Amygdala Network Dysfunction Links Depressive Symptom and Memory Deficit in Elderly with Amnesic Mild Cognitive Impairment

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Introduction: The public health implications of depression and memory impairment in the geriatric population are enormous [1]. However, little is known about the nature of the neuropathophysiology underlying the depressive symptoms and memory impairment. The purpose of this study was to identify neural correlates of depressive symptoms and memory deficits in the amygdala network in elderly subjects.

Methods: Fifteen amnestic mild cognitive impairment (aMCI) and 18 age-matched control (CN) subjects participated in this study and completed the neuropsychological test. The intrinsic amygdala functional connectivity (AFC) network activity, measured with *m* values, which are Fisher-transformed cross-correlation coefficients, was correlated to Geriatric Depression Scale (GDS) and Rey Auditory Verbal Learning Test delayed recall (RAVLT-DR) scores.

Results: aMCI subjects had significantly higher GDS scores, worse RAVLT-DR scores ($p < 0.01$), and markedly enhanced AFC network activity in the prefrontal, parietal and temporal lobules, and subcortical regions. The AFC network activity was positively correlated with the GDS in the left inferior parietal cortex (IPC), fusiform (FFG), inferior temporal cortex (ITC), right IPC, dorsolateral prefrontal cortex (DLPFC), insula (Ins), thalamus (Tha) and parahippocampus (PHG) in the aMCI group, but only in the left IPC in the CN group; whereas it was positively correlated with RAVLT-DR scores in the left posterior cingulated cortex (PCC) and precuneus (Pre) in both groups, but only negatively correlated in the right postcentral gyrus, inferior frontal gyrus, DLPFC and IPC in the CN group.

Discussion and Conclusion: Growing evidence also has confirmed that there is a certain relationship between depression and memory loss [2]. Moreover, late-life depression is considered a preclinical stage of dementia [3]. Presently, the significant different correlation patterns in the above distinct nodes within the AFC network were identified. This finding suggests that the AFC network has dual effects that link depressive symptoms and memory deficits. The altered neural substrates of the AFC network underlying the emotional and cognitive functions mediation were associated with disease state.

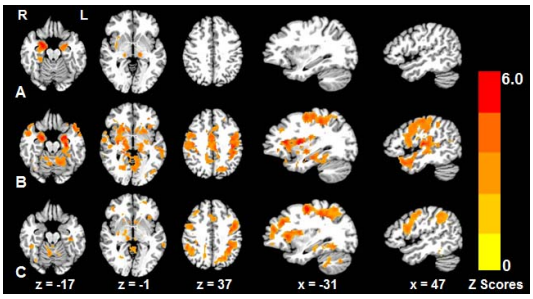
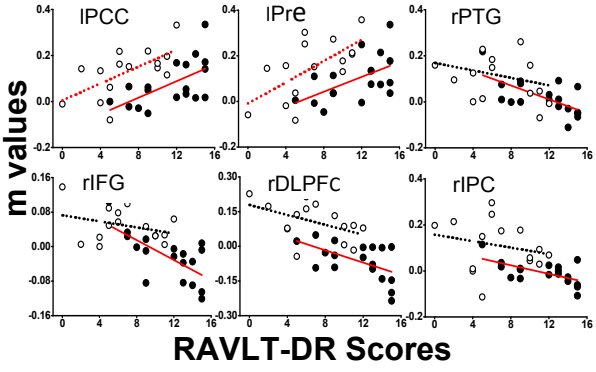


Fig 1. The intrinsic AFC network pattern for CN group **(A)** and for aMCI group **(B)** as well as significantly enhanced intrinsic AFC network in aMCI group than CN group **(C)** ($p < 0.0001$, corrected). R: right; L: left. Color bar presents with *z* scores.



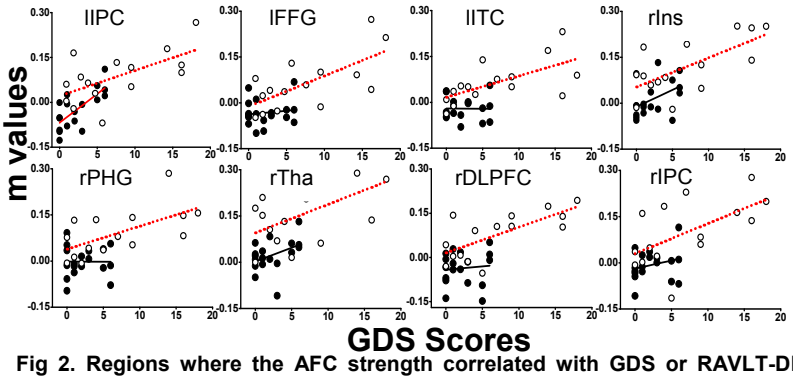


Fig 2. Regions where the AFC strength correlated with GDS or RAVLT-DR scores in CN group (solid circle) and aMCI group (empty circle). Dotted lines are for the aMCI group and solid lines are for the CN group. Red line represents significant correlation ($p < 0.05$), black line is not. **Top:** Quantitative information for regions where AFC strength significantly correlated with GDS scores. For the CN group, AFC strength significantly correlated with GDS scores in lIPC ($p < 0.001$). For the aMCI group, AFC strength significantly correlated with GDS scores in lIPC ($p < 0.015$), lFFG ($p < 0.005$), lITC ($p < 0.012$), rIns ($p < 0.006$), rPHG ($p < 0.016$), rTha ($p < 0.022$), rDLPFC ($p < 0.003$), and rIPC ($p < 0.02$). **Right:** Quantitative information for regions where AFC strength significantly correlated with RAVLT-DR scores. For the CN group, AFC strength significantly correlated with RAVLT-DR scores in lPCC ($p < 0.01$), lPre ($p < 0.02$), rIFG ($p < 0.002$), rPSTG ($p < 0.004$), rDLPFC ($p < 0.02$), and rIPC ($p < 0.007$). For the aMCI group, the AFC strength positively correlated with RAVLT-DR scores in lPCC ($p < 0.01$) and lPre ($p < 0.01$).

Reference: 1. Luiz Pessoa. Nat. Rev. Neurosci.2008, 9, 143-148. 2. Ganguli M, et al. Arch Gen Psychiatry. 2006;63(2):153-160. 3. Steffens DC et al., Arch Gen Psychiatry. 2006;63(2):130-8.

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