Selective impairment of hippocampus and posterior hub areas in Alzheimer’s disease: A MEG-based multiplex network study

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Background:
Although frequency-specific network analyses have shown that functional brain networks are altered in patients with Alzheimer’s disease (AD), the relationships between these frequency-specific network alterations remain largely unknown. Multiplex network analysis is a novel network approach to the study of complex systems consisting of subsystems with different types of connectivity patterns, which could be applied to explore the relationships between frequency-specific networks in AD.

Methods: We used magnetoencephalography (MEG) to integrate five frequency-band specific brain networks in a multiplex framework. Eyes-closed resting-state MEG recordings from 27 AD patients and 26 healthy controls were projected onto atlas-based regions-of-interest (78 cortical and 12 sub-cortical regions) using beam forming. Functional connections between all pairs of ROIs were quantified using a phase-based coupling metric, the phase lag index. Multiplex brain networks were constructed by integrating frequency-specific MEG networks. Several multiplex hub and heterogeneity metrics were computed in order to capture both overall importance of each brain area and heterogeneity of the connectivity patterns across frequency-specific layers.

Results: Different nodal centrality metrics showed consistently that several hub regions, particularly left hippocampus, posterior parts of the default mode network and occipital regions, were disrupted in AD compared to HCs. The connectivity patterns of these vulnerable hub regions in the patients were heterogeneously distributed across layers. Perturbed cognitive function and abnormal CSF amyloid-beta (Aβ42) levels correlated positively with the vulnerability of the hub regions in AD patients.

Conclusions: Our analysis clearly demonstrates that functional networks obtained in different frequency bands do not act as independent entities, but interact with each other. Overall, our MEG-based multiplex network study provides an effective framework to integrate the frequency-specific networks and reveal neuropathological mechanism of hub disruption in AD.