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Relationship between trait anxiety, prefrontal cortex, and attention bias to angry faces in children and adolescents

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ABSTRACT

Using event-related functional magnetic resonance imaging (fMRI) with a visual-probe task that assesses attention to threat, we investigated the cognitive and neurophysiological correlates of trait anxiety in youth. During fMRI acquisition, 16 healthy children and adolescents viewed angry-neutral face pairs and responded to a probe that was on the same (angry-congruent) or opposite (angry-incongruent) side as the angry face. Attention bias scores were calculated by subtracting participants' mean reaction time for angry-congruent trials from angry-incongruent trials. Trait anxiety was positively associated with attention bias towards angry faces. Neurophysiologically, trait anxiety was positively associated with right dorsolateral prefrontal cortex (PFC) activation on a contrast of trials that reflect the attention bias for angry faces (i.e. angry-incongruent versus angry-congruent trials). Trait anxiety was also positively associated with right ventrolateral PFC activation on trials with face stimuli (vesus baseline), irrespective of their emotional content.

Cognitive theories of anxiety suggest that vulnerability to anxiety (i.e. trait anxiety) is associated with perturbed cognitive processing of threats, in particular, attention responses to threat-related information (e.g. Eysenck et al., 2007; Mogg and Bradley, 1998; Williams et al., 1997). Attention bias to threat has been observed for various threat cues, such as threat-related words and angry faces, and has been associated not only with clinical anxiety, but also with trait anxiety within the normal population (Eysenck et al., 2007; for a meta-analysis see Bar-Haim et al., 2007).

Behavioral research has used the visual-probe task to tap anxiety-related attention biases. This task presents a series of face pairs, including angry-neutral pairs, and on each critical trial a target probe replaces either the threat face (threat-congruent condition) or the neutral face (threat-incongruent condition). An attention bias towards threat is reflected by slower reaction times (RTs) on threat-incongruent than threat-congruent trials (as RTs are generally slower to probes which appear in unattended rather than attended spatial locations). More specifically, if a person preferentially directs attention towards a threat cue, and the probe occurs in a different spatial location, this requires reallocation of attentional resources in order to redirect attention from the location of the threat cue to the location of the probe, thereby resulting in slower RTs on threat-incongruent than threat-congruent trials.

Several studies have examined attention bias for threat within the normal population of adults and children. In healthy adults, high trait anxiety is typically associated positively with an attention bias towards threat cues, such as angry faces (Bradley et al., 1998; Mogg and Bradley, 1998, 1999) and threatening words (Broadbent and Broadbent, 1988; see Bar-Haim et al., 2007 for a review). There have been fewer studies of the relationship between trait anxiety and attention bias in normal children, compared with studies of adults. For example, on a visual search task, Hadwin et al. (2003) reported that, in normal children aged 7–10 years, trait anxiety was associated with relatively faster detection of threat faces. Using a visual-probe task, Heim-Dreger et al. (2006) also found that trait anxiety was associated with an attention bias for threat faces in normal children aged 7–10 years. While there have been some mixed findings of anxiety-related attention biases in normal adults and children, these may be accounted for by

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methodological factors. For example, some studies have used the modified Stroop task which provides a less clear-cut index of attention bias (Bar-Haim et al., 2007; Heim-Dreger et al., 2006), or have used control stimuli such as household objects, which differ from angry faces in social salience as well as emotional valence (Mansell et al., 1999). Nevertheless, Bar-Haim et al. (2007) concluded from their extensive meta-analysis that the evidence of an anxiety-related attention bias in children largely resembles that typically found in adults.

Neuroimaging research implicates specific neural circuitry, including the prefrontal cortex (PFC) and amygdala in the detection of and response to threat-related cues in the environment. Anxiety may result from perturbations in this circuitry (e.g. Davis and Whalen, 2001; Hariri et al., 2003; LeDoux, 1996; Monk et al., 2006, 2008), and the PFC, specifically, may be crucial for modulating attention bias to threat (Bishop, 2007; Monk et al., 2006). For example, neuroimaging work on healthy adults has shown that attention modulates response to an aversive face stimulus through the effects of the PFC (Armony and Dolan, 2002; Pourtois et al., 2006). Research in normal adults examining cognitive control has found activation in lateral regions of the dorsal and ventral PFC (Duncan and Owen, 2003; Northoff et al., 2004). While there are close connections between lateral regions of the PFC and other frontal regions (e.g. medial PFC), neuroimaging evidence suggests that the lateral PFC plays a key role in cognitive control (e.g. Northoff et al., 2004). Furthermore, Phillips et al. (2003) proposed that ventral regions of the PFC are involved in identifying the emotional significance of stimuli and automatic regulation of emotional responses, and dorsal regions of the PFC are important for executive functions such as attentional control of emotional stimuli, planning, and effortful regulation of affective states. Other researchers have corroborated that the dorsolateral prefrontal cortex (DLPFC) is involved in allocation of attentional resources and cognitive control processes (Egner and Hirsch, 2005; Kerns et al., 2004; Luks et al., 2007; MacDonald et al., 2000). While there is growing research on the relationship between individual differences in attention responses to threat, PFC function, and anxiety in the normal population, little is known about these relationships in normal youth.

In a clinical study, Monk et al. (2006) investigated both attentional and neural responses to angry faces in adolescents with generalized anxiety disorder, compared with a control group of healthy adolescents. The stimuli were presented in a visual-probe task which concurrently assessed attention bias for threat while neural responses were being monitored using functional magnetic resonance imaging (fMRI). Clinically anxious adolescents showed an attention bias away from angry faces, and enhanced activation of the right ventrolateral prefrontal cortex (VLPFC) in response to angry faces. Monk et al. (2006) did not find any anxiety-related effects in amygdala activation.

The present study examined in healthy children and adolescents: (1) whether trait anxiety is associated with an attention bias for angry faces, (2) the neural correlates of the anxiety-related attentional bias for angry faces, and (3) whether the anxiety-related pattern of attentional and neural responses to threat cues in healthy youth is similar to that previously found in youth with clinical anxiety by Monk et al. (2006). We used angry faces for several reasons. First, humans possess biologically prepared mechanisms sensitive to innate threat stimuli, such as angry faces, facilitating attention allocation towards such threats (Hadwin et al., 2003; Mogg and Bradley, 1999; Öhman et al., 2001; Öhman, 1996). Further, angry faces have ecological validity, are naturalistic, and are emotionally potent in comparison to stimuli such as threatening words which are often limited in threat value (Bradley et al., 1998; Mogg and Bradley, 1999). In addition, previous behavioral research has demonstrated an association between trait anxiety and attention bias towards angry faces in healthy adults and children (e.g. Bradley et al., 1998; Heim-Dreger et al., 2006; Mogg and Bradley, 1999), and we are keen to use a robust paradigm which is likely to elicit an anxiety-related attention bias so we can assess attention bias and neural responses concurrently in an fMRI scanner. Finally, our previous imaging study which examined clinically anxious youth used angry faces (Monk et al., 2006), so we used the same stimuli in order to compare findings across studies and build upon our previous behavioral and fMRI work. In addition, in line with our previous fMRI study and behavioral research, we included happy faces as a comparison to examine whether the behavioral and neural effects were selective to angry faces.

We used a visual-probe task and event-related fMRI to test three hypotheses: First, trait anxiety would be associated with an attention bias for angry faces. Second, trait anxiety would be related to neural responses associated with the attention bias for angry faces, as reflected by the contrast between the angry-incongruent and angry-congruent conditions. This contrast allows us to examine attention allocation and cognitive control, which has been associated with DLPFC engagement (Luks et al., 2007; MacDonald et al., 2000; Phillips et al., 2003). Specifically, if a person has an attention bias to threat and the probe appears in the opposite location (i.e. angry-incongruent trials), this would require attention to be redirected away from the location of the threat cue to the opposite location, in order to respond to the probe. On the other hand, if a person has an attention bias to threat and the probe appears in the same location as the threat (angry-congruent trials), this would not require attention re-orienting away from the location of the threat cue to the probe location (if individuals do not have an attention bias to threat, there should be no difference in the attentional demands of angry-incongruent and angry-congruent trials). Thus, an anxiety-related attention bias to threat should be associated with greater attentional demand (indexed by DLPFC response) on angry-incongruent trials relative to angry-congruent trials. And finally, our third hypothesis was that trait anxiety would be associated with VLPFC activation to angry faces (cf. Monk et al., 2006).

1. Method

1.1. Participants

Twenty healthy children and adolescents participated. Two participants were excluded due to poor performance on the visual-probe task (more than 25% of trials with missing response time (RT) data due to errors or outliers), and two were excluded due to excessive head movement during the fMRI task (greater than 1 voxel). The final sample included 16 healthy children and adolescents (8 males; mean age 15.31 ± 2.02; age range 11–18; mean IQ 112.06 ± 12.06). Participants were recruited through the NIH website, flyers, and word of mouth.

Health status was determined by a physical examination and psychiatric interview (The Kiddie Schedule for Affective Disorders and Schizophrenia; Kaufman et al., 1997). All participants were free of current and past psychiatric disorders including anxiety. Specifically, we excluded for current major depressive disorder, Tourette's syndrome, conduct disorder, post-traumatic stress disorder, obsessive-compulsive disorder, exposure to severe trauma, suicidal ideation, psychosis, pervasive developmental disorder, lifetime history of bipolar disorder, and any type of clinical anxiety disorder. Participants had intelligence quotients above 75 (Weschler, 1999). The NIMH Institutional Review Board approved all procedures, and parents and participants provided written consent/assent.

1.2. Measures

1.2.1. Trait anxiety

Participants completed the trait version of the State-Trait Anxiety Inventory for Children (STAIc; Spielberger, 1973). We collected the state version as well, but we did not include them in analyses since the measure was taken outside of the scanner and so may not be indicative of participants' state in the scanner. Participants used a 3-point scale (1 = "almost never", 2 = "sometimes", 3 = "often") to answer 20 items such as "I worry too much" and "I have trouble making up my mind". Participants'