European Neuropsychopharmacology (2016) **26**, 350–356

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Reduced striatal dopamine $D_{2/3}$ receptor availability in Body Dysmorphic Disorder

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Received 26 May 2015; received in revised form 20 November 2015; accepted 23 November 2015

KEYWORDS
Body Dysmorphic Disorder (BDD);
Dopamine $D_{2/3}$ receptor;
Obsessive Compulsive and Related Disorders (OCRD);
Single Photon Emission Computed Tomography (SPECT)

Abstract
Though the dopaminergic system is implicated in Obsessive Compulsive and Related Disorders (OCRD), the dopaminergic system has never been investigated in-vivo in Body Dysmorphic Disorder (BDD). In line with consistent findings of reduced striatal dopamine $D_{2/3}$ receptor availability in Obsessive Compulsive Disorder (OCD), we hypothesized that the dopamine $D_{2/3}$ receptor availability in the striatum will be lower in patients with BDD in comparison to healthy subjects.
Striatal dopamine $D_{2/3}$ receptor Binding Potential (BP_{ND}) was examined in 12 drug-free BDD patients and 12 control subjects pairwise matched by age, sex, and handedness using [^{123}I]iodobenzamide Single Photon Emission Computed Tomography (SPECT; bolus/constant infusion technique). Regions of interest were the caudate nucleus and the putamen. BP_{ND} was calculated as the ratio of specific striatal to binding in the occipital cortex (representing nonspecific binding).
Compared to controls, dopamine $D_{2/3}$ receptor BP_{ND} was significantly lower in BDD, both in the putamen (p=0.017) and caudate nucleus (p=0.022).
This study provides the first evidence of a disturbed dopaminergic system in BDD patients. Although previously BDD was classified as a separate disorder (somatoform disorder), our findings give pathophysiological support for the recent reclassification of BDD to the OCRD in DSM-5.

1. Introduction

Patients with Body Dysmorphic Disorder (BDD) suffer from a preoccupation with an imagined defect or excessive concern about a slight physical anomaly. BDD is characterized by

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http://dx.doi.org/10.1016/j.euroneuro.2015.11.018
0924-977X/

ritualized behaviors (mirror checking, grooming, camouflaging or reassurance seeking), substantial social isolation and markedly high rates of suicidality (Phillips et al., 2006). The disorder affects up to 2% of the population, but we showed that estimates of BDD prevalence rise till 10% at dermatology, plastic surgery or maxillofacial surgery outpatient clinics (Vulink et al., 2006, 2008). Both youth and adults with BDD have very poor psychosocial functioning and quality of life (Didie et al., 2007).

BDD used to be classified in the DSM-IV as a somatoform disorder, but has recently been removed in DSM-5 to the new Obsessive Compulsive and Related Disorders (OCRD) section, next to Obsessive Compulsive Disorder (OCD) (American Psychiatric Association, 2013). This new classification of BDD is justified by the notion that obsessions and compulsion are core symptoms of the disorder, i.e. obsessions with appearance and compulsive grooming or mirror checking. As a diagnostic group, OCRD may share a common phenomenological core symptom: the development of dependence on a specific, repetitive behavior that is continued despite its negative consequences, resembling addiction. Moreover, OCD shares with addiction disturbances of the brain reward system, e.g. attenuated reward anticipation in the ventral striatum (Figee et al., 2011), excessive ventral frontostriatal connectivity (Harrison et al., 2009; Sakai et al., 2011) and reduced striatal dopamine $D_{2/3}$ receptor binding (Denys et al., 2004). A shared dopaminergic reward dysfunction in OCD and addiction may be explained by abnormal recruitment of this system related to compulsive behaviors. Therefore, it can be assumed that compulsivity in BDD is also rooted in dysfunction of the dopaminergic reward system. Apart from a study that showed excessive frontostriatal responses when BDD patients were viewing pictures of their own faces (Feusner et al., 2010), as of yet, the functional anatomy of the reward system in BDD has never been investigated.

Here, we investigate if BDD has similar dopaminergic abnormalities as OCD, by examining striatal $D_{2/3}$ receptor availability in patients with BDD using Single Photon Emission Computed Tomography (SPECT) and [^{123}I]iodobenzamide (IBZM). Secondary, we will assess the correlation between both symptom severity and dopamine $D_{2/3}$ striatal binding. In line with previous findings in OCD, we hypothesize that the mean Binding Potential (BP_{ND}) of dopamine $D_{2/3}$ receptor availability in the striatum (caudate nucleus and putamen) will be lower in patients with BDD in comparison to healthy subjects. In addition, we hypothesize that symptom severity will negatively correlate with the BP_{ND}.

2. Experimental procedures

The study was conducted between September 2010 and March 2012 at the departments of psychiatry and nuclear medicine at the Academic Medical Center (AMC) in Amsterdam, The Netherlands. This study is in accordance with the principles laid down by the Declaration of Helsinki and was approved by the Medical Ethical Review Committee of the AMC. All participants provided a written informed consent to comply with all study procedures. None of the subjects participated in any other on-going scientific study. We included BDD patients and healthy control subjects. All were between 18 and 65 years of age, right-handed, physically healthy, as confirmed by physical and laboratory examinations. All had normal body mass index BMI (18.5–24.9 kg/m^2), as morbidly obese subjects have lower striatal $D_{2/3}$ receptor availability (van de Giessen et al., 2014). None of the participants had a history of neurological or other medical problems, potentially having central nervous system effects. None of the subjects were pregnant or breast-feeding. Subjects were not allowed to use more than 15 cigarettes and or more than 6 cups of caffeine containing drinks per day, as these substances influence central dopamine metabolism (Brody et al., 2004; Kaasinen et al., 2004). None of the participants had a history of drugs or alcohol abuse.

The BDD patients were consecutively selected in the outpatient clinic of anxiety disorders at the department of psychiatry of the AMC. Study criteria for the patient sample included a primary diagnosis of BDD by the DSM-IV criteria, confirmed by the Structured Clinical Interview of the DSM-IV Axis Diagnosis and a board certified psychiatrist. Patients with comorbid diagnoses except from social phobia were excluded. Patients needed a score of at least 16 on the Body Dysmorphic Disorder Modification of the Yale–Brown Obsessive Compulsive Scale (BDD-Y-BOCS). The BDD-Y-BOCS is a 12-item scale, designed to assess symptom severity during the past week. Total scores range from 0 to 48, higher scores indicating more severe symptoms. Also the Brown Assessment of Beliefs Scale (BABS) was administered to all BDD patients. The BABS is a seven-item scale designed to assess degree of delusion during the past week in a variety of psychiatric disorders. Total scores range from 0 to 24, higher values indicating a higher degree of delusion. When patients had delusional BDD (BABS $>$ 18) they were classified as delusional disorder and not included in our study. Patients did not use psychotropic medication within four weeks before the first test date. Patients received no psychotherapy for at least three months before the first test date.

The control subjects were selected from a historical [^{123}I]IBZM SPECT database at the department of Nuclear Medicine in the AMC. This database consisted of healthy volunteers with no current or life-time psychiatric DSM-IV Axis I, or Axis II disorders. None of the control subjects had ever been treated with psychotropic medication. To minimize the possibility of $D_{2/3}$ receptor density differences, controls were pairwise matched to BDD patients by age ($\pm$2 years), gender and smoking status, since $D_{2/3}$ receptor availability is influenced by natural ageing (Rinne et al., 1993), gender (Pohjalainen et al., 1998) and active smoking of cigarettes (Brody et al., 2004).

2.1. Single Photon Emission Computed Tomography protocol

Two days prior, and on the day of the scan, participants were given 200 mg/day of potassium iodide, to decrease radiation exposure to the thyroid gland. All subjects underwent a measurement of $D_{2/3}$ BP_{ND} with SPECT using the selective radiolabeled $D_{2/3}$ receptor antagonist [^{123}I]IBZM (GE Healthcare, Eindhoven, The Netherlands; radiochemical purity $>$95%), which was given by intravenous infusion, using the sustained equilibrium/constant infusion technique (Laruelle et al., 1995).

A bolus of approximately 100 MBq was administered, followed by 25 MBq/h for 3 consecutive hours. This protocol of administration induces a state of sustained binding equilibrium after 120 min, excluding that changes in cerebral blood flow may influence the $D_{2/3}$ BP_{ND} (Innis et al., 2007). SPECT data were obtained for approximately 60 min, from 120 to 180 min after the initiation of [^{123}I]IBZM administration. SPECT studies were performed using a 12-detector single slice brain-dedicated scanner (Neurofocus 810, which is an upgrade of the Strichmann Medical Equipment, Inc. Medfield, Massachusetts, USA) with a full-width at half maximum (FWHM) resolution of approximately 6.5 mm, throughout the 20 cm field-of-view. After positioning the subjects with the head parallel to the orbitomeatal line, axial slices parallel and upward from the