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BIOMARKERS

POSTER PRESENTATION

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NEUROIMAGING

Neuroinflammation potentiates the effect of amyloid-β on longitudinal tau changes

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Abstract

Background: It has been proposed that microglia release of proinflammatory factors reactive to amyloid plaques constitutes an early event leading to tau pathology. Here, we assessed how the rate of progression of tau-PET and the rate of change in plasma pTau217 are affected by baseline levels of amyloid-β and neuroinflammation.

Methods: We included 93 individuals from TRIAD cohort: 11 young individuals, 57 cognitively unimpaired elderlies, 15 with mild cognitive impairment and 10 individuals with Alzheimer's Disease. Neuroinflammation, tau tangle and amyloid-β (Aβ) deposition were assessed via [^{11}C]PBR28-PET, [^{18}F]MK6240-PET and [^{18}F]AZD4694-PET, respectively. Individuals also had plasma pTau217 quantified using the Alzpath assay. [^{11}C]PBR28-PET positivity was defined as a SUVR of 2.5SD above the mean of the young individuals in the precuneus and posterior cingulate. Voxel-based regression models evaluated the interaction of TSPO- and Aβ-PET with annual change in tau-PET and plasma pTau217. The effect of the interaction on tau-PET was also evaluated at the region-of-interest level using Braak regions. All models were corrected for age, sex and RFT corrected. Comparison of models was made using the Akaike Information Criterion (AIC) and the models' goodness-of-fit was evaluated using R^2 analyses. Models used [^{18}F]MK6240-PET SUVR yearly change as the outcome and used as predictors [^{11}C]PBR28-PET SUVR in the precuneus and posterior cingulate and [^{18}F]AZD4694-PET SUVR in the neocortical region.

Results: Positive associations were found between the interaction of Aβ- and TSPO-PET at baseline predicting the yearly change in tau-PET (Figure 1A). At the ROI level,

the interaction significantly predicts tau load in Braak regions III-IV in [^{11}C]PBR28 positive individuals (Figure 1B). Positive associations were also found between the interaction of Aβ- and TSPO-PET at baseline predicting the yearly change in plasma pTau217 (Figure 2A), which is driven by [^{11}C]PBR28 positive individuals (Figure 2B). In addition, the interaction between Aβ- and TSPO-PET predicting the yearly change in tau-PET is the model with the highest R^2 and the lowest AIC values in Braak regions III-IV-V-VI (Figure 3).

Conclusion: These results support the hypothesis that microglial activation potentiates the effect of Aβ plaques on tau tangle progression and the pTau217 increases across the aging and AD spectrum.

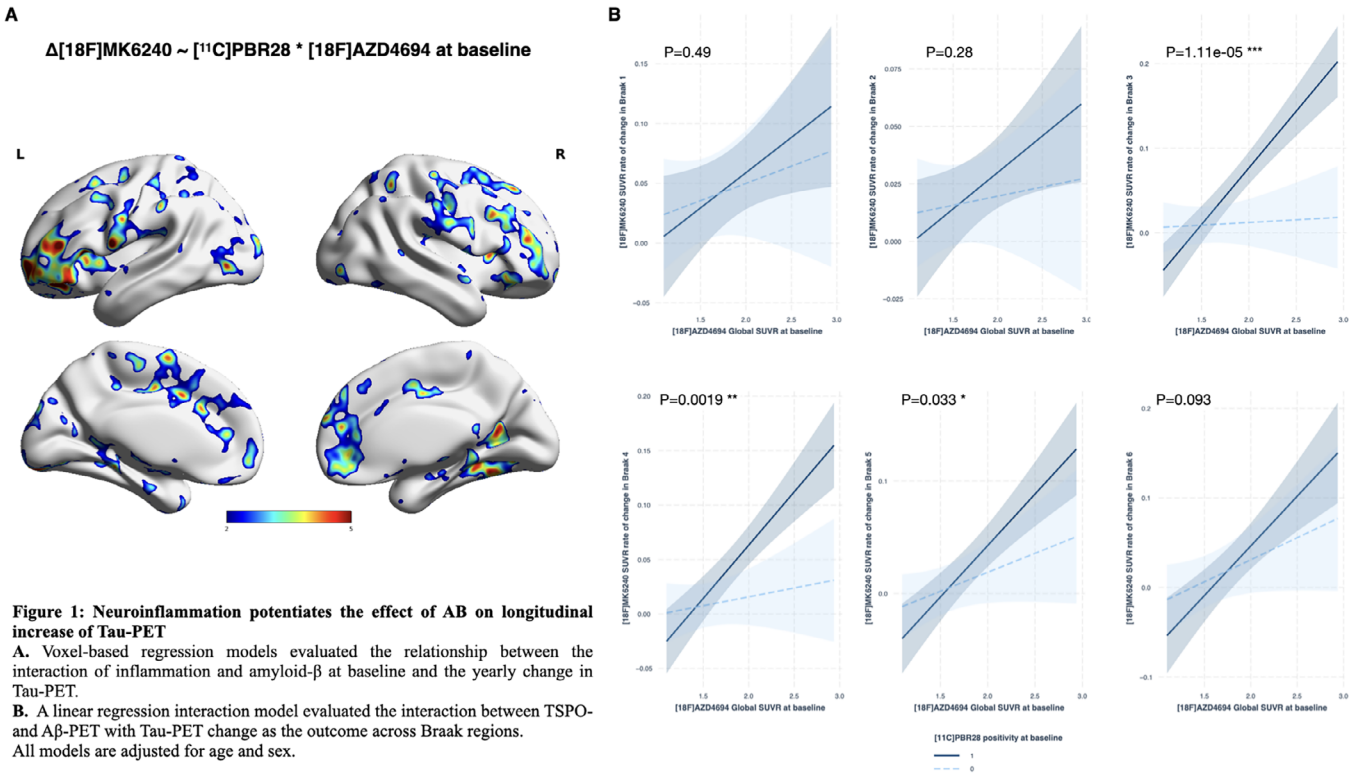

Figure 1: Neuroinflammation potentiates the effect of AB on longitudinal increase of Tau-PET

A. Voxel-based regression models evaluated the relationship between the interaction of inflammation and amyloid-β at baseline and the yearly change in Tau-PET.

B. A linear regression interaction model evaluated the interaction between TSPO- and Aβ-PET with Tau-PET change as the outcome across Braak regions.

All models are adjusted for age and sex.

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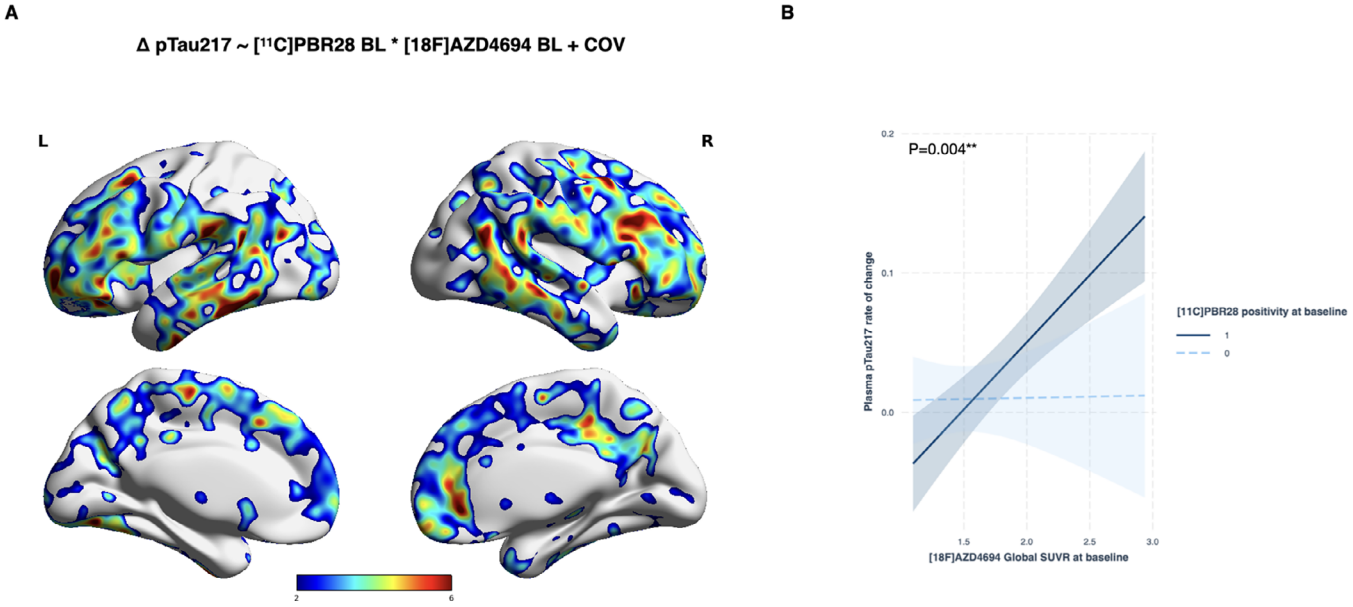

Figure 2: Neuroinflammation potentiates the effect of AB on longitudinal increase of plasma pTau217
A. Voxel-based regression models evaluated the relationship between the interaction of inflammation and amyloid-β at baseline and the yearly change in plasma pTau217.
B. A linear regression interaction model evaluated the interaction between TSPO- and Aβ-PET with plasma pTau217 change as the outcome.

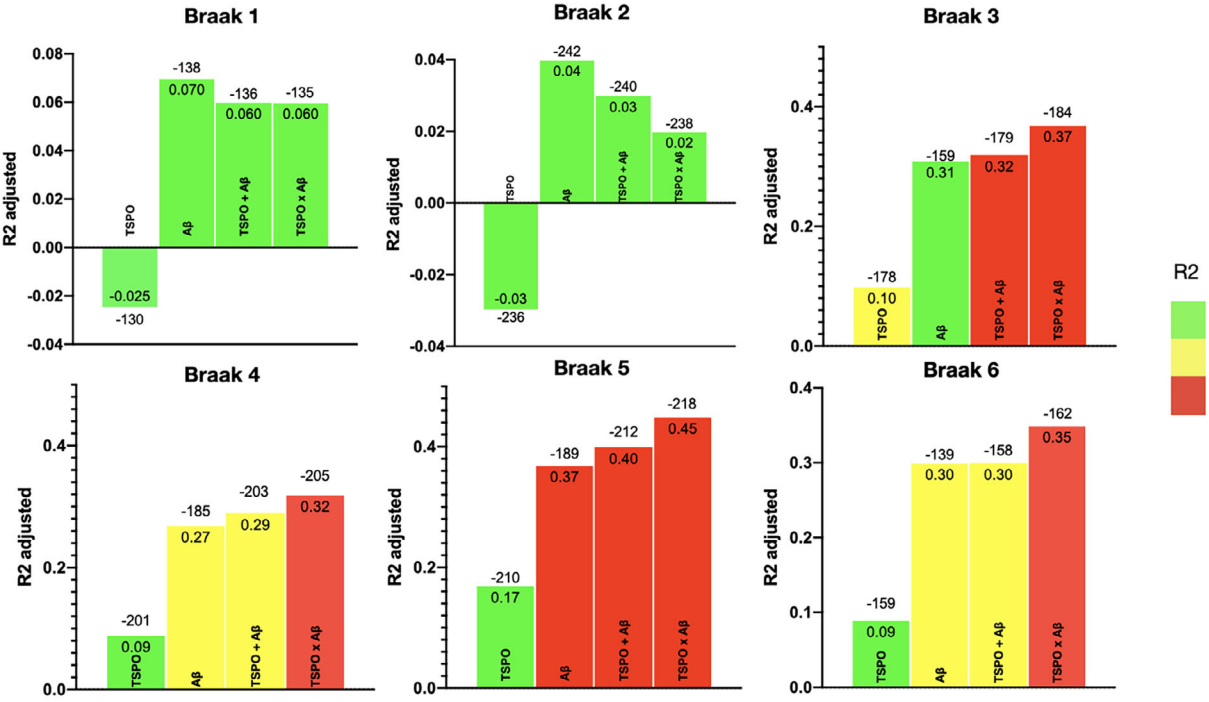

Figure 3: The interaction between inflammation and Aβ is the best predictor of longitudinal Tau-PET change.
R^2 and AIC (above the bars) for different regression models with the yearly change in Tau-PET as the outcome, using amyloid-β-PET and TSPO-PET SUVR as predictors. All models included age and sex as covariates.