



White matter microstructure in body dysmorphic disorder and its clinical correlates

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ABSTRACT

Body dysmorphic disorder (BDD) is characterized by an often-delusional preoccupation with misperceived defects of appearance, causing significant distress and disability. Although previous studies have found functional abnormalities in visual processing, frontostriatal, and limbic systems, no study to date has investigated the microstructure of white matter connecting these systems in BDD. Participants comprised 14 medication-free individuals with BDD and 16 healthy controls who were scanned using diffusion-weighted magnetic resonance imaging (MRI). We utilized probabilistic tractography to reconstruct tracts of interest, and tract-based spatial statistics to investigate whole brain white matter. To estimate white matter microstructure, we used fractional anisotropy (FA), mean diffusivity (MD), and linear and planar anisotropy (c_l and c_p). We correlated diffusion measures with clinical measures of symptom severity and poor insight/delusionality. Poor insight negatively correlated with FA and c_l and positively correlated with MD in the inferior longitudinal fasciculus (ILF) and the forceps major (FM). FA and c_l were lower in the ILF and the inferior fronto-occipital fasciculus and higher in the FM in the BDD group, but differences were nonsignificant. This is the first diffusion-weighted MR investigation of white matter in BDD. Results suggest a relationship between impairments in insight, a clinically important phenotype, and fiber disorganization in tracts connecting visual with emotion/memory processing systems.

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1. Introduction

Body dysmorphic disorder (BDD) is a psychiatric disorder in which individuals are preoccupied with misperceived defects of their appearance (American Psychiatric Association, 2000). Believing that they look disfigured and ugly, they suffer significant distress and functional impairment. BDD affects approximately 0.7–2.4% of the population (Faravelli et al., 1997; Rief et al., 2006; Koran et al., 2008; Buhlmann et al., 2010) and is associated with high lifetime rates of hospitalization (48%) (Phillips and Diaz, 1997) and suicide attempts (22–27.5%) (Veale et al., 1996; Phillips and Diaz, 1997; Phillips et al., 2005a). Insight is usually impaired and 36–60% of BDD patients are delusional (Gunstad and Phillips, 2003; Phillips et al.,

2005b; Mancuso et al., 2010). Despite the severity of this disorder, knowledge of the underlying abnormalities in brain function and structure is still in its early stages.

An important symptom domain in BDD, for which there is emerging evidence, is distortion of visual perception. Distortion of self-perception of appearance may contribute to the conviction of disfigurement and ugliness, and subsequent poor insight or delusionality. Clinically, individuals with BDD focus on details of their appearance at the expense of global aspects. A neuropsychological study using the Rey–Osterrieth Complex Figure Test demonstrated that patients with BDD selectively recalled details instead of larger organizational design features (Deckersbach et al., 2000). Individuals with BDD may also have perceptual distortions for own-face processing; in one study they perceived distortions of digital images of their faces that were not actually present (Yaryura-Tobias et al., 2002).

A previous functional magnetic resonance imaging (fMRI) study (performed in the same participants as the current study) found that individuals with BDD demonstrated abnormalities in

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visual processing (striate and extrastriate visual cortex) and frontostriatal systems (orbitofrontal cortex and caudate) when viewing their face (Feusner et al., 2010a). There was also evidence of abnormalities in emotion processing systems. In addition, BDD symptom severity was correlated with frontostriatal activity and activity in extrastriate visual cortex. Abnormalities in visual systems may therefore represent early stage abnormalities (“bottom-up”) and/or may be the result of “top-down” modulation from emotional processing and/or prefrontal systems.

An earlier fMRI study in BDD using others' faces as stimuli also found a pattern of abnormal information processing, including left hemisphere hyperactivity in an extended face-processing network (Feusner et al., 2007). This pattern, in contrast to the generally right hemisphere-dominant pattern for healthy controls (Haxby et al., 1994), suggests greater detail in encoding and analysis relative to holistic and configural processing. Abnormal interhemispheric sharing of information may be involved, which may also contribute to aberrant visual processing.

The objective of the current study was to explore anatomical white matter connections involved in the neural systems that have been previously found to show abnormal activity in BDD. These white matter tracts include those likely involved in the integration of information between visual processing and the limbic as well as prefrontal systems, and those involved in interhemispheric sharing of information.

The only other studies in BDD that have investigated white matter include three small studies of volumetric brain morphology. Two of these (Rauch et al., 2003; Atmaca et al., 2010), but not the third (Feusner et al., 2009), found greater total white matter in the BDD group relative to healthy controls.

To our knowledge, no study to date has investigated white matter microstructure in BDD using diffusion tensor imaging (DTI). However, a number of DTI studies have investigated white matter integrity in obsessive-compulsive disorder (Szeszko et al., 2005; Cannistraro et al., 2007; Yoo et al., 2007; Menzies et al., 2008; Saito et al., 2008; Garibotto et al., 2010; Bora et al., 2011; Nakamae et al., 2011), which is believed to be related to BDD (Hollander and Wong, 1995; Phillips et al., 2010). Several of these studies (Yoo et al., 2007; Saito et al., 2008; Garibotto et al., 2010; Bora et al., 2011; Nakamae et al., 2011), but not others (Szeszko et al., 2005; Cannistraro et al., 2007; Menzies et al., 2008), found abnormal fractional anisotropy (FA) in the corpus callosum. Across the studies with positive findings, however, there were inconsistencies in regard to both location and direction (higher or lower FA) of the abnormalities within the corpus callosum. Two studies in social anxiety disorder, also thought to be related to BDD (Fang and Hofmann, 2010), suggested abnormalities of FA in the uncinate fasciculus (Phan et al., 2009; Baur et al., 2011). One study in anorexia nervosa, also conceptualized to be related to BDD (Corove and Gleaves, 2001), found abnormalities in the fimbria-fornix (Kazlouski et al., 2011). Overall, a consistent pattern of white matter abnormalities has not emerged in these related disorders. Thus, we based our hypotheses for the current study on the aforementioned functional brain imaging studies in BDD suggesting abnormal activity in extended visual processing systems, in addition to performing exploratory analyses across the white matter of the entire brain.

Magnetic resonance diffusion imaging can provide information on white matter microstructure and anatomical connectivity by measuring the diffusion profile of water molecules. The DTI technique fits an ellipsoid (or “tensor”) to local water diffusivity, providing an estimate of the magnitude and orientation of water diffusion at each voxel. From this, white matter integrity measures based on the three “eigenvalues” of the reconstructed ellipsoid (representing the magnitude of water diffusivity along the three principal directions of the ellipsoid), such as the

fractional anisotropy (FA; a measure of preferential directionality of water diffusion) and mean diffusivity (MD; a measure of overall diffusivity), can be derived (Torrey, 1956; Stejskal, 1965).

One limitation of the standard FA is that it is not designed to probe subvoxel fiber architecture. Thus, low FA values may reflect either abnormal individual fiber integrity (e.g., fiber demyelination) or greater dispersion of fibers (e.g., fiber crossing or mixing, or other disorganization). To help differentiate these, we included DTI-derived geometric indices, linear and planar anisotropy (c_1 and c_2) (Westin et al., 2002), to better quantify the shape of diffusion tensors beyond standard FA and MD.

Based on the previous BDD studies outlined above, we hypothesized that BDD participants would exhibit microstructural white matter abnormalities relative to controls in tracts involved in integration of information between limbic and visual processing systems, between prefrontal systems and visual processing systems, and those involved in interhemispheric sharing of information. We therefore examined the inferior longitudinal fasciculus (ILF), which connects anterior temporal cortex structures (including the amygdala and hippocampus) to the occipital lobe; the inferior fronto-occipital fasciculus (IFOF), which connects prefrontal regions to the occipital lobe; and the forceps major (FM), which connects the right and left occipital lobes (Catani and Schotten, 2008). Moreover, we predicted significant correlations would exist between the degree of microstructural abnormalities in these tracts and important clinical phenotypes of BDD symptom severity as well as poor insight/delusional. We also performed an exploratory voxel-wise analysis of all white matter tracts.

2. Methods

2.1. Participants

The UCLA Institutional Review Board approved the study protocol. Participants comprised 14 unmedicated individuals with BDD and 16 healthy controls, aged 20–48 years, all of whom provided informed consent (Table 1). BDD and control participants of equivalent sex, age, and level of education were recruited from the community (all had participated in a previous fMRI study of own-face processing (Feusner et al., 2010)). All were right-handed as determined by the Edinburgh Handedness Inventory (Oldfield, 1971). Diagnoses were made by J.D.F., who has clinical expertise with this population using the Body Dysmorphic Disorder Module (Phillips et al., 1995), a reliable diagnostic module modeled after the Structured Clinical Interview for the Diagnostic and Statistical Manual (DSM) of Mental Disorders. In addition, we performed a clinical psychiatric evaluation and screened participants with the Mini-International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998).

Exclusion criteria for all participants included: substance abuse or dependence within the past 12 months, lifetime neurological disorder, pregnancy, or any current medical disorder that may affect cerebral metabolism. We excluded BDD participants with any concurrent Axis I disorder besides dysthymia, major depressive disorder

Table 1
Demographics and psychometric scores.

Characteristics	BDD group (N=14)	Control group (N=16)	P value ^a
Age, mean years (S.D.)	26.6 (4.9)	27.3 (5.3)	0.7
Female/male	7/7	8/8	> 0.99
Education, mean years (S.D.)	15.5 (2.8)	16.9 (2.3)	0.150
BDD-YBOCS score, mean (S.D.)	29.85 (4.4)	N/A	N/A
BABS score, mean (S.D.)	15 (3.9)	N/A	N/A
HAMD-17 score, mean (S.D.)	10 (6.7)	1.25 (1.48)	< 0.0001

Abbreviations: BDD: body dysmorphic disorder; BDD-YBOCS: BDD version of the Yale-Brown Obsessive-Compulsive Scale; BABS: Brown Assessment of Beliefs Scale; HAMD-17: 17-item Hamilton Depression Rating Scale.

^a Two-sample *t*-tests for age, education and HAMD-17; χ^2 test for gender.

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