Longitudinal Blood Biomarker Trajectories in Preclinical Alzheimer's Disease

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Background

Positron Emission Tomography (PET) imaging-based biomarkers have been used as the gold standard measure to detect amyloid and tau pathology *in-vivo*.[1] The high cost and the limited availability of PET imaging have paved the way for the development of more cost-effective and minimally invasive biomarkers of Alzheimer's disease (AD) (e.g., blood biomarkers).[2]

Implementation of novel blood biomarkers into clinical practice requires assessment of their dynamic changes across the AD spectrum.[2] Therefore, we **assessed plasma biomarkers' temporal trajectories in cognitively unimpaired older adults with and without evidence of significant AD pathology on PET scans.**

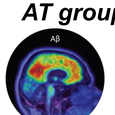
Methods

PREVENT-AD Research Group

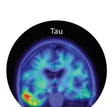
We included participants from the PREVENT-AD cohort, a longitudinal cohort of cognitively unimpaired older adults with a self-reported parental history of AD.

PET sample	A-T- (N =84)	A+T- (N = 27)	A+T+ (N = 15)
Age (SD)	62.8 (4.4)	63.3 (4.6)	66.3 (4.9)
Sex F:M (%F)	60:2 (73.1)	22:7 (75.8)	11:4 (73.3)
Global Amyloid SUVR	1.17 (0.06)	1.56 (0.36)	1.80 (0.45)
Tau Entorhinal SUVR	1.03 (0.09)	1.05 (0.09)	1.34 (0.1)

AT group classification on PET



Amyloid-PET [3,4]
18[F]NAV4694-PET
Global amyloid
Positivity threshold = 1.29

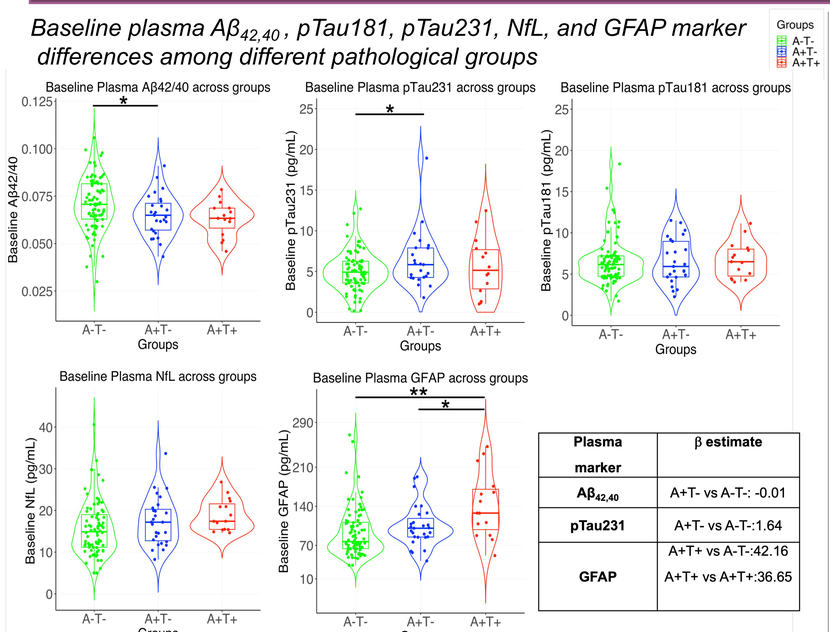


Tau-PET [3]
18[F]AV-1451-PET
Entorhinal cortex
Positivity threshold = 1.23

Blood draws were collected between 2011-2017. **$A\beta_{42}$,$A\beta_{40}$, NfL, and GFAP** were measured using commercial SiMOA multiplex assay. Additionally, plasma **pTau181, pTau231** were measured using in-house SiMOA assay developed at Gothenburg University.[5,6]

Results

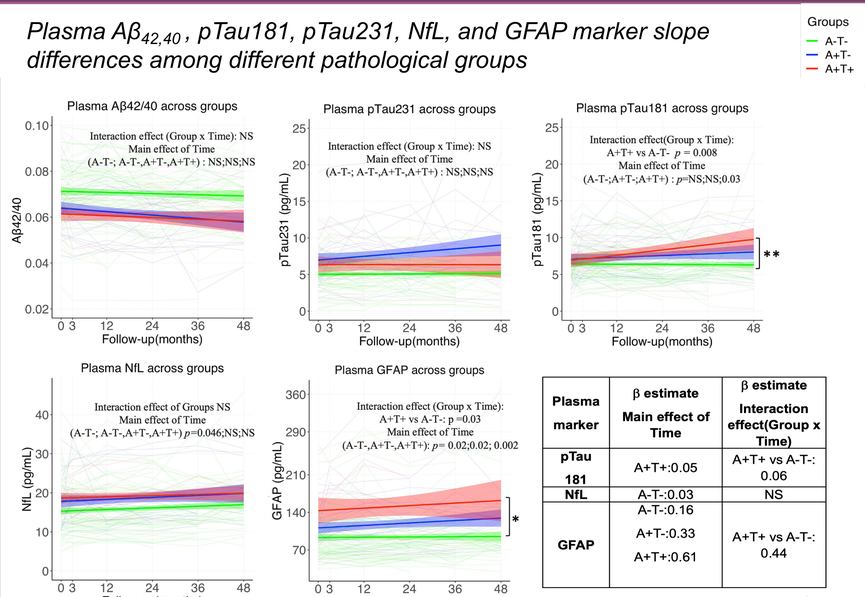
Baseline plasma $A\beta_{42,40}$, pTau181, pTau231, NfL, and GFAP marker differences among different pathological groups



Plasma marker	β estimate
$A\beta_{42,40}$	A+T- vs A-T-: -0.01
pTau231	A+T- vs A-T-:1.64
GFAP	A+T+ vs A-T-:42.16 A+T+ vs A+T+:36.65

Linear regression analyses compared baseline plasma $A\beta_{42,40}$, pTau181, pTau231, NfL, and GFAP markers among different pathological groups assessed on PET. *Notes*: Models included covariates of sex,age at baseline,years of education. β estimates presented for plasma markers above showed significance between groups.* = p<0.05; ** = p<0.01

Plasma $A\beta_{42,40}$, pTau181, pTau231, NfL, and GFAP marker slope differences among different pathological groups



Plasma marker	β estimate Main effect of Time	β estimate Interaction effect(Group x Time)
pTau 181	A+T+:0.05	A+T+ vs A-T-: 0.06
NfL	A-T-:0.03	NS
GFAP	A-T-:0.16 A+T-:0.33 A+T+:0.61	A+T+ vs A-T-: 0.44

NS. Not-significant

Linear mixed-effects models compared longitudinal plasma $A\beta_{42,40}$, pTau181 pTau231, NfL, and GFAP markers rate of change among different pathological groups. *Notes*: Models included covariates of sex,age at baseline,years of education, time difference between initial plasma collection and PET visit. β estimates presented for plasma markers above showed significance between groups. * = p<0.05; ** = p<0.01

Summary

- We observed lower baseline plasma $A\beta_{42,40}$ and higher baseline plasma pTau231 among individuals with amyloid pathology. Higher baseline plasma GFAP differences were also observed among individuals with both amyloid and tau pathologies compared to those with only amyloid or no pathology.
- **Increases in the rate of change in plasma pTau181 and GFAP markers among individuals with both pathologies were observed when compared to those with no pathology**. This suggests the potential utility of plasma markers in tracking individuals with different pathological stages in preclinical Alzheimer's disease.

References:
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