Cognitive Dispersion is not Associated with Cerebrospinal Fluid Biomarkers of Alzheimer's Disease: Results from the European Prevention of Alzheimer's Dementia (EPAD) v500.0 Cohort

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Background: Cognitive dispersion, variation in performance across cognitive domains, is posited as a non-invasive and cost-effective marker of early neurodegeneration. Little work has explored associations between cognitive dispersion and Alzheimer's disease (AD) biomarkers in healthy older adults. Even less is known about the influence or interaction of biomarkers reflecting brain pathophysiology or other risk factors on cognitive dispersion scores.

Objective: The main aim of this study was to examine whether higher cognitive dispersion was associated with cerebrospinal fluid (CSF) levels of amyloid-β (Aβ 42), total tau (t-tau), phosphorylated tau (p-tau), and amyloid positivity in a cohort of older adults at various severities of AD. A secondary aim was to explore which AD risk factors were associated with cognitive dispersion scores.

Methods: Linear and logistic regression analyses explored the associations between dispersion and CSF levels of Aβ 42, t-tau, and p-tau and amyloid positivity (Aβ 42< 1000pg/ml). Relationships between sociodemographics, APOE ε4 status, family history of dementia, and levels of depression and dispersion were also assessed. Results:Dispersion did not emerge as associated with any of the analytes nor amyloid positivity. Older (β=–0.007, SE=0.002, p=0.001) and less educated (β=–0.009, SE=0.003, p=0.009) individuals showed greater dispersion.

Conclusion: Dispersion was not associated with AD pathology, but was associated with age and years of education, highlighting individual differences in cognitive aging. The use of this metric as a screening tool for existing AD pathology is not supported by our analyses. Follow-up work will determine if dispersion scores can predict changes in biomarker levels and/or positivity status longitudinally.

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