Relationship Of Plasma P-tau217 And Neurodegeneration In Early-onset Alzheimer's Disease

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BACKGROUND

We are continuing to refine our understanding of plasma P-tau217 and other biomarkers of Alzheimer's disease (AD). Beyond its utility in the diagnostic evaluation of patients with cognitive impairment (Palmqvist et al. 2021)[1], it remains unclear what the magnitude of this measure tells us about other biomarkers and whether it relates to cognition within samples of AD patients.

Hypotheses:

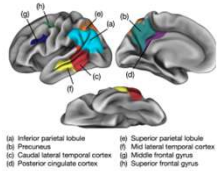
- H1: Based on prior work demonstrating correlations between plasma P-tau217 and medial temporal lobe atrophy in mild cognitive impairment (MCI) late-onset AD (Rabiei rad et al. 2025)[2], we hypothesized that plasma P-tau217 would correlate with atrophy within our early-onset AD (EOAD) MRI atrophy signature (Touroutoglou et al. 2023)[3].
- H2: A combination of plasma P-tau 217 levels and EOAD signature atrophy would explain more variance in cognitive impairment than either alone in a sample of AD patients.

MATERIALS AND METHODS

Participants: We analyzed plasma P-tau217 (AlzPath) data from 204 MCI and mild dementia EOAD patients (mean age: 59 yo, SD =4; 110 Female) from Longitudinal Early-Onset Alzheimer's Disease Study (LEADS).

Data analysis: In each patient, atrophy in the EOAD signature (**Fig. 1)** was calculated as W-scores (i.e., Z-scores adjusted for age and sex relative to a sample of healthy controls).

Fig. 1. EOAD Signature ROIs (Touroutoglou et al. 2023)



We ran a simple regression analysis of the plasma P-tau217 and W-scores in the EOAD signature. Using multiple regression, we examined the contributions of the EOAD signature atrophy and plasma P-tau217 to the severity of cognitive impairment, as indexed by Clinical Dementia Rating Sum-of-Boxes scores (CDR-SB).

RESULTS

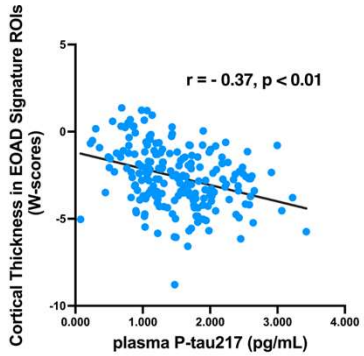


Fig. 1. Relationship between the magnitude of plasma P-tau217 and cortical thickness within the EOAD signature.

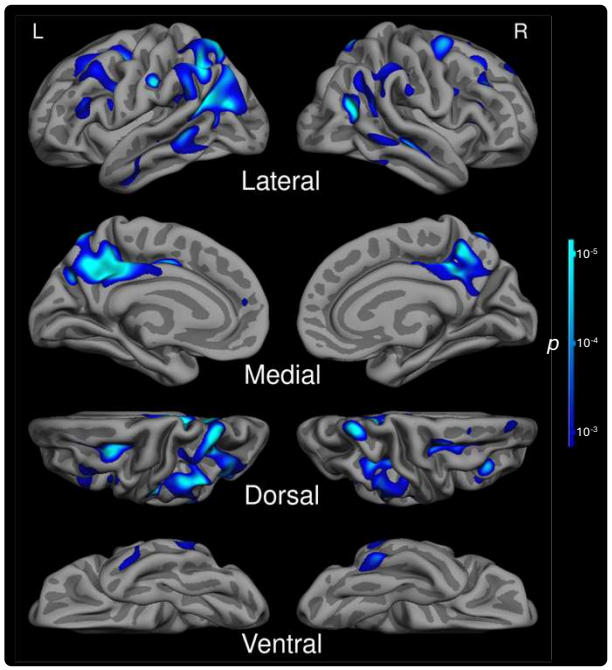


Fig. 2. Whole-brain correlation maps between cortical thickness and plasma P-tau217 biomarker levels. Plasma P-tau217 negatively correlated with thickness, thresholded at an uncorrected *p < 0.01*.

RESULTS CONT.

	CDR-SB scores		
	B	R^2 change	Total R^2
EOAD Signature Cortical Thickness	-.24 [a]	.08	.43
Plasma P-tau217	.16 [b]		

Table 1. Multiple regression analyses showed that a combination of EOAD signature atrophy and plasma P-tau217 levels explained more variance in cognitive impairment than either alone, F (2, 201) = 12.650, p < .01.

Note: Table displays standardized regression coefficients (*B*) as well as the incremental (R^2 change) and total variance (total R^2) in the CDR-SB scores predicted by the independent variables entered into a single multiple linear regression model, accounting for age and sex.
[a]*p* < .01, [b]*p* < .05

CONCLUSIONS/FUTURE DIRECTIONS

- In EOAD patients, plasma P-tau217 levels relate to the magnitude of atrophy within the EOAD cortical signature, highlighting its utility as correlate of MRI-derived measures of neurodegeneration in EOAD.
- The magnitude of these biomarkers together relate to cognitive impairment, which can provide valuable information regarding disease progression for clinical care and clinical trials involving disease-modifying therapies.

REFERENCES & ACKNOWLEDGEMENTS

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[3]Touroutoglou A. et al. Alzheimers Dement.2023;19(Suppl 9):S74-S88.

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