EPAD
European Prevention of
Alzheimer's Dementia Consortium

Application of the ATN classification scheme in a population without dementia Findings from the EPAD cohort

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Background: We classified non-demented European Prevention of Alzheimer's Dementia (EPAD) participants through the amyloid/tau/neurodegeneration (ATN) scheme and assessed their neuropsychological and imaging profiles.

Materials and methods: From 1500 EPAD participants, 312 were excluded. Cerebrospinal fluid cut-offs of 1000 pg/mL for amyloid beta (Aß)1-42 and 27 pg/mL for p-tau181 were validated using Gaussian mixture models. Given strong correlation of p-tau and t-tau (R2 = 0.98, P < 0.001), neurodegeneration was defined by age-adjusted hippocampal volume. Multinomial regressions were used to test whether neuropsychological tests and regional brain volumes could distinguish ATN stages.

Results: Age was 65 ± 7 years, with 58% females and 38% apolipoprotein E (APOE) ε4 carriers; 57.1% were A–T–N–, 32.5% were in the Alzheimer's disease (AD) continuum, and 10.4% suspected non-Alzheimer's pathology. Age and cerebrovascular burden progressed with biomarker positivity (P < 0.001). Cognitive dysfunction appeared with T+. Paradoxically higher regional gray matter volumes were observed in A+T–N– compared to A–T–N– (P < 0.001).

Discussion: In non-demented individuals along the AD continuum, p-tau drives cognitive dysfunction. Memory and language domains are affected in the earliest stages.

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