Threat Monitoring and Attention-Bias Modification in Anxiety and Stress-Related Disorders

Tomer Shechner\textsuperscript{1} and Yair Bar-Haim\textsuperscript{2,3}
\textsuperscript{1}Department of Psychology, University of Haifa; \textsuperscript{2}School of Psychological Sciences, Tel-Aviv University; and \textsuperscript{3}Sagol School of Neuroscience, Tel-Aviv University

Abstract
Extensive research has demonstrated the effects of threat-related attentional bias on anxiety and stress-related disorders. This review summarizes recent findings from clinical affective neuroscience. It takes a multilevel analysis approach by presenting behavioral and neural findings from studies conducted in laboratories, clinical settings, and real-life situations. Building on recent findings, we propose a new working model linking individual tendencies to attend or avoid threats with the level of danger in a given context. Namely, adaptive or pathological response is determined by threat-monitoring flexibility and plasticity in an ever-changing environment. The review culminates by describing the potential therapeutic value of attention-bias modification in the treatment of anxiety and stress-related disorders.

Keywords
attention bias, anxiety, PTSD, attention-bias modification

Humans’ evolutionary adaptedness has carved out a dedicated neuro behavioral system designed to monitor and prioritize potential threats in the environment. Through specific cognitive functions, our brains detect potential threats and select and perform the actions necessary for survival. The threat-monitoring system is designed to monitor and provide solutions to an array of survival problems, from avoiding predators to correctly deciphering social cues that signify danger in everyday situations. Therefore, this system must retain considerable behavioral flexibility and neural plasticity to adapt in an ever-changing environment. Importantly, if the environment changes, prior adaptation may be incompatible with the new circumstances and the survival function may no longer apply. Thus, our threat-monitoring system can be construed as constantly scrutinizing, prioritizing, and calibrating threat signals and potential responses. While constant minute adaptations are required under all circumstances, changes to threat monitoring will be most evident in environments where the degree of genuine danger is highly variable.

The current review summarizes recent findings linking threat-related attention biases to anxiety and stress-related disorders. We begin by summarizing the behavioral and neural underpinnings of attention biases and their relation to anxiety, focusing on contemporary concepts and advances in this research field. Next, we describe adaptive versus pathological responses of the threat-monitoring system and offer a tentative working model linking threat-related attention biases to the degree of contextual danger. Finally, in the last section, we briefly review the clinical implications of research on attention-bias modification (ABM) reflecting therapeutic efforts to actively change maladaptive threat monitoring.

Attention Biases in Anxiety
Systematic perturbations in threat-related information processing, such as attention biases to threat, have been assigned a prominent role in the etiology and maintenance of anxiety and stress-related disorders (Cisler & Koster, 2010; Van Bockstaele et al., 2014; Yiend, 2010). Much empirical evidence indicates that the attentional system of anxious individuals is distinctively sensitive to, and biased in favor of, threat. Tasks used to measure

Corresponding Author:
Yair Bar-Haim, School of Psychological Sciences, Tel-Aviv University, Tel-Aviv 69978, Israel
E-mail: yair1@post.tau.ac.il
attention biases typically present stimuli with different emotional valence, requiring participants to detect or recognize targets appearing in their vicinity (e.g., the dot-probe task; the emotional spatial cuing task). Attention bias is commonly inferred by differences in behavioral response times to targets appearing in the locations of threat as compared to neutral cues (Van Bockstaele et al., 2014). Meta-analyses have yielded moderate effect sizes of attention bias toward threat among anxious youth and adults and no threat bias in non-anxious populations (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007). A similar result and effect size was reported in a meta-analysis examining threat-related attention biases in anxious versus non-anxious participants using eye-tracking technology (Armstrong & Olatunji, 2012). While the effect size of threat-related attention bias in anxiety is moderate, meta-analyses compiling large numbers of studies have indicated no publication bias and very large fail-safe indices.

The Neurocognitive Architecture Supporting Threat Monitoring

Neuroimaging studies have delineated frontolimbic neural circuitries supporting attention allocation toward and away from threats (Bishop, 2008; Heeren, De Raedt, Koster, & Philippot, 2013; Shechner, Britton, et al., 2012). Activation in the amygdala and anterior cingulate has been associated with rapid and enhanced sensitivity to threat stimuli (Carlson et al., 2012; Etkin et al., 2004). Areas in the prefrontal cortex (PFC) have been associated with attention-control mechanisms (Browning, Holmes, Murphy, Goodwin, & Harmer, 2010; Corbetta & Shulman, 2002). Specifically, the ventrolateral PFC (vlPFC) supports a shift function, possibly interacting with the amygdala so as to redirect attention in light of changing environmental factors (Corbetta & Shulman, 2002). The dorsolateral PFC (dlPFC) supports maintenance of task goals to retain performance in the presence of emotionally valenced distractors (Bishop, 2008, 2009). Finally, the dorsomedial PFC (dmPFC) plays a monitoring function with a special role at the interface between affect and motor responding, while the ventromedial PFC (vmPFC) modulates limbic processing in support of context-relevant emotion regulation (Etkin, Egner, & Kalisch, 2011). Together, these brain regions are thought to function as an integrated neural network that evaluates and responds to potential threats in the environment.

Neuroimaging studies using the dot-probe task in anxious patients have consistently demonstrated perturbations in brain function in fronto-amygdala regions, particularly the vlPFC and dlPFC, which are associated with attention processes (Britton et al., 2012; Fani et al., 2012; Monk et al., 2008; Telzer et al., 2008). For example, lower vlPFC engagement in anxious relative to non-anxious individuals occurs specifically during the probe phase of the dot-probe task, rather than during the presentation of a threat cue. This implicates vlPFC more strongly in the directing of attention than in the response to threat (Britton et al., 2012). Importantly, other recent studies have linked individual differences in anxiety to differences in the connectivity between fronto-amygdala regions (Hardee et al., 2013; Monk et al., 2008). Specifically, fronto-amygdala connectivity was weaker in anxious relative to non-anxious participants. The weaker threat-related negative connectivity between the PFC and the amygdala in anxious participants has been interpreted as reflecting amygdalar hyper-responsiveness to minor threats in the absence of a compensatory increase in modulation by the PFC. Figure 1 depicts the key structures in the circuitry underlying threat monitoring.

Additional support for the role of fronto-amygdala circuitry in threat-related attention biases in anxiety has come from studies reporting that cognitive behavioral therapy and pharmacological treatment (SSRIs) induce changes in vlPFC and amygdala activation during performance of a dot-probe task (Maslowsky et al., 2010). Furthermore, direct training of threat-related attention has also been shown to correlate with changes in these same brain circuitries (Britton et al., 2015; Carlson et al., 2012; Eldar & Bar-Haim, 2010; Mansson et al., 2013; Taylor et al., 2014). Taken together, perturbed activation and
connectivity in fronto-amygdala regions represents a potential target biomarker for translational research.

Effects of Context on Threat Monitoring

Recent evidence has suggested that immediately present threat cues are processed differently depending on the particular context in which they appear. For example, in extremely stressful contexts, attention has been shown to shift away from threats, potentially alleviating the emotional hardship of acute stress. Context has been shown to modulate attention in response to signs of danger. For example, threat avoidance was found in a field study of non-anxious individuals in a life-threatening context (Bar-Haim et al., 2010), among soldiers exposed to a stressful combat simulation (Wald et al., 2011), and in several laboratory studies using milder threat inductions (Helfinstein, White, Bar-Haim, & Fox, 2008; Shechner, Pele, Pine, Fox, & Bar-Haim, 2012). Together, these data strongly suggest that threat-related attention biases may be more multifaceted and varied than originally conceptualized. Rather than reflecting a static individual trait quality, these recent findings suggest that threat monitoring involves active plasticity and responsiveness to contextual danger. This context-dependent modulation of attentional threat monitoring offers a unique window into the plasticity of threat–attention interaction and its role in psychological adaptation.

Attentional Variability and Threat Monitoring

For many years, threat-related attention bias was conceptualized as a trait-like characteristic of anxious individuals. Specifically, most theories linking threat bias and anxiety focused on the downstream cognitive effects associated with maintaining attention on minor threats (for a review, see Cisler & Koster, 2010). This assumption, however, is not in line with the required flexibility and dynamism of the ever-changing context of real-life threat monitoring. To address this theoretical gap, recent studies have started to measure the inherent variability and fluctuation of threat-related attentional bias (Naim et al., 2015; Price et al., 2015; Zvielli, Bernstein, & Koster, 2015). In particular, traumatic stress exposure and subsequent posttraumatic stress disorder (PTSD) have been associated with enhanced attention-bias variability in a variety of samples (Badura-Brack et al., 2015; Iacoviello et al., 2014; Naim et al., 2015). These attentional fluctuations resemble the wider symptom clusters of PTSD: hypervigilance and avoidance/dissociation. Elevated attention-bias variability may, in this way, reflect a loss of attentional control and aberrant buffering of threat-related attention among patients with PTSD. Interestingly, recent trials of ABM in combat veterans demonstrated that reductions in attention-bias variability partially mediated reductions in PTSD symptoms, thereby suggesting that targeting dynamic fluctuations in attention may prove useful for PTSD patients. Elevated variability in attention bias also emerged for spider-phobic participants relative to non-anxious controls (Zvielli et al., 2015), but not for participants with social anxiety disorder relative to controls (Naim et al., 2015). Taken together, these results suggest that further research is needed to delineate the specific associations between attention-bias variability and psychopathology.

Interplay Between Contextual Danger and Threat Monitoring in Predicting Psychopathology and Adaptive Response

In light of this emerging perspective on the nature of threat monitoring, we propose a tentative working model (Fig. 2). We posit that high congruence between the degree of contextual danger and dominant patterns of threat monitoring (i.e., threat-vigilance or threat-avoidance tendencies) should lead to an adaptive response. In contrast, incongruence between context and threat-monitoring pattern should result in a maladaptive response. The top panel of Figure 2 depicts congruence between contextual danger and threat monitoring. Elevated threat vigilance is expected and of paramount importance in dangerous contexts, where it leads to more adaptive responses, whereas in safe contexts, avoiding and even ignoring minor threat cues is thought to promote better adaptation. These conditions represent congruence between contextual demands and the level of threat monitoring, which leads to adaptive psychological and behavioral responses. The bottom panel of Figure 2 represents incongruence between contextual danger and threat monitoring, which leads to maladaptive responses in the form of anxiety and stress-related symptoms. Most studies conducted under safe conditions have reported elevated threat vigilance in anxiety disorders (Armstrong & Olatanji, 2012; Bar-Haim et al., 2007; Yiend, 2010), reflecting an incongruence between contextual danger and threat-monitoring pattern. In the same vein, threat avoidance displayed under objectively dangerous circumstances has been associated with stress-related symptoms and PTSD (Bar-Haim et al., 2007; Wald et al., 2013; Wald et al., 2011).

Importantly, the proposed model does not imply that attention to threat in a genuinely dangerous environment will not elicit anxiety. In such a context, elevated anxiety
would be appropriate and is likely to drive adaptive outcomes. In contrast, when the environment is safe but an individual still attends to whatever minor threats are present, then this too could elicit anxiety. However, this elevated anxiety will be inappropriate in such a situation and likely to drive maladaptive outcomes. This tentative working model descriptively accounts for most of the results on threat-related attentional biases in anxious and healthy individuals. More information is now needed on the cognitive and neural mechanisms that govern plasticity or rigidity in this adaptation-driven system.

**Contextual Considerations for Attention-Bias Modification**

The elucidation of specific aberrations in threat monitoring in anxious patients and the observed association between traumatic exposure and threat-monitoring patterns present specific targets for intervention and prevention. One such intervention protocol—ABM—involves computerized cognitive-training strategies designed to alter biases in threat-related attention. For example, in a dot-probe task designed to shift attention away from threat, two stimuli, one threat-related and one neutral (e.g., a threatening vs. neutral word or picture), are briefly and concurrently shown during each trial; their removal is followed by a small target probe, which most frequently (e.g., on 90% of trials) appears in the location just occupied by the neutral stimulus. Patients are required to discriminate as quickly as possible between two variants of the probe (e.g., one or two dots) without compromising accuracy. Because target location is systematically manipulated to increase the proportion of targets appearing at the location of the neutral stimulus, attending to these contingencies can assist in task performance (Abend et al., 2013; Abend, Pine, Fox, & Bar-Haim, 2014). Thus, the desired rectification of attention bias is implicitly and gradually induced over repeated training trials.

One implication of our proposed tentative model of the interplay between environmental context, threat

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**Fig. 2.** A schematic showing how the congruence model of the threat-monitoring system describes the interplay between contextual danger and threat monitoring in predicting psychopathology.
monitoring, and psychological adaptedness is that ABM should train people to ignore or avoid threat signals in environments where no genuine danger is present but to be vigilant for threat signals in environments where genuine danger is present. This approach calls for serious consideration of actual environmental factors in treatment development and practice if they are to be maximized. Indeed, most ABM studies to date have focused on the treatment of anxious patients in what would be typically considered safe environments. Meta-analyses focusing specifically on ABM designed to shift attention away from threat have yielded moderate and significant effect sizes in alleviating anxiety symptoms (Hakamata et al., 2010; Linetzky, Pergamin-Hight, Pine, & Bar-Haim, 2015; Mogoase, David, & Koster, 2014), but see Cristea, Kok, and Cuijpers (2015) for a different interpretation of the efficacy of cognitive-bias modification for anxiety and depression.

Two recent studies of ABM applied to prevent PTSD in combat-deployed soldiers have provided further support for the importance of considering context in ABM treatment designs. In one randomized controlled trial of 719 soldiers, four sessions of ABM designed to shift attention toward threat were delivered before deployment to combat. This context-congruent ABM significantly reduced risk for post-combat PTSD (Wald, Fruchter, et al., 2016). In a different study, soldiers were either engaged in ABM toward threat or completed a control task in tactical assembly areas just before combat deployment (Wald, Bitton, et al., 2016). Results from this study indicated that ABM moderated the association between combat exposure and stress symptoms. These preliminary studies support the notion that enhanced vigilance in a genuinely dangerous context promotes adaptive psychological responses. Taken together, the extant ABM findings suggest that adaptive psychological responses depend not only on the direction of threat-related attention but also on the congruence between threat attendance and the level of actual danger present in the environment.

**Conclusion**

Three decades of extensive research on threat-related attention biases in anxiety, and roughly a decade of research on ABM training and contextual impact on attention bias, have led us to a deeper understanding of the behavioral and neural subsets of threat monitoring and its relation to anxiety and stress-related disorders. Novel models that take into account the delicate interplay between personal tendencies and aspects of the environment, along with the growing technological development in areas such as neuroimaging and computing, have begun to open exciting avenues for research and clinical applications that will surely emerge in the coming years.

**Recommended Reading**


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**References**


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