Limited Default Network in Bipolar Disorder by BOLD-based fMRI

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Background

The consistent and characteristic default network (tripod component) of resting rhythm has been detected by utilizing BOLD-based fMRI at both 1.5T and 3T field strength (Yeh et al, 2005). The resting tripod component involved bilateral occipital, precuneus, posterior cingulate, inferior parietal lobule and medial prefrontal cortices (Yeh et al, 2002 and 2006). Similar tripod component coexists with task-relevant signal components in sensori-motor or cognitive tasks (e.g. naming task), and implies the functional connectivity (Laufs et al, 2003). To study the change of functional connectivity in bipolar disorder (BD), tripod components were derived from sessions of N-back memory fMRI studies for 11 patients with bipolar disorders (types I or II) in euthymic state and 9 normal subjects. By identifying the default network using independent component analyses and spatiotemporal constrains, limited default network of BD was identified as one of the neuro-imaging state markers for BD.

Materials and Methods

(1) N-back fMRI

Twelve right-handed euthymic BD patient and twelve normal subjects (gender matched as male : female = 6 : 6 for each group, age matched as 35.2 +/- 11.3 and 33.4 +/- 12.4 years old, respectively) were recruited by filling written IRB consent form and evaluation of a psychiatrist using DSM-IV criteria. Blocked fMRI paradigm of N-back was constructed using English letters with jittered intervals and counter-balanced schemes in STIM2 (Neuroscan Inc., VA, USA). With a mirror projection for visual stimuli, patients and subjects were instructed to response as soon as possible by pushing button during the 1-Back and 2-Back fMRI blocks interleaved with resting blocks of eye fixation (1B-fix-2B-fix-1B-fix-2B-fix-2B-fix-1B-fix). With the head fixation using a vacuum pillow, images were acquired using a 3T Medspec S300 system (Bruker GmbH, Ettlingen, Germany) equipped with an actively shielded gradient coil, a quadrature transceiver of head. Single-shot echo planar images (64x64 matrix, slice thickness/ gap = 5/1 mm, 20 slices) covering whole brain were acquired with a flip angle = 90 degree, echo time (TE) = 50 ms, repetition time (TR) = 2000 ms, dummy scan (DS) = 5 for reaching stable magnetization and repetition number (NR) = 240.

(2) Data Analyses

Off-line analysis using modified AFNI (Analysis of Functional NeuroImages, NIMH, Bethesda, USA) ensured the head motion with head translation < 2 mm and head rotation < 1 degree. Studies (one of patient and two of subject studies) of head motion exceeding the motion criteria mentioned above were rejected from data analysis, because no preprocessing of motion correction was applied for independent component analyses (ICA). Identification of tripod component, except for one normal subject, was obtained by informax ICA (Computational Neurobiology Laboratory, The Salk Institute for Biological Studies, La Jolla, USA) and spatial correlates of normalized coordinate system for the characteristic tripod resting component, Averaged temporal template derived from ICA tripod component was applied as the regressor for GLM estimation in SPM2 (Functional Imaging Laboratory, Wellcome Department of Imaging Neuroscience, UCL, London, UK). Two level statistical evaluation using random-effect analysis was performed with statistical criteria of $p<0.001/n>0$ for the first level and $p<0.05/n>100$ for the second level, respectively.

Results

Co-existence of task-relevant (memory task) and task-irrelevant (tripod component) activities was demonstrated in one BD patient for spatiotemporal correlates (**Figure 1**). Consistent identification of tripod component (**Figure 2**) represented the connectivity of default mechanisms in both groups of BD (n=11) and normal subjects (n=9). And random-effect group analyses demonstrated the decreased default connectivity in BD group (**Figure 3**), especially right insula and bilateral dorsal lateral prefrontal regions (**Figure 3**, right).

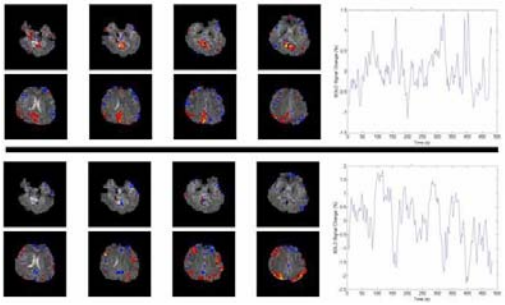

Figure 1 : Co-existence of tripod component (default mechanism, upper raw) and task-relevant (memory correlates, lower raw) activities (left : spatial extension and right : time courses) was verified in a BP patient with paradigm design of N-back task.

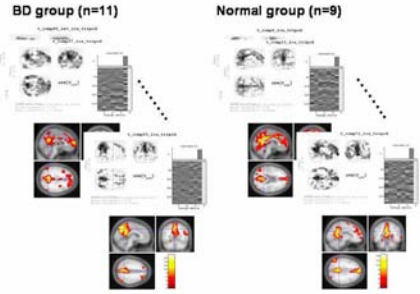

Figure 2 : Connectivity of default mechanism in groups of BD (n=11) and normal subjects (n=9) by analyses combining informax ICA and SPM.

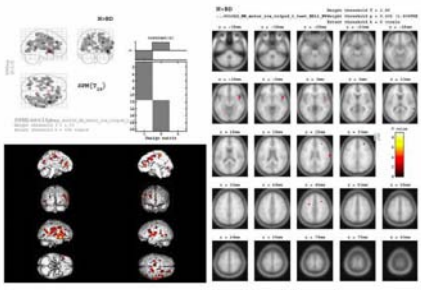

Figure 3 : Random-effect analysis of BD and normal groups showed limited default connectivity of BD group in statistical criteria of $p<0.05/n>100$ (left) and $p<0.005/n>0$ (right)

Conclusions

Correlates of the tripod component (default mechanism) mainly involved posterior medial (interpretation of environment), posterior lateral, ventral medial prefrontal (integration of information from internal/external environments) and dorsal medial prefrontal cortices (monitoring and reporting one's mental states). For the BOLD-based fMRI studies of N-back task, both groups of BD and normal subjects showed co-existence of task-irrelevant tripod component and task-relevant activities of memory correlates. Random-effect analysis confirmed the limited default connectivity in right insula and bilateral dorsal lateral prefrontal areas for the BD group, who may have deficit in emotional and executive functions. But further study will be required for evaluating this finding as one of the neuro-imaging state markers for BD.

Acknowledgement

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References

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