Published in final edited form as:
Body Image. 2008 March ; 5(1): . doi:10.1016/j.bodyim.2007.11.002.

The Pathophysiology of Body Dysmorphic Disorder

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Abstract

Body dysmorphic disorder (BDD) is an often severe and disabling condition, affecting up to 2% of the population. Despite its prevalence and clinical significance, very little is known about the pathophysiology of BDD. However, clues to its possible neurobiological substrates and abnormalities in information processing are starting to emerge. This article reviews findings from genetic, brain lesion, neuroimaging, neuropsychological, and psychopharmacological studies that have allowed us to develop a tentative model of the functional neuroanatomy of BDD. There is likely a complex interplay of dysfunctions in several brain networks underlying the pathophysiology of BDD. A combination of dysfunctions in frontal-subcortical circuits, temporal, parietal, and limbic structures, and possibly involving hemispheric imbalances in information processing, may produce both the characteristic symptoms and neurocognitive deficits seen in BDD. An improved understanding of the pathophysiology of BDD will be crucial to guide the development of better treatments.

Keywords

body dysmorphic disorder; pathophysiology; perception

Introduction

Body dysmorphic disorder (BDD) is defined by the *Diagnostic and Statistical Manual of Mental Disorders, 4th ed.* (DSM-IV-TR) (American Psychiatric Association., 2000) as a preoccupation with an imagined defect in physical appearance or excessive concern about a slight physical anomaly that causes significant impairment or distress. It is believed to affect close to 2% of the general population (Rief, Buhlmann, Wilhelm, Borkenhagen, & Brahler, 2006), and up to 13% in psychiatric settings (Grant, Kim, & Crow, 2001; Phillips, Nierenberg, Brendel, & Fava, 1996; Wilhelm, Otto, Zucker, & Pollack, 1997). BDD is an under-recognized disorder that causes significant suffering, disability, and functional impairment (Phillips, 2000; Veale et al., 1996).

Very little is known about the etiology or pathophysiology of BDD, as few studies have addressed this directly. This review of the pathophysiology of BDD explores what has been elucidated thus far from research on the genetics, neuroanatomy, neuropsychology, and psychopharmacology of BDD, as well as secondary BDD symptoms resulting from brain damage and medical illnesses. In addition, the brain networks that mediate body image

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distortion, self-recognition, and emotional reactions to visual stimuli are reviewed. This information is synthesized to produce preliminary hypotheses of the pathophysiological processes most likely to mediate the symptoms of BDD, in the interest of stimulating further research in this area.

Genetics of BDD

Genetic factors are likely to play an important role in the etiology of BDD, as evidenced by its pattern of heritability (Bienvenu et al., 2000). Eight percent of individuals with BDD have a family member with a lifetime diagnosis of BDD, which is four to eight times the prevalence in the general population. BDD shares heredity with obsessive-compulsive disorder (OCD), as family studies have shown that 7% of BDD patients were found to have a first-degree relative with OCD (Phillips, Gunderson, Mallya, McElroy, & Carter, 1998), and first-degree relatives of OCD probands have a six times higher lifetime prevalence of BDD than do relatives of controls (Bienvenu et al., 2000).

There has been scant research on molecular genetic data to inform our understanding of the etiology of BDD. Only one preliminary genetic association study has been performed thus far. Richter et al. (2004) found an association between the gamma-aminobutyric acid (GABA)A-γ2 gene and BDD and comorbid BDD + OCD, but not with OCD alone. There was also a trend toward association with the serotonin transporter promoter polymorphism (5-HTTPRL) short allele (Richter et al., 2004). This area of research clearly needs to expand.

Neuroimaging Studies in BDD

Brain imaging studies can be extremely useful in identifying structural and functional brain abnormalities, and can be designed to parse out specific cognitive and emotional processes that may contribute to symptomatology in patients with a given disorder. Functional brain imaging research has led to a greater understanding of the neurobiological mediation of OCD, for example, indicating that OCD symptoms are mediated by overactivity along a neural circuit connecting the orbitofrontal cortex, basal ganglia, and thalamus (Saxena, Bota, & Brody, 2001; Saxena, Brody, Schwartz, & Baxter, 1998).

Unfortunately, only two brain imaging studies of BDD have been published thus far. A preliminary volumetric magnetic resonance imaging (MRI) study found leftward shift in caudate volume asymmetry and greater total white matter volume in eight women with BDD than in eight female controls (Rauch et al., 2003). This study implicates similar regions or networks in BDD as in OCD, although previous findings in OCD are a rightward shift in caudate asymmetry and lesser total white matter (Saxena et al., 2001). A small functional imaging study of six BDD patients, using single photon emission computed tomography (SPECT), showed variable, discrepant findings – relative perfusion deficits in bilateral anterior-medial temporal and occipital regions and asymmetric perfusion in parietal lobes (Carey, Seedat, Warwick, van Heerden, & Stein, 2004). This study, however, had no control or comparison group and did not make any quantitative measurements of regional brain activity. Moreover, two of the six BDD patients had comorbid major depression, and one had comorbid OCD, making it difficult to know whether the perfusion abnormalities were associated specifically with BDD or due to the comorbid conditions.

Recently, the first functional imaging study to compare BDD patients to controls examined visual information processing of faces, with respect to spatial frequency (Feusner, Townsend, Bystritsky, & Bookheimer, 2006). Twelve BDD patients and twelve healthy controls underwent functional magnetic resonance imaging (fMRI) while matching photographs of faces. Some of the faces were digitally altered to remove the high or low

spatial frequencies, which created images that contained configural or detail information, respectively. BDD participants showed greater left hemisphere activity relative to controls for all face tasks, particularly in lateral aspects of the prefrontal cortex and the temporal lobe. They also activated dorsal anterior cingulate gyrus for the low spatial frequency (LSF) face task. Controls, on the other hand, activated left-sided prefrontal cortex and dorsal anterior cingulate gyrus only for the high spatial frequency (HSF) face task. Greater left-sided activity for LSF and normal faces suggests a predominance of detail encoding and analysis, a pattern evident in controls only for HSF faces. This suggests that BDD patients may process faces in a piecemeal manner, while healthy controls' perception of faces may be more configural and holistic. These laterality patterns in the BDD participants suggest a bias for local, or detail-oriented, processing of faces over global processing.

Another finding in the BDD group was abnormal activation of amygdalae for the LSF and HSF face tasks. In contrast, the controls showed activation of the amygdalae for the NSF task, but reduced activity or deactivation for the LSF and HSF tasks. Amygdala activation did not correlate with any behavioral measures. This suggests an abnormal hyperresponsivity of the amygdala that appears specific to LSF and HSF visual information.

The results from this fMRI study suggest that BDD participants show fundamental differences from controls in visual processing, with different laterality of activation patterns in areas representing an extended visual processing network, and abnormal amygdala activation. These abnormalities may be associated with BDD patients' apparent perceptual distortions; they may focus in excruciating detail on specific facial features and lose the larger, overall context of the whole face. As this experiment used others' faces and not their own, it will be important for future studies to investigate the processing of their own faces as they may experience greater distortions and because of the possibility of the influence of emotional arousal.

Neuropsychology of BDD

Neuropsychological studies have provided some important evidence of abnormal perceptual and emotional information processing, as well as memory deficits, in patients with BDD. Hanes (1998) found that both BDD and OCD patients, compared to normal controls, showed poor performance on tests of executive function, including response inhibition and planning, but normal performance on measures of memory and motor function. Deckersbach et al. (2000) found that BDD patients differed significantly from healthy controls on both verbal and nonverbal learning and memory indices. Group differences in free recall were statistically mediated by deficits in organizational strategies in BDD patients, who tended to use a strategy of focusing on details rather than recalling the overall organization and properties of visual stimuli or verbal information, consonant with how individuals with BDD may process faces (Feusner, Townsend et al., 2006). In addition, this deficit in memory organization strategy was similar to the pattern previously observed in OCD and recently in anorexia nervosa, and is thought to reflect dysfunction in frontal-striatal circuits and prefrontal regions that mediate executive functioning (Deckersbach et al., 2000 ; Savage et al., 2000; Sherman et al., 2006). However, some recall deficits in BDD patients remained even after partialing out the effects of organization, suggesting potential involvement of more fundamental memory consolidation structures, such as the hippocampus (Deckersbach et al., 2000).

Other studies have shown that BDD patients exhibit selective processing of threat and distraction by emotional cues, similar to patients with anxiety disorders (Buhlmann, McNally, Wilhelm, & Florin, 2002). Relative to healthy controls, BDD patients exhibited greater interference for positive and negative words in the emotional Stroop paradigm,

regardless of disorder-relevance, than for neutral words. Interference tended to be greatest for positive words related to BDD, such as “attractive” and “beauty.” In another study, BDD patients demonstrated negative interpretive biases in ambiguous situations (Buhlmann, Wilhelm et al., 2002). They rated the likelihood that others are negatively judging their appearance and social behavior significantly higher than did controls or OCD patients. These data demonstrate that BDD patients are vulnerable to distraction by emotional cues in general, and by words and situations related to their current concerns in particular. These patterns of cognitive and emotional processing suggest that BDD may be related to anxiety disorders such as social phobia (Buhlmann, McNally et al., 2002; Buhlmann, Wilhelm et al., 2002).

BDD patients also show abnormalities in explicit and implicit perception of emotional expressions. Buhlmann, McNally, Etcoff, Tuschen-Caffier, & Wilhelm (2004) tested BDD patients, OCD patients, and healthy controls and found no differences among the three groups in the ability to discriminate general facial features. However, the BDD and OCD groups were less accurate than controls in identifying facial expressions of emotion. BDD patients misidentified facial expressions as angry more often than did OCD patients or controls. In a different study, BDD patients were also found to have particular difficulty identifying emotional expressions in self-referent scenarios, such as imagining that the person in the picture is a bank teller looking at them. They misinterpreted more expressions as contemptuous and angry in self-referent scenarios than did controls, but did not have significantly more difficulty identifying emotional expressions in other-referent scenarios, such as imagining that the teller is looking at their friend (Buhlmann et al., 2004). Feusner, Bystritsky, & Bookheimer (2006) studied implicit processing of faces with emotional expressions in a face matching task. They found delayed responses and a higher error rate in patients with BDD relative to healthy controls, suggesting abnormalities in implicit processing of emotional expressions. Ideas of reference in BDD might be related to a bias toward explicitly or implicitly misinterpreting other people's emotional expressions as angry and rejecting, which in turn might reinforce patients' concerns about their perceived ugliness and social undesirability.

Perceptual distortions of their own faces may contribute to preoccupation with perceived defects and poor insight in BDD patients. Yaryura-Tobias, Neziroglu, Chang et al. (2002) compared three groups of ten participants each (BDD, OCD, and a non-psychiatric control group) using a computerized perceptual program. The participants were asked to make changes to a computerized image of their faces. In addition, they underwent affective and perceptual testing. The groups did not differ on affective and perceptual organizational measures, although the OCD group reported a higher level of anxiety. Fifty percent of participants with BDD and 40% of those with OCD but no controls perceived distortions that were not actually present when observing computerized images of their own faces. The authors suggested that this may be an indication of visual perception defects in BDD, and symmetry and perfectionism in OCD, which may have influenced body image perception.

These neuropsychological data in BDD, taken together, suggest possible dysfunction in frontal-subcortical circuits involved in executive functioning, memory structures such as the hippocampus, and regions involved in facial emotion perception, such as the inferior frontal, right parietal, and occipito-temporal cortices, insula, striatum, and amygdala (Adolphs, Demasio, Tranel, & Demasio, 1996; Gur, Skolnik, & Gur, 1994; Sprengelmeyer, Rausch, Eysel, & Przuntek, 1998). BDD patients may have *over*activity in structures involved in mediating attentional biases and social anxiety, such as the amygdala (Stein, Goldin, Sareen, Zorrilla, & Brown, 2002). However, the functional neuroanatomy of executive dysfunction, perceptual distortions, and attentional biases in BDD has yet to be directly studied.

Another source of indirect, although potentially valuable, information about the pathophysiology of BDD comes from case reports and case series of medical and neurological illnesses that manifest with body dysmorphic or related symptoms. These cases of "secondary BDD" can help in generating hypotheses about neurobiological processes and brain systems that may contribute to "primary" BDD.

Secondary BDD

Medical Illnesses Presenting with BDD Symptoms

Several authors have reported cases of BDD symptoms developing as a result of medical illnesses. In some of these, BDD symptoms have developed in patients with inflammatory diseases. Examples include a 22 year-old male with subacute sclerosing panencephalitis (SSPE) who presented with BDD symptoms (Salib, 1988), a 17 year-old male who developed BDD symptoms after an episode of Bell's Palsy, and a 22 year-old male who developed BDD symptoms immediately after the onset of ulcerative colitis (Gabbay, O'Dowd, Weiss, & Asnis, 2002). These cases suggest that inflammatory processes might play a role in the development or exacerbation of BDD symptoms. Another case report described exacerbation of BDD symptoms in an 18 year-old subsequent to streptococcal pharyngitis (Mathew, 2001). This suggests that BDD could be a manifestation or variant of pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANDAS), believed to be due to post-streptococcal auto-antibodies that cross-react to basal ganglia tissue (Snider & Swedo, 2004).

BDD Symptoms Related to Temporal Lobe Damage

Overall, the brain networks that mediate BDD symptoms remain to be elucidated. However, indirect evidence from case reports of secondary BDD symptoms resulting from brain lesions have provided some clues as to which structures might be involved. Several reports implicate dysfunction of the temporal lobes in the development of secondary BDD and similar symptoms. In one case, a 49 year-old male with right temporal lobe epilepsy developed delusional olfactory reference syndrome (Devinsky, Khan, & Alper, 1998). This is considered a variant of BDD and is characterized by a belief that one is emitting a terrible odor that is noticeable and disgusting to everyone nearby. In another case, a 24 year-old male developed BDD six weeks after suffering an inflammatory brain process with mass effect in the left hemisphere (Gabbay et al., 2003). He became preoccupied with the shape of his nose (believing it was too wide) and developed severe ideas of reference, compulsions of repeatedly checking the appearance of his face in the mirror, asking for reassurance, and desiring cosmetic surgery. MRI of his brain later showed mild left temporal and frontal atrophy. Naga, Devinsky, & Barr (2004) characterized 10 patients who developed somatoform disorders after anterior temporal lobectomy, including two who developed BDD. Somatoform disorders were far more common after right temporal resection than left temporal resection, suggesting that right temporal damage might contribute to idiopathic BDD. Temporal lobectomy frequently produces occipital lobe hypometabolism and visual field defects (Wong, Swartz, Gee, & Mandelkern, 2004), depression and anxiety symptoms (Wrench, Wilson, & Bladin, 2004), and can even lead to psychosis (Mace & Trimble, 1991; Stevens, 1990). Normal perception of body image is disturbed by localized lesions of the non-dominant (right) temporal lobe and posterior parietal lobe (Trimble, 1988). Conceivably, right temporal lobe lesions could reproduce many of the symptoms seen in BDD such as abnormal visual perception, distortion of body image, depressed mood, anxiety, somatic preoccupations and delusions (Saxena & Feusner, 2006).

Neurobiology of Body Image Distortion

Functional brain imaging studies of body image distortion provide another line of evidence implicating temporal lobe dysfunction in the pathophysiology of BDD. The processing of unpleasant words about body image activates mesial temporal lobe structures, including the parahippocampal gyrus (PHG) and amygdala. There are significant gender differences to this phenomenon: women activate PHG, amygdala, thalamus, and striatum while men activate left hippocampus, PHG, left fusiform gyrus, superior temporal gyrus, and apical superior frontal gyrus (SFG) (Shirao, Okamoto, Mantani, Okamoto, & Yamawaki, 2005; Shirao, Okamoto, Okada, Okamoto, & Yamawaki, 2003). Interestingly, the magnitude of right PHG activation correlated with the subjective rating of pleasantness of words concerning body image, so that the most unpleasant ratings were associated with the least right PHG activation (Shirao et al., 2005). Further, women with the most severe psychological and behavioral eating disorder-related symptoms had the least right PHG and left apical SFG activation (Shirao et al. 2003, 2005). Chronic distortions of body self-image might therefore be related to right PHG dysfunction. This might result in hypersensitivity to potentially negative words and cognitions about body image. Unfortunately, similar imaging studies have not yet been conducted in participants with BDD or any other psychiatric disorder. Based on the frequent negative interpretive, emotional, and perceptual biases demonstrated in patients with BDD (Buhlmann, Etcoff, & Wilhelm, 2006; Buhlmann et al., 2004; Gur et al., 1994; Veale, 2004; Yaryura-Tobias, Neziroglu, Chang et al., 2002; Yaryura-Tobias, Neziroglu, & Torres-Gallegos, 2002), we would predict that they would show marked deficits in right PHG activation compared to controls, as well as much greater ratings of unpleasantness of words concerning body image.

BDD has many important features in common with eating disorders (ED) including distorted body image, poor insight, childhood or adolescent onset, and chronic course. Further, up to 32% of BDD patients have a lifetime comorbid ED (Ruffolo, Phillips, Menard, Fay, & Weisberg, 2006). Both BDD and ED patients experience significant distortions of their own body image much more than images of others. The brain processes visual stimuli about the self differently than about others, and also has distinct responses to distorted body images. In healthy controls, researchers have found that recognition of one's own face, compared to unfamiliar faces, selectively activates the right temporo-parieto-occipital junction, right supramarginal gyrus (part of the inferior parietal lobule - IPL), right inferior frontal gyrus (IFG), and the left fusiform gyrus (Sugiura et al., 2005; Uddin, Kaplan, Molnar-Szakacs, Zaidel, & Iacoboni, 2005). These same regions, along with the dorsolateral prefrontal cortex (DLPFC), are also reliably activated in healthy women viewing distorted body images (Kurosaki, Shirao, Yamashita, Okamoto, & Yamawaki, 2006; Uher et al., 2005; Wagner, Ruf, Braus, & Schmidt, 2003).

Patients with ED appear to process distorted visual stimuli of their own bodies via different brain networks than healthy controls. Female adolescents with anorexia nervosa showed significantly greater activation of the IPL and DLPFC than controls when viewing distorted body pictures (Wagner et al., 2003). Hyperactivation of IPL occurred only when these patients viewed distorted images of themselves, not those of others. Conversely, controls did not show any IPL activation differences between viewing distorted images of themselves versus others. In a different study, women with ED showed *less* activation than controls in right IPL, bilateral fusiform gyrus, and right IFG, when viewing line drawings of fat and thin versus normal-weight bodies of other women (Uher et al., 2005). Instead, they showed greater activation of the right putamen and thalamus. In addition, the degree of ED patients' body image distortion correlated with activation of the right amygdala, while ratings of aversiveness correlated with activation of the right apical SFG.

Overall, these results suggest that individuals with distorted body images may have a neurobiologically-based response bias toward abnormal visual perception and negative appraisal of their appearance, perhaps mediated by diminished tonic activity in parieto-temporal cortex, elevated activity in striatum, and exaggerated responses of the IPL and right subcortical and limbic structures specifically during distorted visual self-perception. Indeed, several functional neuroimaging studies of patients with anorexia nervosa have found abnormally low parietal and temporal cortex activity and high activity in the striatum at resting-state baseline (Frank, Bailer, Henry, Wagner, & Kaye, 2004). Such studies have not been performed in patients with BDD, but similar results to those seen in ED have been predicted (Saxena et al., 2006).

A core feature of BDD is the negative emotional response to visual perception of body parts that a patient thinks are ugly or deformed. BDD patients frequently feel disgusted by their appearance and believe that others also view them as disgusting. This suggests that BDD patients might have pathological hyperactivation of limbic structures that mediate disgust and aversion to visual stimuli, such as the insula and amygdala (Murphy, Nimmo-Smith, & Lawrence, 2003; Stark et al., 2003; Wright, He, Shapira, Goodman, & Liu, 2004), as has been found in OCD patients (Schienle, Schafer, Stark, Walter, & Vaitl, 2005; Shapira et al., 2003).

Neurochemistry of BDD

Several studies have investigated the role of serotonin (5-HT) in BDD. Marazziti et al. (1999) studied platelet 5-HT transporter binding density in a group of 6 patients with BDD, 5 with impulse dyscontrol, 5 with kleptomania, 6 with Tourette's syndrome, and 1 with trichotillomania (“OCD-related disorders”) and compared them to 20 patients with OCD and 20 healthy subjects (Marazziti, Dell'Osso, & Presta, 1999). They found significantly lower platelet 5-HT transporter binding density in the OCD and OCD-related disorders compared to controls, suggesting a shared abnormality at the level of the presynaptic 5-HT transporter.

In a case report, dietary depletion of tryptophan, a 5-HT precursor amino acid, produced acute exacerbation of BDD symptoms and tearfulness in a patient with BDD and OCD who had been treated successfully with a serotonin reuptake inhibitor (SRI) (Barr, Goodman, & Price, 1992). Tryptophan depletion did not exacerbate her OCD symptoms, nor did it exacerbate OCD symptoms in other SRI-treated OCD patients (Barr, Goodman, & McDougle, 1994; Smeraldi, Diaferia, & Erzogovesi, 1996). These findings suggest that response of BDD and depressive symptoms to SRIs is more dependent on the availability of serotonin than are OCD symptoms.

Additional indirect evidence exists of the involvement of serotonergic transmission in BDD. In one patient, the 5-HT2 receptor agonist psilocybin temporarily alleviated BDD symptoms (Hanes, 1996). Interestingly, psilocybin has also been found to alleviate OCD symptoms (Moreno & Delgado, 1997). In contrast, dependence on the 5-HT2 antagonist cyproheptadine has been associated with new onset of BDD symptoms (Craven & Rodin, 1987). There are also preliminary findings that the serotonin agonist mCPP but not placebo causes exacerbation of preoccupations with perceived bodily defects in patients with BDD (Hollander & Wong, 1995). Other indirect evidence comes from several open and controlled treatment studies that demonstrated that high-dose SRIs (Perugi et al., 1996; Phillips, Albertini, & Rasmussen, 2002; Phillips, Dwight, & McElroy, 1998; Phillips & Najjar, 2003) but not desipramine (Hollander et al., 1999), a primarily noradrenergic medication, are effective for treating BDD. However, perturbations of the serotonergic system that exacerbate or alleviate BDD symptoms do not prove that abnormalities of the serotonergic system necessarily underlie the pathophysiology of BDD.

A Tentative Model of the Pathophysiology of BDD

The pathophysiology of BDD likely involves a complex interplay of dysfunctions in several brain networks. Hemispheric imbalance may also play a crucial role. The right hemisphere appears dominant in regulating emotions and body image (Devinsky, 2000). This is supported by the preponderance of secondary BDD cases occurring with right temporal lobe lesions (Devinsky et al., 1998; Gabbay et al., 2003 ; Naga et al., 2004). Right hemisphere lesions can also cause secondary psychotic symptoms, including somatic delusions (Malloy & Richardson, 1994; Price & Mesulam, 1985). A hemispheric imbalance in extended visual processing networks for faces, with greater left-sided activation in prefrontal and lateral temporal regions may contribute to visual detail biases (Feusner, Townsend et al., 2006). In addition, the insula, amygdala, and apical SFG mediate reactions of disgust and aversion to visual perceptions (Ruffolo et al., 2006 ; Shapira et al., 2003; Sugiura et al., 2005; Uddin et al., 2005), a fundamental process in BDD.

Dysfunction in frontal-striatal circuits may also be involved in the pathophysiology of BDD. Evidence of this comes from the phenomenology of obsessive thoughts and compulsive behaviors, the pattern of neurocognitive deficits (Deckersbach et al., 2000 ; Hanes, 1998), and the findings from the one preliminary structural neuroimaging study of BDD published thus far (Rauch et al., 2003). In addition, there are reports of successful neurosurgical interventions in individuals with treatment refractory BDD that target these frontal-striatal circuits. A modified leucotomy (Hay, 1970), capsulotomy, anterior cingulotomy, and subcaudate tractotomy have been reported to be effective for BDD, although in two cases anterior internal capsulotomy was ineffective (Hadley, Newcorn, & Hollander, 2002).

In their review of delusions secondary to brain damage and neurological illnesses, Malloy et al. (1994) concluded that "… a pattern of right hemisphere damage superimposed on dysfunctional frontal systems may be a necessary component of the development of fixed delusions" (p. 463). In idiopathic BDD, the specific structures involved are likely to be those that mediate body image, self-recognition, and perceptual distortions, such as the right PHG, dorsal occipital cortex, temporo-parieto-occipital junction, fusiform gyrus, IPL, IFG, and DLPFC (Frank et al., 2004; Murphy et al., 2003; Shapira et al., 2003; Shirao et al. 2003, 2005; Stark et al., 2003; Trimble, 1988; Wright et al., 2004). Therefore, a putative model of the pathophysiology of BDD encompasses possible abnormalities in some combination of the structures and circuits listed above (Saxena et al., 2006).

Dysfunction of the dorsal occipital cortex, right temporo-parieto-occipital junction, fusiform gyrus, IPL, IFG, and/or DLPFC could give rise to BDD patients' distorted perceptions of their faces and bodies. DLPFC dysfunction might also contribute to an inability to correct the perceptual distortions generated by other dysfunctional systems, leading to continuing misinterpretations. Dysfunction of the ventromedial PFC, responsible for inhibiting limbic responses to aversive stimuli (Phelps, Delgado, Nearing, & LeDoux, 2004), could account for BDD patients' inability to inhibit their reactions of disgust and anxiety in response to perceived bodily flaws, perhaps mediated by excessive activity in the amygdala (Feusner, Townsend et al., 2006). When BDD patients think about their body and appearance, insufficient right PHG activation could give rise to negative self-appraisals of their appearance, negative interpretive biases, and ideas of reference. Frontal-occipital-temporal circuits with greater left-sided activity may mediate the bias for detailed rather than holistic visual processing. Frontal-striatal circuit abnormalities may contribute to executive dysfunction and to the repetitive, intrusive nature of obsessive thoughts and compulsive behaviors in BDD.

Serotonergic transmission may also modulate BDD symptoms at the level of frontal-subcortical circuitry and/or the limbic system. This may lead to either a worsening or an improvement in symptoms, depending on the specific perturbation. The beneficial effect of SRIs in treating BDD may be due to several mechanisms. These include enhancing serotonergic inhibition of amygdala and insula, which reduces negative affect and social anxiety (Furmark et al., 2002), and/or increasing 5-HT release in paralimbic cortex and basal ganglia structures, critical in ameliorating obsessive-compulsive symptoms (Saxena et al., 2001; Saxena et al., 1998).

Conclusions

The pathophysiology of BDD by and large still remains unknown. Nevertheless, evidence from studies of brain-damaged patients as well as neuroimaging studies of brain activation patterns for visual perception, body image distortion, and emotional processing have allowed us to develop a tentative model for the neuroanatomical dysfunctions that may underlie the symptoms of BDD. A combination of frontal-striatal circuit dysfunction, hemispheric imbalances (perhaps involving the right PHG, dorsal occipital cortex, IPL, fusiform gyrus, IFG, and greater left prefrontal and temporal activation for processing faces), and hyper-responsiveness of the amygdala and insula may be involved in mediating the symptoms and neuropsychological deficits of BDD.

Additional research is necessary to determine the pathophysiology of BDD. Cognitive and emotional activation studies could identify abnormalities in specific information processing systems involved in the symptoms of BDD. Baseline functional neuroimaging studies using positron emission tomography (PET) or SPECT imaging to compare BDD patients with healthy controls could identify relatively stable, underlying abnormalities of regional brain activity in BDD. Neurophysiology, neuropathology, and genetic studies could identify abnormalities at the tissue, cellular, and molecular level in BDD. A better understanding of the pathophysiology of BDD could facilitate the development of improved somatic and psychotherapeutic treatments for this distressing and disabling disorder.

Acknowledgments

None.

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Table 1
Imbalances, networks, and regions possibly involved in the pathophysiology of BDD

Imbalance, network, or region implicated	Evidence
Hemispheric imbalances	
•Anterior temporal lobe	Lesion studies
•Parahippocampal gyrus	Body image and eating disorder studies
•Dorsal occipital cortex	Studies of self perception in healthy controls
•IFG and lateral temporal lobe	Face processing fMRI study of BDD
•IPL	Eating disorder studies
•Fusiform gyrus	• Studies of processing faces and body image words in healthy controls • Eating disorder studies
Frontal-striatal circuits	• Obsessive thoughts and compulsive behaviors • Morphometric MRI study of BDD • Neuropsychological studies of BDD • PANDAS variant case report
Amygdala hyper-reactivity	Face processing fMRI study of BDD
Insula hyper-reactivity	Studies of disgust and aversion in healthy controls and OCD
5-HT system	• Lower platelet 5-HT transporter density in BDD • Case reports: tryptophan depletion, 5-HT agonists and antagonists • Improvement of BDD symptoms with SRIs

BDD=body dysmorphic disorder; IFG=inferior frontal gyrus; IPL=inferior parietal lobule; fMRI=functional magnetic resonance imaging; MRI=magnetic resonance imaging; PANDAS=pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection; OCD=obsessive-compulsive disorder; 5-HT=5-hydroxytryptamine (serotonin); SRI=serotonin reuptake inhibitor