Functional Connectivity Differences Across the Alzheimer's Disease Continuum: A Neural ROI-Based Analysis in Relation to Depression

Luka Cvijanovic[1], Meiheng Liang[2], Meichen Yu[2]

[1]Indiana University School of Medicine; [2]Department of Radiology & Imaging Sciences, Indiana University School of Medicine

Background: Alzheimer's disease (AD) is a neurodegenerative disease characterized by β-amyloid plaques and tau tangles, leading to symptoms like memory loss, agnosia, and apraxia. A common AD comorbidity includes depression. While some studies identify midlife depression as a risk factor for AD development, others interpret depression as a manifestation of AD itself. Though emerging literature supports both models, the underlying mechanisms linking the two remain poorly understood. We hypothesized that functional connectivity in the default-mode network (DMN), somatomotor network (SMN), and salience network (SN) would be reduced in association with both AD and depression.

Methods: 178 participants (ages 65-90, positive β-amyloid) fMRI datasets collected, split into 68 ROIs per the Desikan-Killiany atlas. Depressive symptoms were assessed via the NPI and GDS questionnaires. Participants were subdivided into 4 groups: preclinical AD patients without depressive symptoms; preclinical AD patients with depressive symptoms; prodromal and AD patients without depressive symptoms; and prodromal and AD patients with depressive symptoms. This data was residualized to correct for age and sex, then analyzed via non-parametric tests, e.g., Kruskal-Wallis.

Results: Six significantly different functional connectivity regions were found across groups: $p < 0.001$, bankssts; $0.001 < p < 0.01$, precentral, postcentral, and superiortemporal; and $0.01 < p < 0.05$, lateralorbitofrontal and paracentral. Post hoc tests revealed that preclinical AD patients had greater connectivity relative to prodromal + AD patients, with and without depression. Depression specific regions included the paracentral and lateralorbitofrontal ROIs.

Conclusion: The DMN and SMN are implicated in AD development through the bankssts & superiortemporal regions, and the pre-, post-, & paracentral regions, respectively, in patients both with and without depression. The SN and DMN are implicated in depression through the lateralorbitofrontal region, in preclinical AD. And lastly, the SMN and SN are implicated in depression through the paracentral region, specifically in AD patients.