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Eigenvector centrality dynamics are related to Alzheimer's disease pathological changes in non-demented individuals

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Amyloid-β accumulation starts in highly connected brain regions and is associated with functional connectivity alterations in the early stages of Alzheimer's disease. This regional vulnerability is related to the high neuronal activity and strong fluctuations typical of these regions. Recently, dynamic functional connectivity was introduced to investigate changes in functional network organization over time. High dynamic functional connectivity variations indicate increased regional flexibility to participate in multiple subnetworks, promoting functional integration. Currently, only a limited number of studies have explored the temporal dynamics of functional connectivity in the pre-dementia stages of Alzheimer's disease. We study the associations between abnormal cerebrospinal fluid amyloid and both static and dynamic properties of functional hubs, using eigenvector centrality, and their relationship with cognitive performance, in 701 non-demented participants from the European Prevention of Alzheimer's Dementia cohort. Voxel-wise eigenvector centrality was computed for the whole functional magnetic resonance imaging time series (static), and within a sliding window (dynamic). Differences in static eigenvector centrality between amyloid positive (A+) and negative (A-) participants and amyloid-tau groups were found in a general linear model. Dynamic eigenvector centrality standard deviation and range were compared between groups within clusters of significant static eigenvector centrality differences, and within 10 canonical resting-state networks. The effect of the interaction between amyloid status and cognitive performance on dynamic eigenvector centrality variability was also evaluated with linear models. Models were corrected for age, sex, and education level. Lower static centrality was found in A+ participants in posterior brain areas including a parietal and an occipital cluster; higher static centrality was found in a medio-frontal cluster. Lower eigenvector centrality variability (standard deviation) occurred in A+ participants in the frontal cluster. The default mode network and the dorsal visual networks of A+ participants had lower dynamic eigenvector centrality variability. Centrality variability in the default mode network and dorsal visual networks were associated with cognitive performance in the A- and A+ groups, with lower variability being observed in A+ participants with good cognitive scores. Our results support the role and timing of eigenvector centrality alterations in very early stages of Alzheimer's disease and show that centrality variability over time adds relevant information on the dynamic patterns that cause static eigenvector centrality alterations. We propose that dynamic eigenvector centrality is an early biomarker of the interplay between early Alzheimer's disease pathology and cognitive decline.

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