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Attention modification program in individuals with Generalized Anxiety Disorder

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Abstract

Research suggests that individuals with Generalized Anxiety Disorder (GAD) show an attention bias for threat-relevant information. However, few studies have examined the causal role of attention bias in the maintenance of anxiety and whether modification of such biases may reduce pathological anxiety symptoms. In the current paper, we tested the hypothesis that an eight-session attention modification program would (a) decrease attention bias to threat and (b) reduce symptoms of GAD. Participants completed a probe detection task by identifying letters ("E" or "F") replacing one member of a pair of words. We trained attention by including a contingency between the location of the probe and the non-threat word in one group (Attention Modification program, AMP) and not in the other (Attention Control condition, ACC). Participants in the AMP showed change in attention bias and a decrease in anxiety, as indicated by both self report and interviewer measures. These effects were not present in the ACC group. These results are consistent with the hypothesis that attention plays a causal role in the maintenance of GAD and suggest that altering attention mechanisms may effectively reduce anxiety.

Researchers have used a wide range of methods borrowed from cognitive psychology to examine attention bias to threat in individuals with Generalized Anxiety Disorder (GAD;Mathews & MacLeod, 1985, 1986; MacLeod, Mathews, & Tata, 1986; Mogg, Millar, & Bradley, 2000). Research using these methods has consistently produced evidence that patients with GAD preferentially attend to threat relevant stimuli over neutral stimuli when the two compete for processing priority.

In a seminal study, MacLeod, Mathews, and Tata (1986) developed the probe detection paradigm to measure attention bias to threat in GAD. In this paradigm, participants see two words, one above the other, on a computer screen. One word is neutral (e.g., table), and the other word has a threatening meaning (e.g., disease). Participants are asked to read the upper word and ignore the lower word. On critical trials (25%), either the upper or the lower word is replaced with a dot probe (·) and participants are asked to signal the presence of the probe by pressing a button. MacLeod et al. (1986) found that individuals with Generalized Anxiety Disorder detect probes that replace threat words, either in the upper or the lower portion of the screen, faster than probes that replace neutral words. Thus, clinically anxious individuals with GAD consistently showed an attention bias toward threat. On the other hand, non-anxious controls tended to demonstrate an attention bias away from threat in this paradigm. In a later replication of this study, MacLeod and Mathews (1988) calculated an attention bias score in this paradigm by subtracting the mean response latency for trials where the probe replaced the

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threat stimuli from the mean response latency for trials where the probe replaced the neutral stimuli, such that larger numbers revealed greater bias for threat. Using this index, these authors again found that individuals with GAD show an attention bias toward threat.

Two recent reviews of attention bias in anxiety provide clear evidence for an attention bias for threat in GAD. Mogg and Bradley (2005) reviewed 10 studies using the probe detection task and concluded that individuals with GAD show an attention bias for threat that is absent in non-anxious controls. A second meta-analysis conducted by Bar-Haim, Lamy, Pergamin, Bakermans-Kraneberg, and van IJzendoorn (2007) examined attention bias across 172 studies (N = 2263 anxious, N = 1768 non-anxious), concluding that this bias is a consistent and reliable finding using a variety of paradigms. In summary, there is reason to believe that individuals with GAD have an attention bias toward threat relevant information that is absent or less pronounced in non-anxious individuals.

However, most existing research has not allowed the examination of the causal relationship between attention and generalized anxiety disorder because these studies have used correlational designs. Conclusions regarding the causal role of attention bias in maintaining anxiety can only be gleaned from research designs where participants are randomly assigned to conditions and their attention is experimentally manipulated. We now turn to studies using this design.

Macleod, Rutherford, Campbell, Ebsworthy, & Holker (2002) selected 64 undergraduate students from a large participant pool who scored in the middle third of the distribution of a self-report measure of trait anxiety. These participants were then randomly assigned to one of two probe detection tasks that were designed to train attention. Each task comprised 672 trials in which pairs of words (one threat, one neutral) were presented, one above the other, on a computer screen. In the *Attend Threat condition*, probes appeared in the position of the threat word on 576 training trials. The remaining 96 trials were designed to provide a measure of attention bias to threat words. In these test trials, threat word position and probe position were fully crossed as in a typical probe detection task, thus permitting measurement of a participant's tendency to attend preferentially to threat-relevant or neutral words. In the *Attend Neutral condition*, probes appeared in the position of the neutral word on 576 of the trials, with the remaining 96 trials again providing a measure of attention bias. Participants were asked to indicate which type of probe (i.e., single dot or a double dot) had appeared in each trial by pressing a corresponding button as rapidly and accurately as they could. Following the training task and a brief (4 min) rest, the authors manipulated the participants' level of stress by presenting them with a series of unsolvable anagrams and telling them that video recordings of participants who performed particularly well or poorly would be shown to other students. Results indicated that after training participants in the Attend Threat condition showed faster response latencies for detecting probes that replaced threat words than probes that replaced neutral words. Participants in the Attend Neutral condition showed the opposite pattern of results. Moreover, this training extended to word pairs containing novel threat-relevant words and was not confined to specifically trained word pairs. More importantly, participants in the Attend Threat condition reported a greater elevation of negative emotion in response to an experimental stressor.

In their second study, MacLeod et al. (2002) successfully replicated the findings of their first study. During this second study participants' levels of negative affect were measured prior to attention training as well as subsequent to training. This modification provided a baseline against which the effects of attention training could be compared. Results again showed that participants in the Attend Threat condition reported greater elevation of negative emotion in response to the experimental stressor than did those in the Attend Neutral condition. Groups did not differ in their levels of negative affect before the training procedure or after training prior to the stressor. Thus, the difference between the two groups appears to reflect the creation of differing affective vulnerability to stress that is manifested only after the presentation of the stressor. MacLeod et al. (2002) suggested that their findings have potentially important theoretical and practical implications. At the theoretical level, their results provide the strongest support to date for the hypothesis that individual differences in the allocation of attention to threat-relevant information are causally important in mediating vulnerability to negative affectivity. At the practical level, it may be possible to utilize such attention training procedures clinically to ameliorate anxiety symptoms.

Although the results for the above study are consistent with the hypothesis that change in attention bias can lead to change in anxiety vulnerability, several issues need further examination. First, because the two conditions in the above studies both actively trained attention (i.e., either toward threat or away from threat), it is not possible to determine the effect of each training session compared to a baseline condition without training contingencies. Thus, in the current study we compared the effects of an Attention Modification Program (AMP) to a baseline condition where there was no contingency between the location of the probe and the location of the threat or neutral information. We predicted that the AMP would lead to decreased attention to threat and anxiety symptoms compared to the Attention Control Condition (ACC).

Second, although prior research has demonstrated effective attention training procedures in non-patient samples, researchers have not examined the role of attention training in clinical populations. Therefore, we sought to extend attention training procedures to populations with clinical levels of anxiety (i.e., GAD). Application of information processing bias modification to alleviating anxiety symptoms is important because a substantial portion of individuals with GAD presenting for treatment do not respond to current therapies (psychotherapy: 52%, Fisher & Durham 1999; medication: 43%, Gorman, 2003), and for many, the most effective treatments are unavailable or difficult to access. Although researchers have established a relationship between GAD and attention bias to threatening information, this knowledge has yet to be translated into effective treatments for this disorder, thus making examination of such training procedures informative for advancing available treatment options.

Finally, no study has examined attention training procedures with materials specific to each individual's perception of threat. Due to the varied nature of concerns for individuals with GAD, we asked each participant to select the words most relevant to his or her own concern. In summary, the current study examined the effect of a multiple-session attention training program similar to that described by Macleod et al. (2002) on anxiety in individuals with GAD.

Methods

Participants

Participants were 29 treatment-seeking individuals meeting the diagnostic criteria for GAD, based on a diagnostic interview using the Structured Clinical Interview for the DSM-IV (SCID; First, Spitzer, Gibbon, & Williams, 1994). Participants were included in the study if they: (a) had a principal DSM-IV (APA, 1994) Axis I diagnosis of GAD, (b) showed no evidence of suicidal intent, (c) showed no evidence of current substance abuse, (d) had no evidence of current or past schizophrenia, bipolar disorder, or organic mental disorder, (e) were not currently participating in CBT, and (f) had no change in other psychosocial treatments or medication during the 12 weeks prior to study entry. Participants were asked at post-assessment if they had obtained any additional form of treatment during the study. None reported any additional treatment, and no participant dropped from the study.

Materials and Tasks

We administered clinician-rated measures, self-report measures, and information processing measures before the first training session (pre-training) and after the final training session (post-training). Clinician ratings were made by raters blind to treatment condition. The interviewer measures included the SCID Anxiety Disorders Module (First et al., 1994), the Hamilton Rating Scale for Anxiety (Mathews & MacLeod, 1985, 1986HRSA; Hamilton, 1959), and the Hamilton Rating Scale for Depression (HAM-D; Hamilton, 1960). Interview-based assessments were administered to all participants by post doctoral and doctoral level students with at least two years of cognitive-behavioral training. We trained and maintained reliability for all interviews in a three-phase process. The certification procedure required the SCID-IV trainee to first view videotaped and live administrations of the Hamilton scales and SCID-IV by senior interviewers; trainees' ratings of these interviews were then compared to those of the senior interviewer. Next, the trainee administered three HRSA, HAM-D, and SCID-IV interviews in the presence of the senior interviewer with the requirements that (a) the trainee's diagnoses matched those of the senior interviewer and (b) the Hamilton scales ratings differed by no more than five points from the senior interviewer's ratings. Finally, each interviewer maintained a video-based record of their interviews throughout the study. All assessment interviews were reviewed during weekly meetings. If a trained rater no longer met the reliability criterion he or she underwent further training using a different set of training tapes until the criterion was reached again. The inter-rater reliability for the primary outcome measure (HRSA) for the current study was high (r=0.94).

Self-report measures included the Spielberger State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983), the Beck Depression Inventory II (BDI-II; Beck, Steer, & Brown, 1996), the Worry Domains Questionnaire (WDQ; Tallis, Eysenck, & Mathews, 1992), and the Penn State Worry Questionnaire (PSWQ; Meyer et al., 1990). Our information processing measure was an alternate version of the probe detection task. This task was identical in terms of probe location to the ACC procedure, but used an alternate set of stimuli to test for generalizability of the training to a new set of materials.

Procedure

Participants were randomly assigned to one of two conditions: Attention Modification Program (AMP; n = 14) or Attention Control Condition (ACC; n = 15). The participants, independent assessors, and research assistants working with the participants were blind to participant condition. To maintain the blind, each participant received an envelope that contained a condition number that they entered into the computer to start the assigned computer program. Groups did not differ significantly on any clinician-administered or self-report measure at pre-training (*p*s > .2).

The stimuli used in the attention training were derived from words used by McLeod et al. (2002). These authors created two sets of 48 words that were relevant to fears of individuals with general anxiety (sets A and B) and two sets of 48 matched neutral words. In the current study, half of the participants in each group saw a particular word set during training (set A) and were then tested pre-training and post-training using the other word set (set B). Thus, the tests of attention were conducted on a different set of words than the one used during training. To ensure the relevance of the particular words used during training for each participant, we used an idiographic material selection procedure. Prior to training, we asked each participant to rate the emotionality (−3 to +3) of each of the words from the two sets. Twenty words that were rated as most emotionally negative by that participant from the training set were then used as the threat words in the training task. During testing, all words from the alternate set were used.

Participants were seated approximately 30 cm from the computer screen. Words were presented in the center of the screen, approximately 1.5 cm from one another in size 12 Arial font, for 500ms. Word pairs for each participant were presented in a different random order. The computer program was written in Delphi (Borland, Inc.) for this experiment.

Participants in both groups completed the training procedures two times per week (on different days) for four weeks, for a total of eight completed sessions. Participants were informed that they would be randomly assigned to one of two attention training groups. The protocol was described to the participants by the clinician administering the interview as an experimental procedure to determine the efficacy of a computer treatment for anxiety. Participants were informed that, depending on their random group assignment, the computer program they would complete could be either a placebo condition that was not designed to influence their anxiety or an experimental treatment condition that was designed to reduce their anxiety. This protocol was approved by the university's Institutional Review Board (IRB).

Attention Modification Program (AMP)

During each session, participants saw 240 trials that consisted of the various combinations of probe type (E or F), probe position (top orbottom), and word type (Neutral or Threat). Of the 240 trials, 80 included only neutral words: 2 (probe type) × 2 (probe position) × 20 (word pairs). The remaining 160 trials included one neutral word and one threat word: 2 (probe type) × 2 (probe position) × 2 (threat word position) × 20 (word pairs). On trials where participants saw one neutral word and one threat word (i.e., 66% of the trials), the probe always followed the neutral word. Thus, although there was no specific instruction to direct attention away from threat word, on 66% of the trials the position of the neutral word indicated the position of the probe.

Attention Control Condition (ACC)

The ACC condition was identical to the AMP procedure except that during the presentation of the trials where a threat word was present, the probe appeared with equal frequency in the position of the threat and neutral word. Thus, neither threat nor neutral words provided information regarding the position of the probe, and there was no contingency between the position of either threat or neutral words, and the position of the probes.

Results

Groups did not differ on age, education or gender at pre-training (*p*s > .4). Table 1 summarizes these results.

Measure of Attention Bias

Our first goal was to demonstrate change in bias from pre-training to post-training in the AMP group using the novel words from the test set. These data are summarized in Table 2.

We calculated bias scores as per MacLeod et al. (1988); these data are depicted in Figure 1. We submitted participants' bias scores for words in the test set to a 2 (Group: AMP, ACC) × 2 (Time: pre-training, post-training) ANOVA with repeated measures on the second factor. The main effects of Group, $F(1, 27) = 1.53$, $p = .22$, and Time, $F(1, 27) = 0.80$, $p = .39$, were not significant. However, there was a significant interaction of Group × Time, $F(1, 27) = 5.40$, $p < .03$. To follow up this interaction we conducted simple effects analyses. Simple effect of Time revealed that the participants in the AMP group showed a reduction in their attention bias from pre-training to post-training, $t(13) = 3.21$, $p \times .007$, d = 3.3 while those in the ACC group did not, $t(14) = -.84$, $p = .41$, d = -1.0. Simple effect of Group revealed that groups did not differ in their bias score at pre-training, $t(27) = 0.46$, $p = .65$. However the AMP group showed significantly lower bias scores than the ACC group at post-training, $t(27) = 2.18$, $p < .05$.

Measures of Anxiety and Depression

We submitted participants' scores on self-report and interviewer measures to separate 2 (Group: AMP, ACC) × 2 (Time: pre-training, post-training) ANOVAs with repeated measurement on the second factor. These analyses are summarized in Table 3. With the exception of the HAMD and the PSWQ, all interactions of Group × Time were significant (*p*s<.05).

To examine change in each we followed significant interactions with paired t-tests. For self-report measures, these analyses revealed that participants in the AMP group showed a significant decrease in their scores from pre-training to post-training on the STAT-T, t (13) = 4.76, $p < .001$, d= 1.40, STAI-S, t (13) = 4.27, $p < .001$, d = 1.81, BDI, t (13) = 2.69, $p < .02$, d= 0.90, and WDQ, t (13) = 4.30, $p < .001$, d= 1.14. The same paired t-tests in the ACC group did not reveal significant changes on the STAI-T, t (14) = 1.89, $p < .08$, d = 0.27, STAI-S, t (14) = 0.35, $p < .74$, d = .11, BDI, t (14) = 0.40,$p < .70$, d = .07, or WDQ, t (14) = 1.35, $p < .20$, d = 0.36. Similar analyses on the interviewer administered measures revealed that the AMP group showed a significant decrease in their scores on the HRSA, t (13) = 4.27, $p < .001$, d = 1.36. In contrast, the ACC group did not show a significant changed in their HRSA scores, t (14) = 1.47, $p < .16$, d = 0.31.

We also examined the number of participants who no longer met DSM-IV diagnosis for GAD at post treatment. These analyses revealed that a significantly larger proportion of the participants in the AMP group (50%) compared to the ACC group (13%) no longer met diagnostic criteria for GAD after training, $X^2(1) = 4.55$, $p < .03$.

Mediational Analyses

To test the hypothesis that the AMP exerted its influence on anxiety and depression through change in attention bias to threat, we conducted mediational analyses following the procedure described by MacKinnon and colleagues (MacKinnon, Fairchild, & Fritz, 2007; MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002). In brief, this procedure tests the product of the coefficients for the effects of (1) the independent variable (Group: AMP, ACC) to the mediator (attention bias after training) (α), and (2) the mediator to the dependent variable (change in scores, HRSA, STAI-T, STAI-S, BDI, WDQ, from pre- to post-training) when the independent variable is taken into account (β). This procedure is a variation on the Sobel (1982) test that accounts for the non-normal distribution of the αβ path through the construction of asymmetric confidence intervals (MacKinnon, Fritz, Williams, & Lockwood, 2007). Our results indicated that the 95% confidence interval of the indirect path (αβ.) did not overlap with zero for change in anxiety for HRSA (lower limit = .015, upper limit = .343). The same indirect paths for all other measures (STAI-T, STAI-S, BDI, WDQ) overlapped with zero, indicating an absence of a significant mediation.

Discussion

Participants undergoing the Attention Modification Program demonstrated a decrease in attention bias to threat and a decrease in anxiety symptoms. Fifty percent of participants in the AMP were classified as responders (no longer meeting DSM diagnosis for GAD) compared to 13% of participants in the ACC. At post treatment, independent assessors rated participants completing the AMP as significantly less anxious from pre- to post-training. Finally, participants' self-report of anxiety and depressive symptoms corroborated the interviewer ratings. These data suggest that our intervention reduced anxiety. These results are promising, considering the short duration (i.e., four weeks) of the intervention and absence of therapist

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contact. The AMP group showed less bias for threat than the ACC group after training. Moreover, this change in bias was not specific to the words used for training, but generalized to a different word set used at pre-training and post-training assessments. These results suggest that the AMP group experienced a reduction in attention bias toward threat compared to the ACC group.

Although our predictions concerned the impact of attention modification on anxiety, we observed similar effects on self-reported depressive symptoms. These results are not surprising in light of the high comorbidity between anxiety and depression, especially in individuals with GAD (Nutt, Argyropoulos, Hood, & Potokar, 2006). However, our mediational analyses only supported the indirect effect of the attention training procedure on our interviewer measure of anxiety (HRSA) through reduction in attention bias. This finding could reflect the differential sensitivity of our various measures or alternatively the relative efficacy of the training on each construct. Future research should examine the potential mechanisms of attention training program effects on depressive symptoms as well as on anxiety.

These results have theoretical and practical implications for information processing bias modification for anxiety. At the theoretical level, our results provide strong support for the hypothesis that the allocation of attention to threat-relevant information causally contributes to the anxiety symptoms experienced by individuals with GAD. At the practical level, our findings suggest that it may be possible to utilize such attention training procedures clinically, either independent of, or to augment already established treatments for anxiety such as CBT or medication. Despite its high prevalence, many individuals with GAD who need treatment do not receive it for a variety of reasons. Additionally, many individuals who present for treatment do not respond (Fisher & Durham 1999; Gorman, 2003). This intervention may provide an effective and efficient treatment accessible to both individuals who are not receiving any treatment and those who do not respond to traditional treatments. Moreover, this study suggests that basic findings from experimental psychopathology research can be translated into efficacious treatments for individuals with clinical levels of anxiety.

A number of meta-analyses have compared effective treatments for GAD (i.e., cognitive-behavioral therapy and pharmacological treatment). Three meta-analyses of treatment outcome for GAD (Borkovec & Ruscio, 2001; Gould, Saffren, Washington, & Otto, 2004; Lydiard & Monnier, 2004) have suggested some variability in the estimates of effect sizes. However, psychosocial treatments have resulted in between group average effect sizes ranging from 0.71-0.90 and pharmacological treatments from .42-.90 (Gelenberg et. al., 2000; Moller, Volz, Reimann, & Stoll, 2001; Rickels, Pollack, Sheehan & Haskins, 2000). The effect sizes for the current study (0.72-0.88) place this treatment in the range of current treatments for GAD.

Our study has limitations. First, our sample size was relatively small, limiting the generalizibility of our results. Second, we only obtained a significant interaction of Group × Time on one of our two self-report measures of worry (i.e., on WDQ but not on PSWQ). Furthermore, examination of effect sizes indicated that the training was more effective for general anxiety symptoms than for worry symptoms. Therefore, this study does not provide a clear discrimination of the symptoms of GAD that may be most amenable to change using attention training. Third, we did not include an independent measure of attention bias in our study. Future work should include different measures of attention bias (e.g., Posner task, Stroop task) to examine the generalizability of attention training to other measures of attention.

In summary, our results suggest that the translation of basic psychopathology research to address a clinical condition may prove useful in developing new interventions. Moreover, these interventions may help identify the mechanisms that are involved in the pathogenesis of psychiatric conditions. Future studies should examine the additive and/or interactive effects of attention training and traditional interventions (i.e., medication and CBT), as well as the combination of other types of information processing training (e.g., interpretation modification).

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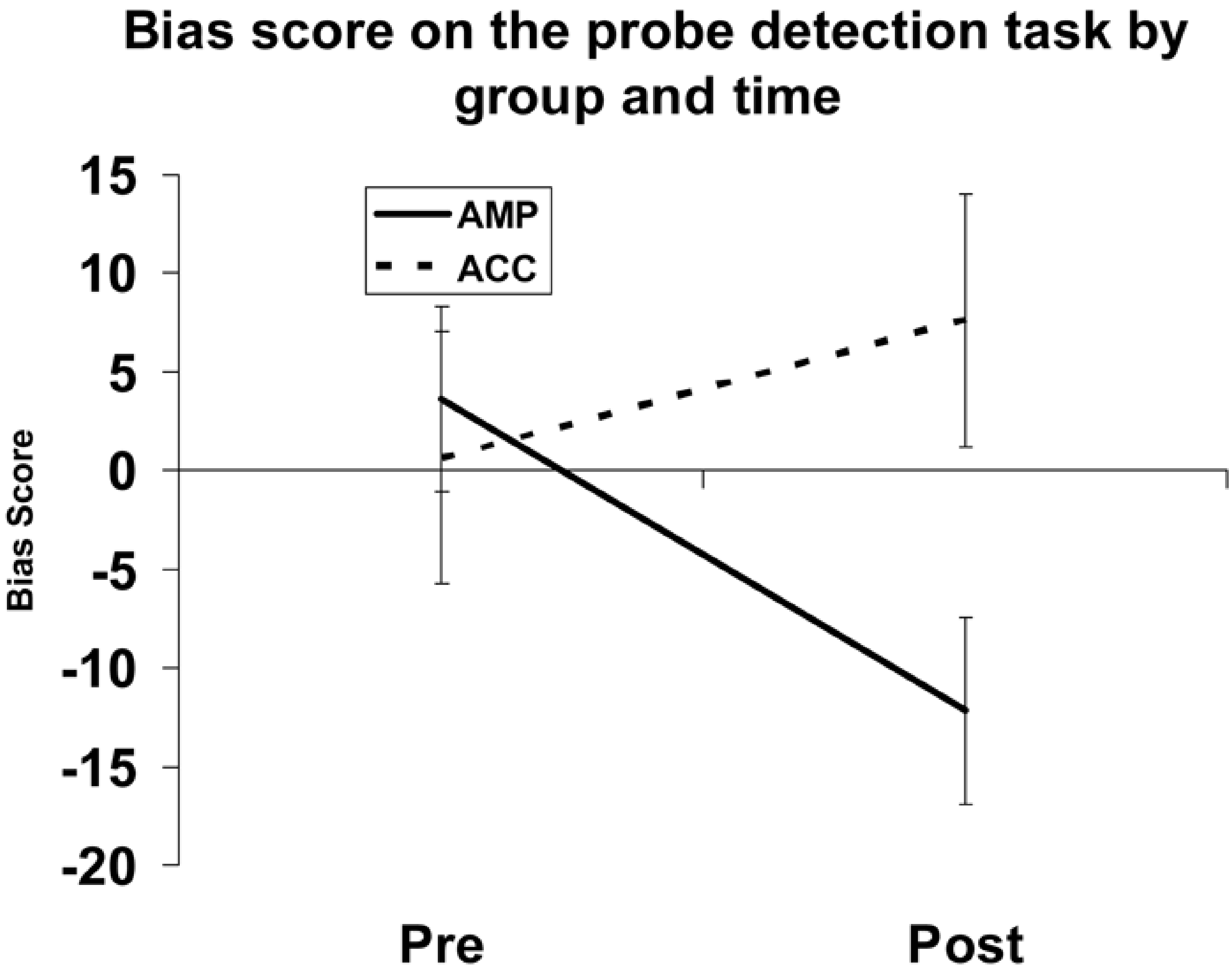

Figure 1.
Change in attention bias

Table 1

Demographic Characteristics

	AMP (n=14)	**ACC (n=15)**
Women, Number (%)	7 (50%)	7 (47%)
Age (SD)	26 (6.14)	25 (8.87)
Education in years	15.7 (2.02)	15.4 (1.68)

Note: AMP: Attention Modification Program; ACC: Attention Control Condition

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Table 2

Means and standard deviations of response latencies by group on the probe detection task

	AMP M (SD)		ACC M (SD)	
	Pre-training	**Post-training**	**Pre-training**	**Post-training**
Probe position				
Top				
Threat word				
Top	589 (175)	526 (100)	635 (206)	543 (115)
Bottom	593 (179)	510 (89)	641 (214)	553 (135)
Bottom				
Threat word				
Top	584 (199)	508 (100)	629 (214)	539 (120)
Bottom	581 (193)	514 (94)	633 (213)	533 (114)

Note: AMP: Attention Modification Program; ACC: Attention Control Condition.

Table 3

Means and standard deviations for self-report and interviewer measures

	AMP		ACC		Results		
	Pre	**Post**	**Pre**	**Post**	**Group**	**Time**	**Group × Time**
	M (SD)	**M (SD)**	**M (SD)**	**M (SD)**	**F (p)**	**F (p)**	**F (p)**
STAI-T	60.9	47.3	58.6	55.6	0.72	26.72	10.84
	(8.9)	(10.4)	(10.2)	(12.3)	(0.4)	(0.00)	(0.003)
STAI-S	59.1	41.4	51.1	49.8	0.00	11.81	8.87
	(10.5)	(8.9)	(9.8)	(13.7)	(0.9)	(0.002)	(0.006)
BDI-II	24.6	14.5	22.8	22.1	0.70	7.17	5.50
	(12.3)	(10.0)	(8.9)	(12.0)	(0.4)	(0.01)	(0.03)
WDQ	86.5	66.5	86.8	80.9	1.81	16.54	4.96
	(16.7)	(18.4)	(14.3)	(18.2)	(0.2)	(0.00)	(0.04)
PSWQ	70.6	63.0	67.8	63.9	0.11	10.70	1.15
	(4.7)	(11.2)	(7.6)	(10.9)	(0.7)	(0.003)	(0.29)
HRSA	20.3	11.9	19.0	16.7	0.58	20.34	6.46
	(6.5)	(5.7)	(7.6)	(7.4)	(0.45)	(0.001)	(0.02)
HAMD	10.4	6.4	12.0	10.3	3.29	10.20	1.73
	(5.4)	(4.4)	(4.7)	(4.3)	(0.08)	(0.004)	(0.20)

Note: AMP: Attention Modification Program; ACC: Attention Control Condition; STAI (S/T): The State-Trait Anxiety Inventory (State/Trait, Spielberger et al., 1983), BDI-II: The Beck Depression Inventory-II; WDQ: Worry Domains Questionnaire (Tallis, Eysenck, & Mathews, 1992); PSWQ: Penn State Worry Questionnaire (Meyer et al., 1990), HRSA : Hamilton Rating scale for Anxiety (Hamilton, 1959), HAM-D : Hamilton Rating scale for Depression (Hamilton, 1959); Degrees of freedom for all effects (1, 27).