



## Neural responses to emotional faces in women recovered from anorexia nervosa

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### ABSTRACT

Impairments in emotional processing have been associated with anorexia nervosa. However, it is unknown whether neural and behavioural differences in the processing of emotional stimuli persist following recovery. The aim of this study was to investigate the neural processing of emotional faces in individuals recovered from anorexia nervosa compared with healthy controls. Thirty-two participants (16 recovered anorexia nervosa, 16 healthy controls) underwent a functional magnetic resonance imaging (fMRI) scan. Participants viewed fearful and happy emotional faces and indicated the gender of the face presented. Whole brain analysis revealed no significant differences between the groups to the contrasts of fear versus happy and vice versa. Region of interest analysis demonstrated no significant differences in the neural response to happy or fearful stimuli between the groups in the amygdala or fusiform gyrus. These results suggest that processing of emotional faces may not be aberrant after recovery from anorexia nervosa.

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### 1. Introduction

Facial expressions are a form of nonverbal communication that indicates a person's attitude, intention and emotion (Ekman and Friesen, 1969). They also are easily identifiable signals for environmental events. For example, facial expressions of fear have evolved to indicate the presence of imminent threat, and happy faces may positively reinforce a particular behaviour (Rolls, 1999). Perceiving emotion in the faces of others is therefore fundamental to successful human communication and interaction (Knapp and Hall, 2009).

There are now a plethora of neuroimaging studies that involve the presentation of stimuli conveying basic facial emotions such as fear, sadness, happiness and surprise. In healthy adults, the recognition of an emotionally salient stimulus is thought to recruit limbic structures such as the amygdala and insula as well as prefrontal (such as the anterior cingulate) and visual processing areas (such as the inferior occipital and fusiform gyrus) (Kesler/West et al., 2001; Murphy et al., 2003; Phillips et al., 2003a,b). There is also evidence that such brain regions may be differentially activated depending on the valence of the emotion displayed; for example, the amygdala has been implicated in fear processing (LeDoux, 2003). However, recent frameworks of emotion processing suggest that such brain regions may have a more general role in responding to emotionally salient information (Costafreda et al., 2008).

The eating disorder anorexia nervosa has been associated with impairment in emotion processing (Jansch et al., 2009; Joos et al., 2009)

and more specifically with the concept of alexithymia, a trait characterised by the inability to recognise, describe and express emotions (Bydlowski et al., 2005; Pollatos et al., 2008). It has been suggested that emotions may play a role in the disorder's maintenance, as well as being direct triggers for eating-disordered behaviours such as binge eating, engagement in excessive exercise and self-induced vomiting (Fairburn et al., 2003; Schmidt and Treasure, 2006; Harrison et al., 2009).

Research on emotional processing in anorexia nervosa has employed both self-report measures and experimental paradigms. Using measures such as the Toronto Alexithymia Scale (Taylor et al., 1985), some studies have found that individuals with anorexia nervosa show significant impairment in emotional processing compared to healthy controls (Zonneville-Bender et al., 2004; Speranza et al., 2007).

In terms of experimental studies in anorexia nervosa, Jansch and colleagues used a facial emotion recognition task and reported that individuals with anorexia nervosa had poorer emotion recognition, slower reaction times and a higher level of misclassification compared to healthy controls (Jansch et al., 2009). Similarly, Kucharska-Pietura and colleagues demonstrated that anorexia nervosa was associated with deficits in the recognition of basic negative emotions, particularly sadness and fear (Kucharska-Pietura et al., 2004). The last finding is supported by a recent study indicating that those with anorexia nervosa have an attention bias towards negative facial expression (Cserjési et al., 2011). However, other studies have failed to replicate significant group differences in emotion processing. Kessler and colleagues conducted an emotion recognition test and did not find any significant differences between individuals with an eating disorder (either anorexia nervosa or bulimia nervosa) and healthy controls (Kessler et al., 2006) and similarly, in an emotion decoding

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study, no significant differences were found between a currently ill and healthy participant group (Mendlewicz et al., 2005).

There are important confounding variables in studies of emotion processing in anorexia nervosa which may explain the conflicting results. Few studies take account of comorbid symptoms. This is especially important given that anorexia nervosa is highly comorbid with depression and anxiety (Herzog et al., 1992), and these disorders are consistently associated with impairment in emotion processing (Stein et al., 2007; Bourke et al., 2010). Therefore, deficits in emotion processing found in anorexia nervosa participants may not be due to eating disorder symptoms but rather to elevated levels of depression or anxiety. For example, a recent study reported that obsessive–compulsive symptoms are a stronger predictor of discrimination accuracy of sad faces than a diagnosis of anorexia nervosa (Castro et al., 2010).

Further, medication status of anorexia nervosa participants is rarely reported or controlled for in the analysis. This is surprising considering research which has shown the effects of antidepressant medication on emotion processing in healthy and depressed participants (Harmer, 2008; Harmer et al., 2009; McCabe et al., 2009) as well as those diagnosed with anorexia nervosa (Jansch et al., 2009). Failure to assess or control for medication status could confound results when comparing emotion processing between individuals with anorexia nervosa and controls. Alternatively, it could be that aberrancies in the processing of emotional stimuli may not be a core component of the disorder. Either way, the variance in results warrants the need for further research in this area.

When individuals are underweight as in acute anorexia nervosa, cognitive and physiological systems are severely disturbed (Kaye et al., 2009) and so it is not possible to determine whether any abnormalities in emotion processing are a cause or consequence of starvation. Investigating emotion processing after weight restoration therefore avoids this confound.

Few studies have investigated emotion processing in the recovered state. In one study it was reported that those recovered from anorexia nervosa were significantly less accurate than healthy controls in recognising emotional expressions from the eyes (Harrison et al., 2010). However, Oldershaw and colleagues also used a "reading the mind in the eyes" emotion-recognition task and found that for positively valenced stimuli, individuals recovered from anorexia nervosa scored midway between an acute anorexia nervosa group and healthy controls, but the recovered participants were not significantly different from either (Oldershaw et al., 2010). The latter result suggests that deficits in the ability to infer emotions may emerge secondary to starvation as suggested by recent accounts of anorexia nervosa (Park et al., 2011) instead of being a primary deficit.

Recently, researchers have also started to consider the neurobiological basis of emotion processing in anorexia nervosa. In an electroencephalography (EEG) study, participants with anorexia nervosa exhibited increased N200 amplitudes to neutral, sad, and disgusted faces and decreased P300 amplitudes in response to aversive emotional faces (Pollatos et al., 2008). It was suggested that this may represent alterations in encoding emotional stimuli and also diminished cognitive processing ability, particularly with respect to negative emotional faces in anorexia nervosa (Pollatos et al., 2008).

In a second EEG study, it was shown that anorexia nervosa participants demonstrate significant reductions in both early and late event related potentials compared with healthy controls when asked to identify facial expressions (Hatch et al., 2011). This was found for both overtly and covertly presented stimuli and at both baseline and following weight regain. The authors suggest that anorexia nervosa may be associated with disturbances in non-conscious neural activity in response to innately important stimuli, such as identifying facial emotions, and this supports an integrative neuroscience model which proposes that automatic disturbances in emotion processing are candidate biological markers for the disorder (Hatch et al., 2010). However, participants in this study still demonstrated

significant eating disorder psychopathology even after regaining weight, and so it is uncertain whether the deficits observed represent biological markers of the illness or are associated with the remaining eating disorder symptoms.

To our knowledge, no studies have employed functional magnetic resonance imaging (fMRI) to examine the neural response to face stimuli in those recovered from anorexia nervosa. The current study therefore investigated the neural response to emotional faces in individuals recovered from anorexia nervosa using fMRI.

Descriptions of eating disorders emphasize the role of fear in the disorder's onset and maintenance, for example, fear of calories and fear of weight gain or fatness (Ellison et al., 1998; Harvey et al., 2002); fearful faces were therefore selected for investigation. The response to the negative emotion of fear was contrasted with happy facial expressions as neuroimaging studies have reported that brief presentation of such stimuli can reliably activate brain circuitry underpinning emotion processing in health and psychopathology (Norbury et al., 2009; Miskowiak et al., 2010; Rawlings et al., 2010).

Further, neuroimaging studies have consistently implicated the amygdala and the reciprocally connected fusiform gyrus in the perception of fearful and happy faces in healthy participants (Breiter et al., 1996; Phillips et al., 1998; Phillips et al., 2001; Murphy et al., 2003; Surguladze et al., 2003) and these regions received attention in neuroimaging studies of anorexia nervosa employing other stimuli (Uher et al., 2005; Vocks et al., 2010; Joos et al., 2011). We therefore conducted a region of interest analysis on these areas, and we hypothesized that individuals recovered from anorexia nervosa would have aberrant neural responses to both happy and fearful face stimuli in the brain regions that have been shown to be activated by this task, namely the amygdala and fusiform gyrus.

## 2. Methods and material

### 2.1. Participants

Sixteen women who had previously met DSM criteria for restricting-type anorexia nervosa (mean age = 23.06, S.D. = 3.55) and sixteen healthy controls (mean age = 24.10, S.D. = 2.91) were recruited for this study. Nine of the recovered anorexia nervosa participants had fulfilled the criteria for major depressive disorder (MDD) during their lifetime and three participants had fulfilled the criteria for obsessive-compulsive disorder (OCD).

Criteria for inclusion in the recovered group included (a) a history of DSM-IV anorexia nervosa as assessed by the Structured Clinical Interview for DSM (Spitzer et al., 2004), (b) maintenance of a body-mass index (BMI) of between 18.5 and 25 kg/m<sup>2</sup> for 12 months, (c) regular menstruation for 12 months and (d) no use of psychoactive medications, such as antidepressants, in the previous 12 months. In addition, recovered anorexia nervosa participants had to score within one standard deviation of the Eating Disorder Examination – Questionnaire (EDE-Q) global mean scores for young women (Mond et al., 2006).

For assessment of current levels of eating disorder, depression or anxiety symptoms, self-assessments were carried out using the EDE-Q (Fairburn and Beglin, 2008), the Beck Depression Inventory (BDI) (Beck et al., 2002) and the State-Trait Anxiety Inventory (STAI) (Spielberger et al., 1983). On the day of scanning, all participants also completed visual analogue scales and the Positive and Negative Affect Scale (PANAS) to assess current mood (Watson et al., 1988). All participants were free from medication, except for the contraceptive pill. Informed consent was obtained from both groups of participants.

### 2.2. fMRI data acquisition

All images were acquired using a 1.5-T Siemens Avanto scanner located at the Oxford Centre for Clinical Magnetic Resonance Research. Functional imaging consisted of 35 T2\*-weighted echo-planar image (EPI) slices (TR = 3000 ms, TE = 50 ms, matrix 64 × 64, slice thickness = 3 mm), 3.0 × 3.0 × 3.0 mm voxels. A Turbo FLASH sequence (TR = 12 ms, TE = 5.65 ms), voxel size = 1 mm<sup>3</sup>, was also acquired to facilitate later co-registration of the fMRI data into standard space.

### 2.3. fMRI task design

The fMRI paradigm consisted of a block design with presentations of fearful and happy facial expressions (NimStim Face Stimulus Set\*). A gender discrimination task was employed in which participants were requested to decide upon the sex of each face and press one of two buttons accordingly with the right thumb. The gender discrimination task was employed as a low level cognitive task which does not interfere

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