Reduced cortical thickness in body dysmorphic disorder.

Sally A Grace[a*], Ben Buchanan[b], Jerome J Maller[b], Wei Lin Toh[a,b], David J Castle[c,d], and Susan L Rossell[a,b,c]

[a] Brain and Psychological Sciences Research Centre, Swinburne University, Melbourne, Australia
[b] Monash Alfred Psychiatry Research Centre, Monash University, Melbourne Australia
[c] Psychiatry, St Vincent's Hospital, Melbourne, Australia
[d] Psychiatry, University of Melbourne, Melbourne, Australia

* **Corresponding author:**
Miss Sally Grace
Brain and Psychological Sciences Research Centre
Advanced Technology Building
Burwood Rd
Hawthorn, VIC 3122
Australia
Phone: +613 9214 8415
Email: sgrace@swin.edu.au

Abstract

Recent neuroimaging studies in body dysmorphic disorder (BDD) have implicated abnormal structure and function of occipito-temporal and fronto-limbic regions in the potential pathophysiology of the disorder. To date, morphometric investigations have yielded inconsistent results, and have suggested that clinical symptoms may mediate morphometric abnormalities in BDD. We measured Grey Matter (GM) cortical thickness in 20 participants with BDD and 20 healthy control participants matched on age, gender and handedness. We observed cortical thinning in BDD patients compared with healthy control participants within the left middle temporal and left inferior parietal gyrus. No significant relationships between cortical thickness and BDD symptom severity, insight, social anxiety and depression were observed within the BDD group. Thinning within left temporal and left inferior parietal regions supports the involvement of these regions in the pathophysiology of BDD.

Keywords: cerebral cortex, grey matter, magnetic resonance imaging, psychiatry.

1. Introduction

Body dysmorphic disorder (BDD) is a psychiatric disorder characterized by preoccupations with an objectively absent 'defect' in physical appearance (American Psychiatric Association, 2013). BDD is relatively common with reported prevalence rates between 1-2% in the general population (Mufaddel et al., 2013; Rief et al., 2006). Without treatment, BDD is associated with high levels of distress, poor insight manifesting as delusions, significant impairment in social and occupational functioning, and suicidal ideations (DeMarco et al., 1998; Phillips et al., 2006). In studies of cognition BDD has been associated with deficits in memory, executive functioning, and holistic visual processing, which have been linked to abnormalities in occipito-temporal and fronto-limbic regions (Feusner et al., 2011; Feusner et al., 2007; Hanes, 1998; Li et al., 2015).

Morphometric MRI investigations have identified neuroanatomical abnormalities in BDD patients. Previous voxel-based morphometry (VBM), anatomical tracing, and volumetric segmentation data in BDD samples have demonstrated significant total whole-brain volume and grey matter (GM) volume reductions (Buchanan et al., 2014), as well as larger total white matter volumes (Atmaca et al., 2010; Rauch et al., 2003). In BDD samples, regional reductions in brain volume have also been identified within the bilateral orbitofrontal cortex (OFC), bilateral anterior cingulate (Rauch et al., 2003), right orbitofrontal cortex, bilateral thalamus, left anterior cingulate cortex, left hippocampus and left amygdala, relative to controls (Buchanan et al., 2014), as well as larger left hemispheric caudate volumes (Rauch et al., 2003). A noticeable trend within these data is that morphometric abnormalities between BDD and healthy control groups appear to be mediated by clinical variables. For example, significant positive correlations of illness duration with bilateral orbito-frontal cortex (OFC) volumes (Atmaca et al., 2010), and right OFC volumes (Buchanan et al., 2014) have been observed in BDD samples. One study reported positive correlations of BDD

symptom severity (as measured by the Yale-Brown Obsessive-Compulsive Disorder Scale; BDD-YBOCS; Phillips et al., 1997) with GM volumes in the left inferior frontal gyrus and right amygdala despite no significant overall group differences in brain morphometry (Feusner et al., 2009).

Further highlighting the sensitive influence of clinical variables on brain morphometry in BDD, a recent analysis of cortical thickness in BDD reported no group differences in cortical thickness in a sample of 49 BDD patients and 44 demographically matched healthy control participants (Madsen et al., 2015). They did, however, find significant associations between anxiety severity and GM cortical thinning in the left superior temporal cortex and greater GM volume in the right caudate nucleus (Madsen et al., 2015). Altogether, this suggests that in general, studies of brain morphometry in BDD have yielded inconsistent results.

There are some methodological issues that are important when considering existing neuroimaging findings in BDD. Heterogeneous analysis techniques and sample characteristics have a significant impact on the generalisability of the findings. With the exception of two studies (Buchanan et al., 2014; Madsen et al., 2015) the sample sizes involved were small (i.e. <12 BDD patients compared to controls), and gender ratios, patient comorbidities and medication use are inconsistent.

To our knowledge, only one examination of cortical thickness has been performed in a sample of BDD participants. Thus, the aim of this study was to further extant morphometric data in BDD through an examination of cortical thickness and its relationship with clinical variables in participants with BDD compared with a sample of demographically matched healthy controls. We computed Pearson correlations between grey matter thickness and clinical variables within the BDD group. Specifically, we hypothesised that reported anxiety

severity within the BDD sample would correlate with grey matter thinning within the temporal lobe.

2. Methods

2.1.Participants

Participants comprised 20 individuals with BDD and 20 healthy control participants, aged between 19 and 64 years, all of whom provided informed consent (Table 1). Recruitment for the BDD group was conducted via referrals from St Vincent's Hospital Body Image Clinic in Melbourne, Australia, where clients were identified as having BDD and introduced to the research project (all had participated in a previous MRI study examining brain connectivity in BDD (Buchanan et al., 2013)). BDD diagnosis was confirmed by the research team using the Body Dysmorphic Disorder Diagnostic Module (BDD-DM) and symptom severity was recorded using the Yale–Brown Obsessive Compulsive Scale Modified for Body Dysmorphic Disorder (BDD-YBOCS; Phillips et al., 1997). All but two of the BDD sample was taking psychoactive medication: five quetiapine, four escitalopram, two duloxetine, two desvenlafaxine, two diazepam, and one each paroxetine, mirtazapine, lorazepam, methylphenidate, sodium valproate or clomipramine. Depressive symptoms were assessed using the Zung Self-Rating Depression Scale which is a brief self-administered survey to quantify the current depressive symptoms experienced by adult patients (Zung, 1965). Social anxiety symptoms were measured using the Social Interaction Anxiety Scale (SIAS), a self-report scale designed to measure social interaction anxiety (Mattick and Clarke, 1998). Degree of conviction and insight into beliefs (i.e. degree of delusionality) was measured using the Brown Assessment of Beliefs Scale (BABS; Eisen et al., 1998).

The control group comprised members of the public who had no personal or family history of a mental disorder. All participants had English as their preferred language and a

Wechsler Test of Adult Reading (WTAR) pre-morbid intelligence quotient (IQ) score of >80. Participants were assessed with the Mini-International Neuropsychiatric Interview (MINI500) and BDD-DM. Handedness was assessed with the Edinburgh Handedness Inventory (EHI; Oldfield, 1971). A more detailed account of selection criteria and demographic characteristics is described elsewhere (Buchanan et al., 2013).

Exclusion criteria for all participants included: past or current psychotic disorder, alcohol or substance abuse history, intellectual or cognitive impairment, and metal implants or neurological disturbances (e.g. trauma brain injury). BDD participants were excluded if they had past or current diagnoses of OCD, bulimia nervosa, anorexia nervosa, or a comorbid mental disorder that was considered as their primary diagnosis, ensuring that all individuals in the clinical sample had BDD as their primary diagnosis.

2.2.Magnetic resonance imaging (MRI) acquisition

Participants were scanned using a 3T scanner (Siemens Magnetom Tim Trio, Germany) at the Murdoch Children's Research Institute (Royal Children's Hospital, Melbourne, Australia). An AC-PC aligned high-resolution structural T1-weighted MPRAGE sequence (512 slices; slice thickness = 1 mm; TE = 2.15 ms; TR = 1900 ms; field of view = 256 mm; in plane resolution 0.5×0.5 mm^2) was acquired allowing high-quality data for structural brain image processing.

2.3. MRI scan processing and calculation of cortical thickness

2.3.1. Quantification of cortical thickness.

Cortical reconstruction and segmentation was performed with the Freesurfer 5.3 (FS) image analysis suite (http://surfer.nmr.mgh.harvard.edu/). FS output was checked on a slice-by-slice basis with the FreeSurfer viewer (freeview) for any segmentations that were not

correct. They were then viewed as 3-dimensional renderings with tksurfer. Cortical thickness group analysis was undertaken within Qdec (Query, Design, Estimate, Contrast. A Graphical User Interface tool for FS; https://surfer.nmr.mgh.harvard.edu/fswiki/FsTutorial/QdecGroupAnalysis_freeview). BDD and control groups were compared for thickness difference, followed by correlational analyses between FS variables (whole cortex) and clinical scores in those with BDD. The subsequent parameters within Qdec were used for all of the analyses: Measure=Thickness, Smoothing=10, Monte Carlo simulation used to correct for multiple comparisons using a threshold of 1.3 (p<0.05) and the appropriate two-tailed tests were applied.

2.3.2. *Statistical Analysis.*

FreeSurfer data were statistically analysed using in SPSS for Windows version 19.0 (SPSS, Chicago, IL). Simple chi-square and analysis of variance (ANOVA) were employed to compare differences in GM thickness within- and between- the groups, covarying for the effects of age. We did not control for the effects of gender as there was not a statistically significant gender difference between the groups. Correlations between total GM thickness and the clinical variables were also performed. Group comparisons in demographic and clinical data were computed using independent samples t tests at p=0.05. Analyses were also computed to investigate whether there were subcortical differences between groups, and whether subcortical volumes were associated with BDD symptoms. However, as the focus of the study was cortical thickness (and not subcortical regions), and as all of these results were not significant, all mention of these analyses have been omitted.

3. Results

3.1.Participants

Table 1 presents demographic and clinical information for the BDD and control groups. The two participant groups were well matched on age, sex, education, estimated IQ, and handedness. The mean BDD severity was in the 'moderate' range, defined as scores between 16 and 30 on the BDD-YBOCS (Phillips et al., 1997). The areas of aesthetic concern in our sample related predominantly to the face, skin and hair, but included other body areas, such as breasts and legs.

Table 1 about here.

3.2. FreeSurfer comparisons between control and BDD groups

3.2.1. Cortical thickness between healthy control and BDD groups.

There were two significant clusters within the left hemisphere demonstrating group differences (controls thicker than BDD), but none within the right hemisphere nor frontal or medial aspects of the left hemisphere (Table 2 and Fig. 1).

Table 2 about here

3.2.2. Correlations between cortical thickness and clinical variables.

There were no significant correlations evident between GM thickness and any of the clinical variables (BDD-YBOCS, BABS, SIAS and Zung scores) in the BDD group.

Fig. 1 about here.

4. Discussion

This study demonstrates cortical thinning in left inferior parietal and left middle temporal regions in a group of BDD participants relative to demographically matched healthy

controls. Hypothesised correlations between GM thinning in the temporal lobe and anxiety severity within the BDD patient sample were not supported by this data set.

We observed significantly reduced cortical thickness in the left inferior parietal and left temporal cortices in the BDD group compared to healthy controls, highlighting the potential role of the left temporal cortex in BDD pathophysiology. While group differences in temporal lobe morphometry have not been previously found in BDD research, temporal regions have been implicated in both functional neuroimaging investigations and in the network architecture of BDD. First, abnormal functional activation in temporal regions has been consistently evident in BDD cohorts during visual processing tasks (Feusner et al., 2011; Feusner et al., 2007). Suggesting that in BDD, visual processing abnormalities are tightly linked to functional activity differences in the temporal lobe. Second, impaired structural integrity within white matter connections between the temporal lobe and frontal and occipital regions has been implicated in BDD (Buchanan et al., 2013). Third, investigations into brain network organisation in BDD have found greater edge betweenness centrality for connections between the left temporal and left occipital pole nodes, suggesting this connection has a heightened influence on the whole brain network (Arienzo et al., 2013). On a local network level, this connection is strongly associated with BDD-YBOCS symptom severity (Arienzo et al., 2013). Together, this suggests that abnormalities in both the structure and function of the temporal lobe may contribute to BDD symptomatology and pathophysiology.

Cortical thinning within the left inferior parietal lobe may also contribute to BDD pathophysiology through its role in face and self-perception. The potential role for the parietal lobe in BDD pathophysiology has been proposed in a previous single photon emission computed tomography (SPECT) pilot study of six BDD patients, demonstrating asymmetric perfusion in the parietal lobes (Carey et al., 2004). In addition, previous research

has suggested that the parietal lobe has a role in somatosensory disturbances in BDD (Kaplan et al., 2014; Yaryura-Tobias et al., 2002). In healthy cohorts, research has implicated the temporal and parietal network in self-facial recognition, and the recognition of faces and basic emotions in others (Sprengelmeyer et al., 1998; Sugiura et al., 2005). However, the relationship between parietal cortical thinning and pathological dysfunction needs to be established in a sample of BDD patients.

No significant correlations were evident between the clinical measures and GM thickness in the BDD group. This findings does not support a previous study which found a significant correlation between GM thickness within superior temporal gyrus and anxiety ratings (Madsen et al., 2015), using the Hamilton Anxiety Rating Scale (HAMA; Hamilton, 1959). The scale used to measure anxiety within our sample (the SIAS; Mattick and Clarke, 1998) measures social anxiety and not general anxiety as the HAMA does, thus, discrepancies between these findings may be due to the measurement of different domains of anxiety.

There are several limitations to consider when interpreting the discrepant results between the current study and previous morphometric analyses in BDD. It requires mention that our sample was heterogeneous with regard to DSM-IV Axis I comorbidities and medication use, which may have influenced the relationship between clinical variables and GM thickness. The participants in our sample were taking psychiatric medications and had comorbid diagnoses. Available literature on the nosology of BDD recognises that comorbidity is a common occurrence in BDD samples, with the most common comorbid lifetime axis I disorders being major depression, social phobia and obsessive-compulsive disorder (Gunstad and Phillips, 2003; Phillips et al., 2005). Furthermore, pharmacotherapy is considered to be essential in the first line of treatment of BDD patients (Phillips, 2010). Thus, the patient sample used in the current study could be considered representative of the BDD

population. An additional limitation when considering discrepant results is the use of normalisation techniques whilst measuring brain volumes. The other published paper examining cortical thickness applied normalization with intracranial volume (Madsen et al., 2015). We did not given that cortical thickness is a local cytoarchitectural measure, and when comparing regionally vertex-by-vertex, correction for influences of overall brain volume do not apply (Lerch and Evans, 2005) [1]. Theoretically, despite the use of the same analysis software in the current and previous cortical thickness analyses, these factors may lead to differences across studies. The addition of a second clinical group, for example obsessive compulsive disorder (OCD), could also help to determine whether the observed differences are specific to BDD or characteristic symptom-related changes to neuroanatomy. Finally, the sample size of the present study was markedly smaller than that of Madsen et al. (2015), which may have impacted the on the generalisability of the current results. Further large-scale morphometric examinations are required in BDD samples to address these limitations and confirm temporal lobe abnormalities in the pathophysiology of BDD.

In conclusion, we found that BDD patients had significantly thinner GM cortical thickness within the left middle temporal and left inferior parietal cortices than demographically matched controls. Contradicting a previous analysis of cortical thickness in BDD, we did not find any significant associations between clinical measures and brain morphometry in BDD. Further studies are required to corroborate the association of symptomatology with brain morphometry BDD. These studies could also incorporate a study design that probes the function of these regions specifically to elucidate the relationship between structural abnormalities in these regions with functional outcomes.

[1] Additionally, we examined cortical thickness differences between the groups whilst controlling for total brain volume (TBV) to ensure our analysis approach was valid. Controlling for TBV did not change the direction or significance findings that are reported in this study.

Conflict of interest

All authors have no interests to declare generally and in relation to the present study.

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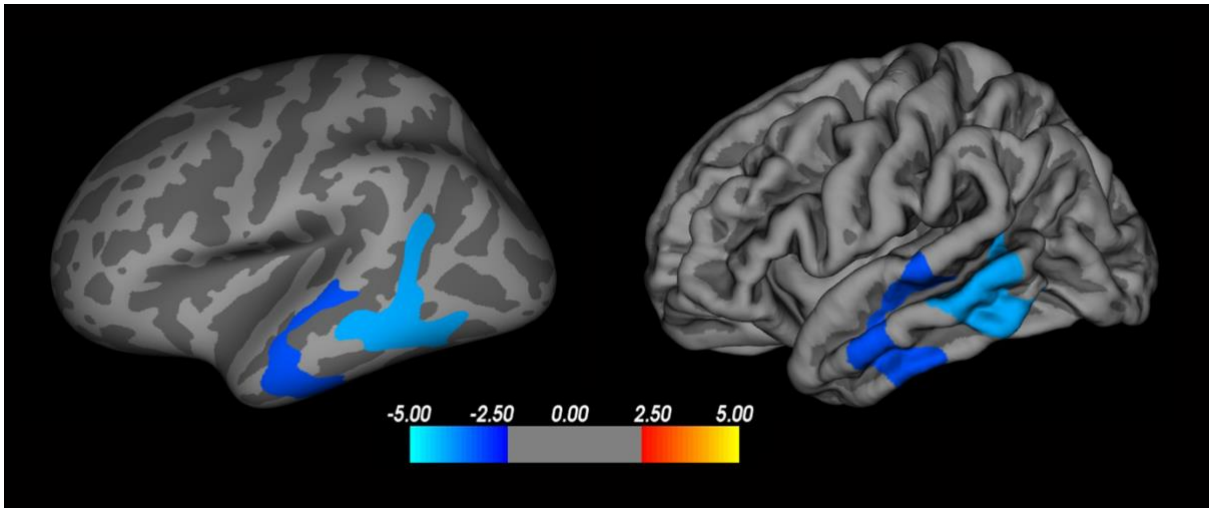

Fig. 1. Freesurfer results for cortical thicknesses between the groups (BDD < Healthy Controls), figures on the left represent the clusters superimposed over Freesurfers‘ inflated brain and the figures on the right are superimposed on the pial surface of the brain.

Table 1. Demographic and clinical variables for the BDD and control groups

	BDD (*n*=20)	**Healthy Controls (*n*=20)**	**Group Comparison (df = 38)**
Demographic Characteristics			
Age (years)	34.6 (11.5)	31.9 (11.4)	$p = 0.45$
Years of Education	14.9 (2.4)	16.3 (3.0)	$p = 0.11$
WTAR IQ estimate	106 (10.7)	110 (6.5)	$p = 0.13$
Handedness (L/R)	3/17	3/17	
Sex (M/F)	6/14	6/14	
Clinical Variables			
BDD severity (BDD-YBOCS)	24.9 (9.6)		
Duration of Illness (years)	10.8 (6.9)		
BABS	15.71 (7.9)		
Zung	46 (11.26)		
SIAS	41.7 (17.58)		

Note: Data presented as mean (SD).

BABS=Brown Assessment of Beliefs Scale total score; BDD=Body dysmorphic disorder; WTAR=Wechsler Test of Adult Reading; Zung=Zung Self-Rating Depression Scale total score.

Table 2. Significant cluster detected in the left hemisphere between patients with BDD and healthy control participants after multiple corrections and controlling for age and total brain volume

Group	Hem	Cluster Number	Max	VtxMax	Size (mm\widehat2)	TalX	TalY	TalZ	CWP	CWPlow	CWPHi	Annotation
BDD vs HC (raw)	Left	1	-.3886	47713	1706.66	-45.6	-47.9	17.6	0.00010	-	-	Inferior parietal
	Left	2	-3.170	136798	1366.80	-55.7	-10.6	-18.4	0.001100	-	-	Middle temporal

Note: BDD=Body dysmorphic disorder; HC=Healthy controls; Hem=Hemisphere; L=Left; R=Right; Max=Maximum -log10(p value) in the cluster (negative value means greater in the BDD group), VtxMax=Vertex number at the maximum, Size(mm^2)=Surface area (mm^2) of cluster, TalX=Talairach (MNI305) coordinate of the maximum for x direction, TalY=Talairach (MNI305) coordinate of the maximum for y direction, TalZ=Talairach (MNI305) coordinate of the maximum for z direction, CWP=p-value of the cluster, CWPLow=Lower 90% confidence interval; CWPHi=Higher 90% confidence interval for CWP, Annotation=Annotation of segmented region as defined by Freesurfer.