Decreased posterior default mode network for depression patients

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Introduction: Alterations of default mode network (DMN) from resting state fMRI have been observed for patients with major depression [1,2]. Some studies reported increased connectivity strengths for depressed patients, while contradictory findings were also reported [3], indicating that depression is a very complicated brain disorder. In this study, we combined Independent Component Analysis (ICA) and seed based connectivity analysis to study the posterior DMN network between patients and normal controls, as well as pre-treatment and post-treatment conditions. Consistent results of decreased DMN connectivity were found for patients between posterior cingulate cortex (PCC) and other regions.

Methods: Subjects: 23 major depression patients (9 males) and 25 normal controls (10 males) participated in this study. This study was conducted at Xi'an Central Hospital, China. Patients were diagnosed based on Structured Clinical Interview for DSM-IV and Hamilton Depression Rating Scale (HDRS). Treatment of patients consisted of the sertraline in a fixed-dosing design over 8 weeks (50-100 mg/day). Patients were evaluated and scanned at beginning of week 1 and end of week 8. MRI scans: The MR images were acquired with a 1.5 Tesla GE Excite MRI system (GE Health care, Milwaukee, WI, USA). Resting state functional images were acquired with a single shot gradient recalled echo planar imaging sequence (TR = 2500 ms, TE = 35 ms, 4 mm isotropic resolution, and scan time of 6:15 minutes). A high resolution T1-weighted image was acquired with 3D SPGR sequence. Data Analysis: All functional data were motion corrected in FSL (http://fsl.fmrib.ox.ac.uk/). We computed translation motion and rotational motion from the log file of motion correction [4]. The functional images were first analyzed using MELODIC with 20 components to find the default mode network. Anterior and posterior sub-networks were found in good correspondence to DMN. Because dissociation of anterior and posterior sub-network of DMN in ICA is very tricky, we decided to switch to seed-based approach. A seed at PCC with highest intensity was selected from group ICA of all subjects and all sessions. The MNI coordinates of the seed is [0 -58 34]. Then a seed based network analysis was performed. Aided by the anatomical image, the functional images normalized to MNI template and smoothed with a kernel of 6 mm. After regressing out head motion, white matter and the CSF time signals, and band-pass filtering between 0.01-0.10 Hz, a PCC network was obtained for each subject/session by computing the cross-correlation coefficient of time courses between PCC seed and other voxels. The correlation coefficient was converted to Z-score using Fisher's formulae. Two-sample t-test was used to compare PCC networks between different group (pre-treatment patients, post-treatment patients, and controls).

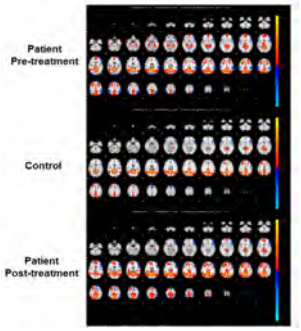

Fig. 1. Posterior DMN network derived from Group ICA for patients pre- and post-treatment, and normal controls.

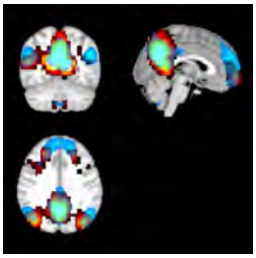

Fig. 2. Posterior DMN (red-yellow) superimposed by PCC-based network (blue-cyan) from control groups shows large overlap of the two networks.

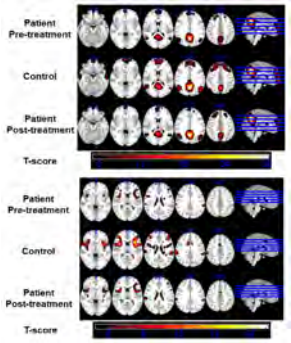

Fig. 3. PCC correlated networks (top) and anti-correlated networks (bottom).

Results: The Hamilton depression score was 25.3 ± 3.9 before treatment. After treatment, the score dropped to 5.3 ± 2.8 while the score for controls was 0.6 ± 1.0. No significant difference was observed for the head motion parameters between Groups ($p > 0.2$ for all paired comparisons with two-sample t-test). Two DMN-related networks were detected from ICA. Similar to Ref. 2, we labeled the one with highest amplitude near PCC as posterior DMN. Spatial maps of posterior DMN are shown in Fig. 1. We see a clear decrease of connectivity in posterior DMN in pre-treatment patients compared to normal controls. Patients after treatment show similar DMN pattern as normal controls. Fig. 2 shows similar spatial pattern for seed based network of PCC as compared with posterior DMN network derived from ICA. The PCC correlated networks and PCC anti-correlated networks are displayed in fig. 3 for all three groups. For PCC correlated network, there is more frontal and temporal connectivity for controls. For PCC anti-correlated network, the controls also show stronger connectivity to insula and cingulate gyrus. The difference can be seen clearer from a two-sample t-test. Fig. 4 shows the statistical results of network difference between three groups. As expected from Fig. 3, both controls and post-treatment groups showed significantly higher negative connectivity between PCC and cingulate gyrus, which is part of the anti-correlated network. On the other hand, only controls showed significant higher connectivity between PCC and frontal and temporal regions. No treatment-related significant difference was found for PCC correlated network.

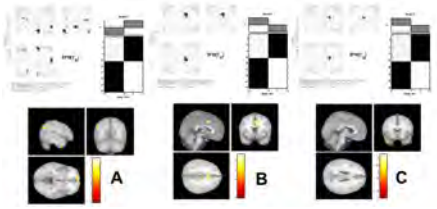

Fig. 4. Statistical results show network differences between pre-treatment patients between normal controls (A: correlated network; B: PCC anti-correlated network) and post-treatment patients (C: PCC anti-correlated network). For all analysis, $p = 0.005$ uncorrected, cluster size = 100 voxels.

Discussion: Our results showed significant difference of the posterior default mode sub-network between major depression patients and normal controls. Specifically, normal controls exhibited higher connectivity between PCC and frontal/temporal regions. The treatment does improve the connectivity strength of patients, especially in the anti-correlated network. These differences were unlikely induced by difference in head motion.

References: 1. Greicius MD et al., Biol Psychiatry. 2007, 62:429-37. 2. Li B et al., Biol Psychiatry. 2013;74:48–54. 3. Veer IM et al., Front Syst Neurosci. 2010, 4, pii:41. 4. Van Dijk K.R., et al., Neuroimage. 2012; 59:431-438.