

# Neural mechanism on hypofunction of working memory maintenance with anxiety-provoking distracter in patients with obsessive compulsive disorder and generalized anxiety disorder

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**Synopsis:** Patients with obsessive compulsive disorder (OCD) and generalized anxiety disorder (GAD) are associated with abnormalities in the processing and regulation of anxiety as well as cognitive deficits. The purpose of this study was to discriminate the brain activation patterns associated with the anxiety-provoking distracter during the working memory (WM) maintenance for the human faces between patients with OCD and GAD, and healthy controls by using a function magnetic resonance imaging (fMRI).

**Subjects and methods:** A total of 12 patients with OCD (mean age = 31.3±7.4 years), 12 Patients with GAD (mean age = 33.4±9.3 years), and 12 healthy controls (mean age = 33.3±7.8 years) underwent the functional MRI on a 3.0 Tesla MR Scanner (Siemens Medical Solutions, Germany).

The activation paradigm consisted of a string of memory preparation - encoding - WM maintenance - distracter - retrieval. As for the encoding task, three different human faces sequentially appear once on a quartile coordinate. During the delay time following the encoding, the subjects were asked to maintain the WM for the encoded faces. Then, the distracters were presented, and the subjects were instructed to look at the distracters while maintaining the WM. The distracters consisted of an anxiety-provoking picture and a neutral picture. In the retrieval task, either of the face presented in the encoding task or a new face was presented. The brain activation mapping and the resulting qualification were processed by SPM8.

**Results and discussion:** The average scores of perceived anxious emotion for anxiety-provoking picture were 7.8±1.4, 7.1±1.4, and 7.7±1.4 in patients with OCD, patients with GAD, and healthy controls, respectively (p=0.523). Scores for the face recognition task with anxiety-provoking distracters were 67.8±9.1%, 64.7±14.4%, and 68.3±11.9% in patients with OCD, patients with GAD, and healthy controls, respectively (p=0.753), while the scores for neutral distracters were 62.1±15.7%, 66.3±19.6%, and 70.0±12.1%, respectively (p=0.682).

In the healthy controls, the anxiety-provoking distracters showed significantly stronger activities as compared with neutral distracters in the brain areas including the ventromedial prefrontal cortex (VMPFC), ventrolateral prefrontal cortex (VLPFC), middle temporal gyrus (MTG), inferior temporal gyrus (ITG), fusiform gyrus (FG), and superior parietal gyrus (SPG) (p<0.005) (Figs. 1,2). The patients with OCD and GAD showed significantly stronger activities in the superior temporal gyrus (STG), hippocampus (Hi), parahippocampal gyrus (PHG), amygdala (Amg), and the same brain areas activated in healthy controls (Figs. 1,2).

In the between-group analysis, there were differential brain activation patterns of the VLPFC, ITG, FG, and SPG in three groups during the WM maintenance with anxiety-provoking pictures (Table 1, Fig. 3). The patients with OCD showed significantly decreased activities in the VLPFC, ITG, FG, and SPG during the WM maintenance with the anxiety-provoking distracters as contrast to healthy controls, whereas the patients with GAD

significantly decreased activities in the same brain areas excluding the VLPFC. The BOLD signal changes of the DLPFC (x, y, z = 36, 12, 36) in the GAD group were negatively correlated with the levels of Generalized Anxiety Disorder 7 (GAD-7) (Spearman's rho = -0.71, p = 0.004) during the WM maintenance with the anxiety-provoking distracters (Fig. 4). Moreover, the levels of Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) were positively correlated with the BOLD signal changes in the amygdala (x,y,z = -22, -5, -14) in patients with OCD (Spearman's rho = 0.80, p = 0.002) (Fig. 5).

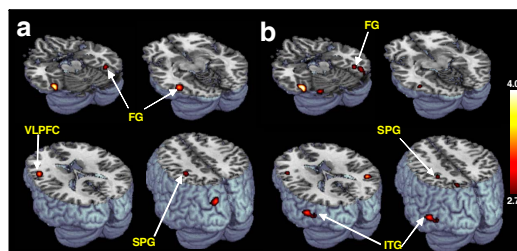
**Conclusion:** It is concluded that, for the first time, our findings provide the evidence for the differential brain activation patterns associated with the effect of anxiety-provoking distracter between healthy controls and patients with OCD and GAD during the delay interval of the WM task.

## References:

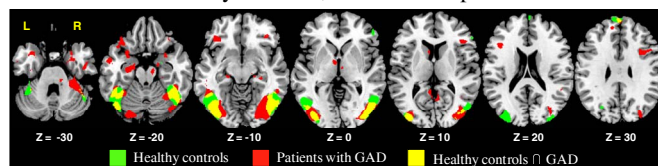
1. Dolcos et al, *Brain Res.* 2007;1152:171-181
2. Etkin et al, *Am. J. Psychiatry* 2011;168:968-978

## Acknowledgment:

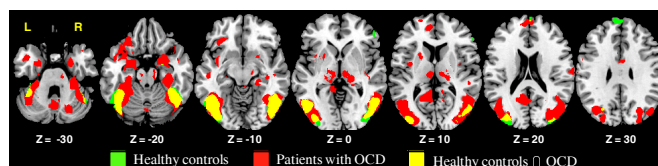
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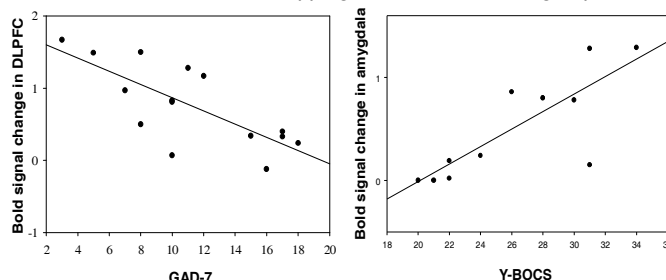
**Fig.3.** Brain areas predominantly activated in healthy controls over patients with GAD (a) and OCD (b) during WM maintenance of the target faces following anxiety-provoking distracters (p<0.005).



**Fig. 1.** Differential brain activation maps resulting from the contrast of anxiety-provoking over neutral distracter during WM of target faces in healthy controls (green) and patients with GAD (red), in which yellow activation indicates the overlapping areas between two groups.



**Fig. 2.** Differential brain activation maps resulting from the contrast of anxiety-provoking over neutral distracter during WM of target faces in healthy controls (green) and patients with OCD (red), in which yellow activation indicates the overlapping areas between two groups.



**Fig. 4.** The BOLD signal changes of the DLPFC (x, y, z = 36, 12, 36) were negatively correlated with the levels of GAD-7 during the WM maintenance with the anxiety-provoking distracters in the patients with GAD (Spearman's rho = -0.71, p = 0.004).

**Fig. 5.** The BOLD signal changes of the amygdala (x, y, z = -22, -5, -14) were positively correlated with the levels of Y-BOCS during the WM maintenance with the anxiety-provoking distracters in patients with OCD (Spearman's rho = 0.80, p=0.002).

Brain areas	F value	MNI coordinates (x, y, z)	Post-hoc t-test (t-value, p<0.005)			
			Con. <sup>a</sup> > GAD	Con. > OCD	GAD > OCD	OCD > GAD
VLPFC	10.13	56 30 28	-	4.48	-	-
Inferior temporal gyrus	13.24	-50 -56 -18	4.32	4.78	-	-
Fusiform gyrus	10.50	-46 -55 -18	3.79	4.28	-	-
Superior parietal gyrus	8.42	26 -71 54	2.85	4.06	-	-

<sup>a</sup>Con.: healthy controls