Psychiatry Research: Neuroimaging 232 (2015) 115–122

Contents lists available at ScienceDirect

Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

Cortical thickness and brain volumetric analysis in body dysmorphic disorder

Sarah K. Madsen [a,b,*], Alex Zai [c], Tara Pirnia [c], Donatello Arienzo [d], Liang Zhan [a,c], Teena D. Moody [d], Paul M. Thompson [a,b,c,d], Jamie D. Feusner [d]

[a] Imaging Genetics Center, Institute for Neuroimaging & Informatics, Department of Neurology, University of Southern California, Marina del Rey, CA, USA
[b] Departments of Neurology, Psychiatry, Radiology, Pediatrics, Engineering, & Ophthalmology, University of Southern California, Los Angles, CA, USA
[c] Department of Neurology, University of California Los Angeles, Los Angeles, CA, USA
[d] Semel Institute for Neuroscience and Human Behavior, Department of Psychiatry, University of California Los Angeles, Los Angles, CA, USA

ARTICLE INFO

Article history:
Received 1 July 2014
Received in revised form
11 December 2014
Accepted 8 February 2015
Available online 26 February 2015

Keywords:
Gray matter
Cortical thickness
Voxel-based morphometry
Volume
MRI
Anxiety

ABSTRACT

Individuals with body dysmorphic disorder (BDD) suffer from preoccupations with perceived defects in physical appearance, causing severe distress and disability. Although BDD affects 1–2% of the population, the neurobiology is not understood. Discrepant results in previous volumetric studies may be due to small sample sizes, and no study has investigated cortical thickness in BDD. The current study is the largest neuroimaging analysis of BDD. Participants included 49 medication-free, right-handed individuals with DSM-IV BDD and 44 healthy controls matched by age, sex, and education. Using high-resolution T1-weighted magnetic resonance imaging, we computed vertex-wise gray matter (GM) thickness on the cortical surface and GM volume using voxel-based morphometry. We also computed volumes in cortical and subcortical regions of interest. In addition to group comparisons, we investigated associations with symptom severity, insight, and anxiety within the BDD group. In BDD, greater anxiety was significantly associated with thinner GM in the left superior temporal cortex and greater GM volume in the right caudate nucleus. There were no significant differences in cortical thickness, GM volume, or volumes in regions of interest between BDD and control subjects. Subtle associations with clinical symptoms may characterize brain morphometric patterns in BDD, rather than large group differences in brain structure.

1. Introduction

Body dysmorphic disorder (BDD) is an under-studied psychiatric disorder, despite its relatively high prevalence (1–2%) (Mufaddel et al., 2013). Individuals with BDD are preoccupied with perceived defects in their physical appearance (American Psychiatric Association, 2013). These concerns are often obsessive, resulting in significant distress and disability. Due to similar symptoms, heredity, and comorbidity, BDD is conceptualized as an obsessive-compulsive related disorder (Phillips et al., 2010). BDD is also associated with depression and anxiety. In addition, those with BDD often have low insight into their psychiatric illness and exaggerate perceived "defects," even though they are not noticeable or very slight to others (American Psychiatric Association, 2013).

There have only been a small number of neuropsychological and neuroimaging studies in BDD, and its neurobiology remains largely unknown. Of the four studies of brain morphometry in BDD (Rauch et al., 2003; Feusner et al., 2009; Atmaca et al., 2010; Buchanan et al., 2014), two found greater total white matter (WM) volume (Rauch et al., 2003; Atmaca et al., 2010) and two found smaller volumes in frontostriatal systems (anterior cingulate and the orbitofrontal cortices) (Atmaca et al., 2010; Buchanan et al., 2014). However, these studies had small sample sizes, and the results are discrepant. Moreover, these studies investigated whole brain or region of interest (ROI) volume measurements, but they did not assess gray matter (GM) thickness, which may be a more sensitive tool to uncover subtle or diffuse morphometric abnormalities.

Neuropsychological, psychophysical, and functional magnetic resonance imaging (fMRI) studies suggest that the pathophysiology of BDD involves abnormalities in executive functioning, visuospatial processing and memory, processing of emotional faces, and visual systems (for review, see Madsen et al., 2013). Several fMRI studies demonstrate an imbalance of global versus detailed processing when BDD patients view images of their own and others' faces and of objects (Deckersbach et al., 2000; Feusner et al., 2007; Feusner et al., 2010, 2011; Jefferies et al., 2012). Two studies found abnormal hypoactivity in primary and/or secondary

* Correspondence to:: Imaging Genetics Center, Laboratory of Neuro Imaging, Institute of Neuroimaging and Informatics, Keck School of Medicine of USC, 2001 North Soto Street – Room 102, Los Angeles, CA 90033, USA. Tel.: +1 310 822 1511.
E-mail address: Sarah.Madsen@ini.usc.edu (S.K. Madsen).

http://dx.doi.org/10.1016/j.pscychresns.2015.02.003
0925-4927/

visual processing systems, and one also found hyperactive frontostriatal systems for own-face stimuli. Abnormal neural activity plays a role in BDD, but whether there are structural abnormalities in these systems has not been established.

This is the first study to examine cortical thickness in individuals with BDD, and the largest to investigate brain morphometry. Differences in brain structure and function, specifically in visual processing regions of the brain, may underlie the dysfunctional preoccupation with details in physical appearance that are core BDD symptoms. We hypothesized that there would be regional differences (greater or lesser) in GM thickness and volumes between BDD patients and controls. Specifically, we expected between-group differences in frontostriatal and visual processing systems, where previous studies found abnormal volumes (Rauch et al., 2003; Atmaca et al., 2010; Buchanan et al., 2014) and/or functioning (Feusner et al., 2007, 2010, 2011). We also predicted significant associations between clinical symptoms and both cortical thickness and volumes. Knowledge of neuroanatomical abnormalities in BDD could contribute to mechanistic understandings of the pathophysiology.

2. Methods

2.1. Participants

The UCLA Institutional Review Board approved this study, and we obtained written informed consent from participants.

Ninety-three right-handed medication-free individuals, recruited from the community, participated. Each participant received a clinical evaluation by J.D.F., who has clinical expertise in BDD. Individuals who met criteria for BDD (Phillips et al., 1995) and who had a score of 20 on the BDD version of the Yale–Brown Obsessive–Compulsive Scale (BDD-YBOCS; Phillips et al., 1997) were eligible. We used the Mini International Neuropsychiatric Inventory to determine comorbid diagnoses (Sheehan et al., 1998). Severity of other psychiatric symptoms was measured using validated clinical scales as follows: the Hamilton Anxiety Rating Scale (HAMA; Hamilton, 1959), the Brown Assessment of Beliefs scale (BABS, measuring insight about perceived defects and psychiatric illness; Eisen et al., 1998), and either the 17-item Hamilton Depression Rating Scale (HAMD-17, administered to $n=26$; Hamilton, 1960; Snaith, 1977) or the Montgomery–Åsberg Depression Rating Scale (MADRS, administered to $n=44$; Montgomery and Åsberg, 1979; Williams and Kobak, 2008). (Two depression scales were used because the dataset combined two similar protocols, one of which administered the MADRS and the other the HAMD-17.) Duration of illness data was available in $n=36$ BDD participants.

We excluded participants either currently taking psychoactive medications or having taken them within 8 weeks of the study, as well as participants currently in cognitive-behavioral therapy. Additional exclusion criteria included the following: lifetime neurological disorders, any current medical disorder affecting cerebral metabolism, recent substance abuse or dependence, or Axis I disorder comorbidity. Major depressive disorder (MDD), dysthymic disorder, generalized anxiety disorder (GAD), and social anxiety disorder (SAD) were allowed because anxiety and depression are common symptoms in BDD (American Psychiatric Association, 2013), and excluding these disorders would lead to a non-representative study group. However, BDD had to be the primary diagnosis.

2.2. Brain image acquisition

We acquired high-resolution T1-weighted 3D structural MRI brain scans on Siemens Allegra ($n=29$) or Trio ($n=41$) scanners, using a Magnetization Prepared Rapid Acquisition Gradient Echo (MP-RAGE) sequence. On the Allegra, images were obtained with a repetition time (TR)=2.3 s, echo time (TE)=2.93 ms, flip angle=8°, field of view=256 × 256, and voxel size=1.3 × 1.3 × 1 mm^3. On the Trio, images were obtained with a repetition time (TR)=1.9 s, echo time (TE)=2.26 ms, flip angle=9°, field of view=250 × 250, and voxel size=1 × 1 × 1 mm^3.

2.3. Brain tissue segmentation

Researchers were blind to diagnosis throughout data processing.

We used the FAST Automated Segmentation Tool in FSL (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FAST) (Zhang et al., 2001) to obtain segmentations from each participant's brain MRI scan. Subcortical and cortical GM and WM segmentations were manually edited by trained experts (A.Z., T.P., J.D.F.). Raters achieved 99% inter-rater reliability, as defined by number of overlapping voxels, on a training set of $n=5$.

2.4. Parcellation and cortical thickness analysis

We used FreeSurfer (v5.0.0, http://surfer.nmr.mgh.harvard.edu/) to obtain ROIs from the 2006 Desikan-Killiany atlas and 3D maps of cortical GM thickness. Technical details have been described previously (Fischl and Dale, 2000; Fischl et al., 2002). Briefly, the processing pipeline involves removal of non-brain tissue, intensity normalization, tessellation of the cortical GM/WM boundary, alignment of cortical anatomy, segmentation of total GM volume for left and right hemispheres, smoothing, and creation of 3D surfaces with GM thickness at each surface point in left and right hemispheres.

We excluded data from five participants due to scanner artifacts that prevented accurate cortical segmentations. We created separate cortical GM maps smoothed

Table 1
Demographics and psychometrics.

	Healthy controls	BDD	
N:	44	49	–
Age	25.34 ± 7.80 years	26.43 ± 7.79	$p=0.50$
Sex	30 Females 14 Males	37 Females 12 Males	$p=0.58$
Scanner:	21 Trio 23 Allegra	23 Trio 26 Allegra	$p>0.99$
Illness duration (years):	–	12.42 ± 9.56	–
BDD-YBOCS	–	29.82 ± 5.51	–
BABS	–	15.15 ± 3.31	–
HAMA	1.59 ± 1.54	12.39 ± 7.89	$p<0.01$*
HAMD (26 BDD subjects, 23 HC subjects)	1.35 ± 1.50	10.92 ± 6.53	$p<0.01$*
MADRS (23 BDD subjects, 21 HC subjects)	0.57 ± 0.93	17.87 ± 8.10	$p<0.01$*
Comorbidity	–	None ($n=23$) Agoraphobia ($n=1$) Dysthymia ($n=1$) Dysthymia, GAD ($n=2$) GAD ($n=5$) MDD ($n=9$) GAD, MDD ($n=6$) GAD, MDD, social phobia ($n=1$) SAD ($n=2$)	–

The demographic and psychometric information for the body dysmorphic disorder (BDD) and healthy control participants is listed (mean ± standard deviation), along with *p*-values for two-tailed unpaired *t*-tests for continuous variables and chi-squared tests for binary variables.