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Neural correlates of the processing of self-referent emotional information in bulimia nervosa

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ABSTRACT

There is increasing interest in understanding the roles of distorted beliefs about the self, ostensibly unrelated to eating, weight and shape, in eating disorders (EDs), but little is known about their neural correlates. We therefore used functional magnetic resonance imaging to investigate the neural correlates of self-referent emotional processing in EDs. During the scan, unmedicated patients with bulimia nervosa ($n = 11$) and healthy controls ($n = 16$) responded to personality words previously found to be related to negative self beliefs in EDs and depression. Rating of the negative personality descriptors resulted in reduced activation in patients compared to controls in parietal, occipital and limbic areas including the amygdala. There was no evidence that reduced activity in patients was secondary to increased cognitive control. Different patterns of neural activation between patients and controls may be the result of either habituation to personally relevant negative self beliefs or of emotional blunting in patients.

1. Introduction

Recent developments in cognitive theories for eating disorders (EDs) include a role for distorted beliefs about the self with content ostensibly unconnected to weight, shape or eating (e.g. Cooper, Wells, & Todd, 2004; Waller et al., 2007). The content of self beliefs in EDs is negatively valenced and although its specific content has been elusive, evidence suggests it can be distinguished from that more typical of depression (Cooper & Cowen, 2009; Fairchild & Cooper, 2010). For example, self loathing beliefs are common in EDs, while beliefs of abandonment and deprivation are more typical of depression (Fairchild & Cooper, 2010). In practice, because of high comorbidity both types of belief are common in EDs (Fairchild & Cooper, 2010). Despite the theoretical importance of negative self beliefs (NSBs), there have been no studies to date investigating the neural correlates of these beliefs in EDs. This information could be useful in understanding the role and mechanisms of negative self beliefs (NSBs) in EDs and in supporting the development of treatment strategies.

Processing information about the self has been associated with increased activation across a network of areas such as the medial prefrontal gyrus (MFG), posterior cingulate and the precuneus (e.g. Fossati et al., 2003; Kelley et al., 2002; Lemogne et al., 2009; Rameson, Satpute, & Lieberman, 2010; Whitfield-Gabrieli et al., 2011). For example, asking participants to make a judgement about whether personality traits were self related (self condition) or generally desirable traits (general condition) resulted in an MFG activation that was unique to the self condition (Fossati et al., 2003) and such effects may be enhanced in emotional disorders such as depression (Lemogne et al., 2009). Emotional responses to NSBs further activate regions known to be important in emotional processing more generally such as the amygdala (Goldin, Manber-Ball, Werner, Heimberg, & Gross, 2009). It has been suggested that higher order cortical areas such as anterior cingulate cortex (ACC) and medial and lateral prefrontal cortices are important in regulating emotion (Ochsner & Gross, 2005). Dysfunction in these higher order cortical circuits could contribute psychopathology. For example, although to the best of our knowledge there are no studies of the regulation of negative self beliefs in EDs, a study in another emotional disorder, social anxiety, has demonstrated that higher cognitive control regions are important in regulating emotional responses to NSBs, but these regions are less recruited in individuals with social anxiety disorder than in healthy controls (Goldin et al., 2009).

The present study considered the neural correlates of processing NSBs in unmedicated patients with BN. Although there have been no studies to date of the processing of self-referent emotional information in EDs, studies in the related disorder of

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depression have revealed aberrant patterns of activations in the MFG in patients (Lemogne et al., 2009). We therefore hypothesised that there would be altered patterns of activation in brain regions known to be important in the processing of NSBs (MFG) and in emotional responses to NSBs (amygdala). Such differences might be secondary to differences in the cognitive regulation of emotional responses to NSB involving higher order cognitive control regions. This seemed especially pertinent given the literature suggesting that negative self beliefs in EDs drive processes designed to regulate their associated affect and behaviour (Waller et al., 2007), as well as the evidence that BN may be associated with impaired cognitive control and impulsivity (Steiger & Bruce, 2007). Although there is considerable overlap between NSBs in ED and depression there is also emerging evidence suggest possible to distinguish between the content of beliefs between the two groups of disorders (Cooper & Cowen, 2009; Fairchild & Cooper, 2010). We were therefore additionally interested in exploring whether there would be different neural responses to NSBs that have previously been associated with depression and those that have previously been associated with EDs and whether the NSBs associated with eating disorders would lead to the largest group differences.

2. Methods

2.1. Participants

Twenty-seven right-handed females (11 BN; 16 control) gave informed consent to participate in the study. Groups from this community sample were determined using the Structured Clinical Interview for DSM-IV (SCID; First, Spitzer, Gibbon, & Williams, 1996). BN participants who additionally met criteria for previous or current major depression were not excluded (6 BN participants met criteria for current or previous depression), due to the high comorbidity of BN and depression [reported at 63% in clinically based samples (Brewerton et al., 1995) and 36% in community samples (Dansky et al., 1998)]. No patients were engaged in any form of treatment at the time they took part in the study, but all were given guidance and support for seeking treatment after the study. Healthy volunteers were screened to be free of any current or previous DSM-IV Axis 1 diagnosis and not currently dieting. All volunteers were screened to be free of psychotropic medication, with the exception of one patient who had taken an antihistamine tablet in the morning prior to scanning in the afternoon.

Participants also completed the Eating Attitudes Test-26 (EAT-26; Garner, Olmsted, Bohr, & Garfinkel, 1982) and the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983).

2.2. Task design

Participants were presented with 60 personality characteristic words which they rated as either "me" (could be used to describe them) or "not me" (vice versa) in a rapid event related design. Specifically, participants were told that they would be presented with personality characteristic words which they should rate as "me" if they thought they did apply to them or could be used to describe them and "not me" if the reverse was true. Thirty of these words were relevant to ED NSBs (e.g. evil and monstrous) and 30 to depression NSBs (e.g. numb and excluded), as determined by an exploratory factor analytic study looking at the relationship between ED and depressive symptoms and NSBs (Cooper & Cowen, 2009) (see Supplementary material for a full list of stimuli). Stimuli were presented in randomised order in an event-related design. Each trial consisted of a central fixation cross of 500 ms, followed by the presentation of a word for 4500 ms and a further fixation cross for 5000 ms using E-Prime (version 1.0; Psychology Software Tools Inc., Pittsburgh, PA, USA) and projected onto an opaque screen at the foot of the scanner bore, which participants viewed using angled mirrors. Participants' responses were made via an MRI-compatible keypad.

2.3. fMRI data acquisition and analysis

Imaging data were collected using a 1.5T Siemens Sonata scanner. fMRI data analysis was carried out using FSL version 5.98 (Smith et al., 2004). Functional imaging consisted of 23 contiguous T_2*-weighted echo-planar image (EPI) slices [repetition time (TR) = 2000 ms, echo time (TE) = 28 ms, field of view (FOV) 192 × 192, slice thickness 4 mm]. A turbo FLASH sequence TR = 12 ms, TE = 5.65 ms, voxel size = 1 mm^3 was also acquired to facilitate later coregistration of the fMRI data into standard space.

Preprocessing included within subject image realignment (Jenkinson, Bannister, Brady, & Smith, 2002), non-brain removal (Smith, 2002), spatial normalisation [to Montreal Neurological Institute (MNI) 152 stereotactic template], spatial smoothing using a Gaussian kernel (5 mm full-width-half-maximum), and high-pass temporal filtering (to a maximum of 0.008 Hz).

In the first level analysis, activation maps were computed using the general GLM with local autocorrelation correction (Woolrich, Ripley, Brady, & Smith, 2001). Two explanatory variables were modelled: ED relevant and depression relevant words. These explanatory variables were modelled by convolving the onset of each word with a haemodynamic response function, using a variant of a γ function (i.e. a normalisation of the probability density function of the γ function) with a standard deviation of 3 s and a mean lag of 6 s. In addition, temporal derivatives were included in the model as covariates of no interest to increase statistical sensitivity. Contrasts of interest were ED relevant words vs baseline (implicit baseline representing all the variance in the model that is not explicitly modelled), depression relevant words vs baseline (implicit baseline representing all the variance in the model that is not explicitly modelled), ED relevant vs depression relevant (and vice versa).

In the second level analysis data, individual subject's data were combined using full mixed-effects analysis (Woolrich, Behrens, Beckmann, Jenkinson, & Smith, 2004). This mixed-effects approach accounts for within subject variability and allows population inferences to do be drawn. Significant activations were identified using a cluster-based threshold of statistical images [$Z = 2.00$ and a (corrected) spatial extent threshold of $p < 0.05$ (Friston, Worsley, Frackowiak, Mazziotta, & Evans, 1994)]

Given the strong a priori evidence implicating the MFG and amygdala in the processing of self related words and emotional stimuli, and the anterior cingulate and dorsolateral prefrontal cortex (DLPFC) in the regulation of emotional responses to NSBs, region-of-interest (ROI) analyses were performed in addition to a whole brain analysis using 5 mm spheres generated around a central co-ordinate taken from previous papers employing emotional tasks. The following Talairach coordinates were used: (−)24, −4, 20 (amygdala); (−)6, 48, 18 (MFG); (−)7, −20, 29 (cingulate); (−)48, 7, 36 (DLPFC) (Goldin et al., 2009; Lemogne et al., 2009; Surguladze et al., 2005). Percent signal change in relevant contrasts was extracted and these data were analysed using ANOVA.

Because of the potential confound of between group differences in anxiety and depression, significant analyses were also re-run controlling for these variables. This was done either by including the HADS depression and anxiety scores as confounding variables in the second level analysis in FSL, or in the case of extracted signal change as confounding variables in the ANOVA.

3. Results

Compared to healthy volunteers (HVs), the BN patient group had a significantly higher score on the EAT-26 [mean (SD) 3.38 (4.41) vs 29.55 (11.99), $F(1,25) = 64.57$, $p < 0.01$], as well as greater levels of depression and anxiety [HAD-D: 1.40 (1.45) vs 6.00 (4.40); $F(1,25) = 14.41$, $p < 0.01$, HAD-A: 5.87 (3.81) vs 9.81 (3.99); $F(1,25) = 6.55$, $p = 0.02$, data from one control participant missing]. Mean duration of illness for the BN group was 6.94 years (SD 5.56; data from two participants missing). The two groups did not differ in age [27.38 (5.44) vs 24.55 (4.97); $F(1,25) = 1.89$, $p = 0.18$].

3.1. Behavioural results

Patients endorsed more of both the ED and depression relevant personality words as me than controls (ED: $F(1,25) = 7.62$, $p = 0.01$; depression: $F(1,25) = 11.34$, $p < 0.01$; Table 1). Both groups

Table 1
Behavioural data.

	Controls	Patients
No ED words rated as "me"	0.94 (1.18)	6.18 (7.44)
No ED words rated as "not me"	28.81 (1.33)	23.45 (7.57)
RT to rate ED words as "me"	2116.96 (745.08)	2114.59 (369.25)
RT to rate ED words as "not me"	1311.21 (341.33)	1795.06 (678.28)
No depression words rated as "me"	3.88 (5.43)	13.55 (9.44)
No depression words rated as "not me"	26.00 (5.68)	15.82 (9.83)
RT to rate depression words as "me"	2472.34 (883.33)	1978.45 (487.40)
RT to rate depression words as "not me"	1527.07 (491.90)	2125.61 (550.30)

Table shows means and (standard deviations). Reaction times are shown in milliseconds. RT, reaction time; ED words, ED NSB relevant personality characteristic words; depression words, depression NSB relevant personality characteristic words.