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Functional neuroanatomy of body shape perception in healthy and eating disordered women

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Abstract

Background: Abnormalities in perception and evaluation of body shape are hallmark of eating disorders.

Method: Brain responses to line drawings of underweight, normal weight and overweight female bodies were measured using functional magnetic resonance imaging in 9 women with bulimia nervosa, 13 with anorexia nervosa and 18 healthy women. Participants rated the stimuli for fear and disgust.

Results: In the three groups, the lateral fusiform gyrus, inferior parietal cortex and lateral prefrontal cortex were activated in response to body shapes compared to the control condition (drawings of houses). The responses in the lateral fusiform gyrus and in the parietal cortex were less strong in patients with eating disorders compared to healthy controls. Patients with eating disorders rated the body shapes in all weight categories as more aversive than did healthy women. In the group with eating disorders, the aversion ratings correlated positively with activity in the right medial apical prefrontal cortex.

Conclusion: Processing of female body shapes engages a distributed neural network, parts of which are underactive in women with eating disorders. The considerable variability in subjective emotional reaction to body shapes in patients with eating disorders is associated with differential activity in the prefrontal cortex.

Introduction

Western society attributes central importance to body weight and shape. Women, in particular, are under pressure to pursue a slender body ideal, which is unattainable for the vast majority (Nichter and Nichter 1991; Thompson et al 1999). Consequently, dissatisfaction with one's own body weight and shape has become a rule rather than exception (Rodin et al 1985). While most women are concerned about their weight and shape, the 'undue influence of body shape and weight on self-evaluation' is a core symptom of the eating disorders and is common to anorexia (AN) and bulimia nervosa (BN) (American Psychiatric Association 1994).

Body weight and shape dissatisfaction, and discrepancy between actual and ideal body weight, are strongest in BN (Cash and Deagle 1997). In AN, body weight dissatisfaction is often masked by actually being underweight, but it resurfaces with weight gain and complicates the recovery process (Fairburn et al 1993). Weight and shape dissatisfaction precedes and predicts the onset of disordered eating behaviour (Cattarin and Thompson 1994; Killen et al 1996; Stice and Shaw 2002), influences the outcome of cognitive-behavioural treatment (Wilson et al 1999), and is modified in the course of effective therapy (Probst et al 1999). Even after successful management of eating behaviour, the persistence of weight and shape concerns is a predictor of relapse (Carter et al 2004; Fairburn et al 1993; Halmi et al 2002).

Related to concerns about weight and shape in eating disorders is 'a disturbance in the way in which one's body weight or shape is experienced' (American Psychiatric Association 1994). This manifests as systematic overestimation of one's own body size, and this bias is stronger in AN than BN (Cash and Deagle 1997). Disturbance in body size estimation is likely to involve perceptual and affective components (Thompson et al 1999). The weight and shape concerns can bias estimates of body size in a concern-congruent manner, with the body being perceived as heavier and larger than it is. Individuals with eating disorders may also have functional abnormalities in brain systems concerned with processing body size or body image (Grunwald et al 2001; Smeets and Kosslyn 2001).

Given the importance of body image for mental health and the interest into the neurobiological underpinnings of mental disorders, there has been a dearth of investigations into the neural correlates of normal and pathological body image. Most have focused on two brain systems; one involved in visual perception of images of the body and involving the extrastriate body area (EBA) (Downing et al 2001) and the other denoting a mental map of one's own body - the body schema. The EBA is located in the lateral occipito-temporal cortex and responds to visual images of human bodies and body parts (Downing et al 2001). The representation of one's own body schema depends on neural circuits involving the right parietal cortex and its connections to the thalamus (McGlynn and Schacter 1989).

In patients with eating disorders, the limited extant research has focused on neural systems involved in body schema. Smeets and Kosslyn (2001) hypothesised that distorted perception of one's own body in AN is mediated by a failure to integrate the general body schema in the left hemisphere with the concrete examples encoded in the right hemisphere. Results of a divided visual field experiment supported this theory, with more and quicker misattributions of enlarged own body images projected to the left hemisphere in AN patients. Grunwald and

colleagues (2001) hypothesised that misperception of own body size in eating disorder patients is one aspect of a more widespread disturbance in haptic (active tactile) perception and is associated with functional disturbance in the right parietal cortex. This was supported by the finding of decreased theta power in the right parietal region on the electroencephalographs of AN patients during a haptic perception task.

Recently, functional magnetic resonance imaging (fMRI) has been used to study cerebral reactions to distorted own or other female bodies in adolescent patients with AN and age- and gender-matched healthy controls (Seeger et al 2002; Wagner et al 2003). While a pilot study in three patients reported specific responses in the right amygdala and in the brainstem to their own versus another woman's body (Seeger et al 2002), a group analysis of 13 patients did not replicate these findings (Wagner et al 2003). In the latter investigation, most responses to own body images were common to healthy and AN subjects and included extensive dorsolateral prefrontal, supplementary motor, insular, inferior parietal, fusiform and cingulate cortical areas. Only the response to own distorted bodies in the right inferior parietal lobule was higher in the AN group than in the healthy controls (Wagner et al 2003). Compared to Seeger et al (2002), the results of the latter study are more credible as they are based on a formal group comparison. Also, the functional localisation of the disturbance in the inferior parietal cortex corresponds to previous research on body schema (Grunwald et al 2001; McGlynn and Schacter 1989; Smeets and Kosslyn 2001).

However, some aspects of the methodology make the interpretation of the results of Wagner et al (2003) problematic. Firstly, own and other body images were compared to scrambled meaningless stimuli but not to meaningful non-body images. Subsequently, the extensive neural network detected as activated in this contrast reflects not only body-image-related but also general object-recognition processes. Secondly, as only distorted body images were used, it is unclear whether the obtained cerebral responses relate to the content per se (own or other body) or to the fact that the images were unnaturally distorted. Thirdly, the subjects participated in a preparatory session, when the images were taken and distorted to 'maximum unacceptability'. This means that there was a previous active exposure to the target images and differences in brain responses to own and other images may be due to priming from the preparatory session.

The present study sought to investigate the neural correlates of body image in eating disorder patients and controls by examining cerebral response to body pictures. It complements the investigations by Seeger et al (2002) and Wagner et al (2003), as the three methodological issues raised above were addressed. Simple line drawings of female bodies of different sizes (underweight, normal and overweight bodies) were contrasted to meaningful objects - line drawings of houses. The drawings were designed to focus the subjects' attention on the body size and shape and to minimise additional information. The contrast between body and house conditions sought to identify the neural substrate of body perception. Contrasts between bodies of different sizes were designed to capture the processes related to body size perception and evaluation. Subjective ratings were used to identify the neural bases of individual differences in the affective appraisal of body shapes. These ratings were carried out post-scanning, so there was no pre-scanning exposure to the stimuli. As the degree of body image distortion varies across the spectrum of eating disorders (Cash and Deagle 1997), the present study included groups of patients with both AN and BN.

Six specific hypotheses were tested.

Hypothesis I: across all participants, there will be category-specific responses to bodies (as contrasted to houses) in the lateral occipitotemporal cortices (EBA) (Downing et al 2001) and in the right parietal cortex (body schema system) (Grunwald et al 2001; McGlynn and Schacter 1989; Smeets and Kosslyn 2001).

Hypothesis II: the overweight bodies would be perceived as aversive by all participants and would elicit greater responses in the amygdala and insula (Murphy et al 2003; Phan et al 2002).

Hypothesis III: body-stimuli would lead to differential activation in the EBA and the body schema parietal circuitry in patients compared to controls, reflecting dysfunction in body image processing. This would be independent of the size of the image; therefore, we expected no interaction of stimulus body size with activity in EBA and parietal regions.

Hypothesis IV: eating disorder patients would find body shapes more aversive than controls and would show greater responses in the medial prefrontal cortex, insula and amygdala (Ellison et al 1998; Seeger et al 2002; Uher et al 2004; Wagner et al 2003).

Hypothesis V: the systematic distortion of body ideal in favour of a thinner physique would be reflected by greater response in the emotion-processing regions (amygdala, insula, medial prefrontal cortex) to pictures of overweight and normal weight bodies in patients versus controls.

Hypothesis VI: there would be significant correlations between subjective ratings of negative affect to the body shapes and neural activity in the brain regions underlying emotion processing, such as the amygdala and the medial prefrontal cortex.

Method

Participants

Twenty-two patients with eating disorders were recruited from the inpatient (n=9) and outpatient (n=13) services of the South London and Maudsley Trust. Eighteen healthy women (CO) were recruited by advertisement and screened for abnormal eating habits (underweight, binge-eating, self-induced vomiting, purging), neurological or psychiatric disease. Lifetime diagnosis and inclusion criteria were ascertained using the structured EAT-AET interview based on Eating Disorder Examination (Fairburn and Cooper 1993) and customised for the use in genetic studies (Ribases et al 2004). Nine patients fulfilled DSM-IV criteria for BN; all of them reported bingeing and self-induced vomiting at least once a day; two of them had a history of AN. Thirteen patients fulfilled DSM-IV criteria for AN; seven of restrictive (RAN) and 6 of binge-purge (BPAN) subtype (American Psychiatric Association 1994). Exclusion criteria for all groups were metallic implants, psychotropic medication other than antidepressants, claustrophobia, psychosis and alcohol or drug dependence.

The mean age \pm S.D. was 29.6 \pm 9.3 in the BN group, 25.4 \pm 10.2 in the AN group and 26.6 \pm 8.6 in controls; between group differences in age were non-significant ($F_{2,37}=0.5$; $p>0.1$). Current body mass index (BMI) was lower in AN (16.2 \pm 1.6) than in BN (22.6 \pm 2.5) and controls (22.4 \pm 3.0). One control and one AN patient were left-handed. The mean disease duration was 14.2 \pm 8.6 years in BN and 11.8 \pm 10.2 years in AN patients. Nine participants (5 BN and 4 AN) were taking antidepressant medication (SSRI).

After description of the study, written consent was obtained as approved by the South London and Maudsley Ethical Committee. All participants also completed experiments with food and emotional images, which are reported separately (Uher et al 2003; Uher et al 2004).

Stimuli

Three sets of black and white line drawings of female bodies in swimming costumes were custom-created to represent underweight (BMI < 17.5), normal weight (20 < BMI < 25) and overweight (BMI > 27.5) female bodies in similar positions. The drawings were matched to silhouette scales (Fallon and Rozin 1985) and photographs of women with known BMI to fit the selected weight categories. The control stimuli were line drawings of houses of varied sizes and styles. Examples are given in Figure 1.

Procedure

Body and house images were presented on a rear-projecting screen and viewed via a double mirror periscope fitted to the headcoil. Participants were given verbal instruction: "You will be shown drawings of houses and bodies. Look at each of them and think how acceptable such a house / body-shape would be for you." Each image was shown for 2.5 s followed by a blank screen for 0.5 s. Ten body pictures in a 30 second block ('on' condition) were followed by ten control pictures ('off' condition). This sequence was repeated 5 times for each type of stimuli. There were 17 images per category, so that each image was presented three times (with the exception of one image per category being presented only twice). The order of underweight, normal weight and

overweight bodies was counterbalanced between participants. After leaving the scanner, participants rated individual images on 1 to 7 numeric analogue scales for disgust and fear; following written instruction: “What do you feel when looking at this image?” (Scale I: “Fear”, Scale II: “Disgust”; 1–not at all, 7–very much).

Image acquisition

Gradient echo echoplanar images were acquired on a 1.5 Tesla neuro-optimised MR system (GE Medical Systems, Milwaukee, USA). Fifty T_2^* -weighted whole brain volumes were acquired in each condition (repetition time 3s, echo time 40ms) in 16 near-axial 7mm thick slices (0.7mm interslice gap) depicting blood oxygen level dependent (BOLD) contrast with an in-plane resolution of 3mm.

Data analysis

Following motion correction (Bullmore et al 1999a), the BOLD effect was modelled by two Poisson functions with haemodynamic delays of 4 and 8 seconds. The least-squares model of the weighted sum of these two functions was compared with the signal in each voxel to obtain a goodness of fit statistic. The distribution of this statistic under the null hypothesis was calculated by wavelet-based resampling of the time series and refitting the models to the resampled data. Generic group activation maps, depicting regions where the BOLD signal is significantly stronger in response to the active images (body) than to the control images (houses), were constructed by mapping the observed and randomised test statistics into standard space and computing median activation maps. Main effects of group (BN, AN, controls) and stimulus (underweight, normal weight, overweight) and interaction between the two factors were established by cluster-level analysis with data randomisation between groups to determine the sampling distribution of group differences under the null hypothesis. Similarly, correlations of subjective ratings of images with voxel- and cluster-wise values of the goodness of fit were obtained by calculating the Pearson product-moment correlation at each voxel. The probability of occurrence of any cluster in the observed data was computed by reference to the null distribution (Bullmore et al 1999b). In group analyses, all activations above the cluster-wise significance threshold of $p \leq 0.01$ are reported. This provides a reasonable balance between the type I and type II errors (overall probability of the occurrence of a false positive cluster is smaller than 1.0 but larger than 0.05). However, cluster-wise threshold of $p \leq 0.001$ is required for whole brain correction (overall probability of occurrence of any false positive cluster is smaller than 0.05). Subjective ratings were averaged for each category of stimuli and then analysed using ANOVA with planned orthogonal contrasts (Contrast I: all patients versus controls; Contrast II: BN versus AN).

Results

Subjective ratings of stimuli

The ratings of fear and disgust were highly correlated for all categories of stimuli (Pearson’s $0.71 < r < 0.94$) and hence an average of these two is reported as a measure of ‘aversion’ (Figure 1). Images of bodies were rated as

more aversive by patients than by controls ($F_{2,117}=25.9$; $p<0.001$; Contrast I: $t_{1,117}=6.6$; $p<0.001$). This was true for all three categories of body shapes (underweight: $t_{1,37}=3.1$, $p<0.01$; normal: $t_{1,37}=4.1$, $p<0.001$; overweight: $t_{1,37}=6.7$, $p<0.001$). This effect was more marked in AN than BN (Contrast II: $t = 2.0$; $p<0.05$). Further, there was significant group by stimulus interaction ($F_{4,111}=2.8$; $p<0.05$): while healthy participants rated the underweight bodies as most aversive, the eating disordered patients reported more aversion to the overweight bodies. The AN patients reported more aversion to the normal weight bodies, compared to both the BN and control participants.

As can be seen from the error bars and scatter plots (Figure 1), there was considerable variability in subjective ratings within the patient groups. Some patients scored in the range of healthy controls, while others gave much more negative ratings. Specifically, we have identified a group of five subjects (1 BN, 4 AN), who rated images of normal bodies as more aversive than images of underweight bodies, reflecting a severe disturbance in body image. All control subjects rated the underweight bodies as more aversive than the normal weight bodies. To capture the relative preference for an underweight body ideal, an *index of body-image disturbance* was calculated as [(aversion to normal weight bodies – aversion to thin bodies) / (aversion to normal weight bodies + aversion to thin bodies)] for correlational analyses involving the imaging data.

There were no between groups differences in the ratings of the images of houses.

Generic group activation maps

Details of group activation maps are given in Table 1 and Figure 2. In response to body shapes (compared to houses), both patients and healthy women activated the lateral fusiform gyrus (corresponds to EBA, Brodmann's areas 19 and 37), the inferior parietal cortex (maximum response in Brodmann's area 40) and the lateral prefrontal cortex (maximum response in the inferior frontal gyrus, Brodmann's area 44). For all three regions, the body-shape-related activations were stronger and/or more extensive in the right hemisphere (Table 1). The medial aspects of the fusiform and lingual gyri were consistently more active in the control condition with images of houses (Figure 2).

Other activations reached the cluster-wise $p<0.01$ thresholds only in some of the conditions. There were no brain regions that showed greater activation across all participants to overweight, relative to normal weight or underweight bodies. However, in the group of healthy women, the right dorsal anterior cingulate cortex (Brodmann's area 32) was activated in response to overweight bodies and an area in the anterior ventrolateral prefrontal cortex (medial frontal gyrus, Brodmann's areas 47 and 10) was responsive to the underweight body-shapes. In the eating disordered patients, there were activations in subcortical structures (thalamus and putamen) in response to normal and overweight but not underweight body shapes.

Group comparisons

Patients with eating disorders, as a group, showed a weaker reaction to body shapes in the occipitotemporal cortex (including the EBA) and in the parietal cortex than did healthy women (Table 2). These effects were more marked in the AN group who showed weaker activation, relative to both BN patients and controls, in the right and left lateral fusiform gyrus and in the right parietal cortex in response to all three categories of body shapes.

Patients with BN showed activation in the right lateral fusiform gyrus intermediate between the healthy women and those with AN, but did not differ from controls in terms of parietal activation. There were no regions of significantly increased activations in any patient group compared to the healthy controls. There was an interaction between group (patients versus controls) and condition (overweight versus underweight body shapes) in the right fusiform gyrus ($p < 0.01$), which was due to a relatively stronger response in healthy controls to overweight body shapes and in the patients to underweight body shapes.

Correlation of brain activity with subjective ratings

As the variability in the ratings of body shapes within the control group was relatively small, the correlation analysis focussed on patients with eating disorders. Composite activity maps to all three categories of body shapes were used in the correlations. Reactivity to body shapes in the right apical medial prefrontal region (superior frontal gyrus, Brodmann's area 10; $x=14$; $y=60$; $z=4$) correlated positively with the mean aversion rating of body shapes ($r=0.54$; $p < 0.01$). On the other hand, reactivity in the left lateral fusiform gyrus (Brodmann's areas 19 and 37; $x=-47$; $y=-67$; $z=-7$) tended to be lower in those who reported greater subjective aversion to body shapes ($r=-0.45$; $p < 0.05$). The index of body image disturbance (aversion in response to normal relative to underweight bodies) was positively correlated ($r=0.51$; $p < 0.01$) with reactivity in the inferior medial temporal region (including Brodmann's area 34 and the amygdala; $x=14$; $y=0$; $z=-18$). This latter correlation was largely due to three cases with severe body image disturbance and strong reactivity to body shapes in this region (Figure 3).

Discussion

Previous research has indicated that the processing of body image is underpinned by neural systems involved in analysing perceptual aspects of the human body (EBA; Downing et al 2001) and in representing a person's own body schema (right parietal cortex; e.g. McGlynn and Schacter 1989). In the present study, the pattern of brain response to female body shapes is consistent across different categories of stimuli (underweight, normal, overweight) and across groups of participating women (with or without an eating disorder) and includes bilateral activations in the lateral fusiform gyrus, inferior parietal cortex and dorsolateral prefrontal cortex, supporting our Hypothesis I. These findings are consistent with those of Wagner et al (2003), who found activity in these three regions in response to distorted body images in both healthy women and women with anorexia nervosa. The present body-selective activation in the lateral occipital-temporal cortex subsumes the previously identified EBA (Downing et al 2001) but is larger and also includes more ventral areas previously identified as responsive to faces or animals more than to inanimate objects (Chao et al 1999; Ishai et al 1999). This suggests a broader specialisation of this part of the occipitotemporal cortex for animate (humans and animals) as opposed to inanimate (tools, furniture, houses) objects. Furthermore, the right more than left asymmetry in the responses to body shapes is consistent with the right hemispheric dominance for body schema (McGlynn and Schacter 1989). It has been suggested that the characteristic disturbances in body image found in patients with eating disorders (e.g. Cash & Deagle, 1997) may reflect functional abnormalities in these regions (Grunwald et al 2001; Smeets and Kosslyn 2001). In the present study, there was less activity in the occipito-temporal and parietal regions in eating disordered patients compared to controls, with this relative inactivity being more marked in patients with AN. This lower responsiveness in the present patient group is unlikely to be due to non-specific decreases in brain reactivity, as these same patients demonstrated increased or equivalent levels of activation relative to controls in response to food-related or non-specific emotional stimuli (Uher et al 2004). The present findings provide support for Hypothesis III that body image processing brain circuits are dysfunctional in patients with eating disorders. The low functionality of this network may facilitate the development of body image disturbance in some individuals and may be related to deficits in spatial and tactile perception (Grunwald et al 2001; Tchanturia et al 2002). Further research is needed to address the issue of whether this abnormality is a consequence or an antecedent of the eating disorder.

It is important to note that the present findings stand in contrast to the increased reactivity in the inferior parietal lobule in response to own distorted body images in adolescent patients with AN reported by Wagner et al (2003); however, direct comparison across studies is difficult as no negative differences (areas less activated in the AN group) are reported in the latter paper. Furthermore, the relative increase in activity in the study by Wagner et al. was specific to distorted pictures of one's own body and not present to pictures of other bodies. This suggests that this finding reflects the self-relatedness of stimuli or previous exposure, rather than body processing per se.

We anticipated that functional abnormalities in the neural circuits underlying body image processing in patients with eating disorders would be independent of body image stimulus size. However, we found an interaction of body image size with group in the lateral fusiform gyrus. Specifically, relative underactivity in this region in

patients, compared to controls, was evident to images of overweight bodies, but this pattern was reversed to images of underweight bodies. In addition, in the patient group, overall subjective ratings of the aversiveness of the body shapes correlated negatively with activity in the fusiform gyrus, with lower activations being associated with greater subjective aversion. This suggests that dysfunction in the EBA in eating disordered patients is related to the subjectively aversive nature of the stimuli. However, as these findings were relatively weak and unpredicted, further research is clearly warranted.

As expected, patients rated body images as more aversive than controls. Furthermore, AN patients were more averse to normal weight bodies than BN patients and controls. However, these trends in subjective ratings were generally not reflected in the fMRI data. We found no support for Hypothesis II that overweight body shapes would lead to greater activation in brain regions implicated in emotion processing. There was also no evidence supporting Hypothesis IV, as reactivity in emotion processing regions of the brain did not differentiate between eating disorder patients and controls. Neither were there any reliable interactions between body image stimulus size and activation in these regions either within or between groups (Hypothesis V not supported). In the group of patients with eating disorders, we did find activation in the basal ganglia and the thalamus in response to normal and overweight bodies. However, the differences from normal weight condition were not significant and did not generalise to the control group. In the light of these data, it is notable that, although the previous study by Wagner et al (2003) found responses in some emotion processing brain regions (anterior cingulate, insula cortex), that study also did not find any group difference in these regions between AN patients and controls.

This lack of emotion-system activation in response to body images in the present data and in particular the lack of group differences in the present data and in the previous study (Wagner et al., 2003) may be due to a number of factors. For example, the relatively low salience of body shape stimuli for healthy women combined with high variability in subjective perception of different body shapes in patients may have contributed. In addition, metacognitive processes may have confounded the findings; it is possible that women are implicitly performing a self-comparison with the presented body shapes (Stice et al 2003; Tiggemann and Slater 2004). In that case, the aversiveness of an overweight body shape would be balanced by the relatively positive self-comparison and vice versa. Hence, future investigations of neural correlates of body image related processes might profit from more specific paradigms, which would include explicit judgement or comparison of body shape and weight.

It is also possible that the presentation of body shapes as line drawings is not sufficiently evocative. However, line-drawings of body shapes proved to be effective in provoking subjective aversion in the present study and silhouette tests with similar drawings are widely used for evaluation of body image disturbance (Bulik et al 2001; Fallon and Rozin 1985). Nonetheless, more naturalistic stimuli, such as colour photographs may be more effective in a symptom provocation paradigm. For example, slender models presented in visual media have been shown to provoke negative feelings and impair the body image in susceptible young women (Groesz et al 2002); application of such stimuli is warranted in future neuroimaging research on eating disorders.

Given the possibility that line drawings may not have been particularly evocative, it may be that differential reactivity to the current body shape images in emotion processing brain regions was only present in patients who found these stimuli strongly aversive. In the present group of patients with eating disorders, there was indeed a

large between-subject variability in the subjective ratings of the drawings. While many patients rated the images similarly to healthy controls, others gave much more negative ratings. In support of Hypothesis VI, correlation analyses demonstrated that the mean aversion ratings in the patient group were associated positively with activity in the apical medial prefrontal cortex. Furthermore, the index of body image disturbance (coding a relative preference for underweight body shapes) correlated positively with a cluster of activity in the inferior medial temporal lobe, including the amygdala.

This medial prefrontal cortex activation is comparable with reactions to subjectively aversive food stimuli (Uher et al 2003; Uher et al 2004). It appears that while the reactivity in this region to food is present in most eating disordered individuals, the reactivity to body shape stimuli is restricted to a smaller subgroup, for whom such stimuli are subjectively strongly disturbing. However, although these two clusters overlap in the same anatomically defined area (Brodmann's area 10), the activation correlated with body shape ratings is located anterior to the food-responsive cluster. Hence, further investigation will be needed to explore the role of the medial prefrontal cortices in the genesis of symptoms in eating disorders.

In terms of the medial temporal and amygdala activation, on closer inspection it was apparent that this correlation was largely due to the three patients who showed the highest levels of body image disturbance and strongest reactivity to body shapes in this region. It should be noted that this was a post hoc analysis intended to explain the within group variability in the present data. The data must therefore be interpreted with caution. This same region was previously found to be reactive to derogatory body-related words in young women (Shirao et al 2003), to distorted images of own bodies (Seeger et al 2002) and to high-caloric drinks (Ellison et al 1998) in some patients with AN; other studies did not find such associations (Uher et al 2004; Wagner et al 2003). The present data on relatively strong amygdala reactivity in a small subgroup of patients may explain why findings concerning activity in this region were inconsistent in previous reports.

Although the present study is so far the largest in functional neuroimaging research on eating disorders, the nature of our sample limits the generalizability of our findings. Most of the patients included have had a chronic eating disorder and had been ill for many years. It is likely that the role of body image disturbance varies over the course of the illness and factors determining the onset of disorder may no longer be salient at the chronic stage. The factor of illness duration may explain some differences between studies as the study by Wagner et al (2003) was based on a substantially younger and less chronic sample. Finally, while current and lifetime diagnoses of eating disorder have been carefully established, the assessment of comorbidity relied on several screening questions and comprehensive diagnostic interview covering all psychiatric disorders was not employed. The issue of comorbid disorders may need to be formally addressed in future investigations.

In conclusion, in the present study we found a highly consistent pattern of brain activity related to body shape processing in healthy women and in women with eating disorders. Patients with eating disorders exhibited a relative underactivity of these networks and this may underlie the failure to represent and evaluate one's own body in a realistic way.

Table 1: Group activation maps in response to body shapes.

	Brodmann's area	Laterality	Size (voxels)	Talairach's coordinates			Effect size	Significance level
				Tal(x)	Tal(y)	Tal(z)		
BODY SHAPES (COMMON ACTIVATIONS)								
Occipitotemporal (lateral fusiform gyrus)	19,37	Right	287	43	-63	-13	0.59	0.0003
Occipitotemporal (lateral fusiform gyrus)	19,37	Left	231	-43	-67	-8	0.37	0.0003
Parietal	40,7	Right	244	29	-63	48	0.41	0.0003
Parietal (Inferior Parietal Lobule), occipital	40, 19	Left	84	-29	-63	42	0.18	0.0005
Lateral prefrontal	44,9,46,47	Right	192	51	15	26	0.27	0.0003
Lateral prefrontal / Precentral	6,44	Left	35	-47	4	31	0.16	0.0034
HEALTHY WOMEN: UNDERWEIGHT BODY SHAPES								
Ventrolateral prefrontal (medial frontal gyrus)	10,47	Left	10	-36	52	-7	0.10	0.0078
HEALTHY WOMEN: OVERWEIGHT BODY SHAPES								
Anterior cingulate gyrus	32	Right	28	7	15	42	0.12	0.0038
EATING DISORDERS: NORMAL BODY SHAPES								
Putamen		Right	37	11	4	9	0.11	0.0049
Thalamus (dorsomedial)		Right	22	7	-15	4	0.09	0.0084
EATING DISORDERS: OVERWEIGHT BODY SHAPES								
Thalamus		Right	25	11	-4	4	0.14	0.0069

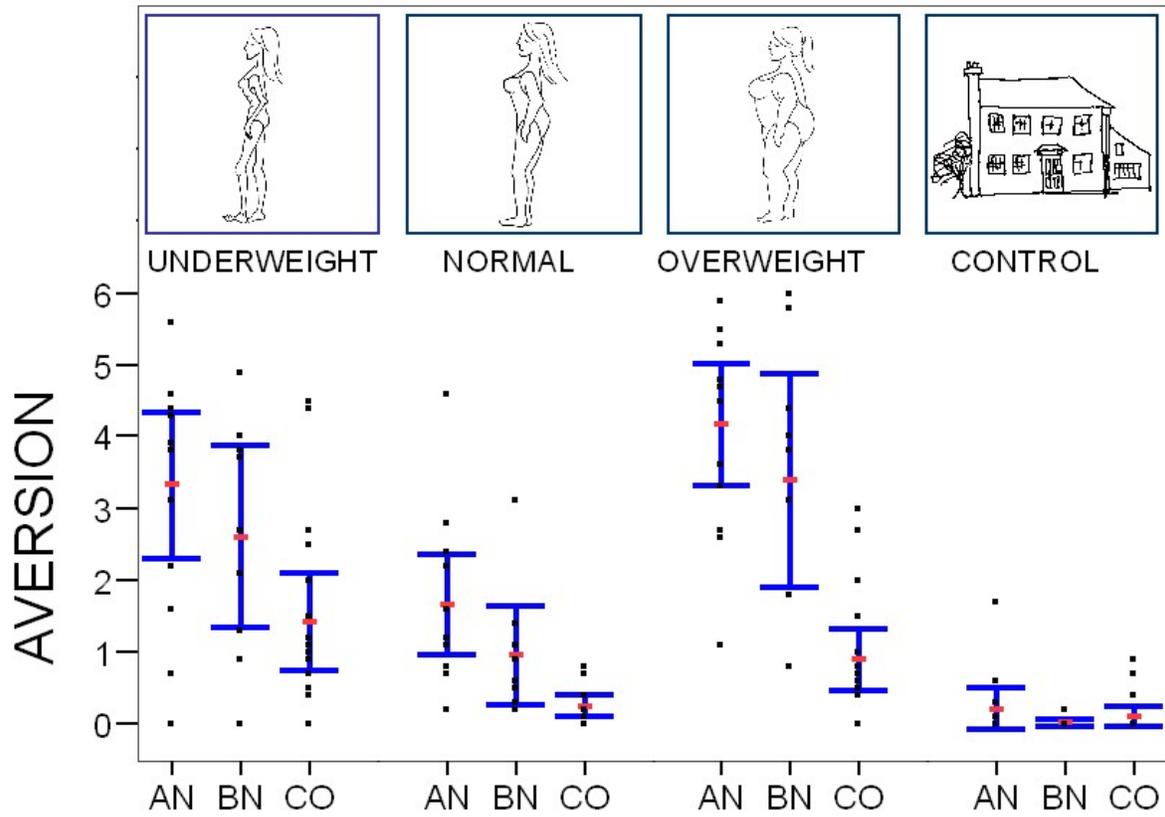
First, activations are given, which are common to all three conditions (underweight, normal, overweight body shapes) and all groups (healthy women, anorexia nervosa, bulimia nervosa); then, other activations are listed under the specific combination of condition and group. All activations, which have been positively associated with the presentation of body shapes at a cluster-wise significance threshold of $p \leq 0.01$, are included. The 'Size' of each cluster is given as number of voxels (each voxel is 60 mm^3). The 'Location' is specified as Talairach's x, y, and z coordinates of the centre of mass for each cluster. The strength of activation is given as 'Effect size' and the 'Probability' of occurrence of an activated cluster by chance in the specific activation map is given as a p value.

Table 2: Group comparisons of activation maps in response to body shapes.

	Brodmann's area	Laterality	Size	Talairach's coordinates			Significance level
				Tal(x)	Tal(y)	Tal(z)	
EATING DISORDERS < HEALTHY WOMEN							
Parietal (inferior lobule)	40	Right	53	33	-56	48	0.0006
Occipitotemporal (lateral fusiform gyrus)	37	Right	107	51	-59	-8	0.007
Occipitotemporal (lateral fusiform gyrus)	19, 37	Left	36	-36	-70	-13	0.008
ANOREXIA NERVOSA < HEALTHY WOMEN							
Parietal (superior parietal lobule)	7	Right	67	29	-67	31	0.006
Occipitotemporal (lateral fusiform gyrus)	37	Right	120	40	-60	-13	0.0002
Occipitotemporal (lateral fusiform gyrus)	37	Left	33	-40	-67	-2	0.008
BULIMIA NERVOSA < HEALTHY WOMEN							
Occipitotemporal (lateral fusiform gyrus)	37	Right	78	51	-59	-8	0.002
ANOREXIA NERVOSA < BULIMIA NERVOSA							
Prefrontal (inferior frontal gyrus)	44	Right	92	51	7	26	0.006
Parietal (superior parietal lobule)	7	Right	132	29	-70	37	0.003
Occipitotemporal (lateral fusiform gyrus)	37	Right	95	51	-59	-13	0.0002

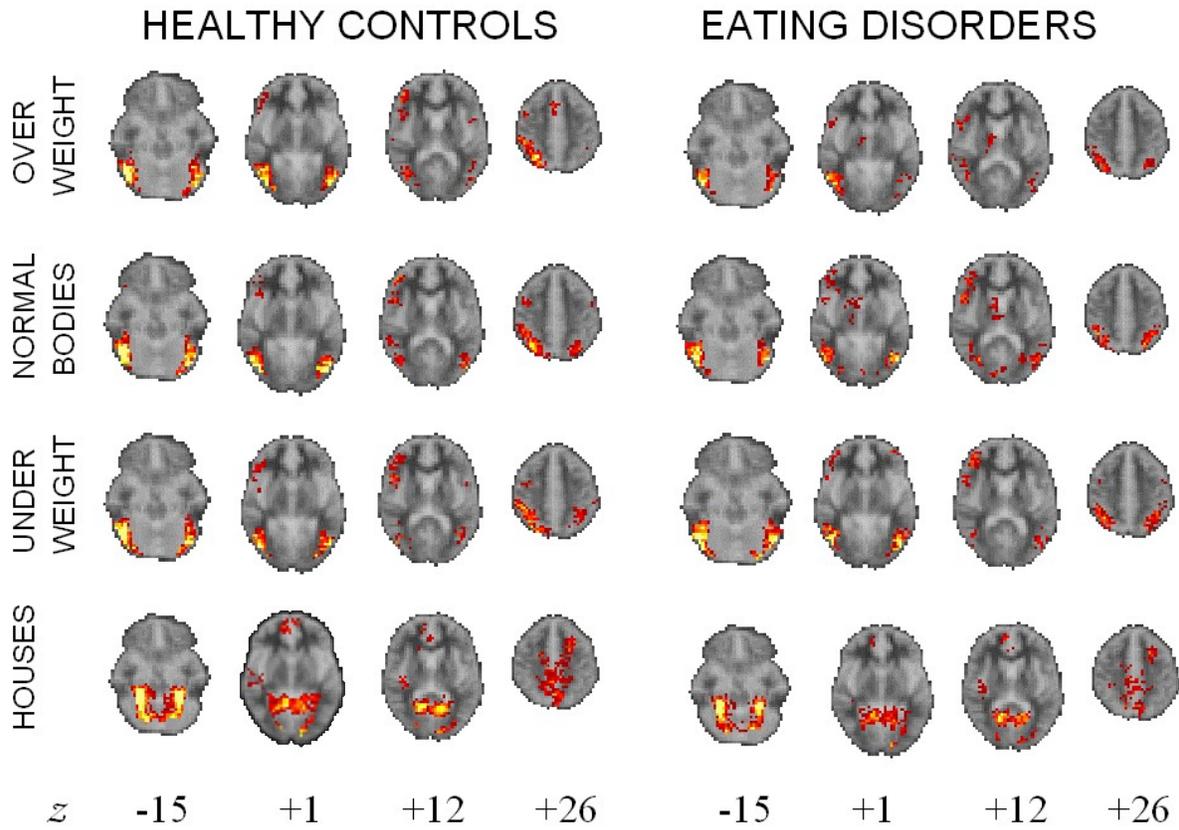
All between groups differences in brain reactions to body shapes at a cluster-wise significance threshold of $p \leq 0.01$ are included. The 'Size' of each cluster is given as number of voxels (each voxel is 60 mm^3). The 'Location' is specified as Talairach's x, y, and z coordinates of the centre of mass for each cluster. The strength of difference is indicated as the 'Probability' of occurrence of an activated cluster by chance in the specific comparison (p value).

Figure 1: Examples of stimuli and subjective ratings of aversion.



The numbers correspond to the average of fear and disgust ratings of all images in the category on a 1-7 numeric analogue scale (1-not at all disgusted/fearful; 7-very much disgusted/fearful). Error bars represent the 95% confidence interval. Groups: AN – anorexia nervosa, BN – bulimia nervosa, CO - healthy female controls.

Figure 2: Generic group activation maps for body shape images.

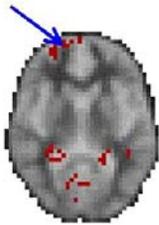


The depicted activations were associated with the active stimuli at the clusterwise level of significance $p \leq 0.01$. Four representative axial slices are shown in radiological convention (right hemisphere is on the left hand side of the image). The vertical position of each slice is determined by the z coordinate, which is given at the bottom of the figure.

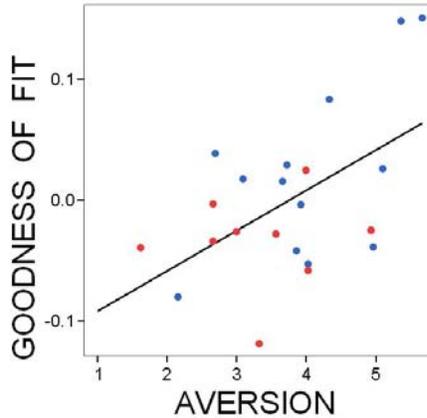
Figure 3: Correlations of subjective rating with brain activity in response to body shape stimuli.

RIGHT APICAL
PREFRONTAL CORTEX

$x = 14, y = 60, z = 4$

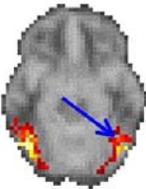


$r = 0.54$
 $p < 0.01$

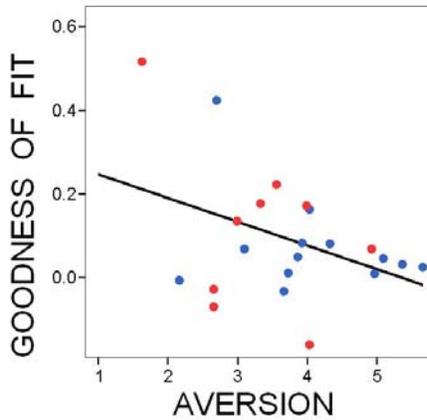


LEFT LATERAL
LINGUAL GYRUS

$x = -47, y = -67, z = -7$

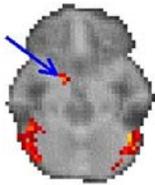


$r = -0.45$
 $p < 0.05$

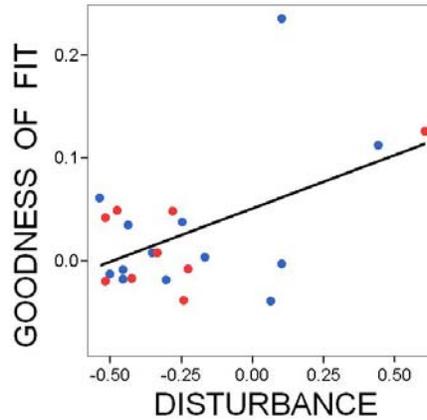


RIGHT AMYGDALA
REGION

$x = 14, y = 0, z = -18$



$r = 0.51$
 $p < 0.01$



• BULIMIA NERVOSA

• ANOREXIA NERVOSA

The brain slices illustrate the clusters from which the values of goodness-of-fit statistics have been extracted. Talairach's coordinates correspond to the centre of mass of each cluster. 'Aversion' is the mean rating of all body shapes on the dimensions of disgust and fear. 'Disturbance' is an index of relative preference for underweight bodies. The fitted lines were derived by linear regression model; the Pearson's correlation coefficient (r) and the level of significance (p) are given for each correlation.

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