Effects of threat context and cardiac sensitivity on fear responding to a 35% CO2 challenge: A test of the context-sensitivity panic vulnerability model

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ABSTRACT

The present study tested several predictions of a context-sensitivity panic vulnerability model emphasizing the interaction between threat context and threat sensitivities. Participants without a history of panic (N = 47) completed both global and domain-specific panic relevant sensitivity measures and were then randomized to undergo a 35% CO2 inhalation challenge in the presence or absence of a cardiac defibrillator (threat context). As predicted by the model, cardiac sensitivity (but not trait anxiety or anxiety sensitivity) potentiated the effects of the presence of the defibrillator on CO2 fear responding. Moreover, as predicted by the model, the observed potentiation effects of cardiac sensitivity on CO2 fear responding were mediated by participants’ threat appraisals connected to the presence of the defibrillator. Theoretical and clinical implications are discussed.

The past two decades have witnessed a proliferation of psychological theories of panic disorder (Barlow, 1988; Beck, Emery, & Greenberg, 1985; Bouton, Mineka, & Barlow, 2001; Chambless & Gracely, 1989; Clark, 1986; McNally, 1990; Wolpe & Rowan, 1988). Fear of anxiety sensations appears as a common thread throughout many of these models. Evidence supporting the link between fear of anxiety sensations and panic comes from several lines of research including (a) descriptive studies showing elevations in anxiety sensitivity (AS) among panic disorder patients (Taylor, Koch, & McNally, 1992; Telch, Jacquin, Smits, & Powers, 2003); (b) laboratory studies demonstrating heightened subjective fear and panic in response to biological challenges such as CO2 inhalation among panic patients (Gorman et al., 1994; Perna, Barbini, Cocchi, Bertani, & Gasperini, 1995); (c) studies showing that patients undergoing cognitive behavioral treatment for panic display significant reductions in anxiety sensitivity (Penava, Otto, Maki, & Pollack, 1998; Telch et al., 1993); (d) evidence suggesting that panic disorder symptom improvement following CBT is mediated by changes in fear of bodily sensations (Smits, Powers, Cho, & Telch, 2004); and (e) prospective studies suggesting that those scoring high on measures of anxiety sensitivity have a significant increased risk for developing subsequent panic attacks (Maller & Reiss, 1992; Schmidt, Lerew, & Jackson, 1997, 1999), panic symptoms (Grant, Beck, & Davila, 2007), or other anxiety disorders (Schmidt & Zvolensky, 2007; Schmidt, Zvolensky, & Maner, 2006).

Although the evidence linking anxiety sensitivity to panic is substantial, some negative findings have emerged (e.g., Koszycki & Bradwejn, 2001; Struzik, Vermani, Duffin, & Katzman, 2004) and even among the positive findings, anxiety sensitivity explains only a small proportion of the variance in panic attack occurrence. These data highlight the importance of identifying additional causal factors implicated in panic. Research examining contextual factors during biological challenge has provided important data on the psychology of panic. For example, Rapee, Mattick, and Murrell (1986) observed greater anxious responding to 50% CO2/air challenge among panic disorder participants who received an explanation for their symptoms compared to panic disorder participants who did not receive such explanation. Similarly, panic patients undergoing a CO2 challenge without a safe person present responded with greater fear, and a greater number of catastrophic

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cognitions than panic patients who did have a safe person present (Carter, Hollon, Carson, & Shelton, 1995). In addition to perceived safety, perceived control has also shown to be predictive of panicking in response to CO2. Panic disorder patients who were led to believe that they could decrease the concentration of CO2 during inhalation were significantly less likely to display CO2-induced panic relative to patients who were not offered this option (Sanderson, Rapee, & Barlow, 1989). However, an attempt to replicate this finding was not successful (Welkowitz, Papp, Martinez, Browne, & Gorman, 1999). Finally, there is some evidence that attentional focus to internal cues moderated the relationship between panic disorder status and fearful responding to CO2 (Schmidt & Trakowski, 1999).

Taken together, results suggest that psychological variables such as perceived safety, perceived control, and perceived predictability influence fearful responding to biological challenge among panic disorder patients. However, it is not clear from these studies whether these variables function as contextual risk factors for heightened fear responding to challenge or whether they become panicogenic only after the emergence of panic disorder. Experiments manipulating these potential threat-enhancing contextual factors in non-clinical participants provide some evidence to suggest that they increase emotional responding to challenge in participants with no history of panic disorder. For example, the effects of perceived control on non-clinical subjects’ emotional response to a 450 mg. Caffeine challenge was examined through an experimental manipulation in which a caffeine antidote pill placebo was made available to half of non-clinical participants with instructions that they could ingest the pill if their caffeine-induced sensations became too uncomfortable (Telch, Silverman, & Schmidt, 1996). Results showed a significant interaction between participants’ anxiety sensitivity and their perceived control assignment. Specifically, those high in anxiety sensitivity showed higher fear when they underwent the caffeine challenge without the placebo caffeine antidote (no perceived control); whereas low anxiety sensitive participants were not affected by the perceived control manipulation.

Additional support for the interactive effects of contextual factors and dispositional factors comes from a study manipulating offset control during 20% CO2 challenge (Zvolensky, Eifert, & Lejuez, 2001). As predicted, only those high in anxiety sensitivity showed heightened fear in the no offset control condition. Finally, using an instructional set manipulation, Telch, Harrington, Smits, and Powers (2005) provided non-clinical participants scoring high or low in anxiety sensitivity with instructions to expect either arousal or relaxation during a single 35% CO2 inhalation. Consistent with the hypothesis that unexpected arousal would be perceived as more threatening, those receiving relaxation instructions were significantly more likely to panic in response to CO2 relative to those receiving arousal instructions. However, consistent with earlier findings, this effect was observed only for those high in anxiety sensitivity.

Taken together these findings suggest that person and contextual factors may interact to influence challenge-induced fear responding. Telch (1995) offered a context-sensitivity vulnerability model to account for the often-observed interaction between anxiety sensitivity and contextual factors in laboratory studies of panic provocation. This formulation proposed that contextual factors, which increase either the anticipated threat of the challenge or the perceived threat of the consequent reactions (somatic, cognitive, or affective) during the challenge will result in greater fear responding. Unlike other psychological formulations of panic that emphasize the threatening misinterpretation of bodily sensations (Clark, 1986) or the enduring tendency to perceive anxiety as threatening (McNally, 1990), the current formulation places central importance on the interaction of context and dispositional tendencies (sensitivities) in predicting panic. It should be emphasized that this model is not a theoretical formulation of panic disorder but rather an explanatory model for the propensity to experience panic in situations that pose no objective threat to the individual (i.e., false alarms). Given the high prevalence of false alarms across the full spectrum of anxiety disorders as well as the general population, the proposed panic vulnerability model has applicability across a broad range of anxiety disorders and non-clinical cases in which panic reactions occur.

The model makes several specific predictions. First, it proposes that certain dispositional tendencies potentiate the likelihood of experiencing panic in certain contexts. The use of the term potentiate here is meant to imply that the combined effects of the specific sensitivity and the specific context are greater than the sum of the individual contributions of the presence of the sensitivity alone or the context alone. Context is defined here as a stimulus that may be internal as in the case of a somatic cue (e.g., chest tightness), threatening thought (I’m going to lose control), or experienced emotion (e.g., anger); or external (e.g., being in a densely crowded place with a small exit). The threat potentiating dispositional sensitivities can be quite broad as in the case of trait anxiety or the trait sensitivity or may be more narrow or domain-specific as in the case of cardiac or respiratory sensitivity.

The model also proposes that the strength of the panic potentiation brought about by a specific dispositional sensitivity will be directly related to the conceptual match between the dispositional variable under investigation and the threat-relevant context (context-sensitivity matching hypothesis). Indirect support for this hypothesis comes from biological challenge studies showing that more narrow-band sensitivities such as physical concerns (Carter, Suchday, & Gore, 2001; Zinbarg et al, 2001) or suffocation concerns (Eke & McNally, 1996; McNally & Eke, 1996; Shiperd, Beck, & Ohtake, 1996) outperform anxiety sensitivity in predicting fear response to provocations that elicit a strong physical/respiratory reaction i.e., CO2 inhalation and voluntary hyperventilation. A final prediction of the model is that dispositional tendencies such as anxiety sensitivity or rejection sensitivity potentiate the panicogenic effects of certain internal or external contextual cues by increasing the likelihood that an objectively non-threatening context will be perceived as threatening. For example, those playing high dissociation sensitivity are more likely to perceive the effects of hyperventilation or marijuana ingestion to be threatening and consequently panic. Similarly, possessing high vestibular sensitivity may contribute to panic when confronting a high platform due to an exaggerated concern of losing one’s balance.

The aim of the present experiment was to perform a preliminary test of the aforementioned context-sensitivity panic vulnerability theory by experimentally examining the singular and interactive effects of a putative threat-enhancing contextual cue (i.e., presence or absence of a cardiac defibrillator) and several putative threat-enhancing dispositional variables (i.e., trait anxiety, anxiety sensitivity, respiratory sensitivity and cardiac sensitivity) among young adults undergoing a 35% CO2 challenge. Our rationale for using a cardiac defibrillator to manipulate threat context was two-fold. First, cardiac concerns are extremely common among panic patients (Sheehan, 1983), hence it seemed appropriate to use a contextual manipulation that was directly related to the threat-relevant concerns of panic attack sufferers. Second, because the presence of a cardiac defibrillator is not inherently threatening, any fear-enhancing effects are more easily attributable to how participants appraise its presence. This was an important feature because one of the major assumptions of the proposed theory is that dispositional factors such as trait anxiety and cardiac sensitivity potentiate the panicogenic effects of
contextual cues by increasing the likelihood that the cue will be perceived as threatening. Three specific predictions from the theory were tested. The potentiation hypothesis was tested by examining whether the interaction of threat context (presence or absence of the defibrillator) by cardiac sensitivity predicted significant variance in subjective fear and probability of panic after controlling for the main effects of both threat context and sensitivity. The sensitivity-context matching hypothesis was tested by examining the relative potentiation strength of each of the dispositional sensitivities. It was hypothesized that the greatest potentiation would be observed for cardiac sensitivity because of its closer conceptual match with the manipulated threat context (i.e., presence of the defibrillator). Lastly, we tested the threat appraisal mediation hypothesis by examining whether any observed potentiation effects were mediated by the perceived threat associated with the presence of the defibrillator.

1. Method

1.1. Participants

Participants (N = 47) were 22 male and 25 female undergraduate students enrolled in an introduction to psychology course at the University of Texas at Austin. They ranged in age from 18 to 27 with a mean of 19.03 (SD = 1.45). Participants were selected from a large sample (N = 1940) undergoing screening and received course credit for their participation. The following exclusion criteria were used: (a) history of panic attacks; (b) history of medical conditions that could be aggravated by inhalation of CO2 including cardiovascular disorders (e.g., cardiac arrhythmia, cardiac failure), respiratory disorders (e.g., asthma, lung fibrosis), high blood pressure, epilepsy, stroke or seizures; (c) use of psychotropic medication during the past two weeks; and (d) pregnant or lactating. Of the 63 participants who volunteered to participate in the experiment, 13 were excluded because of a history of panic attacks, and 3 were excluded because of a history of asthma.

1.2. Design

Participants were randomly assigned to receive a single vital capacity inhalation of 35% CO2 and 65% O2 under one of two threat context conditions (i.e., presence or absence of a cardiac defibrillator). Measures of trait anxiety, anxiety sensitivity, and depression were included in the design as continuous putative fear-enhancing dispositional variables. Indices of fear responding were collected immediately before and after completing the CO2 challenge.

1.3. Measures

1.3.1. Anxiety sensitivity

The Anxiety Sensitivity Index-Revised (ASI-R; Taylor & Cox, 1998) consists of 36 items and was constructed as an extension of the original ASI (Peterson & Reiss, 1987). Respondents are presented with statements expressing concerns about possible negative consequences of anxiety such as “It scares me when my hear beats rapidly.” For each statement, respondents rate each item on a Likert scale ranging from very little (0) to very much (4). The ASI total score is computed by summing responses across the 36 items. Initial factor analytic research on the ASI-R using a clinical sample (Taylor & Cox, 1998) yielded 4 subscales: (a) Fear of respiratory symptoms, (b) Fear of publicly observable anxiety reactions, (c) Fear of cardiovascular symptoms, and (d) Fear of cognitive dyscontrol. However, more recent factor analytic findings from a large cross-cultural non-clinical sample (Zvolensky et al., 2003) revealed only two dimensions: (a) Fear of somatic symptoms; and (b) Social/Cognitive concerns.

1.3.2. Cardiac and respiratory sensitivity

The existing factor analytic studies of the ASI-R did not encompass a subscale that distinctively taps cardiac sensitivity. This was essential for the present study given the nature of our threat context manipulation (presence or absence of cardiac defibrillator) aimed at examining the context-specificity hypothesis. Thus, we newly constructed Cardiac and Respiratory subscales of the ASI-R based on data obtained from an independent sample of undergraduate students (N = 1350). First, two of the authors (MJT and JAJS) independently chose 9 ASI-R items tapping cardiac or respiratory concerns on the basis of their face validity (i.e., #1—4, and 8 for respiratory concerns, and 7, 22, 24, 27 for cardiac concerns). Inter-rater reliability between the two raters for this initial classification was 100%. The first half of the data were subjected to exploratory factor analysis based on maximum likelihood extraction and oblique rotation (delta = 0). This resulted in a two-factor structure explaining 59.2% of the variance. Item #7 and #9 were excluded due to failing to exhibit differential factor loadings. Thus, the final items included three items for the Cardiac sensitivity subscale (i.e., #22, 24, 27) and four items for the Respiratory subscale (#1, 2, 3, 4). Another exploratory factor analysis using the 7 final items revealed that the two factors explained 62.7% of the variance with a clear bifurcation of factor loadings between the two factors. For the cross-validation of the two-factor structure, the other half of the data was subjected to confirmatory factor analysis using Analysis of Moment Structures, Version 4.0 (AMOS; Arbuckle & Wothke, 1999). Results demonstrated a good fit of the model: GFI = 0.94, NFI = 0.95, IFI = 0.95, and CFI = 0.95. Internal consistency (Cronbach Alpha) was 0.87 and 0.85 for the Respiratory and Cardiac subscales, respectively. The Respiratory and Cardiac subscales displayed a correlation of 0.73 and 0.70 with the total scores of the ASI-R, respectively. The correlation between the cardiac and respiratory subscales was 0.35.

1.3.3. Trait anxiety

Trait anxiety was assessed using the State Trait Anxiety Inventory-Trait subscale (Spielberger, Gorschuch, & Lushene, 1970). The subscale is composed of 20-items designed to assess trait anxiety. The items are scored on a four-point Likert scale ranging from Not At All (1) to Very Much So (4). Both scales of the STAI have shown adequate psychometric properties (Knight, Waal-Manning, & Spears, 1983).

1.4. Emotional response to CO2 inhalation

1.4.1. The Acute Panic Inventory (API; Liebowitz, Gorman, Fyer, Dillon, & Klein, 1984)

The API is a widely used self-report instrument for assessing physical and affective reactions to biological challenges. Respondents rate 29 potential CO2 symptoms (e.g., palpitations,
lightheadedness, going crazy, losing control) on a 0 (none) to 3 (extreme) Likert scale. Peak fear during the challenge is assessed using a 0 (not disturbed at all) to 100 (the worst imaginable experience) scale. The API also includes a question to assess the occurrence of panic (yes/no) in response to the challenge.

1.5. Appraisal of danger and safety associated with the presence of the defibrillator

1.5.1. The Defibrillator Appraisal Questionnaire (DAQ)

The DAQ is a 4-item author-constructed scale designed to index participants’ perceived danger and perceived safety associated with the presence of the defibrillator. Participants rated the following items on a 5-point (0 = not at all; 4 = completely) Likert scale: (1) Because of the defibrillator, I felt that I was in a potentially harmful or dangerous situation; (2) I felt safe knowing that should I need assistance, there was an available method of medical aid; (3) The presence of the defibrillator made me question the safety of the challenge; and (4) The presence of the defibrillator reassured me that nothing bad was going to happen to me. Scores on items 1 and 3 were averaged to provide an index of perceived danger associated with the presence of the defibrillator. Similarly, items 2 and 4 were averaged to provide an index of perceived safety associated with the presence of the defibrillator. Examination of the scale used in the current study revealed a coefficient alpha of 0.95 and 0.69 for the two subscales, respectively. Only participants randomized to the defibrillator condition completed this scale.

1.6. Procedures common to both threat context conditions

Following informed consent, participants completed a 9-item medical history questionnaire designed to identify participants with medical or medication contraindications to inhalation of CO2 and panic attack history. Participants then completed the ASI-R and the STAI-T and were randomly assigned to either the Defibrillator or No Defibrillator (i.e., Control). All participants then watched a 2-min video clip demonstrating the inhalation procedure along with the following CO2 challenge instructions:

“For this experiment, you will be administered a carbon dioxide inhalation challenge. Inhaling carbon dioxide is a widely used research procedure for studying anxiety. The gas mixture that you will be inhaling consists of 35% carbon dioxide and 65% oxygen. Both of these components are in the air that we breathe. However, this mixture has a higher concentration of both oxygen and carbon dioxide. It is important that you know that despite the higher concentrations, the gas mixture is not harmful in any way. However, during the inhalation procedure you are likely to experience some unusual or odd sensations, such as faintness and shortness of breath, which should last only for a short period. The procedure will consist of several steps. First, we will have you complete several forms to indicate how you are feeling right now. Next, we will ask you to exhale fully so that all the air is out of your lungs and have you breathe in a full, complete breath of the gas mixture. While breathing in the gas it is important that you hold your nose to insure that only the proper mixture of gas is inhaled. You will hold the gas mixture in your lungs for 5 full secs., after which you will exhale the gas. Next, you will complete a form asking about your reactions to the inhalation of the gas. Let’s have you watch an actual example of a person undergoing the CO2 inhalation procedure.”

Following instructions and demonstration, the procedure was practiced with the experimenter using regular room air. Participants then completed baseline questionnaires.

1.6.1. Defibrillator threat context condition

Prior to inhalation, the experimenter left the room and reentered wheeling in a cart with a defibrillator (Hewlett Packard 43100A). The cart was positioned 2 m directly in front of the participant and the Experimenter provided the following comment: “Oh, I forgot one thing; we need this defibrillator here in the room just in case of an emergency.” Participants then completed the CO2 challenge. Following inhalation, they completed the API and the DAQ.

1.6.2. Control threat context condition

Participants in the control condition underwent the challenge without a defibrillator present, after which they completed the API.

2. Results

2.1. Pre-manipulation equivalence of the groups

Scores on the baseline measures of ASI, STAI, and BDI were within the range of a non-clinical population (see Table 1). There were no significant differences on any of the measures at baseline, indicating that randomization had resulted in comparable groups.

2.2. Test of the potentiation hypothesis

A series of hierarchical regression analyses were conducted to examine the interactive effects between threat context and dispositional variables in predicting peak fear and panic occurrence in response to CO2 inhalation. Support for the potentiation hypothesis is demonstrated if the disposition by threat context interaction significantly predicts CO2 fear/panic after controlling for the main effects of both the sensitivity and threat context variable. Separate hierarchical regression analyses were performed for each of the five dispositional sensitivity variables (i.e., cardiac sensitivity, respiratory sensitivity, anxiety sensitivity, trait anxiety, and depression). All continuous predictors were centered to reduce potential multicollinearity (see Aiken & West, 1991). Primary outcome measures were CO2 peak fear (0—100) and CO2 panic (yes or no).

In Step 1 of the hierarchical regression analysis, Cardiac sensitivity and Threat context (i.e., defibrillator condition) combined accounted for 25.0% of the variance in CO2 Fear, $R^2 = 0.25$, $F (2, 44) = 7.32, p < 0.005$. In Step 2, the interaction term of Cardiac sensitivity by Threat context explained an additional 11.8% of the variance ($R^2$ change $= 0.12, F (1, 43) = 8.03, p < 0.01$). Once the interaction term was entered into the model ($b = 0.41, t = 2.83, p < 0.01$), neither Cardiac sensitivity nor Threat context significantly predicted CO2 fear. Follow-up simple slope analyses revealed that Cardiac sensitivity predicted CO2 fear in the defibrillator condition.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Condition</th>
<th>Control</th>
<th>Defibrillator</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 22)</td>
<td>(n = 25)</td>
<td></td>
</tr>
<tr>
<td>STAI-T</td>
<td>37.59</td>
<td>39.72</td>
<td>11.03</td>
</tr>
<tr>
<td>BDI</td>
<td>9.50</td>
<td>9.32</td>
<td>6.89</td>
</tr>
<tr>
<td>ASI-R Total</td>
<td>30.14</td>
<td>31.40</td>
<td>24.45</td>
</tr>
<tr>
<td>Cardiac sensitivity</td>
<td>2.59</td>
<td>1.60</td>
<td>2.26</td>
</tr>
<tr>
<td>Respiratory sensitivity</td>
<td>3.91</td>
<td>5.16</td>
<td>3.79</td>
</tr>
</tbody>
</table>

Note: STAI-T = State-Trait Anxiety Inventory-Trait Subscale Score; BDI = Beck Depression Inventory; ASI-R Total = Anxiety Sensitivity Index-Revised Total Score; Cardiac sensitivity = Cardiac sensitivity subscale; Respiratory sensitivity = Respiratory sensitivity subscale.
Cardiac sensitivity alone was not a significant predictor of CO2 panic for the defibrillator condition \((b = 7.97, t = 6.39, p < 0.01)\) but not in the control condition \((b = 2.13, t = 1.52, p > 0.10)\); see Fig. 1.

Identical hierarchical regression analyses were performed separately for each of the other sensitivity variables (i.e., respiratory sensitivity, anxiety sensitivity, trait anxiety, and depression). None of these dispositional variables interacted significantly with threat context in predicting CO2 fear (see Fig. 2).

A series of hierarchical logistic regression analyses were conducted on the binary outcome measure of CO2 panic similar to the hierarchical linear regression analyses performed for CO2 fear. Cardiac sensitivity and Threat context were entered into Step 1 and Cardiac sensitivity by Threat context interaction was entered into Step 2. The overall model was significant, \(-2 \log \text{likelihood} = 36.10\), \(c^2 = 15.04, p < 0.005\). Nagelkerke \(R^2\), which is a measure of strength of association similar to \(R^2\) in ordinary least squares regression (Nagelkerke, 1991), increased from 0.15 to 0.41 after entering the interaction of Cardiac sensitivity by Threat context. The Threat context by Cardiac sensitivity interaction was marginally significant, \(\chi^2 (1) = 3.81, p = 0.05\); Odds ratio = 2.37 (95% CI = 1.0, 5.63). However, once the interaction term was entered into the model, Cardiac sensitivity alone was not a significant predictor, \(\chi^2 (1) = 0.001, p = 0.97\); Odds ratio = 1.00 (95% CI = 0.66, 1.49), whereas threat context alone was still significantly predictive, \(\chi^2 (1) = 5.14, p < 0.05\); Odds ratio = 8.72 (95% CI = 1.34, 56.73). Follow-up simple effects analyses were conducted to assess the effects of cardiac sensitivity on CO2 Panic for participants in the defibrillator vs. control condition. Consistent with prediction, Cardiac sensitivity predicted CO2 panic only in the presence of the defibrillator, \(\chi^2 (1) = 4.81, p < 0.05\), Odds ratio = 2.35 (95% CI = 1.10, 5.05).

### Test of the context-sensitivity matching hypothesis

To review, the Context-Sensitivity Matching Hypothesis asserts that the strength of the panic potentiation brought about by a specific dispositional sensitivity will be directly related to the conceptual match between the sensitivity variable under investigation and the threat-relevant context. We tested this formulation by examining the magnitude of potentiation (i.e., \(R^2\) change for the interaction term) across the five dispositional sensitivity variables. Support for the sensitivity-context matching hypothesis is demonstrated if cardiac sensitivity leads to a significantly greater fear potentiation effect (i.e., greater \(R^2\) change for the sensitivity \(\times\) context interaction) relative to the sensitivity \(\times\) context interaction terms for the less context-relevant dispositional sensitivities (e.g., trait anxiety). A series of five hierarchical regression analyses (one for each sensitivity variable) were performed. In each analysis, the effects of threat context (dummy coded 0 or 1) and the centered sensitivity variable were entered in Step 1. The threat context \(\times\) sensitivity interaction term was entered in Step 2. Peak fear in response to the CO2 challenge served as the outcome in all analyses. Consistent with the Context-Sensitivity Matching Hypothesis, the cardiac sensitivity \(\times\) threat context interaction term was the only sensitivity \(\times\) threat context interaction term to significantly contribute to the variance in peak fear (see Fig. 2).

The approach for testing the context-sensitivity matching hypothesis for CO2 panic was identical to that used for CO2 fear. A series of five hierarchical logistic regression analyses (one for each sensitivity variable) were performed. Fig. 3 presents the results of these analyses. Consistent with prediction, of the five threat context \(\times\) sensitivity interactions tested, only the threat context \(\times\) cardiac sensitivity interaction was significant \(\chi^2 (1) = 3.81, p = 0.05\); Odds ratio = 2.37 (95% CI = 1.0, 5.63). Consistent with the context-sensitivity matching hypothesis, the magnitude of the potentiation effect (i.e., 26% of the variance in CO2 panic was accounted for by the interaction of cardiac sensitivity and threat context) was markedly higher than that observed for the other less conceptually matched sensitivities (see Fig. 3).

Follow-up simple effects analyses comparing the percentage of those reporting CO2 panic for the defibrillator vs. no defibrillator conditions as a function of cardiac sensitivity (high vs. low) illustrates the marked potentiation effect of cardiac sensitivity on CO2 panic in the presence of the defibrillator (see Fig. 4). Specifically, 58% of the high cardiac anxiety sensitive participants reported panic during the CO2 inhalation in the presence of the defibrillator relative to only 10% in its absence \(\chi^2 (1) = 4.81, p < 0.05\), Odds ratio = 2.35 (95% CI = 1.10, 5.05)].

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**Fig. 1.** The interactive effect of threat context and cardiac sensitivity on CO2 fear.

**Fig. 2.** Proportion of variance explained in CO2 Fear from a series of hierarchical regression analyses.
2.4. Appraisal mediation hypothesis

The appraisal mediation hypothesis was tested according to the analytic steps outlined by Baron and Kenny (1986). However, because data on the putative mediator — DAQ-Perceived Danger were collected only for participants randomized to the defibrillator condition, our test for mediation focused on whether the relationship between cardiac sensitivity and CO2 fear/panic would be mediated by specific threat appraisals associated with the presence of the defibrillator. In Step 1, the cardiac sensitivity explained 64% of the variance in CO2 fear, $R^2 = 0.640, F(1, 23) = 40.85, p < 0.001$. Likewise, the probability of CO2 Panic was also significantly associated with Cardiac sensitivity, Wald $X^2 (1) = 4.81, p < 0.05$, OR = 1.46 (95% CI, 1.10, 5.05). These data confirm that the first condition for mediation was met.

In Step 2, we tested the association between Cardiac Sensitivity and the proposed mediator (i.e., the $a$ path). Cardiac sensitivity was significantly associated with DAQ-Perceived Danger scores, $R^2 = 0.40, F(1, 23) = 15.62, p < 0.005$. These data confirm that the second condition for mediation was met.

In Step 3, we tested the relationship between the proposed mediator and fearful responding to CO2. DAQ-Perceived Danger was significantly associated with CO2 Fear, $R^2 = 0.316, F(1, 23) = 10.61, p < 0.005$. However, the relationship with CO2 Panic was only marginally significant, Wald $X^2 (1) = 3.29, p = 0.07$ OR = 1.49 (95% CI, 0.97, 2.29). These data confirm that the third necessary condition for mediation was met for CO2 Fear but not for CO2 Panic. Accordingly, we performed subsequent analyses only for CO2 fear.

In Step 4, we tested the relationship between Cardiac Sensitivity and CO2 Fear after controlling for the proposed mediator. According to Baron and Kenny (1986), evidence for full mediation exists when the relationship between the IV and DV is no longer significant after controlling for the effects of the mediator, whereas evidence for partial mediation exists when the relationship between IV and DV is significantly attenuated (but still significant) after controlling for mediator effects. The strength of the relationship between Cardiac Sensitivity and CO2 Fear was reduced considerably after controlling for DAQ-Perceived Danger Scores. This reduction was consistent with partial mediation, since the association between Cardiac Sensitivity and CO2 Fear was still significant after controlling for the mediator, $b = 0.74$, $t = 4.51, p = < 0.001$.

We employed the distribution of products test (MacKinnon, Fairchild, & Fritz, 2007; MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002) to test the significance of the mediated pathway. The distribution of products test involves multiplying the regression coefficients of the two segments of the mediated pathway (i.e., $a \times b$) and calculating the 95% confidence interval (CI) for this product (95% CI). Because the 95% CI (0.057, 0.527) did not include 0, we can conclude that the mediated pathway was statistically significant (MacKinnon et al., 2004).

Finally, we calculated the proportion mediated (PM; Shrout & Bolger, 2002) as an index of the effect size of the mediated pathway. PM is the proportion of the total effect of the independent variable on the dependent variable (i.e., the $c$ path) mediated by the mediator and is calculated by the formula $PM = (a \times b)/c$. The proportion of the effect of cardiac sensitivity on CO2 Fear mediated by perceived danger was 40.95%.

3. Discussion

The central aim of the present study was to test predictions derived from the context-sensitivity vulnerability model of panic that posits a central role for the interaction of threat-enhancing context and threat-enhancing dispositional sensitivities in the pathogenicity of panic. Our approach was to have non-clinical participants with varying levels of trait anxiety, anxiety sensitivity (two commonly-studied dispositional sensitivity measures in the experimental study of panic), respiratory sensitivity and cardiac sensitivity (more domain-specific sensitivity variables) undergo...
a 35% CO₂ challenge in the presence or absence of a threat-relevant contextual cue (i.e., defibrillator).

The prediction that threat-relevant sensitivity variables would potentiate the anxiogenic effects of threat-relevant contexts was supported by the significant interaction observed between the experimentally manipulated threat context (defibrillator present or absent) and cardiac sensitivity. Participants scoring high in cardiac sensitivity showed significantly higher subjective fear and probability of panic in response to CO₂ inhalation in the presence of the defibrillator. In contrast, high cardiac sensitivity in the absence of the defibrillator was not significantly associated with higher subjective fear or probability of panic in response to CO₂ challenge. These findings are consistent with previous biological challenge investigations demonstrating a significant interaction between anxiety sensitivity and manipulated threat contexts such as the presence or absence of a caffeine antidote (Telch et al., 1996) or instructional sets leading to the expectation of either challenge-induced arousal or relaxation (Telch et al., 2005). Taken together, these data argue against an additive model in which dispositional and contextual factors each only independently contribute to the prediction of fearful responding to challenge. Additional support for this contention comes from analyses from the current experiment demonstrating that neither cardiac sensitivity nor threat context (defibrillator condition) predicted unique variance in fear responding after statistically controlling for the effects of the interaction term.

Examination of the other sensitivity variables provides some evidence supporting the specificity of cardiac sensitivity as a potentiator of fear responding to CO₂ in the presence of the defibrillator. Specifically, cardiac sensitivity showed a significant interaction with the defibrillator condition, while respiratory sensitivity and anxiety sensitivity did not. These findings provide preliminary support for the proposed formulation asserting that the conceptual linkage between a threat-relevant sensitivity and context will affect the magnitude of the potentiation effect. Our previous attempt at testing this sensitivity-context matching hypothesis using a dissociation challenge paradigm failed to demonstrate specificity in that both dissociation sensitivity and anxiety sensitivity potentiated fear responding to the challenge equally (see Leonard, Telch, & Owen, 2000). Perhaps limitations of our measure of dissociation sensitivity or the modest potency of our dissociation challenge contributed to the failure to demonstrate specificity of the sensitivity variable.

Our findings may provide some clues as to the potential mechanisms through which the presence of the cardiac defibrillator exerted its effect on the relationship between cardiac sensitivity and fearful responding to CO₂. Our mediational analyses revealed that cardiac sensitivity was a strong predictor of participants’ ratings of perceived danger associated with the defibrillator. In turn, perceived danger associated with the defibrillator significantly predicted fearful responding to the CO₂ challenge. Finally, the effects of the defibrillator’s presence on CO₂ subjective fear was significantly attenuated after controlling for the effects of perceived danger associated with the defibrillator. This finding provides evidence in support of the third prediction derived from the theory, namely asserting that dispositional factors such as cardiac sensitivity potentiate the panicogenic effects of contextual cues by increasing the likelihood that the context will be perceived as threatening.

It should be noted that for purposes of testing the proposed model, we have conceptualized both cardiac sensitivity and anxiety sensitivity as continuous rather than categorical constructs. However, there is some evidence (e.g., Bernstein et al., 2006, 2007; Schmidt, Kotov, Lerew, Joiner, & Ialongo, 2005) suggesting that anxiety sensitivity may be taxonic. To date, tests of the taxonic hypothesis for AS have been mixed (see Broman-Fulks et al., 2008). Conclusions regarding the applicability of the proposed context-sensitivity model to sensitivities that are taxonic in nature await future research.

Several limitations of the study deserve comment. First, although the study of those who have not yet developed naturally occurring false alarm panic reactions has the advantage of ruling out that the putative vulnerability factor under investigation is simply a consequence or concomitant of pre-existing panic, our data only speak directly to predicting fear responding to a laboratory challenge. Prospective risk studies and randomized prevention trials are needed to determine how the interaction of contextual factors and dispositional sensitivities contribute to the onset of naturally occurring panic reactions across the full spectrum of anxiety disorders. Second, a more powerful test of the context-sensitivity matching hypothesis would have been to also include a non-cardiac threat context condition as part of the experimental manipulation in order to demonstrate that elevated cardiac sensitivity potentiates CO₂ fear responding in the presence of the cardiac-relevant contextual cue (i.e., defibrillator) but not in the presence of a safety cue unrelated to cardiac concerns (e.g., epinephrine pen). Third, statistical power to detect modest effects was limited due to our relatively small sample size.

Some clinical implications of our findings deserve mention. First, our data suggest that there may be some therapeutic justification for employing a domain-specific approach in the assessment of threat-relevant sensitivities. Global dispositional measures such as trait anxiety and anxiety sensitivity may lack sufficient specificity to aid the clinician in individually tailoring treatment strategies. In contrast, the inclusion of assessment strategies that assist the clinician in identifying patients’ specific threat-relevant sensitivities such as cardiac sensitivity, respiratory sensitivity, rejection sensitivity, heat sensitivity, fatigue sensitivity, to name a few — may assist clinicians to more effectively tailor intervention strategies to match peoples’ sensitivity profiles. A second treatment implication of our findings comes from our preliminary demonstration that the appraisal of threat connected to the presence of the defibrillator accounted for the observed potentiation effect of cardiac sensitivity on fear responding to CO₂. These data speak to the potential importance of including intervention elements that target patients’ negatively biased appraisals.

Taken together, our findings lend preliminary support for the proposed context-sensitivity panic vulnerability model. Future laboratory and prospective risk studies investigating additional contextual factors and their interaction with both global and domain-specific dispositional sensitivities may yield greater understanding of false alarm fear reactions and their prevention.

References


