Journal of Psychiatric Research 85 (2017) 75–82

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/psychires

Combined "top-down" and "bottom-up" intervention for anxiety sensitivity: Pilot randomized trial testing the additive effect of interpretation bias modification

Daniel W. Capron [a, b, *], Aaron M. Norr [b], Nicholas P. Allan [b], Norman B. Schmidt [b]

[a] Department of Psychology, University of Southern Mississippi, Hattiesburg, MS, USA
[b] Department of Psychology, Florida State University, Tallahassee, FL, USA

ARTICLE INFO

Article history:
Received 3 May 2016
Received in revised form
24 September 2016
Accepted 3 November 2016

ABSTRACT

Objective: Anxiety disorders contribute substantially to the overall public health burden. 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 primarily utilized "top-down" (e.g., psychoeducation) interventions. The goal of the current study was to evaluate the effect of adding a "bottom-up" (interpretation bias modification; CBM-I) intervention to an AS psychoeducation intervention.
Design: Single-site randomized controlled trial. Participants completed either a 1) Psychoeducation + active CBM-I or 2) Psychoeducation + control CBM-I intervention. Change in AS was assessed post-intervention and at a one-month follow-up.
Participants: Individuals with elevated levels of AS.
Intervention: Single-session computer-delivered intervention for AS.
Results: Accounting for baseline ASI-3 scores, post-intervention ASI-3 scores were significantly lower in the combined condition than in the psychoeducation + control CBM-I condition ($\beta = 0.24$, $p < 0.05$; $d = 0.99$). The active CBM-I plus psychoeducation AS intervention was successful in reducing overall AS (59% post-intervention; $p < 0.05$, Cohen's $d = 0.99$) and these reductions were maintained through one-month post-intervention (52%; $p < 0.05$, Cohen's $d = 1.18$). Participants in the active condition reported significantly lower rates of panic responding to a vital-capacity CO_2 challenge (OR = 6.34, 95% CI = 1.07–37.66). Lastly, change in interpretation bias significantly mediated the relationship between treatment condition and post-treatment AS reductions.
Conclusions: The current intervention was efficacious in terms of immediate and one-month AS reductions. Given its brevity, low-cost, low-stigma and portability, this intervention could lead to reducing the burden of anxiety disorders.

It is hard to reconcile the success of cognitive-behavioral anxiety treatments with the staggering burden of anxiety disorders (Hofmann and Smits, 2008). One major issue is that the vast majority of individuals in need of psychological treatment do not receive any services (Kessler et al., 2005). Creating brief, portable and inexpensive interventions could potentially reach more individuals in need and reduce the burden of anxiety psychopathology. One way to attain all three of these criteria would be by developing computerized interventions. Such interventions could be delivered widely via the internet at virtually no cost. Ideally, such interventions would target very specific mechanisms to achieve the greatest reduction in symptoms in the most efficient manner possible. One such mechanism is anxiety sensitivity (AS), or a fear of anxiety-related sensations (e.g., elevated heart rate; Reiss et al., 1986).

AS is elevated in patients across anxiety diagnoses (Olatunji and Wolitzky-Taylor, 2009; Taylor et al., 1992). Further, AS is one of the few well-researched risk factors in prospective examinations of the development of anxiety pathology (Schmidt et al., 1997; Schmidt et al., 2006). These findings, along with others from the literature, led the American Psychiatric Association (2013) to officially recognize AS as a risk factor for anxiety psychopathology in DSM-5.

AS appears to be an excellent candidate for computer-delivered

* Corresponding author. 118 College Dr., #5025, Hattiesburg, MS, 39406, USA.
E-mail address: daniel.capron@usm.edu (D.W. Capron).

http://dx.doi.org/10.1016/j.jpsychires.2016.11.003
0022-3956/

interventions because evidence suggests that it can be significantly reduced using brief treatment protocols focused on the provision of corrective information (e.g., Broman-Fulks and Storey, 2008; Feldner et al., 2008; Gardenswartz and Craske, 2001; Keough and Schmidt, 2012; Schmidt et al., 2007; Watt et al., 2006). Researchers have begun to examine the effects of top-down computer-assisted (combination of computer-delivered and clinician-delivered intervention) and computer-delivered (computer only intervention) AS interventions. For example, Anxiety sensitivity amelioration training (ASAT), is the largest ($N = 404$) and most comprehensive computer-assisted AS intervention (Schmidt et al., 2007). ASAT combined psychoeduation and interoceptive exposure (IE) exercises (i.e. bringing on uncomfortable bodily sensations to prove that they are uncomfortable but not dangerous) and resulted in significantly reduced self-reported AS, compared to a control condition. Subsequent "top-down" AS interventions have found similar results (Keough and Schmidt, 2012; Schmidt et al., 2014).

Despite the positive results of these top-down AS interventions, it is still unknown whether we have reached maximum potency in this area. Converging research suggests that the etiology and maintenance of anxiety disorders occurs via both top-down and bottom-up processing of threat stimuli (see Clark and Beck, 2010 for a review). Since the Clark and Beck (2010) review more nuanced definitions of automatic (i.e., bottom-up) versus non-automatic (i.e., top down) processes have been introduced. For example, Teachman et al. (2012) reviewed four theoretically independent features of automatic cognitive processing (i.e., unconscious, efficient, unintentional, uncontrollable; Bargh, 1994) in relation to anxiety (and depressive) disorders. Their review concluded that most anxiety disorders evidence uncontrollable and likely also unconscious and unintentional biased processing of threat-relevant information. Therefore, the addition of a computer-delivered bottom-up intervention to ASAT could potentially increase potency (relative to extant "top-down" only interventions) without greatly increasing the logistic burden of the study (i.e., by increasing the sample size).

With regard to interventions, we use the term "top-down" to denote interventions that target conscious and intentional processing (e.g., psychoeducation, cognitive restructuring) and "bottom-up" to denote interventions that target unconscious, unintentional processing (e.g., cognitive bias modification). Additionally, it should be noted that some theorists (See Moors and De Houwer, 2006 for a review) have conceptualized automatic cognitive processing as containing unique and independent elements other than those reviewed by Teachman et al. (2012). Therefore, the unique components that make up automatic processing is a research area that is still evolving.

A constellation of procedures known as cognitive bias modification (CBM) have shown promise in the bottom-up computer-delivered treatment of anxiety psychopathology by directly manipulating cognitive biases, including AS. Unlike cognitive behavioral therapy (CBT; top-down), CBM (bottom-up) is not designed to alter the manner in which individuals respond to anxiogenic thoughts, but rather to directly change the underlying cognitive processes that give rise to such thinking (MacLeod and Mathews, 2012). Recent work on CBM has examined changing these biased interpretations (Brettschneider et al., 2015; Joormann et al., 2015; Oglesby et al., 2016). Interpretation bias (IB) in those with anxiety refers to selective information processing, favoring negative/threatening interpretations of ambiguous information. CBM for IB (CBM-I) involves presenting individuals with ambiguous scenarios to train them to make either threatening or non-threatening interpretations. IB is modified by structuring feedback to reinforce non-threatening over threatening interpretations.

Given that AS involves misinterpretation of internal sensations, it appears to be an excellent candidate for CBM-I. Several preliminary CBM-I's for AS have been investigated (Clerkin et al., 2015; MacDonald et al., 2013; Steinman and Teachman, 2010). Steinman and Teachman (2010) found a significant effect of positive CBM-I training on post-task AS in undergraduates with elevated AS. Next, MacDonald et al. (2013) tested community participants and found a significant reduction in self-reported AS that was maintained through a 48-h follow-up. Lastly, Clerkin et al. (2015) found decreases in self-reported AS over two CBM-I sessions (that were on average 2 days apart); however, there was not a significant difference between decreases in the active (28%) and control (20%) conditions. Interestingly, none of the CBM-I intervention studies found significant group differences in response to symptom induction exercises (e.g., straw-breathing, chair spinning, etc.), despite significant self-reported AS reductions following the intervention. These discrepant findings could result from inadequate power as the relative effects seemed comparable between these studies and Schmidt et al. (2007), which had by far ($n = 404$) the largest sample of these studies.

One method to increase statistical power is to increase sample size; however, a more resource effective method is to increase the effect of the intervention. In the present study, we wanted to extend the literature by examining whether adding a "bottom-up" AS intervention (CBM-I) increases the effect of a "top-down" computer-delivered psychoeducation intervention. To test this aim, we added an active or control computer-delivered CBM-I intervention to an active psychoeducation module (ASAT-P; created by removing the interoceptive exposure portion of the ASAT module used in Schmidt et al., 2007). This psychoeducation module discussed misinterpretations related to bodily sensations commonly held by individuals with elevated AS (e.g., if my heart is racing it signifies an impending heart attack) and provided corrective information as to the lack of validity of these beliefs.

In sum, the goal of the present study was to create and test a dissemination-friendly brief AS intervention that improved upon previous AS interventions by adding a CBM-I (bottom-up) to a traditional top-down (i.e., psychoeducation) intervention. We hypothesized that adding CBM-I to a psychoeducation-based AS amelioration intervention (ASAT-P+) would result in significant reductions in AS compared to a control condition that added a placebo CBM-I to the psychoeducation intervention (ASAT-P−). Specifically, participants in the ASAT-P+ condition would: report significantly less self-reported AS (post-treatment and at a one-month follow-up) and show significantly reduced panic responding in response to a CO_2 symptom induction exercise than those in the ASAT-P− condition. Lastly, the CBM-I word-sentence pairs were created for this study. Accordingly, its efficacy had never been assessed. Therefore, we placed the CBM-I (active or placebo) intervention before the ASAT (all participants received active psychoeducation) intervention to test CBM-I specific hypotheses. Based on the reviewed studies, we believed the active CBM-I, assessed before participants received ASAT-P, would lead to self-reported reductions in AS and that change in interpretation bias would be the mechanism (significant mediation of the relationship between treatment condition and change in AS).

1. Method

1.1. 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 university's Institutional Review Board. Participants then completed the battery of baseline measures [e.g., Anxiety Sensitivity Index-3 (ASI-3), Beck Anxiety Index (BAI)] and were randomized with a planned allocation ratio of 1:1 to the active CBM-I add-on condition (ASAT-P+) or control CBM-I add-on condition (ASAT-P−). The simple randomization sequence (1 = ASAT-P+; 2 = ASAT-P−) 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 CBM-I session, participants completed the ASI-3. Next, all participants received the psychoeducation module. Lastly, they completed a battery of post-intervention self-report measures and the vital capacity breath CO_2 challenge. One month from experiment completion the participants were e-mailed the link to a secure website to complete the ASI-3.

1.1.1. Participants

Participants (n = 61) with ASI-3 scores 1.5 SD above the mean were recruited through the psychology department participant pool between September 2012 and April 2013. Pre-intervention demographic characteristics are included in Table 1 and participant flow is included in the CONSORT diagram (Fig. 1). Intervention/data collection occurred in private, sound-attenuated experiment rooms. The required sample size was determined using a power analysis program (Faul et al., 2007) and a large effect size based on previous AS intervention work (Keough and Schmidt, 2012).

1.1.2. Self-report measures

1.1.2.1. Acute panic inventory (API). The API measures symptoms of arousal associated with panic attacks (Liebowitz et al., 1984). It is widely used with CO_2 challenges (Schmidt et al., 2007). The API included a Subjective Units of Distress (SUDS) rating (0–100) of self-reported fear. Baseline internal consistency of the scale was adequate (Cronbach's $\alpha = 0.76$).

1.1.2.2. 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). Baseline internal consistency of the scale was good (Cronbach's $\alpha = 0.85$).

Table 1
Descriptive statistics for baseline measures by treatment condition.

	Active condition		Control condition		F
	Mean	SD	Mean	SD	
ASI-3 total	29.43	11.28	27.74	11.43	0.34
Beck anxiety index	21.00	10.39	19.65	10.63	0.25
Age	18.83	1.02	18.68	0.83	0.43
	Percentage		Percentage		χ^2
Sex					1.39
Male	40.0%		25.8%		
Female	60.0%		74.2%		
Ethnicity					1.00
Caucasian	96.7%		90.3%		
African American	3.3%		9.7%		

Note. $N = 30$ for active condition and $N = 31$ for control condition. ASI-3 = Anxiety Sensitivity Index-3.

1.1.2.3. Beck anxiety inventory (BAI). The BAI is a widely used measure of panic/anxiety symptoms that has been evidenced strong psychometric properties (Beck et al., 1988). Baseline internal consistency of the scale was good (Cronbach's $\alpha = 0.89$).

1.1.3. Behavioral measures

1.1.3.1. 35% CO2 vital capacity inhalation. All participants inhaled a single vital capacity (VC) breath mixture of 35% CO_2 and 65% O_2. All participants were provided with the following instructions regarding the CO_2 procedure: “You will be taking a single vital capacity breath of a gas containing 35% carbon dioxide and 65% oxygen. You will need to exhale completely, and then take a full and complete inhalation using the mouthpiece. Please hold the inhalation for 5 s. I will count to five for you and then you can exhale.” Next, the participant practiced the procedure (i.e., taking a deep VC breath and holding it). Following the practice trial, the experimenter assisted the participant in taking a VC breath delivered via a 4.8L venti-comp bag filled to capacity. The participant, wearing a nostril clamp, exhaled all of the air in his or her lungs and then inhaled from the venti-comp bag via a one-way flow valve. Gas intake volume was indexed by subtracting the amount of gas inhaled by the participant during the provocation relative to the participant's VC. Vital capacity was assessed and CO_2 intake was measured to ensure each participant inhaled a vital capacity breath. A repeated inhalation was used in the 39% of cases where an initial inhalation was less than 80% of VC. Immediate (API) responses to the challenge were then assessed. In the CO2 challenge analyses, we covaried for pre-inhalation SUDS for two reasons. First, we believe it is the standard in the CO2 literature (Schmidt et al., 2007). Second, it not only controls for subjectivity of SUDS ratings but also differences in state arousal immediately before the inhalation.

1.1.3.2. Panic responding. We utilized a stringent 4-fold criteria for defining panic in reaction to a CO_2 challenge developed by Telch et al. (2011). All of the following criteria had to be satisfied for a post-challenge reaction to be classified as panic response: 1) affirmation of panic during challenge, 2) a sudden pre to post inhalation rise in reported fear (i.e., SUDS) ≥ 30 on a 100-point Likert scale, 3) four or more of the DSM-V panic attack symptoms, and 4) a 13-point pre- to post- inhalation rise on the API.

1.2. Top-down intervention

1.2.1. Psychoeducation (ASAT-P)

All participants received a modified version of ASAT (Schmidt et al., 2007) that we refer to in this manuscript as ASAT-P. The original ASAT includes both psychoeducation along with interoceptive exposure (i.e., hyperventilation) exercises. In previous studies using the full ASAT protocol (Keough and Schmidt, 2012; Schmidt et al., 2007), participants met with a trained study therapist to ask questions or get instruction on interoceptive exposure exercises. In this study, only the psychoeducation portion was utilized to make it more amenable to computer-only delivery. This 30 min computerized presentation describes stress and anxiety sensations and attempts to normalize overreactions to these sensations through the provision of accurate information. The complete presentation (with IE material included) has been shown to be effective at reducing AS (Schmidt et al., 2007), but the modified non-IE version (ASAT-P) has never been empirically evaluated.

1.3. CBM-I conditions

1.3.1. Active (+)

The CBM-I was programmed using E-Prime software (Schneider et al., 2002) and is modeled closely on previous work on CBM for

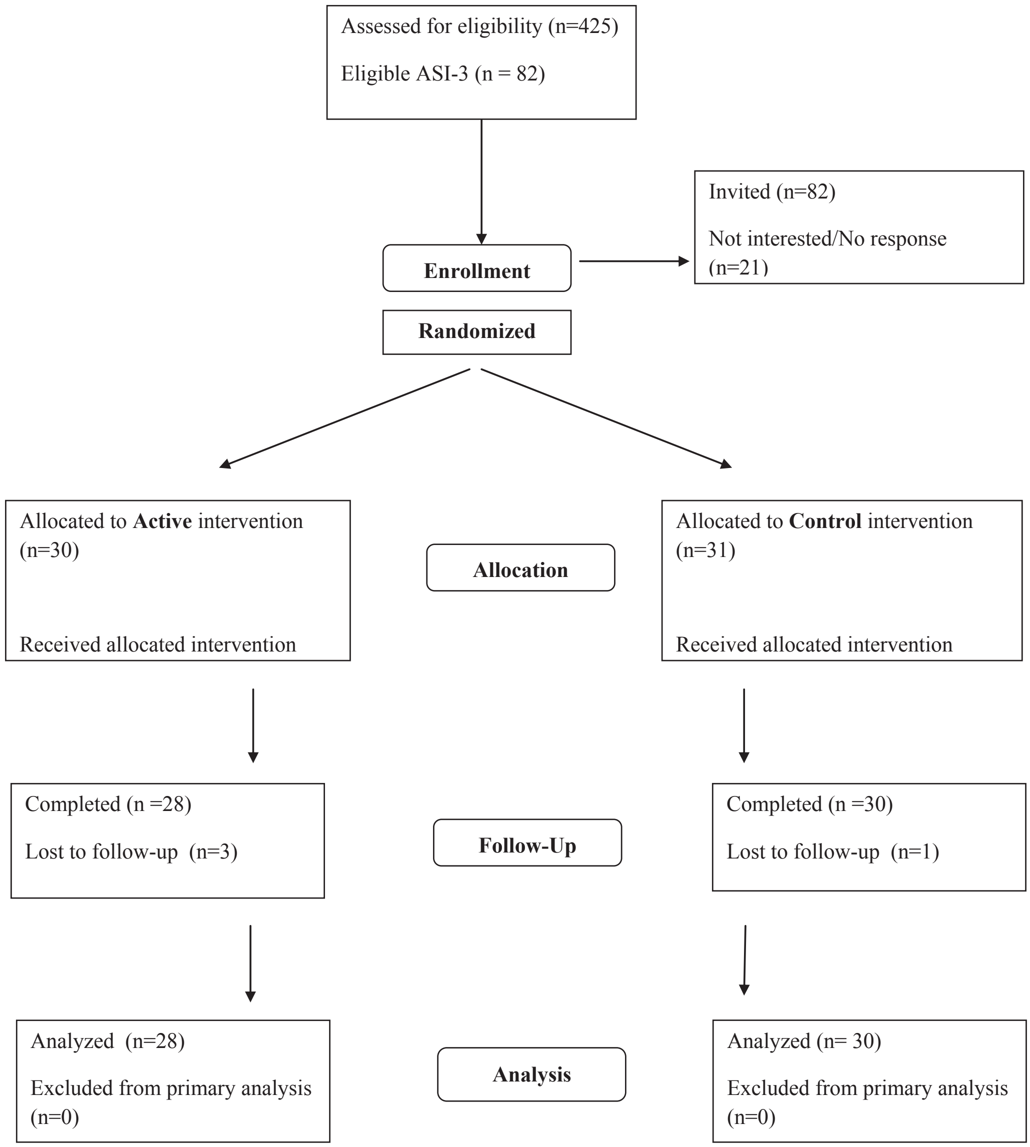

Fig. 1. JARS/CONSORT diagram.

anxiety (Beard and Amir, 2008; Brosan et al., 2011). On each trial, participants were presented with a word (or two-word phrase) for 1 s (e.g., "excited") followed by a sentence (e.g., "You notice your heart is beating faster"). On half the trials, the combination of the word and sentence created a benign meaning (as in the previous example). On the other half of trials, this combination created a threatening meaning (e.g., "stressful" followed by the sentence – "Your mind is full of thoughts"). The word sentence pairings, which were created specifically for this intervention were rated by five independent judges who are published authors on AS. 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. The judges reviewed a list of pairs that had been already revised several times by the authors; therefore, no threshold was used to eliminate items, as all pairs were deemed to have sufficiently high or low valence ratings. Participants were required to judge the relatedness of the word and the sentence, pressing "yes" if they thought the two words were related and "no" if they believe they were unrelated. Participants were given visual feedback during training such that judging the anxious combinations to be "unrelated" and the benign combinations as being "related" would produce a "correct" response. Furthermore, when they judged threatening combinations as being "related" and benign combinations as being "unrelated" they heard a horn blast (approximately 80 dB) and were given feedback that the response was "incorrect". IB is measured by the number of trials in which participants endorsed benign relationships and rejected anxious relationships. 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 5-min break activity (simple math problems). Next, they completed another 80 trials of training. Finally, they were given 40 test trials of novel words and sentences to measure change in IB. The full CBM-I took 15–20 min to complete. Fig. 2 displays the full CBM procedure. This procedure is based on previous IB literature (Brosan et al., 2011).

1.3.2. Control (–)

The procedure for the control CBM-I was identical to the active

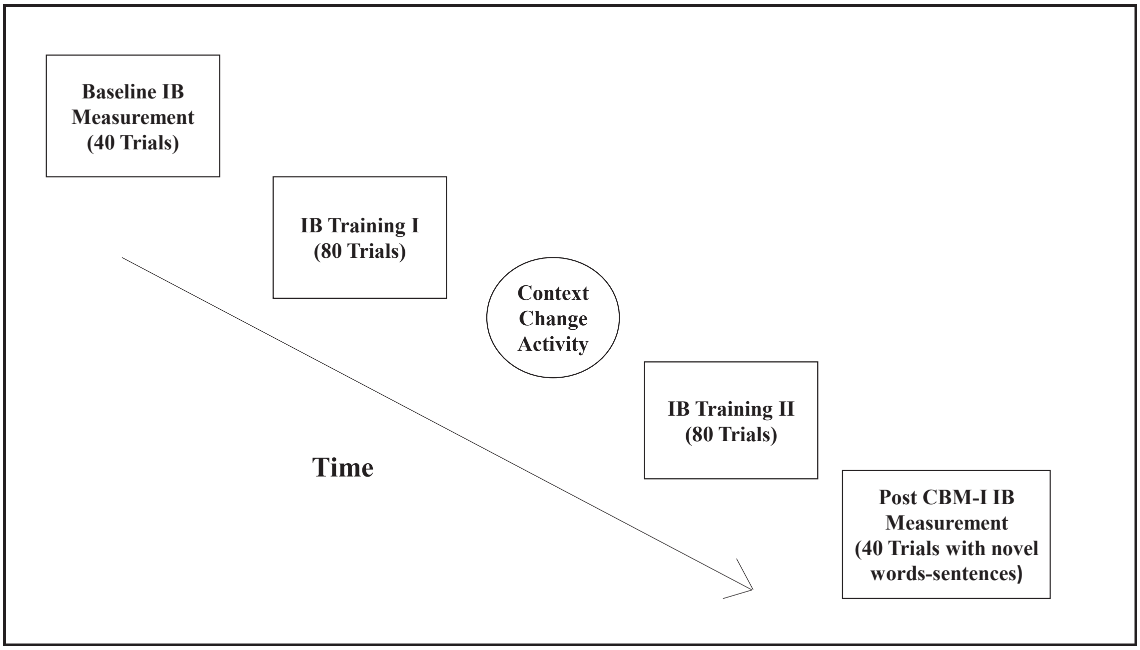

Fig. 2. CBM-I procedural flow.

CBM-I, with the exception that participants were arbitrarily reinforced at a 50% rate. This reinforcement is designed so that on average participants' IB would not be modified, and has been used in previous CBM-I for AS protocols (MacDonald et al., 2013).

2. Results

2.1. Sample and preliminary analysis

Random assignment resulted in fairly even division of participants across the ASAT-P+ ($n = 30$, 49%) and the ASAT-P− conditions ($n = 31$, 51%). Means of the ASI-3, BAI, and several demographic variables are provided in Table 1. Variables were compared across the active and control condition to determine the success of randomization. There were no differences across the ASI-3, the BAI, gender, and ethnicity, indicating that participants appeared to be successfully randomized. There were a total of three participants from the ASAT-P+ condition and one participant from the ASAT-P− condition who did not complete the one-month follow-up. There were no differences in ASI-3 score between those who did and did not complete the 1 month follow-up, $F(1, 59) = 0.314$, $p > 0.05$.

2.2. Primary analyses: combined intervention effects on anxiety sensitivity

The effect of the intervention was evaluated post-intervention and at a one-month follow-up. Means and standard errors of ASI-3 scores at baseline, post-intervention, and at follow-up are provided in Fig. 3. The effect of treatment condition was examined using linear regression (see Table 2). Baseline ASI-3 scores were entered in step 1 and the condition (1 = ASAT-P+, 2 = ASAT-P−) was added in step 2. Accounting for baseline ASI-3 scores, post-intervention ASI-3 scores were significantly lower in the ASAT-P+ condition than in the ASAT-P− condition ($\beta = 0.24$, $p < 0.05$). Cohen's d (calculated based on the formula provided by Feingold, 2009) was 0.99, indicating a large effect of the ASAT-P+ intervention. In addition, accounting for baseline ASI-3 scores, month 1 ASI-3 scores remained significantly lower in the ASAT-P+ condition than in the ASAT-P− condition ($\beta = 0.26$, $p < 0.05$), with an effect size estimate of 1.18. These models were re-analyzed, including an interaction term between baseline ASI-3 scores and treatment condition. There was no significant moderation effect of baseline ASI-3 scores.

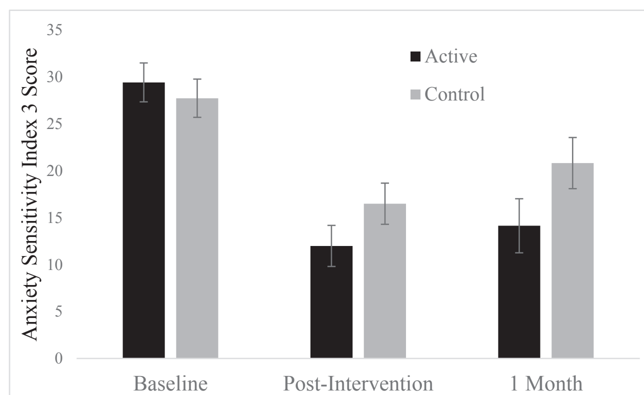

Fig. 3. Anxiety Sensitivity Index-3 Scores by treatment condition across the intervention period. Error bars represent standard errors.

Table 2
Examination of intervention effects on ASI-3 at post-intervention and 1 month follow-up.

Predictor	Post-intervention		Month 1 follow-up	
	ΔR^2	β	ΔR^2	β
Step 1	0.28		0.24	
Baseline ASI-3		0.53^{***}		0.49^{***}
Step 2	0.34		0.31	
Baseline ASI-3		0.56^{***}		0.51^{***}
Treatment condition		0.24^{*}		0.26^{*}

Note. ASI-3 = Anxiety Sensitivity Index-3.
$^{***}p \le 0.001$, $^{*}p \le 0.05$.

2.3. Combined intervention effects on biological challenge

The effects of the intervention on subjective ratings of a CO_2 challenge were also examined. Logistic regression models were examined for presence of panic following a 35% CO_2 challenge. Forty-two participants completed the CO_2 challenge. Ten participants were ineligible for the challenge based on criteria set by the IRB including presence of asthma, benzodiazepine medication use, hypertension and migraines. Eight participants exercised their right to refuse to complete the CO_2 challenge and four participants did not have CO_2 data due to administrative problems (e.g., issues with CO_2 tank). Of these individuals 4 were in the ASAT-P+ condition and eight were in the ASAT-P− condition. There were no significant differences in baseline SUDS between participants who did and did not complete the CO_2 challenge ($p > 0.30$). The model contained 2 predictor variables (pre-challenge SUDS and treatment condition). Pre-challenge SUDS ratings were included to control for the relative subjectivity of SUDS ratings. The full model significantly predicted the presence of panic, $\chi 2$ ($df = 2$, n = 42) = 7.77, $p = 0.02$. The covariate, pre-challenge SUDS (OR = 0.91, Wald = 2.01, $p = 0.15$) was not significantly related to panic status. However, treatment condition (OR = 6.34, 95% CI = 1.07–37.66, Wald = 4.12, $p = 0.04$) was a significant predictor of panic response. Participants in the ASAT-P− only condition (33%) were more than three times as likely to have had a post-CO_2 panic response than participants in the ASAT-P+ condition (9%).

2.4. CBM-I interpretation bias change & mediation analyses

We examined change in interpretation bias as the difference between the percentage of "Correct" responses on 40 novel word-sentence pairs and the percentage of "Correct" scores during the initial 40 "Test" trials before participants were given feedback. In the active CBM-I condition participants answered 61% correctly at baseline and 86% correctly post-CBM-I ($t = -9.46$, $p < 0.001$). In contrast, the control CBM-I condition answered 60% correctly at baseline and 58% correctly post-CBM-I ($t = 0.67$, $p = 0.507$). Thus, it appears the active intervention was successful at training IB. This model was re-analyzed, including an interaction between baseline.

IB and condition. This interaction was not significant.

As recommended, particularly for small samples, estimates of indirect effects were generated using bootstrapping analysis (Preacher and 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 indirect effect of change in interpretive bias on one-month follow-up anxiety sensitivity (ASI-3) was evaluated through simple mediation (Hayes, 2012) controlling for baseline ASI-3, with condition as the independent variable, one-month follow-up ASI-3 score as the dependent variable, and IB change scores during the intervention phase as the mediating variable. Results of 5000 bootstrap resamples demonstrated that the direct effect of condition on follow-up ASI-3 was significant ($B = 8.90$, SE = 4.14, t = 2.15, $p = 0.04$). In addition, the direct effect of condition on change in IB was significant ($B = -0.25$, SE = 0.05, t = −5.40, $p < 0.001$). Critically, the indirect effect of IB change on follow-up ASI-3 scores was significant ($B = -7.30$, SE = 3.91, 95% CI [−16.28, −0.70]).

We also tested baseline to post-intervention change in BAI scores as an alternate mediator. We utilized the same model with change in BAI scores in lieu of change in IB. However, the indirect effect of BAI change on follow-up ASI-3 was not significant (95% CI [−2.31, 1.11]).

3. Discussion

The aim of the present study was to evaluate the effect of adding a bottom-up computer-delivered AS intervention to a top-down psychoeducation intervention. Findings indicated that the addition of CBM-I to psychoeducation was successful in reducing self-reported AS, and that these significant reductions were maintained at a one-month follow-up. The study also found significantly fewer participants in the ASAT-P+ condition reported a panic response to a VC breath CO_2 challenge. Lastly, mediation analyses, covarying for baseline AS, found that the hypothesized mechanism, change in interpretation bias, mediated the relationship between treatment condition and follow-up AS.

The results of this study show there is potential benefit to combining top-down and bottom-up interventions as pathological anxiety appears to be the result of a dysfunctional system consisting of both of these processing modalities and their interaction (Derakshan and Eysenck, 2009; Kim et al., 2011). Indeed, neuroscience research has found evidence of failures in both top-down regulation (Bishop et al., 2004; Williams et al., 2006) and bottom-up processing (Rauch et al., 2000) in the cortical structures of anxiety disorders patients versus healthy controls. An analog of combining top-down and bottom-up cognitive interventions is combining psychotherapy (i.e., conscious, inefficient, intentional, controllable) and pharmacotherapy (i.e., unconscious, efficient, unintentional, uncontrollable). Several randomized controlled trials have shown improved outcomes with combined psychotherapy and pharmacotherapy for anxiety disorders including panic disorder (Barlow et al., 2000), social phobia (Blomhoff et al., 2001), and GAD (Power et al., 1990). However, in a review of this literature, Otto et al. (2005) concluded that adding medication to anxiety psychotherapy is a complex decision and should not be considered the default strategy. In addition, using medication as the bottom-up intervention may not be ideal because the majority of evidence suggests that treatment gains are lost once medication is stopped (Pollack and Smoller, 1996). Even more concerning, in combined psychotherapy/pharmacotherapy treatments the discontinuation of medication can remove the benefits of psychotherapy as well (Barlow et al., 2000; Haug et al., 2003).

Conceptual models of anxiety from cognitive theorists (Beck et al., 1985; Clark, 1986) posit that anxiety is caused and maintained by both the content of cognitive biases (e.g., threat) and biased processes (e.g., interpretation). It follows then that effective computer-delivered treatments for anxiety disorders must correct both the threatening content and the biased process to have maximum potency and the widest impact. In this intervention we have attempted to correct biased content through psychoeducation and biased processes through CBM-I. At first glance it appears top-down and bottom-up constructs must be independent because a process cannot logically be both intentional and unintentional, or conscious and unconscious, simultaneously. However, the results of the study provide indirect evidence for independence (i.e., CBM-I alone condition showed significant AS reductions before psychoeducation and sham-CBM-I with psychoeducation showed significant reductions) and synergy (i.e., the ASAT-P+ had the greatest reductions). Future work in this area could address the degree to which these intervention types are truly independent and/or synergistic, or if it is possible for some anxiety processes to be partially conscious and unconscious concurrently.

Despite its brevity and low resources needed, the combined ASAT-P+ intervention for AS appears to be very effective; reducing AS by 59% post-intervention and maintaining 52% reduction at a one-month follow-up. In comparison, previous AS interventions resulted in mean AS reductions of 28% (therapist delivered psychoeducation plus IE; Keough and Schmidt, 2012), 30% (computer/

therapist delivered psychoeducation plus IE; Schmidt et al., 2007), 32% (computerized psychoeducation plus IE; Schmidt et al., 2014), 34% (group smoking plus AS intervention; Feldner et al., 2008), 41% (exercise; Broman-Fulks and Storey, 2008), and 43% (workshop; Gardenswartz and Craske, 2001). Making comparisons across different AS treatments is difficult based on different levels of baseline AS, different measures (ASI vs. ASI-3), and different lengths of treatment. However, it is important to remember that this intervention is quite undemanding; it requires only a single-session lasting approximately 45–50 min and no trained clinicians. One possibility for the increased effectiveness is the novel combination of a psychoeducation module with a CBM-I intervention. Indirect support for this assertion comes from evidence that adjunctive CBM for attention biases (CBM-A) improved PTSD outcomes for individuals with PTSD going through prolonged exposure or cognitive processing therapy (Kuckertz et al., 2014), and a recent meta analysis that concluded CBM-I can be employed as a useful complementary treatment to usual psychotherapies (Menne-Lothmann et al., 2014). However, it should be noted that adjunctive CBM-A did not significantly improve cognitive behavior therapy for social phobia among 134 women diagnosed with social phobia (Rapee et al., 2013) and a recent meta-analysis including primarily CBM-A studies concluded it is possible that CBM have no significant clinically relevant effects (Cristea et al., 2015).

In regard to CBM-I findings, the current study found that change in IB significantly mediated the relationship between treatment condition and post-treatment ASI-3 total. These findings are consistent with other CBM-I interventions that have resulted in significant IB change and provide evidence against the idea that CBM merely exposes individuals repeatedly to threatening stimuli, decreasing their fear response (versus actually changing IB) (See Beard, 2011 and Salemink et al., 2010 for discussions).

It is important to acknowledge limitations in the current study design. One limitation is the use of an analog sample. However, this sample was elevated on the construct of interest (AS) at mean levels comparable with pre-treatment anxiety disorders patients (Taylor et al., 2007), which suggests this intervention may be helpful in reducing AS in clinical populations. In addition, the sample was relatively small. However, previous research suggested that we would find large intervention effects (Keough and Schmidt, 2012) and the study was sufficiently powered to examine the hypotheses. Replication and extension in a larger, clinical sample of individuals with anxiety disorders is a needed follow-up before strong conclusions can be drawn about the clinical utility of this intervention. Second, our contention that adding CBM-I to psychoeducation would increase (between group) statistical power relies on the contention that there is a synergistic effect from combining these interventions. Although we believe this is a reasonable expectation given extant literature that anxiety disorders result from and are maintained by a combination of bottom-up and top-down processing (Clark and Beck, 2010); this aspect is not explicitly testable with the current design. Third, our alternative mediator analysis used the BAI. However, the BAI may not have sufficient reactivity to detect changes over a one-hour period. Future work in this area would benefit from measuring anxiety with a state measure such as the State-Trait Anxiety Inventory-State version (Spielberger, 1983). Lastly, we did not include an independent measure of change in interpretation bias. However, training effects on the self-report and fear induction exercises, largely mitigate this concern.

In sum, this study suggests an extremely brief, computerized intervention can result in substantial reductions in AS. AS is the most well-known risk factor for anxiety disorders (APA, 2013; Olatunji and Wolitzky-Taylor, 2009). Despite the many well-established treatments for anxiety disorders (Chambless and Ollendick, 2001), anxiety disorders continue to result in substantial burden to society (Kessler et al., 2005), likely because of issues such as access, cost and stigma. This initial pilot study needs to be replicated in larger more clinically severe samples. However, by offering a potential top-down and bottom-up solution to these crucial dissemination issues, these results suggest that computer-delivered interventions for AS could one day reduce the anxiety burden as a first-step in a stepped-care model of anxiety treatment.

Author contributions

Dr. Capron led the creation of the CBM-I intervention, supervised the revision of the psychoeducation intervention, was principal investigator of the execution of the study and completed the initial draft of the manuscript.

Mr. Norr assisted in the creation of the interventions and revised the manuscript.

Mr. Allan conducted the majority of analyses and wrote the majority of the results section.

Dr. Schmidt supervised the project and provided critical feedback on the manuscript.

Funding

No funding was received for this study.

Conflicts of interest

All authors declare that they have no conflicts of interest.

Acknowledgments

The authors would like to thank Joshua Russell and Brittany Dane for their assistance creating the intervention and running participants.

References

APA, 2013. Diagnostic and Statistical Manual of Mental Disorders (DSM-5®). American Psychiatric Pub.

Bargh, J.A., 1994. The four horsemen of automaticity: Awareness, intention, efficiency, and control in social cognition. In: Wyer Jr., R.S., Srull, T.K. (Eds.), Handbook of social cognition, Vol. 1. LawrenceErlbaum Associates, Hillsdale, NJ, England, pp. 1–4.

Barlow, D.H., Gorman, J.M., Shear, M., Woods, S.W., 2000. Cognitive-behavioral therapy, imipramine, or their combination for panic disorder: a randomized controlled trial. JAMA 283 (19), 2529–2536.

Beard, C., 2011. Cognitive bias modification for anxiety: current evidence and future directions. Expert. Rev. Neurother. 11 (2), 299–311.

Beard, C., Amir, N., 2008. A multi-session interpretation modification program: changes in interpretation and social anxiety symptoms. Behav. Res. Ther. 46 (10), 1135–1141.

Beck, A.T., Emery, G., Greenberg, R.L., 1985. Anxiety Disorders and Phobias: a Cognitive Perspective. Basic Book, New York.

Beck, A.T., Brown, G., Epstein, N., Steer, R.A., 1988. An inventory for measuring clinical anxiety – psychometric properties. J. Consult. Clin. Psych. 56 (6), 893–897.

Bishop, S., Duncan, J., Brett, M., Lawrence, A.D., 2004. Prefrontal cortical function and anxiety: controlling attention to threat-related stimuli. Nat. Neurosci. 7, 184–188.

Blomhoff, S., Haug, T.T., Hellström, K., Holme, I., Humble, M., Madsbu, H.P., Wold, J.E., 2001. Randomised controlled general practice trial of sertraline, exposure therapy and combined treatment in generalised social phobia. Brit. J. Psychiatry 179, 23–30.

Brettschneider, M., Neumann, P., Berger, T., Renneberg, B., Boettcher, J., 2015. Internet-based interpretation bias modification for social anxiety: a pilot study. J. Behav. Ther. Exp. Psy. 49, 21–29.

Broman-Fulks, J.J., Storey, K.M., 2008. Evaluation of a brief aerobic exercise intervention for high anxiety sensitivity. Anxiety Stress Copin. 21, 117–128.

Brosan, L., Hoppitt, L., Shelfer, L., Sillence, A., Mackintosh, B., 2011. Cognitive bias modification for attention and interpretation reduces trait and state anxiety in anxious patients referred to an out-patient service: results from a pilot study. J. Behav. Ther. Exp. Psy 42, 258–264.

Chambless, D.L., Ollendick, T.H., 2001. Empirically supported psychological

interventions: controversies and evidence. Annu. Rev. Psychol. 52, 685–716.
Clark, D.M., 1986. A cognitive approach to panic. Behav. Res. Ther. 24, 461–470.
Clark, D.A., Beck, A.T., 2010. Cognitive theory and therapy of anxiety and depression: convergence with neurobiological findings. Trends Cogn. Sci. 14, 418–424.
Clerkin, E.M., Beard, C., Fisher, C.R., Schofield, C.A., 2015. An attempt to target anxiety sensitivity via cognitive bias modification. PLoS One 10 (2).
Cristea, I.A., Kok, R.N., Cuijpers, P., 2015. Efficacy of cognitive bias modification interventions in anxiety and depression: meta-analysis. Brit. J. Psychiatry 206, 7–16.
Derakshan, N., Eysenck, M.W., 2009. Anxiety, processing efficiency, and cognitive performance: new developments from attentional control theory. Eur. Psychol. 14, 168–176.
Faul, F., Erdfelder, E., Lang, A.-G., Buchner, A., 2007. G*Power 3: a flexible statistical power analysis for the social, behavioral, and biomedical sciences. Behav. Res. Methods 39, 175–191.
Feingold, A., 2009. Effect sizes for growth-modeling analysis for controlled clinical trials in the same metric as for classical analysis. Psychol. Methods 14, 43.
Feldner, M.T., Zvolensky, M.J., Babson, K., Leen-Feldner, E.W., Schmidt, N.B., 2008. An integrated approach to panic prevention targeting the empirically supported risk factors of smoking and anxiety sensitivity: theoretical basis and evidence from a pilot project evaluating feasibility and short-term efficacy. J. Anxiety Disord. 22, 1227–1243.
Gardenswartz, C.A., Craske, M.G., 2001. Prevention of panic disorder. Behav. Ther. 32, 725–737.
Haug, T.T., Blomhoff, S., Hellstrøm, K., Holme, I., Humble, M., Madsbu, H.P., Wold, J.E., 2003. Exposure therapy and sertraline in social phobia: I-year follow-up of a randomised controlled trial. Brit. J. Psychiatry 182, 312–318.
Hayes, A.F., 2012. PROCESS: a Versatile Computational Tool for Observed Variable Mediation, Moderation,and Conditional Process Modeling.
Hofmann, S.G., Smits, J.A., 2008. Cognitive-behavioral therapy for adult anxiety disorders: a meta-analysis of randomized placebo-controlled trials. J. Clin. Psychiatry 69, 621.
Joormann, J., Waugh, C.E., Gotlib, I.H., 2015. Cognitive bias modification for interpretation in major depression effects on memory and stress reactivity. Clin. Psychol. Sci. 3, 126–139.
Keough, M.E., Schmidt, N.B., 2012. Refinement of a brief anxiety sensitivity reduction intervention. J. Consult. Clin. Psych. 80, 766–772.
Kessler, R.C., Demler, O., Frank, R.G., Olfson, M., Pincus, H.A., Walters, E.E., Wang, P., Wells, K.B., Zaslavsky, A.M., 2005. Prevalence and treatment of mental disorders, 1990 to 2003. New Engl. J. Med. 352, 2515–2523.
Kim, M.J., Loucks, R.A., Palmer, A.L., Brown, A.C., Solomon, K.M., Marchante, A.N., Whalen, P.J., 2011. The structural and functional connectivity of the amygdala: from normal emotion to pathological anxiety. Behav. Brain Res. 223, 403–410.
Kuckertz, J.M., Amir, N., Boffa, J.W., Warren, C.K., Rindt, S.E.M., Norman, S., McLay, R., 2014. The effectiveness of an attention bias modification program as an adjunctive treatment for post-traumatic stress disorder. Behav. Res. Ther. 0, 25–35.
Liebowitz, M.R., Gorman, J.M., Fyer, A.J., Dillon, D.J., Klein, D.F., 1984. Effects of naloxone on patients with panic attacks. Am. J. Psychiatry 141, 995–997.
MacDonald, E.M., Koerner, N., Antony, M.M., 2013. Modification of interpretive bias: impact on anxiety sensitivity, information processing and response to induced bodily sensations. Cogn. Ther. Res. 37, 860–871.
Menne-Lothmann, C., Viechtbauer, W., Höhn, P., Kasanova, Z., Haller, S.P., Drukker, M., van Os, J., Wichers, M., Lau, J.Y., 2014. How to boost positive interpretations? A meta-analysis of the effectiveness of cognitive bias modification for interpretation. PLoS One 9, e100925.
MacLeod, C., Mathews, A., 2012. Cognitive bias modification approaches to anxiety. Annu. Rev. Clin. Psychol. 8), 189–217.
Moors, A., De Houwer, J., 2006. Automaticity: A theoretical and conceptual analysis. Psychological Bulletin 132 (2), 297–326. http://dx.doi.org/10.1037/0033-2909.132.2.297.
Oglesby, M.E., Raines, A.M., Short, N.A., Capron, D.W., Schmidt, N.B., 2016. Interpretation bias for uncertain threat: a replication and extension. J. Behav. Ther. Exp. Psy. 51, 35–42.
Olatunji, B.O., Wolitzky-Taylor, K.B., 2009. Anxiety sensitivity and the anxiety disorders: a meta-analytic review and synthesis. Psychol. Bull. 135, 974–999.
Otto, M.W., Smits, J.A.J., Reese, H.E., 2005. Combined psychotherapy and pharmacotherapy for mood and anxiety disorders in adults: review and analysis. Clin. Psychol. Sci. Pr. 12), 72–86.
Pollack, M.H., Smoller, J.W., 1996. Pharmacologic Approaches to Treatment-resistant Panic Disorder. Challenges in Clinical Practice: Pharmacologic and Psychosocial Strategies. Guilford Press, New York, NY, US, pp. 89–112.
Power, K., Simpson, R., Swanson, V., Wallace, L., 1990. Controlled comparison of pharmacological and psychological treatment of generalized anxiety disorder in primary care. Br. J. Gen. Pract. 40, 289–294.
Preacher, K.J., Hayes, A.F., 2004. SPSS and SAS procedures for estimating indirect effects in simple mediation models. Behav. Res. Methods Ins. Com. 36, 717–731.
Rapee, R.M., MacLeod, C., Carpenter, L., Gaston, J.E., Frei, J., Peters, L., Baillie, A.J., 2013. Integrating cognitive bias modification into a standard cognitive behavioural treatment package for social phobia: a randomized controlled trial. Behav. Res. Ther. 51, 207–215.
Rauch, S.L., Whalen, P.J., Shin, L.M., McInerney, S.C., Macklin, M.L., Lasko, N.B., Orr, S.P., Pitman, R.K., 2000. Exaggerated amygdala response to masked facial stimuli in posttraumatic stress disorder: a functional MRI study. Biol. Psychiatry 47, 769–776.
Reiss, S., Peterson, R.A., Gursky, D.M., McNally, R.J., 1986. Anxiety sensitivity, anxiety frequency and the prediction of fearfulness. Behav. Res. Ther. 24, 1–8.
Salemink, E., van den Hout, M., Kindt, M., 2010. How does cognitive bias modification affect Anxiety? Mediation analyses and experimental data. Behav. Cogn. Psychoth. 38, 59–66.
Schmidt, N.B., Capron, D.W., Raines, A.M., Allan, N.P., 2014. Randomized clinical trial evaluating the efficacy of a brief intervention targeting anxiety sensitivity cognitive concerns. J. Consult. Clin. Psychol. 82, 1023–1033.
Schmidt, N.B., Eggleston, A.M., Woolaway-Bickel, K., Fitzpatrick, K.K., Vasey, M.W., Richey, J.A., 2007. Anxiety Sensitivity Amelioration Training (ASAT): a longitudinal primary prevention program targeting cognitive vulnerability. J. Anxiety Disord. 21 (3), 302–319.
Schmidt, N.B., Lerew, D.R., Jackson, R.J., 1997. The role of anxiety sensitivity in the pathogenesis of panic: prospective evaluation of spontaneous panic attacks during acute stress. J. Abnorm. Psychol. 106, 355–364.
Schmidt, N.B., Zvolensky, M.J., Maner, J.K., 2006. Anxiety sensitivity: prospective prediction of panic attacks and Axis I pathology. J. Psychiatry Res. 40, 691–699.
Schneider, W., Eschman, A., Zuccolotto, A., 2002. E-prime (Version 1.1). Psychology Software Tools, Pittsburgh, PA.
Spielberger, C.D., 1983. Manual for the State-trait Anxiety Inventory (STAI).
Steinman, S.A., Teachman, B.A., 2010. Modifying interpretations among individuals high in anxiety sensitivity. J. Anxiety Disord. 24, 71–78.
Taylor, S., Koch, W.J., McNally, R.J., 1992. How does anxiety sensitivity vary across the anxiety disorders. J. Anxiety Disord. 6, 249–259.
Taylor, S., Zvolensky, M.J., Cox, B.J., Deacon, B., Heimberg, R.G., Ledley, D.R., Abramowitz, J.S., Holaway, R.M., Sandin, B., Stewart, S.H., 2007. Robust dimensions of anxiety sensitivity: development and initial validation of the Anxiety Sensitivity Index-3. Psychol. Asses. 19, 176.
Teachman, B.A., Joormann, J., Steinman, S.A., Gotlib, I.H., 2012. Automaticity in anxiety disorders and major depressive disorder. Clinical psychology review 32 (6), 575–603.
Telch, M.J., Harrington, P.J., Smits, J.A.J., Powers, M.B., 2011. Unexpected arousal, anxiety sensitivity, and their interaction on CO2-induced panic: further evidence for the context-sensitivity vulnerability model. J. Anxiety Disord. 25, 645–653.
Watt, M.C., Stewart, S.H., Lefaivre, M.J., Uman, L.S., 2006. A brief cognitive-behavioral approach to reducing anxiety sensitivity decreases pain-related anxiety. Cogn. Behav. Ther. 35, 248–256.
Williams, L.M., Kemp, A.H., Felmingham, K., Barton, M., Olivieri, G., Peduto, A., Gordon, E., Bryant, R.A., 2006. Trauma modulates amygdala and medial prefrontal responses to consciously attended fear. NeuroImage 29 (2), 347–357.