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Working Memory Dysfunction with fMRI Task and Gray Matter Difference in Schizophrenia Patients Using Voxel Based Morphometry

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In this study we performed fMRI studies to compare the activation regions between the schizophrenic patients and controls using the 2-back WM task paradigm. In addition, the gray matter (GM) loss between these two groups was compared using the voxel based morphometry (VBM) analysis. The brain regions showing differences in fMRI and VBM studies were compared to investigate the consequence of structural atrophy on functional activation. This study included 14 schizophrenic patients (M/F: 8/6) and 10 normal controls (M/F: 8/2). The MRI study was conducted on a clinical 1.5T MR scanner. The fMRI employed a gradient-echo echo planar imaging sequence to detect blood oxygenation level dependent signal changes associated with neural activities. We used a 2-back WM test with Korean Alphabet (KA) as target cues. Each stimulus was given to the subject every 2.5 seconds. After the functional session, high-resolution 3D anatomical images were acquired for VBM analysis, using a 3D-FLASH sequence. The images were first normalized to the Montreal Neurological Institute coordinate using a 12-parameter affine transformation, and smoothed with an 8 mm isotropic Gaussian kernel, then averaged to obtain the template. The VBM analysis was performed using the AnCova model with sex, age, onset age, onset duration and MMSE in the design matrix. The voxels with the highest z-values represented the region where GM volume was significantly different between these two groups. The clinical task accuracy of the patient group was $86 \pm 9\%$ and that of the control group was $94 \pm 5\%$. The accuracy was significantly higher in the control ($Z = -2.108$, $p = 0.035$), indicating that working memory was impaired in schizophrenic patients. The regions showing increased activity in controls included the right superior frontal gyrus, middle frontal gyrus, left precuneus, left fusiform, anterior bilateral insula, and left putamen. On the other hand, the patient group showed increased activities in the right inferior frontal gyrus in the lateral PFC and right parietal lobule. A more liberal threshold condition of $p < 0.001$ was applied to examine any threshold-dependence of laterality in activities in PFC, but the activity was still observed solely on the right PFC. The VBM result show reductions in GM in Schizophrenia versus controls in the anterior cingulate, medial frontal, superior temporal, middle temporal and fusiform gyrus.

Keywords : Voxel Based Morphometry, fMRI, Schizophrenia