Altered Brain Activity of Defautl Mode Network in Patients with Liver Cirrhosis

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Introduction

Functional MR imaging studies have shown that certain brain regions, including posterior cingulate cortex (PCC) and ventral anterior cingulate cortex (vACC), consistently show greater activity during resting states. These regions constitute a network to support Default Mode (DM) brain function [1]. It has been suggested that changes in the default mode networks may be associated with neurologic and psychiatric diseases [2]. It has also been applied to investigate status of consciousness [3]. Hepatic encephalopathy (HE) is one of the major complications of liver cirrhosis and a complex neurophysiological syndrome. It will be acts of confusion, personality changes, conscious changes and ups and downs of the neurological manifestations. Our purpose of this study is to investigate abnormalities of default mode networks in patients with liver cirrhosis.

Methods

The subject group comprised 35 patients with liver cirrhosis (54±9 years) and 28 normal healthy subjects (54±10years). The patients were divided into child B (n=210 and child C (n=14) according to the Child-Pugh classification which is a well known method to assess the severity of liver cirrhosis. The functional images were obtained using an EPI sequence with the following parameters: 33 axial slices, image resolution = 3.75*3.75*4, and TR= 2000 ms on a GE 3T scanner in Kaohsiung Chang Gung Memorial Hospital. Each subject was scanned in a resting state for 10 min. All resting data underwent the following preprocess procedure: slice timing, head motion correction, spatial normalization with re-sampling to 2x2x2 mm and smooth with 6mm (FWHM) Gaussian kernel using Statistical Parametric Mapping (SPM5, http://www.fil.ion.ucl.ac.uk/spm). Resting-state fMRI Data Analysis Toolkit (REST, http://restingfmri.sourceforge.net), was used for removing the linear trend of time courses and for temporally band-pass filtering (0.01–0.08 Hz) [4]. Two seed points (radius = 3 mm), one in the vACC (2, 38, -2) and another in the PCC (4, -54, 20), were chosen to generate the functional connectivity (FC) of the vACC and PCC map. Prior to the correlation analysis, a linear regression was performed to remove the effects of nine nuisance covariates: the global mean signal; the white matter signal; the cerebrospinal fluid signal; and six head motion parameters. The correlation coefficient maps were converted into z maps by Fisher's r-to-z transform to improve the normality. Finally, One sample t-test (uncorrected $p<0.001$, extent threshold $k = 30$ voxels) and two-sample t-test (uncorrected $p<0.01$, extent threshold $k = 30$ voxels) were performed to reveal significant functional connectivity maps within and between groups.

Results

The one sample results of FC map seeded in vACC and PCC were showed in Fig.1 and Fig.2, and two sample results across different groups were showed in Figure 3 and Figure 4. The hot and winter color bar indicated significant value of the correction and anti-correction results, respectively. From the one sample study, significant decrease of DM patterns, including the correction and anti-correction regions, were found in patients with liver cirrhosis corresponding to the increase severity of child criteria. In vACC (Fig 3), significant difference was found in caudate, putamen, thalamus and insula between groups and normal subjects. In PCC (Fig. 4), significant difference was found in frontal, parietal, as well as basal ganglia.

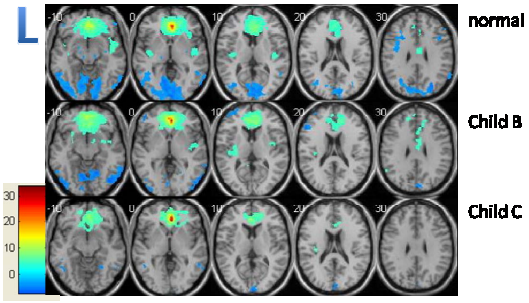

Fig.1 One sample vACC FC maps in different group.

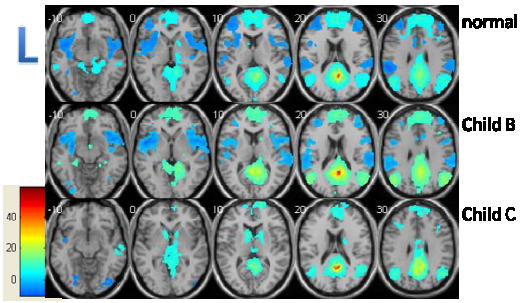

Fig.2 One sample PCC FC maps in different group.

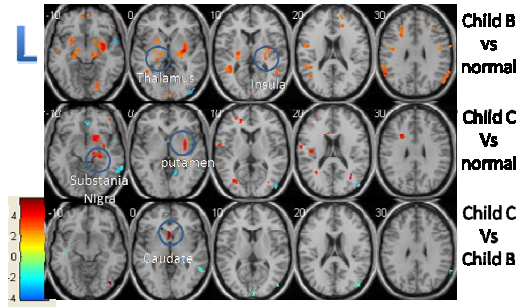

Fig.3 Two sample vACC FC maps between groups.

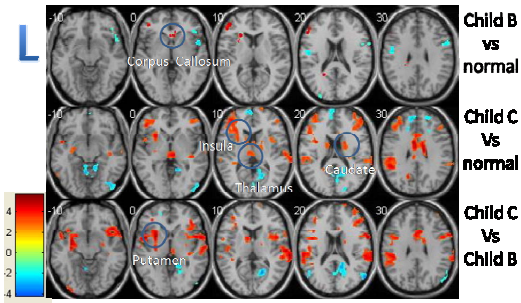

Fig.4 Two sample PCC FC maps between groups.

Discussions and Conclusions

Hepatic encephalopathy (HE) is one of the major complications of liver cirrhosis. Its clinical presentation comprises neuropsychiatric symptoms, altered sleep patterns, changes in the state of vigilance such as somnolence, stupor up to coma and motor deficits. The results from this study suggest that BOLD functional connectivity reflects intrinsic properties of the brain and that the strength of the intrinsic connections can be change in patient with liver cirrhosis. The opposite effect on DM network and anti-DM network supported previous reports that the human brain is intrinsically organized into dynamic, anti-correlated functional networks [3]. Our study supplements previous studies by adding a level of functional detail to the relationship between altered consciousness and intrinsic brain properties. It may improve our ability to monitor the treatment response and prognosis prediction in patient with liver cirrhosis.

References

[1] Greicius et al. Proc Nat Acad of Sci USA. 100 (1): 253-8. 2003. [2] Raichle et al. Proc Nat Acad Sci USA. 98(2):676-82. 2001. [3] Fox et al. Proc Nat Acad of Sci USA. 102(27):9673-8. 2005. [4] Biswal et al. Magn Reson Med 34: 537–541. 1995.