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Learning and Memory Consolidation Processes of Attention-Bias Modification in Anxious and Nonanxious Individuals

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Abstract

Recent evidence suggests that attention-bias-modification (ABM) procedures may reduce anxiety via computerized attention-training tasks. However, the mechanisms underlying the modification of attention patterns in anxiety remain largely unexplored. Here, we compared anxious and nonanxious participants in terms of learning and memory consolidation effects associated with training to attend either toward or away from threat. When trained to attend away from threat, the primary training condition in ABM treatment, anxious participants demonstrated impaired within-session learning. In contrast, consolidation of threat-related learning did not vary as a function of anxiety. These findings suggest that anxious participants have a selective difficulty in altering their threat-related attention patterns during ABM. This specific deficit could explain inconsistent findings in the ABM research base, as well as elucidate potential targets for optimizing ABM protocols in the treatment of anxiety.

Keywords

anxiety, attention-bias modification, learning, memory, consolidation, cognitive training

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Mounting evidence suggests that computerized cognitive training may constitute a viable, cost-effective therapeutic for various psychopathologies, including anxiety, attention-deficit disorder, and schizophrenia (Bar-Haim, 2010; Grynszpan et al., 2011; Klingberg, 2010). Cognitive-training protocols typically rely on repeated practice on tasks targeting specific cognitive processes, such as attention, memory, and executive functions, which have been identified as perturbed in these disorders. Although such training protocols are essentially learning paradigms in which cognitive skills are acquired and trained over time, the learning and memory consolidation processes underlying training effects are typically incompletely specified in available research. Characterizing the specific learning effects taking place during cognitive training is essential for evidence-based enhancement of training efficacy.

Attention-bias-modification (ABM) paradigms are a subtype of computerized cognitive-training interventions that most commonly target threat-related attentional biases in anxiety disorders (Bar-Haim, 2010; MacLeod & Mathews, 2012). ABM protocols systematically train anxious patients to attend away from threat through gradual learning of an implicit attentional contingency between target probes and nonthreat stimuli. Typically given over several practice sessions with multiple trial presentations, ABM training has been robustly shown to lead to reduction in threat bias and anxiety symptoms (Bar-Haim, 2010; Hakamata et al., 2010).

As with most other cognitive-training research, ABM researchers to date have primarily focused on the endpoint outcome of training by measuring induced changes in threat-related attention-bias scores and subsequent reductions in symptoms. Limited attention, however, has

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been given to the specific learning and consolidation processes that produce these changes. Elucidation of these processes and how they affect ABM outcome could guide the design of more effective and durable treatment protocols. Moreover, understanding the underlying operating processes in ABM could help resolve some of the clinical successes and failures reported in the ABM literature (Hakamata et al., 2010; Hallion & Ruscio, 2011).

In a previous study among healthy participants, we began to outline the nature of learning processes in ABM (Abend et al., 2013). We showed that learning to attend to threat cues occurred in two distinct phases previously reported in other forms of nonemotional learning (e.g., Hauptmann & Karni, 2002; Karni, 1996; Karni & Sagi, 1993; Korman, Raz, Flash, & Karni, 2003; Robertson, Pascual-Leone, & Miall, 2004). First, we observed substantial *on-line* (within-session) learning during the initial training session, which reflected repetition-dependent improvement in task performance. Second, we observed *off-line* (between-sessions) learning, that is, enhanced performance after a postpractice rest interval that emerged without additional training and was retained over several months, indexing consolidation into long-term memory (Doyon et al., 2009; Dudai, 2004; Karni, 1996; Karni et al., 1998; McGaugh, 2000; Robertson et al., 2004).

Two aspects of this previous study (Abend et al., 2013) limit its therapeutic relevance. First, study participants were from a nonselected population, whereas ABM is conceived as a therapeutic tool for anxious populations (Bar-Haim, 2010; MacLeod, 2012). Second, the study trained attention toward threat, whereas therapeutic forms of ABM typically train attention away from threat (e.g., Amir et al., 2009; Eldar et al., 2012). If anxious individuals have difficulties learning how to avoid threat cues, they may also exhibit reduced capacity to benefit from ABM. Moreover, the presence of such difficulties would limit the generalizability to anxious participants of ABM research in nonanxious populations. Comparison of ABM-related learning and memory consolidation processes among anxious and nonanxious participants could identify potential impairments in specific phases of attention training. Such impairments could then be directly targeted by adjusting training parameters, thereby ultimately aiding in the design of more efficacious ABM protocols for anxiety (Eberl et al., 2014; MacLeod & Mathews, 2012).

Here, we compared learning and memory consolidation processes among participants with high or low levels of anxiety as we trained their attention either away from threat, toward threat, or in a manner unrelated to threat location. Two sets of findings informed our expectations: the literature on threat-related biases in anxiety and the literature on learning and memory consolidation processes. Given the findings that anxious individuals display a natural tendency to monitor threat (Armstrong & Olatunji, 2012; Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007; Cisler & Koster, 2010), we expected anxious participants to express relative difficulty in learning to attend away from threat. Such deficit could potentially arise from perturbed on-line learning processes, off-line consolidation-dependent learning processes, or both. The current design enabled us to test and identify the perturbed processes with the understanding that identification of specific deficits could lead to different paths of therapeutics development.

Method

Participants

A total of 180 undergraduate students participated in the study (117 females, 63 males; mean age = 23.1 years, *SD* = 2.4, range = 19–33). Selection of participants was based on mass administration of the Trait subscale of the State-Trait Anxiety Inventory (Spielberger, 1983) 3 weeks prior to the present study ($N = 416$). Students who scored in the lower tercile (total score ≤ 34) or upper tercile (≥ 41) were invited to participate. From those who agreed to participate, we randomly selected 90 low-anxious students (56 females, 34 males) and 90 high-anxious students (61 females, 29 males) who then formed the low-anxiety and high-anxiety groups, respectively. Trait anxiety significantly differed between the groups (high-anxiety group: $M = 49.3$, $SD = 6.1$; low-anxiety group: $M = 27.3$, $SD = 2.9$), $F(1, 174) = 942.6$, $p < .001$, $\eta_p^2 = .84$.

Participants within each group were then randomly assigned to six experimental conditions (described later). Participants in these six conditions did not differ in age, $F(5, 84)$s < 1.79, ps > .12, η_p^2s < .10, male-to-female ratio, $\chi^2(5, N = 88) < 2.24$, ps > .82, Vs < .12, or trait anxiety, $F(5, 84)$s < 1.80, ps > .12, η_p^2s < .10. All participants had normal or corrected-to-normal vision. The study was approved by the local ethics committee. Participants provided written informed consent prior to participation and participated in return for course credit.

Attention training

A variant of the dot-probe task (MacLeod, Mathews, & Tata, 1986) frequently used in ABM studies and in our previous work (Abend et al., 2013; Amir et al., 2009; Eldar et al., 2012) was used. For a complete description of the task, see the Attention Training and Procedure sections of Methodological Details in the Supplemental Material available online. In brief, on each trial, a pair of face stimuli, one angry and one neutral, were presented and followed by a target probe appearing in the location vacated by one of the faces. Participants had to

identify the probe as quickly as possible without compromising accuracy (see Fig. S1 in the Supplemental Material).

Three attention-training conditions were compared. In the attend-threat condition, probes were repeatedly presented after the angry faces, thereby establishing the latter as a predictive cue for probe location. In the avoid-threat condition, probes were presented after the neutral faces, which established these as predictive cues. In the control condition, probes were presented with equal probability behind the neutral and angry faces.

Between-sessions rest

All participants completed two sessions. Between-sessions rest was manipulated to examine consolidation-dependent effects on Session 2 performance (off-line learning). In the rest condition, Session 2 started 24 hr after termination of Session 1, a sufficient interval for consolidation processes to occur and for off-line learning gains to emerge (Doyon et al., 2009; Karni et al., 1998; Karni & Sagi, 1993; Robertson et al., 2004). In the no-rest condition, Session 2 immediately followed Session 1. Consolidation effects are not expected that early after practice.

Procedure

A 3 × 2 × 2 factorial design of Training Type (attend threat, avoid threat, control) × Anxiety Group (low, high) × Rest (no rest, rest) was used, with 15 participants in each subcondition. The task was administered in 50-trial blocks with short breaks between blocks (randomly ranging between 60 to 90 s). Session 1 consisted of eight blocks (400 trials in total; ~30 min); Session 2 consisted of four blocks (200 trials; ~15 min). Training condition remained the same for each participant across sessions.

Outcome measures

On-line learning gains, which reflect repetition-dependent performance improvement taking place during the first practice session, were assessed by plotting mean reaction times (RTs) in Blocks 1 to 8, normalized to mean RT in Block 1. As in prior studies of learning, the use of normalized performance gains (Abend et al., 2013; Doyon et al., 2009; Hauptmann & Karni, 2002; Korman et al., 2007) enabled us to more clearly identify learning capacity in the task, by diminishing the influence of individual differences in sensory-motor performance reflected in raw RT measures, as well as between-group differences stemming from the potential effect of anxiety on raw RT (e.g., Eldar & Bar-Haim, 2010; Miskovic & Schmidt, 2012).

Off-line learning gains in task performance reflect improvement in performance in the second session after initiation of memory consolidation processes (Doyon et al., 2009; Dudai, 2004; Karni et al., 1998; Karni & Sagi, 1993; McGaugh, 2000). We assessed off-line gains by plotting mean RTs in Blocks 9 through 12, each normalized to mean RT of the last block of Session 1 (Abend et al., 2013; Doyon et al., 2009; Korman et al., 2007); that is, off-line gains for each participant were calculated as *mean RT of Block 9* minus *mean RT of Block 8*, divided by *mean RT of Block 8*, and so forth, which reflects the percentage of RT reduction relative to Block 8. Positive off-line gains (mean gain > 0) indicate between-sessions improvement in performance.

Data analysis

Outliers and incorrect responses were removed according to prespecified rules (see the Data Analysis section of Methodological Details in the Supplemental Material). Given that on-line and off-line learning are associated with distinct behavioral effects and neural correlates (Doyon & Benali, 2005; Karni et al., 1998; Steele & Penhune, 2010), these learning phases were analyzed separately (e.g., Doyon et al., 2009; Hauptmann & Karni, 2002; Korman et al., 2003; Korman et al., 2007).

The effects of attention-training type and anxiety on on-line learning were assessed using repeated measures analysis of variance (ANOVA) on on-line gains in Blocks 1 through 8. Block (8) served as a within-subjects factor and training type (attend threat, avoid threat, control) and anxiety group (low, high) as between-subjects variables. Post hoc trend analysis was used to examine potential differences in patterns of on-line learning between the experimental conditions.

The effects of training type, anxiety, and rest on off-line learning were assessed using repeated measures ANOVA on off-line gains in Blocks 9 through 12. Block (4) served as a within-subjects factor and training type (attend threat, avoid threat, control), anxiety group (low, high), and rest (no rest, rest) as between-subjects variables.

Significant ANOVA interactions were followed by lower-order ANOVAs and Fisher's least significant difference tests. All tests were two-tailed ($\alpha \leq .05$). Kolmogorov-Smirnov tests on normalized RTs per block and experimental condition revealed that the distribution of normalized RTs in none of the blocks was significantly different from the normal distribution ($ps > .20$), thereby permitting the use of parametric statistical tests.

Results

On-line (within-session) learning

All experimental groups showed significant on-line learning gains reflecting a consistent decrease in mean RT

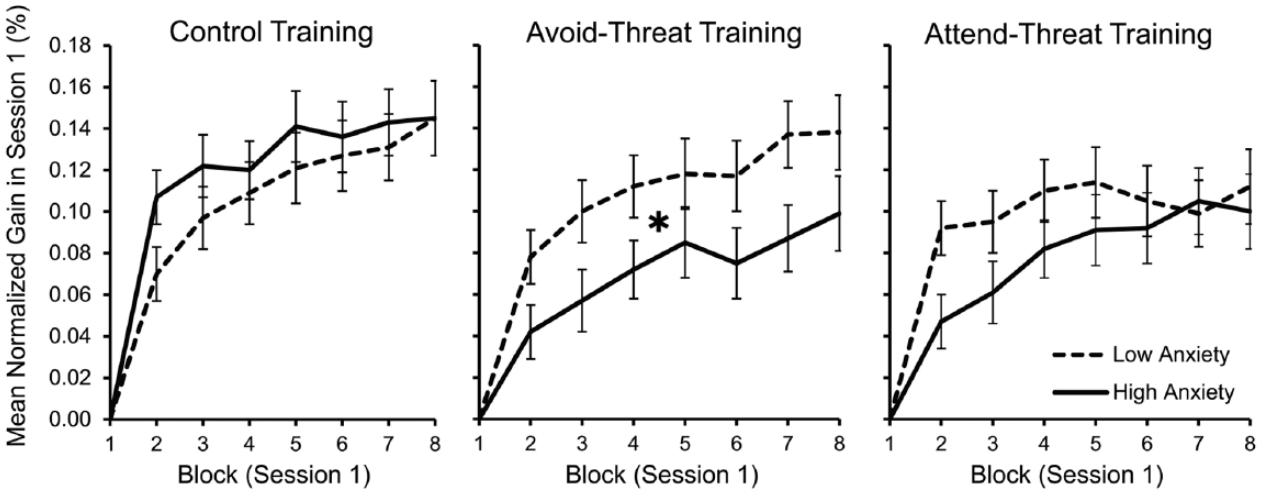

Fig. 1. Mean on-line performance gains in Session 1 blocks by training type (control, avoid threat, attend threat) and anxiety group (low, high). Gains reflect performance improvement relative to Block 1. Asterisk indicates significant difference between groups (*$p < .05$). Error bars signify ±1 standard error of the mean.

with task progression through Session 1 (see Fig. 1). Overall, a mean performance improvement of 12.3% was observed by the end of Session 1, equivalent to a mean reduction in RT of 68 ms across conditions. Comparisons between successive blocks (paired *t* tests, corrected) showed significant improvement in performance between Blocks 1 and 2, Blocks 2 and 3, and Blocks 3 and 4 ($ps < .05$), which indicated that practice-dependent learning in the task reached asymptotic performance after approximately 200 trials.

Formal analysis revealed significant main effects of training type and block on on-line gains—training type: $F(2, 170) = 3.14$, $p < .05$, $\eta_p^2 = .04$; block: $F(7, 1190) = 120.0$, $p < .001$, $\eta_p^2 = .41$. These main effects were qualified by a significant three-way interaction of Training Type × Anxiety Group × Block on on-line gains, $F(14, 1190) = 1.78$, $p = .04$, $\eta_p^2 = .02$, coupled by a significant three-way cubic trend interaction, $F(2, 170) = 3.52$, $p = .03$, $\eta_p^2 = .04$, which suggested that the experimental conditions yielded differential learning patterns in the two groups of participants. To explicate this interaction, we compared on-line learning patterns between the low-anxiety and high-anxiety groups within each of the attention-training conditions. The low- and high-anxiety groups did not differ in learning in the control condition (see Fig. 1, left panel) or in the attend-threat condition (see Fig. 1, right panel), $ps > .28$, $\eta_p^2 s = .02$. However, a main effect of anxiety group was observed in the attention training away from threat condition, $F(1, 56) = 3.98$, $p = .05$, $\eta_p^2 = .07$; the high-anxiety group demonstrated lower mean performance improvement relative to the low-anxiety group (6.5% and 10.0%, respectively; see Fig. 1, middle panel).

For completeness, we also compared the effect of training condition on on-line learning gains within each anxiety group. These post hoc analyses revealed a significant main effect of training type in the high-anxiety group, $F(2, 85) = 4.82$, $p = .01$, $\eta_p^2 = .10$; training toward or away from threat yielded fewer gains than did the control training condition ($p = .02$ and .01, respectively). No difference between training conditions was observed in the low-anxiety group, $F(2, 85) < 1$, $p = .80$, $\eta_p^2 = .01$.

Off-line (between-sessions) learning

In contrast to Session 1, practice in Session 2 was not characterized by an on-line learning curve as evidenced by nonsignificant main or interaction effects of block. Mean off-line gains in the experimental groups are presented in Figure 2. A significant main effect of rest on off-line gains was observed, $F(1, 164) = 11.74$, $p < .001$, $\eta_p^2 = .07$; follow-up one-sample *t* tests revealed that gains were significantly greater than 0 in the rest condition (improvement of 3.1%, $p < .001$) but not in the no-rest condition (0.4%, $p = .43$). Thus, performance in Session 2 was enhanced only after a postpractice rest interval and without any additional on-line learning in the session. Exploratory one-sample *t* tests revealed that after rest, significant off-line gains emerged in the avoid-threat condition (see Fig. 2, middle panel, gray bars) and in the attend-threat condition (see Fig. 2, right panel, gray bars), for both the high- and the low-anxiety groups, $ps < .02$,

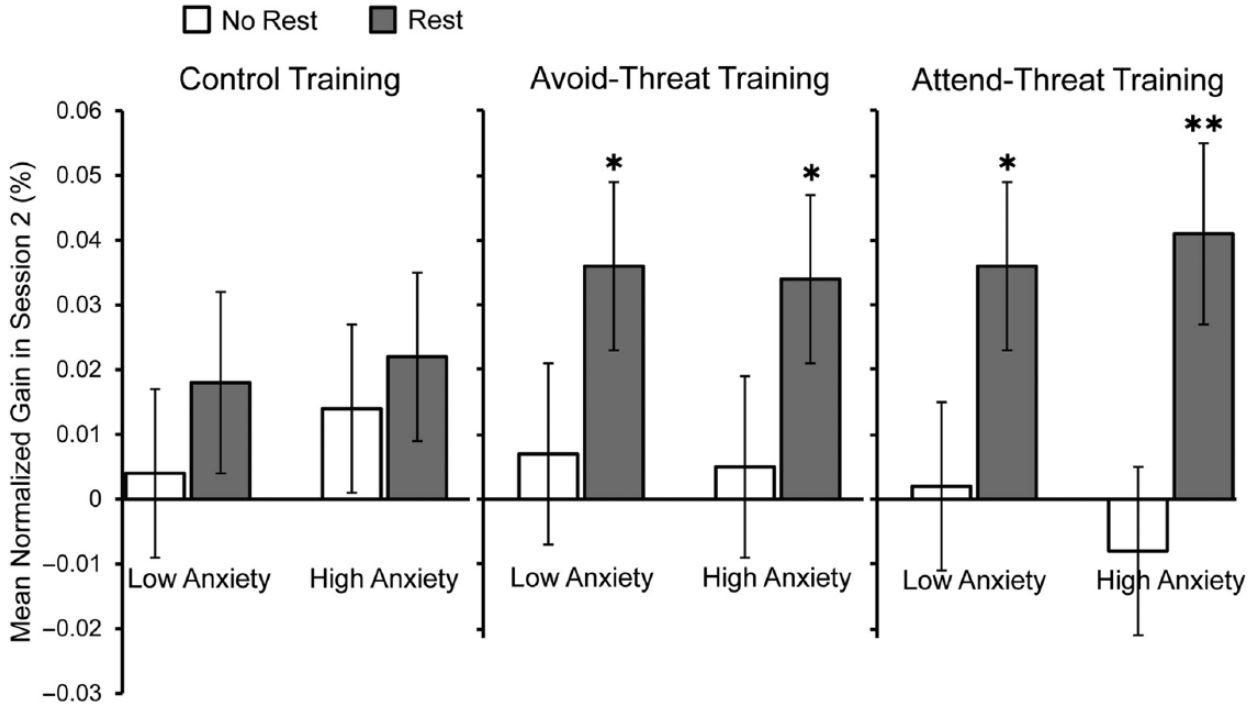

Fig. 2. Mean off-line learning gains in Session 2 by training type (control, avoid threat, attend threat), anxiety group (low, high), and rest (no rest, rest). Gains reflect performance improvement in Session 2 relative to the last block of Session 1. Error bars signify ±1 standard error of the mean. Asterisks indicate significant differences between groups (*$p < .05$, **$p < .01$, for one-sample t tests against 0).

ds > 0.41. Gains did not significantly differ among these four groups, $F(3, 55) = 0.04$, $p > .98$, $\eta_p^2 = .00$. Off-line gains in the control training condition did not differ from 0, ps > .15, ds < 0.34 (see Fig. 2, left panel, gray bars). No other main or interaction effects were observed in this analysis.

Finally, we also assessed whether the anxiety-group difference in on-line gains observed in the avoid-threat training condition in Session 1 remained after a postpractice off-line learning phase and during Session 2. To examine this issue, we normalized mean RTs in Session 2 blocks to the first block of Session 1 (Block 1) and averaged them, thereby generating a measure of total learning gains throughout the two sessions. Total gains did not differ between the anxiety groups in the control and in the attend-threat conditions, ps > .35, η_p^2s < .04. In contrast, after two practice sessions, a trend-level difference between the anxiety groups was still observed in the avoid-threat condition, $t(28) = 1.97$, $p = .06$, $\eta_p^2 = .12$; the high-anxiety group showed fewer overall gains than did the low-anxiety group (M = 12.9% and 18.5%, respectively).

Additional analyses verified that all anxiety- and rest-related effects were specific to threat-related attention training and were not due to simple learning in the dot-probe task. We further confirmed that learning effects did not reflect speed-accuracy trade-off (see Auxiliary Results in the Supplemental Material).

Discussion

The basic learning and memory consolidation processes underlying ABM in anxiety have largely been overlooked in ABM research. This complicates attempts to refine current ABM regimens to target specific learning mechanisms. The current findings offer insights into these plasticity processes in anxiety. First, high anxiety was associated with impaired on-line learning in the avoid-threat training condition, the most frequently used condition in ABM treatment protocols. Such difficulty in learning was expected, given that anxious participants tend to display an attentional bias toward threat, even in the absence of training (Armstrong & Olatunji, 2012; Bar-Haim et al., 2007; Van Bockstaele et al., 2013). The current findings suggest that this intrinsic tendency hinders attempts to alter attention through ABM. Second, despite impaired on-line learning during avoid-threat training, anxious participants demonstrated off-line performance improvement that was comparable in magnitude to that of the low-anxious participants. These results indicate that, unlike on-line learning processes, postpractice consolidation processes are not moderated by trait anxiety.

Taken together, the findings indicate that although anxious individuals may find it more challenging to learn to avoid threat, they are still able to adequately consolidate such learning when given a postpractice rest period.

Nevertheless, after two attention-training sessions, anxious participants still tended to lag behind their nonanxious counterparts in terms of overall learning accumulated, which points to the potential need of additional ABM sessions in clinical settings.

Noting the difficulty of anxious individuals to learn to avoid threat, we argue that a number of task parameters could be adjusted in an attempt to enhance on-line learning in ABM. For example, unlike the current trend to try and restrict on-task time to a bare minimum, increasing the length of training sessions may allow more time for on-line acquisition of the avoid-threat contingency in anxious patients. Indeed, studies have shown that prolonged practice may facilitate subsequent consolidation processes (Hauptmann & Karni, 2002; Hauptmann, Reinhart, Brandt, & Karni, 2005). In addition, in contrast with the common practice in ABM protocols to apply implicit learning, explicitly informing the participants of the embedded attentional contingency may potentially enhance its acquisition (MacLeod, Koster, & Fox, 2009; Smeeton, Williams, Hodges, & Ward, 2005; but see Grafton, Mackintosh, Vujic, & MacLeod, 2013). Alternatively, increasing the reward associated with rapid and accurate probe discrimination could also enhance learning. In most ABM protocols, the attentional contingency is acquired through incidental association rewarded by slight improvement in performance. Introduction of more concrete incentives, such as monetary or symbolic rewards that are proportional to the trained reduction in RT, may lead to more efficient and effective learning of the intended contingency and its consolidation (Abe et al., 2011; Fischer & Born, 2009). Finally, professionals delivering ABM treatment should be aware of the particular perturbations in learning among their anxious patients, thereby calibrating their own expectations as well as providing patients with the needed encouragement and support in learning.

The current data also suggest that consolidation of threat-related attentional learning is not qualitatively degraded in anxious individuals. This finding speaks to the importance of introducing epochs of rest between ABM sessions to allow for off-line memory consolidation and perhaps compensate, to a degree, for difficulties in on-line learning. Thus, the attentional contingency may be more effectively acquired through incremental off-line learning taking place over a number of training sessions. Further research is needed to determine the optimal schedule of training and rest periods in terms of both learning and clinical effects.

This study does not go without limitations. First, we did not study a clinically anxious population. Although threat bias and the effects of ABM have been shown in subclinical (analog) populations as well as in clinical populations (Amir, Weber, Beard, Bomyea, & Taylor, 2008; Bar-Haim et al., 2007; MacLeod, Rutherford, Campbell, Ebsworthy, & Holker, 2002), the use of an analog sample in this study may have attenuated the reported anxiety-related effects. Second, our study design included two sessions of the attention-training task, whereas ABM protocols frequently consist of more sessions (Bar-Haim, 2010). Although this design enabled us to examine the principal effects of learning and memory consolidation in attention training, a complete course of ABM could potentially have uncovered additional, long-term patterns of plasticity.

The controlled experimental design employed in the current study enabled us to uncover specific impaired patterns of on-line learning in anxious individuals, thereby laying the ground for a comprehensive assessment of plasticity effects in a full-course clinical ABM trial. Within a clinical setting, the practical inferences from the current study could be further tested and inform decisions about the structure and delivery parameters of future ABM protocols in clinical practice. Specifically, such future study could explicate association between multisession, training-dependent change in cognitive functions and subsequent symptom reduction. Some of this knowledge can be readily extracted from extant data of ABM clinical trials via secondary analyses of dose-response curves for optimal treatment length (Eberl et al., 2014). ABM researchers also could more closely examine subject-specific learning rates in an attempt to identify moderators of clinical outcome and optimize training procedures. This research focus could pave the way for individualized and adaptive ABM protocols (Klingberg, 2010). From a technical perspective, training-task data files should be designed with learning and consolidation analyses in mind and saved for the duration of the study for future analysis.

In conclusion, ABM shows promise as a treatment for anxiety symptoms and stress vulnerability (Bar-Haim, 2010; Hakamata et al., 2010; MacLeod, 2012), but major questions remain on procedures for enhancing ABM efficacy; in prior studies, few researchers have attempted to elucidate optimal structure and delivery parameters. The present findings demonstrate an anxiety-related deficit in the response of attention to ABM training. This deficit could reduce ABM effectiveness in future studies, unless it is specifically targeted with optimized training regimens. The current results therefore highlight the importance of examining learning processes in ABM as part of the efforts to enhance its therapeutic efficacy.

Author Contributions

R. Abend and Y. Bar-Haim developed the study concept. All authors contributed to the study design. R. Abend collected and analyzed the data. R. Abend and Y. Bar-Haim interpreted the data and drafted the manuscript. D. S. Pine and N. A. Fox

critically revised the manuscript. All authors approved the final version of the manuscript for submission.

Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

Supplemental Material

Additional supporting information may be found at http://cpx.sagepub.com/content/by/supplemental-data

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