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BIOMARKERS

PODIUM PRESENTATION

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Prognostic value of a novel plasma pTau217 assay for amyloid accumulation in healthy elderly

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Abstract

Background: The performance of blood-based phosphorylated tau (pTau) immunoassays to detect asymptomatic Alzheimer's disease (AD) has important implications for therapeutic trials. pTau217 is often recommended as the preferred epitope due to its high fold changes in AD. The current study investigates the ability of a novel pTau217 assay to predict the dynamic phase of amyloid-β (Aβ) accumulation in comparison to the best-performing pTau181 assay.

Methods: Plasma pTau217 was quantified by the ALZPath Simoa assay at the University of Gothenburg in 109 cognitively unimpaired older adults (Flemish Prevent-AD Cohort KU Leuven [F-PACK] cohort). All subjects underwent baseline plasma sampling and longitudinal Aβ-PET (median time interval = 6 years). For a subset of 72 subjects, pTau181 was quantified by the Homebrew ADx Simoa assay. Linear mixed-effects models were used to calculate subject-specific Aβ change and to assess the age-, sex and APOE-corrected predictive value of pTau species for Aβ change, which was assessed in a global and voxelwise manner. Accumulators were defined as having an Aβ rate of change z-score > 1.5 (based on mean & standard deviation within the Aβ- subset). Performance to detect Aβ accumulators was assessed through receiver operating characteristic analyses. Plasma biomarkers were converted to z-scores for effective comparison. Pearson correlations were calculated between pTau181 and pTau217.

Results: Plasma pTau217 levels were higher in Aβ accumulators than non-accumulators with an area under the curve (AUC) of 0.69 (95%CI 0.58-0.81). Moreover, higher pTau217 predicted steeper Aβ accumulation (β_s=0.57, P<.001). Plasma levels of pTau217 strongly correlated with those of pTau181 (r=0.93, Figure 1). In the subgroup with matching pTau181 data, pTau181 was also higher in Aβ accumulators than non-accumulators with an AUC of 0.68 (95%CI 0.53-0.84), which

was comparable to pTau217 (AUC=0.76; P_{DeLong}=.12) or a multibiomarker model including both pTau species (AUC=0.80; P_{DeLong}=.15) in the same subset (Figure 2A). pTau181 demonstrated comparable associations with Aβ accumulation in terms of both strength (β_s=0.53, 95%CI 0.21–0.81 for pTau181 versus β_s =0.48 for pTau217 in this subset) and spatial distribution (Figure 2B).

Conclusions: The novel ALZPath pTau217 assay predicted Aβ accumulation in asymptomatic elderly with comparable performance to the ADx pTau181 assay.

Table 1. Demographic table

Characteristic	All	Non-accumulator	Aβ-accumulator	*P*
N (%)	109	77 (71)	32 (29)	
Age, y	68 ± 6	68 ± 6	69 ± 5	.23
Female, n (%)	52 (48)	37 (48)	15 (47)	1.00
APOE-ε4 carriers, n (%)	56 (48)	34 (44)	22 (69)	**.03**
MMSE, /30	29 [1]	29 [1]	29.5 [1]	.35
Aβ-positive (CL > 23.5), n (%)	12 (11)	0 (0)	12 (38)	**< .001**
Aβ rate of change, CLs/y	0.52 [1.79]	0.22 [0.82]	2.84 [2.54]	**< .001**
Time interval, y	6 ± 2	6 ± 2	6 ± 2	.85
Plasma pTau217, pg/mL	0.31 [0.15]	0.30 [0.14]	0.41 [0.31]	**< .001**
Plasma pTau181, pg/mL	7.83 [5.46]	6.66 [4.24]	10.60 [10.99]	**.002**

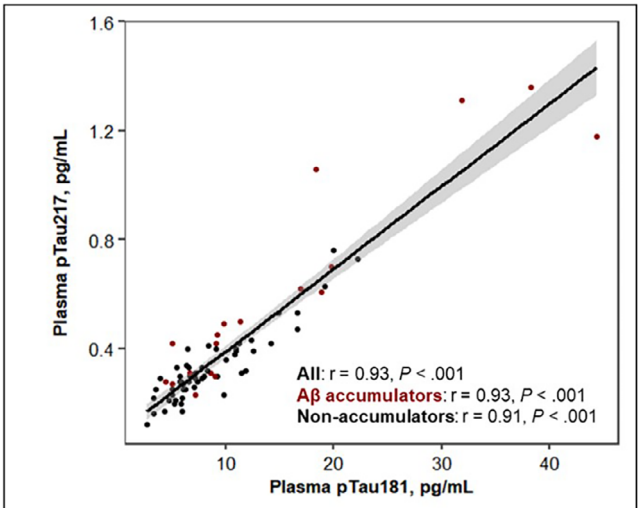

Figure 1. Correlation between plasma pTau217 and pTau181

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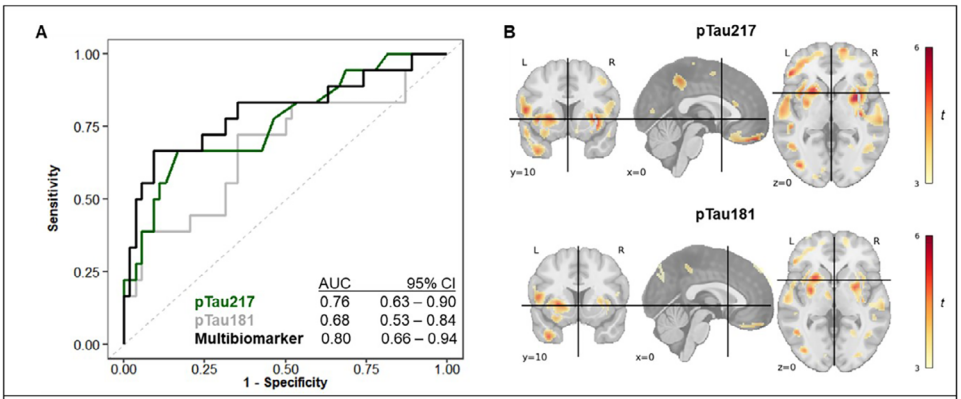

Figure 2. Prognostic value of plasma pTau217 and pTau181 in subset with available pTau181 data for predicting Aβ accumulator status at baseline (A) or longitudinal Aβ accumulation (B).