Development and randomized trial evaluation of a novel computer-delivered anxiety sensitivity intervention

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A B S T R A C T

Objective: Anxiety disorders contribute substantially to the overall public health burden of psychopathology. Anxiety sensitivity (AS), a fear of anxiety related sensations, is one of the few known malleable risk factors for anxiety pathology. Previous AS reduction treatments have utilized highly trained clinicians. A completely-computerized AS treatment would reduce costs and increase dissemination possibilities. Cognitive bias modification for interpretation biases (CBM-I) interventions have shown clinically significant reductions in anxiety symptoms. Another emerging literature focused on learning has shown context-shifting tasks can greatly increase learning without adding logistical burden to an intervention. The current study evaluated a CBM-I for AS that utilized a context-shifting task to deliver twice the treatment dose of extant interventions.
Design: Single-site randomized controlled trial. Participants completed an intervention appointment, as well as one-week and one-month follow-up assessments.
Participants: Individuals with elevated levels of AS.
Intervention: Single-session computer-delivered CBM-I for AS.
Results: Results indicate that the CBM-I for AS was successful in reducing overall AS (62% post-intervention) and these reductions were maintained through one-month post-intervention (64%). Results also revealed that individuals in the active condition reported significantly less incidents of panic responding to a physiological straw-breathing challenge and that change in interpretation bias significantly mediated the relationship between treatment condition and post-treatment AS reductions.
Conclusions: Taken together, the results show that the current CBM-I intervention was strong in terms of immediate and one-month AS reductions. Given its brevity, low cost, low stigma and portability, this intervention could have substantial impact on reducing the burden of anxiety disorders.

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1. Development and evaluation of a novel computer-delivered anxiety sensitivity intervention

Anxiety disorders are the most prevalent class of mental disorders in the United States and increase risk for other disorders (CDC, 2013). Globally, anxiety disorders were the sixth leading cause of disability in 2010 (Baxter, Vos, Scott, Ferrari, & Whiteford, 2014). Although anxiety disorders are often chronic if untreated, much of the burden of anxiety disorders is likely to be avoidable via prevention and early intervention (APA, 1994; Greenberg et al., 1999).

Expectancy theory (Reiss, 1991) proposes that problems with anxiety develop from three sensitivities: anxiety sensitivity (AS), fear of negative evaluation, and injury sensitivity. However, the vast majority of the research on the expectancy theory has focused on AS, defined as a fear of anxiety related sensations (e.g., the fear one will have a heart attack when their heart races). AS is composed of three lower order factors: physical concerns, cognitive concerns, and social concerns (Reiss, Peterson, Gursky, & McNally, 1986; Zinbarg, Barlow, & Brown, 1997). Consistent with expectancy theory, AS is elevated in patients across anxiety diagnoses (Olatunji & Wolitzky-Taylor, 2009; Taylor, Koch, & McNally, 1992). Further, AS is one of the few well-researched risk factors found in prospective examinations to lead to the development of anxiety pathology (Schmidt, Lerew, & Jackson, 1997; Schmidt, Maner, & Zvolensky, 2007). Based on these findings, DSM-5 officially recognizes the significant risk AS plays in the development of anxiety disorders.

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A few extant interventions have shown AS may be a promising intervention target for brief, inexpensive, low-stigma, and portable interventions. Previous AS interventions have been delivered as a one-day workshop (Gardenswartz & Craske, 2001), addition to group therapy for smokers (Feldner, Zvolensky, Babson, Leen-Feldner, & Schmidt, 2008), exercise interventions (Broman-Fulks & Storey, 2008; Smits et al., 2008), and computer-assisted psychoeducation focused interventions (Keough & Schmidt, 2012; Schmidt et al., 2007). Interventions with these qualities could reduce the high burden of anxiety disorders by reaching those who are not currently receiving any efficacious treatment.

One way to create AS interventions that are briefer, less expensive, reduce stigma, and are more portable than existing interventions is by developing a completely computerized version. A constellation of procedures known as cognitive bias modification for interpretation bias (CBM-I) have shown promise in the treatment of anxiety psychopathology by directly manipulating distorted interpretations of benign stimuli (such as those experienced by individuals with elevated AS). CBM-I is delivered via computer and works by presenting individuals with ambiguous information, after which the participant must make a decision that should be facilitated by an interpretation of this ambiguity. Bias is shaped by structuring feedback to reward one style of interpretation over another (usually positive/benign over negative/threatening). Extant CBM-I interventions have resulted in lowered state and trait anxiety (Salemink, van den Hout, & Kindt, 2007), social anxiety (Beard & Amir, 2008; Hoppitt et al., 2014), and worry (Hirsch, Hayes, & Mathews, 2009).

To our knowledge, there have been only a few studies that have tested CBM-I for AS. Individuals with AS have biased interpretations related to internal anxiety sensations (e.g. "When my mind races I worry that I'm going crazy" and "When my stomach is upset, I worry that I might be seriously ill". The first study (Steinman & Teachman, 2010) used a variant of the Mathews and Mackintosh (2000) CBM-I procedure, which only allowed for modifying IB in one direction (i.e. more positive interpretations of ambiguity). In this study, participants in the active condition completed 64 training trials and decreased an average of 29% on the ASI. However, contrary to expectation, the no treatment control decreased an average of 19%. The next CBM-I for AS (MacDonald, Koerner, & Antony, 2013), addressed some limitations of the previous study by using a CBM-I paradigm (Word Sentence Association Paradigm; Beard & Amir, 2008) that guided participants toward making benign interpretations *and* rejecting threat interpretations. In addition, they added a follow-up period (i.e., two days). However, this CBM-I appeared to be less potent. ASI-total scores in the active condition reduced an average of 15% at post-test and 18% at the 48 h follow-up. In contrast to the Steinman and Teachman (2010) study, the control CBM-I condition did not significantly decrease at post-test or follow-up. Lastly, the most recent study, Clerkin, Beard, Fisher, and Schofield (2015); was similar to the MacDonald et al. (2013) report in that they used the Word Sentence Association Paradigm (WSAP) paradigm. However, they divided the training over two sessions (64 training trials per session), which were two days apart. Despite more procedural similarity to the MacDonald et al. (2013) report, their results were similar to the first study (Steinman & Teachman, 2010). The authors reported sizable AS reduction in not only the active (28%) but also the control (20%) CBM-I condition. Interestingly, all three studies provided fearful symptom induction exercises (e.g. straw-breathing, chair spinning, etc.) post-CBM-I but did not find significant differences between active and control participants on these tasks despite significant self-reported AS reductions.

Several gaps remain in the CBM-I for AS literature. First, the longest follow-up period between the previous studies (two days) is very brief. Longer maintenance of treatment gains must be shown before CBM-I can be considered as a clinical tool for treating anxiety. Second, as Clerkin et al. (2015) discuss, no extant work has assessed change in interpretation bias (IB) with novel word-sentence pairs that participants haven't seen during training. Doing so would increase the confidence that CBM-I training leads to meaningful changes in IB; changes that will impact participants as they encounter new anxiety-provoking stimuli in their daily life. In addition, critics of CBM have pointed out that change in self-reported symptoms may not be caused by the purported mechanism, change in interpretation bias. None of the previous studies have performed mediation analyses to directly test whether change in IB is the actual mechanism responsible for self-reported reductions in AS. Finally, questions remain about the clinical utility of these interventions. Although all studies reported significant reduction in self-report AS; two studies found significant AS reduction in the control group and none found statistically significant differences in fearful symptom induction exercises. The authors of these studies have speculated that the lack of significant findings may have been due to a combination of small sample sizes and symptom induction exercises that were not sufficiently challenging. An alternative explanation is that these interventions are not potent enough to have a measurable effect on symptom induction exercises. The CBM-I studies reviewed have not approached the potency of the top non-CBM single session AS interventions (Keough & Schmidt, 2012); suggesting greater AS reduction could be achieved. Efforts have been made to increase the potency of anxiety treatments (i.e. d-cycloserine; mGluR5) in the broader literature; yet, this area has been overlooked in the anxiety CBM literature despite the obvious attraction of making these single-session interventions as efficacious as possible.

Context switching tasks could be employed to add potency to these interventions while keeping them single-session, inexpensive, low-stigma and portable. The context change hypothesis posits that new learning builds up alpha wave interference in the brain, which makes learning less efficient (Pastötter, Schicker, Niedernhuber, & Bäuml, 2011). There are both behavioral and electrophysiological findings in support of the context change hypothesis (Jang & Huber, 2008; Pastötter, Bäuml, & Hanslmayr, 2008; Sederberg et al., 2006). Briefly switching the context of learning resets alpha activity, which allows for new learning to occur without long periods of rest. We believe context changes are an extremely simple, no-cost, and heretofore unutilized method to increase the potency of single-session AS interventions. In the current study we used context shifting to add an extra training session of 80 trials (doubling the total training). In between the two training sessions the participants completed a non-related task (i.e. simple math problems). This task was designed to keep them engaged while providing a context shift from the CBM-I learning. Based on the context shifting hypothesis, this break should not only allow us to double the training dose without overburdening the participant but also increase efficacy of the training.

The current study extended the literature on brief CBM-I in several ways. Primarily, there has been a lack of significant findings for symptom induction exercises in the extant literature. We believe that previous studies have not been potent enough to see significant effects. In the present study, we included a context shifting activity to double the dose of treatment delivered in one session and increase the overall effectiveness of the CBM-I training. Due to this higher dose and congruent with the context change hypothesis, we hypothesized this novel CBM-I paradigm would result in significant condition differences on the symptom induction exercise (i.e., straw-breathing). Specifically, participants completing the active CBM-I would show significantly less fear responding to a straw-breathing challenge than those in the control

condition. In addition, we hypothesized the greater potency of this intervention would also lead to greater reduction in self-reported AS than found in extant studies. Second, this study included a much longer follow-up (one month) than prior work to better determine the durability of these interventions. We hypothesized that treatment-related AS reductions would persist over time. We also assessed change in IB using a novel set of word-sentence associations that participants did not see in training. This provides a test of whether CBM-I training can generalize to new learning. Importantly, we tested if change in IB was the active mechanism behind self-report AS reduction by performing asymmetric bootstrapping mediation analyses. It was hypothesized that change in interpretation bias would significantly mediate change in ASI-3 scores. To corroborate the specificity of this finding we also tested the alternative hypothesis that changes in state emotion (i.e. negative affect) would mediate the relationship between treatment group and AS reduction.

2. Methods

2.1. Trial design and procedure

Participants were invited for the experiment appointment via the psychology department's secure research participant registration website. They began the appointment by reading and signing an informed consent that ensured confidentiality and thoroughly outlined their proposed study involvement. The study was approved by the Florida State University Institutional Review Board. Participants then completed the battery of baseline measures and were randomized with a planned allocation ratio of 1:1.[1] The simple randomization sequence (1 = active; 2 = control) was generated by the random integer generator at random.org. The first author generated the random number sequence. Trained research assistants enrolled participants and opened the matching CBM software program (1 or 2) based on a participant log spreadsheet. Participants and research assistants running participants were blind to intervention group. At the end of the session, participants completed a battery of post-intervention self-report measures and the straw-breathing challenge. One week and again at one month from experiment completion the participants were e-mailed the link to a secure website to complete the ASI-3.

2.2. Participants

Participants were undergraduates screened through the Florida State University psychology participant pool. Individuals were eligible if their mass screening score on the ASI was 1.5 SD above the population mean (Keough & Schmidt, 2012). To ensure the final sample was appropriate for an AS intervention, only participants whose levels of AS remained elevated (>10.7; Schmidt & Joiner, 2002) at the baseline assessment were analyzed. However, due to an extremely small participant pool during the Spring 2013 semester all participants scoring >10.7 on the screening measure were randomized. However, no individuals without elevated AS were included in the final analyzed sample. This resulted in uneven number of participants in the active (n = 48) versus control (n = 41) conditions in the final analyzed data. The required sample size was determined using a power analysis program (Faul, Erdfelder, Lang, & Buchner, 2007) and a medium to large effect size based on pilot data. Participants were compensated for their time with course credit.

The randomized sample was primarily female (82.1%) with an average age of 18.87 (SD = 1.37). The racial representation of the study participants was as follows, Caucasian (88.7%), African American/Black (7.5%), and other (3.8%). A total of 16% of the sample identified as Hispanic or Latino.

2.3. Assessments

2.3.1. Self-report measures

2.3.1.1. Acute panic inventory (API). The API measures symptoms of arousal associated with panic attacks (Liebowitz, Gorman, Fyer, Dillon, & Klein, 1984). It is widely used with CO2 challenges (Norman B. Schmidt et al., 2007). The API includes a SUDS rating (0–100) of self-reported fear. Internal consistency in the present sample was very good ($\alpha = 0.86$).

2.3.1.2. Anxiety sensitivity index-3 (ASI-3). The ASI-3 (Taylor et al., 2007) is based on the original ASI (Reiss et al., 1986) and is a widely used measure of the fear of anxiety-related symptoms. The ASI-3 has established strong psychometric properties (Taylor et al., 2007). Internal consistency in the present sample was very good ($\alpha = 0.88$).

2.3.1.3. Positive and negative affect scales – negative affect (PANAS-NA). The PANAS is a widely used self-report inventory designed to measure global emotional states at the time of assessment (Watson, Clark, & Tellegen, 1988). Items fall into two 10-item subscales that assess positive and negative affect (PA and NA, respectively). Only the NA scale was used in current study. The PANAS-NA showed excellent internal consistency ($\alpha = 0.99$).

2.3.2. Behavioral fear assessment

2.3.2.1. Straw-breathing challenge. Straw-breathing is a safe physiological challenge procedure used to provide a behavioral index of fear responding to a novel stimulus and have been used in previous AS reduction work (Steinman & Teachman, 2010). Participants breathed through a narrow straw, holding their nose closed with their free hand, for as long as they could (up to 2 min). If participants stopped before one minute elapsed, they were instructed, "Please continue a little longer if you are able".

2.3.2.2. Panic responding. Panic was defined using a version of the stringent four-fold criteria gauging reaction to a biological challenge (Telch, Harrington, Smits, & Powers, 2011). All of the following criteria had to be satisfied for a post-challenge reaction to be classified as panic: 1) affirmation of panic during challenge, 2) a sudden pre-to post-challenge rise in reported fear ≥30 on a 100-point Likert scale, 3) four or more of the DSM-V panic attack symptoms, and 4) a 10-point pre-to post-challenge rise on the API.

2.4. Interpretation bias

Consistent with previous CBM-I work (Brosan, Hoppitt, Shelfer, Sillence, & Mackintosh, 2011), interpretation bias was measured as the difference in training-congruent responses (accepting benign interpretation and rejecting anxiety interpretations) between their initial pre-training trial and the post-training trial featuring novel but AS focused word-sentence pairings.

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[1] After completing the CBM-I, participants were further randomized to receive either a cold-pressor challenge or a room temperature arm bath. There was no effect of this challenge on the final results so this part of the experiment has been omitted for space limitation and clarity issues. However, the effect of the cold-pressor challenge and the interaction between CBM-I condition and cold-pressor condition have been covaried in all analyses presented in this manuscript.

3. Description of experimental conditions

3.1. Cognitive bias modification conditions

3.1.1. Bias Interpretation for anxiety sensitivity CBM-I (BIAS)

CBM-I was programmed using E-Prime software (Schneider, Eschman & Zuccolotto, 2002) and is based on a slightly modified version of the WSAP paradigm (Beard & Amir, 2008; Brosan et al., 2011). The modifications made to the original WSAP were showing a word or two-word phrase for 1 s (versus 1 word for 500 ms in Beard & Amir, 2008) and adding an 85 dB horn blast after incorrect responses. In addition, we "flipped" the traditional presentation, using an ambiguous word or two-word phrase followed by a sentence that resolved the word-sentence meaning as threatening or benign. For example, participants were presented with an ambiguous word or two-word phrase for 1 s (e.g. "tingly") followed by a sentence (e.g. "You lightly bang your elbow and it feels funny""). On half the trials the combination of the word/phrase and sentence created a benign meaning (as in the previous example). On the other half of trials this combination created an anxious-threat meaning (e.g., "tingly" followed by the sentence — "Something is terribly wrong with you"). The word sentence pairings, which were created specifically for this intervention were rated by five independent judges who are published authors on anxiety sensitivity. For BIAS, raters indicated how relevant to AS and how threatening the word-sentence pairs were on a 1 (not at all) to 5 (very) scale. The mean AS relevance rating was 4.3, with mean threat ratings of 4.2 for threatening pairs and 1.7 for benign pairs. Participants were required to judge the relatedness of the word/phrase and the sentence. Participants were given feedback during training such that judging the anxious-threat combinations to be "unrelated" and the benign combinations as being "related" would produce a "correct" response. In contrast, if participants produced an "incorrect" response they saw "incorrect" and heard a horn blast (approximately 85 dB). Participants began with 40 test trials with no reinforcement to measure initial IB. They then completed 80 training trials in which their response was reinforced. At this point, they completed a five-minute context-shifting task (simple math problems). The participants then completed another 80 trials of training. Finally, they were given 40 test trials of novel word/sentence pairs to measure change in IB. This procedure is consistent with previous IB literature (Brosan et al., 2011).

3.1.2. Placebo interpretation modification CBM-I (PIM)

PIM was identical to BIAS except that the sentence that followed the cue word was not related to an anxious-threat interpretation of the cue word. For example, the word, "trembling" followed by the sentence "It gets cold in the winter". For PIM, the judges rated the relevance to AS and how related the words were to each other. The mean AS relevance rating was 1.55, with mean relatedness ratings of 4.24 for related pairs and 1.13 for unrelated pairs.

4. Results

4.1. Sample and preliminary analyses

A total of 106 eligible participants were recruited for the study and completed the intervention appointment between September 2013 and April 2014 (See Fig. 1). Data collection stopped when reaching target number of eligible participants; however, previously scheduled appointments were completed. Only those with elevated ASI total scores (>10.7; Schmidt & Joiner, 2002) were included in analyses ($n = 89$). In terms of the online follow-ups, 84% ($n = 75$) completed the week one follow-up and 88% ($n = 78$) completed the month one follow-up. Therefore, the total size of the

sample varies slightly at the different time points. Pretreatment data indicate that random assignment was successful (no significant baseline group differences; Table 1). BIAS participants showed slightly lower baseline IB than PIMS participants (See Table 2).

4.2. Main study hypotheses

4.2.1. Main effect of intervention on overall AS

The effect of CBM-I condition on post-intervention ASI-3 score was examined using linear regression analyses. The regressions were performed with treatment condition as the independent variable (BIAS coded 1; PIM coded 2). The baseline ASI-3 score was included as a covariate. As hypothesized, BIAS had significantly lower post-treatment ASI-3 scores ($t = 5.19$, $\beta = 0.33$, $p < 0.001$, $sr^2 = 0.24$). .

The same analytic strategy was used to assess differences in the treatment conditions from baseline to each follow-up time point. As predicted, BIAS reported significantly lower ASI-3 scores at week one follow-up, ($t = 2.91$, $\beta = 0.25$, $p = 0.005$, $sr^2 = 0.11$), and month one follow-up ($t = 3.16$, $\beta = 0.28$, $p = 0.002$, $sr^2 = 0.11$). There was a substantial percentage of AS reduction in the BIAS condition that maintained through the one-month follow-up (See Fig. 2).

4.2.2. Physiological straw-breathing challenge

To provide a behavioral test of anxiety sensitivity, participants completed a straw-breathing challenge. As hypothesized, a significantly higher percentage of participants in the PIM condition reported an episode of panic responding (41%) utilizing the four-fold criteria adapted from Telch et al. (2011), than participants in BIAS (18%; $\chi 2$ Continuity Correction $= 3.90$, $p = 0.048$). This analysis was followed-up with a logistic regression. CBM-I condition was entered as the IV, self-report panic response (Yes/No) was entered as DV. Pre-strawbreathing API total was entered as a covariate. CBM-I condition was a significant predictor of definitive panic response (Wald $= 5.79$, $p = 0.016$, OR $= 3.84$, 95% CI $= 1.28$, 11.51).

4.2.3. Mechanism analysis — change in IB as mediator between treatment condition and Reduction in AS

The indirect effect of change in interpretive bias was evaluated through simple mediation (Hayes, 2012), with CBM-I condition as the independent variable, baseline to post-intervention ASI-3 change score as the dependent variable, and IB change scores as the mediating variable.[2] IB change was 56% greater in BIAS (See Table 2). All mediation analyses were conducted using PROCESS (Hayes, 2012). Results of 5000 bootstrap resamples demonstrated that the direct effect of condition on ASI-3 change was significant ($B = 8.12$, SE $= 2.10$, $t = 3.87$, $p < 0.001$). In addition, the direct effect of condition on IB change was significant ($B = -2.39$, SE $= 1.11$, $t = -2.16$, $p = 0.034$). Critically, the indirect effect of condition on ASI-3 via IB change was significant (See Fig. 3; $B = 1.02$, SE $= 0.69$, 95% CI [0.11, 2.98]).

Next, we performed comparable mediations to test for mediation effects at week-one follow-up and month-one follow-up. In the week-one follow-up analyses, results of 5000 bootstrap resamples demonstrated that the direct effect of CBM-I condition on IB change was significant ($B = -3.41$, SE $= 1.16$, $t = -2.94$,

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[2] As recommended, particularly for small samples, estimates of indirect effects were generated using bootstrapping analysis (Preacher & Hayes, 2004). In bootstrapping analysis, the most stringent test of an indirect effect (mediation) is if the 95% bias-corrected and accelerated confidence intervals for the indirect effect do not include 0. The structure of these analyses is identical to recent work in the CBM literature (Williams, Blackwell, Mackenzie, Holmes, & Andrews, 2013). There was no evidence of an effect of cold-pressor condition or of an interaction between CBM-I condition and control conditions so simple mediation was performed.
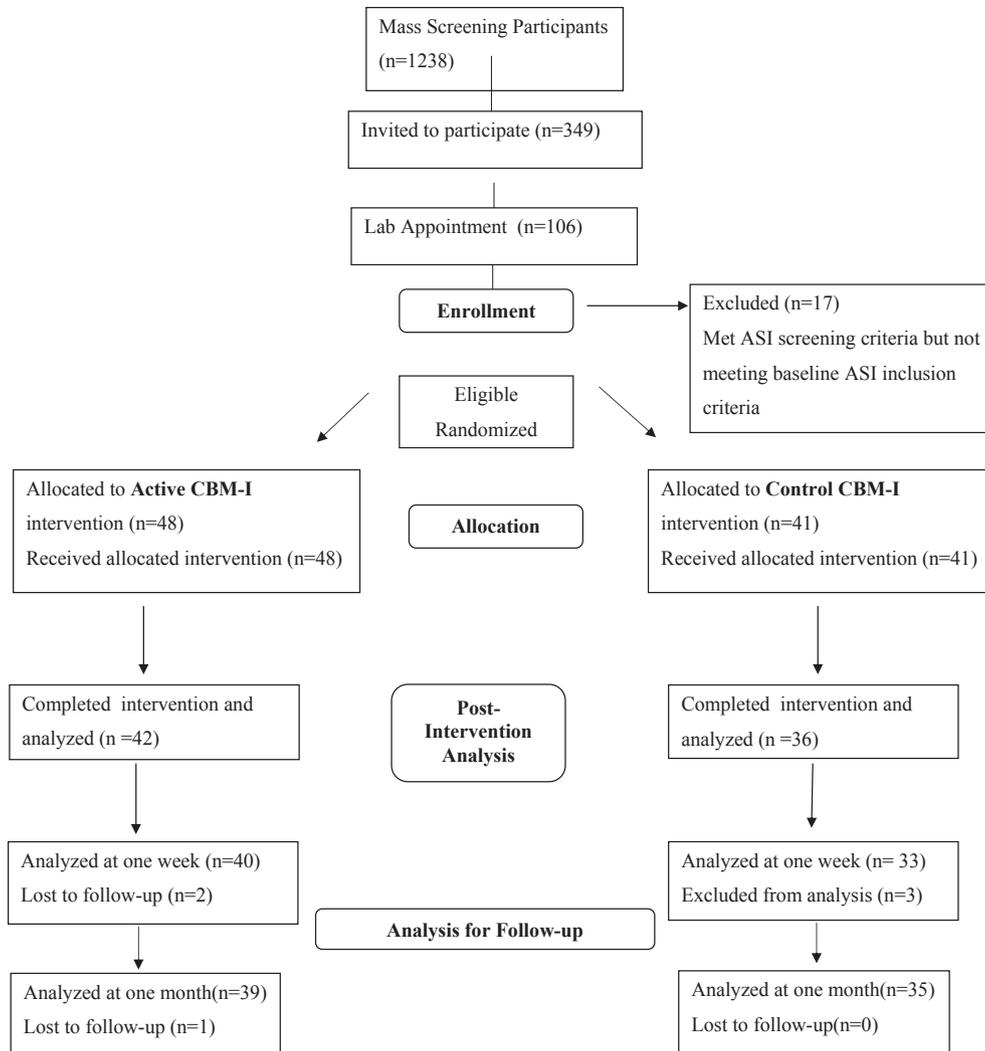
Fig. 1. CONSORT diagram.

$p = 0.004$). However, the direct effect of CBM-I condition on ASI-3 change was not significant ($p = 0.173$). Critically, the indirect effect of condition on ASI-3 via IB change was significant ($B = 1.63$, SE = 0.98, 95% CI [0.16, 4.08]).

In the month-one follow-up analyses, results of 5000 bootstrap resamples demonstrated that the direct effect of condition on IB change was significant ($B = -2.70$, SE = 1.12, $t = -2.41$, $p = 0.018$).

Table 1
Descriptive statistics for pre-intervention measures by treatment condition.

	BIAS		PIM		
	Mean	SD	Mean	SD	t
ASI-3	23.98	10.42	27.09	11.36	−1.35
PANAS-NA	16.91	6.49	16.68	6.78	0.16
	Percentage		Percentage		χ^2
Gender					0.59
Female	77%		85%		
Ethnicity					0.07
Hispanic	17%		15%		
Race					0.55
Caucasian	85%		90%		

Note. BIAS $N = 48$, PIM $N = 41$. ASI-3 = Anxiety sensitivity index − 3. All data is from baseline. All baseline differences are $p > 0.10$.

However, the direct effect of condition on ASI-3 change ($p = 0.095$) and the indirect effect of condition on ASI-3 via IB change were not significant (95% CI [−0.06, 3.14]).

4.2.4. Alternative mediator − state changes in negative affect after CBM-I

State changes in negative affect after the CBM-I were assessed using the PANAS-NA. For the total sample, there was not a significant change in PANAS-NA from Pre to Post ($t = -1.04$, $p = 0.30$). Similarly, there was no significant change in PANAS-NA following the CBM-I for the PIM condition ($p = 0.721$). However, for those in the BIAS condition, there was a significant reduction in PANAS-NA following the CBM-I ($t = -2.27$, $p = 0.028$). Based on the finding of

Table 2
Descriptive statistics for interpretation bias by treatment condition.

	BIAS		PIM	
	Mean	SD	Mean	SD
Baseline IB	29.17	4.70	32.82	5.75
Post-Training IB	35.60	4.31	37.06	2.56
IB Change	6.43	5.14	4.24	4.58

Note. IB = Interpretation bias. BIAS (active) = Bias Interpretation for Anxiety. Sensitivity. PIM (control) = Placebo Interpretation Modification.
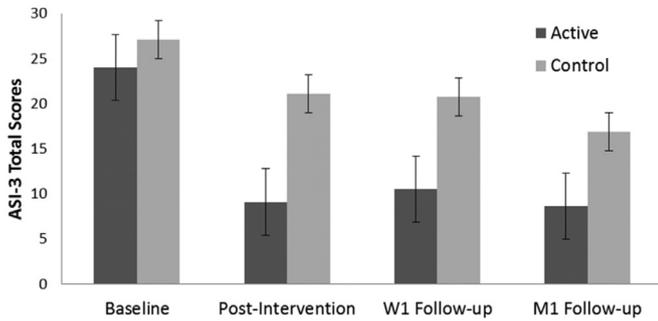
Fig. 2. Reductions in anxiety sensitivity over time. ASI-3 = Anxiety sensitivity index-3. W1 = Week one. M1 = Month one.

significant PANAS-NA reduction in the BIAS condition; a mediation analysis was conducted to see if Post-CBM-I change in PANAS-NA was an alternate mediator of the relationship between CBM-I treatment and change in ASI-3 total. However, results of 5000 asymmetric bootstrap resamples demonstrated that PANAS-NA was not a significant mediator of this relationship (indirect effect 95% CI = −0.63, 0.57).

5. Discussion

The primary aim of the current study was to design and evaluate a brief, low-cost and portable CBM-I based AS reduction intervention. The results from this study indicate that the CBM-I for AS significantly reduced self-reported AS, led to less fear response on a symptom induction exercise, and operated via the hypothesized mechanism (i.e. change in IB). In addition, we extended previous findings by showing that significant self-reported AS reduction was maintained for one month; whereas, the current literature has only assessed the durability of CBM-I for AS effects for a maximum of two days.

The current CBM-I for AS appears to be more effective than previous attempts to reduce AS through CBM-I. The previous protocols resulted in mean AS decreases of 15–28 percent (Clerkin et al., 2015; MacDonald et al., 2013; Steinman & Teachman, 2010).

There were several design differences in the current CBM-I for AS protocol including creating ambiguous words (or two-word phrases) versus ambiguous sentences, increasing the time the word/phrase was displayed from 500 ms to 1 s, adding a buzzer sound to incorrect responses and including a context-shifting task (simple math tasks between CBM-I training sessions). The addition of the math task was designed to double the amount of training a participant received in one-session and increase overall effectiveness of the learning without inducing fatigue (Pastötter et al., 2011). However, although this is a potential explanation for greater AS reductions, this hypothesis was not explicitly tested because of the extra logistical considerations (including more participants). Further, extant work on the context-change hypotheses appears to be based on explicit learning (i.e., encoding lists of words) tasks versus implicit learning tasks such as CBM-I (Pastötter et al., 2008, 2011). Future work is needed to test the effect of this design, given the importance not only to any CBM-I treatment but to all brief psychological interventions. Doubling treatment dose in a very short-amount of time without overwhelming, tiring, or boring participants could be a significant breakthrough for brief psychological interventions.

Participants in the BIAS condition in the current study had a mean 62% decrease in AS at the end of their intervention session. This reduction in global AS is remarkable when compared to previous non-CBM-I AS interventions; such as: 28% (Keough & Schmidt, 2012), 30% (Schmidt et al., 2007), 32% (Schmidt, Capron, Raines, & Allan, 2014), 34% (Feldner et al., 2008), 41% (Broman-Fulks & Storey, 2008), and 43% (Gardenswartz & Craske, 2001). Comparing across different AS treatments is difficult based on different levels of baseline AS, different measures (ASI vs. ASI-3), and different length of treatment. However, it is important to remember that CBM-I for AS is by far the least time-consuming AS reduction intervention, which suggests that it is fair to compare the effects of CBM-I with these extant AS reduction protocols, despite other differences (e.g. baseline severity, AS assessment). It is possible that participants found the CBM-I more engaging than previous (psychoeducation plus IE) approaches. For certain participants the CBM-I may have been like a video game where they were actively involved in choosing whether the word and sentence were
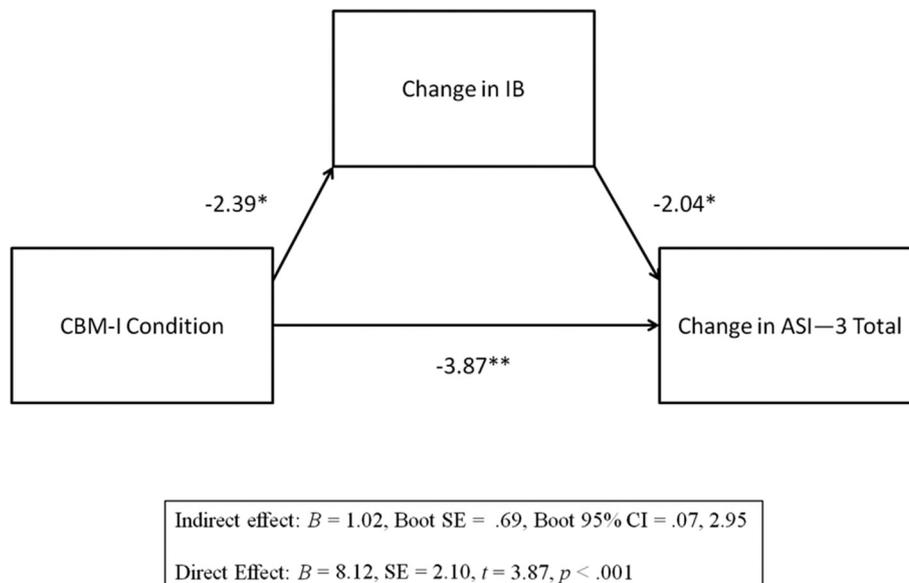

Indirect effect: $B = 1.02$, Boot SE = .69, Boot 95% CI = .07, 2.95

Direct Effect: $B = 8.12$, SE = 2.10, $t = 3.87$, $p < .001$

Fig. 3. Mediating role of change in interpretation bias (IB) in explaining the relation between cognitive bias modification − interpretation bias (CBM-I) condition and changes in ASI-3 total scores between baseline and post-intervention. *$p < 0.05$. **$p < 0.01$.

related every few seconds. In contrast, listening to a psycho-education presentation for 45 min to an hour might have been too passive for some individuals, leading to "zoning out". Active learning has a long history of superior results when compared to passive learning (Benware & Deci, 1984).

Along with these self-reported ASI-3 reductions, a significantly lower percentage of participants in the active condition reported a panic response to the physiological straw-breathing challenge. This is noteworthy because findings in the previous CBM-I for AS reduction literature have not found significant group differences between the active and control conditions on symptom induction exercises. Our explanation is that the current intervention delivered a stronger treatment dose. Our claim is well supported by the finding that self-report AS reductions (62%) were double those found in the strongest previous CBM-I for AS (29%). However, it is important to note that although panic response was measured by four-fold criteria set forth in previous literature (Telch et al., 2011); it is unlikely to capture the true clinical experience of a panic attack.

A discrepancy between strong findings on self-report measures and lack of findings on non-self-report measures has been an issue for the CBM for anxiety field (MacLeod & Mathews, 2012). The previous CBM-Is for AS have been no exception in this regard. The discrepancy between self-report and non-self-report findings has led some to suggest that CBMs are not actually reducing psychopathology but merely training participants to answer self-report measures in a manner that looks like their symptoms have been reduced. This argument is certainly plausible as the stimuli for CBM-I, especially with a specific construct such as AS, will address similar topics as self-report assessments. However, the finding that individuals in the active condition reported significantly lower fear reactivity than the control group during a straw-breathing challenge provides important evidence that the current CBM-I resulted in actual, clinically meaningful reduction in AS.

In the current study we found that change in IB significantly mediated the relationship between CBM-I condition and post-treatment (and week-one follow-up) ASI-3 total. However, it must be noted that change in IB was not a significant mediator of one-month follow-up ASI-3 total so more work needs to be done in this area to clarify the mechanism of change over time. The extant CBM for anxiety literature contains mixed findings for the hypothesized mechanism of change (i.e. change in bias) and many have called for this to be a focus of future CBM research (Beard, 2011; Beard & Amir, 2008; MacLeod & Mathews, 2012). Some critics have suggested that CBM merely exposes individuals repeatedly to threatening stimuli, decreasing their fear response (versus actually changing IB) (See Beard, 2011 and Salemink, van den Hout, & Kindt, 2010 for discussions). The IB mediation findings at post-treatment and one-week follow-up is promising as not all CBM treatments that have shown reduction in self-reported psychopathology have also shown significant change in bias mediation. To our knowledge, this is the first CBM-I to demonstrate IB mediation at a follow-up at least one week from the intervention. However, the lack of significant mediation at one-month follow-up despite increasing treatment gains means more nuanced examinations of potential mechanisms of change are needed in future work.

Contrary to expectations, there was a sizable decrease in AS in the control group overall, and a surprisingly large drop between week-one follow-up and month-one follow-up specifically. The control group saw reductions of approximately 20% through week one and then a substantial decrease to 38% at month one. Significant decreases in the control group have been an issue in previous CBM studies. For example, Steinman and Teachman (2010) reported 20% post-treatment ASI reductions in both a control group that received no training and a control group that received neutral

training. One explanation for the observed AS reductions could be repeated administrations of the ASI-3. There is evidence that merely completing the ASI multiple times results in substantially lower scores (Marsic, Broman-Fulks, & Berman, 2011). Although there are currently no evaluations of repeated administrations of the ASI-3, extant work on earlier versions (i.e. ASI-R) indicates that the only such reduction happens between the first and second administration (Marsic et al., 2011). This effect was controlled for in the current study by using the original ASI as the screening measure and only analyzing participants whose ASI scores remained elevated after the second administration of the measure (at baseline). Future work on the ASI-3 might reveal that repeated administrations results in sizable decreases beyond just the second administration. Given the widespread use of this measure this is an important area for future study.

In regard to the large AS reduction in the control group between week-one and month-one follow-ups, there are several plausible explanations. First, these reductions could be completely unrelated to the intervention. For example, we did not assess medication or psychotherapy during follow-ups so it is possible that a subgroup of individuals sought treatment for their anxiety between the intervention appointment and the one-month follow-up. Another possibility is the design of the PIMS CBM-I. The design was proposed in MacDonald et al. (2013) and used in Clerkin et al. (2015). The PIMS group was shown AS related words ("tremble") with non-threating but related ("It gets cold in winter") or unrelated ("The truck is blue") interpretations. However, there is a possibility that this CBM acted as a diluted intervention because individuals repeatedly paired the AS word with a non-threatening sentence. This possibility is strengthened by the fact that Clerkin et al. (2015) also found a significant decrease in AS using the same control paradigm.

Another area for potential improvement in this literature is the gender distribution of the samples. Our sample had a large percentage of women (82%). However, other studies in this literature have also had a majority of women: 84.5% (Clerkin et al., 2015) and 76% (MacDonald et al., 2013). Given the relatively small samples in this literature the effect of CBM-I for men is being tested on a small number of individuals. To further investigate this issue we ran follow-up analyses to examine gender differences on AS change and found no significant gender differences (all results $p > 0.50$) for AS change in both the active condition and control condition. Future studies should oversample for men, racial minorities, and older adults as University recruiting based primarily on elevated AS appears to result in heavily skewed samples.

It is important to note an additional limitation of the current study that has not been discussed previously. Primarily, the levels of AS in this sample ($M = 25$) were lower than in previous CBM-I for AS interventions from Steinman and Teachman (2010; $M = 35$), Clerkin et al. (2015; $M = 35$), and MacDonald et al. (2013; $M = 40$). However it should be noted that mean baseline AS level was comparable to non-CBM-I computer assisted interventions; such as the study from Keough and Schmidt (2012; $M = 29$) and greater than the original anxiety sensitivity amelioration training from Schmidt et al. (2007; $M = 17$). Given the large treatment reductions observed in the current study as well as the Keough and Schmidt (2012) study, it may be that individuals with moderately elevated AS ($M = 25–29$) are the ideal target for brief computerized AS reduction interventions. Factor mixture modeling studies of the ASI have found that individuals fall into a normative class (ASI < 15), a moderate AS class (ASI 17–22) or a high AS class (ASI > 23) (Allan, Korte, Capron, Raines, & Schmidt, 2014). Perhaps the least severe individuals in this high AS class are most amenable to these interventions because they have high enough AS for the treatment to be relevant but their AS is low enough that it is still readily malleable. Future factor mixture modeling work could be used to

determine who is most likely to benefit from these brief interventions. Individuals with higher elevations on AS, such as those from the MacDonald et al. (2013) report may need more intensive treatment than a one-time computerized intervention. Accordingly, research is needed to examine the CBM-I in more severe samples.

This study suggests an extremely brief, completely computerized intervention can result in substantial reductions in AS. AS is perhaps the most well-known risk factor for anxiety disorders (APA, 2013; Olatunji & Wolitzky-Taylor, 2009). Despite the many well-established treatments for anxiety disorders (Chambless & Ollendick, 2001); anxiety disorders continue to result in substantial burden to society (Kessler, Chiu, Demler, & Walters, 2005) because of issues such as access, cost and stigma. New models of treatment delivery, such as the Muñoz et al. (2015) Massive Open Online Intervention delivery model, which suggest making interventions freely available over the internet, are a great fit for this intervention. By addressing these issues through such a paradigm, CBM-I for AS could have tremendous societal value as a first-step in a stepped-care model of anxiety treatment.

Conflict of Interest Statement

All authors report no conflicts of interest

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