Altered topographical organization of the default-mode network in first-episode remitted geriatric depression.

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Target audience Researchers studied on translational medicine in neuroimaging and neuropsychiatric disorders.

Purpose Cognitive impairment is common in geriatric depression and often persists despite the remission of depressive symptoms [1]. Altered default-mode network (DMN) connectivity and activity seem to occur in depression, although previous findings are partially inconsistent [2, 3], reporting that both increased and decreased functional connectivity. However, importantly, it should be emphasized that the DMN changes in depression may present in a complex way, not as pure increases or decreases. In fact, several previous graph theory-based studies have demonstrated that both whole-brain and sub-brain functional networks possess efficient small-world properties at a low cost [4]. Therefore, in this study, we performed a prospective study to investigate the topological organization of the DMN in patients with remitted geriatric depression (RGD) and whether RGD patients, relative to healthy control subjects, would be more likely to show disrupted topological configuration of the DMN during the resting-state.

Methods Twenty-five RGD patients and twenty-five matched healthy control (HC) subjects underwent cognitive evaluations and resting-state functional magnetic resonance imaging (R-fMRI) scans. The functional connectivity networks were constructed by thresholding Pearson correlation metrics of the DMN regions defined by group independent component analysis (ICA) (**Fig.1**), and their topological properties (e.g., small-world properties and network efficiency) were analyzed by using graph theory-based approaches. Nonparametric permutation tests were further used for group comparisons of topological metrics.

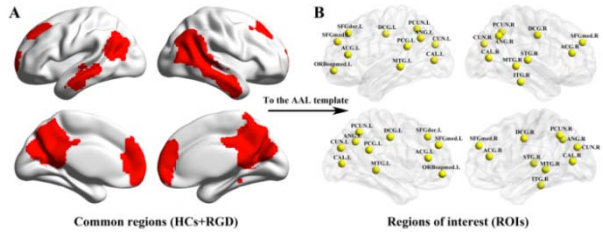

Fig.1. Regions of interest. The common FC map was parcellated by using the automated anatomical labeling (AAL) template.

Results Relative to healthy controls, the RGD patients showed decreased functional connectivity in the posterior regions of the DMN (i.e., the posterior cingulate cortex/precuneus, angular gyrus and middle temporal gyrus) (data not shown). Furthermore, the functional brain networks of both HC subjects and RGD patients showed small-world properties with higher clustering coefficients (i.e., $\gamma>1$) but comparable characteristic path length (i.e., $\lambda\approx1$) relative to random networks (**Fig.2**). However, RGD patients showed abnormal global topology of the DMNs (i.e., increased characteristic path length and reduced global efficiency) compared with healthy controls (**Fig.3**).

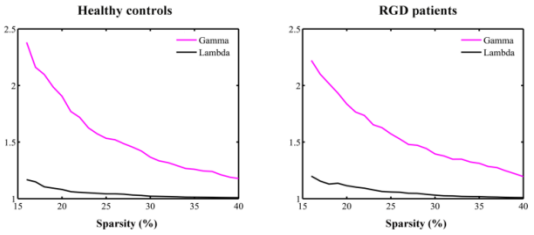

Fig.2. Small-world properties of function brain networks. The graphs show the changes in the γ (C_p^{real}/C_p^{rand}) and λ (L_p^{real}/L_p^{rand}) in healthy controls (left) and RGD patients (right) as a function of sparsity thresholds.

Discussion and Conclusion This study investigated the topological properties of the DMNs in RGD patients using the R-fMRI. These findings provided support for the notion that disease-specific brain networks still possess small-world properties. Moreover, RGD patients showed abnormal global topology of the DMNs (i.e., increased characteristic path length and reduced global efficiency), implying a less optimal organization of the network in RGD. These results highlight the role of the DMN in the RGD pathophysiology and provide insights into the neurobiological mechanisms underlying the cognitive deficits of RGD.

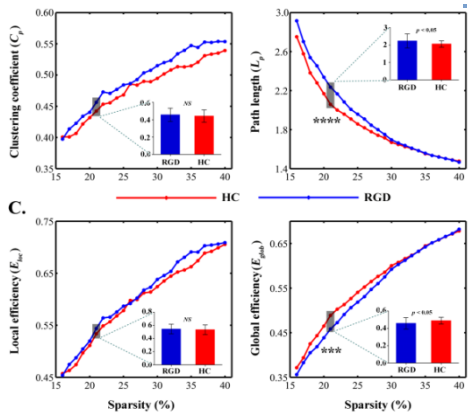

Fig.3. Graphs show small-world parameters and network efficiency of the DMN. Clustering coefficient (**A**), characteristic path length (**B**), local efficiency (**C**) and global efficiency (**D**) of the RGD (bule line) and HC (red line) groups as a function of sparsity thresholds.

References 1. Butters MA, Young JB, Lopez O, et al. Pathways linking late-life depression to persistent cognitive impairment and dementia. Dialogues Clin Neurosci 2008;10:345-57. 2. Li B, Liu L, Friston KJ, et al. A treatment-resistant default mode subnetwork in major depression. Biol Psychiatry 2013;74:48-54. 3. Zhu X, Wang X, Xiao J, et al. Evidence of a dissociation pattern in resting-state default mode network connectivity in first-episode, treatment-naive major depression patients. Biol Psychiatry 2012;71:611-7. 4. Bullmore E, Sporns O. Complex brain networks: graph theoretical analysis of structural and functional systems. Nat Rev Neurosci 2009;10:186-98.