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The Effectiveness of an Attention Bias Modification Program as an Adjunctive Treatment for Post-Traumatic Stress Disorder

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Abstract

Attention bias modification (ABM) may be an effective treatment for anxiety disorders (Beard, Sawyer, & Hofmann, 2012). As individuals with PTSD possess an attentional bias towards threat-relevant information ABM may prove effective in reducing PTSD symptoms. We examined the efficacy of ABM as an adjunct treatment for PTSD in a real-world setting. We administered ABM in conjunction with prolonged exposure or cognitive-processing therapy and medication in a community inpatient treatment facility for military personnel diagnosed with PTSD. Participants were randomized to either ABM or an attention control condition (ACC). While all participants experienced reductions in PTSD symptoms, participants in the ABM group experienced significantly fewer PTSD and depressive symptoms at post-treatment when compared to the ACC group. Moreover, change in plasticity of attentional bias mediated this change in symptoms and initial attentional bias moderated the effects of the treatment. These results suggest that ABM may be an effective adjunct treatment for PTSD.

Keywords

PTSD; attention training; cognitive bias modification

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Post-Traumatic Stress Disorder (PTSD) is a common disorder affecting 3.5 percent of the United States population in any given year (Kessler, Chiu, Demler, & Walters, 2005). This figure is considerably higher for returning military personnel, with rates ranging from 5–20% (Ramchand et al., 2010). Hallmark symptoms of PTSD include re-experiencing symptoms and increased physiological arousal (DSM-IV-TR; American Psychiatric Association, 2000) leading to functional impairment (Schnurr, Lunney, Sengupta, & Waelde, 2003). Moreover, co-morbid depressive disorders and substance abuse are common, causing further distress and disability (Kessler et al., 2005).

Extant research suggests that individuals with PTSD are characterized by an information processing bias for threat-relevant information when compared to non-anxious individuals (e.g., for reviews see Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007; Buckley, Blanchard, & Neill, 2000). Moreover, this information processing bias toward threat relevant information may cause chronic hypervigilance and increased physiological arousal (Thomas, Goegan, Newman, Arndt, & Sears, 2013). Individuals with PTSD may not only experience hypervigilance toward threatening stimuli, but may also have difficulty disengaging their attention from threat following initial attentional capture (for a review see Aupperle, Melrose, Stein, & Paulus, 2012).

One intervention designed to reduce hypervigilance towards and enhance disengagement from threat-related information is attention bias modification (ABM), with several recent meta-analyses suggesting that ABM may result in significant reduction in anxiety symptoms (Beard, Sawyer, & Hofmann, 2012; Hakamata et al., 2010; Hallion & Ruscio, 2011). Given that ABM has demonstrated evidence of efficacy in tightly-controlled randomized controlled trials (RCTs) within laboratory settings (Amir, Beard, Burns, et al., 2009; Amir, Beard, Taylor, et al., 2009; Heeren et al., 2012; Schmidt et al., 2009), it may be well-poised for effectiveness testing. Moreover, the brevity and low cost of this intervention makes it practical for delivery in real-world settings. Whereas efficacy trials are typically conducted in experimenter-controlled environments with standardized protocols for administration of the intervention and assessments, effectiveness trials examine the effects of the treatment under more typical conditions (Flay, 1986).

Several ABM studies have begun to move towards effectiveness testing. However, studies to date have produced mixed results. For example, some studies have failed to produce group differences between ABM and ACC conditions when delivered outside of traditional laboratory-based settings (e.g., internet, smartphone) (Boettcher, Berger & Renneberg, 2012; Carlbring et al., 2012; Enock, Hoffman, & McNally, 2014; Neubauer et al., 2013). These studies examined the effect of ABM as a stand-alone treatment, however, real-world clinical settings often utilize multiple interventions concurrently for anxiety disorders (e.g., pharmacotherapy with psychosocial therapy). Given that comorbid psychiatric disorders is the rule rather than the exception in PTSD (Brady, Killeen, Brewerton, & Lucerini, 2000), combined treatment in the community for individuals with PTSD is particularly prevalent (Foa, Keane, & Friedman, 2000).

Indeed, recent reviews of ABM have called for research examining the effect of ABM as an adjunctive treatment to existing interventions, such as cognitive behavior therapy (CBT) and

pharmacotherapy (Beard, 2011; Hakamata et al., 2010; Hallion & Ruscio, 2011). Several research studies have examined whether ABM results in anxiety reductions over and above the effects of CBT alone (Britton et al., 2013; Rapee et al., 2013; Riemann, Kuckertz, Rozenman, Weersing, & Amir, 2013). One of these studies (Riemann et al., 2013) supported the use of ABM as an adjunctive treatment, while two did not (Britton et al., 2013; Rapee et al., 2013). Both studies that did not find an augmentation effect of ABM were conducted in the context of a research based laboratory setting using highly structured, standardized, and well-monitored provision of CBT. In contrast, ABM was found to augment the effects of CBT and pharmacotherapy when these treatments were administered per routine clinical practice in the context of a residential treatment facility for youth anxiety disorders (Riemann et al., 2013). Thus, there is a need for further study of the effect of ABM as an adjunctive treatment in real world clinical settings.

Although the setting in which attention training is delivered is one factor that may account for some of the discrepant results of ABM studies, factors more proximal to the theory of ABM may also affect outcome (Clarke, Notebaert, & MacLeod, 2014). For example, several studies suggest that level of attentional bias at pre-treatment moderates the effect of ABM, such that individuals with higher levels of attentional bias show greater treatment gains from the intervention (Amir, Taylor, & Donohue, 2011), even when ABM is delivered entirely in non-laboratory settings (Kuckertz et al., 2014). Moreover, ABM is predicated on the notion that change in attentional bias is causally implicated in the maintenance of anxiety symptoms. Consistent with this hypothesis, several studies both inside and outside of laboratory settings have demonstrated that change in attentional bias from pre- to post-treatment mediates the effects of ABM on symptom change (Amir, Beard, Taylor, et al., 2009; Heeren et al., 2012; Kuckertz et al., 2014). As such studies that do not show an effect of the ABM on the intended mechanism (i.e., attentional bias change) would not be expected to demonstrate a corresponding change in symptoms (for a review see Clarke et al., 2014). Indeed, studies that have failed to find group differences in symptoms also failed to find an effect of training on change in attentional bias (Boettcher et al., 2012; Carlbring et al., 2012; Neubauer et al., 2013).

With few exceptions, studies examining attentional bias in the context of ABM (e.g., bias change, moderation, mediation) have conceptualized bias as a static measure over a given time point as the primary construct of interest. For example, the most commonly used bias calculation method is that introduced by MacLeod, Mathews, and Tata (1986). Using this method, researchers calculate attentional bias over a given time period by comparing participant's average response latency to identify a probe following the presentation of a threatening stimulus and the participant's average response latency when the probe follows a neutral stimulus. However, recent research suggests that alternate methods of conceptualizing attentional bias may increase our understanding of cognitive processing in anxiety and its effects on anxiety-related behavior. For example, Iacoviello and colleagues (2014) found that variability of attentional bias rather than attentional bias per se is correlated with PTSD symptoms. Moreover, this variability in attentional bias differentiated individuals exposed to trauma who did and did not develop subsequent PTSD.

Other researchers have also utilized the concept of attentional bias malleability as a predictor of anxiety-related outcomes. For example, Clarke, Chen, and Guastella (2012) demonstrated that plasticity in attentional bias, defined as change in bias within a single session of ABM training, was predictive of treatment response to subsequent CBT, while attentional bias at a static time point was not. Moreover, Najmi and Amir (2010) found that plasticity in attentional bias within a single session of attention training mediated the effect of ABM training on behavioral approach toward feared objects in individuals with obsessive-compulsive symptoms. Thus, the extent to which attentional bias changes within a single session or is trained during ABM may relate to treatment outcome. As static attentional bias (Amir et al., 2011; Kuckertz et al., 2014) and/or plasticity in attentional bias across a single ABM session (Clarke et al., 2012) predict treatment outcome, additional research is needed examining when and for whom these different constructs predict outcome. Similarly, research is needed to clarify the role of these constructs in mediating treatment effects.

To our knowledge, only two studies have investigated the efficacy of ABM in patients with PTSD (Schoorl, Putman, Mooren, Ven Der Weff, & Van Der Does, 2014; Schoorl, Putman, & Van Der Does, 2013). Schoorl and colleagues (2013) administered eight 20-minute sessions of ABM over the course of three weeks to 102 patients with PTSD and assessed PTSD symptoms and attentional bias before and after the treatment as well as at follow-up. ABM and the ACC were equally effective in reducing the symptoms of PTSD with similar effect sizes (ABM, $d = 0.66$; ACC, $d = 0.46$). However, as the authors point out, the ABM procedure was not effective in changing attentional bias in that study. In a second study, Schoorl and colleagues (2014) examined the effect of an eight session ABM program with ideographically selected stimuli for returning war veterans with PTSD in a case series design ($N = 6$). While the authors concluded that ABM was not effective because no participants experienced reductions in PTSD symptoms during the training, five of the six participants demonstrated clinically significant recovery one week following treatment.

To add to the research base on ABM in PTSD as well as to examine questions of moderation/mediation in a real-world setting, we conducted an initial pilot study in which we administered an attention training program in conjunction with a combination of individual, group, and pharmacological treatment to 23 active duty outpatients in a military clinic. After randomization to ABM or ACC, participants completed one session of attention training during their initial clinical assessment. We asked participants to complete two attention training sessions per week for the next four weeks. Statistical comparisons of group differences in change from baseline to four weeks were not significant for any of our dependent variables (i.e., PTSD and depression symptoms). We found that compliance was very low in this setting. Although each participant received instructions to complete the program at least eight times during the four weeks of treatment, the average number of sessions completed outside the clinic was approximately two sessions, with one outlier accounting for this mean in each group. Thus the modal number of sessions completed outside the initial clinical assessment was zero. Low compliance precluded us from examining questions of moderation or mediation, and highlighted the need for protocol adaptation for the administration of ABM in real-world settings.

To address these issues, in this paper we describe the results of an adjunctive ABM program for veterans with PTSD within a community inpatient facility with a dedicated Military Unit for military personnel. We selected this setting in an effort to increase compliance with ABM completion, as well as to allow for comparison in setting with the adjunctive ABM study conducted by Riemann and colleagues (2013). Thus, a goal of the current study was to examine the effectiveness of ABM for PTSD in non-laboratory settings, such as those that combine multiple treatment components (i.e., ABM as an adjunctive treatment). Secondly, it is important to examine the pattern of change (or lack of change in attention training) and moderators of change in any ABM study (Clarke et al., 2014; Kuckertz et al., 2014). More specifically, the plasticity in attentional bias, rather than attentional bias in itself, may be implicated in the maintenance of anxiety symptoms. While some data suggests that plasticity of attentional bias mediates outcome for a single session of ABM (Najmi & Amir, 2010), to date no studies have examined whether change in plasticity over a multi-session of ABM treatment protocol mediates the effect on symptom reductions. To examine effects of static versus plastic attentional bias, we report the results of both (a) static attentional bias at pre-treatment and change in static bias from pre- to post-treatment, and (b) plasticity of attentional bias during the first training session and change in this within-session plasticity of time, as moderating or mediating the treatment effects of ABM.

Method

Participants

Participants were active duty military members (Marine Corps, Army Specialists) receiving treatment at a community inpatient behavioral health unit specializing in treatment of behavioral and chemical dependency services. Thirty-seven individuals consented to participate, and our final sample comprised 29 participants (ABM, $n = 12$; ACC, $n = 17$). Full description of dropout rates is presented in Figure 1. All participants had a diagnosis of PTSD. Substance dependence was the most common other diagnosis. Participants were primarily male (93.1%), ranged in age from 20 to 45 ($M = 25.62$, $SD = 5.79$), and had completed an average of 12.43 years of education ($SD = 1.33$). All participants in the current study received concurrent pharmacotherapy. Demographic information is presented in Table 1.

Program Description

All participants received treatment as usual (TAU) as part of the health unit's standard care regimen. The standard of care for all patients was either prolonged exposure (PE) or Cognitive-Processing Therapy (CPT), depending on the presentation of the individual, as well as psychopharmacology for immediate symptom management. All patients were required to attend group therapies of various formats once per day, including a Cognitive-Behavioral Therapy group, a Process group, adjunctive therapy (choice of art, music, movement, or yoga), gym time, and independent study time to work on homework or complete the attention training program.

In addition, all participants received three individual 60–90 minute sessions per week with a psychologist or post doctoral intern; daily contact with a physician for medication; and daily

contact with their case manager (either a Marriage and Family Therapist or Licensed Clinical Social Worker).

Self-Report Measures

Post-Traumatic Stress Disorder Checklist-Military version (PCL-M)—The PCL-M is a 17-item questionnaire that assesses the severity of PTSD symptoms using a 5-point Likert scale ranging from “not at all” to “extremely,” with a minimum score of 17 and a maximum score of 85 (Weathers, Litz, Herman, Huska, & Keane, 1993). Participants are asked to rate to what extent they experienced PTSD symptoms over the previous month due to prior combat experiences. The military version of the PCL (PCL-M) refers specifically to a traumatic military related event (Weathers, Litz, Huska, & Keane, 1994). Research suggests that the PCL-M has good test-retest reliability ($r = .70$) and internal consistency ($\alpha = .97$; Weathers et al., 1993).

Beck Depression Inventory-II (BDI-II)—The BDI-II (Beck, Steer, & Brown, 1996) is a reliable and well-validated 21-item self-report measure of depressive symptom severity. Each item is scored on a 0 to 3 scale with the total depression score ranging from a minimum of 0 to a maximum of 63.

Attention Training Sessions

Each attention training session comprised 48 pre-session assessment trials, 288 training or control trials (ABM or ACC group, respectively), and 48 post-session assessment trials for a total of 384 trials per session. The program was designed such that all assessment and training trials were delivered within the same session, thus participants remained unaware of the distinction between assessment and training trials. With the exception of the words used, this program was identical to that implemented by Najmi and Amir (2010). Different word stimuli were utilized for the pre-session attentional bias assessment, the training trials (ABM or ACC), and the post-session attentional bias assessment. We created separate pools of stimuli words for assessment and treatment (see Table 2 for a list of all words used in the study). Each pool was divided into four unique word sets (i.e., four sets for assessment, four sets for training). To increase generalizability, stimuli files were randomized for each session such that each participant had an equally likely chance of being presented with any of the four stimuli sets in a given session for training, with a similar procedure for pre- and post-session assessments. Word stimuli sets did not differ between the ABM and ACC conditions. See description below.

Attentional bias assessment—Participants completed an attentional bias assessment at the beginning and end of each treatment session as described above (MacLeod et al., 1986). Each trial began with a fixation cross that appeared in the center of the computer screen for 500 ms. The fixation cross then disappeared and was replaced by a word pair consisting of one threat and one neutral word, presented vertically in the center of the screen for 500 ms, with one word directly above the other. The words then disappeared and a probe (either the letter ‘E’ or the letter ‘F’) appeared in the location of one of the two words. Participants were instructed to decide whether the probe replacing the word was an ‘E’ or an ‘F’ and press the corresponding mouse button (left mouse button for ‘E’ and right mouse button for

'F'). The letter probe remained on the screen until the participant responded. Response latencies for each participant to identify the probe were recorded from the time the probe was presented to the time participants responded. Following each response, there was a 500 ms interval where participants saw a blank screen before the next trial began with a fixation cross. The assessment comprised 48 trials in a given session: 2 (probe type: E or F) x 2 (probe position: top or bottom) x 2 (word type: neutral or threat) x 6 (threat-neutral word pairs). The words that comprise the stimuli for each trial are presented in Table 2. Consistent with previous research (e.g., Najmi & Amir, 2010) attentional bias for any given session before training was calculated as the difference in median response latencies between trials in which the probe replaced the neutral word and trials in which the probe replaced the threat word, with higher bias scores indicating greater attentional bias for threat. More relevant to the goals of the current study, we also administered a measure of bias after each training session that was identical to the pre-training assessment, with the exception that a different set of six words were used than those used during pre training and training trials. This allowed us to calculate an attentional bias plasticity index for each session, defined as pre-session bias minus post-session bias. As training progressed we expected a decrease in this plasticity index as bias at pre-training would be expected to start at a lower level with each successful training session in the ABM group. The ACC group should not show this pattern of change in training over sessions. We also expected that the ABM group should show a decrease in static attentional bias over time, whereas the ACC group should not.

Attention bias modification (ABM)—The ABM comprised a probe detection task as described above, but modified to facilitate the allocation of attention away from threatening material. In this task, the probe always replaced the neutral word of a neutral-threat word pair. The stimuli comprised a different word set than those used during the attentional bias assessments pre- and post-training. Participants completed 288 training trials in a given session: 2 (probe type: E or F) x 2 (threat word position: top or bottom) x 12 (threat-neutral word pairs) x 6 (repetition).

Attention control condition (ACC)—The ACC condition was identical to the ABM procedure with the exception that the probe replaced the threat and neutral words with equal frequency.

Procedure

Both participants and staff were blind to treatment condition. All participants were instructed to complete attention training sessions daily for 14 consecutive days. However, the actual time span over which participants completed their sessions varied (see Table 1). Patients had the choice to complete the attention training during one of two independent study times, either in the morning between 10–11am, or in the evening after 5:30pm. The training was done on a computer in a private and quiet consultation room on the unit where the patients reside. Patients were escorted into the room by a staff member, read the prompt to begin their training, and left to complete the task alone with staff members checking in every 5–15 minutes. Participants initiated ABM/ACC the day the pre-treatment symptom measures were completed, and completed the post-treatment measures the day they

terminated ABM/ACC. All procedures were approved by the Naval Medical Center San Diego, Aurora Hospital, and San Diego State University Institutional Review Boards.

Statistical Analyses

Unless noted otherwise, analyses were conducted for the completer sample. A participant was defined as a completer if they had (a) post-treatment PCL data available, and (b) had initiated the treatment program (i.e., initiated at least one training session).¹

We first compared groups on demographic and clinical characteristics at pre-treatment using *t* tests and chi-squared analyses.

To examine the effect of treatment condition (ABM vs. ACC) on symptom change, we analyzed PTSD symptom severity (PCL) scores at pre-and post-treatment using linear mixed effects models (Laird & Ware, 1982). Specifically we tested the hypothesis that the rate of decrease in PTSD symptom severity from pre- to post-treatment would be larger for the ABM than the ACC group. The model for each group is of the form:

$$PCL_i(t_j) = \beta_0 + \beta_1 t_j + \beta_2 G_j + \beta_3 t_j * G_j + \alpha_{0i} + \varepsilon_{ij}$$

where $PCL_i(t_j)$ is the observed PCL at time t_j for subject i , where G_j is group membership, and where $t_j * G_j$ is the interaction of these two effects. β s are fixed effects and α s are subject specific random effects and alphas are assumed to be from a bivariate Gaussian distribution, and the residuals are from Gaussian distribution. For models with yielded a significant interaction between group and time, we followed the model up by conducting separate models within each group to analyze the effect of time.

Similarly, to examine the effect of treatment condition (ABM vs. ACC) on bias change, we analyzed (a) change in static attentional bias over time, and (b) change in plasticity of attentional bias over time using linear mixed effects models. Specifically we tested the hypothesis that the rate of decrease in (a) static bias and (b) plasticity of bias across treatment would be larger for the ABM than the ACC group. The model for each group is of the form:

$$BIAS_i(t_j) = \beta_0 + \beta_1 t_j + \beta_2 G_j + \beta_3 t_j * G_j + \alpha_{0i} + \varepsilon_{ij}$$

where $BIAS_i(t_j)$ is the observed bias at time t_j for subject i , where G_j is group membership, and where $t_j * G_j$ is the interaction of these two effects. β s are fixed effects and α s are subject specific random effects and alphas are assumed to be from a bivariate Gaussian distribution, and the residuals are from Gaussian distribution. For models with yielded a significant interaction between group and time, we followed the model up by conducting separate models within each group to analyze the effect of time. We included all available data from the first eight sessions in these analyses in order to remain consistent with previous research

¹Within the completer sample ($N = 29$), data were missing as follows: age ($n = 8$), number of days between assessments ($n = 9$), BDI-II at post-treatment ($n = 5$).

examining the role of bias change across eight-session ABM protocols (e.g., Amir, Beard, Taylor et al., 2009; Boettcher et al., 2012; Kuckertz et al., 2014; Neubauer et al., 2013).

We chose to analyze our data using linear mixed effects models rather than repeated-measures ANOVA due to the ability of mixed models to include all available data (Maxwell & Delaney, 2004, Chapter 15) without biased missing data imputation methods such as last observation carried forward (for a review of the advantages of mixed models over repeated-measures ANOVA see Gibbons, Hedeker, & DuToit, 2010). This was particularly relevant to our analysis of attentional bias data, as participants varied in number of attention trainings completed. Missing data were handled using full maximum likelihood estimation. Linear mixed effects models were fitted using the nlme package (Pinheiro, Bates, DebRoy, Sarkar, and the R Core Team, 2014) within R version 2.15.1 (R Development Core Team, 2012). Cohen's d effect sizes (Cohen, 1988) were calculated as follows: $d = 2t / (\text{df})$ (Rosenthal & Rosnow, 1991).

We conducted moderation and mediation analyses using the program PROCESS (Hayes, 2012) within SPSS version 20 (IBM Corp, 2011). We tested separate moderation models to examine whether (a) static attentional bias, defined as the first set of pre-training trials completed in the first attention training session, and/or (b) initial attentional bias plasticity, defined as the change in attentional bias within the first attention training session, moderated treatment response (i.e., examined for change in PTSD and depression symptoms from pre- to post-treatment) between the ABM and ACC groups. Thus, we examined a total of four moderation models. See Figure 2 (model depicted based on Hayes, 2013, Model 1) for a graphical representation of our moderation models. For models that demonstrated a significant moderation effect, we also conducted regions-of-significance analyses using the Johnson–Neyman technique (Johnson & Neyman, 1936) in PROCESS.

Similarly, we conducted a total of four mediation models to examine whether (a) change in static attentional bias, defined as bias from the pre-training trials completed in the first attention training session minus bias from the post-training trials from the last session completed for each participant, and/or (b) change in plasticity of attentional bias, defined as within session change in attentional bias for the first session minus the within session change for the last session completed for each participant, mediated the relationship between treatment group (i.e., ABM, ACC) and symptom reductions (i.e., change in PTSD and depression symptoms from pre- to post-treatment). Following the procedure outlined by Preacher and Hayes (2004) and implemented in PROCESS, we tested the products of (1) the independent variable (Group: ABM, ACC) to the mediator (change in static or plastic attentional bias across treatment; α path), and (2) the mediator to the dependent variable (change in PCL or BDI scores pre- to post-treatment) when the independent variable is taken into account. This procedure is a variation on the Sobel (1982) test that accounts for the non-normal distribution of the $\alpha\beta$ path through bootstrapping procedures (number of resamplings = 5000). Significant mediation effects are indicated when the 95% confidence interval of the indirect path ($\alpha\beta$) does overlap with zero. See Figure 3 for graphical representation of our mediational models.

Results

Baseline Analyses

Groups did not differ in gender [$\chi^2(1) = 0.07, p = .798$], ethnicity [$\chi^2(2) = 2.20, p = .332$], age [$t(27) = 0.95, p = .353$], level of education [$t(19) = -0.69, p = .499$], total length of stay at the treatment facility [$t(27) = -0.66, p = .518$], number of days between assessments [$t(18) = 0.76, p = .458$], type of adjunctive therapy [$\chi^2(2) = 1.32, p = .517$], or percentage of individuals with a substance dependence diagnosis [$\chi^2(1) = 1.45, p = .228$]. Groups also did not differ on severity of PTSD [$t(27) = 0.40, p = .690$] or depressive [$t(27) = 0.25, p = .806$] symptoms at baseline. Participants in the ABM group completed an average of 6.67 sessions ($SD = 5.25$) and participants in the ACC group completed an average of 7.24 ($SD = 5.72$) sessions. Groups did not differ significantly in number of sessions completed [$t(27) = -0.27, p = .787$].

Effect of Attention Training on Attentional Bias

Static Attentional Bias—We first examined the effect of treatment condition on change in static attentional bias over time (i.e., traditional measure of attentional bias). This analyses indicated nonsignificant effects for the main effect of time [$t(110) = -0.96, p = .338, d = 0.18$], main effect of group [$t(27) = -0.54, p = .591, d = 0.21$], and interaction of time and group [$t(110) = 0.96, p = .338, d = 0.18$]. Thus, static attentional bias did not appear to differentially change between groups across treatment.

Plasticity of Attentional Bias²—We also examined the effect of treatment condition on change in plasticity of attentional bias over time. These analyses revealed a main effect of time [$t(93) = -2.26, p = .027, d = 0.47$] and marginally significant effect of group [$t(23) = -1.94, p = .065, d = 0.81$]. Moreover, there was significant interaction of time and group [$t(93) = 2.25, p = .027, d = 0.47$]. Separate models fitted for each group indicated that plasticity of attentional bias decreased over time in the ABM group [$t(39) = -2.13, p = .040, d = 0.68$] but did not change in the ACC group [$t(54) = 0.96, p = .339, d = 0.26$].

Effect of Attention Training on Symptom Measures^{3, 4}

We first examined the effect of training condition on PTSD symptoms (PCL). This analysis indicated a main effect of time [$t(27) = -2.21, p = .036, d = 0.85$] but not group [$t(27) = -1.47, p = .153, d = 0.57$]. Moreover there was a significant interaction of time and group [$t(27) = 2.20, p = .036, d = 0.85$]. Separate models fitted for each group indicated that PTSD symptoms decreased over time in both the ABM group [$t(11) = -5.26, p = .0003, d = 3.17$]

²We note that degrees of freedom for the effect of group differed between our analyses for static attention bias and plasticity of attention bias because during the first session four individuals initiated the pre-session bias assessment and training session, but did not complete the post-session bias assessment and therefore for these participants we could not calculate a bias plasticity index.

³Because length of time between pre- and post-treatment assessments may have varied to some degree between participants, and hence duration of adjunctive therapy, we included length of time between assessments as a covariate. For PCL scores, the interaction of time and treatment condition remained significant ($p = .016$). For BDI-II scores, the interaction of time and treatment condition was marginally significant ($p = .094$).

⁴We also conducted these analyses on an intent-to-treat basis including all 37 randomized participants. The interaction of time and treatment condition remained significant both for PCL scores ($p = .038$) as well as for BDI-II scores ($p = .023$).

as well as in the ACC group [$t(16) = -3.61, p = .002, d = 1.81$]. This decrease was larger in the ABM compared to the ACC condition.

We tested a similar model to determine whether or not there existed an effect of treatment condition on depressive symptom severity (BDI-II). These analyses revealed a main effect of time [$t(22) = -2.51, p = .020, d = 1.07$] but not group [$t(27) = -1.57, p = .127, d = 0.60$]. Moreover, there was a significant interaction of time and group [$t(22) = 2.50, p = .020, d = 1.07$]. Separate models fitted for each group indicated that depressive symptoms decreased over time in both the ABM group [$t(8) = -4.29, p = .003, d = 3.03$] as well as in the ACC group [$t(14) = -3.80, p = .002, d = 2.03$]. This decrease was larger in the ABM compared to the ACC condition.

Moderation Analyses

Static Attentional Bias—We conducted moderational analyses to determine whether static attentional bias at the beginning of treatment (i.e., the set of pre-training trials during the initial attention training session) would moderate the relationship between Group (ABM, ACC) and change in PTSD (PCL) or depressive (BDI-II) symptoms. For change in PCL, our results indicated that the interaction of Group x Static Bias explained a significant proportion of the variance beyond the effect of either of these terms alone, $R^2 = .13, F(1, 25) = 4.62, p = .042$. This interaction is represented in Figure 4, which presents average PCL reductions for the ABM and ACC groups at +1, 0, and -1 standard deviations from the mean initial static attentional bias score (-13.87 ms). Separate regions-of-significance analyses revealed that for participants who presented with initial static attentional bias scores less than -3 ms (i.e., approximately between 0 and +1 standard deviations) to the lowest value observed (-210 ms, or nearly three standard deviations below the mean), those participants who completed ABM experienced significantly greater reductions in PCL scores compared to the ACC group. Using similar methodology, we examined whether attentional bias at baseline moderated the relationship between group and change in depressive symptoms (BDI-II). There were no significant moderation findings for change in depressive symptoms ($p = .383$).

Plasticity of Attentional Bias—We also conducted moderational analyses to determine whether plasticity of attentional bias at the beginning of treatment (i.e., during the first session) would moderate the relationship between Group (ABM, ACC) and change in PTSD (PCL) or depressive (BDI-II) symptoms. We did not find evidence of moderation for change in PTSD symptoms ($p = .209$) nor for change in depressive symptoms ($p = .489$).

Mediation Analyses

Change in Static Attentional Bias—Using change in static attentional bias as a mediator, results revealed that the 95% confidence interval of the indirect path ($\alpha\beta$) did overlap with zero for reduction in PTSD symptoms (lower limit = -2.30, upper limit = 4.52), indicating the absence of a mediation effect. Using a similar methodology, we examined whether difference in change in static attentional bias mediated the relationship between group and change in depressive symptoms (BDI-II). Results revealed that the 95% confidence interval of the indirect path ($\alpha\beta$) included zero for reduction in depressive

symptoms (lower limit = -3.84 , upper limit = 2.63), indicating the absence of a mediation effect. Thus, neither PTSD nor depressive symptom change was moderated by change in static attentional bias.

Change in Plasticity of Attentional Bias—Examining change in plasticity of attentional bias as a mediator using identical methodology, we tested the product of the (1) the independent variable (Group: ABM, ACC) to the mediator (change in bias trainability pre- to post-treatment (α path: unstandardized beta = -135.86 , $SE = 55.37$), and (2) the mediator to the dependent variable (change in PCL-M scores pre- to post-treatment) when the independent variable is taken into account (β path: unstandardized beta = -0.04 , $SE = 0.02$). Results revealed that the 95% confidence interval of the indirect path ($\alpha\beta$) did not overlap with zero for reduction in PTSD symptoms (lower limit = -16.74 , upper limit = -0.13), indicating a mediation effect. Thus, the difference in plasticity of attentional bias from pre- to post-treatment mediated the relationship between ABM conditions and reduction in PTSD symptoms. Next, we examined whether difference in attentional bias trainability mediated the relationship between group and change in depressive symptoms (BDI-II). Results revealed that the 95% confidence interval of the indirect path ($\alpha\beta$) did include zero for reduction in depressive symptoms (lower limit = -7.02 , upper limit = 3.73), indicating the absence of a mediation effect.

General Discussion

The current study suggests that ABM may be beneficial as an adjunct treatment for PTSD for individuals who participate in this intervention. Our study design is consistent with the recommendations of recent reviews (Beard, 2011; Hakamata et al., 2010; Hallion & Ruscio, 2011), calling for research on the combination of ABM with existing treatments, such as CBT and pharmacotherapy. Participants completing ABM in conjunction with standard care at a community inpatient facility experienced significantly greater reductions in symptoms of PTSD and depression than participants receiving standard care and the control version of attention training. Moreover, we found that different forms of attentional bias both mediated as well as moderated the effects of treatment. Specifically, our results suggest that change in attentional bias plasticity across treatment may be an important mechanism through which the treatment (i.e., ABM) exerts its effects on symptom reductions (i.e., mediation effect), and that the effect of ABM on change in symptoms is particularly facilitated for individuals who initially present with a static attention bias away from threat (i.e., moderation effect).

The current study supports the utility of ABM as an adjunctive treatment for PTSD when administered in routine clinical settings. We did not exclude participants on the basis of prior treatment stability, psychiatric comorbidity (e.g., substance dependence), etc. While two recent studies have not yielded incremental effects resulting from ABM administered in combination with ABT, both studies administered highly standardized and specific forms of CBT in the context of an outpatient research setting utilizing specific inclusion and exclusion criteria (Britton et al., 2013; Rapee et al., 2013). Thus, individuals in these studies with relatively uncomplicated diagnostic and treatment profiles may have benefited from ceiling effects of CBT. Conversely, an additional study conducted by Riemann and colleagues (2013) found that addition of ABM to treatment as usual within a residential

setting resulted in improved symptom reduction for highly comorbid youth anxiety cases (Riemann et al., 2013).

While our results suggest that overall, ABM is effective in reducing PTSD symptoms, PTSD as a disorder consists of a variety of symptom clusters. Our results do not speak to the extent to which ABM modifies certain symptom clusters more so than others. For example, one reviewer of this manuscript suggested that ABM may more likely modulate non-specific anxiety symptoms associated with PTSD such as hyperarousal or withdrawal versus re-experiencing symptoms. Indeed, this would be consistent with meta-analyses of ABM suggesting a reduction in general anxiety symptoms (Beard et al., 2012; Hakamata et al., 2010). However, visual attention is thought to serve as the gateway to subsequent information processing systems (Kosslyn, 1999), therefore, it may be the case that modifications in the attentional system and most proximal PTSD symptoms (e.g., hyperarousal) result in cascading effects on other PTSD symptoms such as re-experiencing. While outside the scope of the present study, future research should seek to examine the symptom profile modified by ABM.

However, our results do suggest that in addition to modifying symptoms of PTSD collapsed across symptom clusters, ABM may be effective in targeting depression symptoms in participants with PTSD. Research regarding the efficacy of ABM in reducing depressive symptoms in anxious populations has been mixed. For example, at least two studies (Amir, Beard, Burns, & Bomyea, 2009; Rozenman et al., 2011) found significant decreases in depression following a four-week ABM treatment. However, in their meta-analysis, Hallion and Ruscio (2011) concluded that attention training did not differentially affect depression. Given high rates of comorbidity of depression with PTSD compared to anxiety disorders it is possible that ABM is more effective at targeting depressive symptoms in this population. We note that DSM-IV (American Psychiatric Association, 2000) criteria for PTSD were used in both of our studies, and therefore we examined symptoms of PTSD and depression independently. Revised diagnostic criteria for PTSD in DSM-V (American Psychiatric Association, 2013) include symptoms that are central to both disorders.

Our findings are consistent with randomized trials of other first-line treatments (i.e., Prolonged Exposure, Cognitive-Processing Therapy) that found targeting PTSD symptoms was associated with a reduction in depression as well (Foa et al., 2005; Resick, Nishith, Weaver, Astin, & Feurer, 2002). Moreover, while we selected the stimuli for the current studies to enhance disengagement from trauma-specific content rather than depressive content, it is possible that ABM affected negative emotional processing in general by means of enhanced attentional control (Bair-Haim, 2010; Bar-Haim et al., 2007; Ehlers, Ehling & Kleim, 2012; Eysenck, Derakshan, Santos, & Calvo, 2007).

Further evidence for the role of enhanced attentional control is supported by our moderation analyses examining static attentional bias. While previous research suggests that higher level of static attentional bias *towards* threat corresponds with greater symptom decreases as a result of ABM (Amir et al., 2011; Kuckertz et al., 2014), the findings of the current study suggest the opposite. That is, individuals with greater attentional bias *away* from threat experienced greater symptom reductions as a result of ABM, despite having their attention

trained away from threat. At least two possibilities may explain these findings. First, some previous research supporting attentional control theory has demonstrated lowered anxiety as a result of either training towards or training away from threat (Klumpp & Amir, 2010), although research in this area has been mixed (e.g., Heeren et al., 2012). Given that some research suggests that individuals who develop PTSD may possess both an attentional bias away from threat (Beevers, Lee, Wells, Ellis, & Telch, 2011; Sipos, Bar-Haim, Abend, Adler, & Bliese, 2014; Wald et al., 2013) as well as deficits in attentional control (Aupperle et al., 2012), it may be the case that that training direction (i.e., towards or away from threat) is of less importance than the fact that the training contains a contingency between emotional stimuli and required response in which the individual learns to exert top-down attentional control over presented stimuli. Second, it may be the case that individuals who initially present with a bias away from threat possess a cognitive strength that is more easily maximized through attention training away from threat, relative to individuals who have a pre-existing difficulty attending away from threat. Indeed, a recent study suggested that increased activation in brain areas corresponding to attentional control predicted greater reductions in anxiety symptoms as a result of CBT, presumably because individuals with intact levels of attentional control were better able to utilize this strength to benefit from CBT strategies (Klumpp, Fitzgerald, Angstadt, Post, & Phan, 2014).

Furthermore, reductions in the plasticity of attentional bias within session mediated the effect of ABM on PTSD symptom reductions. While several studies have examined the effect of attentional bias change from pre- to post-treatment as a mediator of ABM outcomes (Amir, Beard, & Taylor, 2009; Heeren et al., 2012; Kuckertz et al., 2014), this is the first study to suggest that change in attentional bias plasticity may explain positive outcomes resulting from ABM. This is consistent with recent suggestion that variability of attentional bias within session is more directly relevant to PTSD symptoms than attentional bias at a single time point (Iacoviello et al., 2014). One possible interpretation of these results is that individuals who were able to learn through ABM to better control the extent to which their attention was differentially affected by emotional stimuli experienced subsequent reductions in PTSD symptoms, whereas this process did not occur in the ACC group. We note that reduction in the attentional bias plasticity index may result from other factors as well, such as decreased concentration to the task as treatment progressed. However, observed differences between ABM and ACC groups would infer that the ABM task was less engaging than the ACC task, and we are not aware of any data that would suggest that this would be the case given that the only difference between the two conditions was the percent contingency between emotional stimuli and probe location. Nonetheless, future research should seek to replicate these effects and examine other possible interpretations of observed patterns in bias change.

Our results suggest that future attention training studies should examine both individual difference factors (i.e., level of bias before treatment) as well as the extent to which the ABM protocol had its intended effect (i.e., change in bias). Consistent with this suggestion, we found that ABM was effective in reducing the symptoms of PTSD and that this effect was mediated by change in attentional bias plasticity. However, we did not find that initial plasticity moderated symptom change. Therefore, our data suggest that static attentional bias

at a single time point (see Amir et al., 2011; Kuckertz et al., 2014) is a better moderator of symptom change than is attentional bias plasticity.

As pointed out by MacKinnon et al. (2012 proceeding of NIMH conference on science of basic change, 2012) meditational analyses can be informative both in trials where an independent variable (IV) produces an effect on the dependant variable (DV) and on trials where this relationship is absent if there is clear measure of the mediator. More specifically, in trials where the IV fails to affect the DV one can address whether the effect was absent because the IV failed to change the mediator or because the mediator changed but it did not affect the DV. To our knowledge no studies that have shown an effect of training on bias have then failed to show an effect of ABM on symptom change. As such, the studies that have failed to show symptom change as a result of ABM are not informative regarding the efficacy of ABM because they did not show that the intervention was effective in changing the mediators of change (see also Clarke et al., 2014).

Despite our ability to show both change in the mediator as well as the dependant variable, our study is limited in that the design did not allow us to demonstrate temporal precedence of the mediator (Kraemer, Kiernan, Essex, & Kupfer, 2008). While our theory driving the current study is that attentional bias is modified as a result of ABM, thus leading to subsequent change in symptoms, it is equally possible that change in symptoms corresponded with later change in bias. Future studies examining the mediating role of attentional bias in ABM should include collection of symptom data at multiple follow up points in order to more precisely examine meditational hypotheses.

Our analyses suggest that ABM resulted in significantly greater symptom reductions for individuals who initiated the program. On average, participants completed 6.7 sessions. Thus, the number of sessions completed indicated suboptimal compliance with the given recommendation to complete the ABM program 14 times over consecutive days. However, this dose is similar to previous studies which have found positive effects of ABM after four consecutive days (Heeren et al., 2012) or eight sessions completed over four weeks (Amir, Beard, Burns et al., 2009; Amir, Beard, Taylor et al. 2009; Kuckertz et al., 2014; Schmidt et al., 2009), and thus the observed treatment response in the current study is not unexpected.

High dropout rate raises concerns regarding the effectiveness of this program in real-world settings. Given that individuals who complete the program appear to benefit from its effects, future research should focus on ways to adapt ABM programs in order to increase compliance. For example, Beard, Weisberg, and Primack (2012) interviewed socially anxious individuals who completed ABM regarding their perceptions and experience with the task. Participants in that study emphasized the importance of being provided a rationale for the program as well as evidence of its efficacy. Moreover, participants emphasized that they would prefer to initiate the program in a medical office setting, but to complete later sessions at home. Finally, Beard et al. reported that some participants found the ABM program strange or monotonous. Consistent with the qualitative work conducted by Beard and colleagues, we suggest that healthcare professionals provide a rationale for ABM prior to administration, and that researchers continue to test versions of the program that increase patient engagement and compliance.

Our study has additional limitations. The small sample size limits the conclusions we can draw from this study. A lack of follow-up data prevents us from examining the temporal stability of benefits derived from ABM. These limitations notwithstanding, this study begins to examine the utility of ABM in real world settings and suggests that completion of ABM may be beneficial in reducing symptoms of PTSD. Moreover, our results suggest that future ABM research should examine the role of different forms of attentional bias, including both static attentional bias as well as plasticity of attentional bias.

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Highlights

- Attention bias modification is effective in reducing symptoms of PTSD
- Attention bias modification for PTSD may also reduce depressive symptoms
- Initial level of attention bias moderates the effect of ABM on PTSD symptom change
- Change in plasticity of attentional bias accounts for the effects of ABM on symptom change

Figure 1. CONSORT flowchart of study participants, point of random assignment, and dropouts at each stage.

Figure 2.
Moderation models tested and associated coefficients for each path.

Figure 3.
Mediation models tested and associated coefficients for each path.

Figure 4.
Moderating effect of static attentional bias on change in PTSD symptoms.

Table 1

Participant Demographics and Symptom Characteristics

	ABM (<i>n</i> = 12)	ACC (<i>n</i> = 17)
Gender (% male)	91.67	94.12
Ethnicity (%)		
Asian American	0.00	11.77
Hispanic	16.67	5.88
White	83.33	82.35
Age (years)	26.83 (5.84)	24.76 (5.77)
Education (years)	12.14 (0.38)	12.57 (1.60)
Substance Dependence Diagnosis (%)	75.00	52.94
PCL Pre	63.08 (9.13)	61.71 (9.04)
PCL Post	42.83 (12.04)	51.65 (14.72)
BDI-II Pre	30.92 (13.46)	29.82 (10.27)
BDI-II Post	14.67 (9.61)	22.07 (14.90)
CPT (% receiving) ^{<i>1</i>}	33.33	17.65
PE (% receiving) ^{<i>1</i>}	50.00	70.59
Medication (% receiving)	100	100
Days Between Assessments	27.11 (9.71)	23.27 (12.35)

Note. BDI-II = Beck Depression Inventory-II; PCL = Post-Traumatic Stress Disorder Checklist; CPT = Cognitive Processing Therapy; PE = Prolonged Exposure.

^{*1*} Four participants received neither CPT nor PE but participated in all other program components.

Table 2

Words Used in the Study

Agony	Chorus	Fear	King	Park	Specialize
Aisle	Civilian	Feather	Knife	Pastel	Spring
Alone	Coconut	Fetch	Laceration	Patrol	Stab
Ambush	Coffeepot	Fire	Lamp	Phrase	Stool
Artillery	Coffin	Firefight	Landmine	Physics	Strawberry
Assault	Combat	Fit	Lemon	Picture	Struggle
Attire	Connection	Flavor	Lethal	Pitcher	Suffocate
Baboon	Convoy	Flounder	List	Plumbing	Suicide
Baghdad	Couch	Garlic	Lollipop	Point	Support
Bagpipe	Courtyard	Grief	Loss	Portion	Symphony
Banana	Crew	Guilt	Massacre	Post	Target
Bank	Cry	Gulf	Measure	Prisoner	Tennis
Battle	Curtain	Gun	Medevac	Punishment	Terror
Bicycle	Curve	Gunner	Mirror	Pupil	Terrorist
Blast	Deathbed	Guppy	Missile	Reading	Thereby
Blood	Desert	Hallmark	Mortar	Recall	Thousand
Bodybag	Destroy	Handle	Mouse	Refugee	Threat
Bomb	Device	Hatred	Murder	Remark	Tile
Bottom	Dinner	Helpless	Mustard	Room	Torture
Brandy	Dinosaur	Horror	Mythology	Sandbox	Turn
Broiler	Disaster	Hostage	Narrative	Sauce	Turntable
Brutal	Dishwasher	Humvee	Nectarine	Scan	UPS
Bubble	Duty	IED	Network	Sculpture	Variable
Bullet	Edit	Inflict	Nightmare	Season	Verse
Burning	Elephant	Injury	Note	Secret	Victim
Bush	Emergency	Insert	Numb	Security	Violin
Camp	Evening	Insurgent	Orange	Shame	Walrus
Capture	Execution	Invader	Oven	Shop	War
Casualty	Explosion	Jihad	Own	Side	Weapon
Catfish	Fallujah	Jockey	Pain	Slaughter	Winter

Chaos	Fatal	Journal	Panic	Snapper	Wound
Chopper	Faucet	Kill	Paralyzed	Softener	Yeast