SOMATIC AWARENESS IN ANXIOUS YOUTH: RELATING TRAIT AND SITUATIONAL SYMPTOMS TO NEURAL MECHANISMS OF THREAT-PROCESSING

by

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The current study examined the relationship between self-reported somatic symptomatology and neural patterns of threat-processing in anxious youth. It attempted to merge discrepant findings regarding somatic awareness in anxiety by differentiating between more chronic somatic anxiety symptoms and an experiential ("situational") awareness of bodily symptoms in response to an acute stressor. Forty-two adolescents (ages 9-13), meeting DSM-IV criteria for GAD, Social Phobia, and/or Separation Anxiety completed a classic dot-probe task in which they indicated the location of a probe that replaced either threatening or neutral faces. Mean BOLD responses on to threat trials were extracted for anatomically defined regions of interest that have been related to anxiety, and this activity was correlated with self-reported somatic subscale scores. Results indicated that, within a sample of anxious youth, chronic somatic anxiety symptomatology was *negatively* correlated with sustained bilateral amygdala activity, while situational somatic symptomatology was associated with increased sustained bilateral anterior insula and caudal anterior cingulate activity. Thus, patients who display blunted emotional reactivity to mild threat cues may be more prone to chronic somatic anxiety symptoms. In addition, patients who maintain an awareness of interoceptive cues during low-grade threat-processing may be more likely to notice and report bodily cues under periods of more acute threat.

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1.0 INTRODUCTION

The current study examined individual differences in anxiety-related somatic symptoms reported by anxiety-disordered youth, and attempted to link patients' awareness of these symptoms with neural patterns of threat-processing. We differentiated between more chronic somatic anxiety symptoms and an experiential awareness of bodily symptoms during high-anxiety situations (i.e., "situational" somatic symptoms). Because somatic symptom reports are presumably dependent on patients' subjective awareness of bodily sensations, we asked whether activation in brain regions subserving attention to threat and interoceptive processing could explain individual differences in chronic and situational somatic symptom rates. In order to detect brain activation during relevant implicit attentional processes, we collected brain activation data while participants performed a basic probe detection task that has been previously used to elicit threat-related attentional biases in anxious youth (i.e., Pine, Guyer, & Leibenluft, 2008).

1.1 THE SIGNIFICANCE OF SOMATIC SYMPTOMS IN PEDIATRIC ANXIETY

Anxiety disorders are the most frequently diagnosed psychiatric syndrome in children and adolescents, with prevalence rates ranging between 12 and 20% (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003). Diagnosed youth often show impairment in the areas of family, academic, and social functioning, and are at high risk for developing additional psychiatric conditions in adulthood (Ezpeleta, Keeler, Erkanli, Costello, & Angold, 2001; Ialongo, Edelsohn,

Werthamer Larsson, Crockett, & Kellam, 1995). Somatic symptomatology is a primary feature of pediatric and adolescent anxiety disorders, and youth with anxiety are significantly more likely than their nonanxious peers to report chronic somatic symptoms (Ginsburg, Riddle, & Davies, 2006). Although research on pediatric anxiety is expanding at an impressive rate, limited attention has been paid to the role that somatic symptoms may play in these disorders.

1.2 LIMITATIONS OF PREVIOUS STUDIES

Previous studies have attempted to link patients' self-reported somatic symptoms to anxiety related elevations in autonomic arousal, but group comparisons between anxious and non-anxious individuals have failed to find reliably higher physiological reactivity in patients (Hoehn-Saric, McLeod, Funderburk, & Kowalski, 2004; Last, 1992; Roemer & Borkovec, 1993). Researchers have also been unable to consistently link individual differences in state and trait physiological arousal with subjective somatic symptoms. (Anderson & Hope, 2009; McLeod, Hoehn-Saric, & Stefan, 1986; F. H. Wilhelm & W. T. Roth, 2001). Recent evidence has suggested that the subjective experience of arousal-related bodily sensations may be more relevant to anxiety pathology than the accurate detection of physiological phenomena (Edelmann & Baker, 2002; Mauss, Wilhelm, & Gross, 2004; F. H. Wilhelm & W. T. Roth, 2001). In addition, previous studies of self-reported somatic anxiety have addressed constructs that are only partially related to the construct of trait somatic awareness. For example, *anxiety sensitivity*—defined as the tendency to catastrophize physical arousal symptoms, (Reiss & McNally, 1985)—is a trait that is characteristic of panic disorder. Some anxious youth with other anxiety disorders score more highly than healthy controls on self-report measures of this

construct (Rabian, Peterson, Richters, & Jensen, 1993; 1995). However, anxiety sensitivity is a construct that refers to a misappraisal bodily sensations rather than a general hyper-awareness of them. Perhaps most importantly, to our knowledge, no research on anxiety-related somatic symptoms in pediatric populations has drawn a distinction between more chronic anxiety-related somatic symptoms and somatic symptoms that occur in response to acute threat. This distinction is important because the relative salience of internal threat stimuli can be affected by one's concurrent engagement with external threat stimuli (Cioffi, 1991).

2.0 BACKGROUND

Both adult and pediatric anxiety disorders have been associated with alterations in the way threat-related information is processed. Much of the previous research on these biases has focused on selective attention to external threat cues (S. J. Bishop, 2008; Puliafico & Kendall, 2006; Roy, et al., 2008), although an excessive attention to somatic sensations has also been named as an anxiety-related attentional bias. Somatic sensations serve as the primary set of threat cues for individuals with panic disorder. However, there have been mixed results regarding the degree to which this is true in other anxiety disorders (e.g., F. Wilhelm & W. Roth, 2001).

The dilemma that served as a motivation for the current study arises from a discrepancy between two bodies of evidence in the pediatric anxiety literature. On one hand, many anxious children and adolescents report significant somatic symptomatology, suggesting that these youth are hyper-aware of bodily sensations. On the other hand, studies from the developmental psychopathology literature indicate that anxious youth have a poor awareness of their own emotional state, a deficit that should theoretically coincide with poor somatic awareness.

Although they are more emotionally reactive, anxious youth appear to be less emotionally self-aware than their non-anxious peers (Suveg & Zeman, 2004; Zeman, Cassano, Perry-Parrish, & Stegall, 2006). They exhibit broad deficits in emotional understanding, including difficulty labeling and differentiating their own emotional states (Southam-Gerow & Kendall, 2000, 2002). Because a precise awareness of one's current emotional state is considered

necessary for adaptive emotion regulation (Cioffi, 1991; Jellesma, Rieffe, Terwogt, & Kneepkens, 2006), it has been argued that anxious youth may benefit from treatments that attempt to increase their knowledge and awareness of their own emotions (Weems, Zakem, Costa, Cannon, & Watts, 2005). Most popular cognitive-behavioral therapy (CBT) protocols for treating pediatric anxiety include a component that teaches patients to attend to subjective somatic sensations during periods of high arousal (Kendall, et al., 2006). Early steps in these interventions aim to *increase* patients' subjective awareness of experiential somatic sensations in order to recognize that they are feeling anxious (Albano & Kendall, 2002; Kendall, Treadwell, Hibbs, & Jensen, 1996). After instruction in proper coping skills, an awareness of somatic anxiety symptomatology during high-arousal situations should cue the individual to engage in learned regulation strategies. The rationale for this aspect of treatment seems to be largely anecdotal, with little empirical evidence. Although low somatic awareness is not explicitly portrayed as an inherent deficit in pediatric anxiety, the use of this treatment component seems to conflict with research findings implying that some anxious youth already pay too much attention to somatic sensations (e.g., Ginsburg, et al., 2006).

2.1 NEURAL FEATURES OF THREAT PROCESSING AND SOMATIC AWARENESS: RELEVANT BRAIN-BASED THEORETICAL MODELS.

Although existing neuroimaging studies have explored anxiety-related individual differences in threat-processing and individual differences in bodily awareness, these two literatures have tended not to intersect. Findings from these two areas can be used to implicate a particular circuit of brain regions that should theoretically show an association with individual differences in

anxiety-related somatic awareness. Based on existing fMRI literature, several brain regions appear to play a role in both the generation of feeling states and the awareness of bodily sensations that co-occur with those feeling states. These regions include the amygdala, the anterior cingulate cortex (ACC), and the anterior insula. While there are several existing theoretical accounts of how this system of brain regions operates, a few particular models are relevant to the current study.

2.1.1 Information-processing models and vigilance-avoidance

Information-processing models of anxiety have emphasized the role of attentional biases in the development and maintenance of anxiety disorders. Individual theoretical models have varied in the extent to which they describe anxiety-related biases as a tendency to preferentially shift attention toward threat-related information (i.e., showing a "hypervigilance" for threat), or away from it (i.e., showing an "avoidance" of threat), and there is some evidence that both kinds of attentional bias may occur at different temporal stages of threat processing. A "vigilance-avoidance" model of anxiety has been proposed (Amir, Foa, & Coles, 1998; Mogg & Bradley, 1998, 1999), in which the time-course of attention allocation is taken into account. The model describes a two-step process in the allocation of attention, in which early attentional vigilance is demonstrated by rapid automatic responses to perceived threat, with a strong orienting response towards novel and threatening stimuli. Avoidance involves the subsequent averting of attention from threat as an attempt to regulate anxious mood state. This sustained cognitive avoidance pattern could maintain anxious responses by preventing individuals from habituating to anxiety-producing stimuli (Mogg & Bradley, 1998). While this model has found some support in studies comparing adult anxiety patients with healthy controls, studies of attentional biases in anxious

children has tended to find either vigilance or avoidance, but not both (McClure, et al., 2007; Daniel S. Pine, et al., 2005; Roy, et al., 2008). To our knowledge, however, no fMRI studies have conceptualized of these attentional biases as individual differences that may perpetuate somatic anxiety symptoms for some patients but not others.

The primary brain mechanisms thought to subserve vigilance and avoidance are the amygdala and the caudal ACC. In the presence of external threat cues, the amygdala signals the presence of affectively salient stimulus features. Amygdala hyper-reactivity is considered a hallmark of selective attention for threat, and anxious youth tend to show greater amygdala activation than controls in response to negative emotional stimuli (Guyer, et al., 2008; McClure, et al., 2007; Monk, et al., 2008; Thomas, et al., 2001). Increased amygdala activity is also thought to give rise to increased activity the caudal ACC, a region implicated in monitoring emotionally relevant behavioral responses and recruiting prefrontal top-down control regions. Hyper-reactivity in the caudal ACC is hypothesized to lead to the overuse of cognitive avoidance as an anxiety-related coping response (S. Bishop, Duncan, Brett, & Lawrence, 2004; Killgore & Yurgelun-Todd, 2005; Thomas, et al., 2001). In imaging studies using supraliminal (i.e. consciously perceptible) stimulus presentation times, anxious subjects who displayed an initially vigilant orienting response for threat subsequently engaged in emotional avoidance, as indicated by blunted late amygdala responses (Derryberry & Rothbart, 1988; Etkin, et al., 2004). Thus, in response to threatening stimuli, increased early but decreased sustained amygdala activity along with increased caudal ACC activity are purported neural features of vigilance-avoidance.

2.1.2 Interoceptive processing and conscious somatic and emotional awareness

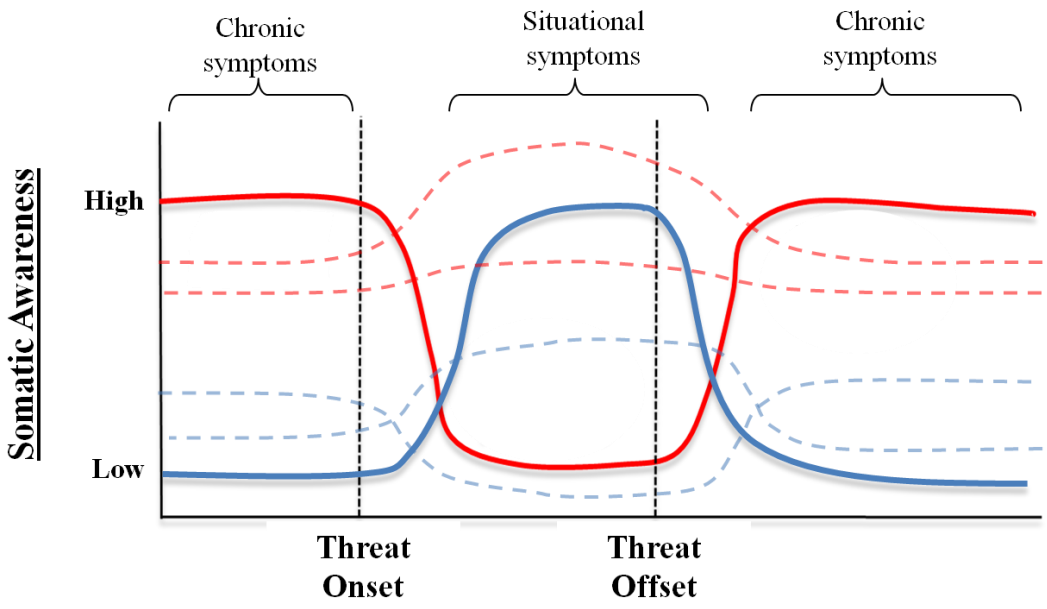
Brain-based models of interoceptive processing have identified neural substrates of the awareness of internal threat-cues. These models emphasize the role of the amygdala in coordinating a synchronized physical arousal response to threat (i.e., S. Bishop, et al., 2004). Internal cues of arousal are picked up by the anterior insula, a region implicated in the perception of somatic sensations and the integration of these sensations into consciously accessible emotional feelings (Craig, 2004; Critchley, Wiens, Rotshtein, Ohman, & Dolan, 2004). Critchley and colleagues have highlighted the anterior insula's role in integrating internal arousal cues with appraisals of external emotional stimuli (Critchley, et al., 2004). Contextualized somatic information is passed on to the rostral ACC, which is involved in assessing the salience of emotional. This portion of the ACC has strong reciprocal connections with the anterior insula, along with a number of brain regions involved in affective and autonomic processing, including the amygdala. According to fMRI research in healthy adults, both the anterior insula and the rostral ACC are active when research subjects pay attention to subjective emotional states and unpleasant visceral sensations (Gregory, et al., 2003; Herwig, Kaffenberger, Jäncke, & Brühl; Pollatos, Kirsch, & Schandry, 2005). Thus, in response to threat-related bodily arousal initiated by the amygdala, anterior insula and rostral ACC activation are considered to be hallmarks of conscious somatic and emotional awareness.

2.2 A MODEL FOR RESOLVING THE DILEMMA: INDIVIDUAL DIFFERENCES IN THE TIME-COURSE OF THREAT-PROCESSING

The brain-based models of threat-processing and interoceptive awareness discussed in the previous section have mainly been used to explain or test for group differences between anxiety-disordered patients and healthy controls. The current study adopts an individual-differences approach in relating brain mechanisms of threat processing and interoceptive awareness to patients' somatic anxiety symptoms. The model put forth in the current study is based on the premise that, within the population of anxious youth, patients who engage in vigilance for or avoidance of external threat cues may have a similar pattern of attending to somatic cues. As such, threat-related brain reactivity patterns associated with a greater processing of external emotional stimuli (i.e., more amygdala activity) and internal bodily cues (i.e., more insula and rostral ACC activity) should be more common in patients who experience more somatic anxiety symptoms. However, some patients may only be aware of anxiety-related somatic cues at specific times, such as during exposure to acute stressors, when arousal is likely to be high. Those patients who are less aware of their own acute stress-related somatic sensations may also be less emotionally self-aware, and may therefore be more likely to engage in maladaptive emotion regulation strategies in response to negatively arousing situations (Suveg & Zeman, 2004).

In addition to accounting for individual differences in somatic awareness, we also sought to combine a time-course model of threat-processing (such as the vigilance-avoidance model described above) with accounts of interoceptive awareness in the brain. And individual patient's level of somatic awareness can therefore be considered a dynamic characteristic varies depending on the context it is measured in. This way, the tendency to experience chronic somatic

anxiety symptoms and the tendency to experience stressor-induced "situational" somatic symptoms can be conceptualized as separate individual difference characteristics that relate independently to threat-related brain functioning. Applying a construct such as vigilance-avoidance could even produce a hypothetical situation in which some anxious youth display both vigilance for chronic somatic symptoms of anxiety and attentional avoidance of uncomfortable bodily sensations during acutely stressful situations. For these individuals, the use of this and other avoidant emotion regulation methods could lead to longer bouts of emotional distress and low-level physiological activation, which in turn could give rise to more chronic somatic anxiety symptoms (Brosschot, Gerin, & Thayer, 2006; Hoehn-Saric, et al., 2004). A representative schematic of this hypothetical process is shown in Figure 1.



This figure is intended to illustrate possible individual differences in the way somatic symptom information is consciously processed by pediatric anxiety patients. For example, the red line depicts a patient who is generally hyper-vigilant for anxiety-related bodily cues and therefore scores high on self-report measures of chronic somatic anxiety symptoms. In the context of external threat, this same patient avoids attending to acute somatic symptoms and reports low levels of situational somatic symptoms. The solid red and blue lines represent two cases in a dataset in which chronic and situational symptoms are inversely correlated, although it is also possible that they are positively correlated (as shown by the sample of dashed lines) or unrelated to one another.

Figure 1. Hypothetical trajectories of somatic awareness.

3.0 THE CURRENT STUDY

In the current study, the tendency to notice and report anxiety-related somatic symptoms was conceptualized as trait that varies between patients, and that also varies within individuals depending on the context in which symptoms are measured. Chronic somatic anxiety symptoms were assessed using the panic/somatic subscale of a well-known anxiety symptom inventory for children. It was assumed that anxious youth who were more chronically aware of or hypervigilant for somatic arousal cues would report more of these kinds of symptoms. As a measure of "situational" somatic awareness, we collected symptom reports from patients just prior to the performance of a social evaluation speech task, when patients were likely to be experiencing high emotional arousal and/or distress. Laboratory tasks that include a social-evaluative component have been shown to lead to increases in cortisol, pro-inflammatory responses, and autonomic arousal (Dickerson, Mycek, & Zaldivar, 2008), and the preparation and performance of a similar speech task has been shown to induce both physiological arousal and subjective anxiety in anxious youth (Gunnar, Talge, & Herrera, 2009; Gunnar, Wewerka, Frenn, Long, & Griggs, 2009).

In order to elicit potentially biased brain activation patterns during threat-processing, we utilized a standard probe-detection task that required participants to respond to simple probes that replace neutral and fearful faces or plain shapes. The Dot Probe paradigm has been used in multiple behavioral and neuroimaging studies to assess attentional biases in pediatric anxiety (Taghavi, Neshat-Doost, Moradi, Yule, & Dalgleish, 1999; M. W. Vasey, El Hag, & Daleiden,

1996). Because of the requirements for attentional control in the presence of distracting emotional stimuli, this task typically engages the amygdala and ACC. We therefore expected task-related activations to reveal individual differences in neural patterns of vigilant and/or avoidant attention allocation.

Based on previous research that chronic somatic symptoms rates increase with overall anxiety severity, we predicted that chronic somatic symptoms of anxiety would be positively correlated with all other (i.e., non-somatic) anxiety symptoms. In accordance with our conceptualization of chronic and situational somatic symptom awareness as distinctive patient characteristics, we also predicted that self-reported chronic and situational symptom rates would be unrelated or inversely correlated.

We further hypothesized that chronic somatic symptom scores would be positively correlated with brain activity patterns implicated in attentional vigilance and avoidance. In other words, we predicted that greater chronic somatic anxiety symptomatology would be associated with: 1) increased initial activation but decreased sustained activation of the bilateral amygdala, and 2) increased activation of the caudal ACC. We also predicted that chronic somatic symptoms would be negatively correlated with patterns implicated in somatic and emotional self-awareness, such that greater symptomatology would be associated with: 3) decreased activation in the bilateral anterior insula, and 4) decreased activation in the rostral ACC.

In devising hypotheses about brain activity and situational somatic symptomatology, we reasoned that patients who showed more reactivity to (i.e., less experiential avoidance of) external and internal stimuli during the presentation of mildly threatening pictures would also notice and report the most intense situational somatic symptoms. We therefore hypothesized that situational somatic symptom scores would be associated with a) greater late amygdala activity,

b) less caudal ACC activity, c) greater anterior insula activity, and d) greater rostral ACC activity.

3.1 METHODS

3.1.1 Participants

Participants included 42 clinically anxious youth (20 male, 22 female), ages 9-13 (*M* = 10.4, *SD* = 1.2). The sample was largely Caucasian, containing only two African American children, and one child of mixed race. Recruitment was conducted as part of a larger study investigating psychological and biological mechanisms of clinical pediatric anxiety at baseline and following CBT. Recruitment methods included advertising, school counselor or teacher referral, and pediatrician referral. All participants met DSM-IV criteria for one or more of the following diagnoses: Generalized Anxiety Disorder (GAD), Social Phobia (SoPH), and/or Separation Anxiety Disorder (SAD).

Exclusion criteria included: the presence of a comorbid primary major depressive disorder (MDD) (subjects with primary GAD and co-morbid MDD that was deemed secondary in terms of course and functional impact were not excluded); current Axis I diagnosis of obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), panic disorder, conduct disorder, substance abuse or dependence, and ADHD combined type or hyperactive-impulsive type; lifetime diagnosis of autism or Asperger's syndrome, bipolar disorder, psychotic depression, schizophrenia, or schizoaffective disorder; IQ < 70; current psychoactive medication use (included anxiolytics and antidepressants); imminent risk of suicide or harm to self or others;

inability to complete questionnaires written in English; and any condition that might prevent participation in fMRI procedures (because of the presence of pacemakers, surgically implanted metal plates, screws or pins, metal braces, or other metal objects in the body). Of the participants used in the current study, 24 (57.1%) presented with a single anxiety diagnosis only (GAD *n* = 15, SAD *n* = 6, SoPH *n* = 3) and 18 (42.9%) had two or more concurrent psychiatric disorders. The frequencies of specific anxiety disorders were as follows: GAD = 31, SAD = 10, SoPH = 9, specific phobia = 6. Additional concurrent psychiatric disorders included ADHD (inattentive subtype, *n* = 2; NOS, *n* = 1), and enuresis (*n* = 3). At the time of the intake, one child reported a history of MDD, and another qualified for a diagnosis of MDD in partial remission.

3.1.2 Self-report measures

3.1.2.1 Chronic somatic anxiety symptoms

The *Screen for Child Anxiety Related Emotional Disorders – Child Version* (SCARED-C; Birmaher, Khetarpal, Cully, Brent, & McKenzie, 2003) is a 41-item self-report questionnaire that asks children to report the frequency of individual anxiety symptoms over the past three months, using a three-point Likert scale. It was designed with five symptom subscales based on individual DSM-IV diagnostic criteria for panic/somatic symptoms, general anxiety, separation anxiety, social anxiety, and significant school avoidance. These subscales have been confirmed by factor analysis and they demonstrate good internal consistency, with coefficient α values ranging between .78 and .87 (B Birmaher, et al., 1999). The *somatic/panic subscale* has a total possible score of 26, and a score above 7 is used as a cutoff for a classification of significant somatic anxiety symptomatology. This subscale has been used to detect somatic symptomatology in diverse non-panic anxious samples (Eley, Stirling, Ehlers, Gregory, & Clark, 2004; Peter

Muris, et al., 1998) and has been found to differentiate anxiety-disordered youth from youth with other forms of internalizing and externalizing psychopathology (B. Birmaher, et al., 1999).

3.1.2.2 Situational somatic anxiety symptoms

After preparing for the speech task (described below), each participant completed the *Child Somatization Inventory (CSI)* (Revised 24-item version; Walker, Beck, Garber, & Lambert, 2008). This instrument is a self-report questionnaire that assesses the perceived severity of 24 nonspecific somatic symptoms including headaches, nausea, dizziness, and chest pain. The revised 24-item scale is a shortened version of the original CSI (Garber, Walker, & Zeman, 1991), which contained 31 items and was constructed to include symptoms from the DSM-III criteria for somatization disorder (Association., 1987). Typically, the child is asked to report the extent to which he or she has been experiencing each of the symptoms on 4-point scale (ranging from *not at all* to *a whole lot*) in the previous 2 weeks. A total score is obtained by summing the ratings, with a highest possible score of 140.

For the purpose of the current study, the CSI was administered as a measure of situational somatic symptoms, with the child being asked to report how much he or she is experiencing each individual symptom "right now", versus in the past two weeks. Because the CSI has not been previously administered in this manner, no relevant statistics on the measure's use are available to report. In the current sample of 42 anxious youth, the measure demonstrated good internal consistency, with a coefficient α of .89.

3.2 PROCEDURE

Following the confirmation of their inclusion in the study, children and their parents provided written informed consent for the child's participation. Participants' diagnoses were assessed using the Schedule for Affective Disorders and Schizophrenia for School-Age Children – Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997). Parent and child interviews were conducted separately, with independent evaluators integrating data from both sources to arrive at a consensual diagnosis. Anxious participants also filled out baseline self-report measures. On their second visit, participants completed the fMRI scan (see below for specific fMRI procedure). On their third visit, participants completed the behavioral speech task described below.

3.2.1 Social-threat speech task

On their third visit to the lab, mother-child dyads were asked to complete a series of structured parent-child interaction tasks designed to elicit affective responses among the children. In the context of the greater study protocol, the speech task was designed to assess the mother's behavior in helping the child plan for and cope with this anxiety-provoking task. For the purpose of the current study, the speech task served as social-evaluative stress induction during which we assessed participants' self-reported situational somatic symptoms. Following the completion of the other parent-child interaction tasks, children were told they would be giving a speech in front of a video camera, and that their performance skills would be assessed and compared to other children's skills. They were not told how long the speech needed to be. Children were asked to rank three potential speech topics in order of how much they would want to speak on that topic.

The topics included “something you have learned from reading a book”, “something you learned recently in science”, and “something that you think is wrong with our government and how you would fix it”. Children were always assigned the topic they ranked as #2. After the 5 minutes of collaborative preparation and discussion about their child’s feelings about the speech, parents were shown back to the waiting room. At this point, just prior to giving the speech, children were handed a copy of the CSI and fill it out with respect to how they were currently feeling. Items were read aloud to children who had difficulty reading the questions.

3.2.2 fMRI Assessment Procedure

After completing training for fMRI tasks and a pre-scan exposure in a mock scanner, participants underwent 10 minutes of structural scanning. They then completed a battery of computerized behavioral tasks during concurrent fMRI assessment, which lasted approximately 40 minutes. Because task order was randomized, the task being analyzed for the current study was completed at different times in the assessment sequence for each participant.

3.2.3 fMRI Dot-Probe Task

In the dot-probe task being used in current study, the task alternated between two trial types: one in which a fearful face was presented on one side of a screen and a neutral face was presented on the other, and one in which 2 circles were presented. “Circle” trials were used as a baseline comparison condition. For both trial types, the face or circle stimuli were followed by a probe. Subjects responded with a button press to identify the location of a probe that replaced either the fearful face (congruent) or the neutral face (incongruent). Face or circle stimuli appeared on

screen for either 200ms or 2000ms before being replaced by the dot-probe screen, which remained on screen for 7-9 seconds, depending on the length of stimulus presentations. The probe following each stimulus trial remained on the screen for 2s. In the current study, stimuli were placed vertically from each other, rather than horizontally, as has been used in previous studies. Participants completed total of 80 trials (20 faces trials and 20 circles trials in each of the long and short conditions), split into two eight-minute blocks. All trials lasted a total of 11.7 seconds, leaving room for the occurrence of potential differences in "early" and "late" brain activity.

3.2.4 Apparatus

fMRI data were collected on the Pittsburgh's Brain Imaging Research Center's 3T Siemens Allegra scanner (as in Project 1 Preliminary data). Visual stimuli were presented on a rear projection screen and viewed through a mirror attached to the head coil. Stimulus presentation and behavioral response/reaction-time collection were conducted via a Windows computer running E-prime (Psychology Software Tools) connected to an RF shielded response box connected to a 5-button glove. Twenty-nine axial slices (3.2mm isotropic voxels) were acquired every 1.67 seconds parallel to the AC-PC line using a T2* weighted reverse EPI pulse sequence (TR=1670ms, TE=25ms, FOV=24cm, flip=72). Scanning began with stimulus onset. Anatomical scans were acquired at the same locations as the functional imaging scans, using a reconstructed MPRAGE pulse sequence.

3.2.5 fMRI Data Preparation

Reconstructed fMRI images were time slice corrected using AFNI's (Cox, 1996) 3dTshift, and resliced using 3dVolReg movement correction algorithm. Images were registered to the first image in the series to correct for head movements. Linear detrending and outlier rescaling were performed using NIScorrect (Jonathan Cohen, Princeton University, and Cameron Carter, University of California, Davis). Outliers over two inter-quartile ranges from the median were rescaled, and all functional data were converted to %-change. Data were temporally smoothed using a four point Gaussian filter to identify robust sustained event-related changes in MR signal. Images for all subjects were co-registered to the MNI reference brain using AIR's alignwarp procedure to compute a 32 parameter non-linear warping algorithm (Woods & Mazziotta, 1993) and spatially smoothed using a 6mm FWHM three dimensional Gaussian filter to accommodate individual differences in anatomy. While data generally suggest that warping to the MNI brain yields adequate registrations of gray matter in children (Hoeksma, Kenemans, Kemner, & van Engeland, 2005), registrations were checked by hand and with the lab's automated diagnostic procedures, including examination of variance maps across images.

3.2.6 Definition of anatomically defined regions

Anatomically defined amygdalae were traced on high resolution structural scans. Anatomically defined rostral and caudal ACC subregions (BA24, and 32 respectively), were defined using the AAL atlas (as in Forbes, et al., 2006). Volumes were cross-rendered to each participant's anatomical data using a 32-parameter non-linear warping algorithm (Woods & Mazziotta, 1993) and rendered in the space of the functional data.

3.2.7 Generation of brain activation scores

In order to generate activity scores for each individual on the dot-probe task, the following steps were taken: At the individual subject level, BOLD percent (%) signal change was calculated for each scan of a trial, using the first scan as a baseline scan. Mean activity from "circle" trials was subtracted from "face" trials data, in order to control for effects of probe location and subjects' general brain reactivity to a suddenly appearing stimulus. This was done for all regions of interest, including the left and right amygdala, left and right anterior insula, and the rostral and caudal cingulate (the last two of which are both midline structures and were not divided into lateral subregions).

4.0 DATA ANALYSES

All group-level statistical analyses were performed in MATLAB and SPSS. Before correlating brain activity with somatic symptom scores, descriptives were run on CSI and SCARED scores to detect outliers. For CSI scores, outliers differing from the median by a an absolute value that exceeded 1.5 times the interquartile range were replaced with Md+/-1.5*IQR. No outliers meeting this criteria were found in the SCARED somatic score distribution. We used Pearson product-moment correlations (*r*) to test *a priori* hypotheses about associations between self-report symptom measures. Correlation statistics were calculated for the association of chronic somatic anxiety symptoms with other chronic anxiety symptoms, and for the association between "chronic" and "situational" somatic symptoms.

Pearson product-moment correlations were also used to test *a priori* hypotheses about associations between threat-related brain activity and somatic symptom reports. For each region of interest, mean BOLD % signal change values were correlated with symptom for each of 6 scans per trial (i.e., from scans 2-7). To control for Type I error, two consecutive scans with a significant correlation at $p<.05$ were required for correlations to be considered significant. This temporal length threshold was derived via randomization tests (1000 simulations in which subjects' observed waveforms were randomly assigned to rumination observed factor scores). These tests were used to determine the number of consecutive scans that would occur by chance at the given significance level less than five percent of the time (i.e., at a frequency of $p<.05$).

In addition, existing research has shown effects of age and gender on somatic anxiety symptomatology. In non-anxious populations, rates of self-reported somatic symptomatology (including both anxiety-specific symptoms and general physical symptoms) appear to increase as children get older and peak during adolescence (P. Muris, Hoeve, Meesters, & Mayer, 2004; Offord, et al., 1987). In addition, females appear to be more likely than males to experience somatic symptoms, and they show a greater age-related increase in the frequency of reported symptoms (Eminson, Benjamin, Shortall, Woods, & Faragher, 2006; Taylor, Szatmari, Boyle, & Offord, 1996). Thus, preliminary correlation analyses were conducted to determine whether participants' age and gender variables were significant predictors of anxiety-related somatic symptoms in a sample of clinically anxious youth.

In order to further validate and explore any significant associations found between brain activity and somatic symptoms, we conducted a series of sensitivity analyses. To confirm that the temporal windows of BOLD activation identified in zero-order correlation analyses were independent predictors of somatic symptoms above and beyond age, gender, and non-somatic anxiety symptoms, we ran subsequent hierarchical regression analyses that accounted for these variables following the correlation analyses. Mean activation values for each temporal window were calculated by summing activation at each scan for all significant scans, and dividing by the number of scans in the window. Hierarchical multiple regression analysis were then run, entering selected preliminary variables (i.e., gender, age, or non-cognitive anxiety when appropriate) as predictors at step one, and the mean activation value for the region of interest at step two.

Lastly, in order to further explore the potential role of patients' attentional biases in observed associations between BOLD activation and somatic symptoms, we used reaction time data from the dot-probe task to calculate behavioral indices of biased attention. As described in

(D.S. Pine, et al., 2005), within-subject bias scores were calculated by subtracting each participant's mean response latency on congruent trials from their mean response latency on incongruent trials. Positive bias scores are thought to indicate an attentional bias toward the fearful face (vigilance), while negative scores indicate attentional bias away from the emotional face (avoidance). We ran Pearson product-moment correlations between these bias scores and somatic symptom scores. For somatic symptom measures that were significantly correlated with attentional bias scores, we entered bias scores into a hierarchical regression as described above.

5.0 RESULTS

5.1 PRELIMINARY ANALYSES

Results testing for a significant effect of gender and age on somatic symptoms indicated a significant relationship between gender and chronic somatic anxiety symptoms, $t(38.8) = -2.69$, $p = .01$, with females reporting more severe symptoms than males, $M_{female}(SD) = 11.3(6.0)$ $M_{male}(SD) = 6.9(4.5)$. There was no effect of gender on situational somatic symptom scores, $t(38.8) = -.798$, $p = .43$. Age was not significantly associated with chronic, $r = .14$, $p = .39$, or situational somatic symptom reports, $r = .05$, $p = .74$. Because gender was a significant predictor of chronic symptoms, we ran sensitivity analyses following the correlation of brain activity with chronic somatic symptoms.

Table 1. Self-report measure descriptives

Measure/subscale	*M*	(*SD*)	Range
Trait symptoms (SCARED-C)	39.4	12.5	19-67
Panic/somatic symptoms	9.2	5.7	1-22
Generalized anxiety symptoms	10.9	3.7	3-16
Separation anxiety symptoms	8.5	3.5	3-16
Social anxiety symptoms	7.6	3.4	0-14
Significant school avoidance	3.2	1.9	0-7
Total non-somatic	30.2	8.4	12-46
CSI (with outliers rescaled)	8.3	9.6	0-31.1

5.1.1 Association between chronic somatic and other chronic anxiety symptoms

Characteristics of the sample's self-report data can be found in Table 1, including patients' scores on all of the SCARED symptom subscales. SCARED total and subscale mean scores are consistent with scores previously reported in clinically anxious youth (B. Birmaher, et al., 1999). In agreement with our hypothesis, rates of chronic somatic anxiety symptoms were positively correlated with other types of anxiety symptoms, $r(42) = .57$, $p < .001$. Thus, participants reporting high levels of somatic symptoms were also more likely to report high levels of non-somatic anxiety symptoms. Because subsequent correlations between brain activity and SCARED somatic scores could be accounted for by a shared association with overall anxiety severity.

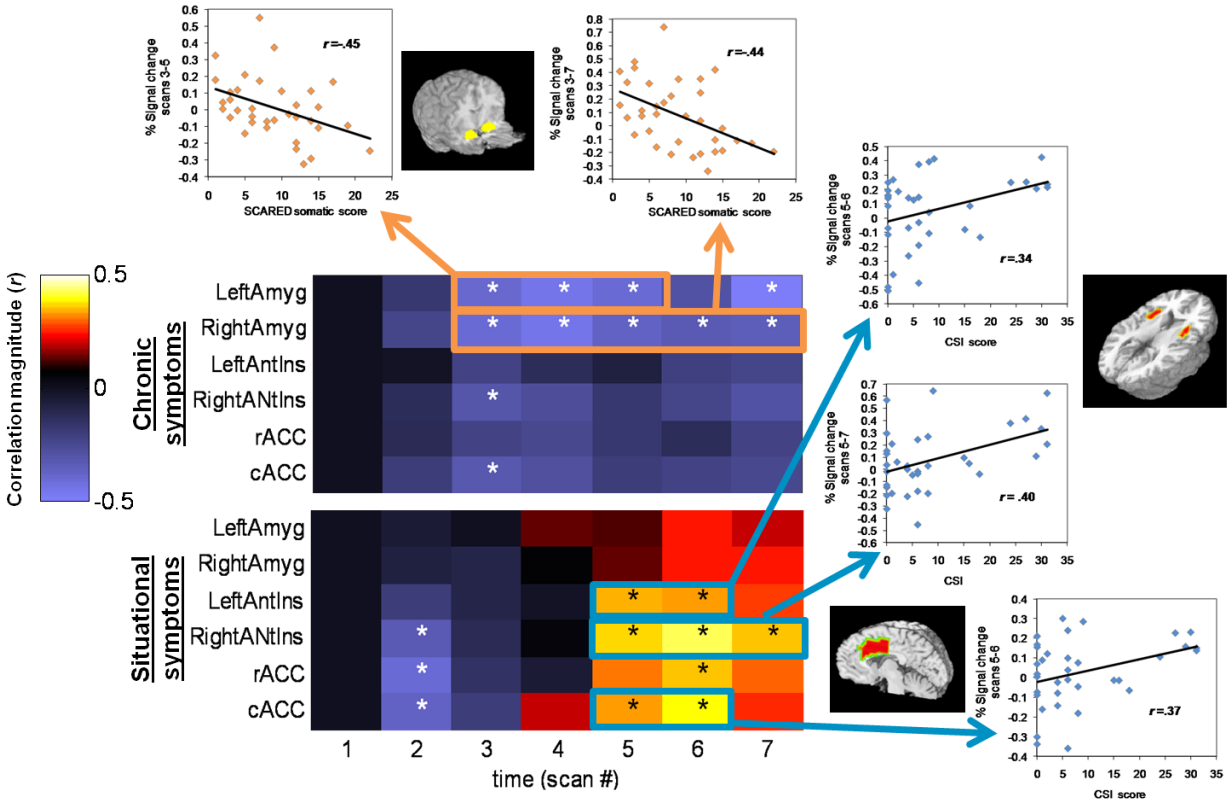
5.1.2 Association between chronic and situational somatic symptoms

In accordance with our hypothesis, situational somatic symptom reports given during acute threat were not significantly associated with rates of chronic somatic anxiety symptomatology, $r = .19$, $p = .22$.

5.1.3 fMRI Results

Figure 2 shows correlation matrices of participants' self-reported somatic symptom levels with mean BOLD activation in each ROI at each scan. Correlation values exceeding a significance threshold of $p < .05$ are marked with an asterisk (*). In order to control for Type I error, only regions in which two or more consecutive scans met this threshold are discussed as significant in

the following results. For descriptive purposes, mean activation values were calculated for the periods of significant correlation, and individuals' mean activation values were correlated with somatic symptom scores. These correlations are the values given in the text below.



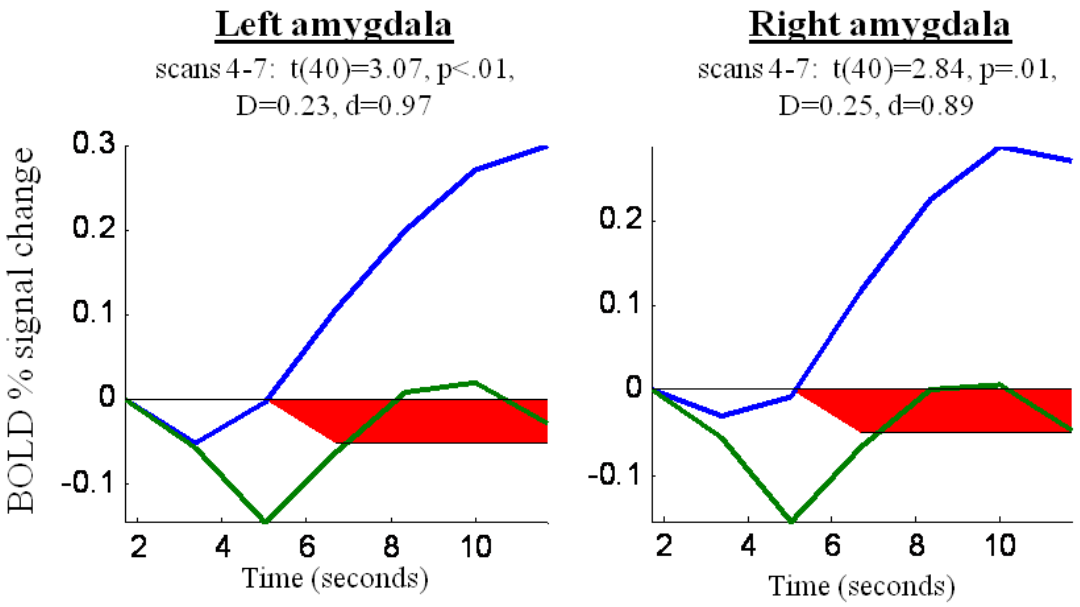
In this figure, color maps represent correlation matrices of each somatic symptoms measure (chronic and situational) with BOLD % signal change across 7 scans (11.7 seconds). Asterisks denote scans at which correlation values were significant at $p<.05$. Only regions whose activity correlated with somatic symptom scores at three or more scans (the temporal threshold determined by randomization tests) were interpreted as significant. Scatterplots show the relationship between patients' symptom scores and mean activation at the significant temporal windows indicted in the corresponding correlation matrix.

Figure 2. Correlations between brain activity in a priori regions of interest and somatic symptom scores.

5.1.4 Association between chronic somatic symptoms and brain activity

In order to test the hypothesis that higher situational somatic anxiety symptom awareness would be associated with lower indices of attentional avoidance, individuals' SCARED-somatic scores were correlated with their brain activity during the dot probe task. (For a table containing correlation and significance values for each scan, please refer to the supplementary data section.) As shown in Figure 2, chronic somatic symptom rates were negatively correlated with bilateral amygdala activity (left: scans 3-5, r = -.45, p = .003; right: scans 3-7, r = -.44, p = .004). No other regions were significantly associated with chronic somatic symptomatology after controlling for Type I error. In the right anterior insula and the caudal ACC, isolated early scans demonstrated negative correlations that did not persist after Type I error correction.

Because correlations do not convey the direction of BOLD % signal change patterns (i.e. whether low chronic somatic patients had greater BOLD activation in the bilateral amygdala or high chronic somatic patients had larger BOLD deactivations), Figure 3a contains graphs illustrating qualitative differences in amygdala activity that characterized high and low chronic somatic symptom reporters (high = green, low = blue). Patients were divided into these groups based on whether their SCARED panic/somatic score fell above or below the cutoff for a designation of "clinically significant" somatic symptoms. Based on these illustrative graphs, negative correlational findings appear to be a result of low chronic somatic patients showing sustained increases in bilateral amygdala activity, while high chronic somatic patients showed a small initial deactivation, followed by a smaller increase in activation.



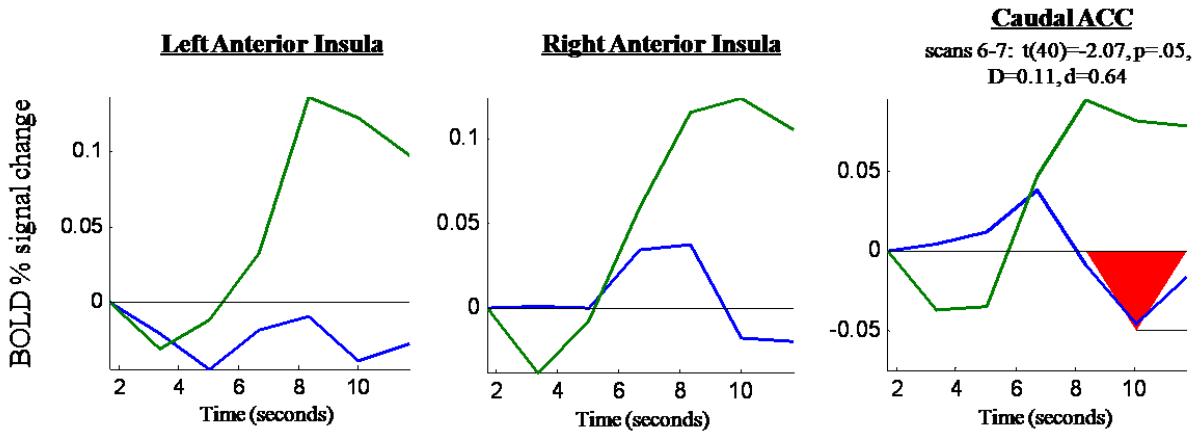
In this figure, the graphs show mean BOLD % signal change across 7 scans (11.7 seconds) for the low chronic somatic group (n = 17) in blue, and the high chronic somatic group (n = 25), in green. Red significance bars denote periods for which the two groups showed significant differences in activation at p<.05. Statistics from independent samples t-tests are shown for comparisons that revealed significant group differences.

Figure 3a. Illustrative group comparison of amygdala activation for patients with high and low chronic somatic symptoms of anxiety

5.1.5 Association between situational somatic symptoms and brain activity

As shown in Figure 2, situational somatic symptom rates were positively correlated with sustained bilateral anterior insula activity, left insula: scans 5-6, r = .34, p = .03; right insula: scans 5-7, r = .40, p = .008. Situational symptoms were also correlated with sustained caudal ACC activity, 5-6, r = .37, p = .02. No other regions were significantly associated with situational somatic symptoms after controlling for Type I error. Isolated early scans in the right anterior insula, rostral ACC, and caudal ACC showed significant negative correlations, and a late scan in the rostral ACC showed a significant positive correlation, but associations did not persist after Type I error correction.

Figure 3b contains graphs illustrating qualitative differences in left and right anterior insula and caudal ACC activity for high and low situational somatic symptom groups (high = green, low = blue). Because no cutoff score has ever been defined for CSI scores collected in the manner we collected them, patients were divided into high and low groups based on a median split (n = 21 for each group). The positive correlation between situational somatic symptoms and right anterior insula activity appears to be a result of high situational somatic patients showing sustained activations in that region, while low situational somatic patients showed little change from baseline. In the caudal ACC, the positive correlation appears to be driven by the high somatic group's sustained activation when low somatic patients showed a small deactivation.



In this figure, the graphs show mean BOLD % signal change across 7 scans (11.7 seconds) for the low situational somatic symptoms group (n = 21) in blue, and the high situational somatic symptoms group (n = 21), in green. Red significance bars denote periods for which the two groups showed significant differences in activation at p<.05. Statistics from independent samples t-tests are shown for comparisons that revealed significant group differences.

Figure 3b. Illustrative group comparison of anterior insula and caudal ACC activation for patients with high and low situational somatic symptoms

5.2 SENSITIVITY ANALYSES

In order to ensure that the brain-somatic symptom association was not attenuated by gender, we ran a hierarchical multiple regression analysis for each ROI in which activity was predictive of chronic symptoms (i.e., the left and right amygdala). Following a stepwise approach, gender was entered at step 1 and the mean activation value for the correlated temporal window was entered at step 2. When gender was used as the sole predictor, it accounted for 15% of the variance in SCARED-somatic scores. Adding left amygdala activity to the model resulted in a significant increase in variance explained, $R^2 = .31$, $\Delta R^2 = .16$, $F(1,39) = 9.16$, $p = .004$, with left amygdala activity serving as a significant independent predictor of chronic symptom scores, $sr^2 = .16$, $p = .004$. The gender variable continued to explain significant independent variance in this second model, $sr^2 = .11$, $p = .02$. When the same analysis was run using right amygdala activity as an additional predictor at step two, amygdala activity again resulted in a significant increase in variance explained, $R^2 = .29$, $\Delta R^2 = .14$, $F(1,39) = 7.4$, $p = .01$. Like the left amygdala, right amygdala activity accounted for significant independent variance in the model, $sr^2 = .14$, $p = .01$, as did the gender variable, $sr^2 = .10$, $p = .03$.

In addition, because non-somatic SCARED scores were significantly correlated with somatic SCARED scores, an additional sensitivity analysis was run to see if the associations between amygdala activity and chronic somatic symptoms were better explained by non-somatic anxiety severity. When entered at step one, non-somatic SCARED scored accounted for 32% of the variance in patients' SCARED-panic/somatic scores. Adding left amygdala activity to the model resulted in a significant increase in variance explained, $R^2 = .43$, $\Delta R^2 = .10$, $F(1,39) = 7.1$, $p = .01$, with left amygdala activity serving as a significant independent predictor of chronic symptom scores, $sr^2 = .10$, $p = .01$. The gender variable continued to explain significant

independent variance in this second model, sr^2 = .22, p = <.001. Statistical results were only slightly weaker, but still significant, when right rather than left amygdala activity was entered at step two, R^2 = .41, ΔR^2 = .09, $F(1,39)$ = 6.1, p = .02. Both right amygdala activity and non-somatic SCARED scores served as significant independent predictors of SCARED somatic scores, sr^2 = .09, p = .01and sr^2 = .22, p <.001, respectively.

5.3 BEHAVIORAL RESULTS AND SENSITIVITY ANALYSES

Participants' attentional bias scores (in milliseconds) ranged from -514 to 674 (average = -20, *SD* = 231). Bias scores were significantly negatively correlated with chronic somatic symptom scores (r = -.31, p = .04), indicating that patients who reported more chronic somatic anxiety symptoms were more likely to show an attentional avoidance of threat, while than patients with fewer chronic symptoms were more likely to show an attentional vigilance for threat. No significant association was found between bias scores and situational somatic symptoms.

In order to test whether correlations between amygdala activity and chronic symptoms could be explained as attentional biases to external threat observed during the dot-probe task, hierarchical regression analyses were run with bias scores entered at step 1 and amygdala activity at step two. When entered at step one, attentional bias scores accounted for 10% of the variance in patients' chronic somatic symptom scores. Adding left amygdala activity to the model resulted in a significant increase in variance explained, R^2 = .26, ΔR^2 = .16, $F(1,39)$ = 8.3, p = .006, with left amygdala activity serving as a significant independent predictor of chronic symptom scores, sr^2 = .16, p = .006. The attentional bias variable no longer explained significant independent variance in this second model, sr^2 = .05, p = .11, although no significant correlation was found

between attentional bias scores and left amygdala activity (r = .20, p = .21). Results were similar when right amygdala activity was entered at step two, R^2 = .27, ΔR^2 = .10, $F(1,39)$ = 9.2, p = .004, although both attentional bias scores and right amygdala activity remained significant independent predictors of somatic chronic anxiety scores, sr^2 = .08, p = .04 and sr^2 = .17, p = .004, respectively. No correlation was found between attentional bias scores and right amygdala activity (r = .07, p = .65). Thus, attentional bias moderated the association between left amygdala activity chronic somatic anxiety symptomatology.

6.0 DISCUSSION

The primary purpose of the current study was to examine the relationship between individual differences in neural patterns of threat-processing and self-reported somatic symptomatology and using fMRI and self-report data from a sample of clinically anxious youth. Taking into consideration discrepant previous findings regarding the degree of somatic awareness possessed by anxious youth, we hoped that differentiating between more chronic somatic anxiety-related symptoms and situational bodily symptoms perceived during an acute stressor.

As expected, participants who reported high levels of chronic anxiety-related somatic symptoms were more likely to report high levels of other chronic anxiety symptoms. This finding is consistent with previously reported associations between somatic symptomatology and overall severity of anxiety symptoms (Beidel, Christ, & Long, 1991). Also in accordance with our hypotheses, our measures of chronic and situational somatic anxiety symptoms were not significantly related to one another. Hence, clinically anxious youth who experience more prominent somatic symptoms of anxiety are not necessarily more aware of bodily symptoms that arise in response to acute stress.

Our hypothesis that individual differences in chronic somatic anxiety symptomatology would be associated with neural indices of early hypervigilance and subsequent attentional avoidance was partially supported. Corresponding to the "avoidance" aspect of the model, sustained bilateral amygdala activity was negatively correlated with chronic somatic symptoms,

even after controlling for the effects of gender and non-somatic anxiety severity. Based on behavioral data analyses, patients who experienced more chronic somatic symptoms were also more likely to show an attentional avoidance of fearful faces, while patients with few chronic somatic symptoms were more likely to display attentional vigilance. Unfortunately, because individual differences in attentional bias were related to symptom rates independently of amygdala activity, we cannot interpret lower amygdala activity as a measure of attentional avoidance. Moreover, higher somatic chronic anxiety was not associated with greater activation in brain areas thought to monitor emotional reactivity and engage higher-level cognitive control regions to down-regulate it (i.e., the ACC). As amygdala activation is considered to be a measure of attentional engagement and emotion processing (Davis & Whalen, 2001; Monk, et al., 2003), these activation patterns could instead indicate that patients who experience more chronic somatic symptoms are simply less emotionally reactive to mild threat stimuli than their less somatic fellow patients. It is important to note that many of items used to assess chronic somatic manifestations of anxiety (on the SCARED panic/somatic subscale) asked patients to report on the frequency with which participants' experienced specific symptoms when they were frightened. Patients who endorse more of these items may in fact be demonstrating a trait awareness of the physiological consequences of their high anxiety.

Our hypothesis that individual differences in situational somatic symptomatology would be associated with neural indices of greater emotional reactivity and somatic awareness in response to threat was also partially supported; patients who reported experiencing more situational somatic symptoms in response to high social-evaluative threat displayed greater sustained activation in the bilateral anterior insula. Based on previous fMRI studies of insula functioning, this pattern could indicate that patients with more severe stressor-induced bodily

symptoms also engage in greater implicit interoceptive monitoring during threat-processing. The majority of fMRI studies that have previously reported a relationship between chronic anxiety symptomatology and insula activation have used tasks that called for explicit interoceptive or emotional self-focus (Critchley, et al., 2004; McClure, et al., 2007; Passarotti, Sweeney, & Pavuluri, 2009), or tasks that involve the anticipation of a highly aversive stimulus (Simmons, Strigo, Matthews, Paulus, & Stein, 2006). In the current study, there were no task demands for interoceptive processing, and the threat-level of stimuli were low. However, the length of the trials (11.7 seconds) left a period of several seconds during which subjects could potentially engage in stimulus-independent thought. During this pause, patients who notice situational somatic symptoms during high threat might also by more likely to return to a subtle focus on bodily sensations.

However, we had also predicted that situational symptom levels would be negatively associated with activity in the caudal ACC, a region implicated in signaling the need for cognitive control resources. Contrary to that prediction, sustained caudal ACC activity was positively associated with situational somatic symptoms. Based on anxiety-related theories of vigilance discussed previously, this activation pattern could be a result of somatically-aware patients maintaining vigilance for the presentation of the next threat stimulus. Although it has been classically thought of as the "cognitive" portion of the anterior cingulate, the caudal ACC also appears to play a role in the generation of phasic autonomic arousal increases during the performance of more demanding tasks that call for effortful cognitive control and attention allocation (Critchley, et al., 2004). It is unlikely that our relatively simple dot probe task elicited such a substantial need for cognitive effort and, in the absence of peripheral physiological data,

we cannot determine whether increased dorsal ACC activity resulted in autonomic arousal increases.

Although the correlational nature of the current study prevents us from discussing threat processing biases as causal byproducts of somatic symptoms, our results suggest that anxious youth who maintain an implicit interoceptive monitoring and action-readiness in response low-grade threat may also be more likely to notice and report bodily threat cues during periods of more acute threat. In addition, anxious youth who display neural indices of blunted emotional responses external threat cues could be at higher risk for experiencing prominent anxiety-related somatic symptoms.

The current study has a number of limitations. First, this study used somatic symptom reports as a measure of patients' subjective experience of their chronic and situational anxiety-related symptoms. Aside from the possible influence of typical flaws in self-report measure (such as experimenter demand characteristics, patients' social desirability, and limited conscious access to internal experience), a number of known factors interact with basic awareness of or attention to bodily sensations. Patients may differ in the degree to which they demonstrate biased appraisals of bodily sensations, and may have differing levels of perceived anxiety control. For youth who feel unable to cope with their anxiety, somatic symptoms are likely to be much more distracting and emotionally distressing. In the current study, we did not attempt to measure negative beliefs about somatic sensations or the perceived ability to handle them. In addition, the tendency to experience somatic anxiety symptoms over time, and the tendency to experience situational somatic anxiety symptoms in response to threat were both conceptualized as trait-like characteristics and presumed to be relatively stable over time. Unfortunately, limited information is available on the temporal stability of these kinds of symptoms. Although individual

differences in stressor-induced physiological reactivity appear to be relatively reliable for intervals of up to several years (Cohen & Hamrick, 2003), research on the stability of subjective physiological stress-reactivity is scarce.

It is also worth noting that the brain imaging data from the present study were recorded during a simple probe detection task that utilized a slow event-related design and images of neutral or fearful human faces. As such, the task would be considered to involve a relatively low level of perceived threat to participants. Previous studies in anxious youth have varied their stimuli by perceived threat level, and have found that patients demonstrate more aberrant amygdala, insula, and ACC activity with respect to controls during periods when threat stimuli were more intense (Nitschke, et al., 2009; Simmons, et al., 2006). If the goal is to determine which pediatric anxiety patients deviate the most from healthy controls, and if somatic threat-processing is more uniform across anxiety patients under higher threat conditions, future studies should use more intensely threatening stimuli before correlating somatic symptom reports with brain activity.

In summary, results from the current study suggest that among anxiety-disordered youth, the tendency to experience chronic somatic anxiety symptoms and the tendency to experience stressor-induced "situational" somatic symptoms are distinct individual difference characteristics. Moreover, these two constructs are associated with unique patterns of threat-related brain activity. Although a great deal of research has being conducted to identify factors responsible for poor emotional self-awareness in anxious youth, this was to our knowledge the first study that attempted to link threat-processing biases with somatic awareness in an attempt to explain this phenomenon. We interpreted positive correlations between situational somatic symptom reports and activation during threat processing as potential evidence that that youth

who maintain interoceptive monitoring during low-level external threat may also be more likely to notice and report bodily cues under periods of more acute threat. In addition, anxious youth who display an attentional avoidance to external and/or subjective emotional threat cues during low-level threat may be more prone to chronic somatic anxiety symptomatology.

APPENDIX A

SUPPLEMENTARY TABLE

Table 2. Correlation values for associations od BOLD %-signal change in a priori ROIs with trait and situational symptom scores

Correlation with trait symptoms

Brain region		**1**	**2**	**3**	**4**	**5**	**6**	**7**
Left Amygdala	corr (*r*)	0	-0.18	***-0.38***	***-0.44***	***-0.40***	-0.29	***-0.48***
	sig (*p*)	0	0.26	***0.01***	***0.003***	***0.009***	0.06	***0.001***
Right Amygdala	corr (*r*)	0	-0.24	***-0.40***	***-0.45***	***-0.36***	***-0.33***	***-0.33***
	sig (*p*)	0	0.13	***0.009***	***0.003***	***0.02***	***0.03***	***0.03***
Left Anterior Insula	corr (*r*)	0	0.00	-0.22	-0.12	-0.07	-0.21	-0.24
	sig (*p*)	0	0.98	0.16	0.43	0.67	0.18	0.13
Right Anterior Insula	corr (*r*)	0	-0.12	***-0.31***	-0.27	-0.18	-0.23	-0.30
	sig (*p*)	0	0.44	***0.05***	0.09	0.26	0.14	0.06
Rostral ACC	corr (*r*)	0	-0.11	-0.22	-0.25	-0.17	-0.13	-0.22
	sig (*p*)	0	0.49	0.16	0.11	0.29	0.42	0.16
Caudal ACC	corr (*r*)	0	-0.19	***-0.32***	-0.28	-0.20	-0.22	-0.24
	sig (*p*)	0	0.22	***0.04***	0.07	0.21	0.17	0.12

Correlation with trait symptoms

Brain region		**1**	**2**	**3**	**4**	**5**	**6**	**7**
Left Amygdala	corr (*r*)	0	-0.04	0.01	0.14	0.12	0.25	0.20
	sig (*p*)	0	0.79	0.94	0.37	0.43	0.12	0.20
Right Amygdala	corr (*r*)	0	-0.06	-0.09	0.06	0.14	0.24	0.25
	sig (*p*)	0	0.69	0.58	0.70	0.37	0.13	0.12
Left Anterior Insula	corr (*r*)	0	-0.21	-0.13	-0.06	***0.34***	***0.31***	0.26
	sig (*p*)	0	0.19	0.41	0.70	***0.03***	***0.05***	0.09

Right Anterior Insula	corr (*r*)	0	***-0.31***	-0.13	0.03	***0.38***	***0.42***	***0.36***
	sig (*p*)	0	***0.04***	0.40	0.84	***0.01***	***0.005***	***0.02***
Rostral ACC	corr (*r*)	0	***-0.40***	-0.14	-0.04	0.30	***0.36***	0.29
	sig (*p*)	0	***0.009***	0.36	0.81	0.05	***0.02***	0.07
Caudal ACC	corr (*r*)	0	***-0.37***	-0.24	0.21	***0.32***	***0.37***	0.27
	sig (*p*)	0	***0.02***	0.21	0.20	***0.03***	***0.01***	0.10

Note: Correlation and significance values in which $p < .05$ are **bolded** and *italicized*.

APPENDIX B

CSI-24-R

YOUR PHYSICAL SYMPTOMS

	How much are you currently bothered by each symptom?	**Not at all**	**A little**	**Some**	**A lot**	**A whole lot**
1.	Headaches	0	1	2	3	4
2.	Faintness or dizziness (feeling faint or dizzy)	0	1	2	3	4
3.	Pain in your heart or chest	0	1	2	3	4
4.	Feeling low in energy or slowed down	0	1	2	3	4
5.	Pains in your lower back	0	1	2	3	4
6.	Sore muscles	0	1	2	3	4
7.	Trouble getting your breath	0	1	2	3	4
8.	Hot or cold spells (suddenly feeling hot or cold for no reason)	0	1	2	3	4
9.	Numbness or tingling in parts of your body	0	1	2	3	4
10.	Weakness (feeling weak) in parts of your body	0	1	2	3	4
11.	Heavy feelings in your arms or legs (when they feel too heavy to move)	0	1	2	3	4
12.	Nausea or upset stomach (feeling like you might throw up, or having an upset stomach)	0	1	2	3	4

YOUR PHYSICAL SYMPTOMS

How much are you currently bothered by each symptom?		Not at all	A little	Some	A lot	A whole lot
13.	Pain in your stomach or abdomen (stomach aches)	0	1	2	3	4
14.	Your heart beating too fast	0	1	2	3	4
15.	Difficulty swallowing	0	1	2	3	4
16.	Losing your voice	0	1	2	3	4
17.	Blurred vision	0	1	2	3	4
18.	Vomiting (or throwing up)	0	1	2	3	4
19.	Feeling bloated or gassy	0	1	2	3	4
20.	Food making you sick	0	1	2	3	4
21.	Pain in your knees, elbows or other joints	0	1	2	3	4
22.	Pain in your arms or legs	0	1	2	3	4

APPENDIX C

SELF REPORT FOR CHILDHOOD ANXIETY RELATED DISORDERS (SCARED) - CHILD FORM

Below is a list of items that describe how people feel. For each item that describes you **for the last 3 months,** please circle the **2** if the item is **very true or often true** of you. Circle the **1** if the item is **somewhat or sometimes true** of you. If the item is **not true** of you, please circle the **0**. Please answer all items as well as you can, even if some do not seem to concern you.

		0 Not true or hardly ever true	**1 Somewhat true or sometimes true**	**2 Very true or often true**
1.	When I feel frightened, it is hard to breathe.	0	1	2
2.	I get headaches when I am at school.	0	1	2
3.	I don't like to be with people I don't know well.	0	1	2
4.	I get scared if I sleep away from home.	0	1	2
5.	I worry about other people liking me.	0	1	2
6.	When I get frightened, I feel like passing out.	0	1	2
7.	I am nervous.	0	1	2
8.	I follow my mother or father wherever they go.	0	1	2
9.	People tell me that I look nervous.	0	1	2
10.	I feel nervous with people I don't know well.	0	1	2
11.	I get stomachaches at school	0	1	2

		0 Not true or hardly ever true	1 Somewhat true or sometimes true	2 Very true or often true
12.	When I get frightened I feel like I am going crazy.	0	1	2
13.	I worry about sleeping alone.	0	1	2
14.	I worry about being as good as other kids.	0	1	2
15.	When I get frightened, I feel like things are not real.	0	1	2
16.	I have nightmares about something bad happening to my parents.	0	1	2
17.	I worry about going to school.	0	1	2
18.	When I get frightened, my heart beats fast.	0	1	2
19.	I get shaky.	0	1	2
20.	I have nightmares about something bad happening to me.	0	1	2
21.	I worry about things working out for me.	0	1	2
22.	When I get frightened I sweat a lot.	0	1	2
23.	I am a worrier.	0	1	2
24.	I get really frightened for no reason at all.	0	1	2
25.	I am afraid to be alone in the house.	0	1	2
26.	It is hard for me to talk with people I don't know well.	0	1	2
27.	When I get frightened, I feel like I am choking.	0	1	2
28.	People tell me that I worry too much.	0	1	2
29.	I don’t like to be away from my family.	0	1	2
30.	I am afraid of having anxiety (or panic) attacks.	0	1	2
31.	I worry that something bad might happen to my parents.	0	1	2
32.	I feel shy with people I don’t know well.	0	1	2
33.	I worry about what is going to happen in the future.	0	1	2
34.	When I get frightened I feel like throwing up.	0	1	2
35.	I worry about how well I do things.	0	1	2
36.	I am scared to go to school.	0	1	2
37.	I worry about things that have already happened.	0	1	2
38.	When I get frightened, I feel dizzy.	0	1	2
39.	I feel nervous when I am with other children or adults and have to do something while they watch me (for example: read aloud, speak, play a game, play a sport).	0	1	2

		0 Not true or hardly ever true	1 Somewhat true or sometimes true	2 Very true or often true
40.	I feel nervous about going to parties, dances, or any place where there will be people I do not know well.	0	1	2
41.	I am shy.	0	1	2

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