Morphologic and cellular metabolic abnormalities in DLPFC in patients with obsessive-compulsive disorder: A voxel-based morphometry and 1H-MRS study

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Purpose: Obsessive-compulsive disorder (OCD) is one of the anxiety disorders, which is characterized by intrusive thoughts (obsessive) and repetitive behaviors (compulsive). Several studies reported that the symptoms of OCD are mainly associated with dysfunction of the cortico-striatal-thalamic circuit (CSTC) and interconnected with the orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), dorsolateral prefrontal cortex (DLPFC), striatum and thalamus in pathogenesis. Among these areas, the DLPFC is little known in the cellular metabolic and morphologic changes in OCD patients. Therefore, this study utilized ^{1}H MRS and VBM analysis to investigate the brain volume and metabolite changes in the patients with OCD.

Subjects and Methods: A total of 28 right-handed subjects consisting of 14 patients with OCD with a duration of illness exceeding 6 years and an educational level over 14 years (mean age, 28.9±7.2 years), who were diagnosed by DSM-IV-RT, and 14 healthy controls (mean age, 32.6±7.1 years) with no history of neurological or psychiatric illness. The subjects underwent on a 3T MRI scanner (Siemens Magnetom Verio, Germany) with an 8-channel receive birdcage head coil. Brain images were acquired using the following parameters: TR/TE = 1900/2.35 ms; flip angle = 90°; FOV = 220×220 mm^2; matrix size = 256×256, voxel size= 0.85×0.85×5 mm^3. MR image data were processed by using SPM8 software with diffeomorphic anatomical registration through exponentiated Lie algebra (DARTEL) algorithm. The single-voxel ^{1}H MRS measurements were performed using a PRESS with TR/TE= 2,000/30 ms, 96 acquisitions (scanning time 3 minutes and 20 seconds), 1,200 Hz spectral width, 1,024 data points, and 8cm^3 (20×20×20 mm) voxel size. The MR spectra were post-processed and analyzed on the right DLPFC by using an MR spectroscopy data analysis package (Siemens Medical Solutions).

Results and Discussion: The regional volume of the white matter (WM) in patients with OCD were different from those of the healthy controls (uncorrected p<0.001, excluded 30voxel). Compared with healthy controls, the OCD patients showed increased WM volumes in the dorsolateral prefrontal cortex (DLPFC), middle frontal gyrus, precuneus, and inferior parietal lobule. On the other hand, significant changes of the gray matter were not observed (Fig. 1 and Table 1). In patients with OCD, the WM volumes in the DLPFC was positively correlated with the scores of Yale-brown obsessive compulsive scale (Y-BOCS) (Pearson's correlation coefficient (γ)=0.58, P<0.03) (Fig. 2). Table 2 compared the levels of the brain metabolites in the DLPFC between the both groups. The metabolic concentrations of β·γ-glutamate/glutamine (β·γ-Glx)/Cr and mI/Cr were significantly different between OCD and healthy controls. Especially, the OCD patients showed a tendency of reduced Glx concentrations in the DLPFC of the CSTC circuits. It should be noticed that the major symptom of OCD disrupted the neurotransmission of Glx, which is a primary excitatory neurotransmitter in the brain. On the other hand, the mI concentration in OCD patients was elevated as contrasted with the controls. Thus, it is assumed that the metabolic abnormality is related with the alteration of phosphatidylinositol 2nd messenger system due to the symptom of OCD.

Conclusion: This study revealed that OCD symptoms are associated with the abnormalities of the localized WM volume and cellular metabolism in the DLPFC, which are presumably related with symptom severity and cognitive dysfunction in patients with OCD. These findings will be helpful for us to understand the neural mechanism associated with OCD.

Reference : 1. Milad MR et al, *Trends Cogn Sci* 2012 ;16(1) : 43-51. 2. Ashburner J & Friston KJ *Neuroimage* 2005; 26(3):839-851.

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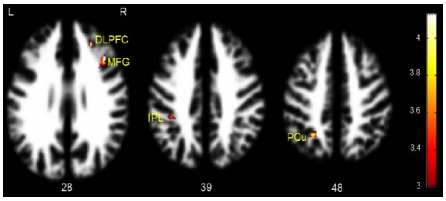

Figure 1. Differential WM volumes in patients with OCD compared to healthy controls (uncorrected P<0.001, excluded 30 voxels). The colored bars show t-values.

Anatomical area	Abbr.	Talairach coordinate			*t*-value
		x	y	z	
Dorsolateral prefrontal cortex	DLPFC	26	39	24	4.05
Middle frontal gyrus	MFG	41	25	25	4.20
Precuneus	PCu	-26	-53	48	4.41
Inferior patietal gyrus	IPG	-36	-37	39	4.04

Note-. Abbr.= abbreviation.

Table 1. Regional WM volume increases in patients with OCD compared to healthy controls (uncorrected P<0.001, excluded 30 voxels)

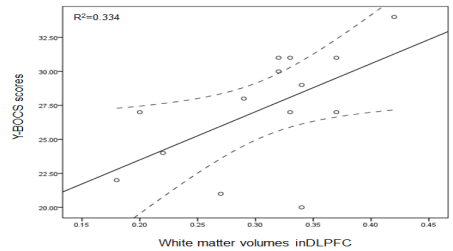

Figure 2. Correlation between WM volumes in the DLPFC and Yale-brown obsessive compulsive scale (Y-BOCS) scores in patients with OCD (P<0.03, Pearson's correlation coefficient=0.58), in which the band with dotted lines shows 95% confidence interval.

	Subject (Mean±SD)		*P value**
	patients with OCD	Healthy controls	
α-Glx/Cr	0.53±0.12 (23 %)	0.46±0.09 (20 %)	0.062
mI/Cr	0.70±0.20 (29 %)	0.46±0.10 (22 %)	0.001
Cho/Cr	0.78±0.08 (10 %)	0.81±0.11 (14 %)	0.447
β,γ-Glx/Cr	0.89±0.19 (21 %)	1.13±0.20 (18 %)	0.004
NAA/Cr	1.64±0.12 (7 %)	1.67±0.12 (7 %)	0.476
Lac/Cr	0.16±0.04 (25 %)	0.20±0.05 (25 %)	0.072
Lip/Cr	0.46±0.06 (13 %)	0.47±0.06 (13 %)	0.519

Data are presented as mean±SD (% CV).
Lip, lipid; Cr, creatine; Lac, lactate; β,γ-Glx, β,γ-glutamate/glutamine; Cho, choline; mI, myo-inositol; α-Glx, α-glutamate/glutamine; NAA, *N*-acetyl aspartate.
The statistical analysis was performed with the Independent T-test.

Table 2. Comparison of the metabolite concentrations in the right DLPFC between patients with OCD and healthy controls.