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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 (versus 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, Derakshan, Santos & Calvo, 2007; Mogg & Bradley, 1998; Williams, Watts, MacLeod & Mathews, 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, Pergamin, Bakermans-Kranenburg, & van Ijzendoorn, 2007).

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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 & Bradley, 1998, 1999) and threatening words (Broadbent & 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 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, Clark, Ehlers, & Chen, 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 & Whalen, 2001; Hariri, Mattay, Tessitore, Fera, & Weinberger, 2003; LeDoux, 1996; Monk, Nelson, McClure, Mogg, Bradley, Leibenluft, Blair, Chen, Charney, Ernst, & Pine, 2006; Monk, Telzer, Mogg, Bradley, Mai, Louro, Chen, McClure, Ernst, Pine, 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, Schwartz, Seghier, Lazeyras, & Vuilleumier, 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, Heinzel, Bermpohl, Niese, Pfennig, Pasual-Leone, & Schluag, 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 & Hirsch, 2005; Kerns, Cohen, MacDonald, Cho, Stenger, & Carter, 2004; Luks, Simpson, Dale, & Hough, 2007; MacDonald, Cohen, Stenger, & Carter, 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 in youth, (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, Lundquist, & Esteves, 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, Mogg, Falla, & Hamilton, 1998; Mogg & 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 & 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).

Method

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 responses 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, Birmaher, Brent, Rao, Flynn, Moreci, Williamson, & Ryan, 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 (Wechsler, 1999). The NIMH Institutional Review Board approved all procedures, and parents and participants provided written consent/assent.

Measures

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' scores on the STAIc ranged from 21–36 ($M = 27.56$, $SD = 4.65$), with higher scores indicating higher trait anxiety. There were no age or gender effects on the STAIc.

Visual-Probe Task—To measure attention bias we used a well-validated visual-probe paradigm that has been employed in research among adults and youth (Mogg & Bradley, 1999; Monk et al., 2006; Pine, Mogg, Bradley, Montgomery, Monk, McClure, Guyer, Ernst, Charney, & Kaufman, 2005). Each trial began with a 500 ms central fixation point, followed by a pair of faces that appeared on the left and right sides of the screen for 500 ms. The faces were replaced by an asterisk-probe which appeared for 1100 ms in the location of one of the preceding faces. Participants were instructed to press one of two buttons as quickly and as accurately as possible to indicate the location of the probe (left or right). Inter-trial interval was 1900 ms.

Participants viewed 80 actors twice across 160 trials. There were five trial types, including two conditions of interest: congruent trials in which an angry-neutral face pair was followed by an asterisk-probe on the same side of the screen as the angry face; and incongruent trials, in which an angry-neutral face pair was followed by an asterisk-probe on the opposite side of the angry face. Control conditions were also included: happy-neutral face pairs (both congruent and incongruent), and neutral-neutral face pairs. There were 32 trials for each of the five conditions. In addition, 40 blank trials (no faces, no probes) were presented to serve as a baseline condition in the fMRI analyses. Trial presentation order was random for each participant (see Figure 1).

Analyses

Behavioral Data Analysis—Incorrect trials were removed from the analyses as well as trials in which participants' RT was < 200 ms or > 800 ms (Monk et al., 2006), resulting in 5.2% ($SD = 5.4$) of trials being removed. Participants were excluded from data analysis if they had more than 25% of trials with missing RT data (due to incorrect responses, non-responses, or outliers which did not fall within the 200–800 ms RT window; Monk et al., 2006). This resulted in the exclusion of two participants. A regression analysis was used to examine the relationship between trait anxiety and attention bias. There was marked variability across individual participants' RTs, so mean RT was entered as a covariate to account for individual differences in overall psychomotor speed. Analyses compared trials when the probe and emotional face were on the same side (congruent) versus opposite side (incongruent). The difference between mean RTs for incongruent and congruent trials provided a measure of attention bias such that positive numbers indicated a bias towards angry faces (i.e., shorter reaction times when the probe appeared on the same side as the angry face).

fMRI Analysis—Imaging used a GE 3-tesla scanner to acquire images with 29 continuous 3.3 mm axial slices, parallel to the AC/PC line. We used echo-planar single shot gradient echo T2* weighting (TR = 2300 ms; TE = 23 ms; FOV = 240 mm; 64×64 matrix; $3.3 \text{ mm} \times 3.75 \text{ mm} \times 3.75 \text{ mm}$ voxel). High-resolution T1-weighted volumetric scans used a magnetization prepared gradient echo sequence (MP-RAGE) [180 1.0 mm axial slices; FOV = 256 mm, NEX = 1, TR = 11.4 ms, TE=4.4 ms; 256×256 matrix; TI = 300 ms, bandwidth 130 Hz/pixel = 33 kHz for 256 pixels in-plane resolution = 1 mm^3].

Functional imaging data were analyzed using AFNI software version 2.56b (Cox, 1999). Participants were removed from the analyses if their head movement was greater than 1 voxel in any direction. This resulted in the exclusion of two participants. Movement was mitigated by registering images to one volume in each run. Incorrect trials and trials not within the accepted RT range were removed from the fMRI analysis. Participants' data were smoothed with a 6 mm full-width at half-maximum isotropic Gaussian filter.

Using a two level procedure, we conducted a random effects fMRI data analysis. At the first (individual) level, multiple regression analyses were run on each participant's individual dataset using the AFNI module 3dDeconvolve. Vectors were created for each of the five conditions (angry-congruent, angry-incongruent, happy-congruent, happy-incongruent, and neutral), with the onset time of each trial for each condition. Blank trials were modeled as an implicit baseline. An additional vector modeled nuisance trials in which the participant responded inappropriately (incorrect responses, non-responses, and RTs that were < 200 or > 800 ms). Using a gamma variate, vectors were transformed into waveforms, and coefficients were created for each participant and condition. Contrast values were calculated by comparison of coefficients for specific conditions. Each participant's anatomical datasets were converted to Talairach space (Talairach & Tournoux, 1988).

At the second (group) level, a regression analysis was done using the AFNI module 3DRegAna on the main contrast of interest, angry-incongruent versus angry-congruent faces, with mean RT as a covariate to be consistent with the behavioral analyses. To examine the relationship between trait anxiety and brain activation, we entered participants' STAIc scores in the regression analysis. We also examined responses to happy-incongruent versus happy-congruent face trials. Finally, we conducted analyses following Monk et al. (2006) to examine the contrast of angry faces versus baseline. We entered participants' STAIc scores and mean RT in the regression to be consistent with our other analyses. For comparison, we also examined happy faces versus baseline and neutral faces versus baseline, in addition to angry faces versus neutral faces and angry faces versus happy faces.

A Monte Carlo simulation (Rissman, Eliassen, & Blumstein, 2003; Monk et al., 2006) was used to control for multiple tests within the primary areas of interest. This method controls for type I errors, offering a reasonable correction for multiple tests during group level analyses in the regions of interest (ROIs). Based on the most frequently reported activation sites in the literature, the analyses were conducted within a priori ROIs limited to Brodmann areas 9 and 46 in the bilateral DLPFC (MacDonald et al., 2000; Pochon, Levy, Poline, Crozier, Lehericy, Pillon, et al., 2001) and the rostral part of the anterior commissure, ventral to the corpus callosum, and lateral to the orbital gyrus in the bilateral VLPFC. Each voxel within these areas that reached significance at the $p < .05$ level was included in the Monte Carlo simulation.

Results

Behavioral Results

In support of our first hypothesis, trait anxiety was significantly associated with an attention bias toward angry faces, $\beta = 0.52$, $p < .05$, $R^2 = 0.38$. For the whole sample, the mean (\pm S.D.) RTs (ms) were 529 (103) to angry-incongruent trials and 520 (97) to angry-congruent trials. There was no evidence that the relationship between trait anxiety and attention bias was confounded by individual differences in overall mean RT, as there was no significant relationship between the latter variable and attention bias scores for angry faces, $\beta = 0.34$, ns, $R^2 = 0.11$. When sex was entered as a covariate, the attention bias towards angry faces remained significant, $\beta = 0.64$, $p < .01$, $R^2 = 0.57$. In addition, males and females showed similar anxiety-related attentional responses to threat (males: $\beta = 0.73$, $p < .05$, females: $\beta = 0.72$, $p < .08$). For happy faces, no relationship was found between attention bias and trait anxiety, $\beta = 0.28$, ns, $R^2 = 0.20$.

fMRI Results

To test our second hypothesis, we examined the neurophysiological correlates of the attentional bias for angry faces by correlating trait anxiety with DLPFC activation in the contrast of angry-incongruent versus angry-congruent trials (which reflects the difference in participants' neural response to angry-incongruent trials and angry-congruent trials). Trait anxiety scores were positively associated with right DLPFC activation on this contrast term, $t(13) = 4.31$, $p < .001$ uncorrected (Talairach-Tournoux Atlas coordinates $x, y, z = 45, 39, 16$; see Figure 2). There was not a parallel response in the left DLPFC, and no other areas of activation reached significance at this level throughout the brain. The Monte Carlo simulation revealed this DLPFC activation to be significant at the $p < .05$ level, corrected for multiple comparisons within the a priori ROI. Furthermore, the relationship between anxiety and DLPFC activation was not significant for the corresponding contrast of trials with happy faces. Finally, to examine further the relationship between anxiety, attention bias, and the DLPFC finding for angry faces, we included participants' attentional bias scores (the difference in RT between angry-incongruent and angry-congruent trials) as a covariate. In this analysis, trait anxiety continued to relate to greater right DLPFC activation, $t(12) = 4.16$, $p = .001$ uncorrected. Lastly, gender was entered as a covariate to examine whether this relationship was affected by sex differences. Trait anxiety continued to relate to greater DLPFC activation, $t(11) = 3.91$, $p < .005$.

To test our third hypothesis, we examined the effect of trait anxiety on the contrast of angry faces versus baseline. Trait anxiety was positively associated with right VLPFC activation, $t(13) = 3.83$, $p = .002$ uncorrected (x, y, z coordinates = 39, 45, 0). The Monte Carlo simulation was significant at $p < .01$ corrected for multiple comparisons within the a priori ROI. Furthermore, there was not a parallel response in the left VLPFC, and no other areas of activation reached significance at this level throughout the brain in this contrast, even when the threshold was relaxed to $p < .05$ uncorrected. Finally, to examine whether individual differences in attention accounted for the VLPFC finding, we included participants' attentional

bias scores as a covariate. In this analysis, trait anxiety continued to relate to greater right VLPFC activation, $t(12) = 3.78, p = .003$ uncorrected.

We conducted further analyses to examine whether the relationship between anxiety and right VLPFC activation was specific to angry faces. At the same VLPFC location in our analysis for angry faces, trait anxiety was related to greater activation in the contrast of happy faces versus baseline, $t(13) = 4.14, p = .001$ uncorrected (x, y, z coordinates = 38, 46, 0), and neutral faces versus baseline, $t(13) = 4.34, p < .001$ uncorrected (x, y, z coordinates = 37, 44, 1). No significant anxiety-related effects were found in the VLPFC in the contrasts of happy faces versus angry faces or neutral faces versus angry faces, suggesting that the VLPFC effect is unspecific to the valence of the emotion.

Discussion

Attention bias for threat cues and lateral PFC activation were both associated with trait anxiety in healthy youth. Specifically, trait anxiety scores significantly correlated with attention bias towards angry faces, relative to neutral faces. Neurophysiologically, trait anxiety was also associated with greater right DLPFC activation on a contrast corresponding to the attentional bias for angry faces (i.e. angry-incongruent versus angry-congruent trials). Additionally, trait anxiety was associated with greater right VLPFC activation, irrespective of the emotional content of the face stimuli. When attention bias scores were entered as a covariate, the relationship between trait anxiety and right DLPFC and VLPFC activation remained significant, suggesting that the relationship between trait anxiety and attention bias for threat do not fully account for differences in brain engagement.

Regarding our first hypothesis, the present finding of an anxiety-related attention bias for angry faces is consistent with previous findings from both adults and youth. These studies have shown that trait anxiety is associated with an attentional bias towards threat cues, such as angry faces in normal adults (Bradley et al, 1998; Mogg & Bradley, 1999) and children (Heim-Dreger et al., 2006). In contrast to the present finding of attentional bias towards angry faces, some previous work among clinically anxious youth using the same behavioral task has found attentional bias away from angry faces. Specifically, this pattern of bias has been found in physically abused children with post-traumatic stress disorder (PTSD; Pine et al., 2005) and in youth with generalized anxiety disorder tested in an fMRI scanner (Monk et al., 2006). Other studies of attention bias in clinically anxious youth have found an enhanced attention bias towards threat (e.g. Taghavi et al., 1999, 2003; Dalgleish et al., 2003; Vasey et al., 1995; Waters, et al., 2008). However, there are notable methodological differences between the clinical studies, which may account for much of the variation in their findings (e.g. type of attentional task, type of anxiety disorder, presence of clinical depression, severity of anxiety symptoms, experimental conditions; see Dalgleish et al., 2003, Pine, 2007, and Waters et al., 2008, for further discussion). For example, many previous studies have used single words (rather than angry faces) as threat stimuli (e.g., Taghavi et al., 1999, 2003; Vasey et al., 1995) and have used the modified Stroop task to assess attention bias (e.g., Dalgleish et al., 2003; Taghavi et al., 1999, 2003). However, interpretation of results from the latter task is complicated, as evidence of an attention bias on this task might reflect either enhanced or suppressed processing of threat (de Ruiter & Brosschot, 1994); thus, the direction of the attention bias is not entirely clear from studies which have used this paradigm. The experimental conditions may also be important in determining findings of attention bias, given that several studies have indicated that stressful contexts and high levels of state anxiety can suppress attentional bias in anxious adults and children (Constans, McCloskey, Vasterling, Brailey & Mathews, 2004; Amir, McNally, Riemann, Burns, Lorenz & Mullen, 1996; Kindt, Brosschot & Everaerd, 1997). Different patterns of bias may also arise from the use of different samples of anxious participants. For example, children with PTSD who have suffered chronic

physical abuse may have acquired a tendency to avoid attending to angry faces, possibly to minimize eye contact and avoid triggering possible aggressive responses in others (Pine et al., 2005). Given that there is not yet enough systematic evidence to provide a conclusive explanation for these mixed findings of attention bias in anxious youth, there is a need for further research, for example, using more direct behavioral measures of attention bias, such as eye tracking. Nevertheless, the present findings are not only valuable in contributing to a growing body of evidence of anxiety-related individual differences in attentional response to threat (Bar-Haim et al., 2007) but also allowed us to test our second hypothesis which focused on relationships among anxiety, attention bias, and PFC function.

To test our second hypothesis, we examined the neural correlates of the anxiety-related attention bias for threat, which involved comparing neural responses across the two main experimental conditions that revealed the attention bias, that is, where the angry face and probe were on different sides (angry-incongruent trials) versus where the angry face and probe were on the same side (angry-congruent trials). Results indicated that trait anxiety was associated with greater right DLPFC activation. This relationship between anxiety and DLPFC activation appeared to be specific to angry faces, as it was not apparent for the corresponding contrast for trials with happy faces. As noted earlier, this DLPFC response may reflect increased attentional demands of angry-incongruent trials, relative to angry-congruent trials, with these attentional demands arising from the anxiety-related attention bias to threat. The behavioral data confirmed that in the present sample trait anxiety was indeed associated with a greater attention bias towards angry faces. Thus, individuals with an anxiety-related attention bias may have needed to make relatively more use of cognitive control mechanisms on angry-incongruent trials in order to reorient their attention from the location of the threat cue to the opposite location to respond to the probe. Interestingly, the relationship between anxiety and DLPFC response also remained significant after covarying for the attention bias measure. Thus, the DLPFC activation effect was not fully explained by the behavioral index of attention bias, which may be explained by this brain region being involved in other aspects of emotion and cognitive processing beyond the attention bias for threat.

In terms of our third hypothesis, we compared neural responses to the different face types versus the baseline condition (as in Monk et al., 2006). There appears to be a notable difference in neural responses to threat cues between youth who vary in non-clinical trait anxiety (in the present study) versus those with clinical anxiety (Monk et al., 2006). That is, in healthy youth, trait anxiety was associated with increased VLPFC activation for all face types, whereas clinical anxiety was associated with increased VLPFC activation specifically for angry faces. This lack of emotion-specificity in the relationship between trait anxiety and VLPFC response in healthy youth suggests that VLPFC activation may reflect the use of cognitive processes involved in general task performance. Thus, in healthy youth, trait anxiety may be associated with greater right VLPFC activation when performing the attentional task, whereas, among clinically anxious youth, the presence of task-irrelevant angry faces may place a particularly high demand on cognitive control processes. However, it is not clear from the current study whether these findings are specific to faces or apply to other non-face stimuli. Future work should include a non-face control condition in order to examine the specificity of the neural response in anxious youth.

Previous neuroimaging research indicates that lateral PFC regions (both VLPFC and DLPFC) commonly show increased activity during cognitive tasks and that these regions play an important role in attentional control functions necessary for maintaining task-specific information about rules or goals (Greicius, Krasnow, Reiss, & Menon, 2003; MacDonald et al., 2000; Yeung, Nystrom, Aronson, & Cohen, 2006). Similarly, Pourtois et al. (2006) suggested that the lateral PFC plays a particularly strong role in the allocation of cognitive resources in the presence of conflict or distracters, a role that Pessoa (2008) suggests is

particularly important for emotional distracters, such as angry faces. Trait vulnerability to emotional disorders such as anxiety, has been associated not only with a bias in increased sensitivity to aversive information (e.g. in automatic stimulus evaluation/appraisal processes), but also with impaired attentional control, which plays an important role in regulating emotional responses to threat (Rothbart & Derryberry, 1981; Derryberry & Reed, 2002). Thus, individual differences in lateral PFC function may be responsible for individual differences in cognitive control, which in turn may be an important component of anxiety vulnerability.

If lateral PFC activation reflects cognitive control processes, the present results may indicate that trait anxiety is associated with greater demands on processing resources to perform the task. This is consistent with cognitive theories which propose that trait anxiety impairs central executive functioning, leading to reduced processing efficiency. Accordingly, trait anxiety is associated with an increased need to allocate extra processing resources to the task in order to maintain performance (Eysenck & Calvo, 1992; Eysenck et al., 2007). Thus, lateral PFC activation may reflect a neural correlate of processing efficiency in healthy youth.

The present findings indicate that, in healthy youth, trait anxiety modulates activity in both the ventral and dorsal areas of the lateral PFC, with the former being influenced by trait anxiety irrespective of the emotional content of the stimuli, and the latter being sensitive to both the attentional cueing effects of threat faces and trait anxiety. Interestingly, a recent study of healthy adults also suggested that individual differences in anxiety influence the levels of DLPFC and VLPFC activation associated with attention allocation to threat cues (Bishop, Duncan, Brett, & Lawrence, 2004). While direct comparison between the studies is complicated by methodological differences (e.g. adults versus youth, different attentional paradigms and stimuli), the present results further highlight the potentially important role of the lateral PFC in modulating attentional responses to threat cues in anxiety.

With regard to the specific roles of the DLPFC and VLPFC, it has previously been suggested that the dorsal and ventral areas of the lateral PFC may support different types of cognitive control and emotion regulation processes. For example, the dorsal areas are implicated in effortful emotion regulation and the ventral regions are more closely involved with automatic detection, appraisal, and regulation of emotion (Ochsner & Gross, 2005; Phillips et al., 2003). It is beyond the scope of the present study to interpret the observed effects of trait anxiety on DLPFC and VLPFC activation in relation to automatic versus effortful cognitive control processes, respectively, as these specific processes were not directly manipulated here. Thus, it would be helpful for future research to examine this issue, for example, by varying the exposure conditions of the stimuli by using brief masked presentation conditions, which would reveal automatic emotion processing effects independent of effortful emotion regulation processes.

Trait anxiety and clinical anxiety are closely related constructs in terms of individual differences in anxiety proneness and vulnerability (Nisita, Petracca, Akiskal, Galli, Gepponi, & Cassano, 1990; Rapee, 1991, 2002). As noted earlier, the present findings suggest that trait anxiety and pathological anxiety in youth are associated with different patterns of lateral PFC activation. Moreover, trait anxiety and clinical anxiety disorders in youth may be associated with different patterns of attention bias to threat. Further investigation is warranted in order to clarify how trait and pathological anxiety may differ not only across different anxiety disorders, but also at different stages of the life span.

A potential limitation of this study is the broad age range and small sample size making it unfeasible to examine the relationship between trait anxiety, attention bias, and PFC function across various ages within childhood and adolescence. Although the study was designed to examine trait anxiety in youth across a wide age-range in order to compare the findings with

those of previous studies (Monk et al., 2006), a larger sample size would help to clarify the developmental implications of these findings and how trait anxiety may ultimately manifest in young adulthood. Future research can examine how the effect of puberty may influence the relationships between trait anxiety, attention bias, and underlying neural mechanisms. Finally, the levels of trait anxiety in the current study reflect a relatively low and narrow range. Thus, future research should examine whether healthy youth with high trait anxiety respond similarly to the youth in this study, or to clinically anxious youth.

In conclusion, the present study indicates that, in healthy children and adolescents, trait anxiety is associated with individual differences in lateral PFC activation when attention is modulated by threat cues. This research is relevant to recent views of anxiety which propose that anxiety vulnerability is associated with individual differences in the operation of neurocognitive mechanisms, such as the PFC, which are involved in the integration of cognitive and emotional responses to threat (e.g. Bishop, 2007; Davidson, 2002). This study also illustrates the advantages of multi-method approaches. fMRI provides important information about the underlying neural mechanisms that relate to attention bias. Future studies using measures such as fMRI, ERPs, and eye tracking can continue to inform us about the core processes underlying anxiety and attentional response to threat.

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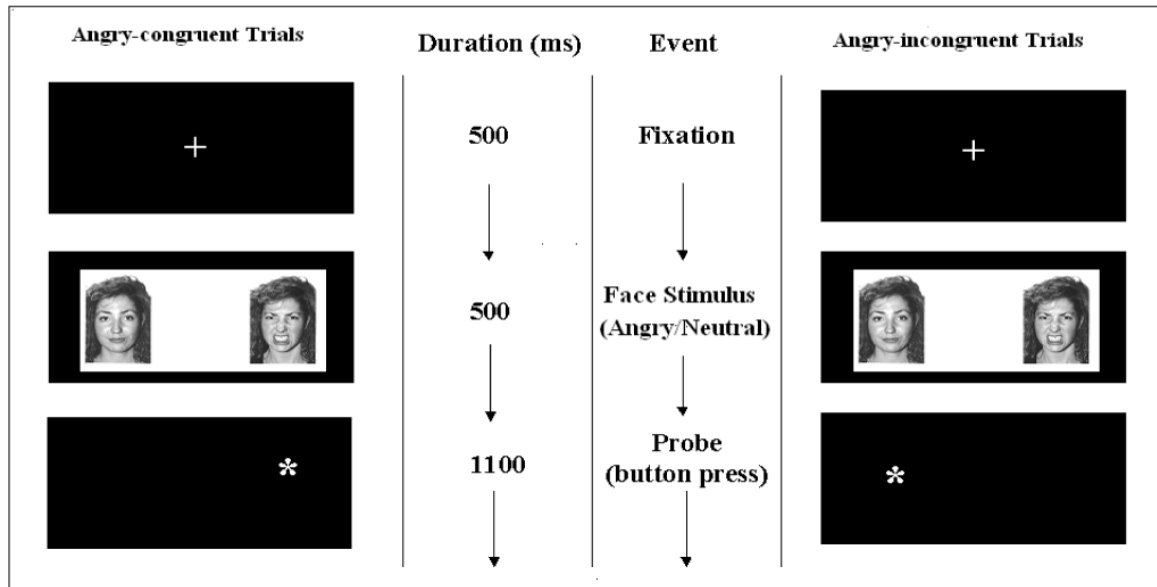


Figure 1.

The figure illustrates the two primary trial types in the task. The right column displays a sample trial of the angry face and probe on different sides (angry-incongruent). The middle two columns show the duration and name of each event. The left column shows a sample trial of the angry face and probe on the same side (angry-congruent). Happy-neutral and neutral-neutral trials were also displayed. The same actor always displays the two facial expressions.

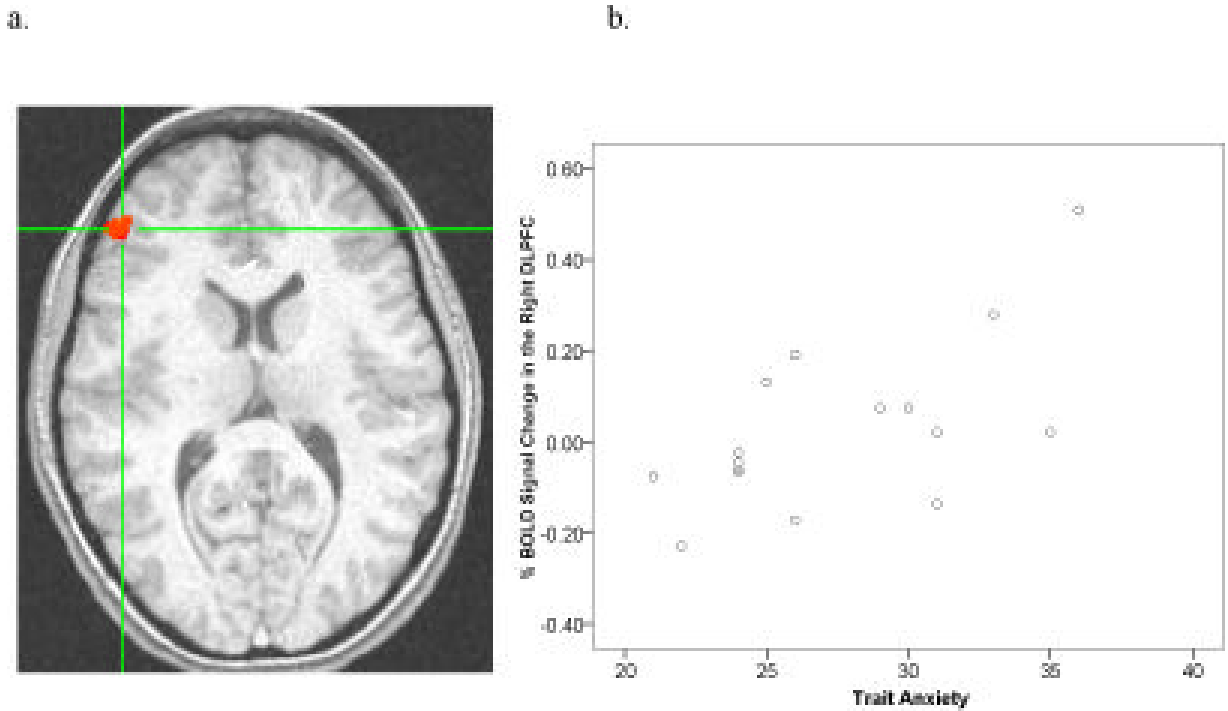


Figure 2(a).

In the comparison of trials in which the angry face and probe were on different sides (incongruent) to trials where the angry face and probe were on the same side (congruent), higher trait anxiety was associated with increased activation in the right DLPFC, $t(13) = 4.31$, $p < .001$ (right is left and left is right) and (b) mean blood oxygenation level-dependent (BOLD) response for participants for the same contrast in the voxel cluster encompassing the activation in the right DLPFC, $r = 0.62$, $p < .01$.