# BRAIN ACTIVATION ASSOCIATED WITH THE ANXIETY-INDUCING DISTRACTOR IN WORKING MEMORY MAINTENANCE IN PATIENTS WITH GENERALIZED ANXIETY DISORDER

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## Synopsis

General anxiety disorder (GAD) affects cognitive function in combination with the process and regulation of emotion. In general, patients with GAD have more difficulty in identifying their own emotions and understanding of emotional experience as compared with healthy controls. Recent studies have investigated the neural activation associated with cognitive processing in response to visual stimulation with facial images in health controls and patients with GAD, and revealed that the cognitive function of facial expression in patients with GAD was impaired.

The purpose of this study is to investigate the neuroanatomy associated with the effect of anxiety-inducing distractor during the delayed-response working memory (WM) task in patients with GAD.

## Subjects and Methods

A total of 36 subjects consisting of 18 patients with GAD (mean age: 37.06±11.03) and 18 healthy controls (mean age: 36.50±7.67) without any history of neurological or psychiatric illness were participated in this study. All of the patients with GAD were diagnosed by DSM-IV. The duration of illness of the patients was 5.02±7.15 years and the averaged score of the anxiety sensitivities (Anxiety Sensitivity Index-Revised: ASI-R) was 63.83±25.08. All the MR experiments were performed on a 3.0 Tesla Magneton Verio MR Scanner (Siemens Medical Solutions, Germany).

The activation paradigm consisted of a string of "cue (1s)–encoding (1s)–delay (4s)–distractor (6s)–button ready (2s)–retrieval (2s)–interstimulus interval (12s)". In the 'encoding' period, three different human faces were presented once. During the 'delay' period, the subjects were instructed to maintain WM of the encoded faces. In the 'distractor' period, anxiety-inducing distractors were presented to evoke emotionally negative images such as traffic accident, threatening behavior and disgusting things. In the 'retrieval' period, either of a new face or the face presented in the 'encoding' period was presented. The brain activation mapping and qualification were performed by using the SPM8. The correlation between localized brain activities and ASI-R scores was analyzed by the simple regression on SPM8.

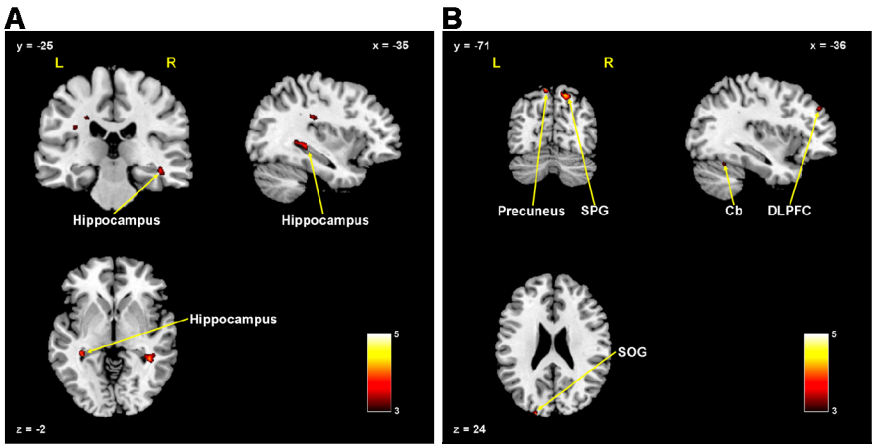


Figure 1. Brain activation map on 3-planes demonstrating full details of predominant activities in patients with GAD as contrasted with healthy controls: (A) GAD over healthy controls and (B) healthy controls over GAD during working memory task with anxiety-inducing distractors, resulting from two sample *t*-test (uncorrected, $p<0.001$). SPG: superior parietal gyrus; Cb: cerebellar cortex; DLPFC: dorsolateral prefrontal cortex; SOG: superior occipital gyrus

## Results and Discussion

The scores for the face recognition task with anxiety-inducing distractors in patients with GAD and healthy controls were 56.11±0.99 % and 66.67±0.69 % ($p<0.05$), respectively. Compared to healthy controls, patients with GAD showed significantly higher activity in the hippocampus; lower activities in the dorsolateral prefrontal cortex (DLPFC), fusiform gyrus, superior parietal gyrus, precuneus, superior occipital gyrus and cerebellar cortex during the anxiety-inducing 'distractor' period ($p<0.001$, Fig. 1).

It is important to note that there was a negative correlation between DLPFC activities and ASI-R scores (Spearman's coefficient ($\gamma$) = -0.61, $p$ = 0.01) in patients with GAD during the anxiety-inducing distractor (Fig. 2). From these results, we assume that anxiety-inducing distractors have the negative effects on cognitive processing in patients with GAD.

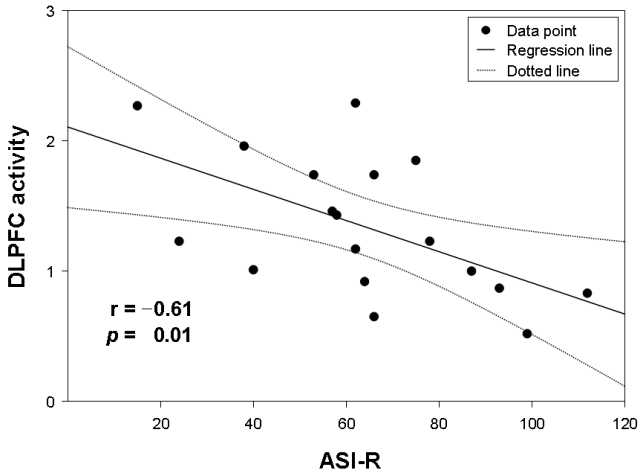


Figure 2. Correlation between DLPFC (x, y, z = 52, 31, 18) activity (change in BOLD signal) and ASI-R score during working memory task with anxiety-inducing distractors in patients with GAD ($p$ = 0.01, Spearman' correlation coefficient ($\gamma$) = -0.61), in which the band with dotted lines shows 95% confidence interval.

## Conclusion

This study revealed the brain activities associated with anxiety-inducing distractor during a delayed-response WM in the patients with GAD. This finding would be helpful to understand the neural mechanisms related to emotional and cognitive regulation in GAD.

## References

1) Dolcos *et al.* Neuropsychologia 2008;46:326-335.

2) Jeffrey *et al.* Depression and anxiety 2012;00:1-9.

## Acknowledgement

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