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Amygdala responses to unattended fearful faces: Interaction between sex and trait anxiety

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Abstract

Trait anxiety and sex have been shown to separately account for some of the observed individual differences in amygdala responses to emotional stimuli, but the combined effect of both factors remains unknown. In this fMRI study, participants varying in trait anxiety scores viewed a series of superimposed face/scene composite images (containing fearful or neutral faces) and were instructed to direct attention to either the face or the scene content. We observed an interaction between sex and trait anxiety in amygdala responses to fearful faces as a function of attention. In females, higher trait anxiety was associated with a stronger amygdala response to unattended fearful faces, whereas no such relationship was present in males. This observed interaction between sex and individual differences in trait anxiety at the level of the brain may have clinical implications for a better understanding of the higher incidence of anxiety disorders in women than men.

Keywords: Amygdala; Anxiety; Attention; Sex differences; Magnetic resonance imaging; Fear

1. Introduction

Functional neuroimaging studies have consistently reported amygdala responses to various types of threat-related stimuli (Davis and Whalen, 2001), supporting the notion of a general role of this structure in the detection of biologically meaningful events across species (LeDoux, 2000). None the less, a growing number of studies point towards the existence of individual differences in the magnitude, location and/or laterality of amygdala responses to emotional material (Hamann and Canli, 2004). For example, sex differences in amygdala responses to emotional stimuli, particularly facial expressions, have been reported (Hamann, 2005; Cahill, 2006). In general, women appear to have larger and more sustained bilateral amygdala activation than men (Hall et al., 2004; McClure et al., 2004; Williams et al., 2005). This is consistent with the observation that women classify emotional expressions, especially those depicting fear, more accurately than men (Hall, 1978; Thayer and Johnsen, 2000; Wild et al., 2001) and may reflect a greater vigilance in females for threat-related stimuli (Williams et al., 2005).

Individual differences in anxiety have also been shown to influence neural responses to threat stimuli, particularly in situations of reduced awareness or attention. For instance, Etkin et al. (2004) found that trait anxiety scores positively correlated with basolateral amygdala responses to masked fearful faces, and Bishop

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et al. (2004) reported that right amygdala responses to fearful faces correlated with state anxiety. In the latter study, an expression-by-attention interaction was also observed: participants with higher state anxiety showed a higher response to fearful faces that were unattended compared to attended ones, while the low state anxiety group exhibited the opposite pattern. Thus, these results suggest a relationship between anxiety levels and automatic amygdala responses to threat. Interestingly, enhanced amygdala responses to threat-related stimuli presented below the threshold of awareness have also been reported in patients with anxiety disorders (Rauch et al., 2003).

While previous studies have highlighted the individual effects of anxiety levels and sex on neural function, it remains unknown whether these variables exert their influence independently, in an additive fashion, or whether a more subtle interaction exists between them. Here, we directly tested, using functional magnetic resonance imaging (fMRI), the effects of trait anxiety and its interaction with sex on the neural responses to fearful faces under different attention conditions. We hypothesized that trait anxiety would influence amygdala responses to unattended faces, as shown in previous studies (Bishop et al., 2004, 2007; Most et al., 2006) and that, critically, this effect would be stronger in female participants, consistent with the proposed greater vigilance for threat stimuli in women.

2. Methods

2.1. Subjects

Forty healthy individuals (age: $M \pm$S.D.$= 23.4 \pm 2.9$, range: 18–31; years of education: $M \pm$S.D.$= 16.9 \pm 1.6$) were recruited through advertisements posted in the McGill University Classifieds. None of the participants had been diagnosed with neurological or psychiatric disorders (including substance abuse) nor were they using prescribed psychotropic medication. All participants had normal or corrected-to-normal vision. At the time of recruitment, participants were assessed for Trait Anxiety using the Trait component of the Spielberger State-Trait Anxiety Inventory (Spielberger, 1983). In order to ensure that higher trait anxiety scores were not reflective of an undiagnosed anxiety disorder, participants underwent psychiatric screening by a clinical psychologist, using the MINI International Neuropsychiatric Interview (Sheehan et al., 1998). All recruitment and testing procedures were approved by the Ethics Review Boards of the Douglas Hospital and the Montreal Neurological Institute, and participants provided written informed consent.

Data from eight subjects were not analyzed due to technical problems (1 subject), unsatisfactory task performance (defined as less than 60% accuracy on either task, 6 subjects), and excessive movement during scanning (greater than 2 mm translation in any direction, 1 subject). In addition, two more subjects were removed from the final analysis because of possible anxious pathology (clinical screening results, 1 subject) or failure to complete the clinical interview (1 subject). The pattern of behavioral and fMRI results when including the data from these two subjects did not differ from that reported here (data not shown).

The final subject sample consisted of 14 females (all right handed, age $M \pm$S.D.$= 22.3 \pm 2.4$) and 16 males (one left-handed; age $M \pm$S.D.$= 24.0 \pm 2.4$). Trait Anxiety scores for both females ($M \pm$S.D.$= 36.7 \pm 8.9$) and males ($M \pm$S.D.$= 38.8 \pm 10.7$) were consistent with those reported for individuals of this age group (Kendall and Sheldrick, 2000). Importantly, there was no significant difference in Trait Anxiety scores between male and female groups ($t(28) = 0.56$, $P > 0.5$).

2.2. Stimuli and task

The stimuli and task employed were similar to those described in Anderson et al. (2003). Stimuli comprised 56 fearful and 56 neutral faces, all of different individuals, which were selected from a larger set of emotional faces previously used and validated by our group (Sergerie et al., 2005, 2006). Theses images, as well as 56 indoor and outdoor scenes, were modified using Adobe Photoshop 7.0 (Adobe Systems, San Jose CA) to achieve consistency in size and contrast, cropped into a 158 by 225 pixel oval and converted to grayscale. The face images were superimposed onto the scenes thereby creating the face/scene composites (see Fig. 1). Two sets (Set A and Set B) of 56 face/scene composites were created (each set containing 28 fearful and 28 neutral faces).

During scanning, participants were instructed, through a visual cue (1000 ms), to make either a male/female judgment (*attend face*) or an interior/exterior judgment (*attend scene*) about a briefly presented (250 ms) face/scene composite image. Each face/scene composite image was presented twice during the experiment, once with the *attend face* and once with the *attend scene* instruction (for an example trial, see Fig. 1). The *attend face* and *attend scene* instructions occurred in an unpredictable, pseudo-random order. The average stimulus onset asynchrony was 5100 ms (median 4250 ms), resulting in a overall task duration of 9:55 min. Participants completed a practice task outside the scanner, using happy faces and a set of scenes not used in the fMRI experiment.