ALTERED BRAIN CONNECTIVITY WITH HIPPOCAMPUS IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER

J. Zhang[1], X. Huang[1,2], S. Liu[1], Q-Z. Wu[1], D. Li[1], L. Chen[1], X. Li[1], F. Li[1], N. Amatya[1], H. Tang[1], W. Kuang[2], and Q. Gong[1,2]

[1]Huaxi MR Research Center (HMRRC), Department of Radiology, West China Hospital of Sichuan University, ChengDu, SiChuan Province, China, People's Republic of, [2]Department of Psychiatry, West China Hospital of Sichuan University

Introduction

Depression is one of the most incapacitating disorders characterized by a range of symptoms affecting both emotion and cognition. The changes in cerebral activations in depressive patients has been reported in the amygdala-hippocampus-cingulate-prefrontal-temporal-occipital network, and hippocampus was suggested to be a core node in functional connectivity study of depression [1]. Particulary, recent study indicated that depressive mood may induced by a disorder-related disruption of functions in hippocampus, prefrontal cortex and anterior cingulate [2]. In the present study we aimed to investigate the resting state functional alterations of patients with major depression when using hippocampus as the seed .

Method

The study was approved by the local ethical committee, and written informed consent was obtained from all subjects. Twenty-four subjects with major depressive disorder (MDD) and 24 age, sex, height, weight, handedness and years of education matched controls were recruited, and were scanned using a gradient-echo echo-planar imaging sequence on a 3T MR imaging system (EXCITE, General Electric, Milwaukee, USA). The severity of depression was rated using the 17-item Hamilton Rating Scale for Depression (HRSD) [3] and the Clinical Global Impression of Severity (CGI-S) [4] scale. To be eligible for the study, patients were required to have a HAMD total score $\geq$ 18 and a CGI-S score $\geq$ 4 on the day of the MR examination. Image preprocessing and statistical analysis was carried out using SPM2 (Welcome Department of Imaging Neuroscience; *http://www.fil.ion.ucl.ac.uk*). For each subject, EPI images were spatially normalized to the Montreal Neurological Institute (MNI) EPI template in SPM2, and each voxel was re-sampled to 3×3×3 mm^3. Subsequently, using the left and right hippocampi as seeds respectively, a method based on the seed-voxel correlation approach was used to examine the relationship of the symptoms and the functional connectivity. This approach includes following steps: (1) Removing signal linear trend from all of the data; (2) Temporally bandpass filtering (0.01–0.08 Hz) for each time series; (3) Correlation analysis of the seed reference with the rest of the brain in a voxel wise manner using the realigned images, and subsequently individual relativity value (r-value) map was produced, and (4) the correlation coefficient be transformed to the normal distribution by Fisher' s z transform before performing the random effect t-tests. After these steps, we did two-sample t-test between normal and patients based on their transformational connectivity relativity value (r-value) maps. $P < 0.05$ with correction for multiple comparisons was deemed significant.

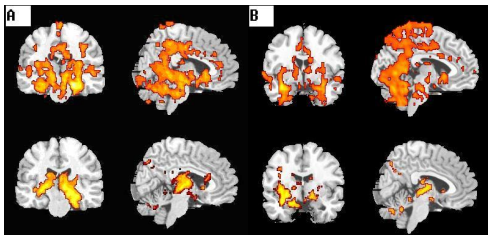

Fig.1 Averaged correlation maps for patient (bottom) and normal (up) group when using the left (A) and right (B) hippocampus as seed respectively.

Results

Using left hippocampus (BA36) as the seed cluster for fcMRI analysis, the right precentral gyrus (BA6), bilateral postcentral gyrus (BA2), bilateral cingulate gyrus (BA24), bilateral temporal regions (BA22, 39), and right precuneus (BA7) were found to be functionally related to BA36 in the normal but only posterior cingulate cortex (B30) and medial temporal lobe were found to be functional related to the same seed area in the patients. (Fig. 1A) When the seed was in right hippocampus, a significantly decreased functional connectivity was observed in patients when it was compared to the normals' (Fig. 1B), including: (1) primary somatosensory cortex (BA1, 2, 3) (2) posterior cingulate cortex (BA31), and (3) part of cerebellum. Furthermore, when the right hippocampus was used as seed, there are more intense functional connectivities in the normals were observed than that of the left hippocampus. However, the difference was reversed in the patients group. Connectivity intensity between hippocampus and other region of whole brain in depression subjects was significantly decreased compared to that of control subjects, according to the results of resting functional connectivity analysis. The brain regions showed significance included: bilateral temporal lobe (BA20, 21), medial prefrontal lobe (BA 8,9), anterior cingulate cortex (BA38) , occipital lobe (BA 18) ($p < 0.005$, corrected)(Fig. 2). When the left hippocampus was made seed,there are more connectivity intensity decreased area between the normals and the patients(Fig. 2A) compared with the right hippocampus was the seed condition. (Fig. 2B)

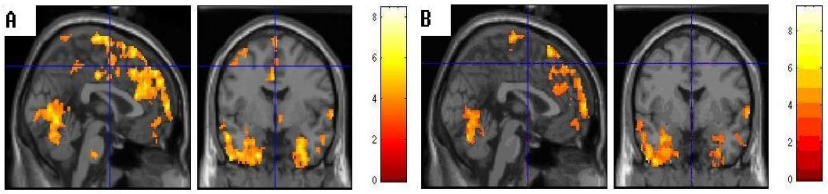

Fig.2 Results of two-sample t-test between two groups using the left (A) and right (B) hippocampus as seeds respectively.

Discussion and Conclusion

The hippocampus plays an important role in emotional and cognitive processes and its volume reductions have been reported in patients with MDD [5]. We identified decreased functional connectivity between the bilateral hippocampus and the other cerebral regions including the temporal lobe, medial frontal lobe, cingulate cortex and cuneus. Changes in brain functional connectivity (FC) between crucial brain regions as observed in the present study support the viewpoint that FC decrease may be a cause of anhedonia, loss of attention, deficient of interest in treatment resistant major depression, suggesting that the FC alteration may be used to assess the disease severity and therapeutic efficacy in patients with major depression.

Reference

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