A Combined Optimized Voxel-Based Morphometry and Resting State Functional Connectivity Investigation in Obsessive-Compulsive Disorder

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Introduction

Neuroimaging studies of obsessive-compulsive disorder (OCD) using the functional magnetic resonance imaging (fMRI) suggested that deficits of the specific cortico-striato-thalamic-cortico (CSTC) circuits were related to the symptoms of OCD (1). Recent morphological MRI studies reported abnormal structural changes of hippocampus and cerebellum in OCD patients (2, 3). However no study has combined these two modalities to explore the whole brain anatomical and functional deficits in OCD yet. The purpose of the current study was to explore structural and functional deficits in OCD using optimized voxel-based morphometry (VBM) and resting-state functional connectivity, and to investigate its relationship to clinical symptoms.

Subjects and Methods

The study was approved by the local ethical committee of West China Hospital of Sichuan University and written informed consent was obtained from all subjects. Twenty patients with OCD (aged 26.8±9.9 years; all right handed, diagnosis based on DSM-IV) and 20 age, sex and handedness matched healthy controls (aged 21.1±9.6 years) were recruited. The MRI examinations were performed via a 3-Tesla GE MRI system with an 8 channel phase array head coil. High resolution T1-weighted images were acquired by a volumetric 3D-SPGR sequence (TR/TE=8.5/3.4msec, flip angle=12°, slice thickness=1mm, 156 axial slices). The resting-state functional MRI images sensitized to changes in BOLD signal levels were obtained via a GE-EPI sequence (TR/TE=2000/30msec, flip angle=90°, slice thickness=5mm with no gap, 30 axial slices, 200 volumes in each run). During MR examination, subjects were instructed to relax with their eyes closed without falling asleep. The high resolution T1-weighted images were preprocessed according to the optimized VBM protocol in SPM5 (http://www.fil.ion.ucl.ac.uk/spm). Two-sample t-test was performed to test the differences of the gray matter volume (GMV) of the OCD patients and controls. The functional connectivity was examined using a method based on a seed voxel correlation approach. The DPARSF software (http://www.restfmri.net) was used to calculate the parametric maps of functional connectivity. For patient data, individual parametric maps of functional connectivity were analyzed with one-sample t-test to identify voxels showing a significant positive or negative correlation to the seed time series using a family-wise error (FWE) correction at P<0.05. For between-group comparison, two-sample t-tests were performed to compare parametric maps of functional connectivity between OCD patients and controls in SPM5. A P value of less than 0.05 was deemed to be significant.

Results

After false discovery rate (FDR) correction, OCD patients demonstrated increased GMV in bilateral thalamus and left cerebellum compared to controls (Figure 1). The mean volume of bilateral thalamus volume in OCD patients was positively correlated (2-tailed Pearson r=0.94, P<0.001). There are no significant correlations between the increased GMV and any clinical measures.

Table 1. Regions demonstrating significantly different functional connectivity with the bilateral thalamus

<table>
<thead>
<tr>
<th>Seed</th>
<th>Connected Region</th>
<th>MNI coordinates</th>
<th>Cluster size</th>
<th>Direction</th>
<th>Z-score</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>R thalamus</td>
<td>R parietal cortex</td>
<td>36 -51 60</td>
<td>42</td>
<td>OCD&gt;HC</td>
<td>3.11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>L thalamus</td>
<td>L parietal cortex</td>
<td>-12 -69 60</td>
<td>34</td>
<td>OCD&gt;HC</td>
<td>3.06</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>L thalamus</td>
<td>L hippocampus</td>
<td>-18 0 -30</td>
<td>10</td>
<td>OCD&gt;HC</td>
<td>2.70</td>
<td>&lt;0.01*</td>
</tr>
</tbody>
</table>

*after small volume correction (SVC); R, right; L, left; HC, healthy controls

Conclusion

Using optimized VBM, the current research finds increased GMV in bilateral thalamus and left cerebellum in OCD patients, indicating that the pathophysiology of OCD is not only associated with GMV abnormalities in CSTC but also in the cerebellum (2). The reduced functional connectivity between bilateral thalamus and bilateral parietal cortex in OCD patients is typically argued to be direct evidence of the neuronal deficits in parietal cortex which is consistent with previous report (3). And the reduced strength of functional connectivity between left thalamus and left hippocampus predicted OCD patients total YBOCS scores, suggesting a direct relationship to global illness severity of OCD.

Reference


Figure 1. Relative to controls, OCD patients had increased GMV in bilateral thalamus and left cerebellum after FDR correction.

Figure 2. Strength of functional connectivity between the left thalamus and left hippocampus predicted the total YBOCS scores of OCD patients.