Cognitive Bias Modification to Enhance Resilience to a Panic Challenge

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Abstract

Interventions targeting the development of resilience are lacking despite evidence that enhancing resilience may lead to decreased incidence of mental and physical illness (Kobasa, 1979), and consequently, less utilization of strained healthcare resources. While most research on resilience has focused on overcoming trauma, the current study targeted resilience among people with high anxiety sensitivity (fear of anxiety symptoms), which is a vulnerability marker for a broad range of anxiety disorders, especially panic disorder. Indeed, increasing resilience to panic-related stressors will likely have important implications for the development and maintenance of anxiety pathology, because those who find it difficult to recover from the relatively common experience of panic symptoms are thought to be most vulnerable to developing diagnosable panic disorder. While research on cognitive bias modification (CBM) interventions has shown they can be effective at reducing cognitive bias and emotional vulnerability in a variety of domains, including anxiety disorders (see Hallion & Ruscio, 2011), focusing on resilience enhancement is a novel application of CBM.

Participants (N = 50) high in anxiety sensitivity were randomly assigned to one of two conditions: four sessions of resilience-enhancing interpretation bias modification (CBM-I), or a control (Sham) condition in which participants completed four sessions of sham tasks similar in format to the CBM-I condition. Following the intervention, participants engaged in a 7.5% steady state carbon dioxide (CO_2) breathing challenge, a reliable elicitor of panic symptoms (Bailey, Argyropoulos, Kendrick, & Nutt, 2005).

In line with hypotheses, those in the CBM-I condition reported a reduction in interpretation bias at post-training (this finding was significant for one measure and not

another), and a trend for a greater reduction in anxiety sensitivity at 2-month follow-up compared to those in the Sham condition. Additionally, those in the CBM-I condition reported less intense cognitive symptoms of panic during the CO_2 challenge, though not less intense physical symptoms or total sum of panic symptoms. Finally, model-predicted values suggested that those in the CBM-I condition experienced less anticipatory anxiety prior to the CO_2 breathing period, and then less anxiety during the recovery period, compared to the Sham condition, but not differences in reactivity to breathing the CO_2-enriched air (though this pattern needs to be interpreted with caution).

While the findings are somewhat mixed, the results of the current study are promising for CBM-I as an intervention to increase resilience to panic attacks for those vulnerable to developing panic disorder. It will be important to replicate this study with a larger sample size, given approximately half of the participants who were initially eligible for the study were excluded from analyses because their anxiety sensitivity score dropped before the start of the study. Additionally, replication with a community treatment-seeking sample will be important. Nonetheless, the current study adds to the CBM-I literature, showing that this training paradigm is able to reduce both maladaptive interpretations and some symptoms of anxiety, especially those tied to threat cognitions. It also contributes to the relatively sparse literature on interventions for adult resilience by showing that CBM-I has the potential to help enhance resilience to stressors, thus promoting prevention for those at risk of developing mental illness.

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Cognitive Bias Modification to Enhance Resilience to a Panic Challenge

Most evidence-based treatments for mental illness focus solely on the development of skills that ultimately minimize reactivity to disorder-relevant stressors, while few focus on the development of resilience, despite low resilience being a shared vulnerability factor across multiple forms of mental illness (Burns, Anstey, & Windsor, 2011; Wingo et al., 2010). Resilience is defined in the current study as the ability to experience attenuated reactivity to an adverse event and to quickly recover or "bounce back" from the event (adapted in part from definitions proposed by Bonanno, 2012; Garmezy, 1991; Luthar, Cicchetti, & Becker, 2000; Roisman, 2005), and is important in determining the impairment caused by such events. In fact, resilience is related to a range of mental health issues, including suicide contemplation (Pietrzak, Russo, Ling, & Southwick, 2011) and anxiety disorders (Pollack, Stein, Davidson, & Ginsberg, 2004). People with vulnerability to panic disorder, for example, may experience greater difficulty recovering from a panic attack (i.e., low resilience; Nillni, Berenz, Rohan, & Zvolensky, 2012), leading to long-term distress and impairment, including intense fear of future attacks and avoidance behavior. Researchers have identified the enhancement of resilience as an important public health issue (Connor & Zhang, 2006), and according to Kumpher (2002), "information on low cost methods for increasing resilience to negative life events is critically needed" (p. 179). Indeed, treatments that increase resilience could lead to significant public health benefits, such as improved quality of life, decreased mortality and disease rates, and reduced utilization of costly mental health resources (Bonanno, Westphal, & Mancini, 2011; Kobasa, 1979).

The current research examines the efficacy of a new intervention for promoting resilience that is an adaptation of cognitive bias modification for interpretation bias (CBM-

I). CBM is a computer-based intervention with adaptations that target a variety of emotional disorders (see MacLeod & Mathews, 2012) and is promising because of its potential advantages over traditional treatments, including likely cost efficiency and the ability to disseminate it widely among underserved and uninsured populations. The current resilience-enhancing CBM-I was administered to a college-aged sample high in anxiety sensitivity (a fear of anxiety symptoms), because anxiety sensitivity is an established vulnerability marker for the development of panic disorder (Hayward, Killen, Kraemer, & Taylor, 2000; Maller & Reiss, 1992; Schmidt, Lerew, & Jackson, 1997). The intervention was designed to train individuals to shift their maladaptive anxiety-relevant interpretations to be more in line with qualities associated with resilience, such as positive emotionality, flexible responding, and self-efficacy beliefs about coping. The impact of this intervention was then examined by presenting participants with a biological challenge (7.5% steady state CO_2 inhalation) that elicits symptoms associated with a panic attack, so that reactivity and recovery in the face of the stressor could be measured.

Definitions of Resilience

Early use of the resilience concept in the social sciences mostly examined the impact of childhood adversity on development (e.g., Garmezy, 1991; Werner, 1995; see Luthar, Cicchetti, & Becker, 2000), but resilience research has since expanded to include the response of adults to a wide variety of potentially traumatic events, including those that are singular, short-lived incidents (see Bonanno, 2012). Multiple researchers have proposed that resilience is determined by the ability to adapt via quick and successful adjustment to stressors or adversity (Collishaw et al., 2007; Feder, Nestler, & Charney, 2009; Garmezy, 1991; Wingo et al., 2010). Further, Bonanno defined resilience as “a stable trajectory of

healthy functioning" (p. 755) following a stressful or aversive event. He suggested that recovery reflected repair after a significant increase in clinical symptoms following a potentially traumatic event (Bonanno et al., 2011).

While Bonanno's definition of resilience emphasizes long-term responses to stress, this is not the only way to study the process of adaptation to stress. In the current study, resilience was examined using more of a proof-of-principle, micro-level approach, rather than focusing on long-term resilience after years of exposure to chronic adversity (e.g., Masten, Best, & Garmezy, 1990) or large-scale traumas, like a terrorist attack (e.g., Bonanno, Galea, Bucciarelli, & Vlahov, 2006). Indeed, while a panic stressor, such as the one used in the current study, is expected to cause distress for those with anxiety sensitivity, it is clearly not expected to have the same impact as a large-scale "trauma," so recovery is operationalized as the return to baseline functioning over a period of minutes rather than longer-term reduction in disorder prevalence. This approach provides a useful and ethical model for examining recovery from an acute stressor, providing helpful clues about how to ultimately enhance longer-term resilience against the potentially harmful impact of panic attacks for those vulnerable to developing panic disorder. Thus, we focus on reduced reactivity and more rapid and complete recovery from a stressor as an indicator of short-term resiliency, but also examine the role of the intervention in preventing future worsening of symptoms (at two-month follow-up) as a preliminary evaluation of more long-term resilience.

Importance of Resilience in Anxiety Disorders

Much of the extant research on adult resilience has focused on combat or injury trauma, or physical and sexual abuse, and the development of post-traumatic stress

disorder (PTSD; Bonanno et al., 2011). However, recovery from subjectively negative events other than trauma, such as a panic attack for someone with high anxiety sensitivity, is also likely dependent upon resilience. Low resilience to panic may be indicated by intense fear, avoidance, vigilance, and arousal following a panic-relevant event. It is this maintenance of fear, or lack of recovery, after an encounter with a stressful event that can make anxiety so debilitating for some people (Kessler et al., 2006). For example, it is estimated that 28% of people will have a panic attack at some point in their lifetime, but only a fraction of those people (approximately 13%) will fail to "bounce back" from the experience, leading to the development of panic disorder (Kessler et al., 2006). It seems likely then that increasing resilience in response to anxiety-related stressors among those who are most at risk could reduce vulnerability to developing an anxiety disorder.

Although trait resilience is a strong predictor of treatment outcome for anxiety and other disorders (Davidson et al., 2012; Min, Lee, Lee, Lee, & Chae, 2012), there are relatively few existing interventions for resilience enhancement in adults, especially outside the context of PTSD. Notwithstanding, existing interventions suggest that they can be effective at increasing general resilience, well-being and vitality, and at reducing symptomology (e.g., Kent, Davis, Stark, & Stewart, 2011; Sood, Prasad, Schroeder, & Varkey, 2011). For example, Kent et al. conducted a randomized controlled trial examining the impact of a 12-week group therapy for resilience on 39 veterans with PTSD. The intervention focused on psychoeducation about resilience and the development of positive emotional experiences and interpersonal support. The results indicated a strong effect for those in the active treatment condition to display more positive emotional health and fewer negative affective symptoms. Other interventions for adult resilience have been aimed at

preventing and reducing workplace stress (e.g., Burton, Pakenham, & Brown, 2010; Millear, Liossis, Shochet, Biggs, & Donald, 2008; Sood et al., 2011). For example, Burton et al. targeted factors commonly associated with resilience (e.g., positive emotionality, finding meaning, and cognitive flexibility) in an 11-week group therapy in a workplace setting. The results were promising, indicating that the intervention was associated with improvements across a myriad of psychological factors, including stress, self-acceptance, mindfulness, and personal growth. Further, after a single 90-minute treatment session designed to increase resilience among physicians, by incorporating attention and interpretation modification as well as relaxation training, participants showed increased self-reported resilience and quality of life and reduced anxiety and stress at a two-month follow-up (Sood et al., 2011). Taken together, these studies suggest that resilience can be enhanced through intervention, and that these interventions can have some lasting effects even after just a single session. The current study aimed to modify an existing cognitive intervention for the enhancement of resilience in response to panic among anxiety sensitive individuals.

Changing Cognitive Biases Tied to Anxiety

The choice of a cognitive training paradigm for the intervention follows from cognitive models of anxiety disorders and fear, which posit that threat-oriented information processing biases causally contribute to the development and maintenance of anxiety (Beck, 1976; Beck & Clark, 1997; Salkovskis, 1985, 1989). These cognitive biases can be defined as the "selective processing of information perceived as signifying a threat or danger to one's personal safety or security" (Beck & Clark, 1997). For instance, people with various forms of anxiety pathology tend to interpret situations as more threatening

than do non-anxious individuals (Stopa & Clark, 2000; Eysenck, Mogg, May, Richards, & Mathews, 1991).

Anxiety sensitivity, or the fear of symptoms of anxiety (Reiss & McNally, 1985), is theorized to derive in part from a catastrophic misinterpretation of bodily sensations that are commonly associated with anxiety and panic attacks, such as a racing heart, shortness of breath, lightheadedness, and nausea (Clark, 1986). Cognitive models of panic disorder posit that catastrophic misinterpretations of bodily sensations and other anxiety cues lead to increased anxiety, which in turn leads to more catastrophic interpretations (Clark, 1986). An example of such a misinterpretation would be someone who experiences a racing heart and makes a catastrophic interpretation that the benign physiological sensation is indicative of a heart attack. Anxiety sensitivity was the anxiety domain selected for the current study because it is a common problem (Telch, Lucas, & Nelson, 1989), and is an established risk factor for anxiety pathology, particularly panic disorder (Reiss, 1991; Schmidt, Zvolensky, & Maner, 2006).

There is considerable evidence supporting the theorized links between anxiety sensitivity, catastrophic interpretation bias, and panic disorder. For instance, McNally, Hornig, Hoffman, and Han (1999) found that higher anxiety sensitivity predicted greater catastrophic misinterpretation bias in a student sample with no history of spontaneous panic. Similarly, research from our lab has found that both a group high in anxiety sensitivity (Teachman, 2005) and a group with panic disorder (Teachman, Smith-Janik, & Saporito, 2007) evidenced a greater interpretation bias related to symptoms of panic attacks compared to a group low in anxiety sensitivity or a healthy control group, respectively. With regard to intervention, researchers found that the strength of

catastrophic misinterpretations prior to treatment for panic disorder was a significant predictor of change in anxiety sensitivity after treatment (Schneider & Schulte, 2008). Additionally, Teachman, Marker and Clerkin (2010) found that catastrophic misinterpretation bias declined over the course of cognitive behavior therapy for panic disorder, and the extent of this decline predicted the degree of subsequent symptom reduction. These results point to the value of shifting interpretation bias to reduce anxious symptoms.

CBM-I interventions are designed to reduce anxiety-congruent threat interpretations and increase anxiety-incongruent, or benign, interpretations. These paradigms are computer-based and involve the repeated pairing of benign resolutions with stimuli that are ambiguous, in that they may be construed as threatening to someone with anxiety. One common variant of CBM-I, which will be used in the current study, is based on the ambiguous scenarios paradigm created my Mathews and Mackintosh (2000), which involves imagining oneself in scenarios that are initially ambiguous, but are disambiguated in either an anxiety-congruent or incongruent way upon completion of a word fragment at the end of the scenario. A previous CBM-I study found that four sessions of this training successfully reduced both negative interpretation biases and self-reported trait anxiety (Mathews, Ridgeway, Cook, & Yiend, 2007). Several studies examining the impact of CBM-I on various forms of anxiety have now been conducted (e.g., Amir, Bomyea, & Beard, 2010; Beard & Amir, 2008; Clerkin & Teachman, 2011; Murphy, Hirsch, Mathews, Smith, & Clark, 2007; Teachman & Addison, 2008), with some success at reducing both interpretation bias and emotional vulnerability.

Notwithstanding these gains in the development of CBM-I (and CBM more broadly), the findings across studies remain quite mixed (see meta-analysis by Cristea, Kok, & Cuijpers, 2015; Hallion & Ruscio, 2011), which suggests the need for further modification of these paradigms to increase their efficacy. Indeed, *if* the effects can be made more robust, CBM paradigms seem likely to offer several advantages over traditional treatments, including potential cost-effectiveness, increased opportunities for dissemination, and enhanced tolerability by patients. Partly because of these possible advantages, CBM-I may be a useful intervention platform for reducing biased interpretations and anxiety symptoms and increasing resilience.

At least one study has successfully reduced anxiety sensitivity by altering catastrophic interpretations using CBM-I (Steinman & Teachman, 2010). However, durability of self-reported anxiety sensitivity symptom change was not examined in this single-session study. Further, only post-training reactivity (and not recovery) was assessed in response to a fairly mild panic stressor consisting of a brief interoceptive exposure, which may explain why there was not strong evidence of training-linked changes in response to the panic stressor (i.e., no training group difference in avoidance was found, and only a marginal trend for a group difference in subjective fear). Thus, the current study expanded the research on CBM-I for anxiety sensitivity by using multiple training sessions to enhance effects, measuring effects at a two-month follow-up, and measuring both initial reactivity and subsequent recovery to a relatively more intense panic stressor.

CBM-I for Resilience. Researchers have recently begun to modify CBM-I to target the development of healthier interpretations upon actually encountering a stressor (e.g., Mackintosh, Mathews, Eckstein, & Hoppitt, 2013). This contrasts with standard CBM, which

typically aims to reduce expectations about the likelihood that negative events will occur. We expected that this effort to target factors more directly linked to resilience, such as beliefs about one's ability to successfully handle a negative event when it occurs, would result in reduced reactivity and hastened recovery from a stressor compared to traditional CBM, because participants would have tools to manage stressors instead of simply relying on the belief that everything will turn out alright.

Several factors that have been empirically linked to increased resilience were thus targeted in the current study, including emotional and cognitive flexibility (Kashdan & Rottenberg, 2010; Waugh, Thompson, & Gotlib, 2011), self-efficacy (Benight & Bandura, 2004; Benight, Swift, Sanger, Smith, & Zepplin, 1999), an ability to assign purpose or meaning to a stressor (Holaday & MacPhearson, 1997), and positive emotional expression within the context of a stressor (Keltner & Bonanno, 1997; Fredrickson, Tugade, Waugh, & Larkin, 2003). For example, emotional and cognitive flexibility, defined as the ability to "flexibly deploy different coping strategies to match the demands of the environment" (Waugh et al.), has been linked to enhanced resilience. Specifically, Waugh et al. used psychophysiological and self-report measures to examine emotional reactivity to images that varied in emotional valence, finding that people with higher levels of trait resilience were better able to alter their emotional response to match the valence of the images compared to those with lower resilience. Self-efficacy also likely has ties to post-traumatic resilience, given that self-efficacy was the most significant predictor of subsequent distress for participants who had survived a natural disaster (Benight et al., 1999). Also, self-efficacy fully mediated the relationships between loss of resources and both post-traumatic distress and optimism (in the expected directions). Another factor, meaning assignment,

has also been examined for its role in adult resilience. Researchers conducted qualitative interviews with burn survivors, and revealed that survivors frequently attributed their ability to recover from the trauma to an ability to assign meaning or importance to the event (Holaday & McPhearson, 1997). Further, Frederickson et al. (2003) examined factors that influenced U.S. college students' resilience after the September 11, 2001 terrorist attacks, finding that the experience of positive emotions (e.g., hope, pride, amusement) in the weeks after the attack fully mediated the relationship between higher pre-attack resilience and both reduced post-attack development of depressive symptoms and greater increase in psychological resources (e.g., optimism and life satisfaction). Thus, in the current study, each of these targets—cognitive flexibility, meaning assignment, self-efficacy, and positive emotions—was incorporated into the CBM-I intervention.

This research is the first to our knowledge to examine whether CBM-I can extend beyond the reduction of reactivity to a stressor and also enhance recovery in a sample vulnerable to developing panic disorder.

The CO_2 Breathing Challenge

One common laboratory method for examining reactivity and recovery related to panic and anxiety sensitivity is the use of biological challenge procedures, which allow for the experience of bodily sensations commonly associated with panic. Specifically, during the carbon dioxide (CO_2) breathing challenge, individuals are asked to breathe air enriched with above-average levels of CO_2. While this challenge is completely safe, it is particularly ecologically valid because it reliably elicits multiple sensations similar to those experienced during a panic attack, such as shortness of breath and lightheadedness (Zvolensky & Eifert, 2001). There are multiple versions of this task, including one involving a single vital

capacity breath of a 35% CO_2 gas mixture (e.g., Schmidt, 1999), and another involving continuous inhalation of a mixture typically ranging between 5%-10% CO_2 (e.g., Sanderson & Wetzler, 1990). There is significant methodological variability across administrations of this task, including the quantity of CO_2 in the gas mixture and the duration of CO_2 breathing time, yet findings from the use of this task as a panic stressor are quite largely consistent (see Zvolensky & Eifert, 2001).

The CO_2 breathing challenge leads to greater fear and a higher frequency of panic attacks or panic symptoms in both people with panic disorder, as well as those with high anxiety sensitivity, compared to non-anxious control participants and those with other anxiety disorders (Griez, de Loof, Pols, Zandbergen, & Lousberg, 1990; Perna, Bertani, Arancio, Ronchi, & Bellodi, 1995; Verberg, Griez, Meijer, & Pols, 1995; see McNally, 1994). Further, multiple studies have shown that anxiety sensitivity is correlated with both self-report and physiological measures of anxiety in response to the CO_2 breathing challenge (Eke & McNally, 1996; Shipherd, Beck, & Ohtake, 2001). For example, Eke and McNally found that anxiety sensitivity, in addition to suffocation fear, but not trait anxiety or CO_2 sensitivity, predicted fear in response to the CO_2 challenge. Additionally, recent research has established the challenge as a reliable measure of panic-relevant arousal via adequate test-retest reliability for subjective fear (Gorlin, Beadel, Teachman, & Roberson-Nay, 2012; Seddon et al., 2011).

An important advantage of the CO_2 breathing challenge is its sensitivity to treatment for panic disorder. Indeed, subjective fear in response to the CO_2 breathing challenge has been reduced after both cognitive-behavioral and psychotropic medication-based treatments (Gorman et al., 1997; Nardi, Valença, Nascimento, Mezzasalma, & Zin, 2000;

Pols, Lousberg, Zandbergen, Griez, 1993). To our knowledge, it has not yet been used to measure the impact of a CBM-I intervention, yet findings suggest it is both a reliable and valid measure of panic vulnerability; hence its use as an outcome measure in the current study.

Overview and Hypotheses

This study evaluated the effects of resilience-enhancing CBM-I on interpretation bias, anxiety sensitivity, and the reaction to and recovery from a 7.5% steady state CO_2 breathing challenge. It was hypothesized that the resilience-enhancing CBM-I would result in increased resilience-congruent interpretations, decreased interpretation bias toward threat (particularly toward physical sensations associated with anxiety), and reduced anxiety sensitivity symptoms. It was also predicted that the active training condition would lead to enhanced resilience in response to panic-relevant stress. Specifically, it was hypothesized that people in the resilience training condition would show less anxious *reactivity* while breathing CO_2 enriched air (as evidenced by a less steep increase in reported anxiety during the challenge, and/or lower overall anxiety level), as well as faster *recovery* (as evidenced by a steeper decline in anxiety, and/or lower overall anxiety level) at the termination of CO_2 breathing, compared to those in the control condition. Additionally, it was hypothesized that, following the CO_2 breathing challenge, participants in the active training condition would be more willing to volunteer for future studies that involve participation in the CO_2 challenge compared to participants in the control condition. Finally, given the sample was college-aged, a particularly vulnerable time for the development of panic disorder (Kessler et al., 2005), it was predicted that those in the

active intervention would either show an improvement or less worsening in anxiety sensitivity at a two-month follow-up, compared to the control condition.

Methods

Participants and Recruitment

Participants (N = 90) were college students invited to participate based on their score on the Anxiety Sensitivity Index (ASI; Reiss, Peterson, Gursky, & McNally, 1986) in a University participant pool pre-selection battery. A college student sample was used, in part as a sample of convenience, and because the period spanning late adolescence through one's early twenties is the most prevalent time for developing panic disorder (Kessler et al., 2005), and high levels of anxiety sensitivity are strongly linked to the experience of panic attacks and panic disorder (Schmidt, Lerew, & Jackson, 1997; see McNally, 2002). Specifically, respondents who scored a 27.5 or greater were invited to participate, because this cutoff reflects a score of at least one standard deviation above the ASI mean for college students (Peterson & Reiss, 1992). This cutoff is also in line with other research showing that an unselected group who had reported experiencing at least one un-cued panic attack reported a mean of 25.3 on the ASI (Rapee, Ancis, & Barlow, 1988).

Anxiety sensitivity was reassessed with the ASI at the beginning of the study. At that point, only 60% (N = 50) of the sample who completed the study (n = 83) continued to meet the cutoff criterion for this construct. Only the data of those who remained high in anxiety sensitivity upon study initiation were used in the current analyses given our desire to examine the intervention's effects in a sample with significant risk for anxiety pathology (rather than participants who were experiencing transient symptoms, or potentially over-reporting on the screener to increase their likelihood of meeting eligibility criteria). See

Figure 1 for an adapted CONSORT (Consolidated Standards of Reporting Trials) flow diagram (Schulz, Altman, & Moher for the CONSORT Group, 2010) of the sample enrollment, allocation, and attrition details. Also, see Appendix A for further discussion of the reliability of this measure and the decision to reduce the sample, and other options that were considered. The final sample of 50 participants had a mean ASI score of 36.48 (*SD* = 5.44), and 52% reported the past experience of a panic attack on the PDSS. Furthermore, the sample had a mean age of 19.31 years (*SD* = 1.14) and was 86% (*n* = 43) female. The racial composition of the sample was reported as 55% (*n* = 27) Caucasian, 31% (*n* = 15) Asian, 10% (*n* = 5) African American, 4% (*n* = 2) biracial or prefer not to answer, and no one reported their ethnicity as Hispanic or Latino. See Table 1 for the demographic characteristics of the sample by study condition.

Potentially eligible participants (based on the initial ASI screener) were invited by e-mail to participate in four study visits (two one and a half hour sessions and two 30 minute sessions). The email contained the exclusion criteria related to the biological challenge procedure for the participant to review (see "exclusion criteria" below). The participant then notified the study team via e-mail if he or she was qualified (based on meeting the exclusion criteria) and willing to participate.

To increase the external validity of the results, participants *were not* excluded based on the following: 1) current/past treatment history, 2) past use of psychotropic medications (current use is also acceptable with some exceptions; see exclusion criteria below), or 3) comorbid psychiatric diagnoses (except for current or past psychosis). Psychiatric comorbidity is common in people with high levels of anxiety (Brown, Campbell,

Lehman, Grisham, & Mancill, 2001), so including these individuals enhanced the generalizability of the results.

Exclusion criteria. The following exclusion criteria (modified from Levitt, Brown, Orsillo, & Barlow, 2004; Pine et al., 2005) were included to protect participants from any possible risk from the CO_2 breathing challenge: 1) Serious, unstable illnesses, including type I and type II diabetes mellitus, hepatic, renal, gastroenterologic, respiratory, cardiovascular, endocrinologic, neurologic, immunologic, or hematologic disease, 2) one or more past seizures without a clear and resolved etiology, 3) a concussion or other head trauma within the past month, 4) current or past episodes of psychosis, 5) currently taking antidepressants or a non-psychotropic medication with psychotropic effects (e.g., beta-adrenergic blockers), unless the dosage has been stable for a minimum of one month prior to the study, and 5) self-reported confirmation or possibility of pregnancy. Additionally, students taking benzodiazepines could participate, but must not have used benzodiazepine medication for at least 48 hours prior to the final session of the study (when the CO_2 challenge takes place). Participants were screened both during the initial e-mail sign-up phase, and again when they arrived for participation in the final study session.

CBM-I Intervention

Ambiguous Scenario Training (adapted from Mathews & Mackintosh, 2000). Participants completed either four 30-minute intervention sessions or four 30-minute control sessions. Within each training session, participants were presented with scenarios designed to be ambiguous, but potentially threatening to someone with high anxiety sensitivity. Specifically, scenarios targeted factors thought to underlie anxiety sensitive individuals' difficulty recovering from a panic stressor (e.g., beliefs about their ability to

handle a negative event when it occurs, such as fixed beliefs that being anxious is catastrophic, and that they will not recover). After the presentation of a scenario, participants were presented with a final sentence containing a word fragment that was completed by selecting the missing letter (there is only one solution to the fragment). This word fragment resolved the ambiguity of each scenario in a resilience-congruent (i.e., healthy) direction. These resolutions trained the development of interpretations that enhance characteristics associated with resilience, such as greater flexibility in responding, greater self-efficacy, finding meaning or a silver lining in response to a stressor, and the expression of positive emotionality despite the presence of a stressor. A sample scenario targeting the use of positive emotional response in light of an anxiety stressor was: "You are at an amusement park and decide to ride a roller coaster with your friends. After you get off the ride, you are a bit dizzy and your legs feel weak. Although this makes you anxious, you can still l_ugh with the rest of your friends about how fun the ride was.." The final sentence and word fragment ("laugh") in this scenario create a resolution that promotes the use of positive emotional expression. Finally, each scenario was followed by a comprehension question that required a "yes" or "no" answer and was designed to reinforce the resolution of the ambiguity. For example, the question for the scenario above was: "Are you able to laugh with the rest of your friends despite feeling anxious?" Participants were not allowed to advance through training until they provided the correct missing letter for the word fragment, and then the correct answer to the comprehension question. See Appendix B for additional sample scenarios.

Control Condition. The Control training condition consisted of a sham variation of the Ambiguous Scenario Training that used scenario content that was neutral in valence

(see Steinman & Teachman, 2014 and Appendix B for examples). In this variation, none of the trials were related to the development of resilience, and approximately 75% of the trials were unrelated to anxiety sensitivity content (the decision to allow 25% of the content to relate to anxiety sensitivity was made to enhance credibility of the control condition). The control task was designed to match the Ambiguous Scenario Training paradigm for task demands, such as attention, time, format, and other nonspecific factors. This control condition was selected as opposed to the more commonly used CBM control condition that presents half of the trials with anxiety-congruent resolutions and half with anxiety-incongruent resolutions, because it has not been determined whether this variation is actually neutral (i.e., whether the positive and negative trials result in no change in interpretation bias; see Clerkin & Teachman, 2010).

The training sessions lasted for 30 minutes each. Participants completed 50 novel scenario trials per training session. If participants completed the trials for a given session prior to the end of the 30 minutes, they then underwent a modified iteration of the same scenarios until the time had expired, following Steinman and Teachman (2014). The second iteration asked participants to read the trials aloud, and the third iteration asked participants to complete three letters from the word fragment in the final sentence.

Materials[1]

See Appendix B for a copy of each measure.

Measure of Trait Resilience.

The Connor-Davidson Resilience Scale (CD-RISC; Connor & Davidson, 2003) is a 25-item measure of trait resilience that was used to characterize the sample and to check for

[1] The Panic Attack Coping Questionnaire was administered after the CO_2 challenge, but is not included in the analyses because it is not central to the current hypotheses.

baseline training group differences in resilience.[2] Participants responded to statements that assess various aspects of resilience (e.g., adaptability to change, distress tolerance, ability to use humor when faced with a problem, meaning assignment, social support) on a five-point scale ranging from "Not True at All" to "True Nearly All of the Time." This measure has shown good reliability and validity (Connor & Davidson, 2003). Cronbach's alpha[3] for the current study was .93.

Measures of Panic Vulnerability.

The Anxiety Sensitivity Index (ASI; Reiss et al., 1986) consists of 16 items that measure the fear of anxiety symptoms (e.g., racing heart, lightheadedness) on a five-point Likert scale ranging from "Very Little" to "Very Much". This self-report measure has excellent psychometric properties (Deacon, Abramowitz, Woods, & Tolin, 2003; Peterson & Reiss, 1993), and was used to screen potential participants, and as a measure of baseline, post-training, and follow-up anxiety sensitivity. Cronbach's alpha for the current study was .60 at pre-study screening, .40 at baseline (both of which were unexpectedly low), .85 at post-training, and .80 at follow-up.

The Panic Disorder Severity Scale (PDSS; Shear et al., 1997) is a seven-item measure used to assess the severity of panic symptoms, including panic attack frequency, anticipatory anxiety, agoraphobia, avoidance, and distress and impairment caused by panic. This measure has adequate psychometric properties (Shear et al., 1997), and was

[2] This measure was initially conceptualized as an outcome measure, but multiple readers of an earlier draft raised questions about the validity of construing a general measure of resilience that is designed to reflect long-standing patterns of adapting to stress as an outcome measure in this context where outcomes are assessed immediately following training and training is specific to anxiety sensitivity/panic resilience.
[3] All reports of Cronbach's alpha are indicators of inter-item consistency.

used to characterize the sample.[4] The PDSS was modified in the current study to allow for self-report (see Houck, Spiegel, Shear, & Stat, 2002). Cronbach's alpha was .76.

Measures of Interpretation Bias.

The Recognition Ratings Task (modified from Mathews & Mackintosh, 2000) is commonly used to examine change in interpretations as a result of CBM-I, and was used in the current study as a measure of resilience-relevant interpretation bias. Both before and after training, participants read six ambiguous, anxiety sensitivity-relevant scenarios. These scenarios had a title, and required participants to complete the missing letter in the final word fragment and answer a comprehension question. These scenarios were similar in format to the CBM-I training scenarios, except the final sentence did not resolve the ambiguity. Participants then engaged in a puzzle task for three minutes as a distracter (adapted from Steinman & Teachman, 2010). Next, participants were shown the title of each scenario, followed by four disambiguated interpretations for that scenario. One interpretation was a positive, or resilience-congruent, interpretation; one was a negative, or resilience-incongruent, interpretation; and the other two served as a positive and a negative foil (i.e., the interpretation was valenced but unrelated to anxiety sensitivity/panic or resilience). Participants made ratings of how similar in meaning each of the four interpretations was to what they recalled from the original scenario, using a one (very different in meaning) to four (very similar in meaning) scale. Cronbach's alpha for the

[4] PDSS was administered at baseline, post-training, and follow-up, but due to the skip pattern in the measure (i.e., you do not proceed to provide severity ratings if you have not had a past history of a full-blown panic attack), only 16 participants completed the full measure at all three time points, so the measure could not be used to assess outcomes. However, the baseline assessment is retained for the information it provides about the presence of reported panic attack history in this high-risk sample.

positive ratings was .85 at baseline and .89 at post-training, and for the negative ratings, the alpha was .85 at baseline and .92 at post-training.

The Brief Body Sensations Interpretation Questionnaire – Physical subscale (BBSIQ-Phys) is a seven-item subscale of a measure assessing anxiety-relevant interpretations, with satisfactory internal consistency (Clark et al., 1997). The seven items related to physical sensations of anxiety were used in the current study to examine the impact of training condition on anxiety sensitivity-relevant interpretation bias. Additionally, unlike Recognition Ratings, the BBSIQ-Phys measures interpretation bias using a format that is dissimilar to the CBM-I training paradigm. For this measure, participants were presented with ambiguous scenarios (e.g. "You notice that your heart is beating quickly and pounding. Why?"), and then three possible disambiguated interpretations, two of which are either neutral or anxiety-incongruent (e.g., "because you have been physically active", "because you are feeling excited"), and one that is anxiety-congruent (e.g., "because there is something wrong with your heart"). Participants were then asked to rate the likelihood of each interpretation being true using a 0-8 Likert scale, ranging from "Not at all likely to be true" to "Extremely likely to be true" (note, the rankings subscale of the BBSIQ was not included in the current study to reduce measurement burden). Cronbach's alpha for the BBSIQ-Phys items was .84 at baseline, .87 at post-training, and .82 at follow-up.

Measures of Reactivity to the CO_2 Challenge.

The Subjective Units of Distress Scale (SUDS; Wolpe, 1969) was used to obtain a subjective rating of anxiety at baseline and at two-minute intervals throughout the CO_2 breathing challenge to measure change in state anxiety. Participants rated their anxiety on a scale between 0 and 100, ranging from "No anxiety" to "Extreme anxiety." The SUDS was

chosen over more comprehensive measures because of its brevity due to the planned frequency of administration.

The Diagnostic Symptom Questionnaire (DSQ; Sanderson, Rapee, & Barlow, 1989) is a 16-item measure of panic attack symptoms that has been commonly used during the CO_2 breathing challenge (Finlay & Forsyth, 2009; Forsyth & Eifert, 1998; Kelly & Forsyth, 2007; Nillni et al., 2012; Poonai et al., 2000). The DSQ was administered once during the baseline assessment (pre-training), once during the pre-CO_2 room-air phase of the CO_2 challenge, twice during the CO_2 breathing period, twice during the post-CO_2 recovery period, and once post-CO_2 challenge (for a total of seven administrations). Apart from the final administration, this measure was abbreviated (DSQ-Abbreviated) to allow for multiple administrations across the CO_2 challenge while minimizing interference during the task (i.e., time spent filling out measures during the CO_2 challenge). Specifically, participants were asked to indicate whether or not they were experiencing each panic symptom by simply circling "yes" or "no" (the intensity Likert-scale ratings were eliminated). In addition to the sum of the number of panic symptoms experienced (DSQ-Sum), participants were then asked to rate how intensely they were experiencing both overall physical (DSQ-Physical) and overall cognitive (DSQ-Cognitive) symptoms of panic on a 9-point Likert scale ranging from "Not at All Noticed" to "Very Strongly Felt". The very final administration (after the CO_2 challenge, with the mask off) was expanded (DSQ-Expanded) to include the same items as the DSQ-Abbreviated in order to assess participants' current experience with panic symptoms, as well as 12 additional items from the original version. These additional items retrospectively assessed various cognitions experienced upon the onset of panic symptoms during the CO_2 challenge that were not otherwise assessed. The

mean Cronbach's alpha for the six administrations of the DSQ-Abbreviated was .78 with a range of .62 to .89. The Cronbach's alpha for the panic-symptom items of the DSQ-Extended was .89.

CO_2 Breathing Challenge Task

The CO_2 challenge task has been used extensively by clinical researchers to study how people respond to the experience of heightened bodily sensations, particularly those tied to panic attacks (Roberson-Nay, Beadel, Gorlin, Latendresse, & Teachman, 2014; Papadopoulos, Rich, Nutt, & Bailey, 2010; Perna et al., 1994; Seddon et al., 2011), and recent work from our lab has shown that it reliably elicits panic-related arousal (Gorlin et al., 2012). After the training task, participants were asked to breathe a steady state 7.5% CO_2 gas mixture (21% oxygen, balance nitrogen) for eight consecutive minutes (with a variety of IRB-approved safety precautions in place; see exclusion criteria above). The gas mixture was administered to the participant through a face mask, worn over the nose and mouth, which maintains a tubal connection to a gas reserve that was kept from view of the participant. This breathing challenge included a five minute baseline room-air phase and an eight minute recovery phase, in which the mask remained in place, but the participant breathed room air. The participants were not told when the initiation and termination of the CO_2 breathing portion of the task occurred, and participants were instructed that they could stop the task at any point if they became too uncomfortable. Throughout the task, subjective fear (SUDS), and symptoms of panic attacks (DSQ-Abbreviated) were measured at regular intervals to examine reactivity and resilience toward this panic-relevant stressor (see Figure 2). Specifically, we administered SUDS every two minutes throughout the task, and the DSQ on seven occasions (including a pre-training baseline assessment and an

immediate post-CO_2 challenge expanded assessment). We decided that the limitations of not administering the CO_2 challenge both before and after training were outweighed by the costs of exposing participants to the challenge before training, which might have affected participants' responses to both the training and post-training measures.

Anxious reactivity was operationalized as self-reported panic symptoms on the DSQ (both the sum of all symptoms and the intensity of physical and cognitive symptoms) and subjective fear (using SUDS) during the CO_2 breathing phase of the task. Additionally, recovery was operationalized via self-reported panic symptoms and subjective fear during the post-CO_2-breathing recovery phase. Note, we recognize there is an interpretive challenge in that it is not entirely clear when the stressor (including actual physiological reactivity in response to breathing the CO_2 enriched air) has offset and recovery has begun; however, this task was selected because it offers a clear point of termination of the CO_2-enriched air, providing considerable standardization and control over the stressor's administration. We have elected in this study to focus on indicators of anxious reactivity and recovery that emphasize the person's subjective reactions to the stressor (separate from the actual level of physiological reactivity), consistent with Bonanno's (2012) focus on "healthy adjustment."

Willingness to Engage in CO_2 Task Again. As a novel and more indirect measure of resilience that focused on willingness to endure future stress, after undergoing the CO_2 breathing challenge, participants were given a sheet of paper that read, "We appreciate your participation in this study. We are looking for participants to participate in other psychology studies for payment and/or credit. Please indicate below whether or not you would allow us to contact you for participation in future studies." There were four

responses provided, and participants were asked to check all that applied to them. The four responses were, “I would be willing to be contacted for paid participation in future psychology studies”, “I would be willing to be contacted for paid participation in future psychology studies that use the CO_2 breathing challenge”, “I would be willing to be contacted for paid participation in future psychology studies, but not ones that include the CO_2 breathing challenge”, and “I would prefer not to be contacted for participation in future studies”. The variable of interest was willingness to participate in future studies that use the CO_2 breathing challenge.

Procedure

Upon arrival to the first laboratory session, participants underwent a detailed informed consent process and were then asked to complete baseline measures of interpretation bias (BBSIQ-Phys and Recognition Ratings), prior panic symptom severity (PDSS), state panic symptoms (DSQ-Abbreviated), state subjective fear (SUDS), and trait resilience (CD-RISC). Participants were then randomly assigned to one of two intervention conditions (resilience-enhancing CBM-I or sham training control condition). After this first training session, participants returned for three additional visits, approximately every three to four days. The second and third visits consisted solely of a 30-minute training session. After completion of training during the fourth session, they once again completed measures of interpretation bias (BBSIQ-Phys and Recognition Ratings), anxiety sensitivity (ASI), and provided demographics information. Next, to examine the impact of training on resilience (incorporating both reactivity and recovery), participants underwent the CO_2 breathing challenge (with subjective fear and panic symptom monitoring, using SUDS and DSQ-Abbreviated), which was immediately followed by a final administration of the DSQ

(DSQ-Expanded), and the assessment of willingness to engage in the CO_2 task in the future. Finally, participants were emailed a request to complete an Internet survey two months after their final laboratory session, which included the measures of anxiety sensitivity (ASI) and interpretation bias (BBSIQ). See Figure 3 for a visual representation of the study procedure. Note, all measures were not administered at follow-up because this administration occurred over email/Internet, and we wanted to minimize participant burden to increase adherence and reduce attrition. This follow-up session was followed by a thorough debriefing conducted over the telephone. The total study took approximately four hours (Visit 1: one and a half hours, Visit 2 and 3: 30 minutes, Visit 4: one and a half hours). Participants received $40 or four credits toward their participant pool requirement for their time, and were offered a five dollar gift card for participating in the follow-up assessment.

Results

Comment on Sample Size and Power Analyses

To determine the probability of detecting training condition differences in interpretation bias, findings from Steinman and Teachman (2010) were used to conduct a power analysis. They found significant CBM-I training condition differences on a post-training Recognition Ratings task for both change in positive and negative anxiety sensitivity interpretations. Taking the average of these two effects, a comparable Cohen's *f* of .41 would result in a 96% likelihood of seeing differences with $n = 22$ per treatment condition (where alpha =.05).

Information on how to derive power for multi-level modeling is lacking (Scherbaum & Ferreter, 2009), but researchers have completed simulation studies to help determine

what size sample will allow for the detection of effects and the minimization of non-convergence of the models (Kreft, 1996; Maas & Hox, 2005; Scherbaum & Ferreter). Results of these power simulations suggest that the detection of a medium effect size with an 86% likelihood (alpha = .05) is possible when the Level 2 sample size (individuals) is 40 and the Level 1 sample size (repeated measurements) is 10 (Scherbaum & Ferreter), which would be met in the current study from sampling SUDS on twelve occasions. Additionally, Maas and Hox (2005) suggest a Level 2 sample size of no less than 30 in order to maximize the chance of model convergence.

Thus, we aimed for a sample of 50 participants per condition to account for potential attrition and adequately power the analyses in the current study. However, our power was reduced given the decision to reduce the sample size and only use those participants who remained high on the ASI prior to starting training. Thus, for the interested reader, a summary of the results run on the full sample both with and without the ASI as a covariate can be found in Appendix C.

Sample Characteristics

The two training groups, "CBM-I" (n = 29) and "Sham" (n = 21), did not differ by gender ($\chi^2(1) = .16$, $p = .691$), race ($\chi^2(4) = 4.91$, $p = .297$), or age ($F_{(2, 47)} = .98$, $p = .975$, $d = .01$). As expected, there were also no significant differences in baseline symptoms of anxiety sensitivity (ASI; $t(48) = -.94$, $p = .350$, $d = -.23$), panic symptoms for those who had reported the past experience of a panic attack (PDSS: $t(48) = 1.19$, $p = .239$, $d = .31$; DSQ: $t(48) = -.71$, $p = .483$, $d = -.20$), baseline anxiety at any of the sessions (SUDS: all p's > .10), or interpretation bias (resilience-congruent Recognition Ratings: $t(48) = -.84$, $p = .403$, $d = -.25$; resilience-incongruent Recognition Ratings: $t(48) = .42$, $p = .550$, $d = .17$, BBSIQ-Phys:

$t(47) = .35$, $p = .727$, $d = .10$). There was, however, a significant difference between groups for baseline trait resilience (CD-RISC: $t(48) = 2.32$, $p = .025$, $d = .66$), such that those in the CBM-I condition reported higher baseline trait resilience ($M = 71.34$, $SD = 13.52$) than the Sham condition ($M = 62.33$, $SD = 13.67$). As a result, baseline trait resilience was included as a covariate in the primary analyses. See Table 2 for means and standard deviations for the baseline (and post-training and follow-up where applicable) dependent and sample characterizing variables.

Change in Interpretation Bias Following Training

Recognition Ratings. A repeated measures analysis of covariance (RM-ANCOVA) was conducted for the Recognition Ratings variable. The within-subject variables were time (pre-training and post-training), valence (positive and negative), content (resilience-congruent, resilience-incongruent), the between-subjects factor was training condition (CBM-I and Sham), and baseline trait resilience was covaried. Because the primary research question involves differences in training condition, only the main effects and findings related to training condition are discussed. There were no significant main effects for condition ($F(1, 47) = .78$, $p = .381$, $\eta^2_p = .02$), time ($F(1, 47) = .29$, $p = .592$, $\eta^2_p = .01$), or valence ($F(1, 47) = 2.29$, $p = .137$, $\eta^2_p = .05$), and there was a non-significant trend for a main effect for content ($F(1, 47) = 3.63$, $p = .063$, $\eta^2_p = .07$). There was, however, a significant condition by time by valence interaction ($F(1, 47) = 5.62$, $p = .022$, $\eta^2_p = .11$), which was subsumed by the expected significant four-way condition by time by valence by content interaction ($F(1, 47) = 5.67$, $p = .021$, $\eta^2_p = .11$).

To follow-up the four-way interaction, four repeated measures ANCOVAs for time by condition were conducted for each of the four Recognition Ratings types: resilience-

congruent, resilience-incongruent, positive foil, and negative foil. For the resilience-congruent Recognition Ratings, there was a non-significant trend for a main effect of condition ($F(1, 47) = 3.99$, $p = .052$, $\eta^2_p = .08$), and a significant condition by time interaction ($F(1, 47) = 6.92$, $p = .011$, $\eta^2_p = .13$). Follow-up independent sample t-tests indicated no significant difference between conditions at baseline ($t(48) = .60$, $p = .550$, $d = .17$), but at post-training, those in the CBM-I condition reported significantly more resilient-congruent interpretations than those in the Sham condition ($t(48) = 3.77$, $p < .0005$, $d = 1.07$), as hypothesized (see Figure 4a). Examining within-subject effects, paired-sample t-tests found that both conditions reported significantly more resilient interpretations at post-training than at baseline (CBM-I: $t(28) = -6.05$, $p < .0005$, $d = -1.12$, Sham: $t(20) = -3.49$, $p = .002$, $d = -.76$), though the effect size was stronger in the CBM-I condition, as expected.

For the resilience-incongruent Recognition Ratings, there was no main effect of condition ($F(1, 47) = 1.97$, $p = .167$, $\eta^2_p = .04$), and a non-significant trend for a condition by time interaction ($F(1, 47) = 3.33$, $p = .074$, $\eta^2_p = .07$). Following up this trend, independent samples t-tests indicated no significant difference between conditions at baseline ($t(48) = -.84$, $p = .403$, $d = -.25$), while those in the CBM-I condition reported significantly fewer resilience-incongruent interpretations than those in the Sham condition at post-training ($t(48) = -2.45$, $p =. 018$, $d = -.71$), consistent with hypotheses. As shown in Figure 4b, paired samples t-tests examining within-subject differences revealed a significant reduction in resilience-incongruent interpretations from pre- to post-training for those in the CBM-I condition ($t(28) = 3.63$, $p = .001$, $d = .67$), but no change for those in the Sham condition ($t(20) = 1.66$, $p = .113$, $d = .23$).

There were no significant main effects for condition or condition by time interactions for the positive or negative foil analyses (p's > .10), indicating that the observed interpretation changes were specific to resilience and anxiety sensitivity content.

BBSIQ-Phys. For the BBSIQ-Phys outcome variable, a 2 (training condition) x 3 (time: pre-training, post-training, and follow-up) repeated measures ANCOVA was conducted with trait resilience as a covariate. There were no significant main effects or interactions detected (all p's >.10).

Change in Anxiety Sensitivity Following Training

To examine the impact of training on anxiety sensitivity, a 2 (training condition) x 3 (time; pre-training, post-training, and follow-up) RM ANCOVA with trait resilience as a covariate was conducted, revealing a main effect of time ($F(2, 39) = 3.89$, $p = .029$, $\eta^2_p = .17$). There was no main effect of condition ($F(1, 40) = 1.69$, $p = .201$, $\eta^2_p = .04$), but there was a non-significant trend for the expected interaction between condition and time ($F(2, 39) = 2.66$, $p = .083$, $\eta^2_p = .12$). Follow up independent sample t-tests were conducted for each time point. While there was no significant condition difference at baseline or post-training, there was a non-significant trend for a difference at follow-up ($t(43) = -1.99$, $p = .053$, $d = -.62$), with those in the CBM-I condition reporting less anxiety sensitivity than those in the Sham condition, possibly indicating delayed training effects (see Figure 5). Examination of within-group differences showed similar patterns across time for both training conditions, with a significant reduction in anxiety sensitivity from baseline to post-training (CBM-I: $t(25) = 5.27$, $p < .00025$, $d = 1.03$; Sham: $t(19) = 3.31$, $p = .004$, $d = .74$) and baseline to follow-up (CBM-I: $t(26) = 6.60$, $p < .00025$, $d = 1.27$; Sham: $t(17) = 4.25$, $p = .001$, $d = 1.00$), but no significant difference from post-training to follow-up (CBM-I: $t(24) = 1.60$,

p = .123, d = .32; Sham: $t(17) = 0.07$, p = .945, d = .02), suggesting gains were maintained. Notably, while both conditions showed reductions in symptoms, the effect sizes tended to be larger for those in the CBM-I condition relative to those in the Sham condition.

Willingness to Participate in Future CO_2 Challenges

A Chi-Square analysis was used to examine training condition differences in rate of endorsement for the item that assessed willingness to participate in future studies that include the CO_2 challenge. The result of the Chi-Square test was non-significant ($\chi^2(1) = 1.34$, p = .247), though low power may have been an issue given 48% of those in the CBM-I condition versus 65% of those in the Sham condition said they were unwilling to participate in future CO_2 challenges, perhaps suggesting more willingness to participate in future CO_2 challenges in the CBM-I condition.

Change Over the Course of the CO_2 Breathing Challenge

Mixed-effect linear regression models (MLR) were used to examine the impact of training condition on subjective fear (SUDS) and panic symptoms (DSQ) over time during the CO_2 breathing challenge using the lme4 package in R (R Core Team, 2013; Bates, Maechler, Bolker, & Walker, 2013). For each analysis, training condition, time (linear and curvilinear), and their 2-way interaction were examined as fixed-effect predictors of the SUDS, DSQ-Sum, DSQ-Cognitive, and DSQ-Physical variables. Trait resilience (as a covariate) was entered into the model as a continuous fixed effect. The Intercept was included as a random effect in each model to control for random variation in individual participants' means for the variable under analysis. Please see Table 3 for correlations between the post-training measures of anxiety and interpretation bias and the measures of the CO_2 breathing challenge, and Table 4 for the full results for each model.

SUDS. The analysis for SUDS revealed a significant main effect of quadratic time (β = 43.08, p = .039) as well as a significant training condition by quadratic time interaction. Best practices for follow-up tests for interactions involving quadratic trends are not well defined, so we chose to apply multiple strategies that map well onto the theory we are interested in testing. First, we followed up with between-group t-tests at each time point, which resulted in no significant differences. However, examination of the effect sizes at each time point suggested that the interaction may have arisen from a combination of individually non-significant differences. Specifically, for the first three measurement points during the room-air pre-CO_2 period (d = -.27, -.20, and -.15, respectively), those in the CBM-I group reported lower anxiety than those in the Sham group, suggesting reduced anticipatory anxiety. There was also a small effect at the final two time points of the CO_2 breathing period (d = .17 and .25), with those in the CBM-I group reporting greater anxiety than those in the Sham group. Finally, there was again a small effect for the final measurement (d = -.17), with the means showing that those in the CBM-I group reported less anxiety after completion of the challenge than those in the Sham group, suggesting greater post-CO_2 recovery.

As is standard practice, we then extracted the predicted values from the model to examine how the predicted trends might differ. The general pattern of change over time for the predicted values (see Figure 6) was characterized by a slower increase in SUDS ratings during the pre-CO_2 breathing period (again, indicating less anticipatory anxiety) for those in the CBM-I condition. Both groups seemed to respond with mostly similar levels of subjective anxiety during the CO_2 breathing period. A difference appeared again during the

recovery period, wherein those in the CBM-I group seemed to recover slightly more than those in the Sham condition.

These multiple follow-up approaches allowed for examination of the significant interaction between condition and quadratic time from different vantage points, but given the multiple tests and small effect sizes, this overall finding should be interpreted with caution.

DSQ. There were significant main effects of quadratic time for the DSQ-Sum, DSQ-Physical, and DSQ-Cognitive variables. Specifically, there was an increase in panic symptoms reported during the CO_2 breathing portion, as would be expected, followed by an observable decrease in symptoms during recovery. Contrary to hypotheses, there was no significant main effect of training condition or interaction between training condition and time for the DSQ-Sum or DSQ-Physical variables. For the DSQ-Cognitive variable, however, there was a significant main effect of condition with those in the CBM-I condition reporting fewer cognitive symptoms of panic across the CO_2 challenge than those in the Sham condition, in line with hypotheses. See Figures 7a and 7b for visual representations of the change in DSQ-Cognitive and DSQ-Physical scores across the task.

Discussion

This study examined the efficacy of a novel application of CBM-I designed to increase resilience following a laboratory-induced panic challenge in a sample with high anxiety sensitivity—a well-established vulnerability marker for panic attacks and panic disorder. CBM-I is designed to alter maladaptive interpretations, and the CBM-I training in the current study was modified to enhance interpretations in a way that promotes the cognitive skills or characteristics associated with resilience (e.g., meaning assignment,

cognitive flexibility, positive emotional expression) as they pertain to anxiety sensitivity. In line with hypotheses, those who underwent CBM-I endorsed more resilience-congruent interpretations and fewer resilience-incongruent interpretations (though this effect was smaller) on the Recognition Ratings task following training compared to those in the Sham condition, but there was no training difference on a measure of panic interpretations that was not focused on resilience. Those in the CBM-I condition also reported a trend for less anxiety sensitivity at follow-up compared to those in the Sham condition, as expected. With regard to the CO_2 challenge task, individuals who completed CBM-I reported less intense cognitive symptoms of panic across the challenge, together with a complex pattern of subjective anxiety suggesting less anticipatory anxiety prior to the CO_2 breathing phase, comparable anxious reactivity during CO_2 administration, and then slightly greater anxiety reduction during the recovery period, compared to the Sham condition. However, there were no training condition differences observed for the total number of panic symptoms or the intensity of physical symptoms reported across the challenge.

Specificity and Timing of CBM-I Training Effects

While there was a significant training condition effect on resilience-congruent interpretations measured by Recognition Ratings, unexpectedly, there were no training condition differences on a measure of panic-relevant interpretations (on the BBSIQ) that is unrelated to resilience characteristics. A recent study found that the match in content between CBM-I training scenarios and the participant's specific fears results in more positive outcomes than for those whose feared situations do not match the content of the scenarios (Beadel, Ritchey, & Teachman, in press), and the current study suggests that the type of interpretations trained (even within a given fear domain) may also impact the

results. Unlike many past versions of CBM-I, this version was not solely designed to reduce an individuals' propensity to misinterpret benign symptoms as catastrophic, as assessed by this second measure of interpretation bias, but rather to bolster interpretations that promote resilience.

Notwithstanding, an alternative possible interpretation for the finding of training effects on Recognition Ratings but not on the BBSIQ, is that the Recognition Ratings task is somewhat similar in format to the scenario training format, which can raise concerns about 'teaching to the test' and shared method variance. While this possibility cannot be eliminated, the overall evidence in this study shows that the active CBM-I condition resulted in change across multiple dependent variables, including interpretation bias, anxiety sensitivity, subjective distress, and panic cognitions, suggesting the overlap in format is unlikely to fully account for the positive training results.

Also consistent with hypotheses, the results suggest that CBM-I positively affected panic vulnerability, based on the CBM-I (vs. Sham) condition's greater reduction in anxiety sensitivity, which is a leading vulnerability factor for the development of panic disorder (Reiss, 1991; Schmidt, Zvolensky, & Maner, 2006). Interestingly, the difference in conditions did not emerge until follow-up, though this finding should be interpreted with caution because the difference was at a non-significant trend, albeit with a medium to large effect size. The delayed effect is somewhat surprising considering at least one single-session CBM-I study has shown a change in anxiety sensitivity directly after training (though with a smaller effect size; see Steinman & Teachman, 2010). Perhaps the resilience component of the CBM-I adapted for this study led to the delay in effects; for instance, one may need to practice the new resilience-enhancing interpretations, such as meaning

assignment, cognitive flexibility, etc. in real-life settings before they can affect a construct like "fear of fear", which is likely activated very rapidly and involuntarily in this vulnerable sample. Clearly, the current study points to the importance of follow-up measurement, as some effects can take longer to manifest.

Impact of CBM-I on Resilient Responding to a Panic Stressor

The CO_2 breathing challenge, a common biological challenge procedure, was administered after training to assess the impact of CBM-I on resilience. Subjective anxiety, total number of panic symptoms, intensity of cognitive panic symptoms, and intensity of physiological panic symptoms were measured across the task, including during the pre-CO_2 room-air phase, the CO_2 breathing phase, and the post-CO_2 room-air recovery phase. Contrary to hypotheses, there was no impact of training condition on the number of panic symptoms reported or the intensity of physiological symptoms of panic. With regard to the number of panic symptoms, it seems probable that the modification of the measure from a 9-point Likert scale to a dichotomous yes/no format reduced the variability in responding, which may explain the null finding. However, in line with hypotheses, there was a main effect for those in the CBM-I condition to report less intensity of cognitive symptoms of panic across the task than those in the Sham condition. While there was not the expected interaction with time, indicating differences specific to rate of decline during the recovery phase, we nonetheless interpret this main effect as enhanced resilience due to the fact that those in the CBM-I condition reacted with less intensity of cognitive symptoms during the CO_2 breathing phase (indicating reduced anxious reactivity) and during the recovery room-air phase (indicating enhanced recovery), both of which are markers of reduced vulnerability to the panic stressor.

It is not completely surprising that there was a condition difference in the expected direction for the intensity of cognitive symptoms, but not for physiological symptoms of panic, because the purpose of the training is more focused on changing the meaning assigned to symptoms rather than reducing the initial activation of physical symptoms of panic. In other words, the resilience training emphasized that one can recover and cope when unpleasant events happen, rather than priming the expectation that unpleasant events would not happen. Interestingly, a related line of research has identified distinct subtypes of panic disorder, including a cognitive subtype, in which an individual experiences high levels of subjective fear and cognitive symptoms, but low levels of physiological arousal (Meuret et al., 2006; Schmidt, Forsyth, Santiago, & Trakowski, 2002). Perhaps the version of CBM-I used in the current study would be best suited to help increase resilience and reduce anxiety for this subtype, though this possibility needs to be examined in future research.

In addition, those in the CBM-I condition appeared to have slightly less anxiety during the pre-CO_2 room-air breathing phase, as well as a slightly greater decline in anxiety during the post-CO_2 recovery phase compared to those in the Sham condition, suggesting effects on both anticipatory anxiety and recovery to the stressor (though between-group follow-up tests showed no significant differences at any time point across the CO_2 challenge despite the significant interaction, so these trends should be interpreted with caution). The training effects on subjective anxiety point to reduced emotional vulnerability in the face of a stressor, which is key to increasing resilience. Notably, subjective anxiety is also part of the criteria for the cognitive subtype of panic, again suggesting that CBM-I may be particularly helpful for this subtype. Additionally, these results point to the importance of

examining emotional vulnerability more broadly by incorporating both pre- and post-task measurement, especially given that we did not see training differences in reactivity during the CO_2 stressor. While many researchers solely examine reactivity during the stressor itself, these findings suggest that differences may emerge during anticipatory and recovery periods, which may help explain why some prior CBM studies have failed to see transfer of cognitive training effects to emotional vulnerability indicators.

Given the promising—but not clear-cut—findings for the subjective anxiety variable and the null findings for the self-reported physical symptoms variable during the CO_2 challenge, a suggestion for future research would be to examine psychophysiological responding across the CO_2 challenge. There is often desynchrony between self-report and physiological measures of anxiety (e.g., Himadi, Boice, & Barlow, 1985; Mavissakalian, 1986), so the psychophysiological findings may show different patterns of response compared to the subjective measures. However, defining the psychophysiological *response* is challenging; given this is a biological challenge, some physiological indices could reflect both the stressful stimulus itself and the dependent "response" variable. As a result, care would have to be taken so that the psychophysiological response variable can be distinguished from the physiological reaction that is caused directly by the task. One possible solution to this may be to measure skin conductance, which is a reliable measure of anxiety-related sympathetic nervous system activity (Dawson, Schell, & Filion, 2007), but not likely a direct physiological result of CO_2 inhalation.

Clinical Implications

While interventions targeting resilience are lacking, a speedy recovery from a stressful event is an important component of maintained well-being and psychosocial

health (Bonanno et al., 2011; Kobasa, 1979). The current study showed that a CBM-I training designed to modify panic-relevant interpretations to enhance resilience is able to help anxiety sensitive individuals experience less distress in response to a subsequent stressor, compared to a control condition. Since most of the existing interventions for adult resilience target combat trauma or workplace stress (see Kent et al., 2011; Sood et al., 2011), there is a clear need for interventions designed to reduce reactivity and hasten recovery in response to other stressful events, such as panic attacks. Research shows that people who have had panic attacks (even without meeting criteria for panic disorder) report impairment in physical and emotional health, occupational functioning, and increased utilization of emergency medical services compared to those who have not experienced panic attacks (Klerman, Weissman, Ouellette, Johnson, & Greenwald, 1991), so easily portable interventions for this population could have substantial benefits. Moreover, it would be interesting to examine whether this resilience adaptation of CBM-I could be modified to also enhance resilience to other types of anxiety stressors, such as negative or humiliating social situations for those vulnerable to social anxiety, or exposure to news about catastrophic negative events for those vulnerable to generalized anxiety disorder.

At the same time, change did not occur reliably for the full range of panic markers investigated. Perhaps the effects of this intervention could be strengthened by incorporating a greater proportion of training scenarios that help reduce the traditional components of interpretation bias for panic, such as a tendency to overestimate the likelihood and severity of threatening outcomes (Wiedemann, Pauli, & Dengler, 2001), or beliefs about one's ability to tolerate anxiety sensations (Schmidt, Richey, & Fitzpatrick, 2006). In addition, it will be helpful to replicate the current study with a motivated,

treatment seeking sample. Anecdotal evidence from participant feedback suggests that they often find CBM-I to be repetitive and uninteresting. Those who are seeking treatment for anxiety and find exposure therapy aversive or fearful may be more motivated to engage with the CBM-I training material as an alternative intervention, which may enhance the results. Indeed, there is research suggesting that higher client motivation for treatment enhances the impact of psychological interventions (Huppert, Barlow, Gorman, Shear, & Woods, 2006; Keijsers, Schaap, Hoogduin, 2000; Zuroff et al., 2007). Providing some brief psychoeducation on the risks associated with high anxiety sensitivity could perhaps enhance motivation for participation.

Limitations and Conclusion

There are several limitations of the current study. First, the sample size is smaller than intended because a significant portion of participants who were eligible based on an initial screener no longer met inclusion criteria by the start of the study, and thus were not used in the analyses. There are several possible explanations for this shift in ASI scores, including an over-reporting of anxiety at the first measurement due to a cohort effect of increased stress during the period of administration (i.e., the first few weeks of the semester), and potential over-reporting of symptoms due to fear of not being able to meet the department's study participation requirements. Second, while this study purposefully targeted college-aged individuals because that is a particularly vulnerable time for the development of anxiety (Kessler et al., 2005), the use of a student sample points to the need for replication with a community sample and other age groups. Third, there was no baseline assessment of the CO_2 breathing challenge, which prohibited a pre- to post-training comparison, though this design decision was deemed important in order to reduce

the possibility of exposure effects or negative expectancies that could confound a second administration of the task. Fourth, there was a baseline condition difference in trait resilience, and although it was covaried in most of the analyses, it is nonetheless a limitation.

Notwithstanding these limitations, this study was the first, to our knowledge, to modify CBM-I to increase resilience to panic sensations for those vulnerable to developing panic disorder. Additionally, this study adds to the growing literature demonstrating that CBM-I is able to modify unhealthy interpretations (see Cristea et al., 2015; Hallion & Ruscio, 2011), and supports the proposed causal link between interpretation bias and anxiety (Wilson, MacLeod, Mathews, & Rutherford, 2006). While the results are somewhat mixed, this study provides preliminary evidence that CBM-I may be able to enhance resilience, a construct that is critical to maintaining psychological wellbeing in the face of life's stressors. Moreover, a significant advantage of this intervention is that it is computer-based and does not require a clinician, so it may one day be easy to disseminate broadly in a cost-effective and non-stigmatizing way. Targeting the factors that have been found to promote resilience may help vulnerable people decrease the distress and impairment associated with a panic attack, and ultimately reduce the likelihood of developing a full-blown disorder.

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Table 1. Sample Demographics by Training Condition.

Variable	CBM-I Condition	Sham Condition
Age Mean (SD)	19.31 (1.07)	19.30 (1.26)
Gender (% Female)	86.2%	85.7%
Race		
% Caucasian	55.2%	52.4%
% Asian	37.9%	19.0%
% African American	6.9%	14.3%
% Biracial	0.0%	4.8%
% No Answer	0.0%	9.5%
Ethnicity		
% Hispanic	0.0%	0.0%

Table 2. Descriptive Statistics for the Sample Characterizing and Pre-to-Post Training Dependent Variables.

Variable	CBM-I Condition *M (SD)*			Sham Condition *M (SD)*		
	Pre	Post	Follow-Up	Pre	Post	Follow-Up
Resilience-Congruent Recognition Ratings	40.90 (6.85)	48.76 (5.23)		39.76 (6.19)	42.81 (5.85)	
Resilience-Incongruent Recognition Ratings	31.10 (8.25)	25.86 (7.70)		32.86 (5.56)	31.05 (6.92)	
Physical Interpretations (BBSIQ-Phys)	2.53 (1.45)	1.70 (1.07)	1.81 (1.07)	2.39 (1.29)	2.03 (1.19)	2.36 (1.33)
Anxiety Sensitivity (ASI)	35.86 (5.01)	27.65 (9.13)	26.48 (9.01)	37.33 (5.99)	32.20 (9.04)	31.61 (7.55)
Panic Disorder Symptoms (PDSS)	1.12 (0.59)			0.98 (0.26)		
Trait Resilience (CD-RISC)	71.34 (13.52)			62.33 (13.67)		

Note. BBSIQ-Phys = the physical sensation subscale of the Brief Body Sensations Interpretation Questionnaire, ASI = Anxiety Sensitivity Index, PDSS = Panic Disorder Severity Scale, CD-RISC = Connor-Davidson Resilience Scale.

Table. 3. Correlations between Post-Training Anxiety Measures and Measures of the CO2 Breathing Challenge

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12,	13.	14.	15.	16.
1. ASI PT	--															
2. Resilience-Congruent Interpretations PT	-.45**	--														
3. Resilience-Incongruent Interpretations PT	.34*	-.29*	--													
4. Panic-Relevant Interpretations PT	.60**	-.34**	.34**	--												
5. SUDS Pre-CO_2	.43**	-.42**	.26*	.42**	--											
6. SUDS CO_2 Breathing	.39**	-.36**	.23	.39**	.84**	--										
7. SUDS CO_2 Recovery	.44**	-.31*	.32*	.43**	.83**	.82**	--									
8. DSQ Sum Pre-CO_2	.16	-.29*	.14	.18	.39**	.20	.32*	--								
9. DSQ Sum Avg CO_2 Breathing	.31*	-.33*	.18	.27*	.27*	.39**	.28*	.18	--							
10. DSQ Sum Avg Recovery	-.20	.04	-.16	-.12	.02	.07	.02	.14	.52**	--						
11. DSQ Cognitive Pre-CO_2	.16	-.15	.08	.20	-.04	-.04	-.07	.44**	.07	.08	--					
12. DSQ Cognitive Avg CO_2 Breathing	.27*	-.20	.17	.08	.16	.25*	.12	-.08	.62**	.37**	.08	--				
13. DSQ Cognitive Avg Recovery	-.19	-.15	-.05	-.21	-.00	.13	.03	-.24	.40**	.80**	-.08	.53**	--			
14. DSQ Physical Pre-CO_2	.15	-.29*	.14	.16	.42**	.22	.35**	.99**	.18	.13	.31*	-.10	-.24	--		
15. DSQ Physical Avg CO_2 Breathing	.28*	-.32*	.16	.29*	.26*	.38**	.29*	.22	.98**	.50**	.05	.45**	.32*	.23	--	
16. DSQ Physical Avg Recovery	-.20	.05	-.12	-.10	.02	.06	.02	.21	.52**	.99**	.11	.32*	.72**	.20	.51**	--

Note. * = < .05, ** < .01, PT = post-training, SUDS = Subjective Units of Distress Scale, Resilience Congruent Interpretations = resilience congruent Recognition Ratings, Resilience Incongruent Interpretations = resilience incongruent Recognition Ratings, Panic Relevant Interpretations = Brief Body Sensations Interpretation Questionnaire – Physical Subscale, DSQ =

Diagnostic Symptom Questionnaire and Physical refers to the physical intensity item and cognitive refers to the cognitive intensity item. For the DSQ measurements during the CO_2 breathing and recovery period, the average across the two scores was used. For the SUDS variable, the average rating across measurements was used for the Pre-CO_2, CO_2 breathing and Recovery periods.

Table 4. Results for Mixed Effect Linear Regression Models for Dependent Variables of the CO_2 Breathing Challenge.

	Estimate (β)	Standard Error	df	t	p
SUDS					
Intercept	36.11	15.96	45	2.26	.029*
ME Condition	1.50	6.00	46	0.25	.803
ME Time	-28.82	21.51	42	-1.34	.187
ME Time^2	-195.44	13.36	447	-14.63	.000***
Interaction: Condition x Time	-17.21	33.56	42	-0.51	.611
Interaction: Condition x Time^2	43.08	20.85	445	2.07	.039*
DSQ-SUM					
Intercept	3.77	1.19	53	3.16	.002**
ME Condition	0.06	0.58	51	0.11	.912
ME Time	9.82	4.32	43	2.27	.028*
ME Time^2	-12.49	2.80	183	-4.46	.000
Interaction: Condition x Time	-6.41	6.80	44	-0.94	.350
Interaction: Condition x Time^2	-6.43	4.37	186	-1.47	.142
DSQ-Physical					
Intercept	4.54	0.87	52	5.21	.000***
ME Condition	0.54	0.35	51	1.53	.133
ME Time	1.61	2.39	44	0.67	.505
ME Time^2	-12.71	1.96	185	-6.48	.000***
Interaction: Condition x Time	-1.63	3.77	44	-0.43	.667
Interaction: Condition x Time^2	-2.28	3.08	187	-0.74	.460
DSQ-Cognitive					
Intercept	3.61	0.94	52	3.84	.000***
ME Condition	0.79	0.39	50	2.04	.047*
ME Time	1.13	3.03	44	0.37	.710
ME Time^2	-6.14	1.95	185	-3.15	.001**
Interaction: Condition x Time	0.93	4.71	45	0.20	.844
Interaction: Condition x Time^2	-3.50	3.04	186	-1.15	.251

Figure 1. CONSORT Flow Diagram

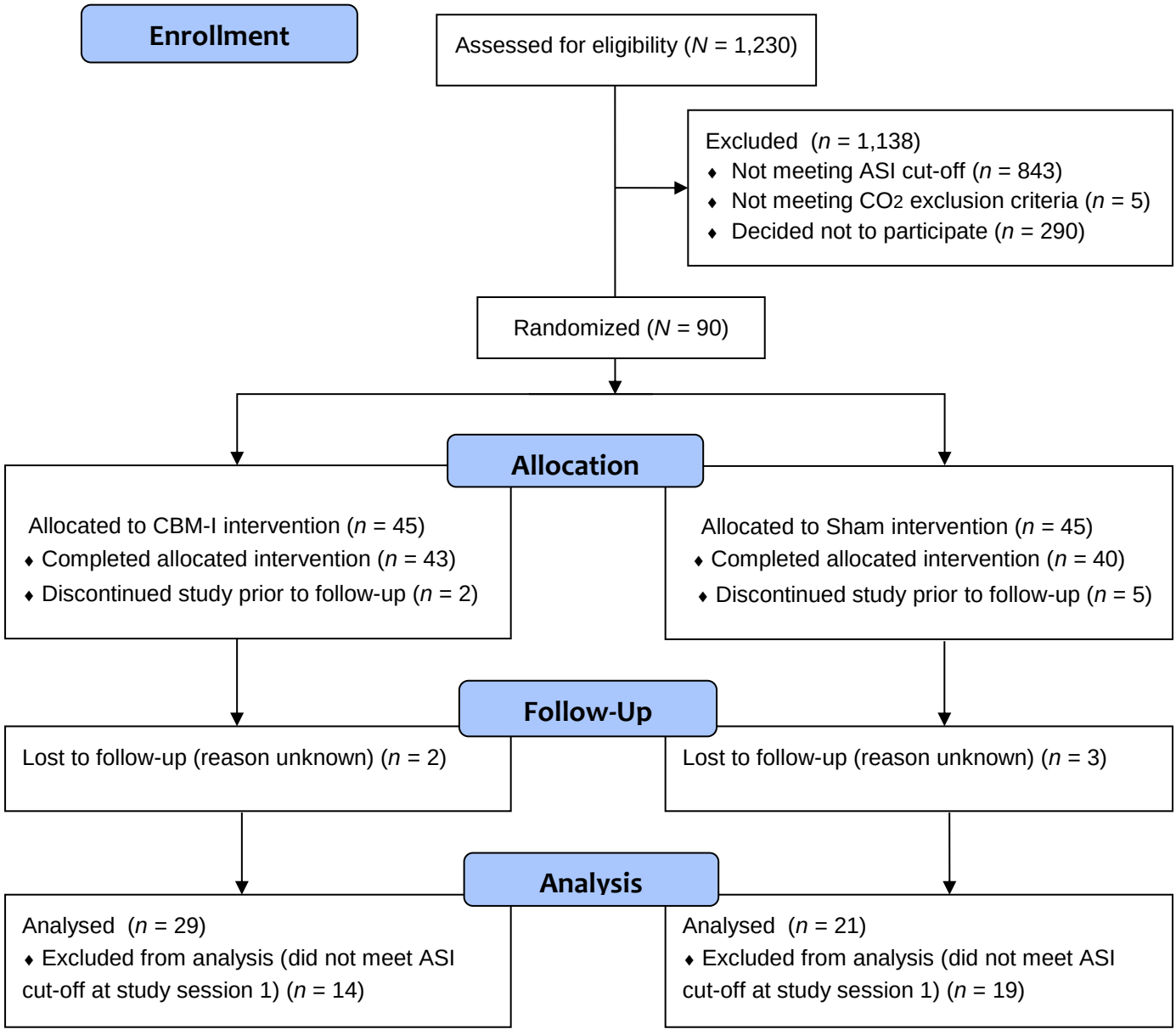


Figure 2. CO_2 Breathing Challenge Procedure.

Pre-Training Baseline		Pre-CO_2 Room Air Phase (Mask On)				CO_2 Breathing Phase (Mask On)								Post-CO_2 Room Air Recovery Phase (Mask On)								Immediate Post-CO_2 Challenge (Mask Off)
	Minute:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
S D			S D		S		S D		S		S D		S		S D		S		S D		S	S D-E

Note. S = SUDS, D = DSQ-Abbreviated, D-E = DSQ-Expanded.

Figure 3. Study Procedure.

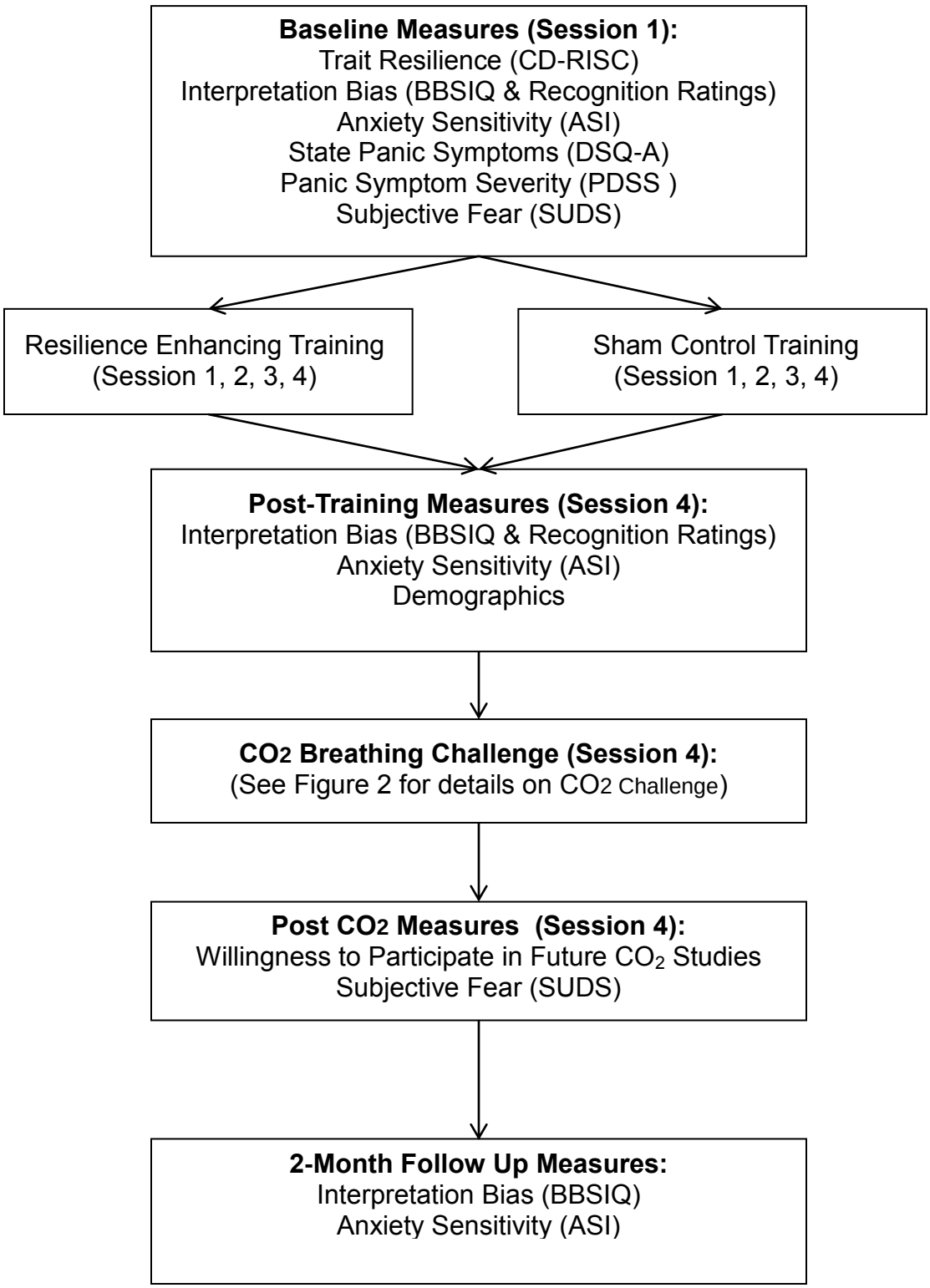


Figure 4a. Resilience-Congruent Recognition Ratings from Pre- to Post-Training.

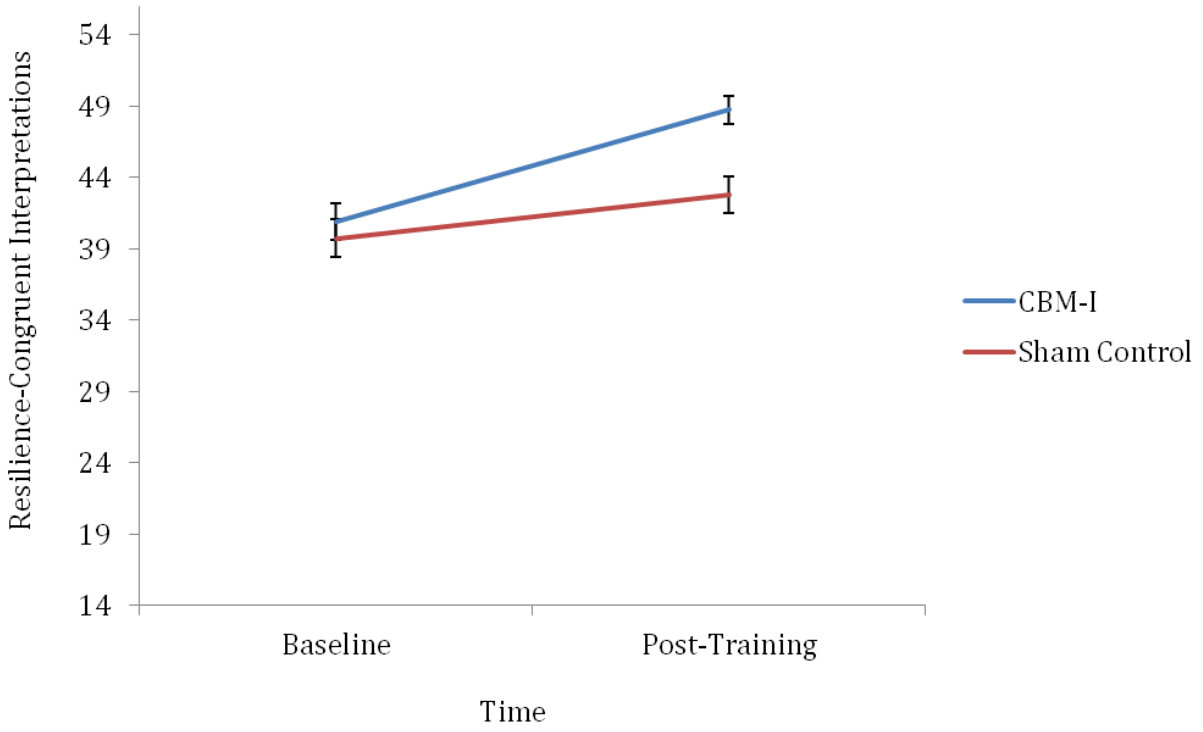


Figure 4b. Resilience-Incongruent Recognition Ratings from Pre- to Post-Training.

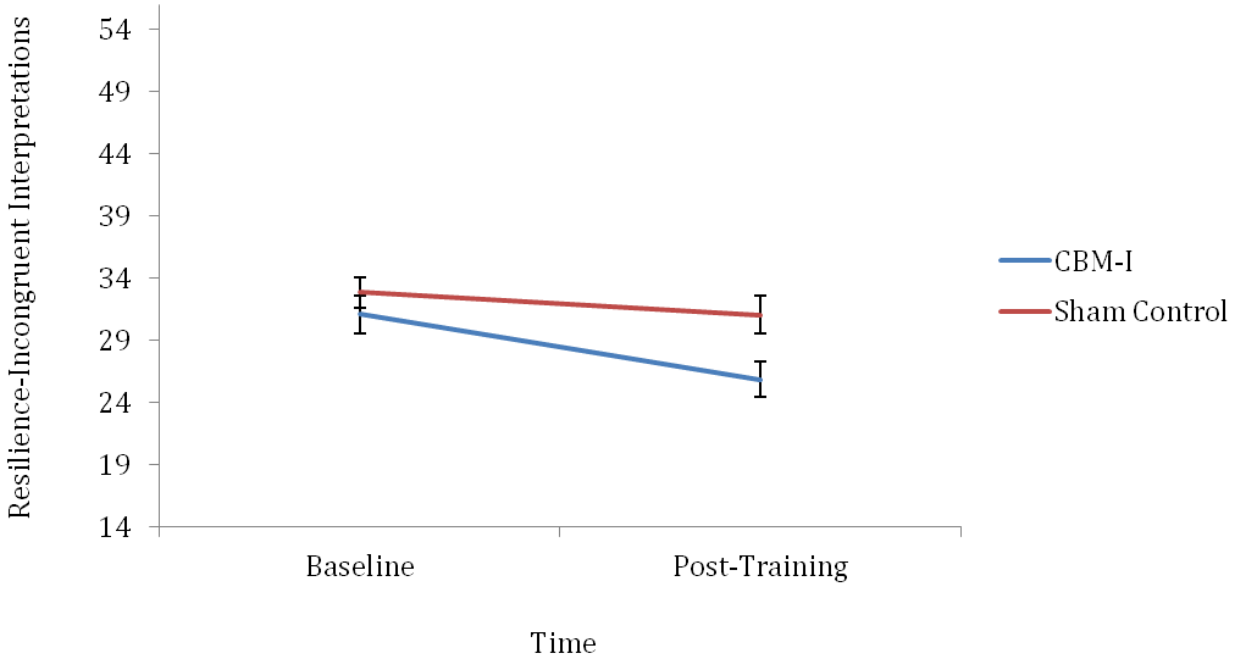


Figure 5. Anxiety Sensitivity from Pre-Training to Follow-Up.

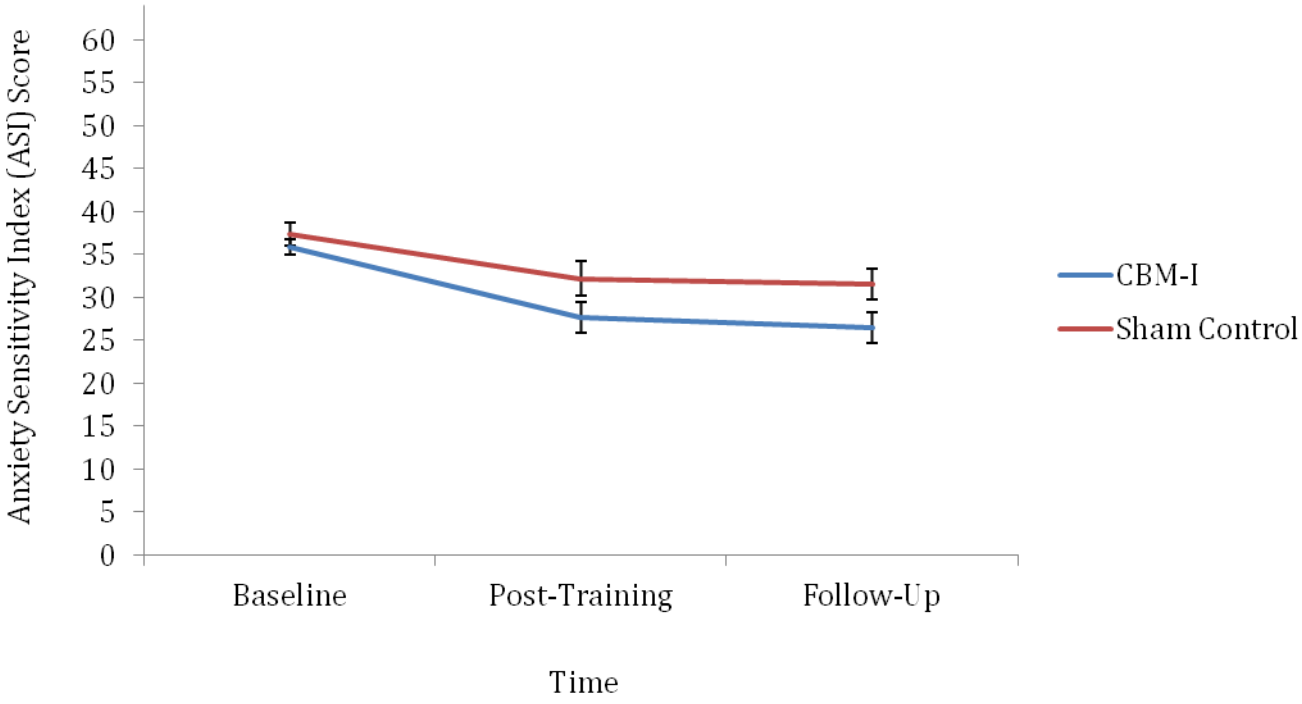
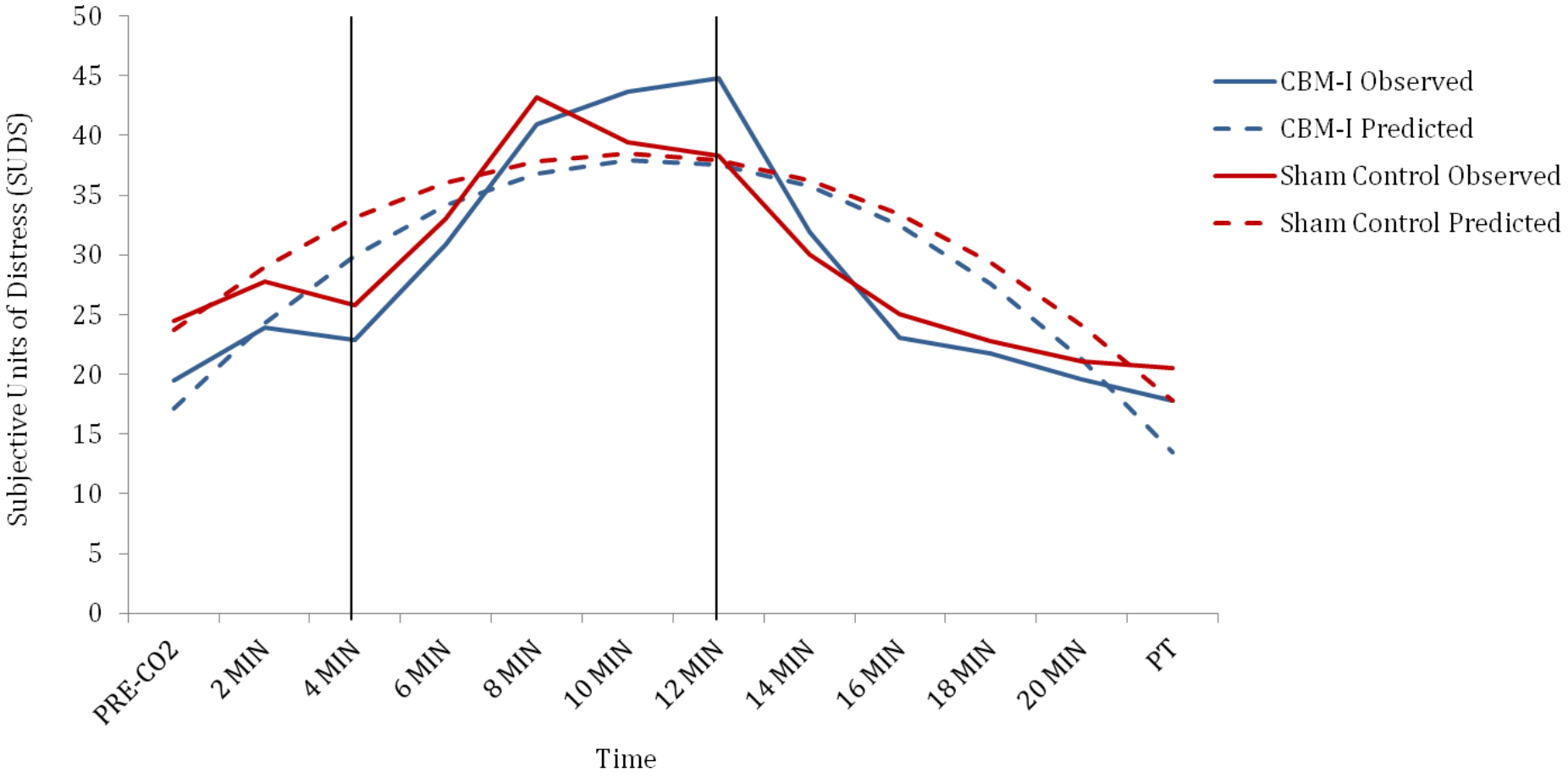


Figure 6. Observed and Predicted Values for Subjective Anxiety Across the CO_2 Challenge.



Note. Pre-CO2 is a baseline measurement before the start of the task, and PT indicates a final measurement after the task when the breathing mask has been removed. The vertical black line at the 5-minute mark indicates the initiation of the CO2 breathing phase, and the vertical black line at the 13-minute mark indicates the termination of the CO2 breathing phase.

Figure 7a. Intensity of Cognitive Symptoms of Panic Across the CO_2 Challenge.

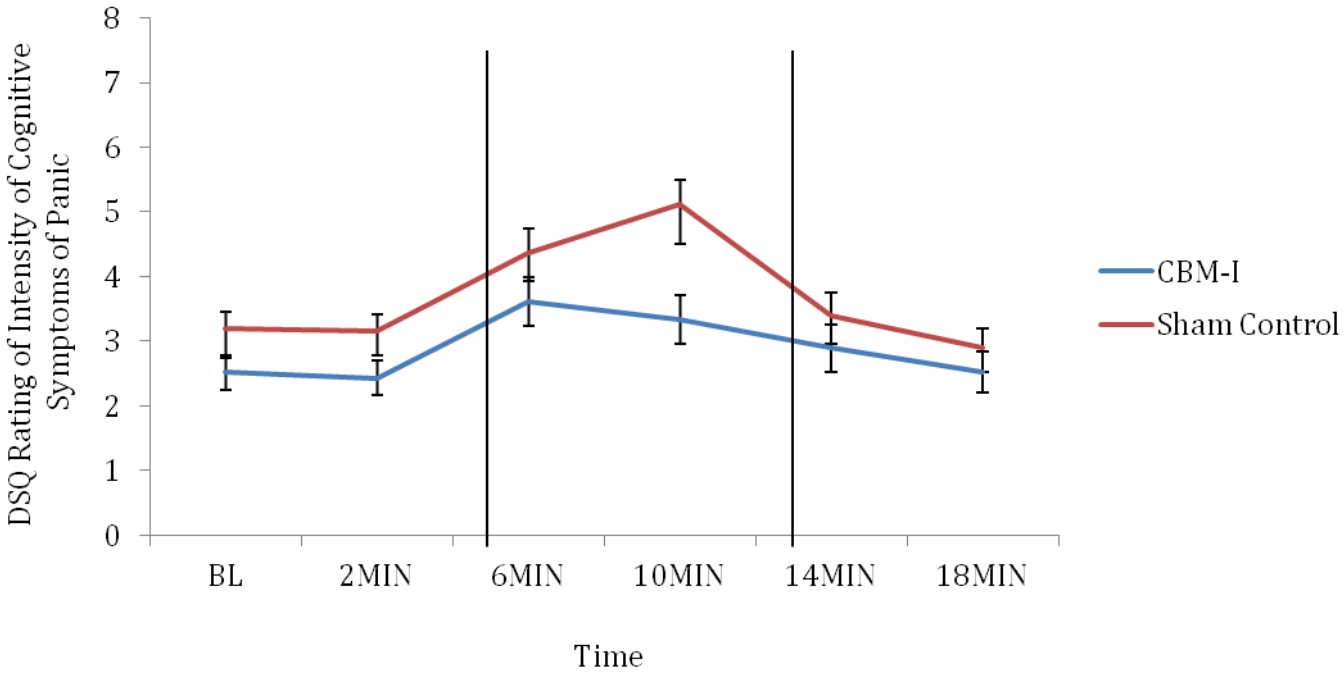
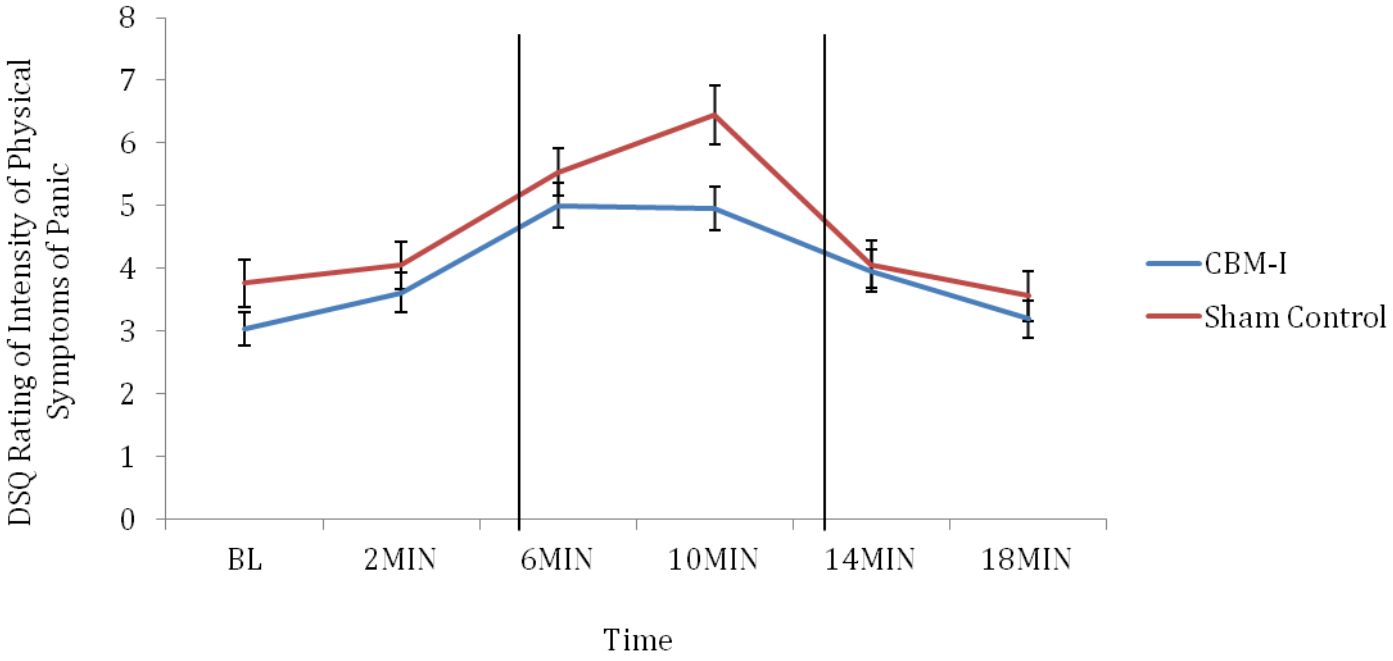


Figure 7b. Intensity of Physical Symptoms of Panic Across the CO_2 Challenge.



Note. DSQ = Diagnostic Symptom Questionnaire, BL = Baseline. The vertical black line at the 5-minute mark indicates the initiation of the CO2 breathing phase, and the vertical black line at the 13-minute mark indicates the termination of the CO2 breathing phase.

Appendix A

Across multiple studies, the ASI has shown consistently adequate test-retest reliability, even for measurements administered years apart (e.g., Maller & Reiss, 1992; Reiss, Peterson, Gurskey, & McNally, 1986; Rodriguez, Bruce, Pagano, Spencer, & Keller, 2004). However, in the current study, the two administrations of the ASI, separated by no more than three months, approximately 40% of the recruited study sample no longer met the cutoff criteria (≥ 28) at the first session of the study. Due to the theoretical importance of high anxiety sensitivity on the intended effect of both the intervention and the panic stressor, we decided to reduce the study sample to include only those who continued to meet the cutoff criterion across both measurements. Before making this decision, other options were considered in an effort to better understand and preserve more of the sample.

First, we examined the relative reliability as a standard measure of test-retest reliability across the repeated measurements. The intraclass correlation (ICC) was .25, which indicates poor test-retest reliability (an ICC of .75 or above is typically interpreted as adequate reliability; Portney & Watkins, 2000). As a result, we examined this further by also calculating the absolute reliability, which provides the estimated amount by which a repeated measurement would be expected to vary based on normal within-participant variability and measurement error (see Chuang, Wu, & Hsieh, 2014). Measures of absolute reliability include the standard error of measurement (SEM) and the smallest real difference (SRD). The SEM, which is the smallest difference across the two measurements that would still indicate true change, was 6.62. The SRD, or the amount of change necessary to exceed expected measurement error to indicate true change at a 90% confidence

interval, was 6.08. The mean difference between the two measurements was 7.03 (Pre-selection: M = 37.77, SD = 6.40; Session 1: M = 30.74, SD = 8.90). Since the actual mean difference is greater than both the SEM and the SRD, the absolute reliability is poor and the change across time reflects true change (see Beckerman et al., 2001; Chuang et al., 2014).

Second, in order to address the drastic reduction in scores across the two measurement points for some people, we considered extending the extent of permissible change across measurement points (conceptually related to the relative reliability examination) using a threshold value indicating the maximum change between the scores that would be acceptable for inclusion in the analyses. The modal shift was a decrease of nine points (roughly 12% of the sample showed this particular reduction), and the cumulative percentage of the sample that decreased nine points or less (including those who showed an increase from pre-test to Session 1) was 66.7% (N = 54). As a result, we considered removing the 27 individuals who decreased by 10 or more points, but ultimately decided against this approach because it eliminated five individuals who decreased by at least that much but remained above the cutoff at the second administration (i.e., it cut individuals who were still high in anxiety sensitivity), and included nine individuals who decreased by less than 10 points but remained below the cutoff at the second administration.

Third, a scatterplot of the Session 1 ASI scores was examined for score distribution with the purpose of identifying whether there was a clearly identifiable group with high anxiety sensitivity that encompassed a portion of individuals below the identified cutoff. On the contrary, the scores followed a fairly normal distribution (a negative skew would have

been expected and ideal), thus precluding us from adjusting our cutoff in a way that would not be arbitrary.

A final approach considered was to include the full sample and run the analyses with the Session 1 ASI as a covariate in order to control for the variability in responding at the start of the study. Ultimately, we chose not to adopt this method due to the low reliability of the first two administrations of the ASI—we decided that including only a sample that was consistently high in ASI would provide the best opportunity of examining a truly and reliably high anxiety sensitive sample, despite the resulting reduction in power. While the test-retest reliability was not greatly increased in this pared down sample (ICC = .31), this was determined to be the best option, and this study should be replicated with larger sample that is reliably high in anxiety sensitivity. Notwithstanding, we include a brief summary of the analyses rerun with the full sample for the interested reader.

Appendix B

Connor-Davidson Resilience Scale 25 (CD-RISC-25)

initials ☐☐☐ *ID#* ☐☐☐☐☐☐☐ *date* ☐☐/☐☐/☐☐☐☐ *visit* ☐☐ *age* ☐☐

*For each item, please mark an "x" in the box below that best indicates how much you agree with the following statements as they apply to you over the last **month**. If a particular situation has not occurred recently, answer according to how you think you would have felt.*

		not true at all (0)	rarely true (1)	sometimes true (2)	often true (3)	true nearly all the time (4)
1.	I am able to adapt when changes occur.	☐	☐	☐	☐	☐
2.	I have at least one close and secure relationship that helps me when I am stressed.	☐	☐	☐	☐	☐
3.	When there are no clear solutions to my problems, sometimes fate or God can help.	☐	☐	☐	☐	☐
4.	I can deal with whatever comes my way.	☐	☐	☐	☐	☐
5.	Past successes give me confidence in dealing with new challenges and difficulties.	☐	☐	☐	☐	☐
6.	I try to see the humorous side of things when I am faced with problems.	☐	☐	☐	☐	☐
7.	Having to cope with stress can make me stronger.	☐	☐	☐	☐	☐
8.	I tend to bounce back after illness, injury, or other hardships.	☐	☐	☐	☐	☐
9.	Good or bad, I believe that most things happen for a reason.	☐	☐	☐	☐	☐
10.	I give my best effort no matter what the outcome may be.	☐	☐	☐	☐	☐
11.	I believe I can achieve my goals, even if there are obstacles.	☐	☐	☐	☐	☐
12.	Even when things look hopeless, I don't give up.	☐	☐	☐	☐	☐
13.	During times of stress/crisis, I know where to turn for help.	☐	☐	☐	☐	☐
14.	Under pressure, I stay focused and think clearly.	☐	☐	☐	☐	☐
15.	I prefer to take the lead in solving problems rather than letting others make all the decisions.	☐	☐	☐	☐	☐
16.	I am not easily discouraged by failure.	☐	☐	☐	☐	☐
17.	I think of myself as a strong person when dealing with life's challenges and difficulties.	☐	☐	☐	☐	☐
18.	I can make unpopular or difficult decisions that affect other people, if it is necessary.	☐	☐	☐	☐	☐
19.	I am able to handle unpleasant or painful feelings like sadness, fear, and anger.	☐	☐	☐	☐	☐
20.	In dealing with life's problems, sometimes you have to act on a hunch without knowing why.	☐	☐	☐	☐	☐
21.	I have a strong sense of purpose in life.	☐	☐	☐	☐	☐
22.	I feel in control of my life.	☐	☐	☐	☐	☐
23.	I like challenges.	☐	☐	☐	☐	☐
24.	I work to attain my goals no matter what roadblocks I encounter along the way.	☐	☐	☐	☐	☐
25.	I take pride in my achievements.	☐	☐	☐	☐	☐

09-2011

Anxiety Sensitivity Index

Circle the one phrase that best represents the extent to which you agree with the item. If any of the items concern something that is not part of your experience (e.g. “It scares me when I feel shaky” for someone who has never trembled or had the “shakes”) answer on the basis of how you think you might feel *if you had* such an experience.

1. It is important to me not to appear nervous.
Very Little A Little Some Much Very Much

2. When I cannot keep my mind on a task, I worry that I might be going crazy.
Very Little A Little Some Much Very Much

3. It scares me when I feel “shaky” (trembling).
Very Little A Little Some Much Very Much

4. It scares me when I feel faint.
Very Little A Little Some Much Very Much

5. It is important to me to stay in control of my emotions.
Very Little A Little Some Much Very Much

6. It scares me when my heart beats rapidly.
Very Little A Little Some Much Very Much

7. It embarrasses me when my stomach growls.
Very Little A Little Some Much Very Much

8. It scares me when I am nauseous.
Very Little A Little Some Much Very Much

9. When I notice that my heart is beating rapidly, I worry that I might have had a heart attack.
Very Little A Little Some Much Very Much

10. It scares me when I become short of breath.
Very Little A Little Some Much Very Much

11. When my stomach is upset, I worry that I might be seriously ill.
Very Little A Little Some Much Very Much

12. It scares me when I am unable to keep my mind on a task.
Very Little A Little Some Much Very Much

13. Other people notice when I feel shaky.
Very Little A Little Some Much Very Much

14. Unusual body sensations scare me.
Very Little A Little Some Much Very Much

15. When I am nervous, I worry that I might be mentally ill.
Very Little A Little Some Much Very Much

16. It scares me when I am nervous.
Very Little A Little Some Much Very Much

Panic Disorder Severity Scale (PDSS)

Questions about Panic Attacks

A panic attack is a sudden rush of intense fear or discomfort that is accompanied by at least four of the following physical symptoms: pounding heart or accelerated heart rate, sweating, trembling or shaking, shortness of breath, choking feeling, chest pain, nausea or stomach difficulties, feeling dizzy, unsteady, lightheaded, or faint, feeling that things are unreal around you or a feeling that you are separated from yourself, fear of losing control or going crazy, fear of dying, numbness or tingling sensations, chills or hot flashes.

The intense fear and physical symptoms that come with a panic attack develop very suddenly and typically reach their most severe point within approximately 10 minutes after the start of the panic attack. While it is common to feel nervousness or worry before or after an attack, panic attacks are different from general feelings of anxiety because of their sudden onset and the intense fear and physical symptoms that accompany the attack.

Have you ever had a panic attack? **Yes / No**

If no, please hand this form to the experimenter. You do not need to fill out the rest of this form**. If yes,** please circle the appropriate response to the questions below:

1. How frequently do you have panic attacks?

0 – None.
1 – Mild (Panic-like sensations or limited symptom attacks or less than one full panic attack a week).
2 – Moderate (one or more full panic attacks a week).
3 – Severe (daily attacks reported or several a week).
4 – Extreme (attacks occur more than once a day).

2. How much distress do you experience during panic attacks?

0 – None.
1 – Mild, infrequent and not too intense.
2 – Moderate, regular and intense, but still manageable.
3 – Severe, very frequent and very intense.
4 – Extreme distress with all attacks.

3. How much anxiety do you feel in anticipation of future panic attacks?

0 – None.
1 – Mild, occasional worry about when next panic attack will occur.
2 – Moderate, frequent worry about next attack.
3 – Severe, preoccupied with very disturbing worry about next attack.
4 – Extreme, near constant and disabling worry.

4. To what extent do you avoid particular situations because you fear having a panic attack in that situation?

0 – None.
1 – Definite fear or discomfort and desire to avoid at lease one situation, but will confront or endure situation under most circumstances.
2 – Definite fear or discomfort and desire to avoid up to three situations, and will regularly avoid at least one of the situations.
3 – Definite fear or discomfort and desire to avoid more than three situations, and will regularly avoid two or more situations but many confront if accompanied by a trusted companion.
4 – Definite fear and avoidance of several situations, and there are definite and major modifications in lifestyle because of avoidance.

5. To what extent do you avoid particular sensations because you fear having a panic attack?

0 – None.
1—Definite discomfort with one or more physical sensations, but will endure sensations under most circumstances.
2 – Definite discomfort with and desire to avoid fully experiencing one or more physical sensations, and have reduced certain activities to limit sensations.
3 – Definite discomfort with and desire to avoid experiencing one or more physical sensations, and consistently avoids at least one activity to prevent experiencing sensations.

4—Definite discomfort with and desire to avoid experiencing one or more physical sensations, and consistently avoids more than one activity to prevent experiencing sensations.

6. To what extent do panic attacks impair or interfere in work functioning?

0 – None.
1 – Mild, slight interference with occupational activities, but overall performance is not impaired.
2 – Moderate, definite interference with occupational performance but still manageable.
3 – Severe, causes substantial impairment in work performance.
4 – Extreme, incapacitating.

7. To what extent do panic attacks impair or interfere in social functioning?

0 – None.
1 – Mild, slight interference with social activities, but overall performance is not impaired.
2 – Moderate, definite interference with social performance but still manageable.
3 – Severe, causes substantial impairment in social performance.
4 – Extreme, incapacitating.

Diagnostic Symptom Questionnaire - Expanded (DSQ-Expanded)

Below is a list of symptoms which various people sometimes notice during a gas inhalation. These experiences are very individual; some people notice almost all the symptoms, others notice hardly any. For each symptom listed below indicate if you are experiencing it now by circling “yes” or “no”.

Physical Feelings:

1. Numbness or tingling in face or extremities yes/no
2. Trembling or shaking yes/no
3. Dizziness, lightheadedness, or unsteadiness yes/no
4. Pounding or racing heart yes/no
5. Breathlessness or smothering sensation yes/no
6. Faintness yes/no
7. Chest tightness or pain yes/no
8. Choking yes/no
9. Sweating yes/no
10. Hot flushes or cold chills yes/no
11. Feeling unreal or in a dream yes/no
12. Nausea or abdominal distress yes/no

Fearful Thoughts:

13. Fear of dying yes/no
14. Fear of going crazy yes/no
15. Fear of losing control yes/no

Please use the following scale to rate the current overall intensity of the physical feelings and fearful thoughts you endorsed above.

0 . . . 1	. . . 2	. . . 3 . . .	4 . . . . 5 . . .	6 . . .	7 . . . 8
Not at all noticed	slightly felt	moderately felt	strongly felt	very strongly felt	

16. What is the overall intensity of your current physical feelings? _____

17. What is the overall intensity of your current fearful thoughts? _____

18. Using the same scale, what is the overall intensity of your current sensation of panic or fear?

_____

When you first noticed the physical feelings (listed previously) during the task, did you have any of the following thoughts:

19. I feel relaxed	yes/no
20. I feel like I might be dying	yes/no
21. This is dangerous	yes/no
22. There is nothing to fear	yes/no
23. This is quite pleasant	yes/no
24. I feel like I might be having a heart attack	yes/no
25. I am going to faint or fall	yes/no
26. I need help	yes/no
27. I am safe here	yes/no
28. Something is wrong	yes/no

---

29. When you started to notice the physical feelings you listed previously, how much <u>control</u> did you believe you had over the feelings once you noticed them? (circle one number)

0 . . . 1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8

no control at all	a little control	moderate control	a lot of control	total control

---

30. How much <u>control</u> did you believe you had over AVOIDING the occurrence of a panic attack? (circle one number)

0 . . . 1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8

no control at all	a little control	moderate control	a lot of control	total control

---

Diagnostic Symptom Questionnaire - Abbreviated (DSQ-Abbreviated)

Below is a list of symptoms which various people sometimes notice during a gas inhalation. These experiences are very individual; some people notice almost all the symptoms, others notice hardly any. For each symptom listed below indicate if you are experiencing it now by circling “yes” or “no”.

Physical Feelings:

1. Numbness or tingling in face or extremities yes/no
2. Trembling or shaking yes/no
3. Dizziness, lightheadedness, or unsteadiness yes/no
4. Pounding or racing heart yes/no
5. Breathlessness or smothering sensation yes/no
6. Faintness yes/no
7. Chest tightness or pain yes/no
8. Choking yes/no
9. Sweating yes/no
10. Hot flushes or cold chills yes/no
11. Feeling unreal or in a dream yes/no
12. Nausea or abdominal distress yes/no

Fearful Thoughts:

13. Fear of dying yes/no
14. Fear of going crazy yes/no
15. Fear of losing control yes/no

Please use the following scale to rate the current overall intensity of the physical feelings and fearful thoughts you endorsed above.

0 . . . 1	. . . 2	. . . 3 . . .	4 . . . . 5 . . .	6 . . .	7 . . . 8
Not at all noticed	slightly felt	moderately felt	strongly felt		very strongly felt

16. What is the overall intensity of your current physical feelings? _____

17. What is the overall intensity of your current fearful thoughts? _____

Brief Body Sensations Interpretation Questionnaire

BBSIQ

Instructions for Part 1

Here are some outline descriptions of situations in which it is not quite clear what is happening. After each one, you will see three possible explanations for the situation. Please rate the extent to which you think each of the three explanations for a situation would be likely to be true if you found yourself in that situation.

Use the scale below for your ratings. Put a number between 0 and 8 next to each of the three explanations in the text. Please write your answer (from 0-8) on the line beside the word 'Rating' for each of the possible explanations.

0----------1----------2----------3----------4----------5----------6----------7----------8

Not at all likely	**A little**	**Moderately**	**Very**	**Extremely likely**

1. You have visitors over for dinner and they leave sooner than you expected. Why?

Rating_____	a)	They did not wish to outstay their welcome.
Rating_____	b)	They had another pressing engagement to go to.
Rating_____	c)	They did not enjoy the visit and were bored with your company.

2. You feel short of breath. Why?

Rating_____	a)	You are developing the flu.
Rating_____	b)	You are about to suffocate or stop breathing.
Rating_____	c)	You are physically "out of shape".

3. Your vision has become slightly blurred. Why?

Rating_____	a)	You have strained your eyes slightly.
Rating_____	b)	You need to get glasses or change your existing glasses.
Rating_____	c)	This is the sign of a serious illness.

4. You go into a shop and the assistant ignores you. Why?

Rating_____	a)	They are bored with their job, and this makes them rude.
Rating_____	b)	They are concentrating very hard on something else.
Rating_____	c)	They find you irritating and resent your presence.

5. You feel lightheaded and weak. Why?

Rating_____	a)	You are about to faint.
Rating_____	b)	You need to get something to eat.
Rating_____	c)	You didn't get enough sleep last night.

6. You smell smoke. What's burning?

Rating_____	a)	Your house is on fire.
Rating_____	b)	Some food is burning.
Rating_____	c)	Someone is smoking a cigarette.

7. A friend suggests that you change the way that you're doing a job in your own house. Why?

Rating_____	a)	They are trying to be helpful.
Rating_____	b)	They think you're incompetent.
Rating_____	c)	They have done the job more often and know an easier way.

8. Your chest feels uncomfortable and tight. Why?

Rating_____ a) You have indigestion
Rating_____ b) You have a sore muscle
Rating_____ c) Something is wrong with your heart

9. You wake with a jolt in the middle of the night, thinking you heard a noise, but all is quiet. What woke you up?

Rating_____ a) You were woken by a dream.
Rating_____ b) A burglar broke into your house.
Rating_____ c) A door or window rattled in the wind.

10. You are introduced to someone at a party who fails to reply to a question you ask. Why?

Rating_____ a) They did not hear the question.
Rating_____ b) They think you are uninteresting and boring.
Rating_____ c) They were preoccupied with something else at the time.

11. You notice that your heart is beating quickly and pounding. Why?

Rating_____ a) Because you have been physically active.
Rating_____ b) Because there is something wrong with your heart.
Rating_____ c) Because you are feeling excited.

12. You suddenly feel confused and are having difficulty thinking straight. Why?

Rating_____ a) You are going out of your mind.
Rating_____ b) You are coming down with a cold.
Rating_____ c) You've been working too hard and need a rest.

13. A letter marked "URGENT" arrives. What is in the letter?

Rating_____ a) It is junk mail designed to attract your attention.
Rating_____ b) You forgot to pay a bill.
Rating_____ c) News that someone you know has died or is seriously ill.

14. You notice that your heart is pounding, you feel breathless, dizzy and unreal. Why?

Rating_____ a) You have been overdoing it and are overtired.
Rating_____ b) Something you ate disagreed with you.
Rating_____ c) You are dangerously ill or going mad.

Measure of Willingness to Participate in Future CO_2 Studies

We appreciate your participation in this study. We are looking for participants to participate in other psychology studies for payment and/or credit. Please indicate below whether or not you would allow us to contact you for participation in future studies.

Email ID:_____ Participant ID:_____

Please check <u>any</u> of the following options (check all that apply):

- I would be **<u>willing</u>** to be contacted for paid participation in future psychology studies. _____
- I would be **<u>willing</u>** to be contacted for paid participation in future psychology studies that use the CO_2 breathing challenge. _____
- I would be **<u>willing</u>** to be contacted for paid participation in future psychology studies, but **<u>not</u>** ones that include the CO_2 breathing challenge. _____
- I would prefer **<u>not</u>** to be contacted for participation in any future studies. _____

Resilience Enhancing Training: Ambiguous Scenario Examples

1.) A scenario targeting positive emotionality:

Scenario: You are climbing the stairs to your apartment with friends. When you get to the top, you feel winded. Although this feeling makes you anxious, you see that your friends are also out of breath and all of you lau_h at yourselves and relax. (Missing letter: g)

Comprehension question: Are you able to laugh although you feel anxious? (Answer: Yes)

2.) A scenario targeting self-efficacy/coping potential:

Scenario: You are swimming laps at the pool. After a couple of laps you feel out of breath and decide to stop for a minute. Although gasping for breath makes you feel anxious, you decide to keep swimming, knowing you can han_le your anxiety. (Missing Letter: d)

Comprehension question: Are you unable to keep swimming because you feel anxious? (Answer: No)

3.) A scenario targeting meaning assignment:

Scenario: You are strolling through the city with a friend. As you walk, you suddenly feel a sense of lightheadedness and nausea. This instantly triggers some worry, but you know that with each experience like this, you are improving yourself by becoming better at tol_rating your anxiety. (Missing letter: e)

Comprehension question: Is there any personal growth to come from your experience with anxiety? (Answer: Yes)

4.) A scenario targeting flexible responding:

Scenario: You have three exams on the same day. The night before, you wake up in the middle of the night sweating heavily and you have heart palpitations. You are about to jump out of bed, but then reconsider and lay back down to rest, doing some slow breathing to c_lm yourself before falling back to sleep. (Missing letter: a)

Comprehension question: Are you able to successfully address your anxiety? (Answer: Yes)

Control Condition: Neutral Scenario Examples

Scenario: You go to the grocery store. While you are there, you buy eggs, bread, and juice. You forget to purchase m_lk. (Missing letter: i)

Comprehension Question: Did you remember to buy milk? (Answer: No)

Scenario: You are watering your household plants. As you make your way around the house, you notice that one of your plants is wilting. You decide to move the plant into more direct sunli_ht. (Missing letter: g)

Comprehension Question: Are you watering your plants? (Answer: Yes)

Scenario: You are on a date. You are eating dinner at a new restaurant in town. You turn to your date and ask a questi_n. (Missing letter: o)

Comprehension Question: Are you eating at a restaurant? (Answer: Yes)

Scenario: You are taking a train to New York. On the ride, you strike up a conversation with the passenger sitting next to you. You exchange information and decide to keep in to_ch. (Missing letter: u)

Comprehension Question: Are you riding on an airplane? (Answer: No)

All Conditions: Recognition Ratings Examples

1.) A Recognition Ratings item targeting meaning assignment:

Title: **THE HIKE**

Scenario: You go on a three-hour hike with your family through the mountains of Virginia. The next day, you feel fatigued and weak when you wake up. You get up and sit on the edge of your _ed. (Missing letter: b)

Comprehension Question: Did you go on a hike with your classmates? (Answer: No)

Disambiguated Interpretations:

Positive Anxiety Sensitivity Resilience: As you think about feeling fatigued and weak, you feel good because you know that they are indicators that you are building muscle strength and endurance.

Negative Anxiety Sensitivity Resilience: As you think about these sensations, you feel scared because you know that they are indicators that something may be wrong with your body.

Positive Foil: As you think about these sensations, you recall all the laughs you had with your family on the hike yesterday.

Negative Foil: As you think about these sensations, you recall something important that you forgot to do yesterday.

2.) A Recognition Ratings item targeting positive emotionality:

Title: **THE DANCE CLUB**

Scenario: You are at a dance club on the weekend with friends. The noise and dancing has made you feel excited, and your heart is racing fast. The next song is one that you k_ow. (Missing letter: n)

Comprehension Question: Are you at a concert? (Answer: No)

Disambiguated Interpretations:

Positive Anxiety Sensitivity Resilience: Your heart racing makes you nervous, but you smile when you realize that you haven't had this much fun in a long time.

Negative Anxiety Sensitivity Resilience: Your heart racing makes you nervous, and you can't focus on anything other than how worried you are.

Positive Foil: Your heart racing makes you nervous, and then you see a friend you really like who you haven't seen in a while.

Negative Foil: Your heart racing makes you nervous, and then you see somebody that you don't like.

Participant Screener

To determine your eligibility for this study, please indicate whether you have (or have had) any of the following:

- Current asthma for which you are receiving medication (e.g. via an inhaler).
- One or more past seizures without a clear and resolved etiology.
- Current or past episodes of psychosis.
- Have taken any of the following psychiatric medications:
    - Initiated an antidepressant medication (e.g. an SSRI like Prozac, Lexapro, etc.) within the past 4 weeks (use longer than four consecutive weeks is acceptable).
    - Have taken (or will need to take) benzodiazepine medication (e.g. Xanax, Valium, etc.) within 48 hours prior to study participation.
    - Are currently taking a non-psychiatric medication with psychiatric effects (e.g., beta-adrenergic blockers).
- Serious, unstable illnesses including type I and II diabetes mellitus, hepatic, renal, gastroenterologic, respiratory, cardiovascular, endocrinologic, neurologic, immunologic, or hematologic disease.
- Current or suspected pregnancy.

If one or more of the above items apply to you, please check here: ____

If none of the above items apply to you, please check here: ____

Consent Form

Consent of an Adult to Be in a Research Study

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Participant's Name_____ Subject ID # _____

Principal Investigator: Bethany Teachman, Ph.D.
University of Virginia
Department of Psychology
102 Gilmer Hall, PO Box 400400
(434) 924-0676

Sponsor: National Institute on Aging (National Institutes of Health)

What is the purpose of this form?

This form will help you decide if you want to be in the research study. You need to be informed about the study, before you can decide if you want to be in it. You do not have to be in the study if you do not want to. You should have all your questions answered before you give your permission or consent to be in the study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will get a copy of this signed form.

Who is funding this study?

This study is being funded by the National Institute on Aging, a division of the U.S. National Institutes of Health (NIH).

Why is this research being done?

The purpose of the study is to examine the ability of a computer-based intervention to change thinking patterns that affect anxiety. You will be assigned to either an active intervention condition or to a "control" condition (a condition that is similar in some ways to the active intervention condition, but which we do not expect to be as effective). You can find out at the end of the study which condition you were in, and if you were in the control condition and wish to receive the active intervention condition, we would be happy to provide you with that program. (There is no charge and no additional compensation for participating in this additional program after the study is complete.)

You are being asked to participate in this study because you are a healthy volunteer between 18 and 64 years of age, and because your responses on a questionnaire you completed as part of the pre-selection survey qualify you to participate in this study.

We will recruit 115 participants to be in this study at UVA.

Note: All the procedures are being done strictly for research purposes only. You will not receive any direct benefit from the study procedures, though you will receive information about how to obtain mental health services if you desire them.

How long will this study take?

Your participation in this study will require 4 study visits, totaling four hours (Visits 1 will be 1 ½ hours, Visits 2 and 3 will each be 30 minutes, and Visit 4 will be 2 hours). These visits will occur approximately 3-5 days apart, totaling approximately 9-15 days. You will also be asked to take a brief survey that will take approximately 10 minutes over the internet approximately 2 months after your final visit.

What will happen if you are in the study?

SCREENING and STUDY PROCEDURES

If you agree to participate, you will sign this consent form before any study related procedures take place. All visits will take place in Gilmer Hall in either room 208 or in the 024 suite, and the follow-up assessment will be completed from your personal computer.

Visit 1 (Day 1-will last about 1 ½ hours):

During the first visit, you will be asked to complete a series of questionnaires that ask about various aspects of your past and current thoughts, feelings, and behaviors. These questionnaires will take about 45 minutes to complete.

You will then engage in a computer task that will require you to read and imagine yourself in a series of scenarios and then complete word fragments (by filling in missing letters) within each scenario. This will take about 30 minutes to complete.

Visit 2 and 3 (Day 2 and 3 will last about 30 minutes, and will take place in 3-5 day intervals): During your second and third visit, you will again engage in the same computer task.

Visit 4 (Day 4 will last about 2 hours, and will take place 3-5 days after Visit 3):
At the fourth study visit, you will complete a brief screening form. If the screening form confirms that you are eligible for this part of the study, you will continue with the study procedures for Visit 4. Your eligibility or ineligibility based on the screening form will not jeopardize your receipt of payment for participating in this study.

During your fourth visit, after engaging in the computer task for the final time, you will again complete questionnaires that ask about your thoughts, feelings, and behaviors.

You will then be asked to complete a breathing task that requires you to wear an air mask while breathing regular room air for a period of time, then breathing room air containing a small amount of carbon-dioxide (CO_2), followed by another brief period of regular room air. Before you begin the breathing task, the experimenter will provide you with more detailed information about how the task works and what you can expect from it. You will then be asked to sign a Consent Addendum if you are willing to participate in that portion of the study. If you do not wish to participate or you feel too uncomfortable at any point during the study, you may withdraw from that part of the study without penalty.

What are the risks of being in this study?

Although unlikely, some emotional distress may arise from completing of questionnaires that assess mood and anxiety symptoms.

In addition, there is minimal risk of harm to you other than possible temporary discomfort or distress (e.g., during the breathing task) as a result of participating in this experiment. You will receive more information about the breathing task and the possible risks associated with it during Visit 4.

Other unexpected risks:
You may have side effects that we do not expect or know to watch for now. Please let the study leader know if you have any problems.

Could you be helped by being in this study?

You will not benefit from being in this study. However, the information researchers get from this study may help others in the future. Additionally, the study may help us understand how people's thoughts, beliefs, and behaviors may be related to their experience of discomfort or distress in response to physical stressors, which may ultimately help us discover ways of relieving that discomfort or distress.

What are your other choices if you do not join this study?

The only choice is not to be in this study.

If you are a patient at UVa, your usual care will not be affected if you decide not to participate in this study.
If you are an employee of UVa, your job will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will receive $45 by check for finishing this study, as well as a $5 Amazon.com gift card for completing the follow-up internet survey (done 2 months after Visit 4). You should receive your payment about 2 weeks after your visit(s).

Additionally, participants will receive payment for each study visit attended ($20 for the 2 hour visit, $15 for the 1 ½ hour visit, and $5 for the 30 minute visits.)

Your check will be available to be picked up or sent out by mail up to 14 business days after finishing the study (Visit 4).

The income may be reported to the IRS as income.

Will being in this study cost you any money?

Being in this study will not cost you any money.

What if you are hurt in this study?

If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover. You do not give up any legal rights, such as seeking compensation for injury, by signing this form.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You will be debriefed if you withdraw from the study. There is no penalty for withdrawing. You will still receive full compensation for the number of study visits that you have attended at the time of withdrawal.

Even if you do not change your mind, the study leader can take you out of the study.

How will your personal information be shared?

The UVA researchers are asking for your permission to gather, use, and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you will still receive course payment for attending this study session and you can continue to participate in research at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, email address, gender, and ethnicity. In addition, we will collect legal name, address, and social security number only for participants who choose the monetary compensation option.

Who will see your private information?

- The researchers to make sure they observe the effects of the study and understand its results

- People or committees that oversee the study to make sure it is conducted correctly
- In the unlikely event that we learn of possible child or elderly abuse, or danger to self or others, we must inform a legal authority for safety purposes

The information collected from you might be published in a scientific journal. This would be done in a way that protects your privacy. No one will be able to find out from the journal article that you were in the study.

What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you retract it. To retract it, please send a letter to the researchers listed on this form. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation. UVA researchers will do everything possible to protect your privacy.

The information collected about you will be kept confidential by UVA as required by the federal Privacy Rule. Your information will not be released outside of UVA unless it is permitted by law.

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures
- Report an illness, injury, or other problem that you think may be related to your participation in the study
- Leave the study before it is finished
- Express a concern about the study

Bethany A. Teachman, Ph.D.
University of Virginia, Department of Psychology
102 Gilmer Hall, rm. 207 Charlottesville, VA 22903 Telephone: (434) 924-0676.

What if you have a concern about a study?

You may also report a concern about a study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483
Charlottesville, Virginia 22908 Telephone: 434-924-2620

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the

problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

Signatures

What does your signature mean?

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you understand the information given to you about the study and in this form. If you sign the form it means that you agree to join the study.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Consent From Impartial Witness

If this consent form is read to the subject because the subject is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The subject may place an X on the Participant Signature line above.

I agree the information in this informed consent form was presented orally in my presence to the subject and the subject had the opportunity to ask any questions he/she had about the study. I also agree that the subject freely gave their informed consent to participate in this trial.

_____	_____	_____
IMPARTIAL WITNESS (SIGNATURE)	IMPARTIAL WITNESS (PRINT)	DATE

Consent Addendum

Participant's Name _____Subject ID # _____

ADDENDUM TO CONSENT

Carbon Dioxide Challenge Task

This addendum to the consent form is to provide you with additional information regarding the study in which you are participating.

You will be asked to complete a breathing task that requires you to wear an air mask while breathing regular room air for a period of time, then breathing room air containing a small amount of carbon-dioxide (CO_2), followed by another brief period of regular room air. This is called the Carbon Dioxide Challenge Task.

Some people may find this breathing task anxiety-provoking or physically uncomfortable while others do not experience any discomfort. Though the breathing task may cause some temporary discomfort, it has no lasting harmful physical effects. If you feel too uncomfortable at any point during the study, you may withdraw without penalty. Also, you will be offered relaxation exercises should you experience any ongoing discomfort.

Throughout the breathing task, we will be monitoring your emotions, thoughts, as well as your heart rate, perspiration (sweat) level, breath volume, and breathing rate through non-invasive psychophysiological data collection procedures.

Carbon Dioxide Challenge Task Procedures:

- You will be breathing room air for some portion of time, and room air mixed with a small amount of carbon dioxide for some portion of time.
- You will breathe the room air for a total of 12 minutes and the carbon dioxide air for a total of 8 minutes.
- We cannot tell you when you will be breathing the room air versus the air enriched with carbon dioxide.
- Breathing carbon dioxide enriched air may cause you to feel a number of physical sensations, such as rapid heartbeat, dizziness, or chest pressure, and it may make you feel anxious.
- If you do feel anxious, the anxiety usually goes away within a few minutes.
- If the task causes you to feel anxious or uncomfortable and your anxiety does not go away within a few minutes after removing the face mask, please let the experimenter know.
- Also, if you feel uncomfortable and want to stop the breathing task, you can do so at any time without penalty.

Note: If you do not choose to participate in this phase of the study, you will still receive full course credit for your participation.

All other sections of the original consent form still apply. Please refer to it for any questions you might have.

Contact Names and Numbers

If you have any questions about this study, you should talk to Dr. Bethany Teachman at (434) 924-0676.

If you have any questions regarding research participants' rights, please contact the Chair of the Institutional Review Board for Health Sciences Research of the University of Virginia at (434) 924-2109 or the IRB-HSR staff at (434) 924-5152.

Conclusion

You will receive a signed copy of this form to keep.

I HAVE READ, OR HAD READ TO ME, THE ABOVE INFORMATION BEFORE SIGNING THIS ADDENDUM. I HAVE BEEN OFFERED AN OPPORTUNITY TO ASK QUESTIONS AND HAVE RECEIVED ANSWERS THAT FULLY SATISFY THOSE QUESTIONS.

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Debriefing Form

Debriefing

Thank you for participating in our study. The general purpose of this research is to understand the effectiveness of a training program designed to modify interpretation biases. Interpretation bias, or the propensity to interpret ambiguous stimuli in a threatening manner, has been found to be associated with panic disorder and the fear of anxiety sensations, as well as other anxiety disorders. The purpose of this training is to teach persons to interpret ambiguous situations in a way that promotes resilience in response to a panic symptoms or panic attacks. For example, a person with an interpretation bias may interpret the experience of having a racing heart as meaning that they are in danger of having a heart attack. After training, that same person is more likely to feel that symptoms of anxiety are manageable and not catastrophic, and may even find real-life stressors to be less anxiety-provoking. We are hoping to learn whether this training can help people recover more quickly in response to a panic stressor, which we conceptualize as enhanced resilience.

For this study, half of the participants received a resilience-enhancing training session, where all of the word fragment resolutions reinforced a resolution consistent with resilient thinking (e.g., believing that one will recover from a difficult event), and half of the participants received a sham training session, where the scenarios were not related to altering interpretations or enhancing resilience. We are interested to see whether this training leads to differences on various measures of interpretation bias, panic symptoms, and coping skills. We also are interested in examining whether training impacts reactivity and recovery in response to a carbon dioxide (CO_2) breathing challenge, which is a well-validated panic stressor. We hypothesize that those in the resilience-enhancing training condition will show less anxious reactivity (i.e., fear, panic symptoms, and physiological arousal) during the CO_2 breathing period, and quicker recovery during the post-CO_2 room-air breathing period.

The CO_2 breathing challenge task that you completed has been used extensively by researchers to study how people respond to the experience of heightened physical sensations, particularly those sensations related to anxiety and panic disorder. During this task, you breathed room air infused with a relatively small amount (7.5%) of CO_2 for 8 minutes, with 4 minutes of regular room air before and 8 minutes of regular room air after the CO_2 inhalation. The CO_2 challenge task you completed is completely safe and has no lasting harmful physical effects. However, some people do experience physical discomfort (such as racing heart, dizziness, etc.) while completing the 7.5% CO_2 challenge task, which is normal and generally wears off within several minutes of returning to normal room air breathing.

If you are interested in learning more about the training program or the use of the CO_2 challenge task to study anxiety and panic disorder see:

- Hallion, L. S., & Ruscio, A. M., (2011). A meta-analysis of the effect of cognitive bias modification on anxiety and depression. *Psychological Bulletin, 137*(6), 940-958.
- Rassovsky, Y., Kushner, M. G., Schwarze, N. J., & Wangensteen, O. D. (2000). Psychological and physiological predictors of response to carbon dioxide challenge in individuals with panic disorder. *Journal of Abnormal Psychology, 109*, 616-623.
- Steinman, S. A., & Teachman, B. A. (2010). Modifying interpretations among individuals high in anxiety sensitivity. *Journal of Anxiety Disorders, 24,* 71-78.

We invited people for participation in this study based on their responses on a prescreening questionnaire that examined anxiety sensitivity, or the fear of anxiety symptoms. The experimenter does not know your score for this questionnaire. High anxiety sensitivity is sometimes associated with panic disorder. This does <u>not</u> mean you have panic disorder or an anxiety disorder. However, if you feel especially concerned about your mood or anxiety symptoms, or about your anxiety levels in response to the breathing task, please feel free to phone Jessica Cruz at (434) 243-7646 about options for

counseling. Alternatively, you could also phone the **UVA Counseling and Psychological Services (434-243-5556) or the Mary D. Ainsworth Psychological Clinic in the Psychology Department (434-982-4737).**

Once again, thank you for participating in our study. If you have any further questions regarding any aspects of this research, please contact Dr. Bethany Teachman at (434) 924-0676 or Jessica Cruz at (434) 243-7646. In addition, if you have any concerns about any aspect of the experiment, you may contact Dr. Richard Stevenson, Chair, Institutional Review Board for Health Sciences Research, Suite 400, Morton Bldg., One Morton Dr., University of Virginia, P.O. Box 800392 Charlottesville, VA 22908. Telephone: (434) 924-0245 Email: rds8z@virginia.edu

Appendix C

Variable	High ASI Participants (Sample Used in Dissertation)	Full Sample	Full Sample with ASI as Covariate
Resilience-Congruent Recognition Ratings	Significant Condition by Time Interaction (CBM > Sham)	Significant Condition by Time Interaction (CBM > Sham)	Significant Condition by Time Interaction (CBM > Sham)
Resilience-Incongruent Recognition Ratings	NS Trend Condition by Time Interaction (CBM < Sham)	Significant Condition by Time Interaction (CBM < Sham)	Significant Condition by Time Interaction (CBM < Sham)
Panic-Relevant Interpretations (BBSIQ)	Non-Significant	NS Trend Condition by Time Interaction (CBM > Sham at Baseline)	NS Trend Condition by Time Interaction (CBM > Sham at Baseline)
Anxiety Sensitivity (ASI)	NS Trend Condition by Time Interaction (CBM < Sham at Follow-up)	Non-Significant	Non-Significant
CO_2 Challenge Subjective Anxiety (SUDS)	Significant Condition by Quadratic Time Interaction	Non-Significant	NS Trend Condition by Quadratic Time Interaction
CO_2 Challenge Panic Symptom Sum (DSQ-SUM)	Non-Significant	Model Unable to Converge	Model Unable to Converge
CO_2 Challenge Cognitive Panic Symptom Severity (DSQ-Cognitive)	Significant Main Effect (CBM < Sham)	Non-Significant	Non-Significant
CO_2 Challenge Physical Panic Symptom Severity (DSQ-Physical)	Non-Significant	Non-Significant	Non-Significant

Note. BBSIQ = Brief Body Sensations Interpretation Questionnaire, ASI = Anxiety Sensitivity Index, SUDS = Subjective Units of Distress Scale, DSQ = Diagnostic Symptom Questionnaire