The role of attention bias to threat in anxiety: mechanisms, modulators and open questions

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Individuals at risk of developing anxiety and those with (sub-) clinical anxiety have robust attention biases to irrelevant threats, among them facilitated engagement, difficulty in disengaging and later avoidance of threat. These attention biases are thought to be associated with abnormal activation and connectivity in prefrontal-limbic-sensory neural circuits. Attention biases were shown to be related to other processing biases, but more empirical data are needed to better understand the causal role of each processing bias and to develop effective treatments. These attention biases have further been suggested as playing a causal role in anxiety, although mixed findings from attention bias modification studies challenge this contention.

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This review focuses on the role played by attention biases to irrelevant threat in anxiety. The review briefly summarizes recent evidence for attention biases among healthy participants, individuals at risk of developing anxiety and individuals with (sub) clinical anxiety. It then discusses possible causal relationships between attention biases and other information-processing biases in anxiety and discusses findings from two common types of attention training: attention bias modification (ABM) and executive attention control. Finally, the review poses open questions and offers suggestions for future studies.

Biased attention toward threat among healthy participants, individuals at risk and individuals with (sub) clinical anxiety

Healthy individuals exhibit facilitated early engagement of attention when confronted with threatening stimuli, as well as difficulty ignoring negative distractors [3,4,5,6,7]. Nevertheless, this prioritized attention to negative information among healthy participants is modulated by different factors, including context [8], perceptual [9] and cognitive [10] load, processing type [11], modality [12], distance from threat [13] and interaction between modulating factors [14,15]. Recent findings suggest that low-level sensory features may explain prioritized processing. As a category, task-irrelevant faces attracted more attention than a control stimulus (i.e., a butterfly), possibly due to low-frequency information sufficient for global face processing. Yet contrary to the common view that irrelevant threatening faces are specifically prioritized due to their evolutionary value, irrelevant angry faces attracted no more attention than neutral ones [16].

Populations at high risk of developing anxiety, such as individuals with dispositional negativity (a tendency to feel and express more frequent and severe negative affect and anxiety), demonstrated enhanced attention biases compared to healthy controls. Dispositional negativity is characterized by faster orienting of attention and slower disengagement from distracting threats, as well as enhanced caution and increased alertness in potentially threatening situations. Indirect evidence suggests that dispositional negativity is accompanied by enhanced amygdala activation and abnormal connectivity between the amygdala and dorsolateral prefrontal regions, which may underlie these various attention biases [17].

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Individuals with clinical or subclinical levels of anxiety demonstrate robust attention biases to task-irrelevant threats [18,19]. Notebaert et al. [20] also showed that attention biases toward threat cues among highly anxious participants are not modulated by the ability to avoid danger. These biases may be due to reduced prefrontal and enhanced limbic and sensory activation in anxiety, reflecting reduced regulatory control over threat vigilance.

In sum, individuals at risk of developing anxiety and those with (sub) clinical anxiety show biased attention to threat, even when irrelevant, while healthy participants show prioritized attention only to task-relevant threat. Attention biases to irrelevant threat may result from abnormal prefrontal-limbic-sensory regulatory circuits.

**Relation between attention biases and other information processing biases**

Anxiety is characterized by abnormalities in other aspects of information processing, including maladaptive abnormalities in sensory perception of threatening items, atypical memory of negative items, negative interpretation of ambiguous cues and negative expectations regarding the future [2].

To date, most research on biased information processing in anxiety has focused on attention. Furthermore, only a few studies have examined possible relations between different biases. Therefore, although understanding the causal relationships between specific biases in anxiety is important for developing treatments targeting the core causal processes, the existing literature does not allow suggesting a directional model.

A recent review [21] underlines the role of expectation and attentional processes in the prioritized perception of threatening stimuli among healthy individuals. Threat-related cues, compared to neutral cues, result in enhanced activation of sensory, decision-related and attention-related fronto-parietal neurons that enhance perceptual sensitivity and decrease reaction times. Grupe and Nitsche [22] propose that abnormal uncertainty regarding future events among anxious individuals involves increased amygdala activation, yielding increased hypervigilance, avoidance and poor control associated with abnormal activation in sensory, prefrontal, striatal and limbic regions.

Recent findings suggest that expectancy is not always related to faster threat perception. In one study, participants with high trait anxiety exhibited higher perceptual sensitivity in the presence of relevant threat (i.e., electric shock), but worse performance in the absence of threat [23]. Another study demonstrated that threat perception is not always modulated by anticipation or anxiety. When participants were shown a visual search array preceded by anticipatory cues and were asked to report a task-relevant deviant bird or spider, the anticipatory cues predicted reactions to neutral bird targets but had no effect on reactions to threatening spider targets [24]. These results were found among participants with both high and low fear of spiders, in line with biological preparedness. Taken together, these results suggest that the influence of biased expectancies on attention and perception in anxiety is modulated by various factors. More data are needed to draw firm conclusions.

Attention biases may be related to another type of perception bias. Participants with extreme spider phobia perceived the actual size of spiders as bigger than did less fearful controls [25]. A similar perception bias was lowered by exposure to spiders [26]. In line with these findings, new event-related potentials (ERPs) research indicates that emotions influence very early ERP components in visual areas [27]. Sensory biases occur during early processing stages, similar to enhanced vigilance and delayed disengagement of attention. More research is needed to better understand the relation between attention and size perception biases.

In sum, attention, expectancy and perception biases are evident in anxiety, but only a few studies have investigated their causal relationships, with inconclusive findings. More data are needed to understand these causal relations and underlying prefrontal-limbic-sensory abnormalities.

**Insights from attention training**

Many studies employ cognitive training, which is thought to modify attention biases. This type of research seeks to better understand the causal role of attention in anxiety and to alleviate clinical symptoms. Yet the results of such interventions are mixed [28**]. In ABM techniques, two stimuli — commonly neutral and threatening — are presented in parallel. Participants are trained to focus their attention on neutral rather than threatening stimuli. Threat vigilance/avoidance is calculated by comparing reaction times to targets appearing in locations previously occupied by threatening versus neutral cues. Analysis of pooled patient-level datasets from highly anxious individuals demonstrated ABM’s modest but significant effect on remission and attention bias [29]. ABM’s effectiveness was limited to patients younger than 37, patients assessed by clinicians and training conducted in laboratory settings. Considering these limitations, the authors suggest developing more engaging ABM paradigms and/or combining ABM with other treatments. Another review of ABM in highly anxious individuals [30**] underscores the disappointing results of threat-avoidance ABM, especially if the training did not take place in the lab. In addition, anxiolytic effects were not related to alterations in attention bias following ABM. The fact that fear and overt threat behavior may not always be ‘synchronized’,
such that fear reports are not always accompanied by anxious vigilance or avoidance behavior, may at least partially explain these disappointing findings [31].

Heeren et al. [32] indicate that ABM’s effects may be due to threat vigilance or inhibitory control mechanisms. The review concluded that anxiety reduction during ABM was associated with improved goal-directed control [30**], in line with evidence for ABM’s impact on prefrontal activation and prefrontal-visual cortex connectivity [33]. These results should be taken with caution as the change in prefrontal activation following ABM was not replicated in another study [34].

In another common type of training aimed at improving emotion control, participants performed a difficult executive task (e.g., distraction inhibition in a Flanker task, memorizing items in working memory). While executive training has been shown to alleviate rumination [35] and trait anxiety [36], results are difficult to replicate [37,38]. Executive training effects were reflected in enhanced connectivity between limbic and prefrontal regions [39] and reduced prefrontal and supramarginal task-activation [40], suggesting that symptomatic improvement is due to a better balance between top-down control mechanisms and bottom-up threat detection.

In sum, current views point to modest effects of ABM and executive training on anxiety symptoms, possibly via modulation of prefrontal-limbic-sensory connectivity. Future research is warranted to fine tune the optimal conditions for this training and develop more engaging training effective outside laboratory settings. Furthermore, direct within-subject comparison between ABM and executive training may shed light on the similarities and differences between these two methods, thus facilitating the development of more effective methods.

Conclusions, applications and future directions

The evidence summarized here demonstrates the presence of enhanced vigilance, delayed disengagement and avoidance of irrelevant threatening cues among anxious participants and those prone to develop anxiety. Healthy individuals prioritize relevant threats only. These differences were related to abnormalities in prefrontal regulatory influences over limbic and sensory regions related to threat detection in anxiety. Expectancy and attention biases may result in enhanced perceptual sensitivity that characterizes anxiety via prefrontal-limbic-sensory pathways. Yet findings are mixed and more data are needed to understand the directional relationships among attention, expectancy and perception biases. Threat avoidance and executive attention training have moderate effects, possibly through their impact on prefrontal-limbic-sensory circuits. Nevertheless, these training methods are difficult to replicate.

The above findings show that more research is needed to understand the causal role and neural underpinnings of specific attention abnormalities in anxiety. This understanding is essential for developing targeted psychological and pharmacological treatments. For example, the attention subsystem driving a patient’s most significant symptoms may differ from patient to patient. Developing more sensitive measures to assess specific attention biases and their impact on other biases will assist clinicians in developing individually-tailored treatments that target core causal biases and not their byproducts. In addition, a better understanding of changes in attention processes and anxiety symptoms following attention modification over time will facilitate better assessment of training protocols, which in turn may lead to more effective training.

Future comprehensive research is warranted to examine the factors moderating attention training efficacy. So far studies have focused on a single moderator that explains only some of the data variance. Large-scale studies using advanced statistical methods (e.g., machine-learning tools) have the potential to solve inconsistencies in the existing literature. Such studies can take into account various moderating factors both prior to and during training in order to develop individually tailored training protocols. For example, the mechanisms targeted for training (e.g., orienting, avoidance, inhibition or working memory) may differ between populations [32,41], while factors such as length and frequency may differ between trainees. In attempting to solve these inconsistencies and develop more effective training, new protocols should target perceptual mechanisms [42] or employ new stimuli [43]. For example, following training that enhanced attention bias toward positive stimuli, participants with high levels of worry or physiological arousal exhibited reduced worry symptoms and attentional changes, as indicated by behavior and ERP components [44]. These new training methods seem promising, but future replications are needed to test their efficacy.

Open questions remain regarding the dynamic mutual influences of the cognitive and neural systems modulating valence processing. The development of advanced data acquisition and analysis methods may help resolve these questions. For example, although researchers agree that the amygdala plays a central role in the network that subserves valence processing, its exact role is being debated. Some researchers have proposed that the thalamic pulvinar nucleus is involved in tagging stimuli as threatening, while the amygdala orchestrates the responses [5**,45]. Today such a proposition can be examined directly using high-resolution fMRI. Exciting developments in neuroimaging analysis offer opportunities for better characterizing the dynamics of valence processing [46,47] and of interactions between neural networks [48]. These methods can resolve long-standing
debates regarding the role of different systems in valence processing among healthy and anxious individuals.

**Conflict of interest statement**
Nothing declared.

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**References and recommended reading**

Papers of particular interest, published within the period of review, have been highlighted as:

● of special interest

**of outstanding interest**


   In the new edition of The nature of emotion: Fundamental questions, Shackman and Lapate highlight the mutual influences and strong connections between the neurocognitive systems mediating emotion and attention. The chapter provides an excellent summary of contemporary views and recent findings.


   In this introduction paper, the authors summarize findings on attention bias modification and provide useful practical future research directions.


   A review paper that summarizes findings from a large number of multisession ABM studies in high-anxious individuals. The authors conclude that the impact of ABM on anxious symptoms is not larger compared to control attention trainings. Furthermore, they suggest that general attentional mechanisms, such as vigilance or attention control, are atypical in anxiety. They further note that ABM towards positive stimuli may be more promising compared to presenting negative cues.


30 Emotion-cognition interactions


