Prediction of Alzheimer's disease biomarker status defined by the 'ATN framework' among cognitively healthy individuals: results from the EPAD longitudinal cohort study

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Background: The Amyloid/Tau/Neurodegeneration (ATN) framework has been proposed as a means of evidencing the biological state of Alzheimer's disease (AD). Predicting ATN status in pre-dementia individuals therefore provides an important opportunity for targeted recruitment into AD interventional studies. We investigated the extent to which ATN-defined biomarker status can be predicted by known AD risk factors as well as vascular-related composite risk scores.

Methods: One thousand ten cognitively healthy older adults were allocated to one of five ATN-defined biomarker categories. Multinomial logistic regression tested risk factors including age, sex, education, APOE4, family history of dementia, cognitive function, vascular risk indices (high systolic blood pressure, body mass index (BMI), high cholesterol, physical inactivity, ever smoked, blood pressure medication, diabetes, prior cardiovascular disease, atrial fibrillation and white matter lesion (WML) volume), and three vascular-related composite scores, to predict five ATN subgroups; ROC curve models estimated their added value in predicting pathology.

Results: Age, APOE4, family history, BMI, MMSE and white matter lesions (WML) volume differed between ATN biomarker groups. Prediction of Alzheimer's disease pathology (versus normal AD biomarkers) improved by 7% after adding family history, BMI, MMSE and WML to a ROC curve that included age, sex and APOE4. Risk composite scores did not add value.

Conclusions: ATN-defined Alzheimer's disease biomarker status prediction among cognitively healthy individuals is possible through a combination of constitutional and cardiovascular risk factors but established dementia composite risk scores do not appear to add value in this context.