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Evaluating Emotional Sensitivity and Tolerance Factors in the Prediction of Panic-Relevant Responding to a Biological Challenge

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Abstract

The current study investigated anxiety sensitivity, distress tolerance (Simons & Gaher, 2005), and discomfort intolerance (Schmidt, Richey, Cromer, & Buckner, 2007) in relation to panic-relevant responding (i.e., panic attack symptoms and panic-relevant cognitions) to a 10% carbon-dioxide enriched air challenge. Participants were 216 adults (52.6% female; $M_{age} = 22.4$, $SD = 9.0$). A series of hierarchical multiple regressions was conducted with covariates of negative affectivity and past-year panic attack history in step one of the model, and anxiety sensitivity, discomfort intolerance, and distress tolerance entered simultaneously into step two. Results indicated that anxiety sensitivity, but not distress tolerance or discomfort intolerance, was significantly incrementally predictive of physical panic attack symptoms and cognitive panic attack symptoms. Additionally, anxiety sensitivity was significantly predictive of variance in panic attack status during the challenge. These findings emphasize the important, unique role of anxiety sensitivity in predicting risk for panic psychopathology, even when considered in the context of other theoretically-relevant emotion vulnerability variables.

Over the past 20 years, there has been a focused effort placed on advancing our understanding of the role of cognitive-affective vulnerability factors in the etiology and maintenance of panic psychopathology (Barlow, 2002; Beck & Clark, 1997; Clark, 1986; McNally, 2002). This work has led to notable scientific and clinical progress both in terms of identifying cognitive-affective factors related to onset and maintenance of panic psychopathology as well as

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¹Additional hierarchical regression analyses were conducted with the proposed model predicting heart rate, respiration rate, and skin conductance at minute 4 of the biological challenge. The additional covariate of baseline heart rate, respiration rate, or skin conductance was included in step one of the model. None of the predictor variables of interest (ASI, DTS, or DIS) were significantly related to challenge steps of physiological responding (p 's > .05).

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development of efficacious therapeutic approaches for such clinical problems (Barlow, 2002).

One of the most promising lines of inquiry has focused on anxiety sensitivity (Bernstein & Zvolensky, 2007; Taylor, 1999). Anxiety sensitivity is the fear of anxiety and arousal-related sensations and their consequences (Reiss & McNally, 1985). Anxiety sensitivity has been conceptualized as a relatively stable, though clinically malleable, cognitive predisposition (McNally, 2002). When anxious, individuals high in anxiety sensitivity may be more apt to become acutely fearful due to beliefs that these internal anxiety sensations have harmful personal physical, psychological, or social consequences (Fedoroff, Taylor, Asmundson, & Koch, 2000; Rodriguez, Bruce, Pagano, Spencer, & Keller, 2004; Zinbarg, Barlow, & Brown, 1997). In fact, anxiety sensitivity, across numerous studies, is concurrently and prospectively associated with more severe anxiety symptoms and panic psychopathology; effects not attributable to trait anxiety or negative affectivity (Feldner, Zvolensky, Schmidt, & Smith, 2008; Hayward, Killen, Kraemer, & Taylor, 2000; Li & Zinbarg, 2007; Maller & Reiss, 1992; McLeish, Zvolensky, & Bucossi, 2007; Schmidt, Lerew, & Jackson, 1997, 1999; Schmidt, Zvolensky, & Maner, 2006). Additionally, laboratory studies have consistently confirmed that anxiety sensitivity measured prior to a biological challenge paradigm is a significant predictor of post-challenge anxiety symptoms and panic attacks (Eke & McNally, 1996; Leen-Feldner, Feldner, Bernstein, McCormick, & Zvolensky, 2005; Rabian, Embry, & McIntyre, 1999; Schmidt, 1999; Zvolensky, Feldner, Eifert, & Stewart, 2001); effects, again, evident above and beyond negative affectivity and trait anxiety. Although empirical work on anxiety sensitivity has indicated that it represents a central cognitive factor in fear acquisition to interoceptive stimuli, there has been considerably less effort to integrate conceptually related work on tolerance (cf, sensitivity) of aversive stimuli, which is of theoretical relevance to models of panic psychopathology (Bernstein, Zvolensky, Vujanovic, & Moos, in press; Zvolensky & Otto, 2007). Such limitation is unfortunate, as anxiety sensitivity is related to distress tolerance constructs (e.g., Bernstein et al., in press), and as discussed below, distress tolerance factors may be related to panic psychopathology (Marshall, Zvolensky, Vujanovic, et al., 2008; Schmidt & Trakowski, 1999). Indeed, like anxiety sensitivity, distress tolerance variables may theoretically motivate avoidance and paradoxically amplify anxiety states.

Discomfort intolerance is a tolerance-related construct of particular relevance in the context of anxiety sensitivity and panic vulnerability. Discomfort intolerance is operationalized as individual differences in capacity to withstand *uncomfortable physical sensations* (Schmidt & Lerew, 1998; Schmidt, Richey, Cromer, & Buckner, 2007; Schmidt, Richey, & Fitzpatrick, 2006). Conceptually, discomfort intolerance may be relevant to vulnerability for panic psychopathology because persons less able to tolerate aversive physical sensations (e.g., anxious arousal) may be less able to withstand such stimuli, and therefore, escape or avoid situations (e.g., public settings) or activities (e.g., exercise) that may trigger them (Schmidt & Lerew, 1998); possibly, placing themselves at greater risk for maladaptive panic-relevant avoidance learning. Schmidt and colleagues (2006), using the Discomfort Intolerance Scale (DIS), have found discomfort intolerance is (a) elevated among clinical samples, particularly persons with panic disorder, compared to persons without a clinical disorder; and (b) moderately concurrently and prospectively associated with measures of anxiety symptoms, with weaker associations for indices of depressive symptoms (Schmidt et al., 2006). Discomfort intolerance has been initially explored in relation to anxious and fearful responding to laboratory stressors. For example, using a carbon dioxide-enriched air (CO₂) paradigm among clinical ($n = 45$) and non-clinical ($n = 45$) samples, Schmidt and Trakowski (1999) found discomfort intolerance was significantly predictive of a greater fear response only among the nonclinical group. The lack of an effect in the clinical group may have been due to a truncated range of discomfort intolerance among that group (Schmidt & Trakowski, 1999). Other studies have found that discomfort intolerance is related to statistically significant, but

small, increases in anxiety symptoms during biological challenge among non-clinical participants in a laboratory setting (Bonn-Miller, Zvolensky, & Bernstein, 2009; Schmidt et al., 2007). These data collectively suggest that discomfort intolerance may be related to anxious and fearful responding to bodily sensations, although a comprehensive examination of this construct in the context of other related tolerance factors (see subsequent paragraph), has not been completed.

Like discomfort intolerance, distress tolerance is another tolerance construct of theoretical relevance to anxiety sensitivity and panic psychopathology vulnerability (Bernstein et al., in press). Simons and Gaher (2005) conceptualize distress tolerance as an individual's ability to withstand negative psychological or *emotional* states (Simons & Gaher, 2005). Initial study has shown that distress tolerance, as measured by the Distress Tolerance Scale (DTS; Simons & Gaher, 2005), is negatively associated with measures of affective distress (negative affectivity) and dysregulation (lability). Other work has found that lower levels of distress tolerance, particularly under conditions of higher degrees of life stress, are related to greater endorsement of poor mental health outcomes (e.g., depressive symptoms; Anestis et al., 2007; O'Leirigh, Ironson, & Smits, 2007; Zvolensky, Marshall et al., 2009). For example, Buckner and colleagues (2007) found that DTS scores concurrently mediated the relationship between depressive symptoms and both marijuana and alcohol use problems. Overall, distress tolerance is related to a variety of psychological symptoms. These data, although limited, highlight the potential role of distress tolerance as a risk marker for a variety of psychopathological symptoms. It is presently unclear, however, whether distress tolerance relates to anxious and fearful responding to panic-relevant bodily sensations. Theoretically, persons less capable of tolerating acute anxiety and related emotional states elicited by physiological arousal may be more apt to experience such sensations as intense and uncontrollable and thereby paradoxically amplify the anxiety.

Together, several studies suggest that anxiety sensitivity plays an important role in the experience of anxiety and panic. However, no study has directly examined anxiety sensitivity in the context of discomfort intolerance and distress tolerance in a biological challenge paradigm. Given that anxiety sensitivity is related to both discomfort intolerance (Schmidt et al., 2006) and distress tolerance (Zvolensky et al., 2009), and both discomfort intolerance and distress tolerance are putatively related to greater risk for anxiety symptoms, there is a need for a direct test of the incremental predictive validity of anxiety sensitivity beyond these two tolerance variables, as well as the incremental predictive utility of distress tolerance and discomfort intolerance beyond anxiety sensitivity. Therefore, the primary purpose of the present investigation was to concurrently examine the predictive power of anxiety sensitivity relative to discomfort intolerance and distress tolerance in regard to panic-relevant self-reported symptoms following direct exposure to perturbation in bodily sensations. It was hypothesized that, when examined concurrently, anxiety sensitivity, but not distress tolerance or discomfort intolerance, would significantly predict DSM-IV panic attacks in the laboratory, as well as intensity of cognitive and physical panic attack sensations. These effects were expected to be evident above and beyond negative affectivity, lifetime panic attack history, and shared variance with both discomfort intolerance and distress tolerance. Our hypothesis was grounded in the large body of literature identifying AS as a unique risk factor in the pathogenesis of panic-spectrum problems; and despite their theoretical promise, the lack of strong empirical evidence to-date that distress tolerance or discomfort intolerance would account for unique variance beyond AS.

Method

Participants

Participants were 216 adults (52.6% female; $M_{age} = 22.4$, $SD = 9.0$) recruited from the greater Burlington, VT community via flyers and advertisements in local newspapers. The racial distribution generally reflected that of the State of Vermont (State of Vermont Department of Health, 2007), with 91.1% of the total sample identifying as Caucasian, 1.9% African-American, 1.5% Hispanic, .7% Asian, and 4.8% as Other. Approximately 42.6% of participants reported being daily smokers, averaging 13.8 ($SD = 6.9$) cigarettes per day. With regard to alcohol consumption, 75.6% reported drinking alcohol at least 2-4 times per month as measured by the Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 1992). Participants reported a mean alcohol consumption score (frequency-by-quantity per occasion; Stewart, Zvolensky, & Eifert, 2001) of 6.8 ($SD = 4.9$). Additionally, participants scored a mean of 9.8 ($SD = 6.42$) on the AUDIT, indicating at least moderate alcohol problems, with 63.1% meeting criteria for current alcohol use problems (i.e., scoring 8 or greater on the AUDIT; Babor et al., 1992).

Exclusionary criteria for the current study included: (1) limited mental competency or the 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. Exclusionary criteria help ensure the safety of participants during the biological challenge wherein fear reactivity to bodily sensations was tested and rule out alternative explanations related to any observed effects (e.g., effects being due to psychopathology rather than the studied variables; Forsyth & Zvolensky, 2002). Individuals with current nicotine dependence were not excluded from the current study, given that one of the larger investigations providing data for these analyses explicitly focused on relations between smoking and panic responsivity.

Pre-Challenge Measures

The Structured Clinical Interview-Non-Patient Version for DSM-IV (SCID-N/P; First, Spitzer, Gibbon, & Williams, 1995) screening questions were administered to rule out psychopathology and assess for current suicidal ideation (see exclusionary criteria). In the present study, each SCID was reviewed by the principal investigator (PI) to ensure interrater agreement on inclusion/exclusion criteria. No disagreements between the SCID interviewer and the PI regarding inclusion/exclusion were observed.

The *Smoking History Questionnaire* (SHQ; Brown et al., 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, Antony et al., 2005).

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). There is a large body of literature attesting to the psychometric properties of the AUDIT (Saunders, Aasland, Babor, de la Fuente, & Grant, 1993). The current study utilized: (1) frequency and quantity items to index current alcohol consumption (an average frequency-by-quantity per occasion composite score; Stewart et al., 2001), and (2) total score to measure alcohol use problems (Babor et al., 1992).

The *Positive Affect Negative Affect Scale* (PANAS; Watson, Clark, & Tellegen, 1988) is a 20-item measure in which respondents indicate, on a 5-point Likert-type scale (1 = “very slightly or not at all” to 5 = “extremely”), the extent to which they generally feel different feelings and

emotions (e.g., “*Hostile*”). The PANAS is a well-established mood measure commonly used in psychopathology research (Watson et al., 1988), and factor analysis indicates that the PANAS assesses the global dimension of negative affect (PANAS-NA). The PANAS-NA subscale of the PANAS has demonstrated good convergent and discriminant validity (Watson, 2000).

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 different types of fears, including fears of anxiety-related somatic, cognitive, and social cues.

The *Discomfort Intolerance Scale* (DIS; Schmidt, Richey, & Fitzpatrick, 2006) is a 5-item measure on which participants indicate, on a 7-point Likert-type scale (0 = *not at all like me* to 6 = *extremely like me*), the degree of agreement towards statements related to their tolerance of discomfort. Aside from a global score, factor analysis indicates that the DIS is comprised of two distinct sub-factors entitled Intolerance of Discomfort or Pain (2 items; e.g., “I can tolerate a great deal of physical discomfort” - reverse scored), and Avoidance of Physical Discomfort (3 items; e.g., “I take extreme measures to avoid feeling physically uncomfortable”). We utilized the DIS total score in the present study to measure the global discomfort intolerance factor (Schmidt et al., 2006, 2007).

The *Distress Tolerance Scale* (DTS; Simons & Gaher, 2005) is a 14-item self-report measure, in which respondents indicate, on a 5-point Likert-type scale (1 = “*strongly agree*” to 5 = “*strongly disagree*”), the extent to which they can experience and withstand distressing psychological states (Simons & Gaher, 2005). The DTS encompasses four types of emotional distress items including: perceived ability to tolerate emotional distress (e.g., I can’t handle feeling distressed or upset), subjective appraisal of distress (e.g., My feelings of distress or being upset are not acceptable), attention being absorbed by negative emotions (e.g., When I feel distressed or upset, I cannot help but concentrate on how bad the distress actually feels), and regulation efforts to alleviate distress (e.g., When I feel distressed or upset I must do something about it immediately; Simons & Gaher, 2005). High levels of distress tolerance are indicated by higher scores on the DTS (Simons & Gaher, 2005). We employed the total DTS score in the current study: (a) to facilitate comparability to past research (Simons & Gaher, 2005), and (b) because the hypotheses being evaluated pertained to a global distress tolerance construct. The present study utilized the original 14-item scale; the final, published scale is identical to the one utilized except that it includes a 15th item. Because the 14- and 15-item versions of the DTS differ by only one item, it is expected that their psychometric properties are likely very similar (Simons & Gaher, 2005).

The *Diagnostic Sensations Questionnaire* (DSQ; Sanderson, Rapee, & Barlow, 1988, 1989) is a measure of panic responsiveness. In the present study, the DSQ was used to assess DSM-IV panic attack symptoms immediately post-challenge. The DSQ lists DSM-IV panic symptoms and yields composite scores for a mean intensity level of symptoms. The DSQ consists of both physical (e.g., “Pounding or racing heart”) and cognitive (e.g., “Fear of going crazy”) subscales. Past work has successfully used these symptom composites to index the intensity of panic symptoms in challenge studies (Forsyth, Eifert, & Canna, 2000; Schmidt, Forsyth, Santiago, & Trakowski, 2002). In the current study, post-challenge panic attacks were coded

dichotomously (yes/no), such that individuals met criteria for a panic attack if they reported four or more symptoms (one of which had to be cognitive) and a “sensation of panic” at a moderate severity rating or greater. This more conservative definition of a panic attack has been used successfully in past challenge work (Marshall et al., 2008).

Physiological assessment

A J&J Engineering I-330-C2 system was used to digitally record physiological data online at a sample rate of 1024 samples per second across channels using J&J Engineering PhysiLab Software. Two physiological variables were examined for the current study (Venables & Christie, 1980): respiration rate (a measure of breaths per minute), and heart rate (a measure of beats per minute). Respiration rate was obtained using a Pneumograph sensor cable with PS-2 sensors as a manipulation check. The sensors were placed across the chest and secured with a Velcro strap, allowing a measure of chest excursion during respiration. 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.

Materials and Apparatus

Laboratory sessions were conducted in a 3-meter × 3-meter experimental room in the Department of Psychology at the University of Vermont. After completing physiological hookup and providing experimental instructions (see Procedure for details), the experimenter ran and observed study participants from an adjacent control room containing an apparatus designed to provide participants with either room air or a mixture of 10% carbon dioxide-enriched air. Carbon dioxide 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. In addition to a one-way mirror, a video and audio monitoring system allowed the experimenter to observe all session events.

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-screener was administered by a trained research assistant via telephone. Those meeting inclusionary criteria were scheduled to attend a single laboratory session. Upon arrival, participants completed a written informed consent, as well as the pre-experimental measures. Each participant then completed the biological challenge procedure, which consisted of electrode placement for physiological measurement, a 10-minute adaptation period (breathing room air through the C-PAP mask), 4-minute 10% carbon dioxide-enriched air challenge, and 5-minute recovery period (breathing room air through the mask again). Participants completed the DSQ immediately following the 4-minute challenge period. Physiological data were gathered continuously throughout the experimental portion of the study. After the study, participants were debriefed and compensated \$20.

Data Analytic Plan

A hierarchical logistic regression and a series of hierarchical linear regressions (Cohen & Cohen, 1983) were conducted to test the hypothesis that, when entered concurrently, anxiety sensitivity, but not distress tolerance or discomfort intolerance, would predict post-challenge panic attack status (yes/no), as well as dimensional DSQ Physical and Cognitive panic attack symptoms, above and beyond the covariates of negative affectivity and past year panic attack history. Negative affectivity (PANAS-NA) and past year panic attack history (PA) were entered as covariates into step one of the regression, and the predictor variables of anxiety sensitivity (ASI total), distress tolerance (DTS total), and discomfort intolerance (DIS total)

were entered into step two. The criterion variable in the logistic regression was post-challenge panic attack status (yes/no). The criterion variables in the linear regressions were DSQ Physical symptoms and DSQ Cognitive symptoms. In this procedure, any variance in the dependent variables accounted for by one or more independent variables within each step, cannot be accounted for by shared variance with the other simultaneously entered independent variables in that step; and any incremental variance accounted for by step two is unique to those predictor variables and cannot be attributed to variables in step one; (Cohen & Cohen, 1993).

Results

A manipulation check was first conducted to ensure that the CO₂ challenge elicited clinically meaningful physiological arousal. Specifically, paired samples t-tests were conducted between baseline (i.e., last minute of baseline) and challenge (i.e., last minute of CO₂ challenge) heart rate (HR) and respiration rates. A paired samples t-test showed that challenge HR levels ($M = 90.72$, $SD = 14.19$) were significantly greater than baseline HR levels ($M = 81.01$, $SD = 10.32$; $t = 10.30$, $p < .001$). A paired samples t-test showed that challenge respiration levels ($M = 19.70$, $SD = 4.03$) were significantly greater than baseline respiration levels ($M = 16.11$, $SD = 3.33$; $t = 10.63$, $p < .001$).¹

Zero-order correlations were examined among the variables of interest (see Table 1). Correlations between ASI and DTS ($r = -.43$, $p > .001$), DTS and DIS ($r = -.25$, $p > .001$) and ASI and DIS ($r = .26$, $p > .001$) were all significant. ASI total scores were significantly positively correlated with all outcome variables: post-challenge panic attack status ($r = .36$, $p < .001$), DSQ Physical symptoms ($r = .28$, $p < .001$), and DSQ Cognitive symptoms ($r = .42$, $p < .001$). DTS total scores were significantly, albeit moderately, correlated with post-challenge panic attacks ($r = -.23$, $p < .01$) and DSQ Cognitive symptoms ($r = -.26$, $p < .001$), but not DSQ Physical symptoms ($r = -.09$, $p > .01$). DIS scores were statistically significantly correlated, albeit weakly, with all outcome measures: post-challenge panic attack status ($r = .17$, $p < .05$), DSQ Physical symptoms ($r = .18$, $p < .01$), and DSQ Cognitive symptoms ($r = .22$, $p < .01$).

See Tables 2 and 3 for a summary of all regression results. The total model, including all covariates and predictors, significantly predicted 19.3% of variance in challenge panic attack status ($p < .001$). Step one of the model significantly predicted 7.1% of variance in panic attack status ($p < .01$); only NA was a unique significant predictor ($OR = 1.08$, $95\%CI = 1.02 - 1.14$, $p = .01$). Panic attack history did not account for unique variance in challenge panic attack status independent of negative affect. Step two of the model significantly predicted an additional 12.2% of variance in panic attack status ($p < .001$); only anxiety sensitivity was a unique significant predictor ($OR = 1.09$, $95\%CI = 1.04 - 1.14$, $p < .01$). Thus, neither distress tolerance nor discomfort intolerance accounted for unique variance in panic attack status above and beyond the covariates and anxiety sensitivity.

The model significantly predicted 10.0% of variance in DSQ Physical symptoms ($F = 4.64$, $p < .001$). Step one of the model accounted for 3.5% of variance ($p < .05$); only negative affectivity was a unique significant predictor ($t = 2.28$, $\beta = .16$, $sr^2 = .02$, $p < .05$). Panic attack history did not account for unique variance in DSQ Physical symptoms independent of negative affect. Step two of the model accounted for an additional 6.5% of variance ($p < .01$); only anxiety sensitivity was a unique significant predictor ($t = 3.23$, $\beta = .25$, $sr^2 = .04$, $p < .01$). Again, neither distress tolerance nor discomfort intolerance accounted for unique variance in DSQ Physical symptoms above and beyond the covariates and anxiety sensitivity.

The model significantly predicted 19.4% of variance in DSQ Cognitive symptoms ($F = 10.08$, $p < .001$). Step one of the model accounted for 5.9% of variance ($p < .01$); only NA was a unique significant predictor ($t = 2.95$, $\beta = .20$, $sr^2 = .04$, $p < .01$). Panic attack history did not

account for unique variance in DSQ Cognitive symptoms independent of negative affect. Step two of the model accounted for an additional 13.6% of variance ($p < .001$); only anxiety sensitivity was a unique significant predictor ($t = 4.73$, $\beta = .35$, $sr^2 = .08$, $p < .001$). Please see Table 3 for regression output₁. Again, neither distress tolerance nor discomfort intolerance accounted for unique variance in DSQ Cognitive symptoms above and beyond the covariates and anxiety sensitivity.

Discussion

The role of anxiety sensitivity, relative to tolerance factors, in panic responding to a biological challenge in the laboratory has not yet been investigated. Previous studies have documented associations between anxiety sensitivity and distress tolerance and discomfort intolerance; and preliminary findings and theory indicate that these variables may each be associated with panic. The current study aimed to evaluate whether anxiety sensitivity is uniquely predictive of panic attack occurrence and intensity in the laboratory above and beyond negative affectivity and panic attack history, as well as after controlling for shared variance with distress tolerance and discomfort intolerance.

As predicted, anxiety sensitivity was correlated significantly with all outcome variables at the zero-order level; as well as incrementally above and beyond negative affectivity, panic attack history, distress tolerance, and discomfort intolerance. Specifically, anxiety sensitivity was uniquely predictive of (categorical) panic attack onset during the challenge, as well as the intensity of physical and cognitive panic attack symptoms in response to the challenge. In addition, distress tolerance and discomfort intolerance, were significantly related to panic outcome variables at the zero-order level; though the effect sizes of these zero-order correlations were relatively small in size ($r = .17$ - $-.26$). However, neither distress tolerance nor discomfort intolerance were uniquely predictive of panic attack symptoms above and beyond the covariates and anxiety sensitivity. These findings suggest that sensitivity to internal signs of anxiety and fear of their outcomes is associated with greater panic responding to a biological challenge in the laboratory, independent of levels of distress tolerance and discomfort intolerance. Although intolerance of negative psychological and physical discomfort have both been found to be associated with an increase in mental health problems (Schmidt et al., 2006; Anestis et al., 2007; O'Clearigh et al., 2007; Zvolensky, Marshall et al., 2009), they did not demonstrate incremental relations to panic in response to the challenge after accounting for negative affectivity, panic attack history, and anxiety sensitivity in the present investigation.

Interestingly, the present study design, though useful to evaluate incremental validity, could theoretically cloud the potential clinical importance of distress tolerance due to the *simultaneous* entry of DTS total and ASI total scores within the regression equation. After covarying out *shared* variance in panic vulnerability explained by anxiety sensitivity *and* distress tolerance - presumably to the product of a common higher-order factor of affect sensitivity and tolerance that may theoretically be related to panic vulnerability (Bernstein et al., in press) - an incremental effect of anxiety sensitivity and a null effect for distress tolerance may be observed. This observed effect, however, may fail to reflect potentially meaningful, common variance in panic vulnerability explained by anxiety sensitivity *and* distress tolerance as well as their putative higher-order factor. Thus, in the present study, it may be that only anxiety sensitivity demonstrated an *incremental* effect in relation to panic vulnerability after accounting for tolerance factors not because tolerance, or a higher-order affect sensitivity and tolerance factor, are not clinically significant but because some of the variance in anxiety sensitivity, specifically that which is not shared with distress tolerance, may *also* be associated with panic. The latter would suggest that anxiety sensitivity is indeed uniquely important, but may miss the potential importance of distress or affective tolerance variables, systematically

associated with individual differences in anxiety sensitivity, for panic vulnerability. Thus, the next step in this line of study may evaluate the role of the hierarchical model of affect sensitivity and tolerance in relation to panic vulnerability, in and out of the laboratory. Such future study may be important in light of the present findings.

The present study has a number of limitations that may help inform future research. First the generalizability of these data is limited as a function of the sample. The sample was composed of a demographically homogenous group of healthy, young adults from the Northeastern United States. It is important that in future study, more diverse populations are studied. Second, measurement of the predictor variables was limited to self-report measurement of anxiety sensitivity, distress tolerance, and discomfort intolerance. Future study may usefully integrate multi-method measures of these variables (e.g., mirror-tracing task to index distress tolerance) beyond self-report; however, unlike for distress tolerance and discomfort intolerance (Leyro, Zvolensky, & Bernstein, 2009), no multi-method measures of anxiety sensitivity have been studied widely (Bernstein & Zvolensky, 2007). Third, the current study included individuals with nicotine dependence. Given established relations between smoking and panic psychopathology (Zvolensky, Feldner, Leen-Feldner, & McLeish, 2005), future work would benefit from evaluating the potential role of nicotine dependence in relations between anxiety sensitivity, distress tolerance, discomfort intolerance, and panic reactivity. Finally, although the biological challenge methods applied in this investigation provide a valid laboratory-based analogue of panic vulnerability, future research may evaluate a similar research question using a prospective design incorporating ecologically valid measurement of clinical panic outside of the laboratory.

In summary, past work focused on anxiety sensitivity and panic vulnerability has not evaluated the unique effect of anxiety sensitivity relative to theoretically important distress tolerance and discomfort intolerance factors. The present study demonstrated the unique predictive power of anxiety sensitivity above and beyond negative affectivity, panic attack history, as well as distress tolerance and discomfort intolerance. These data help highlight the unique importance of anxiety sensitivity in the context of tolerance factors with respect to panic vulnerability, and therefore contribute to the broader field-wide effort to elucidate the key processes underlying the development of panic-spectrum psychopathology.

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Table 1
Zero-Order Correlations and Descriptive Statistics

Variable Name	1	2	3	4	5	6	7	8	Mean (SD) or %	Observed Range
1. Recent PA history (% yes)	1	.23*	.23*	-.22*	.10	.14†	.11	.14†	11.2%	
2. PANAS-NA		1	.42**	-.41**	.22*	.21*	.17†	.22*	17.44 (5.41)	10 - 44
3. ASI			1	-.43**	.26**	.36**	.28**	.42**	16.10 (8.24)	0 - 44
4. DTS				1	-.25**	-.23*	-.09	-.26**	3.63 (0.76)	1.5 - 5.0
5. DIS					1	.17†	.18*	.22*	11.53 (4.98)	0 - 30
6. Post-Challenge PA (% yes)						1	.55**	.80**	25.1%	
7. DSQ-Physical							1	.69**	39.94 (19.55)	0 - 88
8. DSQ-Cognitive								1	7.63 (7.00)	0 - 30

Note:

PANAS-NA = Positive Affect Negative Affect Scale - Negative Affectivity subscale (Watson et al., 2000); ASI = Anxiety Sensitivity Index (Reiss et al., 1986); DTS = Distress Tolerance Scale (Simons & Gaher, 2005); DIS = Discomfort Intolerance Scale (Schmidt et al., 2006); DSQ = Diagnostic Sensations Questionnaire (Sanderson et al., 1988, 1989)

† $p < .05$

* $p < .01$

** $p < .001$

Table 2

Regression Analysis: DSQ Physical and Cognitive Subscales

		F	ΔR^2	t	β	sr^2	p
<i>DSQ-Phys</i>		4.64					<.001
Step 1			.04				<.05
	<i>PA</i>			1.01	.07	.00	ns
	<i>NA</i>			2.28	.16	.02	<.05
Step 2			.07				<.01
	<i>ASI</i>			3.23	.25	.04	<.01
	<i>DTS</i>			1.13	.09	.00	ns
	<i>DIS</i>			1.68	.12	.01	ns
<i>DSQ-Cog</i>		10.08					<.01
Step 1			.06				<.01
	<i>PA</i>			1.38	.10	.01	ns
	<i>NA</i>			2.95	.20	.04	<.01
Step 2			.14				<.001
	<i>ASI</i>			4.73	.35	.08	<.001
	<i>DTS</i>			-0.94	-.07	.00	ns
	<i>DIS</i>			1.58	.10	.01	ns

Note: PA= Recent PA history; NA= Positive Affect Negative Affect Scale (Watson et al., 2000); ASI = Anxiety Sensitivity Index (Reiss et al., 1986); DTS = Distress Tolerance Scale (Simons & Gaher, 2005); DIS = Discomfort Intolerance Scale (Schmidt et al., 2006); DSQ-Phys = Diagnostic Sensations Questionnaire - Physical panic attack symptoms post-challenge, DSQ-Cog = Diagnostic Sensations Questionnaire - Cognitive panic attack symptoms post-challenge (Sanderson et al., 1988, 1989).

Table 3

Logistic Regression Analysis: Challenge Panic Attack Status

		AR ²	OR	95% CI (lower)	95% CI (upper)	p
Block 1		.071				<.01
	PA		1.815	.724	4.551	ns
	NA		1.080	1.019	1.144	<.05
Block 2		.193				
	ASI		1.085	1.035	1.138	<.001
	DTS		.816	.487	1.369	ns
	DIS		1.038	.969	1.112	ns

Note: PA= Recent PA history; NA= Positive Affect Negative Affect Scale (Watson et al., 2000); ASI = Anxiety Sensitivity Index (Reiss et al., 1986); DTS = Distress Tolerance Scale (Simons & Gaher, 2005); DIS = Discomfort Intolerance Scale (Schmidt et al., 2006).