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Enhanced neural reactivity and selective attention to threat in anxiety

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ABSTRACT

Attentional bias towards threat is implicated in the etiology and maintenance of anxiety disorders. We examined the neural correlates of threat bias in anxious and nonanxious participants to shed light on the neural chronometry of this cognitive bias. In this study, event-related potentials (ERPs) were recorded while anxious ($n = 23$) and nonanxious ($n = 23$) young adults performed a probe-discrimination task measuring attentional bias towards threat (angry) and positive (happy) face stimuli. Results showed an attention bias towards threat among anxious participants, but not among nonanxious participants. No bias to positive faces was found. ERP data revealed enhanced C1 amplitude (~80 ms following threat onset) in anxious relative to nonanxious participants when cue displays contained threat faces. Additionally, P2 amplitude to the faces display was higher in the anxious relative to the nonanxious group regardless of emotion condition (angry/happy/neutral). None of the ERP analyses associated with target processing were significant. In conclusion, our data suggest that a core feature of threat processing in anxiety lies in functional perturbations of a brain circuitry that reacts rapidly and vigorously to threat. It is this over-activation that may set the stage for the attention bias towards threat observed in anxious individuals.

1. Introduction

The attentional system of anxious individuals is biased in favor of threat-related stimuli (Bar-Haim et al., 2007; Mogg and Bradley, 1998; Williams et al., 1996). This processing bias has been implicated in the etiology and maintenance of anxiety disorders (Beck and Clark, 1997; Eysenck, 1992; Mathews and Mackintosh, 2000). Furthermore, recent studies have used computerized attention training tasks to modify threat-attention patterns in clinically anxious participants and demonstrated significant reduction in anxiety symptoms and even full clinical remission in considerable percentage of patients (Amir et al., 2009; Schmidt et al., 2009; Bar-Haim, 2010; Hakamata, in press).

One of the most widely used tasks to study and modify attention biases in anxiety is the dot-probe task (Bradley et al., 1997; MacLeod et al., 1986). In this task, two stimuli, one threat-related and one neutral, are shown briefly on each trial, and their offset is followed by a small target in the location just occupied by one of them. Participants are required to respond as fast as possible to the target. Based on the attention literature (Navon and Margalit, 1983; Posner et al., 1980), response latencies to the target provide a "snap-shot" of a participant's attention bias, with faster responses to targets at the attended relative to the unattended location. Faster reaction times (RTs) to targets appearing at the location of threat relative to neutral stimuli are indicative of an attentional bias towards threat and possibly also difficulty to disengage attention from the threatening stimuli (Fox et al., 2001). The opposite pattern indicates avoidance of threat.

Given the practical and theoretical importance of these behavioral findings for the understanding of the etiology of anxiety disorders and for the potential development of novel treatments (Pine et al., 2009), endeavors to delineate the neural substrates of the threat bias have started to emerge (Armony and Dolan, 2001; Pourtois et al., 2006). More specifically, fMRI studies show that anxious patients relative to nonanxious controls demonstrate enhanced activation in the amygdala and ventro-lateral prefrontal cortex (vlPFC) while performing on the dot-probe task (Monk et al., 2006, 2008). It has been suggested that these anxiety-related activation patterns reflect greater sensitivity and hypervigilance to threats as well as perturbations in frontal emotion regulation in anxious participants. Connectivity analyses further suggest that activations in the amygdala and in the PFC of anxious patients are negatively correlated during dot-probe performance, such that increased PFC activation is associated with reduced response of the amygdala (Monk et al., 2008). And, trait-anxiety was found to be positively correlated with activation in the PFC (Telzer et al., 2008). These data are in accord with models implicating the PFC in the down regulation of amygdalar reactivity (LeDoux, 1995, 1996).

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fMRI studies provide important insights on the brain structures associated with threat-related attentional biases in anxious individuals during performance on the dot-probe task. However, performance on this task entails two distinct stages: processing of the emotion cues, and processing of and responding to the targets that follow them. To gain better understanding of the underlying neural correlates of these cognitive processes and their timing, researchers have taken advantage of the superior temporal resolution provided by event-related potential (ERP) techniques. Of particular interest were ERP components known to be modulated by emotion stimuli and spatial attention.

ERP dot-probe studies with healthy adults have shown threat-related modulation in the C1 component time locked to the faces display (Pourtois et al., 2004) and in the P1 component time locked to target onset (Pourtois et al., 2004; Santesso et al., 2008). The C1 component (50–100 ms post-stimulus) was more intense for displays containing threat faces relative to displays containing non-threatening faces (Pourtois et al., 2004). The C1 is the first ERP component triggered by the appearance of a stimulus in the visual field, and is thought to be pre-attentive and independent of spatial attention (Clark et al., 1995; Clark and Hillyard, 1996; Foxe and Simpson, 2002; Fu et al., 2005; Hillyard and Anllo-Vento, 1998; Stolarova et al., 2006). It has been suggested that modulation of the C1 by the emotional valence of the cue display on the dot-probe task could be the consequence of an interaction between the primary visual cortex and subcortical limbic structures responsible for the detection of threats (Pourtois et al., 2004; Stolarova et al., 2006). The P1 component (peaking ~130 ms post-stimulus onset) was found to be enhanced for targets replacing threatening faces compared to happy or neutral faces (Pourtois et al., 2004; Santesso et al., 2008). Augmentation of the P1 component was also found among high trait anxious individuals when performing on different cue-target attention tasks (Li et al., 2005, 2007). These findings were attributed to greater attention allocation to the threatening relative to non-threatening stimuli, and are in line with basic ERP spatial attention research showing P1 modulation by early visuospatial orienting (Clark and Hillyard, 1996; Hillyard and Anllo-Vento, 1998; Mangun, 1995; Mangun and Buck, 1998; Luck et al., 2000).

To our knowledge, only three ERP studies used the dot-probe task to test the chronometry of threat bias in anxious relative to nonanxious control participants (Fox et al., 2008; Mueller et al., 2009; Helfinstein et al., 2008). Fox et al. (2008) used a go/no-go dot-probe task and found that angry face cues elicited an enhanced N2pc component in anxious but not in nonanxious individuals. Mueller et al. (2009) also used a go/no-go variant of the dot-probe task and found that compared to controls, patients with social anxiety disorder showed enhanced P1 amplitudes to angry–neutral versus happy–neutral face pairs. However, unlike the findings in nonselected populations, these authors also found decreased P1 amplitudes to probes replacing emotional (angry and happy) versus neutral faces. Finally, Helfinstein et al. (2008) used the dot-probe task with a prime word before each trial, and showed enhanced P1 and N1 components to the faces display among anxious relative to nonanxious participants. However, all the trails in this particular study contained pairs of angry–neutral faces, thus it was impossible to specifically tie this result to the threatening emotion. These studies used modified versions of the dot-probe task, thus leaving unspecified the neural chronometry associated with performance on the classic dot-probe task, which makes the association of these findings with previous behavioral and imaging fMRI data more difficult.

Here, we examine the chronometry of attention bias to threat and to positive stimuli in anxious relative to nonanxious individuals. ERPs were collected while participants performed a classic dot-probe task. Displays consisting of angry–neutral, happy–neutral, and neutral–neutral face pairs were followed by a target probe. We expected to replicate the established finding of attentional bias towards threat in anxious participants. That is, faster RTs to targets replacing angry faces than to targets replacing neutral faces in anxious individuals but not in nonanxious controls (Bar-Haim et al., 2007; Mogg and Bradley, 1999). Following Pourtois et al. (2004) and Santesso et al. (2008) who used the dot-probe task with nonselected samples, we also expected that this behavioral pattern will be mirrored by enhanced C1 negativity in anxious relative to nonanxious participants during the faces display when containing threat faces but not when containing happy faces or only neutral faces. This finding would indicate enhanced pre-attentive threat processing in anxious participants. Finally, previous studies were equivocal in their data on P1 amplitude time locked to target onset with Mueller et al. (2009) reporting reduced P1 amplitude for targets appearing at the location of emotional (angry and happy faces) relative to the neutral face in anxious individuals and other studies (Pourtois et al., 2004; Santesso et al., 2008) report enhanced P1 for threatening stimuli in nonselected populations, our analyses remain exploratory in nature. All in all, we expected to complement the extant ERP (Pourtois et al., 2004; Santesso et al., 2008; Li et al., 2005, 2007; Fox et al., 2008; Mueller et al., 2009; Helfinstein et al., 2008) and fMRI findings (Monk et al., 2006, 2008; Telzer et al., 2008) illuminating further the association between anxiety, attention, and brain activation using the classic dot-probe task.

2. Methods

2.1. Participants

Participants were selected from a pool of 190 undergraduate students based on their scores on the trait scale of the State-Trait Anxiety Inventory (STAI-T) (Spilberger et al., 1983). The anxious group consisted of 23 students (17 females, $M_{age} = 22.54$ years, SD = 1.17) with the highest trait-anxiety scores. The nonanxious group comprises 23 students (13 females, $M_{age} = 22.52$ years, SD = 1.23) with the lowest scores on this scale. The groups differed on trait-anxiety (anxious: $M = 55.52$, SD = 8.62; nonanxious: $M = 26.61$, SD = 1.97) and state anxiety (anxious: $M = 50.96$, SD = 7.51; nonanxious: $M = 27.04$, SD = 5.17), $ts(44) = 15.67$ and 12.56, respectively, $ps < 0.0001$. STAI-T mean score of the anxious group exceeded the normal functioning range and was similar to those found among clinically anxious patients (Fisher and Durham, 1999; Yong-Ku et al., 2009).

2.2. The dot-probe task

2.2.1. Stimuli

The fixation display was a gray plus sign (2 cm × 2 cm) presented in the center of the screen. The face stimuli were achromatic photographs (55 mm × 80 mm) of 12 different actors taken from the NimStim stimulus set (Tottenham et al., 2009), each of which displayed three possible expressions of emotion: angry, happy, and neutral (all open mouth). The original NimStim stimuli are chromatic. Adobe Photoshop software was used to convert the stimuli to grayscale and equate their luminance and contrast values. Each faces display was made up of two photographs of the same actor, presented at equal distances at the left and right sides of the screen (center-to-center distance of 16.5 cm) and in the upper visual field. There were three types of face pairs: angry–neutral, happy–neutral, and neutral–neutral (36 different pairs in total). The target display consisted of two dots (5 mm center-to-center). Each dot subtended 2 mm in diameter. The dot pair was oriented either horizontally (..) or vertically (:) and appeared at the location of the center of either the left or the right photograph of each face pair.

2.2.2. Dot-probe procedure

Each trial in the dot-probe task began with a 500 ms fixation display followed by the faces display for 500 ms, which was immediately replaced by the target display for 200 ms. Following target display the screen went blank for an inter-trial interval (ITI) of 1300 ms after which a new trial began. Participants had to determine the orientation of the dots by pressing one of two pre-specified buttons.

2.2.3. Design

The three types of face pairs (angry–neutral, happy–neutral, and neutral–neutral) made up the three conditions of emotion and were pre-