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CLINICAL MANIFESTATIONS

POSTER PRESENTATION

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NEUROPSYCHIATRY AND BEHAVIORAL NEUROLOGY

Investigating the additive effects of Alzheimer's disease biomarker staging and subjective cognitive decline in the prediction of clinical progression

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Abstract

Background: The identification of cognitively unimpaired individuals at risk of short-term cognitive decline is a critical task for Alzheimer´s disease (AD) research. Cognitively normal individuals with amyloid and/or tau pathology have a high risk for short-term cognitive decline. However, not all of these individuals show clinical progression. Individuals in clinical stage 2 of AD, characterized e.g. by subjective cognitive decline (SCD), are thought to be temporally closer to clinical progression to mild cognitive impairment (MCI), but this hypothesis has not been rigorously investigated yet.

Method: We included 195 memory clinic SCD patients and 83 cognitively normal participants without SCD (CN) with baseline CSF and longitudinal cognitive data from the observational DELCODE study. Participants were categorized into three AD biomarker stages (A-T-, A+T-, A+T+) based on their baseline CSF Aβ42/40 and p-tau$_{181}$ status. The groups were compared in their longitudinal preclinical Alzheimer´s cognitive composite (PACC5) trajectories and average time until progression to MCI. Group differences in the time until progression to MCI, over eight years of follow-up, were estimated with restricted mean survival time models. All analyses were adjusted for demographic covariates.

Result: Compared to the A-T- group (62 CN, 123 SCD), A+T- (16 CN, 49 SCD) and A+T+ (5 CN, 23 SCD) participants showed significantly accelerated PACC5 decline and a faster progression to MCI (A+T-: 2.7 [-5.7-11.2] and A+T+: 22.4 [8.1-36.8] months earlier than A-T-;). SCD patients had a significantly faster PACC5 decline and progression to MCI (15.5 [9.8-21.1] months) than CN participants. The effects of SCD and the biomarker stages on both outcome measures remained significant when the predictors were entered in the same models. In exploratory analyses, SCD patients tended to show a faster progression to MCI than CN participants within the same biomarker group (A+T-: 19.0 [6.3-31.7] and A+T+: 14.0 [-20.8-48.8] months earlier than CN in same biomarker group).

Conclusion: SCD provides incremental information for the identification of individuals at high risk of imminent cognitive decline beyond a biomarker-based classification of AD pathology. In cognitively unimpaired individuals, the clinical stage should be taken into account additionally to AD biomarkers for an improved prediction of the time until clinical progression.