# Bias-contingent attention bias modification and attention control training in treatment of PTSD: a randomized control trial

Amit Lazarov[1,*], Benjamin Suarez-Jimenez[2,*], Rany Abend[3], Reut Naim[4],
Erel Shvil[5], Liat Helpman[2], Xi Zhu[2], Santiago Papini[6], Ariel Duroski[5], Rony Rom[5],
Franklin R. Schneier[2], Daniel S. Pine[3], Yair Bar-Haim[7] and Yuval Neria[2]

[1]Department of Psychiatry, Columbia University Medical Center and New York State Psychiatric Institute, New York, NY, USA, and School of Psychological Sciences, Tel Aviv University, Tel Aviv, Israel; [2]Department of Psychiatry, Columbia University Medical Center and New York State Psychiatric Institute, New York, NY, USA; [3]Section on Developmental Affective Neuroscience, National Institute of Mental Health, Bethesda, MD, USA; [4]School of Psychological Sciences, Tel Aviv University, Tel Aviv, Israel; [5]New York State Psychiatric Institute, New York, NY, USA; [6]Department of Psychology, The University of Texas at Austin, Institute for Mental Health Research, TX, USA and [7]School of Psychological Sciences and Sagol School of Neuroscience, Tel Aviv University, Tel Aviv, Israel

## Abstract

**Background.** Randomized control trials (RCTs) comparing attention control training (ACT) and attention bias modification (ABM) in posttraumatic stress disorder (PTSD) have shown mixed results. The current RCT extends the extant literature by comparing the efficacy of ACT and a novel bias-contingent-ABM (BC-ABM), in which direction of training is contingent upon the direction of pre-treatment attention bias (AB), in a sample of civilian patients with PTSD.

**Methods.** Fifty treatment-seeking civilian patients with PTSD were randomly assigned to either ACT or BC-ABM. Clinician and self-report measures of PTSD and depression, as well as AB and attention bias variability (ABV), were acquired pre- and post-treatment.

**Results.** ACT yielded greater reductions in PTSD and depressive symptoms on both clinician-rated and self-reported measures compared with BC-ABM. The BC-ABM condition successfully shifted ABs in the intended training direction. In the ACT group, there was no significant change in ABV or AB from pre- to post-treatment.

**Conclusions.** The current RCT extends previous results in being the first to apply ABM that is contingent upon AB at pre-treatment. This personalized BC-ABM approach is associated with significant reductions in symptoms. However, ACT produces even greater reductions, thereby emerging as a promising treatment for PTSD.

Posttraumatic stress disorder (PTSD) is a persistent and disabling condition unless there is a timely targeted intervention (Blanchard *et al.*, 2003). While numerous psychological and pharmacological treatments exist (Bradley *et al.*, 2005; Sullivan and Neria, 2009), poor clinical response creates a need to identify new targets for therapeutic intervention (Difede *et al.*, 2014). Threat-related ABs may represent such a target (Buckley *et al.*, 2000; Brewin and Holmes, 2003). Indeed, cognitive models of PTSD implicate different information processing biases in this disorder (Buckley *et al.*, 2000; Brewin and Holmes, 2003), including biased attention for threat- and trauma-related information (Chemtob *et al.*, 1988; Foa *et al.*, 1989; Litz and Keane, 1989; Foa *et al.*, 1991; Foa and Rothbaum, 1998; Ehlers and Clark, 2000; Aupperle *et al.*, 2012).

Computerized protocols targeting AB were examined more extensively in randomized controlled trials (RCTs) of anxiety disorders than PTSD (Bar-Haim, 2010; Linetzky *et al.*, 2015). The four RCTs conducted in PTSD all compared the clinical efficacy of two training variants: attention bias modification (ABM) and attention control training (ACT). ABM is designed to reduce AB to threat through systematic, implicit training (Bar-Haim, 2010). Using an adaptation of the dot-probe task (MacLeod *et al.*, 1986), participants are trained to shift attention to neutral over threat stimuli. ACT, originally used as a control condition for ABM protocols as it is not designed to shift attention in any specific direction (Bar-Haim, 2010; Schoorl *et al.*, 2013; Kuckertz *et al.*, 2014*a*), is thought to enhance attentional control in the context of threat (Badura-Brack *et al.*, 2015). ACT uses a balanced version of the dot-probe task, in which participants are implicitly encouraged to ignore threat-neutral locations to maximize task performance (Badura-Brack *et al.*, 2015).

The four RCTs in PTSD have shown mixed results (Schoorl *et al.*, 2013; Kuckertz *et al.*, 2014*a*; Badura-Brack *et al.*, 2015). Initial studies had shown no differences (Schoorl *et al.*, 2013) or greater symptom reduction for ABM over ACT (Kuckertz *et al.*, 2014*a*). A more recent paper reported data from two independent stand-alone trials of Israel Defense Forces

and US Military veterans with PTSD, both showing an advantage for ACT over ABM in symptom reduction (Badura-Brack et al., 2015).

These mixed findings could arise from unique aspects of attention perturbation in PTSD. Greater variability across patients in PTSD, relative to anxiety disorders (Badura-Brack et al., 2015; Naim et al., 2015), could limit the efficacy of traditional away-from-threat ABM procedures. Previous research reported both ABs toward (Bryant and Harvey, 1997; Buckley et al., 2000; Bardeen and Orcutt, 2011) and away from threat (Bar-Haim et al., 2010; Fani et al., 2011; Sipos et al., 2014) in PTSD, raising questions about the most appropriate form of ABM in PTSD (Badura-Brack et al., 2015), especially as the degree and direction of pre-treatment AB were found to moderate ABM efficacy (Amir et al., 2011; Kuckertz et al., 2014a; Kuckertz et al., 2014b). Thus, tailoring ABM training to the nature of bias at pre-treatment may improve ABM efficacy. Alternatively, different approaches may be needed, since patients with PTSD also manifest increased within-session variability in threat-related attention than patients with anxiety disorders, a phenomenon termed AB variability (ABV; Badura-Brack et al., 2015, Naim et al., 2015). This PTSD-specific perturbation may reflect impaired attention control as opposed to a bias in attention allocation (Bardeen and Orcutt, 2011; Badura-Brack et al., 2015). In this case, ACT might be a more suitable training protocol for PTSD (Badura-Brack et al., 2015).

We compare the efficacy of ACT (Badura-Brack et al., 2015) and a bias-contingent-ABM (BC-ABM) protocol, in which training direction was contingent upon the direction of each patient's pre-treatment bias. Specifically, patients with a bias away from threat at baseline were trained towards threat, whereas patients with a bias towards threat at baseline were trained away from threat. We expected the BC-ABM group to manifest a change in AB and the ACT group to manifest a reduction in ABV. Clinical effects hypotheses were non-directional, given inconsistencies in prior RCTs of PTSD.

## Method

### Participants

For progress through the study, see CONSORT Fig. 1. Fifty civilian treatment-seeking patients with PTSD ($M_{age}$ = 35.68, S.D. = 10.22; Range = 21–34; 19 males) were randomly assigned to receive ACT or BC-ABM. Groups did not differ on baseline variables $ps$>0.12 (Table 1). Nine patients (18%) discontinued treatment (ACT = 5, BC-ABM = 4) with no group difference in drop-out, $\chi^2_{(1)}$ = 0.25, $p$ = 0.62. This dropout rate appears to be lower than prior RCTs of PTSD (Imel et al., 2013; Schoorl et al., 2013; Kuckertz et al., 2014a; Badura-Brack et al., 2015). Within the BC-ABM group, 15 patients showed bias toward threat at pre-treatment, while 11 showed the opposite pattern (For descriptive statistics of these sub-groups see Table 2). The New York State Psychiatric Institute Institutional Review Board approved the study. Participants provided written informed consent. ClinicalTrials.gov identifier: NCT01888653.

### Diagnoses and inclusion criteria

Participants were recruited via the website of the PTSD Research and Treatment Program, Anxiety Disorders Clinic, New York State Psychiatric Institute and local media. Potential participants were phone-screened using the 17-item PTSD Checklist-Civilian (PCL-C; Weathers et al., 1991). Those with PCL-C scores ⩾30 were invited to the clinic for a complete clinical assessment by an independent evaluator, a PhD-level psychologist trained to 85% reliability with a senior clinician on all interview-based measures. Rater reliability was ascertained based on three test-cases that were independently scored and then reviewed and compared with those of the senior clinician, with Cohen's kappa being above 0.7 for all three. Weekly sessions were conducted to monitor and review diagnostic decisions. Primary and co-morbid diagnoses were ascertained using the Structured Clinical Interview for DSM-IV (SCID; First et al., 1995). PTSD diagnosis was further established using the Clinician-Administered PTSD Scale (CAPS; Blake et al., 1995), with a cutoff score ⩾50 as an inclusion criterion.

Additional inclusion criteria were: (a) primary diagnosis of PTSD; (b) 18–60 years of age; (c) normal or corrected-to-normal vision; and (d) AB toward or away from threat >3 ms. We used the 3 ms criterion as this was the minimum group average bias reported in previous RCTs in PTSD (Schoorl et al., 2013; Badura-Brack et al., 2015). Exclusion criteria were: (a) current Axis-I disorder other than PTSD [except for mild-to-moderate major depressive disorder (MDD), indicated by a Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) score ⩽25]; (b) history of psychosis; (c) personality disorder; (d) risk for violence to self or others; (e) prior participation in ABM; (f) concurrent psychotropic medication or psychotherapy; and (g) unstable or untreated medical illness. The final sample included 17 participants with co-morbid MDD (9 in BC-ABM).

## Outcome measures

### Primary outcome – clinician-rated PTSD

The severity of PTSD symptoms, measured by the CAPS (Blake et al., 1995), served as the primary outcome. The CAPS is a structured interview diagnosing PTSD based on DSM-IV criteria. It has been widely used in research demonstrating excellent reliability, convergent and discriminant validity, diagnostic utility and sensitivity to change (Weathers et al., 2001). Cronbach's $\alpha$ in the current sample was 0.68.

Clinically significant change (CSC) was taken as ⩾30% reduction in CAPS score at post-treatment as per previous scoring practices for the measurement of CSC in PTSD (Hien et al., 2010).

### Secondary outcome – self-reported PTSD

The PCL-C (Weathers et al., 1991) indexed self-reported PTSD symptom severity and served as a secondary outcome. The PCL-C is a 17-item questionnaire assessing the presence and severity of symptoms in civilian populations. The PCL-C has been used extensively in research and clinical settings and has good internal consistency, test-retest reliability, and convergent and discriminant validity (Ruggiero et al., 2003). Cronbach's $\alpha$ in the current sample was 0.86.

### Depression

Clinician-rated depressive symptoms were measured using the HRSD (Hamilton, 1960), administered using the Structured Interview Guide for the Hamilton Rating Scale for Depression (SIGH-D; Williams, 1988). The SIGH-D is a 17-item measure of depression covering core symptoms with strong psychometric properties in clinical samples (Williams, 1988). Cronbach's $\alpha$ in the current sample was 0.68. Depression was further assessed using the self-reported Beck Depression Inventory-II (BDI-II;
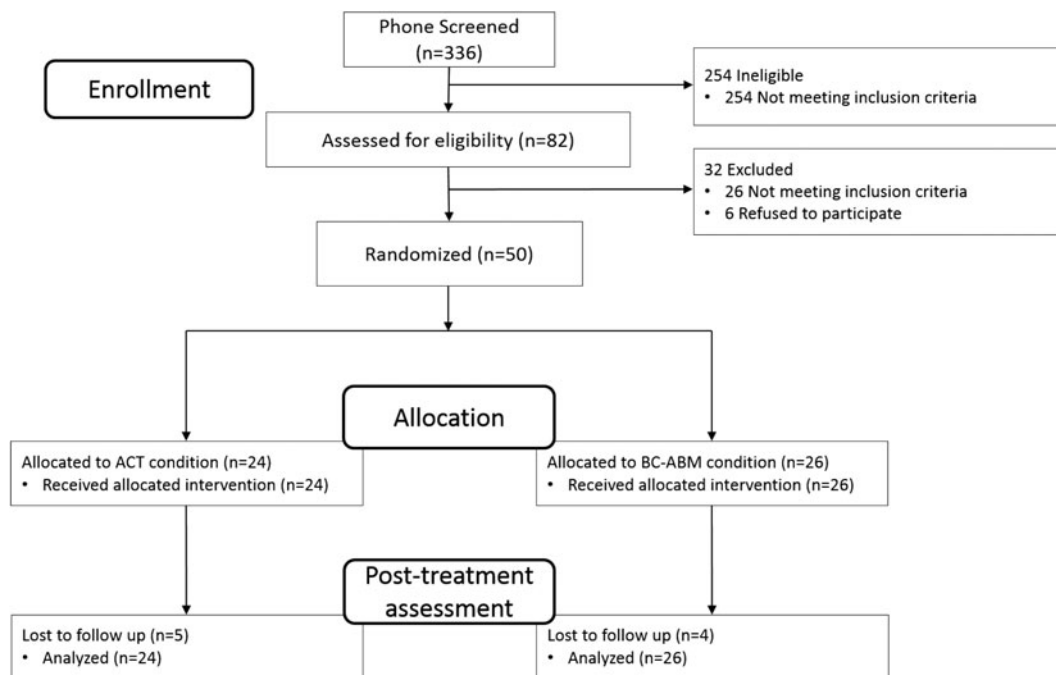
**Fig. 1.** Consort Diagram.

**Table 1.** Demographic characteristics, PTSD and depression symptoms, and AB indices by a group at pretreatment and posttreatment

| | BC-ABM group (n = 26) | | ACT group (n = 24) | |
|---|---|---|---|---|
| | *M* | S.D. | *M* | S.D. |
| Age | 34.27 | 10.15 | 37.21 | 10.29 |
| Years of education | 15.32 | 2.19 | 15.22 | 2.14 |
| Gender ration (M:W) | 9:17 | – | 10:14 | – |
| CAPS (pre-treatment) | 62.23 | 10.39 | 65.00 | 12.08 |
| CAPS (post-treatment) | 46.27 | 16.77 | 38.56 | 24.44 |
| PCL (pre-treatment) | 57.31 | 9.66 | 62.12 | 11.16 |
| PCL (post-treatment) | 49.47 | 11.77 | 41.90 | 14.50 |
| HRSD (Pre-treatment) | 11.77 | 5.18 | 13.00 | 4.82 |
| HRSD (Post-treatment) | 10.06 | 4.54 | 7.22 | 5.92 |
| BDI-II (pre-treatment) | 24.58 | 12.36 | 25.87 | 11.34 |
| BDI-II (post-treatment) | 21.52 | 14.17 | 14.74 | 13.22 |
| AB (pre-treatment) | 10.80 | 33.27 | 3.50 | 30.69 |
| AB (post-treatment) | −0.24 | 17.95 | −11.44 | 31.65 |
| ABV (pre-treatment) | 0.07 | 0.02 | 0.07 | 0.03 |
| ABV (post-treatment) | 0.07 | 0.02 | 0.07 | 0.05 |

PTSD, Posttraumatic Stress Disorder; BC-ABM, Bias Contingent Attention Bias Modification; ACT, Attention Control Training; CAPS, Clinician-Administered PTSD Scale; PCL, PTSD Checklist; HRSD, Hamilton Rating Scale for Depression; BDI-II, Beck Depression Inventory – II; AB, Attention Bias; ABV, Attention Bias Variability.

**Table 2.** Demographic characteristics, PTSD and depression symptoms, and AB indices by BC-ABM sub-group at pre-treatment and post-treatment

| | Bias toward (n = 15) | | Bias away (n = 11) | |
|---|---|---|---|---|
| | *M* | S.D. | *M* | S.D. |
| Age | 35.13 | 9.14 | 33.09 | 11.74 |
| Years of education | 15.00 | 2.30 | 15.75 | 2.04 |
| Gender ration (M:W) | 5:10 | – | 4:7 | – |
| AB (pre-treatment) | 31.43 | 27.79 | −17.32 | 13.33 |
| AB (post-treatment) | 0.77 | 15.26 | −3.66 | 21.36 |
| CAPS (pre-treatment) | 62.73 | 10.91 | 61.54 | 10.11 |
| CAPS (post-treatment) | 44.65 | 11.93 | 48.93 | 23.45 |
| PCL (pre-treatment) | 55.20 | 10.10 | 60.18 | 8.63 |
| PCL (post-treatment) | 48.06 | 11.08 | 51.62 | 12.27 |
| HRSD (Pre-treatment) | 11.93 | 4.44 | 11.54 | 6.26 |
| HRSD (Post-treatment) | 9.69 | 4.49 | 10.75 | 4.15 |
| BDI-II (pre-treatment) | 22.73 | 11.89 | 27.09 | 13.11 |
| BDI-II (post-treatment) | 18.30 | 11.81 | 25.64 | 14.72 |
| ABV (pre-treatment) | 0.07 | 0.02 | 0.07 | 0.02 |
| ABV (post-treatment) | 0.07 | 0.02 | 0.07 | 0.03 |

PTSD, Posttraumatic Stress Disorder; BC-ABM, Bias-contingent Attention Bias Modification; CAPS, Clinician-Administered PTSD Scale; PCL, PTSD Checklist; HRSD, Hamilton Rating Scale for Depression; BDI-II, Beck Depression Inventory – II; AB, Attention Bias; ABV, Attention Bias Variability.

Beck et al., 1996). The BDI-II assesses the presence of 21 depression-related symptoms. It has high internal consistency in clinical and non-clinical samples, and good test-retest reliability (Beck et al., 1996). Cronbach's α in the current sample was 0.92.

### AB assessment and training

For assessment of AB pre- and post-treatment as well as for ABM we used a faces-based variant of the dot-probe task following the TAU-NIMH ABMT Initiative protocol (http://people.socsci.tau.ac.il/mu/anxietytrauma/research/).

### The dot-probe task

In each trial of the dot-probe task used in the study, a fixation cross appeared for 500 ms, followed by a pair of faces of the same actor presented one above the other for 500 ms. Next, a probe display (either '<' or '>') appeared in the location of one of the previously presented faces. The probe remained on the screen until response, which was followed by an inter-trial interval of 500 ms. Participants were instructed to indicate the orientation of the arrowhead probe via a corresponding keyboard press and to perform the task as quickly as possible without compromising accuracy.

The face stimuli were photographs of 20 individuals (10 male, 10 female), with closed-mouth, taken from the NimStim gallery (Tottenham et al., 2009), with each actor contributing one angry and one neutral facial expression. Faces were presented in angry–neutral or neutral–neutral pairs. The face stimuli were split into two sets, A and B, each consisting of 10 actors (5 male).

### Threat bias assessment

The bias assessment task included a total of 120 trials, with 80 angry-neutral trials and 40 neutral-neutral trials. For the pre-treatment assessment, participants were randomly assigned to complete the task with either set A or B of face stimuli, with the opposite set used later for training. Angry face location, probe location, and probe type were fully counterbalanced across trials. In line with previous ABM research (Naim et al., 2015; Lazarov et al., 2017a), for each participant we first excluded inaccurate responses, trials with response latencies <150 ms or >1200 ms, and trials with response latencies ± 2.5 S.D.s from the participant's mean (<2% of all trials, with no group differences).

### Attention indices

In line with previous RCTs in PTSD (Badura-Brack et al., 2015), two attention indices were computed: threat-related AB and ABV.

Threat-related AB was calculated for each participant as the differences between the mean reaction time (RT) on threat-incongruent trials (i.e. the probe appeared in the location previously occupied by the neutral face) and mean RT on threat-congruent trials (i.e. the probe appeared in the location previously occupied by the angry face), such that positive values indicate bias toward threat and a negative value reflects a bias away from threat.

Individual ABV scores were calculated in accordance with previous studies employing this measure in PTSD (Badura-Brack et al., 2015; Naim et al., 2015). Specifically, a 4-step process was employed: (1) a trial-by-trial moving average algorithm computed mean RTs for all successive 10 neutral trial blocks and all successive 10 threat trial blocks; (2) successive AB scores were calculated by subtracting the first threat block average from the first neutral block average, the second threat block average from the second neutral block average, etc., forming a series of consecutive AB scores; (3) the standard deviation of these successive bias scores was then calculated, providing an index of variation in AB throughout the session; and (4) this standard deviation score was divided by the participant's mean overall RT to control for associations between mean and variance. Thus, AB variability reflects the within-session variability in threat-related AB, normalized to individual task performance (Badura-Brack et al., 2015; Naim et al., 2015).

### Attention bias modification and attention control training

The training protocol consisted of 160 trials per session with 120 angry-neutral and 40 neutral-neutral trials. Each participant was trained with an alternative set of faces to the one used in the assessment task (i.e. if measured with set A then trained with set B and vice-versa). In the ABM condition, training was contingent on the bias measured at pre-treatment. Specifically, for those showing a bias toward the threat, the target appeared at the neutral-face location in 100% of the threat-neutral trials, while for those showing a bias away from the threat, the target appeared at the threat-face location in 100% of the threat-neutral trials. Thus, both BC-ABM variants introduced a contingency between the target location and face valence. In the ACT condition, threat-face location, probe location, and probe type were fully counterbalanced with no contingency between face valence and probe location, thus resembling the assessment task.

### General procedure

The study design was a parallel-group RCT: two groups (ACT, BC-ABM) and two assessment points (pre-treatment, post-treatment). Participants were randomly assigned to a treatment condition in a 1:1 ratio, stratified by age and gender, by a staff member not involved in the study. Participants were assessed at each time point using the CAPS (primary outcome measure), PCL-C (secondary outcome measure), HRSD, and BDI-II. Attention indices (AB, ABV) were also measured. All participants were assessed at each time point using the clinician-rated measures, self-report questionnaires, and attention measures. Data collection occurred January 2014 to March 2018.

Consenting participants underwent a clinical assessment at pre-treatment by an independent evaluator blind to group assignment and all aspects of treatment. Participants were informed that the purpose of the study was to evaluate the efficacy of a novel computerized treatment for PTSD. Those meeting clinical inclusion criteria completed the attention assessment task to verify an AB score ⩾3 ms. Sixteen participants were excluded at this stage. Treatment consisted of eight bi-weekly 20-min sessions conducted over 4 weeks. Post-treatment assessment was conducted 1 week after the last training session. Study personnel and participants were blind to treatment group assignment.

### Data analysis

Independent samples t tests were used to compare between-groups descriptive characteristics at pre-treatment, with a $\chi^2$ test for gender distribution. Treatment effects were tested using Generalized Estimating Equations (GEE; Zeger and Liang, 1986; Zeger et al., 1988), as recommended for RCTs (Vens and Ziegler, 2012). GEE accounts for correlated repeated-measurements and accommodates missing data under the missing-at-random assumption, by computing estimated marginal means, thus serving as an intention-to-treat analysis strategy

which includes data from all randomized participants who provided at least one data point. To represent within-subject dependencies in the models, we specified an unstructured covariance matrix. Overall effects of ACT relative to BC-ABM on clinician-rated (CAPS, HRSD) and self-reported (PCL-C, BDI-II) PTSD and depression symptoms were estimated using models containing main effects of group and time, and their interaction. The time-by-group interaction terms reflect the outcomes of interest in an intention-to-treat analysis (Badura-Brack *et al.*, 2015) and test the treatment effect hypothesis of greater improvement (decrease) in symptoms over time for one group relative to the other. A $\chi^2$ test was used to compare groups on CSC.

Effects of training on attention indices (AB and ABV) were examined per condition, as conditions diverged in training method and goal. Specifically, training-related changes in AB were examined in the BC-ABM group, while changes in ABV were examined in the ACT group.

All statistical tests were 2-sided, using $\alpha \leqslant 0.05$. Effect sizes are reported using Cohen's $d$ when appropriate.

## Results

### Primary outcome (CAPS)

Figure 2a illustrates the results of the GEE model for CAPS scores. A main effect of time, $Wald = 73.73$, $p < 0.0001$, was qualified by a time-by-group interaction, $Wald = 4.51$, $p = 0.03$, reflecting a mean change in CAPS score that is 10.48 points larger for the ACT group ($M = 26.44$, S.D. $= 16.09$) relative to the BC-ABM group ($M = 15.96$, S.D. $= 15.75$), Cohen's $d = 0.60$. Follow-up analyses indicated a reduction in CAPS scores from pre- to post-treatment in both groups, with large effect sizes (BC-ABM group, $p < 0.0001$, $d = 1.14$; ACT group, $p < 0.0001$, $d = 1.37$). Rates of CSC did not differ between groups, $\chi^2 = 2.18$, $p = 0.14$, with 54% of patients in the ACT group and 38% of patients in the BC-ABM demonstrating CSC.

### Secondary outcome (PCL)

Figure 2b illustrates the results of the GEE model for PCL scores. A main effect of time, $Wald = 51.56$, $p < 0.0001$, was qualified by a time-by-group interaction, $Wald = 10.04$, $p = 0.002$, reflecting a mean change in PCL scores that is 12.38 points larger for the ACT group ($M = 20.22$, S.D. $= 15.07$) relative to the BC-ABM group ($M = 7.84$, S.D. $= 10.24$), Cohen's $d = 0.90$. Follow-up analyses indicated large reductions in PCL scores from pre- to post-treatment in both groups (ACT, $p < 0.0001$, $d = 1.56$; BC-ABM, $p < 0.0001$, $d = 0.73$).

### Depression (HRSD, BDI-II)

Figure 2c illustrates the results of the GEE model for HRSD scores. A main effect of time, $Wald = 29.89$, $p < 0.0001$, was qualified by a time-by-group interaction, $Wald = 8.84$, $p = 0.003$, reflecting a mean change in HRSD score that is 4.07 points larger for ACT ($M = 5.78$, S.D. $= 4.54$) relative to BC-ABM ($M = 1.71$, S.D. $= 4.51$), Cohen's $d = 0.84$. Follow-up analyses indicated a reduction in HRSD scores from pre- to post-treatment for the ACT group ($p < 0.0001$, $d = 1.07$), with a non-significant trend-level reduction in the BC-ABM group ($p = 0.06$, $d = 0.35$).

Figure 2d illustrates the results of the GEE model for BDI-II scores. A main effect of time, $Wald = 15.28$, $p < 0.0001$, was qualified by a time-by-group interaction, $Wald = 4.96$, $p = 0.02$, reflecting a mean change in BDI-II score that is 8.07 points larger for ACT ($M = 11.13$, S.D. $= 14.96$) relative to BC-ABM ($M = 3.06$, S.D. $= 7.63$), Cohen's $d = 0.64$. Follow-up analyses indicated a significant reduction in BDI-II scores from pre- to posttreatment in both groups (ACT, $p = 0.001$, $d = 1.04$; BC-ABM, $p = 0.05$, $d = 0.23$).

### Treatment-related change in attention measures

#### Bias-contingent attention bias modification

Analysis of AB at pre-treatment for the two BC-ABM sub-groups (i.e. bias-toward, bias-away) showed the expected group difference, $t_{(24)} = 5.36$, $p < 0.001$. One-sample $t$ tests against zero further revealed that at pre-treatment both the bias-toward group, $t_{(14)} = 4.38$, $p = 0.001$, and the bias-away group, $t_{(10)} = -4.31$, $p = 0.002$, had significant mean ABs in the expected direction (see Table 2 for a description of the two BC-ABM sub-groups).

The results from the GEE model for threat-related AB by sub-group and session is depicted in Fig. 3. A group-by-time interaction, $Wald = 15.34$, $p < 0.001$, corroborated a differential training effect in the two sub-groups, with both showing a significant shift in AB in the intended direction, $p = 0.001$ for the bias-toward sub-group and $p = 0.04$ for the bias-away group. Follow-up analysis revealed no group difference in AB at post-treatment, $p = 0.56$, with two separate one-sample $t$ tests against zero indicating non-significant ABs at post-treatment in either the bias-toward or bias-away sub-groups, $ps = 0.86$ and $0.49$, respectively.

#### Attention control training

Contrary to predictions, change in ABV from pre- to post-treatment in the ACT group was not significant, $Wald = 0.07$, $p = 0.79$. Change in the AB measure was also non-significant, $Wald = 1.98$, $p = 0.16$.

## Discussion

This RCT compared the efficacy of two attention training protocols in PTSD: a BC-ABM procedure, in which direction of training was contingent upon the direction of AB at pre-treatment, and ACT. ACT was more effective than BC-ABM across all measures of PTSD and depression symptom severity. A significant shift in AB was noted in the intended training direction for both BC-ABM sub-groups. In the ACT group, no significant change was noted in ABV or AB from pre- to post-treatment.

The greater efficacy of ACT over ABM in reducing PTSD symptoms is in line with some but not other RCTs in PTSD. Similar results were obtained in two recent RCTs in veterans with PTSD that applied the same TAU-NIMH ABMT Initiative protocol as a standalone treatment as used in the current study (Badura-Brack *et al.*, 2015). Conversely, our results diverge from two other RCTs using methods that depart from the present study on several important study-design features. The first study recruited patients awaiting another treatment at a mental health-care department (Schoorl *et al.*, 2013), which could limit treatment efficacy. Not choosing ABM a-priori as a treatment avenue might also involve low treatment expectations, which has been associated with low treatment response (Krell *et al.*, 2004). This study also used pictorial stimuli rather than standard face stimuli as used in the current study. The second study provided ABM/ACT in conjunction with other treatments in an inpatient facility for military personnel with PTSD (Kuckertz
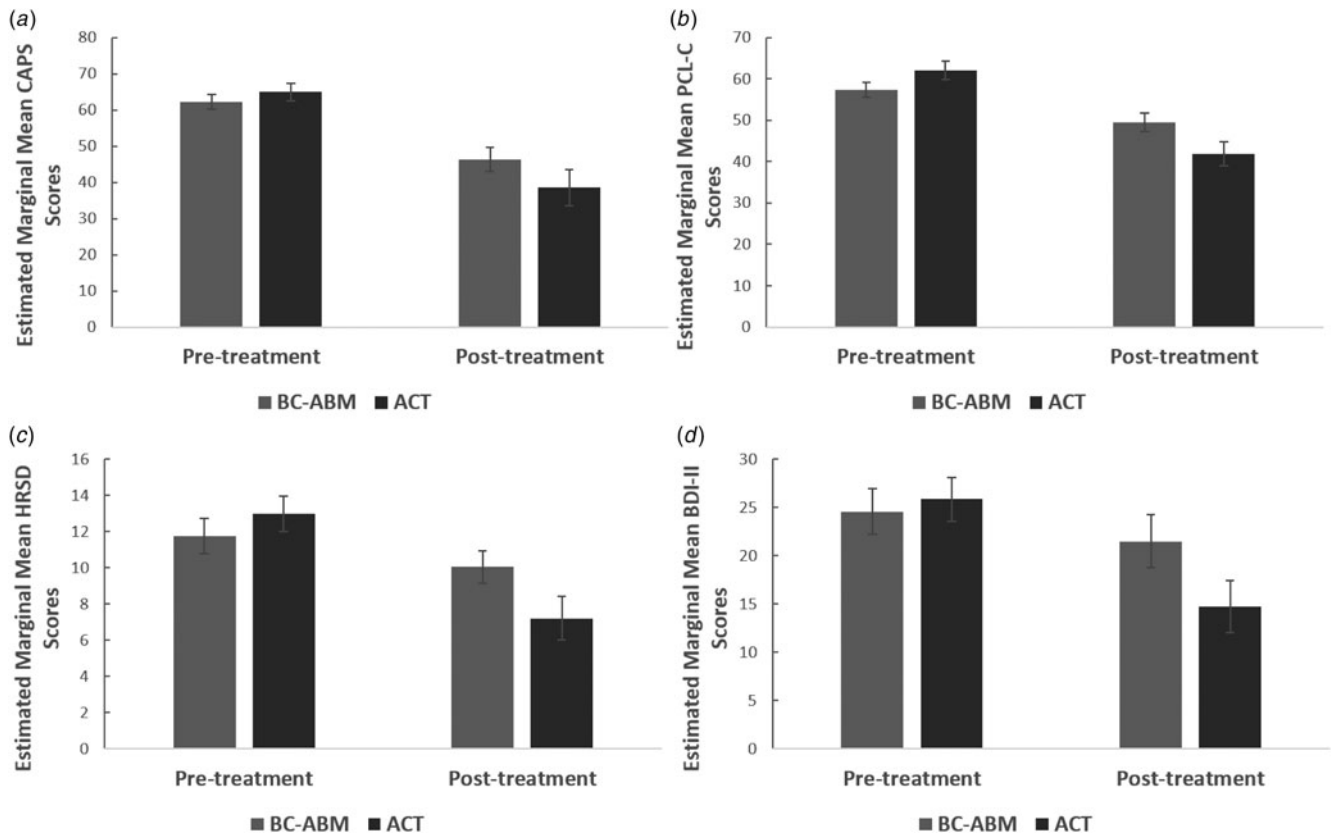
**Fig. 2.** Mean (*a*) CAPS scores, (*b*) PCL scores, (*c*) HRSD scores, and (*d*) BDI-II scores by group (BC-ABM, ACT) and Time (pretreatment, posttreatment). *Note*. CAPS, Clinician-Administered PTSD Scale; PCL, PTSD Checklist; HRSD, Hamilton Rating Scale for Depression; BDI-II, Beck Depression Inventory – II; BC-ABM, Bias contingent attention bias modification; ACT, Attention control training. Error bars denote standard error.
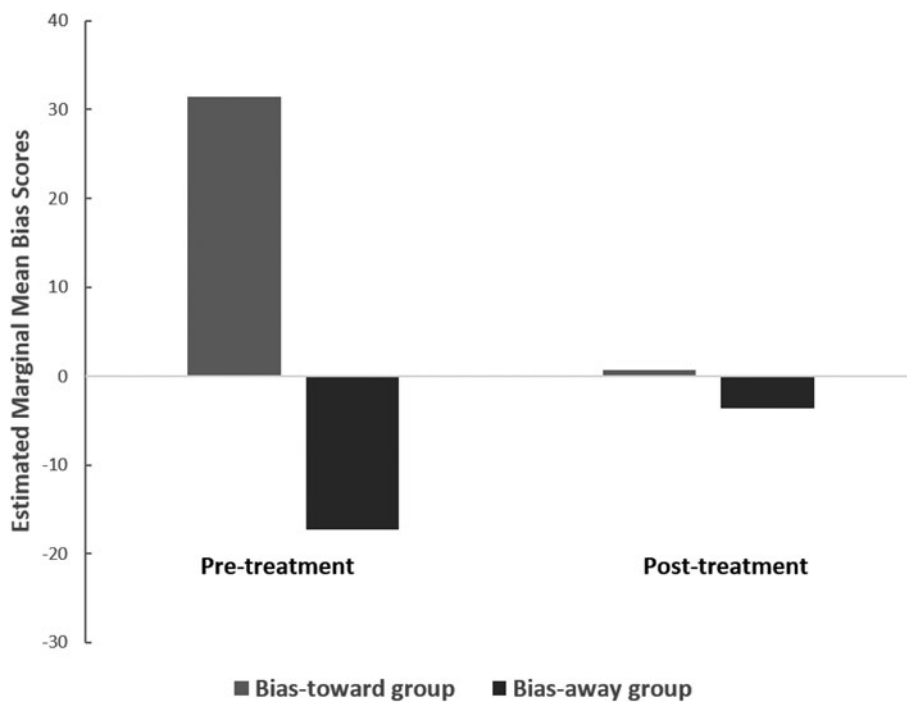


**Fig. 3.** Mean Bias scores by group (Bias-toward, Bias-away) and Time (pretreatment, posttreatment) for the bias contingent attention bias modification (BC-ABM) group.

*et al.*, 2014*a*), thereupon using attention training as an adjuvant. In light of the extant findings, additional RCTs are needed to determine the relative efficacy of ABM and ACT as adjuvants to other PTSD treatments, as was done in other anxiety disorders (Lazarov *et al.*, 2017*b*).

Here we used the direction of AB at pre-treatment to determine the direction of subsequent attentional training within ABM. We reasoned that 'normalizing' ABs may generate better clinical outcomes than training all patients to attend away from threat regardless of their baseline bias. Indeed, BC-ABM produced a significant reduction in symptoms, with both sub-groups demonstrating a reduction in AB following treatment, such that no bias was evident at post-treatment. These results lend support to the distinction between the process of AB change and the ability of specific ABM procedures to evoke this change (Clarke *et al.*, 2014; Basanovic *et al.*, 2017). Thus, ABM procedures may be efficacious in symptom reduction only when they also succeed in changing pre-treatment ABs (MacLeod and Clarke, 2015; MacLeod and Grafton, 2016). Hence, ignoring the direction of AB at pre-treatment could contribute to the lower clinical efficacy of ABM relative to ACT reported in previous RCTs (Badura-Brack *et al.*, 2015). However, in line with these RCTs, we again found ACT to be superior to this new bias-contingent treatment, with a between-intervention effect size of 0.60. While the BC-ABM condition generated an effect size of 1.14, the ACT group manifested an even larger effect size of 1.37. Similar patterns emerged for self-reported PTSD symptoms (*d*s = .73 and 1.56 for BC-ABM and ACT, respectively). Thus, a large clinical effect size for ACT manifested in three independent RCTs, two in military veterans (Badura-Brack *et al.*, 2015) and one in civilians.

The present study also found changes in clinician-rated and self-reported depression symptoms resembling those noted for PTSD symptoms, namely, a reduction in scores in both groups with greater reduction in the ACT compared with the BC-ABM group. This results pattern resembles prior studies that found corresponding changes in PTSD and depression symptoms (Kuckertz *et al.*, 2014*a*; Badura-Brack *et al.*, 2015), while departing from studies examining MDD that typically report poorer clinical outcomes for attention training protocols (Hallion and Ruscio, 2011). This may suggest that attention training is better suited for reducing depressive symptoms co-occurring with PTSD than when occurring as a primary psychiatric condition (Kuckertz *et al.*, 2014*a*). Initiated prior to DSM-5 release, the present study used DSM-IV-based PTSD measures. However, DSM-5 integrates more thoroughly depressive symptoms into the symptomology of PTSD. Thus, current findings may translate seamlessly to the new diagnostic scheme of DSM-5, a prediction that could be verified by additional RCTs applying DSM-5-based PTSD measures.

Despite significant symptom reductions with BC-ABM and corresponding reductions in ABs in this group, reductions in symptoms with ACT were still greater. However, unlike previous RCTs favoring ACT, which noted a mediation of this clinical effect via pre-to-post treatment reduction in ABV (Badura-Brack *et al.*, 2015), we failed to replicate this finding. This may reflect low statistical power, a possibility that could be addressed by future studies employing larger sample sizes. However, what else might be driving enhanced symptom reduction in ACT over ABM? Theory (Eysenck *et al.*, 2007) and research (Bardeen and Orcutt, 2011; Bardeen *et al.*, 2016; Basanovic *et al.*, 2017) suggest that attention control, defined as the capacity to voluntary and effortful execute goal-directed attention deployment while

ignoring conflicting attentional demands (Sarapas *et al.*, 2017), is an important modulator of attention. Attention control was found to be positively associated with the magnitude of AB change following ABM (Basanovic *et al.*, 2017) and to moderate the association between posttraumatic symptoms and AB. Specifically, among those relatively higher in posttraumatic symptoms (like the current sample), attention control was positively related to the ability to shift attention away from threat stimuli (Bardeen and Orcutt, 2011; Bardeen *et al.*, 2016). In line with such findings, it is possible that ACT enhances attention control, which increased the ability of patients to engage/disengage stimuli at will, possibly leading to better clinical efficacy. Thus, while both training protocols exerted positive therapeutic effects, ACT emerged as favorable, possibly through its more robust effect on attention control in the context of threat (Badura-Brack *et al.*, 2015; Basanovic *et al.*, 2017). Still, it remains unclear whether an ACT procedure delivered in a non-threat context would produce similar reductions in symptoms. Future research could further examine this possibility by employing ACT protocols with non-emotional cues such as two different geometrical shapes, thus training attention control in a non-emotional, non-threat context.

Certain study limitations should be considered. First, while ACT is designed to train attention control in the context of attentional threat deployment, we did not directly assess attention control, and hence cannot conclusively determine that it was indeed enhanced in the ACT group. Future research could include specific attention control measures (Bardeen *et al.*, 2016; Basanovic *et al.*, 2017) to explore this possibility. Second, although lack of follow-up assessment has been noted in previous RCTs in PTSD (Kuckertz *et al.*, 2014*a*; Badura-Brack *et al.*, 2015) we were unable to address this shortcoming in the present study, as patients who did not show clinical improvement at post-treatment were referred for additional treatment within our clinic. Third, and related to the previous shortcoming, while the observed changes in AB from pre- to post-treatment in both BC-ABM sub-groups are perfectly aligned with the trained expectations, these might also simply reflect regression to the mean rather than training effects. Future studies including a follow-up assessment could address this possibility. Fourth, while away-from-threat training comprised a sub-group within BC-ABM, the present study did not include a standard 'away-from-threat' ABM group, preventing a direct comparison of its efficacy to that of BC-ABM. However, current results indicated an effect size of 1.14 for BC-ABM, which is considerably larger than previously reported for anxiety disorders (Bar-Haim, 2010; Linetzky *et al.*, 2015) and PTSD (Schoorl *et al.*, 2013). Relatedly, we did not include a placebo control group with no attention training, designed as a potentially inactive treatment, which would have enabled us to control for placebo or other non-specific treatment effects, especially regarding the BC-ABM group. However, because the effect sizes of both groups (1.37 for the ACT and 1.14 for BC-ABM) are considerably higher than those of waiting list and pill-placebo control groups in PTSD trials (Van Etten and Taylor, 1998; Bradley *et al.*, 2005; Schoorl *et al.*, 2013) this possibility seems unlikely. Fifth, we recruited patients with PTSD with no co-morbidities except for mild-to-moderate depression, potentially reducing the generalizability of findings as co-morbidity rates in PTSD are high (Brady *et al.*, 2000). Including only PTSD patients with AB toward or away from threat >3 ms also hinders findings' generalizability as some PTSD patients do not reach this threshold. Future studies could apply more inclusive criteria to address

these issues. In a related vein, while angry faces are considered threatening for PTSD patients with inter-personal traumatic events (Meffert *et al.*, 2008), these faces might be less relevant, and hence less effective, for patients with other types of traumatic experiences. Finally, while in accordance with sample sizes employed in previous RCTs in PTSD that compared ABM and ACT using the same training protocol (Badura-Brack *et al.*, 2015), the sample size was not based on a power analysis. Hence, current findings should be considered while acknowledging the relative small sample size used for comparing two potentially active treatments. Still, significant results and large effect sizes emerged, clearly favoring ACT over BC-ABM in PTSD.

Despite the limitations, current results suggest ACT to be advantageous over ABM in reducing PTSD and depression symptoms among a civilian PTSD sample, even when training is contingent upon AB at pre-treatment. As the current study aligns with two recent RCTs also favoring ACT over ABM in combat-related PTSD (Badura-Brack *et al.*, 2015), it appears that current therapeutic efforts, as well as future research, should focus on ACT and its underlying mechanisms of therapeutic change. Future research could explore and develop novel ways to improve the clinical efficacy of ACT, possibly through better understanding the effects of ACT on attention allocation via attention control, aiming to maximize current patient care.

**Conflict of interest.** None.

**Ethical standards.** The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

# References

Amir N, Taylor CT and Donohue MC (2011) Predictors of response to an attention modification program in generalized social phobia. *Journal of Consulting and Clinical Psychology* **79**, 533–541.

Aupperle RL, Melrose AJ, Stein MB and Paulus MP (2012) Executive function and PTSD: disengaging from trauma. *Neuropharmacology* **62**, 686–694.

Badura-Brack AS, Naim R, Ryan TJ, Levy O, Abend R, Khanna MM, McDermott TJ, Pine DS and Bar-Haim Y (2015) Effect of attention training on attention bias variability and PTSD symptoms: randomized controlled trials in Israeli and U.S. Combat Veterans. *American Journal of Psychiatry* **172**, 1233–1241.

Bardeen JR and Orcutt HK (2011) Attentional control as a moderator of the relationship between posttraumatic stress symptoms and attentional threat bias. *Journal of Anxiety Disorders* **25**, 1008–1018.

Bardeen JR, Tull MT, Daniel TA, Evenden J and Stevens EN (2016) A preliminary investigation of the time course of attention bias variability in posttraumatic stress disorder: the moderating role of attentional control. *Behaviour Change* **33**, 94–111.

Bar-Haim Y (2010) Research review: attention bias modification (ABM): a novel treatment for anxiety disorders. *Journal of Child Psychology and Psychiatry* **51**, 859–870.

Bar-Haim Y, Holoshitz Y, Eldar S, Frenkel TI, Muller D, Charney DS, Pine DS, Fox NA and Wald I (2010) Life-threatening danger and suppression of attention bias to threat. *American Journal of Psychiatry* **167**, 694–698.

Basanovic J, Notebaert L, Grafton B, Hirsch CR and Clarke PJF (2017) Attentional control predicts change in bias in response to attentional bias modification. *Behaviour Research and Therapy* **99**, 47–56.

Beck AT, Steer RA and Brown GK (1996) *BDI-II Manual*, 2nd Edn. San Antonio: Harcourt Brace & Company.

Blake DD, Weathers FW, Nagy LM, Kaloupek DG, Gusman FD, Charney DS and Keane TM (1995) The development of a Clinician-Administered PTSD Scale. *Journal of Traumatic Stress* **8**, 75–90.

Blanchard EB, Hickling EJ, Devineni T, Veazey CH, Galovski TE, Mundy E, Malta LS and Buckley TC (2003) A controlled evaluation of cognitive behaviorial therapy for posttraumatic stress in motor vehicle accident survivors. *Behaviour Research and Therapy* **41**, 79–96.

Bradley R, Greene J, Russ E, Dutra L and Westen D (2005) A multidimensional meta-analysis of psychotherapy for PTSD. *American Journal of Psychiatry* **162**, 214–227.

Brady KT, Killeen TK, Brewerton T and Lucerini S (2000) Comorbidity of psychiatric disorders and posttraumatic stress disorder. *Journal of Clinical Psychiatry* **61**, 22–32.

Brewin CR and Holmes EA (2003) Psychological theories of posttraumatic stress disorder. *Clinical Psychology Review* **23**, 339–376.

Bryant RA and Harvey AG (1997) Attentional bias in posttraumatic stress disorder. *Journal of Traumatic Stress* **10**, 635–644.

Buckley TC, Blanchard EB and Neill WT (2000) Information processing and PTSD: a review of the empirical literature. *Clinical Psychology Review* **20**, 1041–1065.

Chemtob CM, Roitblat HL, Hamada RS, Carlson JG and Twentyman CT (1988) A cognitive action theory of Post-Traumatic Stress Disorder. *Journal of Anxiety Disorders* **2**, 253–275.

Clarke PJF, Notebaert L and MacLeod C (2014) Absence of evidence or evidence of absence: reflecting on therapeutic implementations of attentional bias modification. *BMC Psychiatry* **14**, 8.

Difede J, Olden M and Cukor J (2014) Evidence-based treatment of posttraumatic stress disorder. *Annual Review of Medicine* **65**, 319–332.

Ehlers A and Clark DM (2000) A cognitive model of posttraumatic stress disorder. *Behaviour Research and Therapy* **38**, 319–345.

Eysenck MW, Derakshan N, Santos R and Calvo MG (2007) Anxiety and cognitive performance: attentional control theory. *Emotion* **7**, 336–353.

Fani N, Bradley-Davino B, Ressler KJ and McClure-Tone EB (2011) Attention bias in adult survivors of childhood maltreatment with and without posttraumatic stress disorder. *Cognitive Therapy and Research* **35**, 57–67.

First MB, Spitzer RL, Gibbon M and Williams JBW (1995) *Structured Clinical Interview for DSM-IV Axis I Disorders*. New York: New York State Psychiatric Institute.

Foa EB and Rothbaum BO (1998) *Treating the Trauma of Rape: Cognitive-Behavioral Therapy for PTSD. Treatment Manuals for Practitioners*. New York: Guilford Press.

Foa EB, Steketee G and Rothbaum BO (1989) Behavioral cognitive conceptualizations of post-traumatic stress disorder. *Behavior Therapy* **20**, 155–176.

Foa EB, Feske U, Murdock TB, Kozak MJ and Mccarthy PR (1991) Processing of threat-related information in rape victims. *Journal of Abnormal Psychology* **100**, 156–162.

Hallion LS and Ruscio AM (2011) A meta-analysis of the effect of cognitive bias modification on anxiety and depression. *Psychological Bulletin* **137**, 940–958.

Hamilton M (1960) A rating scale for depression. *Journal of Neurology Neurosurgery and Psychiatry* **23**, 56–62.

Hien DA, Jiang HP, Campbell ANC, Hu MC, Miele GM, Cohen LR, Brigham GS, Capstick C, Kulaga A, Robinson J, Suarez-Morales L and Nunes EV (2010) Do treatment improvements in PTSD severity affect substance use outcomes? A secondary analysis from a randomized clinical trial in NIDA's clinical trials network. *American Journal of Psychiatry* **167**, 95–101.

Imel ZE, Laska K, Jakupcak M and Simpson TL (2013) Meta-analysis of dropout in treatments for posttraumatic stress disorder. *Journal of Consulting and Clinical Psychology* **81**, 394–404.

Krell HV, Leuchter AF, Morgan M, Cook IA and Abrams M (2004) Subject expectations of treatment effectiveness and outcome of treatment with an

experimental antidepressant. *The Journal of Clinical Psychiatry* **65**, 1174–1179.

**Kuckertz JM, Amir N, Boffa JW, Warren CK, Rindt SEM, Norman S, Ram V, Ziajko L, Webb-Murphy J and McLay R** (2014*a*) The effectiveness of an attention bias modification program as an adjunctive treatment for post-traumatic stress disorder. *Behaviour Research and Therapy* **63**, 25–35.

**Kuckertz JM, Gildebrant E, Liliequist B, Karlstrom P, Vappling C, Bodlund O, Stenlund T, Hofmann SG, Andersson G, Amir N and Carlbring P** (2014*b*) Moderation and mediation of the effect of attention training in social anxiety disorder. *Behaviour Research and Therapy* **53**, 30–40.

**Lazarov A, Abend R, Seidner S, Pine DS and Bar-Haim Y** (2017*a*) The effects of training contingency awareness during attention bias modification on learning and stress reactivity. *Behavior Therapy* **48**, 638–650.

**Lazarov A, Marom S, Yahalom N, Pine DS, Hermesh H and Bar-Haim Y** (2017*b*) Attention bias modification augments cognitive-behavioral group therapy for social anxiety disorder: a randomized controlled trial. *Psychological Medicine* **48**, 2177–2185.

**Linetzky M, Pergamin-Hight L, Pine DS and Bar-Haim Y** (2015) Quantitative evaluation of the clinical efficacy of attention bias modification treatment for anxiety disorders. *Depression and Anxiety* **32**, 383–391.

**Litz BT and Keane TM** (1989) Information processing in anxiety disorders: application to the understanding of post-traumatic stress disorder. *Clinical Psychology Review* **9**, 243–257.

**MacLeod C and Clarke PJF** (2015) The attentional bias modification approach to anxiety intervention. *Clinical Psychological Science* **3**, 58–78.

**MacLeod C and Grafton B** (2016) Anxiety-linked attentional bias and its modification: illustrating the importance of distinguishing processes and procedures in experimental psychopathology research. *Behaviour Research and Therapy* **86**, 68–86.

**MacLeod C, Mathews A and Tata P** (1986) Attentional bias in emotional disorders. *Journal of Abnormal Psychology* **95**, 15–20.

**Meffert SM, Metzler TJ, Henn-Haase C, McCaslin S, Inslicht S, Chemtob C, Neylan T and Marmar CR** (2008) A prospective study of trait anger and PTSD symptoms in police. *Journal of Traumatic Stress* **21**, 410–416.

**Naim R, Abend R, Wald I, Eldar S, Levi O, Fruchter E, Ginat K, Halpern P, Sipos ML, Adler AB, Bliese PD, Quartana PJ, Pine DS and Bar-Haim Y** (2015) Threat-related attention bias variability and posttraumatic stress. *American Journal of Psychiatry* **172**, 1242–1250.

**Ruggiero KJ, Del Ben K, Scotti JR and Rabalais AE** (2003) Psychometric properties of the PTSD checklist – civilian version. *Journal of Traumatic Stress* **16**, 495–502.

**Sarapas C, Weinberg A, Langenecker SA and Shankman SA** (2017) Relationships among attention networks and physiological responding to threat. *Brain and Cognition* **111**, 63–72.

**Schoorl M, Putman P and van Der Does W** (2013) Attentional bias modification in posttraumatic stress disorder: a randomized controlled trial. *Psychotherapy and Psychosomatics* **82**, 99–105.

**Sipos ML, Bar-Haim Y, Abend R, Adler AB and Bliese PD** (2014) Postdeployment threat-related attention bias interacts with combat exposure to account for PTSD and anxiety symptoms in soldiers. *Depression and Anxiety* **31**, 124–129.

**Sullivan GM and Neria Y** (2009) Pharmacotherapy of PTSD: current status and controversies. *Psychiatric Annals* **39**, 342–347.

**Tottenham N, Tanaka J, Leon A, McCarry T, Nurse M, Hare T, Marcus D, Westerlund A, Casey BJ and Nelson CB** (2009) The NimStim set of facial expressions: judgments from untrained research participants. *Psychiatry Research* **168**, 242–249.

**Van Etten ML and Taylor S** (1998) Comparative efficacy of treatments for post-traumatic stress disorder: a meta-analysis. *Clinical Psychology & Psychotherapy* **5**, 126–144.

**Vens M and Ziegler A** (2012) Generalized estimating equations and regression diagnostics for longitudinal controlled clinical trials: a case study. *Computational Statistics & Data Analysis* **56**, 1232–1242.

**Weathers F, Litz BT, Huska JA and Keane TM** (1991) *The PTSD Checklist (PCL)*. Boston, VA: Medical Centre: Boston.

**Weathers FW, Keane TM and Davidson JRT** (2001) Clinician-administered PTSD scale: a review of the first ten years of research. *Depression and Anxiety* **13**, 132–156.

**Williams JBW** (1988) A structured interview guide for the Hamilton depression rating-scale. *Archives of General Psychiatry* **45**, 742–747.

**Zeger SL and Liang KY** (1986) Longitudinal data-analysis for discrete and continuous outcomes. *Biometrics* **42**, 121–130.

**Zeger SL, Liang KY and Albert PS** (1988) Models for longitudinal data – a generalized estimating equation approach. *Biometrics* **44**, 1049–1060.