Resting-state functional network abnormalities in major depressive disorder with self-harm: a connectome analysis

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Introduction

Major depressive disorder (MDD) is a public health problem in recent years. MDD is characterized by emotional imbalance with extremely in emotional processing. MDD patient with self-harm may eventually result in the death. Previous studies showed abnormal functional connectivity between specific brain regions [1], and few studies demonstrated the functional network can be observed by the large-scale structural pathways interconnecting [2]. Graph theory is capable of evaluating the topological organization of the human brain [3]. Therefore, in this study we tried to find out the functional connectomic difference between MDD patients and healthy subjects based on resting-state functional magnetic resonance imaging (rs-fMRI) using graph theoretical and network-based statistic (NBS) analyses.

Materials and Methods

According to Hamilton Depression Rating Scale (HAM-D), 18 participants were separated into two groups, 9 MDD patients and 9 healthy subjects. All participants were scanned to obtain rs-fMRI data using 1.5T MRI (Signa HDxt, GE Medical System, USA) with an 8-channel head coil. All subjects were instructed to relax with their eyes closed, to think of nothing in particular, and not to fall asleep. The functional images were obtained using the echo planar image (EPI) sequence. Image parameter were TR/TE = 2000 ms/30 ms, matrix = 64 × 64, FOV = 250 × 250 mm^2, number of repetition = 300 and 33 axial slices aligned along AC-PC lines.

In data analysis, each participant's functional image was spatially normalized to the Automated Anatomical Labeling (AAL) template in Montreal Neurological Institute (MNI) naive space using Statistical Parametric Mapping (SPM), and connectivity matrix was obtained after functional connectivity analysis. Graph theoretical analysis was then applied to investigate systematical alteration of whole brain functional topological organization, including small-worldness (σ), clustering coefficient (C), normalized clustering coefficient (γ), shortest path length (L), normalized shortest path length (λ), local efficiency (E_{local}), global efficiency (E_{global}), modularity, assortativity and transitivity. The NBS analysis was then applied to evaluate systematical alteration of whole brain functional connectivity in MDD patients.

Results and Discussions

Small world topology was observed in both MDD patients and healthy subjects. Compared to healthy subjects we found lower σ, γ and E_{local}, but higher λ, L, C, E_{global}, modularity, assortativity and transitivity in MDD patients. In particular, σ, γ, λ, L and E_{global} reached the significant difference ($p < 0.05$) (Fig. 1). The results indicated there was a less efficient functional network in MDD patients with poor ability of local segregation and global integration. The whole functional network of MDD patients and healthy subjects could be visualized in figure 2A and 2B, respectively. More connections between nodes in MDD patients were found, so the network was more like random network. The abnormalities of network may associate with the depressive symptoms in MDD patients. The NBS revealed one connected sub-networks that were disrupted in MDD patients. The altered sub-network mainly comprised edges between the right frontal superior orbital gyrus and left frontal medial orbital gyrus, left insula and right middle cingulum gurus; between right frontal superior orbital gyrus and left insula, right middle cingulum gtrus; between left frontal inferior orbital gyrus, left insula and right thalamus (Fig. 2C). Graph theoretical and NBS analyses revealed that MDD patients exhibit a disruption in the topological organization of functional brain networks. The results may let us understand the emotional abnormalities and cognitive bias of MDD patients.

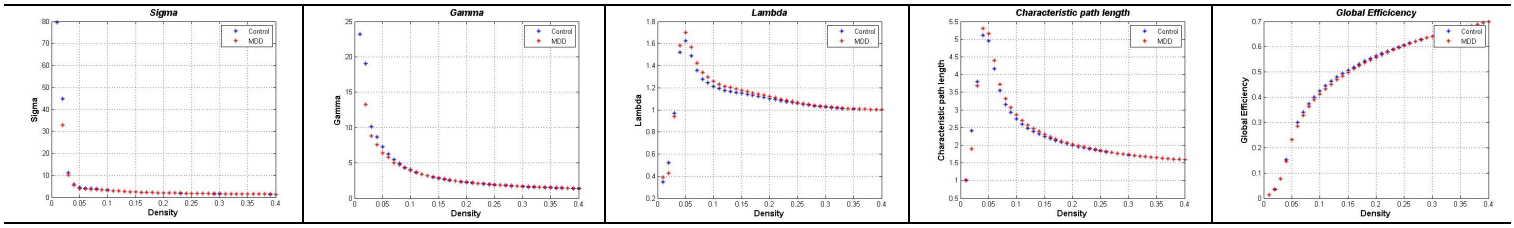

Figure 1: Significant altered topological measures between MDD patients and healthy subjects included σ, γ, λ, L and E_{global}.

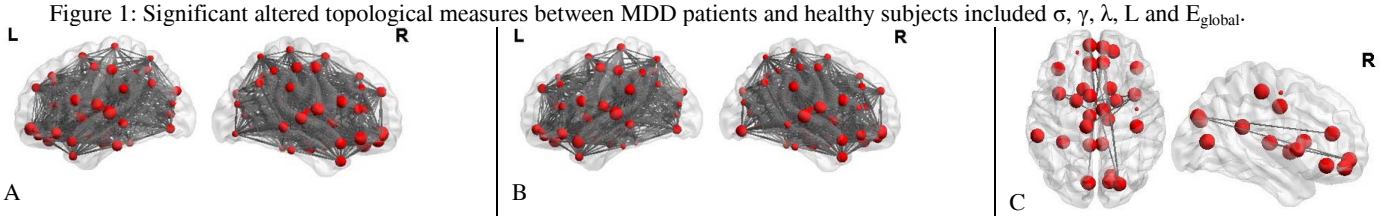

Figure 2: Visualization of functional connectivity network in (A) MDD patients and (B) healthy subjects using graph theoretical analysis. (C) The altered sub-networks in MDD patients compared to healthy subjects using NBS analysis.

Conclusions

Graph theoretical and NBS analyses revealed that MDD patients exhibit a disruption in the topological organization of functional brain networks, including the changes of local segregation and global integration in MDD patients. The abnormalities may let us know the functional disturbances of mood in the disease. In the future, the finding may be the clue to classify MDD patients and provide the reference for clinical diagnosis.

References

[1] Chenwang Jin et al., Neuroscience Letters 2011; 503: 105-109. [2] Zhiliang Long et al., Progress in Neuro-Psychopharmacology & Biological Psychiatry 2014; 56: 18-26. [3] Li M et al., Brain Connect 2014; 4(2): 145-56.