Gender differences in brain activity generated by unpleasant word stimuli concerning body image: an fMRI study

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Background We have previously reported that the temporomesial area, including the amygdala, is activated in women when processing unpleasant words concerning body image.

Aims To detect gender differences in brain activation during processing of these words.

Method Functional magnetic resonance imaging was used to investigate 13 men and 13 women during an emotional decision task consisting of unpleasant words concerning body image and neutral words.

Results The left medial prefrontal cortex and hippocampus were activated only among men, and the left amygdala was activated only among women during the task; activation in the apical prefrontal region was significantly greater in men than in women.

Conclusions Our data suggest that the prefrontal region is responsible for the gender differences in the processing of words concerning body image, and may also be responsible for gender differences in susceptibility to eating disorders.

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Eating disorders, which have been associated with concerns about body shape and size (American Psychiatric Association, 1994), are about 10 times more common in women than in men (Weissman & Olfson, 1995). A possible reason for this difference in susceptibility might be a gender difference in the neural processing of unpleasant information about body image. We previously reported that women showed amygdalar activation while processing unpleasant words concerning body image and perceived these words to be emotionally negative (Shirao *et al*, 2003*a*). The medial prefrontal cortex has connections to the amygdala, constituting an interaction zone between emotional and cognitive processing (Drevets & Raichle, 1998). In this study we compared the brain activation between men and women while processing these words. We predicted that the amygdala would be less activated and the medial prefrontal cortex more activated in men than in women during the emotional decision task.

METHOD

Study sample

An age-matched sample of 13 men (mean age 25.3 years, s.d.=2.8, range 21–30) and 13 women (mean age 25.2 years, s.d.=3.2, range 21–30) participated in this study (P=0.949 by two-tailed, two-sample Student's t test). Participants were recruited by community announcement and paid incentives equivalent to their transportation expenses. All of them were right-handed and were native Japanese speakers. Handedness was determined using the Edinburgh Handedness Inventory (Oldfield, 1971). According to self-report, participants had no history of psychiatric, neurological or other major medical illness, and had never been treated with a psychotropic medication. There was no significant difference in the average years of education between men and women: men 15.2 (s.d.=1.6) *v.* women 14.9 (s.d.=2.5); P=0.645 by two-tailed, two-sample Student's t-test. The average body mass index of the men was 22.4 kg/m^2 (s.d.=3.2, range 18.0–31.3) and that of the women was 21.5 kg/m^2 (s.d.=3.7, range 18.8–28.4); P=0.543 by two-tailed two-sample Student's t-test. The average of the total Eating Disorder Inventory – 2 (EDI–2; Garner, 1991) scores of men was 45.5 (s.d.=28.4, range 9–103) and that of women was 37.9 (s.d.=23.5, range 7–85); P=0.330 by two-tailed Wilcoxon single-rank test. The average score for the item 'body dissatisfaction' for the men was 7.43 (s.d.=5.45, range 2–19) and for the women was 11.31 (s.d.=7.00, range 0–22); P=0.330 by two-tailed Wilcoxon single-rank test. The study was conducted using a protocol approved by the ethics committee of Hiroshima University School of Medicine. All individuals provided written informed consent for participation in the study.

Emotional decision task

We used the emotional decision task developed by Tabert *et al* (2001), with some modifications. The words used in the task were selected from the database of Toglia & Battig (1978), which includes 2854 words that have been rated on several items such as familiarity and pleasantness, on a scale of 1 (very unfamiliar; very unpleasant) to 7 (very familiar; very pleasant), with 4 as the mid-point. For our study, 30 neutral words were selected from the database and translated into Japanese. We also selected 30 highly unpleasant words concerning body image, chosen from Japanese-language dictionaries and thesauri. The two groups of words did not significantly differ with regard to word length (mean length in Japanese letters: body image words 3.2, neutral words 3.1; P=0.575 by two-tailed, two-sample Student's t-test). Our previous validation study comparing women who had eating disorders with a control group of healthy women showed that there was no significant difference in familiarity between the two categories of words (eating disorder group mean familiarity score: body image words 4.2; neutral words 4.1, P=0.727; control group mean familiarity score: body image words 3.9, neutral words 4.1, P=0.218, by two-tailed Wilcoxon single-rank test) and there was no significant difference in the familiarity ratings of words concerning body image between women with eating disorders and the control group (P=0.365 by two-tailed Wilcoxon single-rank test), whereas there were significant differences in pleasantness between the two categories of words (mean pleasantness score in the eating disorder group: body image words 2.4, neutral words 3.9, P=0.0002; mean pleasantness score in the control group: body image words 3.0, neutral words 4.0, P=0.0001, by two-tailed Wilcoxon single-rank test) and there were significant differences in the ratings of pleasantness between the eating disorders group and the control group (P=0.030 by two-tailed Wilcoxon single-rank test) (Shirao *et al*, 2003*b*). Both lists of words contained nouns, verbs, adjectives and adverbs.

The selected words were used to generate sets of unpleasant words concerning body image and sets of neutral words. Each word set comprised a unique combination of three words. The word sets were presented in six alternating blocks of two conditions (the task condition and the control condition) in three cycles (Fig. 1). During the task condition unpleasant word sets were presented, and during the control condition neutral word sets were presented. Each block began with a 3 s cue identifying the condition by displaying the word 'task' or 'control'. Five word sets were presented in each block. Each word set was shown for 4 s with a 1.4 s interstimulus interval (Fig. 1). The blood oxygen level-dependent (BOLD) response was recorded during three blocks of unpleasant words and three blocks of neutral words. During each interstimulus interval, a fixation cross placed centrally on the screen replaced the word set. Baseline functional magnetic resonance images were obtained during a 9 s period prior to the first block of trials, during which the individual viewed a centrally placed fixation cross. During each trial, the word set was projected to the centre of the person's field of view by a Super Video Graphics adapter computer-controlled projection system. The timing of presentation of word sets was controlled by Presentation Software Version 0.51 (Neurobehavioral Systems, Inc., San Francisco, CA, USA) and the word sets were presented in a randomised order. Immediately before functional magnetic resonance imaging (fMRI) scanning was begun, each participant was given ten practice trials (five unpleasant word sets and five neutral word sets). The words presented in the practice trials did not overlap with the experimental words.

Participants were instructed to select the most unpleasant word from each set of unpleasant words based on their personal knowledge and experience, and for each set of neutral words, participants were instructed to select the word that they thought was the most neutral; they indicated their choice by pressing one of three buttons on a response pad in the MRI scanner.

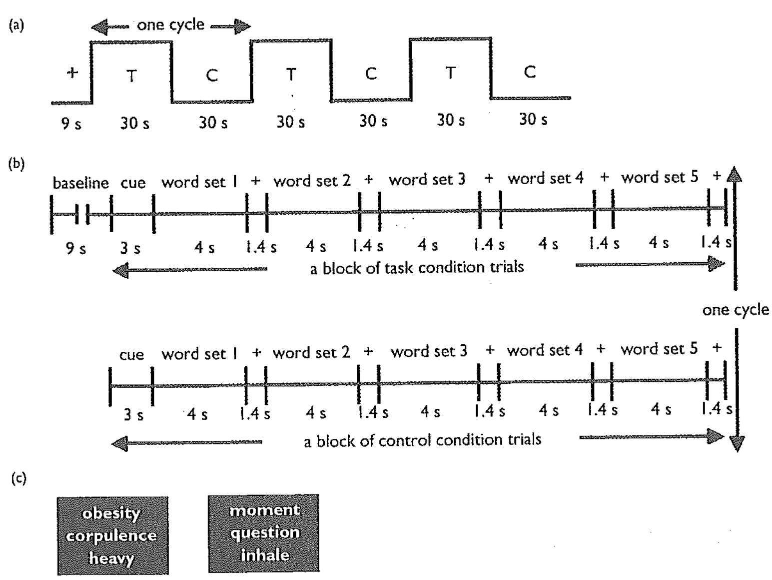

Fig. 1 Design of the study task. (a) Six alternating blocks of task condition (T) trials and control condition (C) trials were presented successively; the total scan time was 189 s (3 min and 9 s), yielding 63 images of 28 axial slices (1764 images). (b) Blocks of task condition and control condition trials were preceded by a baseline imaging period. Each block began with a cue ('task' or 'control'). The participant selected the word judged to be the most unpleasant or most neutral in each word set, by pressing one of three buttons. (C) Translations of typical word sets presented in this study (left-hand block, task condition; right-hand block, control condition).

Image acquisition and processing

The MRI scanner used was a Magnex Eclipse 1.5 T Power Drive 250 (Shimadzu Medical Systems, Kyoto, Japan). A time-course series of 63 volumes was acquired with T_2*-weighted, gradient echo, echo planar imaging (EPI) sequences. Each volume consisted of 28 slices, each 4.0 mm thick with no gap, encompassing the entire brain. The interval between two successive acquisitions of the same image (time to repetition, TR) was 3000 ms, the time to echo (TE) was 55 ms and the flip angle was 90°. The field of view was 256 mm and the matrix size 64 × 64, giving voxel dimensions of 4.0 mm × 4.0 mm × 4.0 mm. After fMRI scanning, structural scans were acquired using a T_1-weighted gradient echo pulse sequence (TR 12 ms, TE 4.5 ms, flip angle 20°, field of view 256 mm, voxel dimensions 1.0 mm × 1.0 mm × 1.0 mm), to facilitate localisation and co-registration of the functional data.

Image processing and statistical analysis were performed using Statistical Parametric Mapping (SPM) 99 software (Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab (Mathworks, Inc., Natick, MA, USA). The first two volumes of the fMRI run (pre-task period) were discarded because the magnetisation was unsteady, and the remaining 61 volumes were used for the statistical analysis. Images were corrected for motion and realigned with the first scan of the session, which served as the reference. The T_1 anatomical images were co-registered to the first functional images in each individual and aligned to a standard stereotaxic space, using the Montreal Neurological Institute (MNI) T_1 template in SPM99. The calculated non-linear transformation was applied to all functional images for spatial normalisation. Finally, the fMRI images were smoothed with a 12 mm full-width, half-maximum Gaussian filter.

Using group analysis according to a random effect model that allowed inference to the general population (Friston *et al*, 1999), we first identified brain regions that showed a significantly greater response to unpleasant word sets in comparison with the response to neutral word sets among male and among female participants, as brain areas related to the cognition of unpleasant word stimuli concerning body image in men and women, respectively. We then took the data of 13 of the 15 women who had participated in our previous study (Shirao *et al*, 2003*a*) and directly compared the activation of the entire brain in the male and female sub-samples using the two-sample Student's *t*-test. The resulting set of voxel values for each contrast constituted an SPM{t} map. The SPM{t} maps were then interpreted by referring to the probabilistic behaviour of Gaussian random fields. The data were given an initial threshold at an uncorrected $P<0.001$ at the voxel level, and regions about which we had an *a priori* hypothesis were reported at this threshold (Elliott *et al*, 2000). For regions about which there was no clear hypothesis, a more stringent threshold of $P<0.05$ corrected at the cluster level of multiple comparison was used. The *x*, *y* and *z* coordinates provided by SPM, which were in MNI brain space, were converted to the *x*, *y* and *z* coordinates in Talairach & Tournoux's (TT) brain space (Talairach & Tournoux, 1988) using the following formulae:

(a) $x_{TT}=x_{MNI}\times 0.88-0.8$;

(b) $y_{TT}=y_{MNI}\times 0.97-3.32$;

(c) $z_{TT}=y_{MNI}\times 0.05+z_{MNI}\times 0.88-0.44$.

Labels for brain activation foci were obtained in Talairach coordinates using the Talairach Daemon software (Research Imaging Center, University of Texas, TX, USA), which provides accuracy similar to that of neuroanatomical experts (Lancaster *et al*, 2000). The labelling of areas given by this software was then confirmed by comparison with activation maps overlaid on MNI-normalised structural images.

Evaluation of pleasantness and familiarity of the word stimuli

Each participant was asked to rate the pleasantness and familiarity of all the words presented in the tasks on a scale from 1 (very unfamiliar; very unpleasant) to 7 (very familiar; very pleasant), immediately after scanning. For this rating procedure the list of words was presented in randomised order in a table format.

RESULTS

Rating of words

The ratings of familiarity with the two categories of words did not significantly differ among men (mean familiarity score: unpleasant words 3.8, neutral words 4.4, $P=0.054$ by two-tailed Wilcoxon single-rank test) or women (mean familiarity score: unpleasant words 4.3, neutral words 4.3, $P=0.456$). However, all participants rated the unpleasant words concerning body image as significantly more unpleasant than the neutral words (mean pleasantness score: unpleasant words 3.1, neutral words 4.1, $P=0.007$ in men; unpleasant words 2.7, neutral words 4.1, $P=0.002$ in women). Neither the ratings of pleasantness nor the ratings of familiarity in each word category significantly differed between the male and female groups.

Brain activation

In men there was significantly greater activation of the left hippocampus, left superior temporal gyrus, left fusiform gyrus and left medial frontal gyrus when the emotional decision task involved unpleasant words compared with neutral words, whereas the women showed significantly greater activity of the left parahippocampal gyrus including amygdala, left thalamus and right caudate body in the same comparison (Table 1, Fig. 2).

The two-sample Student's *t*-test revealed that there was a significantly higher BOLD response in the left apical prefrontal region in men than in women during the unpleasant word task compared with neutral word task (Table 1, Fig. 3). No brain area showed significantly higher activation in women than in men during any of the tasks.

Correlation between psychological data and brain activation

Among the 13 women participants, activation in the left apical prefrontal area, which was significantly lower than that in men during the unpleasant words task, was negatively correlated with the total EDI–2 score (Spearman's rank-order correlation analysis: correlational coefficient -0.699, $P=0.008$). There was no correlation between any brain area showing significant BOLD response and the EDI–2 scores or the pleasantness rating of the unpleasant words.

DISCUSSION

We used the emotional decision task to examine the brain areas engaged in the perception of unpleasant words concerning body image and to compare the patterns of brain activation in men and women. Our results showed that the left medial part of the frontal gyrus, the left limbic area excluding the amygdala, the left superior temporal gyrus and the left fusiform gyrus play an important part in processing

Table 1 Relative increases in brain activity associated with unpleasant words concerning body image (task) and neutral words (control)

	Cluster	BA	*t* score	Coordinates[1]		
				x	*y*	*z*
Men (*n*=13)						
Left hippocampus	696*		9.59	−32	−13	−13
Left superior temporal gyrus		21	6.54	−50	−7	−8
Left fusiform gyrus		20	6.35	−43	−25	−17
Left medial frontal gyrus	359*	9	5.71	−4	53	9
Left superior frontal gyrus		10	5.34	−15	51	18
Women (*n*=13)						
Left parahippocampal gyrus	404*	37	7.08	−17	−13	−15
Left thalamus	485*		6.08	−3	−11	11
Right caudate body			4.65	10	1	5
Men > women						
Left apical prefrontal region	144	9	4.36	−15	49	20

BA, Brodmann area.
1. Stereotaxic coordinates were derived from Talairach & Tournoux (1988) and refer to the medial–lateral position (*x*) relative to the midline (positive=right), anterior–posterior position (*y*) relative to the anterior commissure (positive=anterior) and superior–inferior position (*z*) relative to the comissural line (positive=superior).
*Areas exceeding the extent threshold of $P<0.05$ corrected at the cluster level, all other areas exceeding the height threshold of $P<0.001$ uncorrected at the cluster level and belonging to a cluster of activation with an extent of at least 140 voxels are displayed.

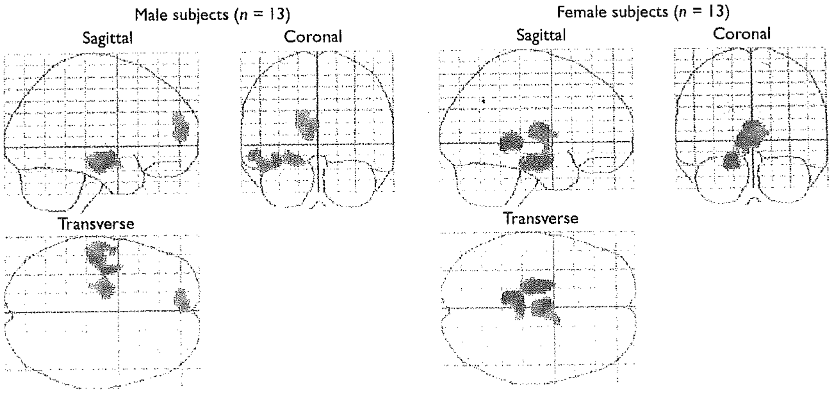

Fig. 2 Brain areas showing significantly greater activation during the task condition compared with the control condition. Three-dimensional 'look-through' projections of statistical parametric maps of the brain regions are shown (one-sample Student's *t*-test; corrected $P<0.05$ at the cluster level; $n=13$; d.f.=12).

unpleasant words concerning body image in men.

Lack of amygdalar activation in men

Consistent with our hypothesis, the amygdala did not show significant activation among men; however, the gender difference of the BOLD response in the amygdala was not significant by two-sample Student's *t*-test.

The amygdala has been suggested by many studies to be strongly associated with stimuli signalling threat. Human lesion and imaging studies consistently indicate that the amygdala is concerned in fear conditioning (Morris *et al*, 1998), in the recognition of fearful facial expressions (Adolphs, 1999) and in the evocation of fearful emotional responses from direct stimulation (Halgren *et al*, 1978). The amygdala is also considered to be important in the detection of environmental threat (Scott *et al*, 1997), including verbal stimuli (Isenberg *et al*, 1999). Therefore, the lack of significant activation in the amygdala among men suggests that men may not process unpleasant words concerning body image as fearful information, whereas women seem to do so.

Medial prefrontal cortex and emotional processing

The significant activation in the medial part of the frontal gyrus – Brodmann areas (BAs) 9 and 10; medial prefrontal cortex – was only detected in men, and there was a significantly higher BOLD response in men than in women in the left apical prefrontal region (BA 9) when performing the unpleasant word task compared with the neutral word task by two-sample Student's *t*-test. These results were consistent with our hypothesis. Many previous studies have suggested that the medial prefrontal cortex might have a role generally in emotional processing. It is reported that visual stimuli that evoke emotions, such as films or pictures, activated the medial prefrontal cortex, and that recall of various emotions such as happiness, sadness and disgust, and a mixture of these emotions, all separately engaged this brain region (Lane *et al*, 1997; Reiman *et al*, 1997). Several more recent studies suggest that when people turn their attention inwards to assess self-relevant attributes or emotional awareness, activity increases in the medial prefrontal cortex (Johnson *et al*, 2002; Zysset *et al*, 2002). The medial prefrontal cortex has connections to limbic structures, including the amygdala, constituting an interaction zone between emotional processing and cognitive processing (Drevets & Raichle, 1998), and this region may have a role in modulating the emotional response in the amygdala and other limbic structures. Limbic structures, including the amygdala, are likely to respond to emotional stimuli at a sensory or perceptual level (Reiman *et al*, 1997), whereas the medial prefrontal cortex may be involved in the cognitive aspects of emotional processing, such as attention to emotion, appraisal or identification of emotion (Drevets & Raichle, 1998). From this viewpoint, the gender differences detected in our study may demonstrate differences of cognitive pattern in men and women. Our results suggest the possibility that men processed the emotional decision task including words concerning body image more cognitively rather than emotionally, and activation in the medial prefrontal cortex was prominent; on the other hand, women processed this task more emotionally rather than cognitively, and the medial prefrontal cortex did not exhibit any significant activation. Both men and women perceived the unpleasantness of the words concerning body image to the same degree, according to their subjective ratings, but the fMRI data suggest that their processes are different: women are likely to use more intuitive processing whereas men use more rational processing. This discrepancy between the genders in cognitive style related to body image may contribute to the large gender difference in susceptibility to eating disorders.

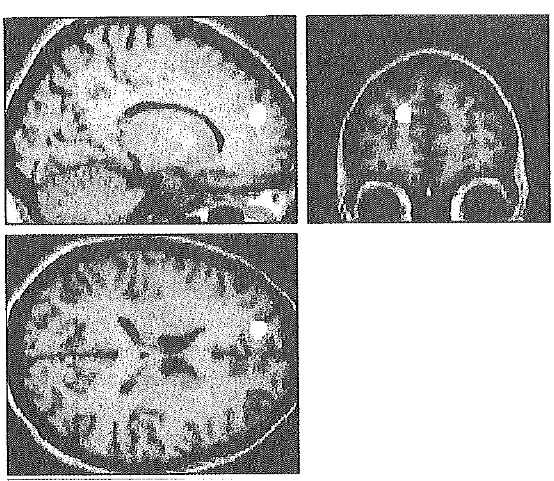

Fig. 3 Brain regions showing significantly greater activation in men than in women during the task condition of the emotional decision task compared with the control condition. Clusters of activation are overlaid onto a T_1-weighted anatomical magnetic resonance image. The white spots show areas of high activation. Two-sample Student's *t*-test; uncorrected $P<0.001$ in height; $n=26$ (13 men, 13 women); d.f.=24.

Another possible explanation of the different patterns of activation in the medial prefrontal cortex between men and women may be the difference in men's familiarity with the unpleasant word set compared with the neutral words. Although the ratings of familiarity were not different between men and women ($P=0.133$ by Mann–Whitney U test), there was a trend for male participants to be less familiar with the unpleasant words concerning body image than with the neutral words ($P=0.054$ by two-tailed Wilcoxon single-rank test). When processing unfamiliar words concerning body image, men might turn more attention inwards, and subsequently the BOLD response in the medial prefrontal cortex was higher than while processing neutral words.

Among women, correlational analysis revealed that the BOLD response in the left apical prefrontal region (BA 9), which was significantly lower in women than in men, was negatively correlated with total EDI–2 scores; in other words women with higher EDI–2 scores exhibited lower activity in this brain area. These results suggest the possibility that the apical prefrontal region might be involved in the pathophysiology of eating disorders.

Comparison with other neuroimaging studies

To our knowledge, two fMRI studies concerning body image distortion have investigated the effects of pictorial body image stimuli in women with anorexia nervosa and healthy controls (Seeger *et al*, 2002; Wagner *et al*, 2003). One study reported that patients with anorexia nervosa showed activation in the right amygdala, right fusiform gyrus and brain-stem associated with stimulation with their own body image whereas healthy controls showed activation only in the fusiform gyrus (Seeger *et al*, 2002), and the other reported that patients with anorexia nervosa showed greater activation in the prefrontal cortex and the inferior parietal lobule than did controls (Wagner *et al*, 2003). The latter authors explain the discrepancy between these results as a consequence of the design of the task. Many differences in the experimental conditions between these studies and ours make it difficult to compare the brain activation data, but a possible explanation of the discrepancy between the study by Wagner *et al* (2003) and our study is the age of the participants: those in the former study were adolescents (approximately 15 years old), whereas we recruited young adults (approximately 25 years old). An fMRI study which investigated the brain activation of adult and adolescent men and women while processing emotional facial expressions reported that the adult men and adolescents (both boys and girls) showed significant activation in the bilateral orbitofrontal cortex and anterior cingulate cortex in response to an angry face, whereas the adult women showed significant activation in the left amygdala in addition to these brain areas (McClure *et al*, 2004). These results suggest that the patterns of neural responses to emotional stimuli may be different in adults and adolescents.

A positron emission tomography study of gender differences in brain activation patterns during recognition of emotional facial expressions revealed that greater amygdalar activation was observed in women and greater medial frontal activation was observed in men (Hall *et al*, 2004); these authors suggest that men might take a more analytic approach and might regulate their emotional reaction to the stimuli more than women. Although the categories of stimuli are different, these results support our findings.

Study limitations

Our study has some limitations. First, we did not administer a structured interview when selecting the participants; however, they had no psychiatric or neurological illness at the time of their participation, although we cannot rule out its occurrence in the future. Second, participants were asked to rate only the unpleasantness and familiarity of the words used. If we had also asked about the fearfulness induced by the stimuli, we might have found gender differences in subjective rating and the results with brain image data would have been more clear-cut. Last, although our data

CLINICAL IMPLICATIONS

- Gender differences in brain activation suggest differences between men and women in the style of cognition toward unpleasant stimuli concerning body image.
- This discrepancy in cognitive style may have relevance to the large gender difference in susceptibility to eating disorders.
- The medial prefrontal cortex may be the brain area linked to the pathophysiology of eating disorder.

LIMITATIONS

- We did not use a structured interview when selecting participants.
- We asked the participants to rate only pleasantness and familiarity of the word stimuli and we could find no clear relationship between brain activation and the subjective rating of the words concerning body image.
- It is unclear whether the patterns of activation in the prefrontal area were specific to the stimuli concerning body image.

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suggest that there is differential activation of the brains of men and women when processing unpleasant words concerning body image, we cannot conclude whether these results are specific to unpleasant stimuli concerning body image or would apply to a wide range of unpleasant stimuli. Among women, a lower BOLD response in the prefrontal region compared with men while processing unpleasant words concerning body image exhibited a negative correlation with the total EDI–2 score, but it is unclear whether this brain region is the focal area responsible for susceptibility to eating disorders.

In conclusion, our study revealed that the paralimbic area including the amygdala was activated only in women and that the left medial prefrontal cortex was activated only in men while performing the emotional decision task with unpleasant words concerning body image. These results suggest that gender differences in brain activation might explain the differences in the style of cognition towards unpleasant stimuli concerning body image. Further studies comparing people who have eating disorders with healthy controls and which include general unpleasant word stimuli to contrast with words specific to body image are needed to elucidate the neural substrate responsible for the onset of eating disorders.

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Reduced Activation of Posterior Cingulate Cortex During Imagery in Subjects with High Degrees of Alexithymia: A Functional Magnetic Resonance Imaging Study

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Background: *Although the brain areas involved in imagery have been reported, the neural bases of individual differences in imagery remain to be elucidated. People with high degrees of alexithymia (HDA) are known to have constricted imaginal capacities. The purpose of this study was to investigate neural correlates of imagery disturbance in subjects with HDA.*

Methods: *A functional magnetic resonance imaging (fMRI) study was undertaken in 10 subjects with HDA and 10 subjects with low degrees of alexithymia (LDA), who were selected according to their scores on the 20-item Toronto Alexithymia Scale (TAS-20). The two groups' regional cerebral activation was compared during various imagery conditions. In those conditions, the subjects imaged a past happy (PH) event, a past sad (PS) event, a past neutral (PN) event, a future happy (FH) event, a future sad (FS) event, and a future neutral (FN) event. The activation levels during these conditions were compared with those during a rest condition (REST).*

Results: *The t tests showed that the mean subjective ratings of both the vividness of the imagery and the intensity of emotion during the imagery were higher in the subjects with LDA than in those with HDA for the PS and FS imagery conditions. On the other hand, relative to the LDA group, the HDA group showed significantly less activation in the posterior cingulate cortex (PCC) during the PH and FH imagery conditions compared with REST and during the FH imagery condition compared with the FN imagery condition.*

Conclusion: *The present results suggest an association between an HDA and reduced activation of the PCC during happy imagery. Given the function of this brain region, these results might be related to a dysfunction of episodic memory retrieval during happy imagery in subjects with HDA.*

Key Words: Alexithymia, imagery, posterior cingulate cortex, fMRI, future, happy

The brain areas involved in imagery have been investigated by neuroimaging studies in normal subjects. These studies revealed that, in addition to primary and secondary sensory areas (Cabeza and Nyberg 2000; Chen et al 1998; Halpern 2001; Le Bihan et al 1993; Shergill et al 2001; Yoo et al 2003), brain areas with other major cognitive functions, such as language, memory, and movement, are activated during imagery (Mellet et al 1998). The neural bases of individual differences in imagery, however, remain to be elucidated.

Alexithymia, a personality construct, was introduced by Nemiah and Sifneos in the early 1970s. The concept evolved initially from clinical observations of patients with psychosomatic disorders (Nemiah et al 1976). The salient features of this construct are as follows: 1) difficulty identifying and describing subjective feelings; 2) difficulty distinguishing between feelings and bodily sensations of emotional arousal; 3) constricted imaginal capacities; and 4) an externally oriented cognitive style (Nemiah et al 1976). Recently, high prevalences of alexithymia have been reported in various psychiatric disorders, such as somatoform disorders (53%, Cox et al 1994), anxiety disorders (46.7%, Parker et al 1993; 41%, Shipko et al 1983), and substance dependence (51%, Taylor et al 1990). An approximately 10% prevalence has been reported even in normal populations (Honkalampi et al 2000; Salminen et al 1999). Taylor (2000) stated in his review that alexithymia is a deficit in emotional regulation that reflects three kinds of deficits: 1) deficits in the cognitive–experiential component of emotion response systems; 2) deficits at the level of interpersonal regulation of emotion; and 3) constricted imaginal capacities. Several studies have investigated imaginal capacity in people with alexithymia. Nemiah et al (1977) reported that whereas control subjects increased their oxygen consumption when instructed to think various emotional thoughts, subjects with alexithymia showed no such increase in these conditions. Whereas imaginal capacity correlates with hypnotic susceptibility (Varga 2001), Frankel et al (1977) reported a high prevalence of alexithymia in subjects with low hypnotic susceptibility. Hyer et al (1990) studied the responses of posttraumatic stress disorder patients who were listening to accounts of their own traumatic experiences and found that the more alexithymic the subject was, the less his heart rate differed between the stressor period and the baseline. Friedlander et al (1997) compared the responses of people with alexithymia with those of people without it to an autogenic relaxation exercise with guided imagery; the former reported less enjoyment and poorer (less vivid) imagery during relaxation than did the latter. These studies suggest that people with high degrees of alexithymia (HDA) might have low imaginal capacities and show less physical reactivity during imagery with emotional contents; however, these studies relied on indirect methods to characterize the brain function of people with alexithymia.

Imagery can be defined as the manipulation of sensory information that comes from memory without information from actual sensory input (Cabeza and Nyberg 2000). The memory is

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subdivided into working memory, episodic memory, and semantic memory. Of these subcategories, the one most closely tied to the emotions of daily life is episodic memory, especially "autobiographical memory" (Rubin 1998). Because alexithymia is conceptualized as a multifaceted construct consisting of factors related logically to each other (Taylor et al 1997), the imagery disturbance of alexithymia is considered to be related to other factors, such as difficulty in identifying and describing feelings (i.e., in processing emotion). In fact, experimental studies suggest that imagery disturbance in subjects with alexithymia is related to emotion processing, as mentioned in the previous paragraph. Thus, we considered that subjects with HDA might have difficulty in retrieval of autobiographical memory. On the other hand, the restricted imaginal capacities of people with alexithymia have been considered to limit the extent to which individuals with HDA can modulate anxiety and other emotions by fantasy, dreams, interest, and play (Krystal 1988; Mightes and Cohen 1992). Thus, previous clinical reports have emphasized disturbances in imaging experiences that had not and were not going to occur, as well as past experiences. Furthermore, in examining the types of emotion that accompany imaging, the previous reports seem to have emphasized the difficulty that people with alexithymia have in imaging positive things to modulate negative emotions such as anxiety. So, we planned a functional magnetic resonance imaging (fMRI) study to directly investigate neural correlates of imagery disturbance in the subjects with HDA with the imagery task in which subjects recall affect-laden autobiographical memories or imagine affect-laden future episodes accompanied by positive (happy) or negative (sad) emotions.

Recent positron emission tomography (PET) and fMRI studies have suggested that episodic memory retrieval is associated with activation of the prefrontal, medial–temporal, medial parieto–occipital (posterior cingulate cortex [PCC], including the retrosplenial cortex and precuneus), lateral parietal, anterior cingulate, occipital, and cerebellar regions (Cabeza and Nyberg 2000). On the other hand, it has been reported that the retrieval of autobiographical memory, which is a kind of episodic memory, often activates the medial–frontal region and the left hippocampus and sometimes activates the medial parieto–occipital area (MPOA) (Maguire 2001). These studies suggested a relatively consistent activation of the prefrontal and medial–temporal cortices in episodic/autobiographical memory retrieval; however, there are also inconsistencies among studies of autobiographical memory retrieval, especially regarding the activation of the MPOA. Although several studies have reported the activation of this area (e.g., Maguire and Mummery 1999; Ryan et al 2001), a considerable number have reported no activation of this area (e.g., Conway et al 1999; Markowitsh et al 1997) during the retrieval of autobiographical memory. Meanwhile, emotional stimuli have been reported to consistently activate this area (Maddock 1999). Furthermore, whereas mental imagery is known to be a major component of episodic memory recall (Tulving 1983), MPOA in imagery domain studies seems to be specifically recruited whenever the generation of the mental image relies on the reactivation of a memorized percept (Ghaem et al 1997; Kosslyn et al 1993; Mellet et al 1995; Roland and Gulyas 1995). So, both episodic memory recall and imagery might share the MPOA as a common region. We considered that the inconsistencies concerning the activation of MPOA across studies might reflect not only differences among tasks but also individual differences in personality traits, in individual patterns of reactions to emotional stimuli, or in individual imaginal capacities such as alexithymia. We therefore studied brain activity during imagery in volunteers and investigated the relationship between this brain activity and the level of alexithymia, while paying attention to MPOA (PCC and precuneus; Brodmann's areas 7, 23, 29, 30, 31). We hypothesized that the activation of the MPOA varies with the 20-item Toronto Alexithymia Scale (TAS-20) score during imagery, especially during emotional imagery conditions.

Meanwhile, although no study to date has used neuroimaging techniques to investigate the relationship between brain activation during imagery and alexithymic characteristics, two neuroimaging studies of alexithymia have recently been conducted (Berthoz et al 2002; Kano et al 2003). These studies suggested that there was no difference in the limbic structure between subjects with alexithymia and those without, and that the impairment of anterior cingulate cortex (ACC) functioning might be associated with alexithymia. Moreover, the medial prefrontal cortex (MPFC), adjacent to the ACC, also was activated in numerous neuroimaging studies of emotion (Phan et al 2002) and was reported to be impaired in subjects with alexithymia (Berthoz et al 2002). So, we were also interested in whether the ACC (Brodmann's areas 24, 32, 33) and MPFC (the medial regions of Brodmann's areas 8, 9, 10, 11) are associated with imagery disturbance in subjects with alexithymia.

Methods and Materials

Subjects

We recruited 14 men and six women aged 20–30 years, who were right-handed, nonanxious, and nondepressed (on the basis of Hospital Anxiety and Depression Scale scores; Zigmond and Snaith 1983; Zigmond et al 1993) from among 38 male and 22 female volunteers according to their alexithymia scores on the Japanese version of the TAS-20. The volunteers were recruited through community announcements and were paid incentives corresponding to their transportation expenses. The TAS-20 is the most psychometrically valid and commonly used measurement of alexithymia (Bagby 1994a, 1994b), and the Japanese version also has high construct validity and reliability (Fukunishi et al 1997). It is a self-report questionnaire containing 20 items rated on a 5-point scale. A high score indicates HDA. In accordance with methods used by Berthoz et al (2002), 10 subjects (7 men and 3 women) with high ($\geq$56) TAS-20 scores were placed into an HDA group, and 10 subjects (7 men and 3 women) with lower ($\leq$ 44) scores, who were age- and handedness-matched to the HDA group, were placed into an LDA group. The subjects in the HDA and LDA groups were aged 25.9 $\pm$ 3.3 years and 23.7 $\pm$ 3.0 years, respectively (mean $\pm$ SD), and their TAS-20 scores were 61.9 $\pm$ 4.0 and 37.9 $\pm$ 3.9, respectively.

All subjects were identified as right-handed according to the Edinburgh inventory (Oldfield 1971). According to the self-reported responses, the subjects had no history of psychiatric, neurologic, or other major medical illness and had never been treated with a psychotropic medication. After the study was described completely to the subjects, written informed consent was obtained from all of them. This study was approved by the Institutional Review Board and the Ethics Committee of Hiroshima University Hospital, Japan. The subjects received course credit for their participation.

Experimental Design

We developed our task by modifying that used in the study by George et al (1995). Before the scanning session, each subject was asked to name specific events that, when imaged, would make him or her happy (one past and one future event) or sad (one past and one future event). Each subject was also asked to image a specific time when he or she was or would be emotionally neutral—that is, not experiencing any particular emotion (one past and one future event). As for the future events, the subjects were asked to imagine, in the greatest possible detail, specific events that they could realistically expect to occur. The researcher then reviewed each event to assess whether the emotion was appropriate (e.g., not a mixture of happiness and sadness or anger) to the type of event. Additional specific sensory stimuli were elicited that could possibly aid in imaging the event (e.g., the exact place where the subject was or would be at the peak moment of emotion or the clothing, time of year, sights, sounds, or smells associated with that moment). Finally, each subject was asked to supply key words that would simply represent each event (e.g., travel with friends, death of grandmother, brushing teeth).

We used a periodic design involving the presentation of an activation condition for 30 sec followed by a baseline condition for 18 sec. This cycle was repeated 18 times over the course of 864 sec. During the activation condition, subjects were cued by the visual presentation of Japanese words representing the six event conditions: "past happy" (PH), "past sad" (PS), "past neutral" (PN), "future happy" (FH), "future sad" (FS), and "future neutral" (FN); key words were also used to cue the subjects to generate imagery of each event. When the words were presented, the subjects were instructed to image each previously agreed-upon event to make themselves feel the emotions and senses that they would feel as if the past or future event was actually happening. Each word was presented for 30 sec. During the baseline condition (REST), the subjects were shown a cross symbol ("+") and instructed to see only that symbol, with no imagery internally. Each presentation of the symbol lasted 18 sec. During each trial, the words were projected to the center of the subject's field of view with a super video graphics array computer-controlled projection system. The order in which the activation conditions were presented was counterbalanced across the subjects. Each trial was started by presenting the cross symbol for 9 sec; this initial presentation was excluded from the analyses. For each event, each subject's ratings of the vividness of his or her imagery and the intensity of the emotion were recorded immediately after the scanning session. Two nongraduated visual analogue scales were used: one assessed the vividness of the imagery (range, 0–10), from imaging nothing to imaging extremely vividly; and the other assessed the intensity of emotion during the imagery (range, 0–10), from feeling nothing to feeling extremely intensely.

Image Acquisition

Functional magnetic resonance imaging was performed with a Magnex Eclipse 1.5-T Power Drive 250 (Shimadzu Medical Systems, Kyoto, Japan). A time-course series of 291 volumes was acquired with T2-weighted, gradient echo, echo planar imaging sequences. Each volume consisted of 28 slices, with a slice thickness of 4 mm with no gap, and entirely covered the cerebral and cerebellar cortices. The interval between successive acquisitions of the same image (TR) was 3000 msec, the echo time (TE) was 55 msec, and the flip angle was 90°. The field of view (FOV) was 256 mm, and the matrix size was 64×64, giving voxel dimensions of $4 \times 4 \times 4$ mm. Scan acquisition was synchronized to the onset of the trial. After functional scanning, structural scans were acquired with a T1-weighted gradient echo pulse sequence (TR = 12 msec; TE = 4.5 msec; flip angle = 20°; FOV = 256 mm; voxel dimensions of $1 \times 1 \times 1$ mm), which facilitated localization.

Analysis

Image processing and statistical analyses were carried out with Statistical Parametric Mapping (SPM99) software (Wellcome Department of Cognitive Neurology, London, United Kingdom) implemented in Matlab (Mathworks, Natick, Massachusetts). The first three volumes of the fMRI run were discarded because the magnetic resonance signal was unsteady. The remaining 288 volumes were used for the analysis. Images were corrected for motion and realigned with the first scan of the session, which served as the reference. For each subject, the T1 anatomic images were coregistered to the first functional images and aligned to a standard stereotaxic space, with the Montreal Neurological Institute (MNI) T1 template in SPM99. The calculated nonlinear transformation was applied to all functional images for spatial normalization. Finally, the functional magnetic resonance images were smoothed with a 10-mm full-width at half-maximum Gaussian filter.

The group analysis was performed at two levels. At the first level, each subject's signal time course was modeled with a delayed boxcar function convolved with a hemodynamic response function in the context of a general linear model. One contrast image per subject was created by contrasting each activation condition (PH, PS, PN, FH, FS, FN) with the baseline condition (REST) and by contrasting each emotional condition with the neutral condition. In the second step, with group analysis according to a random effect model that allows inference to the general source populations (Friston et al 1999), we first identified regions that showed significant responses during each activation condition (PH, PS, PN, FH, FS, FN) compared with the baseline condition (REST) and during each emotional condition compared with the neutral condition (PH > PN, PS > PN, FH > FN, FS > FN) in the HDA and LDA groups, with the one-sample t test. Next, the images were entered into a two-sample t test (to locate brain regions in which the two groups differed significantly) and into a regression analysis (to locate brain regions in which the magnitude of brain activation correlated significantly with the TAS-20 score). Although there were inequalities in the amount of data between the REST condition and the experimental conditions (6 vs. 10), SPM99 performed these analyses, correcting the inequalities of data size. The resulting set of voxel values for each contrast constituted an SPM (t) map. The SPM(t) maps were then interpreted by referring to the probabilistic behavior of Gaussian random fields. The data were thresholded at $p < .001$ uncorrected at the voxel level and at $p < .05$ corrected at the cluster level for regions about which there was no clear hypothesis. Moreover, for regions about which we had an a priori hypothesis (ACC, MPFC, and MPOA), the height and extent of thresholds were set to $p < .001$ uncorrected and $p < .05$ uncorrected, respectively (as justified by Friston 1997).

The x, y, and z coordinates provided by SPM, which were in the MNI brain space, were converted to the x, y, and z coordinates in Talairach and Tournoux's (TT) brain space (Talairach and Tournoux 1988) with the following formula: (TT-x = MNI-x $\times$ .88 − .8; TT-y = MNI-y $\times$ .97 − 3.32; TT-z = MNI-y $\times$ .05 + MNI-z $\times$ .88 − .44). Labels for brain activation foci were obtained in Talairach coordinates with Talairach Daemon software (Research Imaging Center, University of Texas, San Antonio, Texas), the accuracy of which is similar to that of neuroanatomic experts (Lancaster et al 2000).

The accuracy of the labeling of the areas given by this software was then confirmed by comparison with activation maps overlaid on MNI-normalized structural magnetic resonance images.

Results

Subjective Ratings

The *t* tests showed that the mean subjective ratings of the vividness of the imagery were higher in the LDA group than in the HDA group for the PH, PS, and FS conditions. On the other hand, the mean subjective ratings of the intensity of emotion during the imagery were higher in the LDA group than in the HDA group for the PS and FS conditions (Table 1). The examples of the events that subjects imaged during the imagery conditions were sea bathing, party with friends, travel abroad; death of grandmother, death of dog, loss of bag; brushing teeth, cleaning, going to school; honeymoon, playing with child, entrance to ideal occupation; death of mother, loneliness at work, failing to pass on to the next grade; and washing face, changing clothes, driving for PH, PS, PN, FH, FS, FN conditions, respectively. There were no significant differences between the groups in the mean subjective remoteness of the time when the imaged event occurred or would occur in any of the imagery conditions.

fMRI Results (Brain Activation During Imagery Conditions Within Groups)

In the LDA group, at the higher level of significance (height and extent thresholds, respectively, set to $p < .001$ and $p < .05$ corrected), there was significantly greater activation of the PCC in PH and FH than in REST and of the left superior frontal gyrus in PS compared with REST. Moreover, at the lower level of significance (height and extent thresholds, respectively, set to $p < .001$ and $p < .05$ uncorrected), the ACC and right precuneus were significantly more active in PN than in REST and in FH than in FN, respectively. In the HDA group, at the higher level of significance (height and extent thresholds, respectively, set to $p < .001$ and $p < .05$ corrected), there was significantly greater activation of the fusiform gyrus and cerebellum in PH, PN, and FH than in REST (Table 2).

fMRI Results (Comparison of Brain Activation Between Groups)

With the threshold of significance at $p < .001$ uncorrected at the voxel level and at $p < .05$ corrected at the cluster level, FH (FH compared with REST) induced less activation in the HDA subjects than in the LDA subjects in the bilateral PCC (Table 3, Figure 1). These were the only regions showing between-group differences at this level of significance.

Moreover, at the lower level of significance (height and extent thresholds, respectively, set to $p < .001$ and $p < .05$ uncorrected), PH compared with REST and FH compared with FN induced less PCC activation in the HDA group than in the LDA group (Table 3, Figures 2 and 3).

fMRI Results (Regression Analysis)

Regression analysis revealed a significant inverse correlation between the TAS-20 score and the magnitude of brain activation of the bilateral PCC in PH compared with REST (x, y, z = −6, −54, 9; area 30; *t* value 5.26; 1595 voxels; $r = -.846$; $p < .001$), in FH compared with REST (x, y, z = −8, −50, 9; area 30; *t* value 7.83; 1363 voxels; $r = -.810$; $p < .001$), and in FH compared with FN (x, y, z = 6, −62, 21; area 31; *t* value 6.52; 669 voxels; $r = -.812$; $p < .001$) at the higher level of significance (height and extent thresholds, respectively, set to $p < .001$ and $p < .05$ corrected). The Talairach coordinates presented in each parenthesis represents the coordinates in which the local maximum within the cluster was observed. No significant correlation was observed in any other investigated contrasts.

Discussion

As expected, the activation of the MPOA varied with the TAS-20 score (the degrees of alexithymia) during imagery. During FH imagery, the activation in the PCC was significantly lower in the HDA subjects than in the LDA subjects. Also in FH imagery, a significant inverse correlation was found between the TAS-20 score and the magnitude of PCC activation. These results support our hypothesis that the inconsistencies about the activation of MPOA across studies reflect individual differences in personality traits such as alexithymia. The variability of activation in this area according to alexithymic characteristics might explain why prior studies, which did not control for personality, reported various outcomes.

A qualitative comparison of the brain activation detected by one-sample *t* test in the two groups suggests other findings in addition to the intergroup difference in PCC activation. The LDA

Table 1. Subjective Ratings of Vividness of Imagery and Intensity of Emotion During Imagery

Imagery Condition	TAS-20 Group	Vividness of Imagery			Intensity of Emotion During Imagery		
		Mean	SD	*p*	Mean	SD	*p*
Past Happy	HDA	6.1	2.2	.007	6.0	1.8	.068
	LDA	8.3	.75		7.5	1.7	
Past Sad	HDA	4.6	2.7	.031	4.1	2.7	.009
	LDA	7.4	2.6		7.6	2.6	
Past Neutral	HDA	4.2	2.2	.052	2.3	1.9	.188
	LDA	6.3	2.3		3.8	2.8	
Future Happy	HDA	6.5	2.7	.133	5.9	2.7	.086
	LDA	8.1	1.9		7.8	1.8	
Future Sad	HDA	3.9	3.1	.003	3.7	2.8	.010
	LDA	7.7	1.8		7.0	2.4	
Future Neutral	HDA	4.5	2.2	.325	2.3	1.6	.321
	LDA	5.7	2.8		3.5	3.1	

Two nongraduated visual analogue scales were used (the vividness of imagery [imaging nothing to imaging extremely vividly] and the intensity of emotion during imagery [from feeling nothing to feeling extremely intense]). HDA, high degrees of alexithymia group: the subjects with a total 20-item Toronto Alexithymia Scale (TAS-20) score of ≥56; LDA, low degrees of alexithymia group: the subjects with a total TAS-20 score of ≤44; *p* = value of *t* test.

Table 2. Brain Regions Showing Significant Activation During Imagery Task

				Talairach Coordinates[b]		
	k[a]	BA	*t* score	x	y	z
Low Degrees of Alexithymia Group						
Past happy > REST						
Left posterior cingulate gyrus	325[c]	30	6.93	−4	−54	8
Past sad > REST						
Left superior frontal gyrus	229[c]	8	9.22	−4	22	48
Past neutral > REST						
Left anterior cingulate gyrus	128[d]	24	6.85	−3	4	47
Future happy > REST						
Left posterior cingulate gyrus	528[c]	30	9.85	−6	−54	9
Right posterior cingulate gyrus		30	6.25	6	−50	17
Right posterior cingulate gyrus		23	5.56	4	−58	14
Future happy > future neutral						
Right precuneus	97[d]	31	8.35	6	−62	25
High Degrees of Alexithymia Group						
Past happy > REST						
Left cerebellum anterior lobe	369[c]		10.54	−32	−48	−22
Left fusiform gyrus		37	7.81	−36	−60	−19
Left cerebellum posterior lobe			6.63	−31	−63	−25
Past neutral > REST						
Right cerebellum posterior lobe	398[c]		10.48	38	−73	−20
Right fusiform gyrus		18	6.40	24	−85	−19
Right cerebellum posterior lobe			5.75	19	−75	−22
Left fusiform gyrus[c]	179[c]	18	5.75	−20	−85	−20
Left cerebellum posterior lobe			4.76	−36	−73	−23
Future Happy > REST						
Left cerebellum anterior lobe[c]	566[c]		9.25	−36	−40	−30
Left cerebellum posterior lobe			6.78	−29	−75	−24
Left fusiform gyrus		19	5.81	−41	−75	−11

BA, Brodmann's Area; REST, during a rest condition.
[a]Number of voxels in cluster.
[b]Coordinates of the local points of maximal activation included in the cluster.
[c]Differences were significant at $p < .001$ (uncorrected) for voxel level and $p < .05$ (corrected) for cluster extent.
[d]Differences were significant at $p < .001$ (uncorrected) for voxel level and $p < .05$ (uncorrected) for cluster extent.

group showed significantly greater activity of the MPFC, which also extends to the ACC, during PS imagery, but the HDA group did not. This is partially in line with the ACC deficit model of alexithymia (Berthoz et al 2002; Lane et al 1997). There seems to be greater activation in the fusiform gyrus and cerebellum in the HDA group than in the LDA group, which might reflect visual attention (Allen et al 1997; Mangun et al 1998); however, such a comparison does not allow us to measure voxel-by-voxel differences in the magnitude of activation between the groups. A more formal test of the null hypothesis of no between-group difference in activation was provided by a two-sample *t* test at each voxel. A direct comparison between the groups showed significantly lower brain activation in the PCC of the HDA group than in that of the LDA group during FH imagery.

Table 3. Brain Regions Showing Significant Activation in Nonalexithymic Group Compared with Alexithymic Group During Imagery Task

				Talairach Coordinates[b]		
Area	k[a]	BA	*t* score	x	y	z
Past Happy > REST						
Left posterior cingulate gyrus	220[c]	30	4.53	−4	−56	7
Left posterior cingulate gyrus		31	4.23	−1	−60	25
Left posterior cingulate gyrus		23	3.93	−8	−58	18
Future Happy > REST						
Left posterior cingulate gyrus	1150[d]	30	6.97	−4	22	48
Right posterior cingulate gyrus		31	5.61	8	−54	25
Future Happy > Future Neutral						
Right posterior cingulate gyrus	277[c]	31	5.58	6	−59	23

BA, Brodmann's Area; REST, during a rest condition.
[a]Number of voxels in cluster.
[b]Coordinates of the local points of maximal activation included in the cluster.
[c]Differences were significant at $p < .001$ (uncorrected) for voxel level and $p < .05$ (uncorrected) for cluster extent.
[d]Differences were significant at $p < .001$ (uncorrected) for voxel level and $p < .05$ (corrected) for cluster extent.

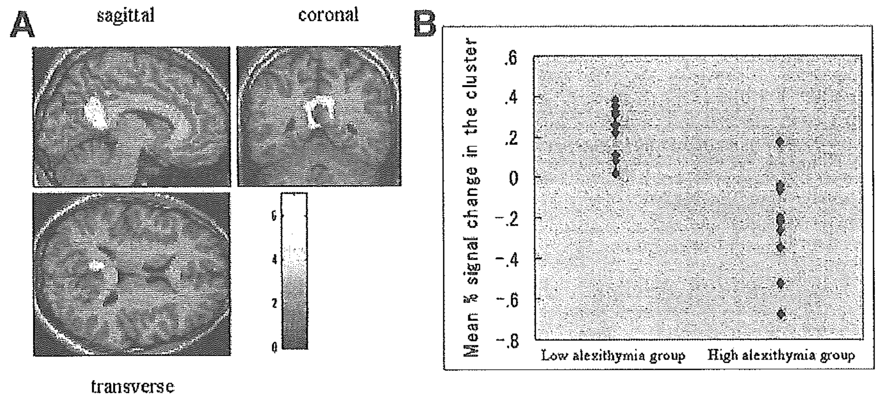

Figure 1. The region significantly less activated in the high degree of alexithymia group compared with the low degree of alexithymia group **(A)** (thresholded at $p < .001$ uncorrected at the voxel level and at $p < .05$ corrected at the cluster level for significance) and the associated adjusted responses for the between-group comparisons **(B)** (mean percentages of signal changes in the cluster) in the future happy imagery condition compared with the REST condition.

There is considerable evidence that the PCC has functions related to episodic memory (Andreasen et al 1995; Grasby et al 1993; Henson et al 1999; Maddock et al 2001). A review of functional imaging studies showed that the caudal part of the PCC was the cortical region most consistently activated by emotional stimuli compared with nominally matched, emotionally neutral stimuli (Maddock 1999). Moreover, it has been speculated that the PCC plays a role in the modulation of memory by emotionally arousing stimuli (Maddock 1999).

The PCC has strong reciprocal connections with regions engaged in memory processing, such as medial–temporal lobe memory structures and the thalamus (Bentovoglio et al 1993; Suzuki and Amaral 1994). It is also reciprocally connected to regions engaged in emotional processing, such as the ACC and the orbitofrontal cortex (Goldman-Rakic et al 1984; Musil and Olsen 1993; Van Hoesen et al 1993). These neuroanatomic findings also suggest that the PCC is involved in both memory and emotion. It is especially interesting that the ACC and PCC are connected reciprocally, whereas recent neuroimaging studies have suggested that the ACC has neural correlates of alexithymia (Berthoz et al 2002 ; Kano et al 2003). Although in our imagery task the activation of the ACC is not related to the degrees of alexithymia, the disturbance of both the ACC and PCC might comprise the various features of alexithymia having interaction.

One possible explanation for the difference between the groups in brain activation during FH imagery is that people with HDA can construct FH imagery, but in a different way than people with LDA do. It is known that the primary and secondary sensory cortices (such as the visual or auditory cortex) are activated during imagery (Cabeza and Nyberg 2000; Shergill et al 2001). But the activation of these areas did not significantly differ between subjects with HDA and subjects with LDA in any of the imagery conditions. So, we can't consider that people with HDA are less imaginal, at least on the sensory level. Together with the function of the PCC mentioned in the previous paragraph, our results indicate that subjects with LDA use memories of past emotional events to create FH imagery, but subjects with HDA rarely or never do. On the other hand, the evaluation of an emotionally salient stimulus engages a variety of cognitive processes, many of which have been considered to rely on episodic-memory retrieval (Pratto 1994). Another explanation is that the activation of the PCC is associated with the evaluation of emotional stimuli that depend on episodic memories, and subjects with HDA evaluate their FH imagery as less exciting than do subjects with LDA.

Moreover, the blood oxygen level–dependent response presented during PH and FH imagery compared with REST suggests a deactivation of the PCC in the HDA group. Recently, functional imaging studies have shown that certain brain regions, including the PCC, consistently show greater activity during resting states than during cognitive tasks. Furthermore, it has been hypothesized that these brain regions constitute a default mode network (Greicius et al 2003; Raichle et al 2001). Raichle et al (2001) speculated that in the default state, information broadly arising in the external and internal milieus is gathered and evaluated and that when focused attention is required, activity within these areas might be attenuated. The HDA group demonstrated significant activation in the fusiform gyrus and not in the PCC, whereas the LDA group demonstrated the reverse pattern of activation in the one-sample *t* test. The fusiform gyrus is related to visual attention (e.g., Mangun et al 1998). Considering the external oriented cognitive style of alexithymia (Nemiah et al 1976; Taylor et al 1997), we speculated that because the HDA subjects might have been more engaged in visual attention to displayed cue letters than in the retrieval of episodic memory, deactivation of the PCC might have been greater in subjects with HDA than in

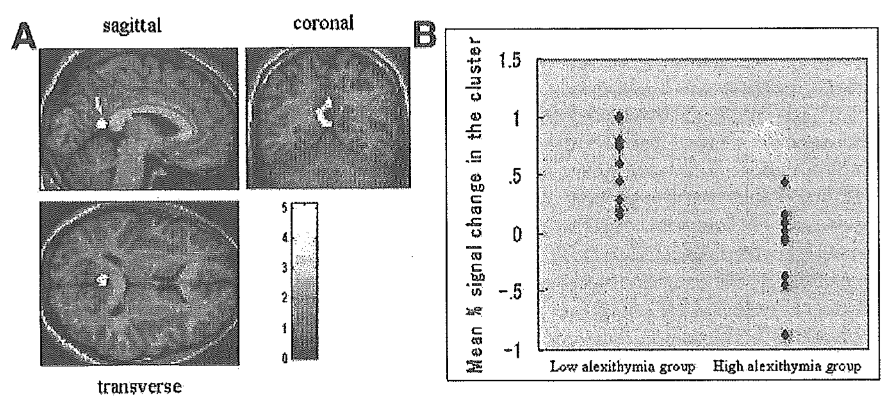

Figure 2. The region significantly less activated in the high degree of alexithymia group compared with the low degree of alexithymia group **(A)** (thresholded at $p < .001$ uncorrected at the voxel level and at $p < .05$ corrected at the cluster level for significance) and the associated adjusted responses for the between-group comparisons **(B)** (mean percentages of signal changes in the cluster) in the past happy imagery condition compared with the REST condition.

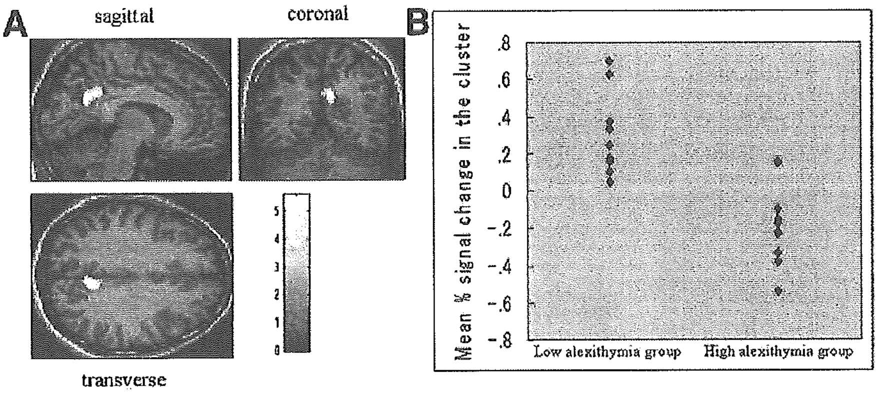

Figure 3. The region significantly less activated in the high degree of alexithymia group compared with the low degree of alexithymia group (**A**) (thresholded at $p < .001$ uncorrected at the voxel level and at $p < .05$ corrected at the cluster level for significance) and the associated adjusted responses for the between-group comparisons (**B**) (mean percentages of signal changes in the cluster) in the future happy imagery condition compared with the future neutral condition.

those with LDA, and the deactivation might likely have contributed to the between-group results.

At a lower level of significance, the PCC was less active in the HDA group than in the LDA group during the PH imagery condition compared with REST. These results, together with the result of the group comparison in FH > REST and FH > FN contrasts, suggest that it is difficult for individuals with HDA to imagine happy events. Our results support the speculation of previous researchers that the restricted imaginal capacities of people with alexithymia limit the extent to which individuals with HDA can modulate negative emotions by imaginative activities that have positive connotations, such as fantasy, dreams, interest, and play (Krystal 1988; Mightes and Cohen 1992). According to Bagby et al (1994b), within the correlation between the TAS-20 and the subscales of extraversion, alexithymia was associated significantly and negatively with the tendency to experience positive emotions. Our data support their idea that alexithymia is associated with a low proneness to experience positive emotions; however, in the PH > PN contrast, there was no significant difference between the groups. Our subjects usually chose daily acts as PN events, and these events were often more recent and more familiar than PH events. Meanwhile, the recency (Piefke et al 2003) and familiarity (Kosaka et al 2003) of autobiographical memory seem to increase PCC activity. The recency and familiarity of PN events might have confounded and diminished the difference between PH and PN conditions in the activation of PCC. To reach a conclusion about the difference in happy imagery between these two groups, further studies controlling these factors are needed.

There is another possible explanation for the groups having differed significantly only in the FH imagery condition. That is, our results might support the speculation of previous researchers that individuals with HDA find it hard to imagine something that they have never experienced. Clinical observations suggest that individuals with HDA seem to be swayed too much by minutiae of superficial "external" things and cannot imagine invisible, intangible things, such as mental content or the future (Marty and de M'Uzan 1963; Taylor et al 1997). They can recall intact their past experience, but they cannot process their experience or imagine events they have never experienced. Our results, however, suggested that the groups did not differ from each other in the FS and FN imagery conditions compared with REST. For FN events, our subjects usually chose daily acts that they had already experienced. We consider that this might explain why the groups did not differ in the FN condition. Moreover, although we did not discuss this in the Results section, the PCC was less active in the HDA group than in the LDA group during FS compared with REST and in FS compared with FN (number of voxels in cluster: 96 and 97, respectively) when the threshold was set at an uncorrected $p < .001$ at the voxel level in an a priori hypothesized region (Elliott et al 2000). On the other hand, there was no difference between the groups in PCC activation during PS compared with REST or during PS compared with PN, even at this lower threshold.

Meanwhile, discrepancies were observed between brain activation and subjective rating results. In general, the different responses to sad and happy imagery conditions were as follows. There were no significant differences in brain activation between the HDA and LDA groups in sad imagery conditions, but there were such differences in subjective ratings between the groups. For happy imagery conditions, on the other hand, the opposite was found: there were no significant differences between the groups in subjective ratings, but such differences were found in brain activation. These results seem to be paradoxical. We speculate that there were no significant differences between the groups in brain activation during sad imagery in the scan, but there might have been differences between the groups in brain activation when the subjects reported the subjective ratings after the scan. Several investigators suggested that alexithymia might involve a "decoupling" of the subjective and physiologic components of the emotional response to stressful stimuli—that is, a higher degree of alexithymia was associated with fewer subjective responses and greater physiologic reactivity (Martin and Pihl 1986; Papciak et al 1985). The results of these previous studies might suggest that subjects with alexithymia have deficiencies in conscious awareness of emotion. In previous neuroimaging studies of alexithymia, the ACC and MPFC have been reported as the neural correlates of conscious awareness of emotion. Studies of decoupling theory have focused exclusively on negative emotion. Berthoz et al (2002) reported that the activation of the ACC/MPFC was lower during negative stimuli and higher during positive stimuli in people with alexithymia than in people without it. Kano et al (2003) found that although the activation of ACC was lower in subjects with alexithymia than in those without it in response to an angry face, there was no difference between groups in the ACC activation in response to a happy face. These results also suggest that "decoupling" occurs in relation to negative emotion but not to positive emotion. If so, when brain activations differ between HDA and LDA subjects during happy imagery, subjective ratings should also differ between HDA and LDA subjects. In this study, however, no significant differences were found in subjective ratings of intensity of emotion during the happy imagery conditions. This might have been influenced by the difference in effect size between brain activation and subjective rating. Neuroimaging is a much more powerful tool than traditional behavior methods for detecting subtle relationships between two variables (Canli and Amin 2002). In fact, in spite of the small sample size, subjective ratings of the intensity of emotion tended to be higher in the LDA group than in the HDA group for PH and FH, although not significantly.

On the other hand, to our surprise, there was no significant difference in the activation of the ACC/MPFC region between the groups for which we had an a priori hypothesis. The small sample size might explain the absence of such a difference. In fact, a qualitative comparison of brain activation by the one-sample t test suggested that the LDA group had significantly greater activity than the HDA group in the ACC/MPFC region during PS imagery. And if the subjects with HDA had poorer imaginal capacity than those with LDA, the activation of this area during the control condition, that is, REST condition (during which free recall could occur) and the neutral imagery condition, could be greater in the LDA group. In fact, ACC activation in the LDA group was significantly greater in PN than in REST in this study, whereas no ACC activation was found in the HDA group during PN. Furthermore, the brain activity detected by the one-sample t test was poorer than it was in George et al (1995), which showed bilateral limbic and paralimbic activation, including that of the ACC/MPFC. We considered that factors such as the shorter time interval among tasks, which might have resulted in mutual influence, or the shorter duration of imagery generation in this study than in the PET study of George et al (1995) might have influenced these differences in results between the two studies. Next, no difference between the groups was observed in the limbic structure (i.e., the amygdala, the hippocampal formation, and the hypothalamus), which plays a central role in emotional responses to simple perceptual aspects of stimuli. This finding is consistent with previous studies that found that the limbic area is not associated with alexithymia (Berthoz et al 2002; Kano et al 2003). Furthermore, no difference between the groups was observed in the insular cortex or in the orbitofrontal cortex; these cortices have been discussed in numerous neuroimaging studies about emotional recall/imagery (Phan et al 2002) and general emotional processing (Bechara et al 2000). This absence of activity might be attributable to the imaging method used. Whereas activation of these regions has been reported mainly in PET studies, it is known to be difficult to detect the activation of these areas by fMRI for susceptibility artifact (Ojemann et al 1997). Thus, our study cannot conclude that there is no relationship between emotional imagery disturbance related to alexithymia and these important brain regions, except for the PCC. Further studies considering these points are needed.

There are some limitations to this study. First, because of the small sample size, we might have failed to identify activation differences between HDA and LDA in other imagery conditions. Second, the sensory modalities of imagery (e.g., auditory, olfactory) involved in each event, in addition to visual sensation, differed not only between subjects but within each subject. This might have been a confounding factor, although it is difficult to control these factors because autobiographical memory is usually multimodal and because imagery, in which sensory modality is restricted, is different from daily experiences, especially emotional ones. Third, the subjects' retrospective ratings of their imagery and intensity of emotion might have been inaccurate, especially if the subjects with HDA had trouble with episodic memory. Finally, some subjects might have been unable to refrain from imagery and emotion or other cognitive activity during the rest periods. The level of each subject's cognitive activity during these rest periods might also be a confounding factor. Further studies considering these points are needed.

In conclusion, the present study revealed that the reduced activation of PCC in subjects with HDA was associated with the disturbance of FH imagery. The disturbance of FH imagery can reduce motivation and hope, and it might be an important factor in the construction of deficits in the emotional regulation of alexithymia. We suggest that PCC might play a crucial role in alexithymia-related imagery disturbance. Although this study has several limitations, the present results are meaningful as the first report to demonstrate neural correlates of imagery disturbance in alexithymia.

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Distorted Images of One's Own Body Activates the Prefrontal Cortex and Limbic/Paralimbic System in Young Women: A Functional Magnetic Resonance Imaging Study

Mitsuhaya Kurosaki, Naoko Shirao, Hidehisa Yamashita, Yasumasa Okamoto, and Shigeto Yamawaki

Background: *Our aim was to study the gender differences in brain activation upon viewing visual stimuli of distorted images of one's own body.*

Methods: *We performed functional magnetic resonance imaging on 11 healthy young men and 11 healthy young women using the "body image tasks" which consisted of fat, real, and thin shapes of the subject's own body.*

Results: *Comparison of the brain activation upon performing the fat-image task versus real-image task showed significant activation of the bilateral prefrontal cortex and left parahippocampal area including the amygdala in the women, and significant activation of the right occipital lobe including the primary and secondary visual cortices in the men. Comparison of brain activation upon performing the thin-image task versus real-image task showed significant activation of the left prefrontal cortex, left limbic area including the cingulate gyrus and paralimbic area including the insula in women, and significant activation of the occipital lobe including the left primary and secondary visual cortices in men.*

Conclusions: *These results suggest that women tend to perceive distorted images of their own bodies by complex cognitive processing of emotion, whereas men tend to perceive distorted images of their own bodies by object visual processing and spatial visual processing.*

Key Words: Body image, functional MRI, prefrontal cortex, amygdala, gender differences, eating disorders

Young women not only are more concerned about body shape and size, but also more harshly judge their own body shape and size than men. Eating disorders (EDs) are one category of psychiatric illness having a larger incidence among women than among men; women are approximately 10 times more likely to experience a lifetime episode of ED than men (Weissman et al 1995). One possible cause of this gender difference in susceptibility to ED may be that the cognitive processing of visual information about body image differs between men and women, and women are more sensitive to information about body image than men.

Several functional magnetic resonance imaging (fMRI) studies on EDs have investigated brain activation upon presentation of images of foods or body shape. In fMRI studies, women with an ED showed an activation of the limbic/paralimbic system and medial prefrontal cortex (PFC) upon viewing images of high caloric foods (Ellison et al 1998; Uher et al 2003, 2004). Functional MRI studies in which female subjects were shown their own distorted images indicated that women with ED showed activation of the limbic system, PFC and the parietal lobe (Seeger et al 2002; Wagner et al 2003). A few neuroimaging studies specifically investigated gender differences in brain activation. Shirao et al (2005) reported that in an emotional decision task involving unpleasant word stimuli about body image, men showed increased PFC activation whereas women showed only amygdala activation.

However, there has been no study on gender differences in the pattern of brain activation upon viewing distorted images of one's own body. We hypothesized that the differences in brain activation while processing body image stimuli between the two genders involve a discrepancy in activation of the limbic area including the amygdala, paralimbic area and prefrontal cortex. We used fMRI to investigate the brain activity of young men and young women while they were engaged in a "body image task" using distorted images and real images of the subject's own body.

Methods and Materials

Subjects

Eleven women and 11 men participated in this study. All of the subjects were right-handed as determined by the Edinburgh Handedness Inventory (Oldfield 1971). Subjects were asked to fill out a written questionnaire regarding his/her own medical history. According to the self-reported responses, the subjects had no history of psychiatric, neurological, or other medical illness, and had never been treated with a psychotropic medication. We limited the female subjects in this study to women between the ages of 20 and 30 years, since young women even in the nonclinical population are often sensitive to body image and since ED commonly occurs in young women. To eliminate age-related effects, the subjects of the two genders were age-matched. To minimize the effect of the body shape proportion of the subjects in the two groups, we matched the body mass index (BMI) of the male and female subjects. Also, to minimize the effects of eating behavior, body image distortion and psychological features of the subjects in the two groups, we matched the score of the total Eating Disorder Inventory-2 (EDI-2) of the male and female subjects. The Clinical characteristics of the subjects

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Table 1. Characteristics of the Subjects

	Women (n = 11)	Men (n = 11)	t-value	p-value
Age (y)	24.5 ± 3.4	24.8 ± 3.1	−.194	.8478
Range	21–30	20–30		
BMI (kg/m^2)	19.9 ± 1.3	20.8 ± 1.4	−1.533	.1409
Range	18.1–22.8	18.5–23.8		
EDI-2	45.5 ± 21.4	35.8 ± 14.5	1.247	.2268
Range	21–89	8–60		

p-values were obtained with the unpaired t-test. EDI-2, Eating Disorder Inventory-2; BMI, body mass index.

are summarized in Table 1. The scores on the subscales of EDI-2 are summarized in Table 2. The protocol of this study was approved by the Ethics Committee of Hiroshima University School of Medicine. After a complete description of the study was provided to the subjects, written informed consent was obtained.

Paradigm

The aim of this study was to investigate the neuronal processing of visual stimulation of fat or thin body image. We developed and created the paradigm, which consisted of a pair of distorted body image and real image, so that the subjects would recognize their own body image on comparison of two images. We thought that it was possible to elucidate the cognitive and emotional processing of visual stimulation of fat or thin body image by analyzing fMRI data on performing our paradigm.

Before the fMRI examination, we took digital photographs of each subject's whole body against a monotonous, light-colored background. The subject wore a white T-shirt and blue jeans, and was in the standing position. We changed the width of the image of the individual from −25 to +25% of the width in the original image by using Paint Shop Pro Version 8.02 (Jasc Software, Inc., Eden Prairie, Minnesota), to obtain ten distorted images with different degrees of thinness or fatness. For each subject, we used the following images of the subject: undistorted original image, fat-body images (width at +5, +10, +15, +20, or +25% of the width of the individual in the original image), undistorted original image with a red cross on the body, and thin-body images (width at −5, −10, −15, −20, or −25% of the width of the individual in the original image).

Using these distorted images and original images, we created image sets which consisted of three types of pairs of images: 1) pairs of a fat-body-image (gaining weight image) and real-image (undistorted original image); 2) pairs of the real-image and the real-image with a red cross; and 3) pairs of a thin-body-image (losing weight image) and real-image (Figure 1A). We used the block-designed fMRI paradigm which consisted of three different blocks of tasks: fat-image task, real-image task, thin-image task (Figure 1B). Each block began with a 3-sec cue indicating whether the block consisted of the fat-image task, real-image task, or thin-image task. Five image sets were presented in each block. Each image set was shown for 5 sec with a 1-sec inter-stimulus-interval (ISI). Three different blocks were presented in one cycle. Our paradigm consisted of three cycles (Figure 1C). The blood oxygen level-dependent (BOLD) response was recorded during the three blocks of fat-image task, real-image task, or thin-image task. During each ISI, a fixation-cross placed centrally on the screen replaced the image set. Baseline functional magnetic resonance images were obtained during a 9-sec interval prior to the first block of trials, during which the subject viewed a centrally placed fixation-cross. During each trial, the image set was projected to the center of the subject's field of view via a super video graphics array (SVGA) computer-controlled projection system. The timing of presentation of image sets was controlled by Presentation Software Version .76 (Neurobehavioral Systems, Inc., San Francisco, California) and the image sets were presented in random order.

Immediately before fMRI scanning was begun, the subject was given 2 practice trials (1 fat-image task and 1 real-image task). In the practice trials, sample image sets of a girl were presented instead of pictures of the subject (Figure 1A). The subject was given instructions before the practice trials. In the fat-image tasks and thin-image tasks, the subject was instructed to select the more unpleasant image from each image set. In the real-image tasks, the subject was instructed to select the image with the red cross on the body. The subject was asked to respond by pressing one of two buttons on a response pad in the MRI scanner.

MRI Acquisition and Processing

Functional MRI of the brain was performed with a MAGNEX ECLIPSE 1.5T Power Drive 250 (Shimadzu Medical Systems, Kyoto, Japan). A time-course series of 102 volumes was acquired with T2*-weighted, gradient echo, echo planar imaging (EPI) sequences. Each volume consisted of 28 slices, and the thickness of each slice was 4.0 mm with no gap, encompassing the entire brain. The interval between two successive acquisitions of the same image (TR) was 3000 msec, the echo time (TE) was 55 msec, and the flip angle was 90°. The field of view was 256 mm

Table 2. Scores of the Subscales of EDI-2

	Total	Drive for Thinness	Body Dissatisfaction	Bulimia	Ineffectiveness	Perfectionism
Women	45.5	4.09	9.18	1.82	5.09	.45
Men	35.8	1.27	4.91	.73	4.73	3.73
	Interpersonal Distrust	**Interoceptive Awareness**	**Maturity Fears**	**Asceticism**	**Impulse Regulation**	**Social Insecurity**
Women	4.18	3.91	2.45	3.18	2.73	3.55
Men	4.82	1.45	4.00	4.64	.82	5.82

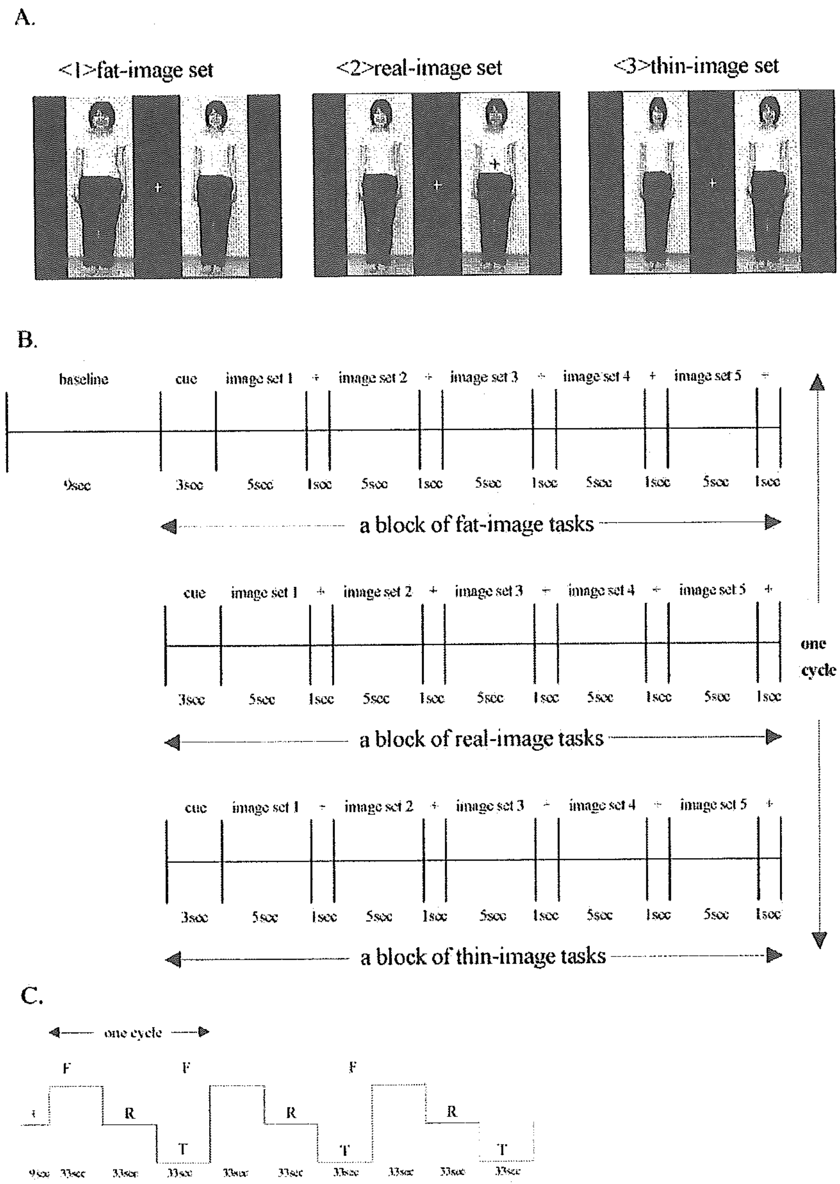

Figure 1. The design of the paradigm used in this study. **(A)** Sample image sets of the subject's own body that were presented to the subject. **(B)** Blocks of fat-image, real-image and thin-image tasks were preceded by baseline. Each block began with a cue indicating "fat," "real" or "thin." The subject was instructed to select the more unpleasant image from each image set for the fat-image task or thin-image task, and to select the image with a red cross on the body for the real-image task, by pressing one of two buttons. **(C)** Overview of block-designed stimulus presentation paradigm for the tasks. Nine alternating blocks of fat-body image (F), real-body image (R), and thin-body image (T) tasks were presented successively. The total scan time was 306 sec (5 min and 6 sec), while yielding 102 images of 28 axial slices (2856 images).

and the matrix size was 64 × 64, giving voxel dimensions of 4.0 × 4.0 × 4.0 mm. After functional MRI scanning, structural scans were acquired using a Tl-weighted gradient echo pulse sequence (TR = 12 msec; TE = 4.5 msec; Flip angle = 20°; field of view (FOV) = 256 mm; voxel dimensions of 1.0 × 1.0 × 1.0 mm), and they facilitated localization and coregistration of the functional data.

Data Analysis

Image processing and statistical analysis were performed using Statistical Parametric Mapping 99 (SPM99) software (Wellcome Department of Cognitive Neurology, London, United Kingdom) implemented in Matlab (Mathworks, Inc., Natick, Massachusetts). The first two volumes of the fMRI run (pre-task period) were discarded because the magnetization was unsteady, and the remaining 100 volumes were used for the statistical analysis. Images were corrected for motion and realigned with the first scan of the session, which served as the reference. The T1 anatomical images were coregistered to the first functional image in each subject and aligned to a standard stereotaxic space, using the Montreal Neurological Institute (MNI) T1 template in SPM99. The calculated nonlinear transformation was applied to all functional images for spatial normalization. Finally, the functional MR images were smoothed with a 12-mm full-width, half-maximum (FWHM) Gaussian filter.

Using group analysis according to a random effect model that allowed inference to the general population (Friston et al 1999), we first identified brain regions that showed a significant response to image sets containing a distorted body image in comparison with the response to image sets containing two real body images among the female subjects and among the male subjects, as brain areas related to the cognition of body image stimuli in women and men, respectively. Next, we directly compared the activation of the entire brain of the subjects of each gender, using the two-sample Student's *t*-test. The resulting set of voxel values for each contrast constituted an SPM {T} map. The

SPM {T} maps were then interpreted by referring to the probabilistic behavior of Gaussian random fields. The data were initially thresholded at $p < .001$ uncorrected at the voxel level, and regions about which we had an a priori hypothesis were reported at this threshold (Elliott et al 2000). For regions about which there was no clear a priori hypothesis, a more stringent threshold of $p < .05$ corrected at the cluster level for multiple comparisons was used. Only regions that survived at this threshold were reported.

The x-, y- and z-coordinates provided by SPM, which were in MNI brain space, were converted to the x-, y-, and z-coordinates in Talairach and Tournoux's (TT) brain space (Talairach and Tournoux 1988) using the following formula: {TT-x = MNI−x * .88 − .8; TT−y = MNI−y * .97 − 3.32; TT−z = MNI−y * .05 + MNI−z * .88 − .44}. Labels for brain activation foci were obtained in Talairach coordinates using the Talairach Daemon software (Research Imaging Center, University of Texas, San Antonio, Texas), which provides accuracy similar to that of neuroanatomical experts (Lancaster et al 2000). The labeling of areas given by this software was then confirmed by comparison with activation maps overlaid on MNI-normalized structural MR images.

Results

Comparison of brain activation upon performing the fat-image task versus the real-image task showed significant activation of the bilateral prefrontal cortex (PFC) (Brodmann area (BA) 13, 47, 9), the left limbic area including the amygdala, and the right cerebellum in the women, and significant activation of the right occipital lobe including the primary and secondary visual cortices (BA 17, 18), the right temporal lobe and parietal lobe, and the left cerebellum in the men while performing the fat-image task.

Comparison of brain activation upon performing the thin-image task versus the real-image task showed significant activation of the left PFC (BA 32, 13), the left limbic area including the cingulate gyrus, the paralimbic area including the insula, and the left cerebellum in the women, and significant activation of the occipital lobe including the left primary and secondary visual cortices (BA 17, 18, 19), the temporal lobe including the bilateral fusiform gyrus, and the right parietal lobe in the men while performing the thin-image task.

Regarding the behavior of the subjects, on each fat-image task, the subjects in both genders tended to select the fat image as more unpleasant image and the women tended to select the fat image more frequently than did men (see Figure 2; Tables 3 and 4).

Discussion

In the present study, upon performing the fat-image task, the PFC and limbic/paralimbic lobe were activated in the women but not in the men, and the dorsal and ventral pathways of the visual system in the occipital, temporal and parietal lobes were activated in the men but not in the women. Our data are the first to demonstrate clear gender differences in brain activation pattern when men and women are confronted with their own distorted body image. These results suggest that the gender differences in brain activation pattern may explain the differences in cognition of distorted body image.

It has been suggested that the amygdala is involved in fear conditioning (Buchel et al 2000; LaBar et al 1998; LeDoux et al 2000; Morris et al 1998), in the recognition of fearful facial expressions (Adolphs et al 1995, 1999), and in evocation of fearful emotional responses from direct stimulation (Halgren et al

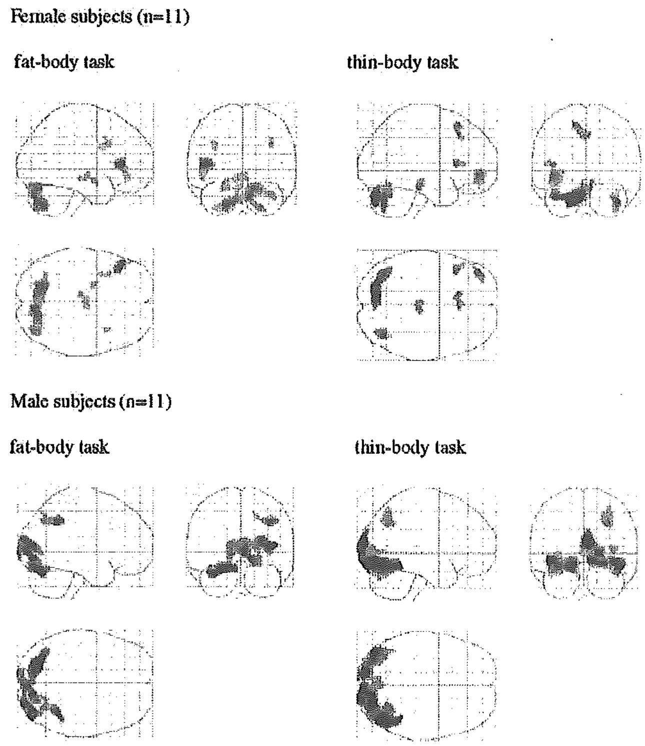

Figure 2. Differences in brain activation pattern between the two genders upon comparison of brain activation while performing the fat-body task and thin-body task. Three-dimensional "look-through" projections of statistical parametric maps of the brain regions are shown. One-sample Student's *t*-test; corrected $p < .05$ at the cluster level; $n = 11$; $df = 10$.

1978). Using fMRI, Ellison et al (1998) found that adult female anorectic patients, when viewing pictures of high-calorie drinks, had increased signal changes in the left amygdala-hippocampal region. They discussed that visual images of high-calorie food are fearful stimuli for patients with anorexia nervosa (AN). An fMRI study on brain reaction to distorted body image reported that female AN patients showed activation of the right amygdala (Seeger et al 2002). Our finding in the present study that the amygdala was activated in the female subjects upon viewing one's own fat body image suggested that a fat shape of her own body was interpreted as fearful information not only in patients with ED, but also in healthy women.

Previous studies suggested that the anterior cingulate gyrus is involved in attention tasks (Casey et al 1997), and in self-monitoring, conflict-resolution, and reward-based decision making (Bush et al 2002; Carter et al 1998; Devinsky et al 1995). Functional MRI studies in female AN patients revealed that the anterior cingulate gyrus was activated when the subjects viewed food stimuli or distorted body images (Ellison et al 1998; Uher et al 2003; Wagner et al 2003). Our finding that the anterior cingulate (BA 32) was activated upon viewing the thin body image only in the women indicates that the attention network was activated in the women and suggests that women tend to perceive their own body image with attentional and self-monitoring processes.

An fMRI study reported that the dorsolateral prefrontal cortex (DLPFC) and orbitofrontal cortex (OFC) are essential for volitional regulation of emotional impulses mediated by limbic/paralimbic structures (Lévesque et al 2003). The medial PFC (MPFC) has connections to limbic/paralimbic structures and

Table 3. Relative Increases in Brain Activity Associated with the Distorted-Body-Image Task Compared with the Real-Image Task

	Cluster	BA	t-Score	x	y	z
Female subjects (n = 11)						
Fat > Real						
Left inferior frontal gyrus[a]	330	13	13.12	−40	26	6
Left middle frontal gyrus[a]		47	4.68	−45	34	−6
Right cerebellum	1456		8.93	6	−79	−34
Right cerebellum			8.00	12	−77	−24
Right inferior frontal gyrus	44	9	5.84	31	10	28
Left amygdala	32		5.42	−20	−3	−15
Left middle frontal gyrus	64	9	4.99	−31	12	29
Left precentral gyrus		6	4.59	−31	3	25
Thin > Real						
Left cerebellum	1028		8.72	−17	−79	−38
Left cerebellum			8.69	−22	−79	−33
Left cerebellum			7.67	−8	−77	−31
Left superior frontal gyrus	169	6	5.81	−13	20	50
Left cingulate gyrus		32	5.31	−1	20	39
Left cingulate gyrus		32	5.05	−8	18	43
Left insula	90	13	5.78	−38	16	8
Left inferior frontal gyrus		13	4.69	−45	26	8
Left inferior frontal gyrus	279	10	5.60	−36	43	−2
Male Subjects (n = 11)						
Fat > Real						
Right middle occipital gyrus[a]	1568	18	8.25	36	−85	4
Right lingual gyrus[a]		17	6.40	3	−89	−5
Right lingual gyrus[a]		18	6.28	12	−81	−11
Left cerebellum	711		8.17	−20	−75	−22
Left cerebellum			6.41	−29	−69	−25
Right superior temporal gyrus	307	39	6.07	31	−52	31
Right precuneus		7	4.61	26	−67	31
Right precuneus		7	4.52	17	−67	37
Thin > Real						
Left inferior occipital gyrus[a]	1255	18	10.93	−38	−81	−11
Left lingual gyrus[a]		17	10.93	−13	−93	−17
Left fusiform gyrus[a]		18	7.20	−29	−83	−17
Right cuneus[a]	2482	18	10.82	3	−93	7
Right fusiform gyrus[a]		19	9.06	34	−69	−13
Right fusiform gyrus[a]		37	8.73	36	−50	−15
Right precuneus[a]	389	7	5.83	26	−63	30

Stereotaxic coordinates were derived from the human atlas of Talairach and *Tournoux* (6) and refer to the medial-lateral position (x) relative to the midline (positive = right), anterior-posterior position (y) relative to the anterior commissure (positive = anterior), and superior-inferior position (z) relative to the commissural line (positive = superior). Only the activated brain areas within the gray matter are displayed. *t*-scores were obtained with one-sample *t*-test. BA, Brodmann area.

[a]Exceeded the extent threshold of $P < .05$ corrected at the cluster level. All other areas that are shown exceeded the height threshold of $P < .001$ uncorrected at the cluster level and belonged to a cluster of activation with an extent of at least 30 voxels.

constitutes an interaction zone between emotional processing and cognitive processing (Drevets et al 1998). When individuals turn their attention inwards to themselves, the activity in the MPFC increases (Johnson et al 2002; Gusnard et al 2001; Kelley et al 2002; Zysset et al 2002). Our finding that the PFC (DLPFC: BA 9,10; OFC: BA 13, 17; MPFC: BA 32) and limbic/paralimbic lobes were activated in the female subjects upon performing both the fat-image task and thin-image task suggests that a woman tends to perceive her body shape with cognitive and emotional processing, regulate emotional stimulation by herself, and turn attention inwards to assess emotional awareness about herself.

On the other hand, there was no significantly greater activation in the PFC and the limbic/paralimbic system upon performing the fat-image task versus the real-image task in the male subjects; on the contrary, the occipital lobe including the primary and secondary visual cortices, the temporal lobe and parietal lobe were activated in the male subjects. Within the visual cortex, the occipitotemporal pathway, or "ventral stream," is crucial for

Table 4. Percentage of Subjects who Selected the Real Image as the More Unpleasant Image in Each Gender (%)

Task	+25	+20	+15	+10	+5	−5	−10	−15	−20	−25
Women	.0	.0	.0	.0	13.3	80.0	60.0	46.7	53.3	13.3
Men	.0	6.1	6.1	18.2	30.3	51.5	33.3	33.3	39.4	30.3