Material and Methods.

Subjects

Three hundred and twenty-nine OCD patients (172 male, mean ± SD age 32.03 ± 9.39 years) and 316 healthy subjects (162 male, mean ± SD age 31.18 ± 9.42 years) were included in the study. Although the OBIC sample originally included 412 OCD subjects and 368 healthy controls, the sample used here corresponds to the demographically matched sample reported in de Wit et al. Since these two samples provided near identical findings in our original voxel-wise volume comparison between OCD patients and healthy controls, for the sake of simplicity and to further control for the confounding effects of between-group differences in demographic variables, of interest in this study, we decided to only report here the results obtained with this optimally matched sample of participants.

Patients were recruited through local outpatient or specialist OCD clinics. A standardized structured interview and the Structured Clinical Interview for DSM-IV Axis I Disorders-Clinician Version (SCID-IV) were used to confirm the OCD diagnosis. Sociodemographic and clinical data such as age at onset, OCD severity, symptom dimension scores and current medication were collected at each center. Exclusion criteria for OCD patients included age under 18 or over 65 years, a current psychotic disorder, a recent history of psychoactive substance abuse or dependence, mental retardation, any severe organic or neurological pathology except tic disorder, and the presence of any contraindication to MRI scanning. Comorbidity with other Axis I disorders was not considered an exclusion criterion provided that OCD was the main diagnosis and the reason for seeking medical assistance. For each control participant, the presence or past history of any psychiatric disorder was excluded prior to inclusion. The other exclusion criteria were the same used for OCD patient selection.

Among OCD sample, 46.5% of the subjects fulfilled criteria for one or more lifetime co-morbid disorders. These were grouped in 7 categories, such as: affective disorders (30.87%), including major depressive disorder, dysthymia, bipolar I and bipolar II; anxiety disorders (21.75%), including panic disorder with and without agoraphobia, social phobia, specific phobia, generalized anxiety disorder, hypochondriasis, and post-traumatic stress disorder; other OCD-spectrum disorders (7.25%); eating disorders (3.70%), including anorexia nervosa, bulimia nervosa and binge eating disorder; attention-deficit hyperactivity disorder (2.48%) and impulse-control disorders (4.93%), including intermittent explosive disorder, pathological gambling, impulsive shopping and hypersexuality.

Materials and Methods

Data acquisition and pre-processing

Acquisition parameters of the scan sequences obtained in each center are described in Supplementary Table 1. After extensive quality control of the images by manual inspection for the presence of artefacts or medical/anatomical abnormalities, images were pre-processed using a standard protocol following the voxel-based morphometry-DARTEL pipeline implemented in the SPM8 software (Statistical Parametric Mapping software, Wellcome Trust Center for Neuroimaging, London, UK). After manual reorientation, images were segmented using the ‘new segment’ algorithm, which in addition to gray matter (GM), white matter and cerebro-spinal fluid tissue probability maps incorporates tissue probability maps of bone, soft tissue and air/background distribution. The ‘new segment’ algorithm segments, normalizes and corrects bias within the same model, although we discarded final output images from this pre-processing step and kept the rigidly transformed versions of GM images (our tissue type of interest), which were used for DARTEL normalization. Thus, with the function ‘create templates’, images were iteratively matched to a template generated from their own mean in order to generate a series of templates with increasing
resolution. Next, native space GM images from study participants were warped (and re-sampled to a resolution of 1.5x1.5x1.5 mm) to the highest resolution gray matter template within a high-dimensional diffeomorphic framework and subsequently registered to the Montreal Neurological Institute (MNI) standard space using the warping parameters of the group template to the tissue prior map in standard space. These spatially normalized GM maps were then modulated by the Jacobian determinants derived from the corresponding flow fields to restore the volumetric information lost during the high-dimensional spatial registration. Finally, bias corrected, tissue segmented, and DARTEL normalized and modulated GM images were smoothed with a 10mm full-width at half-maximum (FWHM) isotropic Gaussian kernel. Such smoothing helped in accounting for putative residual differences across individual brains due to subtle inaccuracies in pre-processing related with the use of brain images from different magnets and subjects with different ethnic backgrounds.

References


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<th>TE (ms)</th>
<th>FA (º)</th>
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N = number of scans included in analysis; FA, flip angle; TR, repetition time; TE, echo time; Matrix size (in voxels; a x b x c; c=number of slices); Voxel size (in mm; a x b x c; a x b=in-plane resolution, c=slice thickness).
Supplementary Figure 1. Whole-brain structural covariance maps of dorsal and ventral caudate seeds corresponding to OCD patients and controls (DC, dorsal caudate; VC, ventral caudate). For illustrative purposes, voxels with $p<0.05$ (uncorrected) are displayed. Colorbar represents $T$ value. Left hemisphere is displayed on the left.

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Supplementary Figure 2. Whole-brain structural covariance maps of dorsal and ventral putaminal seeds corresponding to OCD patients and controls (DCP, dorso-caudal putamen; VRP, ventro-rostral putamen). For illustrative purposes, voxels with \( p<0.05 \) (uncorrected) are displayed. Color bar represents \( T \) value. Left hemisphere is displayed on the left.

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**Supplementary Figure 3.** Whole-brain structural covariance maps of basolateral and centromedial-superficial amygdalar seeds corresponding to OCD patients and controls (BLA, basolateral amygdala; CMS, centromedial-superficial amygdala). For illustrative purposes, voxels with *p*<0.05 (uncorrected) are displayed. Color bar represents T value. Left hemisphere is displayed on the left.