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Regional brain volumes and symptom severity in body dysmorphic disorder

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ABSTRACT

Body dysmorphic disorder (BDD) is a severe psychiatric condition in which individuals are preoccupied with perceived defects in their appearance. Little is known of the pathophysiology or neurobiology of BDD. Recent evidence from a functional MRI study examining visual processing of faces demonstrated abnormal activation patterns in regions including left-sided inferior frontal gyrus (IFG) and amygdala. To investigate morphometric abnormalities, we compared brain volumes from high-resolution T1 magnetic resonance images of 12 unmedicated subjects with BDD to images of 12 matched controls using voxel-based morphometry (VBM). In addition, we compared volumes in specific regions of interest including the IFG, amygdala, caudate, and total grey and white matter and examined correlations with symptom severity. VBM revealed no statistically significant volumetric differences, nor were there significant differences in any of the regions of interest. However, there were significant positive correlations between scores on the BDD version of the Yale–Brown Obsessive–Compulsive Disorder Scale (BDD-YBOCS) and volumes of the left IFG ($r = 0.69$) and the right amygdala ($r = 0.54$). These findings of correlations between BDD symptom severity and volumes of the left IFG and the right amygdala. These are in concordance with the involvement of these regions in pathological face processing, which may contribute to the primary symptomatology.

1. Introduction

Body dysmorphic disorder (BDD) is a severe psychiatric condition in which patients are preoccupied with perceived defects in their appearance. This causes them to believe they are disfigured and ugly, and causes significant suffering and functional impairment. Most patients with BDD have poor insight, and 36–38% are classified as delusional (Eisen et al., 2004; Phillips et al., 2006). BDD affects 1–2% of the population (Faravelli et al., 1997; Otto et al., 2001; Rief et al., 2006), and is associated with high rates of psychiatric hospitalization (48%) (Phillips and Diaz, 1997) and suicide attempts (22–27.5%) (Veale et al., 1996; Phillips and Diaz, 1997; Phillips et al., 2005).

Despite the prevalence and severity of this disorder, very little is known of the pathophysiology or neurobiology of BDD. Only one previous morphometric magnetic resonance imaging (MRI) study in BDD has been published. In this study eight females, some of whom were medicated, demonstrated greater total white matter compared with controls and a leftward shift in caudate asymmetry (Rauch et al., 2003a), which the authors interpreted as suggesting similar striatal pathophysiology to that in obsessive-compulsive disorder (OCD) (Saxena et al., 2001). A small functional imaging study of six BDD patients, using single photon emission computed tomography (SPECT), showed variable, discrepant findings including relative perfusion deficits in bilateral anterior-medial temporal and occipital regions and asymmetric perfusion in parietal lobes (Carey et al., 2004). This study, however, had no control or comparison group. We recently performed a functional magnetic resonance imaging (fMRI) study in BDD that examined visual processing of faces (Feusner et al., 2007). Individuals with BDD as compared with healthy controls demonstrated abnormal activation patterns that included greater left hemisphere activity in regions including the inferior frontal gyrus, as well as abnormal amygdala activation (R>L). No other neuroimaging studies of BDD have been published.

Given these previous findings and the paucity of data on the neurobiology of BDD, the objective of this study was to further investigate regional brain volumes in BDD as compared with healthy controls. Based on our fMRI findings (Feusner et al., 2007), we selected the inferior frontal gyrus (IFG) and the amygdala as regions of interest. Following up the previous morphometric MRI study's findings (Rauch et al., 2003a), we also examined total grey matter (GM), white matter (WM), and the caudate as a region of interest, and calculated laterality quotients. We also tested whether brain volumes in the regions of interest were correlated with symptom severity. In addition, we performed voxel-based morphometry for regional whole-brain analysis to detect any other brain volume differences. We hypothesized that in the BDD group there would be abnormal caudate asymmetry and

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greater total WM. Based on findings from our previous fMRI study in the same cohort of BDD patients, we also hypothesized that they would demonstrate greater volumes of the amygdalae and left IFG, given the previously found hyperactivity in these regions. In addition, we hypothesized that symptom severity would positively correlate with size of the left IFG and bilateral amygdalae. A better understanding of patterns of brain morphometry in BDD could assist in understanding the pathophysiology underlying the clinical symptoms, as well as how it relates to other disorders with similar features.

2. Methods

2.1. Subjects

The UCLA Institutional Review Board approved the protocol for the study. We obtained informed consent from 12 subjects with BDD and 12 healthy controls, ages 18 to 54 (mean 28.7 ± 10), recruited from the community. The BDD group and controls were matched by gender, age, and level of education, and all were right-handed, as determined by the Edinburgh Handedness Inventory (Oldfield, 1971). All BDD subjects met DSM-IV criteria for body dysmorphic disorder, as determined by the first author (Dr. Feusner), who has clinical expertise with this population. Diagnoses were made using the Body Dysmorphic Disorder Module (Phillips et al., 1995), a reliable diagnostic module modeled after the Structured Clinical Interview for DSM. In addition, we screened them for comorbid psychiatric disorders with the Mini International Neuropsychiatric Inventory (MINI) (Sheehan et al., 1998). All BDD subjects were required to have a BDD version of the Yale–Brown Obsessive–Compulsive Disorder Scale (BDD–YBOCS) (Phillips et al., 1997) score of ≥18. We allowed subjects with delusional beliefs.

Exclusion criteria for subjects and controls included active substance abuse, current neurological disorder, pregnancy, and any current medical disorder that may affect cerebral metabolism. We excluded subjects with any concurrent Axis I disorder besides dysthymia, major depressive disorder, or generalized anxiety disorder. As depression and anxiety are so frequently comorbid in this population, we believed it would not be a representative sample to exclude these. We included subjects with a 17-item Hamilton Depression Rating Scale (HAM-D) (Hamilton, 1960) score of <20 and subjects whom the investigator (JF) judged were not actively suicidal. In addition to the BDD-YBOCS and the HAM-D, we also administered the Hamilton Anxiety Scale (HAM-A) (Hamilton, 1969) to all subjects. All participants were free from psychoactive medications for at least 3 weeks before entering the study, and free of fluoxetine for at least 5 weeks. Subjects were not receiving any cognitive–behavioral therapy.

2.2. MRI

We obtained high-resolution T1-weighted three-dimensional magnetic resonance images on a 3-Tesla Allegra (Siemens, Munich, Germany) MRI scanner with 1 mm^3 voxel size for each subject to provide detailed brain anatomy. Magnetization-prepared rapid gradient echo (MP-RAGE) sequences were used, with the parameters: TE = 2.83 ms, TR = 2300 ms, TI = 1100 ms, flip angle = 9.00, field of view = 240 × 256, matrix = 240 × 256, slice thickness 1 mm, 160 slices interleaved.

2.3. Segmentation processing and data analysis

We used FMRIB's Automated Segmentation Tool (part of the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain Software Library—FSL) (Ashburner and Friston, 2000), to acquire total GM and WM volumes. Regions of interest volumes in the caudate and amygdala were acquired from hand-traced coronal slices. The IFG and right and left hemisphere total GM and WM were acquired from hand-traced axial slices. For hand-traced regions of interest, we followed UCLA Laboratory of Neuro Imaging (LONI) protocols for the volumetric parcellation of cortical and sub-cortical regions of interest: *http://cms.loni.ucla.edu/ncrr/protocols.aspx?id=1482*, blinded to all subject demographics. Interrater reliability was 0.94, which we established between investigators (HM and JF) on a training set of five brains. Volumes for each structure were calculated by multiplying the number of voxels by the voxel size (1 × 1 × 1 mm). We normalized values for individual regions of interest (caudate, amygdala, and IFG) to individual total intracranial volumes: raw volume/total intracranial volume * 10^6. Total intracranial volume consisted of total white matter, grey matter, and CSF, excluding the brain stem and cerebellum. Laterality quotients, as an index of regional asymmetry by hemisphere, were calculated as (left − right)/(left + right) (0.5). Additionally, we performed a subanalysis of the females-only, given the previous morphometric study in BDD included only females and given gender differences in regional brain volumes (Good et al., 2001; Mechelli et al., 2005a). We used two-tailed *t*-tests to compare mean volumes between groups, with a threshold of $P<0.05$, uncorrected for multiple comparisons. (Bokde et al., 2005).

2.4. Correlation analyses

In this step we tested the hypothesis that symptom severity is proportional to volumes of the left IFG and the amygdalae, regions found to be hyperactive in the previous fMRI study. We tested correlations between normalized volumes in these regions and scores on the BDD version of the Yale–Brown Obsessive–Compulsive Disorder Scale (BDD–YBOCS) and the Hamilton Rating Scale for Depression (HAM-D) using Pearson product-moment correlations, one-tailed.

2.5. Voxel-based morphometry analyses

Structural data were analyzed with FSL-VBM, a voxel-based morphometry style analysis (Ashburner and Friston, 2000). Structural images were brain-extracted and tissue-segmented (Zhang et al., 2001; Smith, 2002; Smith et al., 2004). GM partial volume images were aligned to MNI152 standard space using nonlinear registration. Resulting images were averaged to create a study-specific template, to which the native GM images were then non-linearly re-registered. These images were then modulated (to correct for local expansion or contraction) by dividing by the Jacobian of the warp field. The modulated segmented images were then smoothed with a Gaussian 4-mm kernel. Finally, a voxel-wise general linear model (GLM) was applied using permutation-based non-parametric testing, forming clusters at $Z>2.3$ and testing clusters for significance at $P<0.05$, corrected for multiple comparisons across space.

3. Results

3.1. Characteristics of the subject group

Table 1 summarizes the demographic and psychometric data for both groups. The average BDD-YBOCS score was 28.7 ± 7.0. One BDD subject had comorbid major depressive disorder, one had dysthymic disorder, two had generalized anxiety disorder, and two had both major depressive disorder and generalized anxiety disorder. The BDD symptoms were the primary concern in every subject. Typical of this population, all 12 subjects had preoccupations with perceived facial defects.

3.2. Volumetric and region of interest analyses

There were no significant differences in total WM or GM between groups as determined by automated segmentation (see Table 2). There were also no significant differences in normalized volumes between groups for the right or left IFG, amygdala, caudate, or for the laterality quotients for any of these regions.

3.3. Correlation analyses

To test the hypotheses that regional brain volumes varied in proportion to severity of symptoms, we performed correlation analyses for the regions of interest. There was a significant correlation between BDD-YBOCS scores and normalized volume of the left IFG ($r=0.69$, $P=0.0067$) (Fig. 1). The right IFG volume was not significantly correlated with the BDD-YBOCS ($r=0.09$, $P=0.4$). Likewise, there were no significant correlations between the right or left IFG and HAM-D scores ($r=0.075$, $P=0.82$; and $r=0.058$, $P=0.86$, respectively).

There was a significant positive correlation between normalized volume of the right amygdala and BDD-YBOCS scores ($r=0.54$, $P=0.034$) (Fig. 2). There was a trend for a positive correlation between BDD-YBOCS scores and normalized volume of the left amygdala ($r=0.43$, $P=0.08$). There was a significant negative correlation between normalized left amygdala volume and HAM-D scores ($r=-0.53$, $P=0.039$). The right

Table 1
Demographics and psychometric scores[a].

	BDD group ($N=12$)	Control group ($N=12$)	P value[b]
Age	28.7 ± 10.0	31.2 ± 11.8	0.57
Gender (F/M)	10/2	10/2	1
Handedness	12R	12R	1
Years of education	15.5 ± 2.9	15.9 ± 1.4	0.66
BDD-YBOCS score	28.7 ± 7.0	0.5 ± 1.0	<0.001
HAM-D score	8.6 ± 5.7	0.83 ± 1.7	<0.001
HAM-A score	12.7 ± 9.8	1.6 ± 1.6	0.002

Abbreviations: BDD: body dysmorphic disorder; BDD-YBOCS: BDD version of the Yale–Brown Obsessive–Compulsive Scale; HAM-D: Hamilton Depression Rating Scale; HAM-A: Hamilton Anxiety Rating Scale.
[a] Data are given as mean ± S.D. unless otherwise indicated.
[b] *t*-test for all comparisons except gender and handedness (χ^2 Test).