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The neural basis of dysfunctional beliefs in non-medicated patients with obsessive–compulsive disorder☆

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ABSTRACT

Dysfunctional beliefs may contribute to the development and maintenance of obsessive–compulsive disorder (OCD) according to some cognitive theories. As little has been investigated about the pathophysiology of dysfunctional beliefs in OCD, this study aimed to determine the anatomical regions that are related to OCD-related dysfunctional beliefs. We first examined 23 non-medicated patients with OCD by magnetic resonance imaging (MRI) and assessed their dysfunctional beliefs using the Obsessive Beliefs Questionnaire-44 (OBQ-44). OBQ-44 has three factors: (1) inflated personal responsibility and the tendency to overestimate threat (OBQ-RT), (2) perfectionism and intolerance of uncertainty (OBQ-PI), and (3) over-importance and over-control of thoughts (OBQ-IC). Voxelwise analysis was used to investigate the correlation between whole brain gray matter volume and each score of OBQ-44 covarying for age, gender, education, severity, and intracranial volume. We found a significant negative correlation between gray matter volume and OBQ-IC scores in the left amygdala; there was no significant correlation with other scores. Comparison of the amygdala volume between patients with OCD and 23 matched healthy controls indicated no volume difference between groups. Taken together, the left amygdala volume may play a role in the presence of certain dysfunctional beliefs in OCD patients.

1. Introduction

Obsessive–compulsive disorder (OCD) is a chronic and disabling neuropsychiatric disorder, characterized by the presence of obsessions, compulsions or both. The cause of obsession is unclear because the content of normal intrusive thoughts and obsessional thoughts is indistinguishable. Unwanted and unacceptable intrusive thoughts, images, and impulses occur in at least 90% of the general population (Salkovskis and Harrison, 1984). While in healthy individuals, these intrusive thoughts, images, or impulses are ignored when perceived as useless, they develop to obsessions in patients with OCD. Salkovskis (1985) hypothesized that appraisals of responsibility and the occurrence of neutralizing activities are critical to the pathogenesis of obsessions. In his model, obsession per se is not the problem, but rather the meaning that is attached to it. After Salkovskis suggested this model, many studies were performed to identify OCD-related dysfunctional beliefs. Obsessive Compulsive Cognitions Working Group (OCCWG) reviewed the literature on OCD-related beliefs and identified 6 domains: (1) inflated responsibility, (2) overestimation of threat, (3) perfectionism, (4) intolerance of uncertainty, (5) over importance of thoughts, and (6) importance of controlling one's thoughts (OCCWG, 1997).

Recent cluster analysis studies have shown that only half of the patients with OCD have elevated dysfunctional beliefs compared to the controls, and from these observations, presence of high and low beliefs OCD subgroups were supposed (Calamari et al., 2006; Taylor et al., 2006). Bradbury et al. (2011) have reported that the high beliefs OCD subgroup tend to exhibit deficits in cognitive flexibility as measured by the Wisconsin Card Sorting Test compared to the low beliefs OCD subgroup. Thus, there might be biological differences between these two subgroups.

Taylor and Jang (2011) suggested that genetic and environmental factors might influence the dysfunctional beliefs and OCD symptoms, and the beliefs also substantially influence symptoms. They reported that beliefs accounted for a mean of 18% of phenotypic variance in OCD symptoms, and genetic and environmental factors accounted for an additional 36% and 47% of phenotypic variance respectively. Given these findings, there might be biological etiology of

Abbreviations: OCD, obsessive–compulsive disorder; OCCWG, Obsessive Compulsive Cognitions Working Group; MRI, magnetic resonance imaging; Y-BOCS, Yale–Brown Obsessive–Compulsive Scale; HDRS, Hamilton Depression Rating Scale; HARS, Hamilton Anxiety Rating Scale; OBQ, Obsessive Beliefs Questionnaire; RT, inflated personal responsibility and the tendency to overestimate threat; PI, perfectionism and intolerance of uncertainty; IC, over-importance and over-control of thoughts; SPM, Statistical Parametric Mapping; GM, gray matter; WM, white matter; CSF, cerebrospinal fluid.

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dysfunctional beliefs. However, the neural substrates of dysfunctional beliefs have not been investigated. Therefore, the aim of the present study was to investigate brain regions that are related to OCD-related dysfunctional beliefs in non-medicated patients with OCD.

2. Methods

2.1. Participants

The subjects included 23 adult patients diagnosed with OCD (based on the DSM-IV criteria) and 23 healthy volunteers matched for age, gender and handedness (see Table 1 for sample characteristics). Patients were recruited at the Kyoto Prefectural University of Medicine Hospital, Kyoto, Japan. All patients were primarily diagnosed using the Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition. All patients had a sole diagnosis of OCD and none had been taking any kind of psychotropic medication for at least 4 weeks before the magnetic resonance imaging (MRI) scanning. Eleven of 23 patients were drug naïve. Only 2 patients had ever received cognitive behavioral therapy, but both of them did not receive it at the time of examination. Exclusion criteria for patients and healthy volunteers included (1) presence of a significant disease such as neurological diseases, pulmonary, cardiac, renal, hepatic, endocrine systems, and metabolic disorders; (2) current or past DSM-IV axis I diagnosis of any psychiatric illness except OCD; and (3) DSM-IV diagnosis of mental retardation and pervasive developmental disorders based on a clinical interview and psychosocial history. There was no history of psychiatric illness in the healthy volunteers as determined by the Structured Clinical Interview for DSM-IV Axis I Disorders-Non-patient Edition. In addition, we confirmed no psychiatric treatment history in any of the healthy volunteers' first-degree relatives. Kyoto Prefectural University of Medicine Research Ethics Committee approved all procedures. All participants gave written, informed consent after receiving a complete description of the study.

2.2. Clinical measurements

All patients were tested with the Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) to assess the severity of OCD symptoms (Nakajima et al., 1995), the 17-item Hamilton Depression Rating Scale (HDRS) to assess the severity of depression (Hamilton, 1967), and the Hamilton Anxiety Rating Scale (HARS) to assess the severity of anxiety (Hamilton, 1959).

Regarding assessment of dysfunctional beliefs, an international group of OCD researchers developed specific operational definitions of cognitive constructs, judged core dimensions of OCD, and constructed self-report measures (Obsessive Beliefs Questionnaire) to assess obsessive beliefs (OCCWG, 1997, 2003). We used the Japanese version of Obsessive Beliefs Questionnaire-44 (OBQ-44) that contains three dimensions: (1) inflated personal responsibility and the tendency to overestimate threat (OBQ-RT), (2) perfectionism and intolerance of uncertainty (OBQ-PI), and (3) over-importance and over-control of thoughts (OBQ-IC) (OCCWG, 2005; Sugiura et al., 2004).

Table 1
Demographic and clinical characteristics of subjects in the OCD and control groups.

Characteristic	Patients with OCD ($n=23$)	Controls ($n=23$)	P-value
Gender, M/F, no.	9/14	10/13	0.77[a]
Handedness, right/left, no.	22/1	22/1	1.00[a]
Age, year	31.5 ± 9.7	29.8 ± 8.8	0.20[b]
Education, year	13.5 ± 2.1	15.3 ± 0.9	0.00[b]
Age of onset, year	24.7 ± 9.8	NA	NA
Duration of illness, year	6.8 ± 8.0	NA	NA
Psychotropic medication naïve/free patients, no.	11/12	No medication	NA
Total Y-BOCS score	25.2 ± 5.3	NA	NA
HDRS score	5.5 ± 4.4	NA	NA
HARS score	7.3 ± 5.5	NA	NA

Abbreviations: HARS, Hamilton Anxiety Rating Scale; HDRS, Hamilton Depression Rating Scale; NA, not applicable; OCD, obsessive–compulsive disorder; Y-BOCS, Yale–Brown Obsessive–Compulsive Scale.
Values represent the mean ± SD score unless otherwise specified. For all scales, high scores denote greater severity.
[a] χ^2 test.
[b] Independent sample t test.

2.3. MRI acquisition

All participants underwent MRI using a 1.5 T MRI system (Philips Medical Systems, Best, The Netherlands). Three-dimensional volumetric acquisition of a T1-weighted gradient echo sequence produced a gapless series of contiguous, thin sagittal sections with the following parameters: flip angle, 15°; acquisition matrix, 256 × 256; field of view, 25 cm; section thickness, 1.5 mm; voxel size, 0.98 mm × 0.98 mm × 1.5 mm; TR, 9.9 ms; TE, 5.8 ms. A board-certified neuroradiologist (K.Y.) reviewed all scans and found no gross abnormalities in any of the subjects.

2.4. Data processing

Statistical Parametric Mapping (SPM) 5 (Wellcome Department of Cognitive Neurology, University College, London) and Voxel-Based Morphometry 5 tools performed image analysis in Matlab 7.5 (Mathworks Inv., Sherborn, MA, USA). We used a unified segmentation model, which combined both normalization and segmentation parameters in a single generative model and led to a better probability image than earlier versions. We applied the affine regularization for "East Asian brains" to the data. The output images of gray matter (GM), white matter (WM) and cerebrospinal fluid (CSF) partitions were re-sliced into 1 × 1 × 1 mm voxels. The voxel values of segmented and normalized GM images were modulated by the Jacobian determinants for non-linear warping only. Gaussian kernels of 10 mm full width at half maximum smoothed the resulting GM images.

2.5. Statistical analysis

Group differences in demographic variables were examined using independent group t tests. The χ^2 test was used to examine differences in joint classifications of discrete variables.

Regarding MRI data, a multiple regression analysis was performed to test the relationship between each OBQ score and regional GM volume. We included intracranial volumes (GM + WM + CSF), age, gender, education and total score of Y-BOCS as covariates to control for the influence of these factors. We used absolute threshold masking (threshold = 0.2) to avoid possible edge effects between different tissue types. We set the significant threshold at P corrected < 0.05 based on Monte Carlo simulations [Ward BD. Simultaneous inference for FMRI data. 2000. http://afni.nimh.nih.gov/afni/doc/manual/AlphaSim]. The corrected threshold corresponds to P uncorrected < 0.001 with a minimum cluster size of 445 mm^3.

In addition, two-sample t-tests between patients and controls were performed in the detected regions using the small volume correction option implemented in SPM5 to investigate whether there is significant volume difference between the two groups. We applied the same statistical threshold and nuisance covariates except severity.

3. Results

The distribution of age, gender, or handedness did not differ between patients with OCD and healthy controls; however, the number of educational years was significantly different between the two groups (Table 1). Mean scores (± standard deviation) of OBQ-RT, OBQ-PI, and OBQ-IC are 54.0 ± 22.5, 56.0 ± 20.8, and 35.0 ± 14.9, respectively.