Investigating reliable amyloid accumulation in Centiloids Results from the AMYPAD Prognostic and Natural History Study

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Abstract:

Introduction: To support clinical trial designs focused on early interventions, our study determined reliable early amyloid-β (Aβ) accumulation based on Centiloids (CL) in pre-dementia populations.

Methods: A total of 1032 participants from the Amyloid Imaging to Prevent Alzheimer's Disease–Prognostic and Natural History Study (AMYPAD-PNHS) and Insight46 who underwent [18F]flutemetamol, [18F]florbetaben or [18F]florbetapir amyloid-PET were included. A normative strategy was used to define reliable accumulation by estimating the 95th percentile of longitudinal measurements in sub-populations (NPNHS = 101/750, NInsight46 = 35/382) expected to remain stable over time. The baseline CL threshold that optimally predicts future accumulation was investigated using precision-recall analyses. Accumulation rates were examined using linear mixed-effect models.

Results: Reliable accumulation in the PNHS was estimated to occur at >3.0 CL/year. Baseline CL of 16 [12,19] best predicted future Aβ-accumulators. Rates of amyloid accumulation were tracer-independent, lower for APOE ε4 non-carriers, and for subjects with higher levels of education.

Discussion: Our results support a 12–20 CL window for inclusion into early secondary prevention studies. Reliable accumulation definition warrants further investigations.

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