EPAD
European Prevention of
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Interactions between apolipoprotein E, sex, and amyloid-beta on cerebrospinal fluid p-tau levels in the European prevention of Alzheimer's dementia longitudinal cohort study (EPAD LCS)

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Background: Alzheimer's Disease, the leading cause of dementia, is over-represented in females. The apolipoprotein E (APOE) ε4 allele is the strongest genetic risk factor for late-onset AD and is associated with aberrant cerebrospinal fluid levels (CSF) of total tau (t-tau), phosphorylated tau (p-tau), and amyloid-β (Aβ). There is some evidence that sex may mediate the relationship between APOE status and CSF tau, however, evidence is mixed.

Methods: We aimed to examine the interaction between sex, APOE ε4 status, CSF Aβ on t-tau and p-tau in 1599 mid-to-late life individuals without a diagnosis of dementia in the European Prevention of Alzheimer's Dementia (EPAD) longitudinal cohort study.

Findings: We found a significant interaction between APOE status, sex, and CSF Aβ on CSF p-tau levels (β = 0·18, p = 0·04). Specifically, there was a stronger association between APOE status and CSF Aβ42 on CSF p-tau in males compared to females. Further, in females with high Aβ levels (reflecting less cortical deposition), ε4 carriers had significantly elevated p-tau levels relative to non-carriers (W = 39663, p = 0·01). However, there were no significant differences in p-tau between male ε4 carriers and non-carriers with high Aβ (W = 23523, p = 0·64).

Interpretation: An interaction between sex and cerebrospinal fluid Aβ may mediate the relationship between APOE status and CSF p-tau. These data suggest tau accumulation may be independent of Aβ in females, but not males.

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