00385 Amyloid and Cerebrovascular Burden Influences on Longitudinal Brain Functional Connectivity Changes in Mild Cognitive Impairment

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Aims: Recent cross-sectional studies have suggested that Alzheimer's disease (AD) and cerebrovascular disease (CeVD) exert divergent effects on brain intrinsic functional networks. However, no study has examined the associations between amyloid-β and CeVD markers and longitudinal functional connectivity (FC) changes. Our study thus sought to examine the effects of baseline amyloid-β and CeVD burden on longitudinal FC changes in amnestic (aMCI) and subcortical vascular mild cognitive impairment (svMCI) patients. We hypothesized that the two MCI subtypes with and without amyloid-β would exhibit divergent network changes over time. Amyloid-β burden would be associated with longitudinal default mode network (DMN) FC disruptions, while CeVD burden would be associated with longitudinal executive control network (ECN) FC changes.

Methodology: We studied 30 aMCI and 55 svMCI patients with annual neuroimaging assessments for 2-4 years. Patients were further classified as PiB (Pittsburgh compound B) positive (PiB+) or negative (PiB-). Individual pairwise FC matrices were first computed for DMN and ECN regions separately using a predefined parcellation scheme. Linear mixed models were then performed to test: 1) the effect of time on pairwise FC for each group separately and 2) the effects of baseline PiB uptake and lacune number (measure of CeVD burden) on pairwise FC in aMCI and svMCI. Nuisance covariates included baseline age, sex and education.

Result: Amyloid-β burden was associated with longitudinal declines in DMN FC, with PiB+ patients showing longitudinal DMN FC declines. In contrast, CeVD burden was associated with longitudinal changes in ECN FC, with svMCI patients showing longitudinal ECN FC increases. This divergent effect was also observed when examining the effect of baseline PiB uptake and lacune number on longitudinal DMN/ECN FC changes in aMCI and svMCI subjects.

Conclusion: Our findings suggest that amyloid-β and CeVD burdens have divergent effects on longitudinal functional network changes in aMCI and svMCI patients.