Psychiatry Research: Neuroimaging 233 (2015) 9–17

Contents lists available at ScienceDirect

Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

Increased activity of frontal and limbic regions to emotional stimuli in children at-risk for anxiety disorders

Rhandi Christensen [a,*], Michael Van Ameringen [b], Geoffrey Hall [c]

[a] Department of Medical Sciences, McMaster University, Hamilton, Ontario, Canada
[b] Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, Ontario, Canada
[c] Department of Psychology, Neuroscience and Behaviour, McMaster University, Hamilton, Ontario, Canada

ARTICLE INFO

Article history:
Received 14 February 2014
Received in revised form
9 November 2014
Accepted 17 April 2015
Available online 30 April 2015

Keywords:
Functional magnetic resonance imaging
Anxiety disorders
Pediatric anxiety
At-risk populations
Social anxiety disorder

ABSTRACT

Neuroimaging studies of children with anxiety disorders are limited, and no study has examined children who are at increased risk for developing anxiety disorders based on parental anxiety. The objective of this study was to examine the function of frontal and limbic brain regions using functional magnetic resonance imaging (fMRI) in children at risk for anxiety disorders. Study participants included high-risk children ($n=20$) who had at least one parent with a primary diagnosis of social anxiety disorder and normal-risk control children ($n=19$). Using fMRI, we measured the blood oxygenation level dependent response while high-risk and normal-risk children were exposed to different emotional facial stimuli. We found greater activation of frontal, temporal and limbic regions in high-risk children relative to normal-risk children during the presentation of emotional stimuli (angry and happy). These regions included the prefrontal cortex, anterior cingulate, hippocampus and insula. Our within-group analysis revealed similar patterns of hyperactivity in high-risk children with and without current anxiety symptoms. To our knowledge, this is the first study to demonstrate functional alterations in emotion-processing brain regions in children who are at risk for anxiety disorders based on parental anxiety. These findings are consistent with previous fMRI studies of pediatric anxiety and behaviorally inhibited children, and they contribute to our understanding of the neural correlates of risk for anxiety disorders.
© 2015 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Functional alterations of emotion-processing brain regions involving fronto-limbic circuitry are thought to be involved in the pathophysiology of anxiety disorders (Birbaumer et al., 1998; Thomas et al., 2001; Stein et al., 2002; Straube et al., 2004; Monk et al., 2006, 2008a; Phan et al., 2006; McClure et al., 2007; Blair et al., 2008; Evan et al., 2008; Guyer et al., 2008; Beesdo et al., 2009; Lau et al., 2009; Ball et al., 2012; Blair et al., 2012). Previous neuroimaging studies of adults with anxiety disorders have found changes in the amygdala, with a consistent finding of amygdala hyperactivity (Birbaumer et al., 1998; Stein et al., 2002; Straube et al., 2004; Phan et al., 2006; Blair et al., 2008; Evans et al., 2008; Ball et al., 2012). Other regions such as the hippocampus, uncus, insula, parahippocampal gyrus, fusiform gyrus, and several frontal regions have also been reported to be overactive in anxious adults (Stein et al., 2002; Wright et al., 2003; Straube et al., 2004; Phan et al., 2006; Blair et al., 2008; Evans et al., 2008; Ball et al., 2012).

While there are numerous neuroimaging studies of anxious adults, neuroimaging studies of children with anxiety disorders are limited, which may be in part due to the challenges associated with scanning younger populations. Of the pediatric neuroimaging studies that have been conducted, there has been a consistent finding of increased limbic and prefrontal activity in children with generalized anxiety disorder, social anxiety disorder and panic disorder (Monk et al., 2006, 2008a; McClure et al., 2007; Guyer et al., 2008; Beesdo et al., 2009; Lau et al., 2009). These functional magnetic resonance imaging (fMRI) studies have used emotion-processing tasks with facial stimuli and have found increased activation of the amygdala, the anterior cingulate and the prefrontal cortex to angry or fearful faces (Monk et al., 2006, 2008a; McClure et al., 2007; Beesdo et al., 2009; Lau et al., 2009).

To better understand the development of anxiety disorders, it is necessary to establish whether neural alterations precede the onset of anxiety or whether they arise as a consequence of the disorder. This may be accomplished by studying at-risk populations who are considered to be at increased risk for developing anxiety disorders. The offspring of individuals with anxiety disorders are at a six- to nine-fold increased risk of developing anxiety disorders (Smoller et al., 2008). Compared with the

* Correspondence to: Anxiety Treatment & Research Centre, Fontbonne Building, F418-1, St. Joseph's Healthcare, 301 James Street South, Hamilton, Ontario, Canada L8P 3B6. Tel.: +1 647 389 9776; fax: +1 905 540 6533.
E-mail address: rhandi.christensen@mail.utoronto.ca (R. Christensen).

http://dx.doi.org/10.1016/j.pscychresns.2015.04.004
0925-4927/© 2015 Elsevier Ireland Ltd. All rights reserved.

prevalence of anxiety disorders in the general population, clinical studies of high-risk populations have found elevated rates of psychopathology among offspring of individuals with anxiety disorders (Capps et al., 1996; Mancini et al., 1996; Merikangas and Dierker, 1998; Beidel and Turner, 1997; Black et al., 2003; Merikangas, 2005). To date, no neuroimaging studies have been conducted with children at risk for developing anxiety disorders based on parental psychopathology. Neuroimaging studies have been conducted in children and youth with behavioural inhibition, a temperamental style that is thought to be a risk factor for or precursor of anxiety disorders (Hardee et al., 2013; Perez-Edgar et al., 2014; Roy et al., 2014).Children of parents with anxiety disorders are more likely to be behaviorally inhibited (Rosenbaum et al., 1988, 1991), and children who are behaviorally inhibited have been found to be at increased risk for developing anxiety disorders. An fMRI study by Hardee et al. (2013) found that behaviorally inhibited children had alterations in amygdala-frontal connectivity. A second fMRI study by Perez-Edgar et al. (2014) demonstrated that behaviorally inhibited adolescents had increased striatal activation, which was also associated with the participant's level of anxiety. These findings suggest that neural alterations may be present in vulnerable populations before the onset of anxiety symptomatology and can be considered markers of risk for anxiety. A previous study examining children at risk for major depressive disorder based on parental anxiety found alterations in amygdala and nucleus accumbens activation to emotional faces (Monk et al., 2008b). The authors suggest that these neural perturbations to emotional stimuli in offspring may reflect vulnerability for major depression (Monk et al., 2008b). Neuroimaging studies using a similar design as that used by Monk et al. (2008b) with at-risk populations based on parental anxiety can clarify whether alterations in neural response reflect a vulnerability to anxiety and can help improve our understanding of the neural correlates of risk for anxiety disorders.

The objective of the present study was to examine the function of emotion-processing brain regions using fMRI in children who are considered to be at increased risk for developing anxiety disorders based on parental anxiety. Our study population included high-risk children of parents with social anxiety disorder and normal-risk control children. We were specifically interested in studying the offspring of individuals with social anxiety disorder for several reasons. First, individuals with social anxiety disorder are thought to possess emotion-processing biases and a hypersensitivity to negative facial emotions (Clark and Wells, 1995; Clark and McManus, 2002; Ball et al., 2012). Consistent with this, previous studies have demonstrated that individuals with social anxiety disorder have alterations in facial emotion processing on a behavioural (Mogg and Bradley 2002) and a neuronal level (Birbaumer et al., 1998; Stein et al., 2002; Straube et al., 2004; Phan et al., 2006; Evans et al., 2008; Goldin et al., 2009; Blair et al., 2011; Ball et al., 2012). Second, we were interested in studying the offspring of adults with social anxiety disorder as previous clinical and neuroimaging studies have not examined this population. Finally, we wanted to study a homogeneous sample of offspring from parents of a specific anxiety disorder rather than offspring from parents with different types of anxiety disorders. We focused our functional analysis on frontal and limbic brain regions as these areas have been previously implicated in the pathogenesis of anxiety disorders. Using event-related fMRI, we compared the blood oxygenation level dependent (BOLD) response while high-risk and normal-risk children were engaged in a dot-probe task and were exposed to masked emotional facial stimuli. Based on previous fMRI studies of pediatric anxiety and behavioural inhibition, we hypothesized that high-risk children would have heightened reactivity of frontal and limbic regions to emotional stimuli.

2. Methods

2.1. Subject selection

The study was approved by our institutional research ethics committee. High-risk children were recruited from the community and from families of patients who were undergoing treatment at the Anxiety Disorders Clinic at McMaster University Medical Centre or the Anxiety Treatment and Research Centre at St. Joseph's Healthcare Hamilton. Normal-risk control children were recruited from the community. Children provided signed assent, and written informed consent was obtained from parents. High-risk children were included in the study if they were between 7 and 12 years of age, right-handed and had at least one parent with a primary diagnosis of social anxiety disorder. High-risk children were excluded if they met criteria for a lifetime psychiatric disorder other than anxiety or mood disorders. Normal-risk children were included in the study if they were between 7 and 12 years of age and right-handed. Normal-risk children were excluded from the study if one or more parent met criteria for a lifetime psychiatric disorder or if the child met criteria for a lifetime psychiatric disorder. Both high-risk and normal-risk children were excluded if the child was currently using any psychoactive substances, had a history of head injury or unstable medical illness, or were unsuitable for MRI scanning.

2.2. Assessment and measures

At the first visit, children and parents were assessed for the presence of psychiatric disorders. Both parents were assessed using the Mini International Neuropsychiatric Interview (MINI; Sheehan et al., 1998). Children were assessed with the Anxiety Disorders Interview Schedule for the DSM-IV—Child Version (ADIS-C), and parents completed the Anxiety Disorders Interview Schedule for the DSM-IV—Parent Version (ADIS-P; Silverman and Nelles, 1988). The Hollingshead Four-Factor Index of Socioeconomic Status was used to determine the socioeconomic status of families (Hollingshead, 1975).

2.3. Dot-probe attention-orienting task

The dot-probe attention-orienting task was developed as a behavioral measure of threat-related attention bias (MacLeod et al., 1986) and has recently been used as an fMRI paradigm to examine emotion processing in anxiety disorders (Monk et al., 2006, 2008a). Previous fMRI studies that have used the dot-probe paradigm in anxious populations have found increased activation of the amygdala and the ventrolateral prefrontal cortex to angry facial stimuli (Monk et al., 2006, 2008a). We chose the dot-probe task as our neuroimaging paradigm because it would allow us to examine functional alterations while subjects were exposed to emotional facial stimuli and it would also allow us to collect behavioural data to determine the presence/absence of a threat-related attention bias in the high-risk group. In previous behavioural studies using the dot-probe task, subliminal exposures yielded a greater attention bias than supraliminal exposures, indicating that conscious processes may not have a prominent role in threat processing (Mogg and Bradley, 2002; Bar-Haim et al., 2007). To target the early, automatic information processing that is thought to be involved in threat processing in the dot-probe task, stimuli should be presented for brief durations or immediately masked (Puliafico and Kendall, 2006). Backward masking is a technique that has been used to interrupt processing of emotionally expressive faces (Esteves and Ohman, 1993; Rolls and Tovee, 1994), and prevent the faces from being consciously perceived by participants (Whalen et al., 1998).

The stimuli used in this task were standardized pictures of male and female emotional faces that were immediately followed by a mask. The faces were taken from standardized batteries (Ekman and Friesen, 1976; Lundqvist et al., 1998). Pictures included equal numbers of male and female faces presented in gray-scale format. Pictures of faces were cropped to remove any non-facial features (e.g., neck and hair) and were framed by a gray background. The faces were 7.5 cm wide and 10.5 cm long in size. Masks were created by cropping a black and white image of a neutral face and re-arranging the cropped pieces in random order. The mask size was 7.5 cm wide and 10.5 cm long. The paradigm was constructed using E-Prime software (Psychology Software Tools Inc., Pittsburgh, PA, USA). Trials start with a fixation point (500 ms) followed by two pictures of an actor's face (17 ms). The two pictures were either neutral+neutral expressions or neutral+emotional expressions. The emotional expressions included happy and angry faces. Immediately after the presentation of the two facial stimuli, the mask appears (68 ms). Finally, the probe, an asterisk, is presented on the screen (1100 ms). Participants were instructed to press a button (left or right) for each trial to indicate which side of the screen the probe is located. The duration of each trial was 3985 ms, and the duration of each intertrial interval was 2300 ms. The intertrial interval served as a baseline for fMRI analysis between groups. There were a total of 200 trials, as follows: 160 trials containing emotional faces and 40 blank trials containing no faces. The paradigm consists of two main emotional trial types (incongruent and congruent) that were used to assess attentional bias for emotional faces. In the congruent trials, the probe appears on the same side of the screen as the emotional

Download English Version:

https://daneshyari.com/en/article/335492

Download Persian Version:

https://daneshyari.com/article/335492

Daneshyari.com