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 (MRI) 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-Telsa 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 MR 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 value 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.

Since VBM analysis showed increased GMV in the left and right thalamus and left cerebellum, each of these three regions were defined as seeds for functional connectivity analysis. When the seeds were located in the left and right thalamus respectively, both OCD patients and controls showed significant positive correlations between the seeds and the activity in the bilateral thalamus, globus pallidus, putamen, hippocampus, parietal cortex, insula and brainstem. The left cerebellum seed region in both groups only showed positive functional connectivity with the bilateral cerebellum regions.

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

Seed	Connected Region	MNI coordinates			Cluster	Analysis		
		X	Y	Z	size	Direction	Z-score	P-value
R thalamus	R parietal cortex	36	-51	60	42	OCD<HC	3.11	<0.01
	L parietal cortex	-12	-69	60	34	OCD<HC	3.06	<0.01
L thalamus	R patiretal cortex	39	-51	60	25	OCD<HC	2.87	<0.01
	L patiretal cortex	-12	-69	57	10	OCD<HC	2.72	<0.01
	L hippocampus	-18	0	-30	10	OCD<HC	2.70	<0.01*

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

When the seed was located in the bilateral thalamus, the OCD patients showed reduced functional connectivity in bilateral parietal cortex than controls (Table 1). Furthermore, when the seed was located in the left thalamus, the OCD patients demonstrated reduced functional connectivity in left hippocampus compared to controls with a small-volume correction (SVC) (Table 1). And the strength of functional connectivity between the left thalamus and left hippocampus was negatively correlated with the total Yale-Brown Obsessive-Compulsive Scale (YBOCS) scores with the patients' age as a covariant (2-tailed Partial Correlation; r=-0.59, P =0.008) (Figure 2)

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

1. Menzies L, et al. Neurosci Biobehav R 2008; 32:525-549.
2. Atmaca M, et al. Prog Neuro-Psychoph 2008; 32:1283-1286.
3. Pujol J, et al. Arch Gen Psychiatry 2004; 61:720.
4. Chamberlain SR, et al. Science 2008; 321:421.

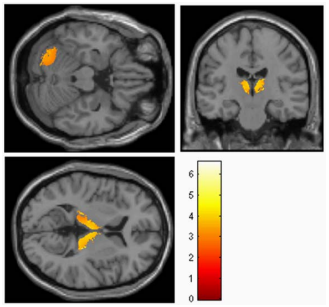

Figure 1. Relative to controls, OCD patients had increased GMV in bilateral thalamus and left cerebellum after FDR correction.

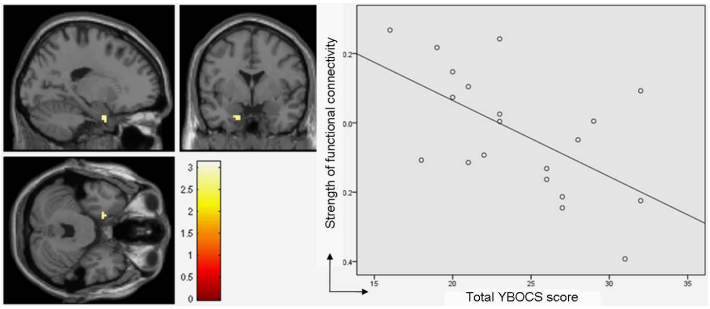

Figure 2. Strength of functional connectivity between the left thalamus and left hippocampus predicted the total YBOCS scores of OCD patients.