Reorganization of brain activity and connectivity in cerebral small vessel disease with cognitive impairment

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Objective: Cerebral small vessel disease (CSVD) is the most common cause of vascular cognitive impairment. However, early identification of vascular cognitive impairment is quite difficult due to the lack of biomarkers that precede and predict the onset of cognitive impairment (CI) in CSVD. The present study aimed to investigate the regional activity, intra-network functional connectivity (FC), inter-network FC and topological properties of resting-state networks in CSVD with and without CI.

Methods: Twenty-four CSVD with CI subjects, 24 CSVD without CI subjects and 46 healthy subjects underwent multimodal MRI scans and neuropsychological tests. Amplitude of low-frequency fluctuations (ALFF) and FC patterns in 5 resting-state networks were explored based on functional MRI data. The association of functional alterations with cognition and structural neuroimaging measures was also assessed in CSVD subjects.

Results: Distinctive patterns of regional brain activity and functional brain connectivity were shown between groups. First, opposite alterations of regional brain activity in parietal regions were shown by CSVD with and without CI groups. Compared with the control group, the CSVD without CI group displayed increased ALFF, whereas the CSVD with CI group displayed decreased ALFF that correlated with worse global cognitive function. Second, the intra-network analysis showed that although similar FC patterns of several networks were shared by CSVD with and without CI groups, the CSVD with CI group additionally displayed increased FC in frontoparietal control network (FPCN) and default mode network (DMN). Interestingly, the increased FC compensated for CI and was associated with white matter hyperintensities (WMH) volume. Third, similarly, the CSVD with CI group additionally displayed decreased FC between FPCN and DMN in the analysis of inter-network FC patterns. However, the decreased inter-network FC was associated with worse global cognitive function. Finally, the analysis of topological properties showed that the intermodule connectivity of FPCN mediated the association between WMH burden and cognitive function in CSVD with CI subjects.

Conclusion: The functional characteristics of CSVD with CI comprise decreased regional brain activity, impaired inter-network connectivity, and increased connectivity within FPCN and DMN that compensates for CI related to structural damages. The decreased regional activity and increased intra-network connectivity provide novel insights into mechanisms underlying the onset of CI in CSVD, and may shed light on the investigation of surrogate markers for CI in CSVD.