Late-onset depression and the BDNF Val66Met polymorphism influence the functional connectivity of hippocampus: a resting-state functional MRI study

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Objective: To investigate the effect of Late-onset depression (LOD) and brain derived neurotrophic factor (BDNF) Val66Met on the hippocampal functional connectivity (FC).

Methods: 26 LOD subjects and 36 gender-, age-, and education-matched normal controls (NC) were recruited. The 62 participants were divided into four groups according to BDNF genotype. All subjects underwent resting state functional magnetic resonance imaging (R-fMRI). Bilateral hippocampal masks were manually traced on high-resolution 3D images as region of interest (ROI) to detect the hippocampal FC. Two-way analysis of covariance (ANCOVA) was performed to explore the main effects of disease and genotype and their interaction on the hippocampal FC. Spearman correlation was used to test the correlation between the FC and the neuropsychological data.

Results: LOD and BDNF Val66Met polymorphism both influence the FC between hippocampus and the occipital cortex. Moreover, LOD is also associated with FC between hippocampus and the orbit-frontal cortex (OFC) and insula, and BDNF Val66Met also influenced the FC between hippocampus and precuneus as well as cerebellum. The interaction of LOD and BDNF Val66Met polymorphism is primarily associated with the FC between hippocampus and the dorsal anterior cingulate cortex, the lateral prefrontal cortex and the angular gyrus. Only the effects of LOD were significantly associated with the neuropsychological data.

Conclusions: LOD, BDNF Val66Met polymorphism and their interaction are all associated with hippocampal FC, but with varying influence on the connective regions. Furthermore, the effects of LOD also have significantly correlations with the neuropsychological data.

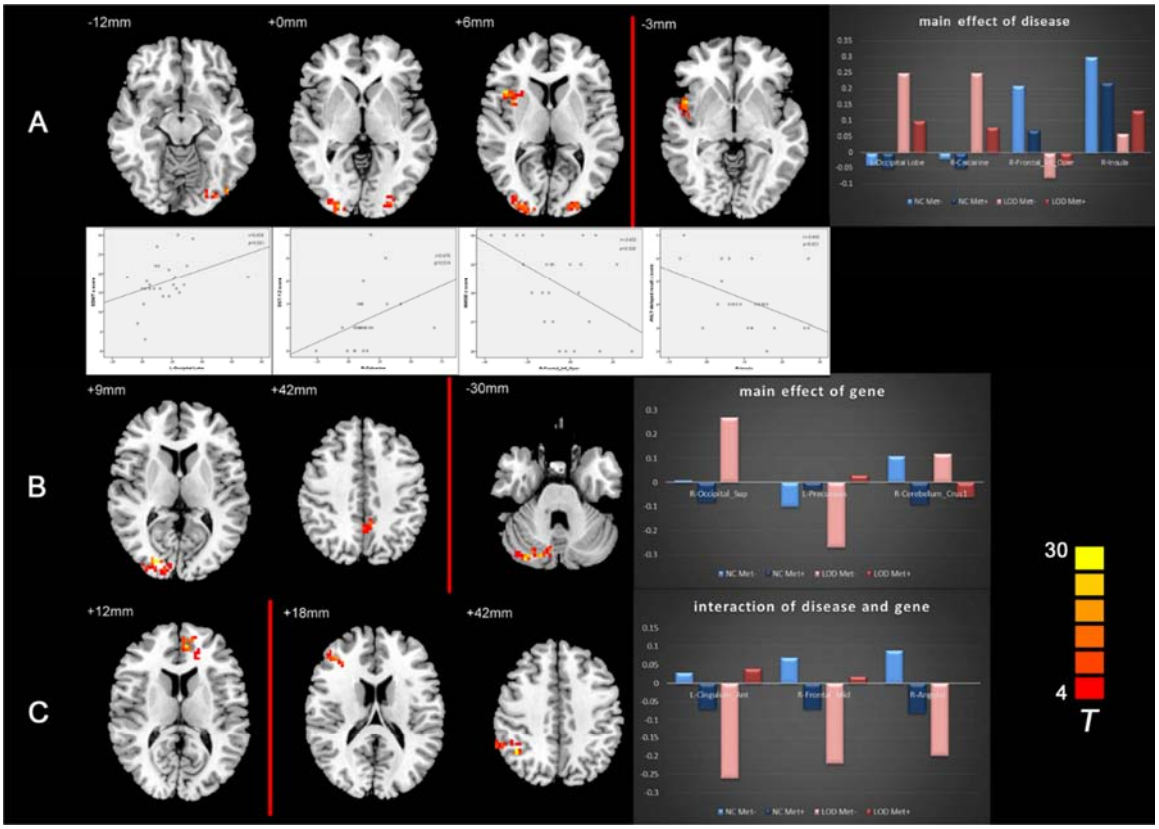

Fig. 1. Regions displaying significant main effect of disease (A), gene (B), interaction of disease and gene (C). The left and right side of the red line exhibit the FC of the left and right hippocampus respectively. A single voxel thresholds of the map resulting from the F-test was set at a $P < 0.05$, and a minimum cluster size of 1215 mm^3 (left hippocampus) /1026 mm^3 (right hippocampus) was used to correct for multiple comparisons, which yielded a corrected threshold of $P< 0.05$, determined by Monte Carlo simulation. Left in the figure indicates right side of the brain. The far right shows the post hoc tested of each brain area (The vertical axis represents the FC z value). And the scatter diagram shows the significant correlation between the changed FC value and the neuropsychological data. Abbreviation: R, right. L, left; Sup, Superior; Mid, Middle; Ant, anterior; LOD, Late-onset depression; NC, normal control.