

Low Medial Temporal Metabolism Correlates with Faster Tau Accumulation and Spread in Early Alzheimer's Disease

P1-02

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Introduction

Tau tangles preferentially deposit early in the medial temporal lobe (MTL) and subsequently spread to other cortices in Alzheimer's disease (AD).

The biological basis underlying this selective vulnerability remains unclear.

This study investigated whether MTL glucose metabolism modulates early tau accumulation and spread in AD.

Methods

Participants with A β /tau/FDG PET within one year were selected from ADNI ($n = 263$) and HABS cohorts ($n = 125$). Resting-state fMRI and follow-up tau PET were available for subsets.

Participants were classified into A-/T-, A+/T-, A+/T_{MTL}+, A+/T_{MOD}+, and A+/T_{High}+. A+/T- and A+/T_{MTL}+, were defined as A+/T_{Early}+, while A+/T_{MOD}+, and A+/T_{High}+, were defined as A+/T_{Advanced}+. MTL FDG were calculated from entorhinal, parahippocampal, and temporal pole cortices and stratified into tertiles (low/mid/high).

Functional connectivity (FC) was derived using the Schaefer 400-parcel atlas. Connectivity-associated tau spread was quantified using FC-tau coupling metrics across the whole cortex and Braak stage III-IV and V-VI regions (β_{Global} / $\beta_{\text{BraakIII-IV}}$ / $\beta_{\text{BraakV-VI}}$).

Results

MTL FDG was among the lowest across AD stages, consistent with Raichle CMRglc atlas.

Across A-/T- and A+/T_{Early}+, low-FDG group exhibited faster tau accumulation and stronger A β - and entorhinal tau-related tau increases compared to mid/high-FDG groups.

Low-FDG group in early stages showed greater connectivity-associated tau spread. Mediation analyses indicated that increased FC between MTL and inferior parietal cortex mediated associations between A β burden and tau accumulation in low-FDG groups.

Conclusion

Lower MTL FDG is related to faster early tau accumulation and spread, potentially through A β -related FC increases highlighting intrinsic metabolic architecture as a potential contributor to early tau vulnerability in AD.

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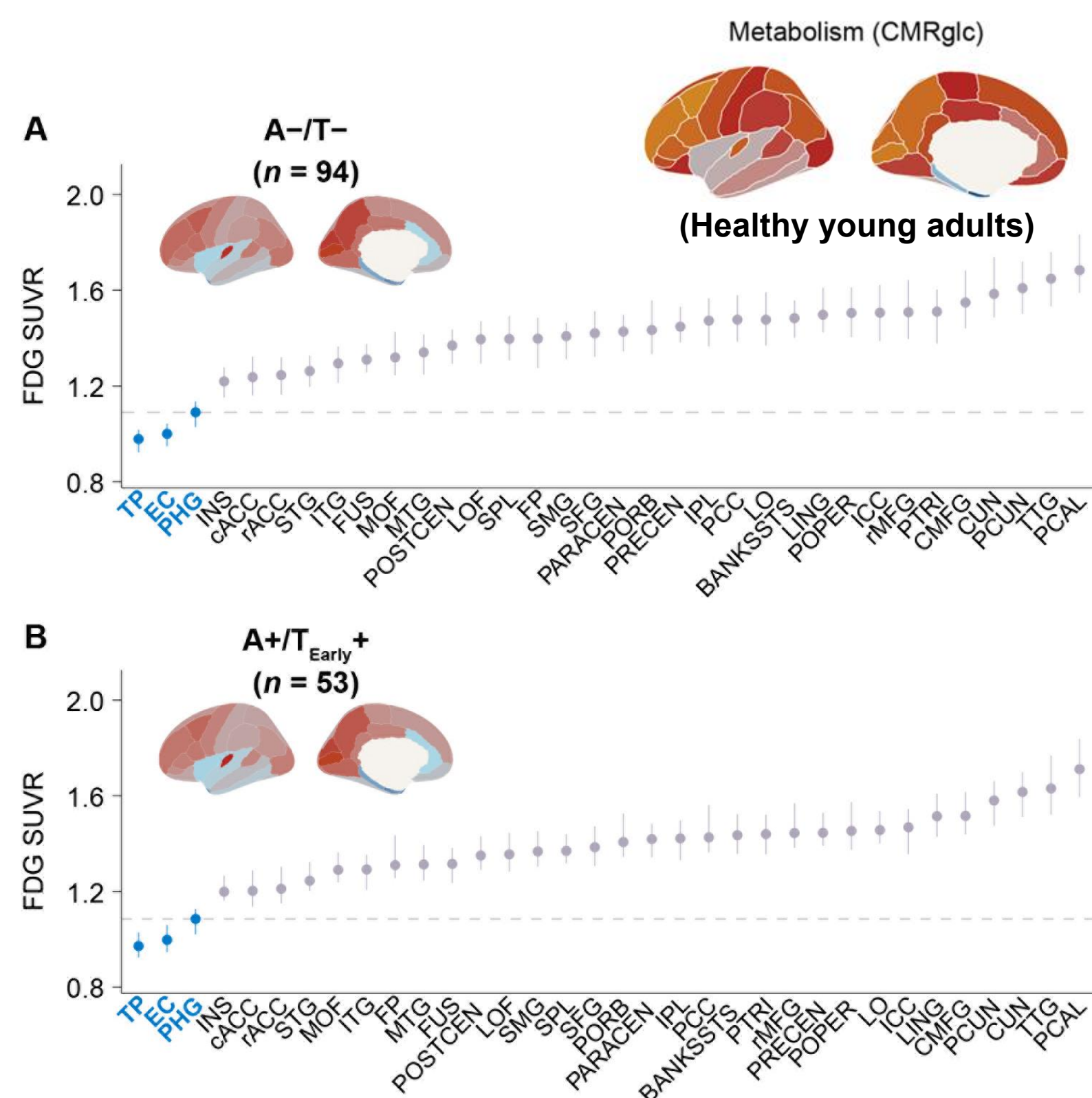


Fig.1. Mean FDG in A-/T- and A+/T_{Early}+, groups.

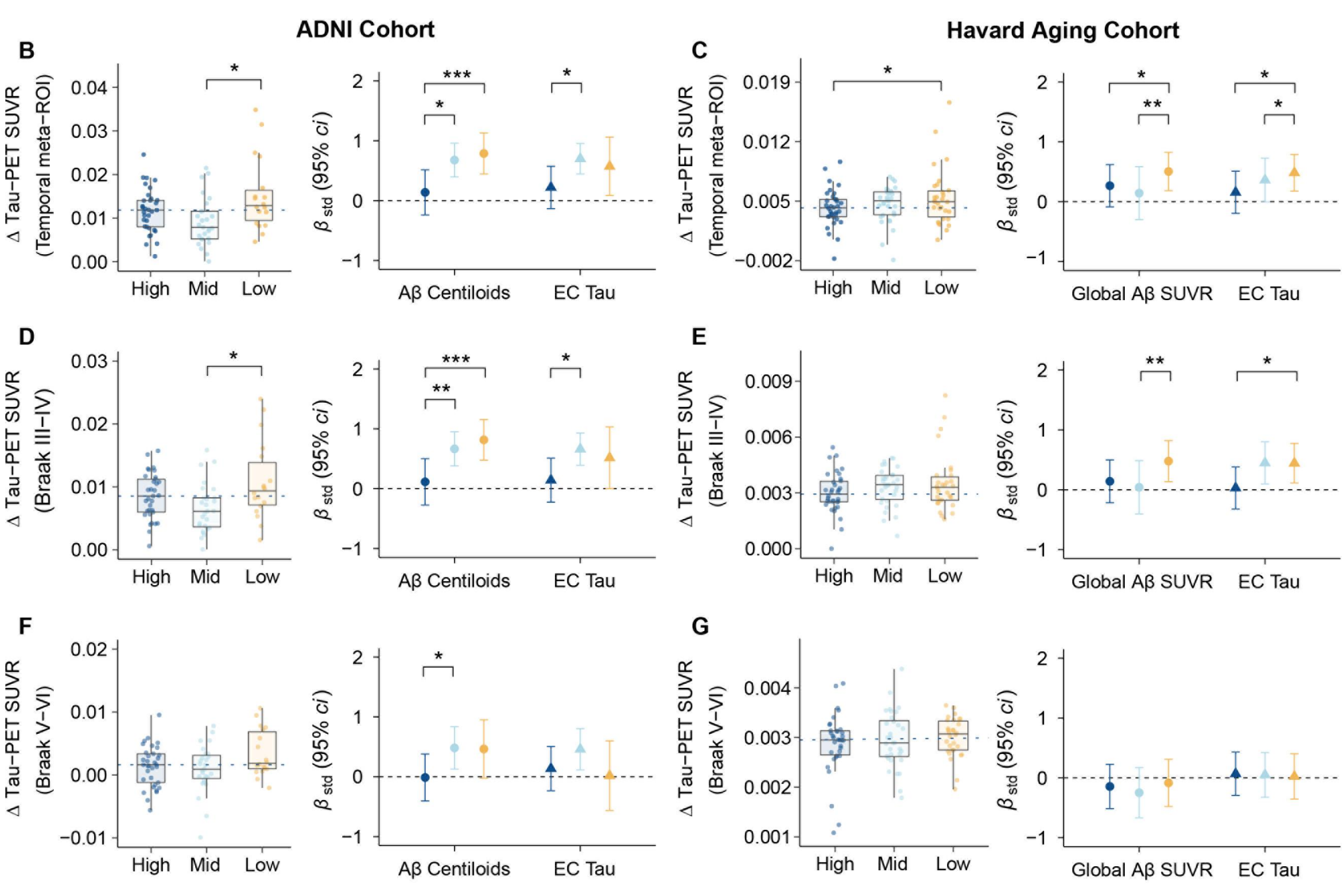


Fig.2. Low MTL FDG is associated with faster longitudinal tau accumulation and stronger A β - and entorhinal tau-related tau increases.

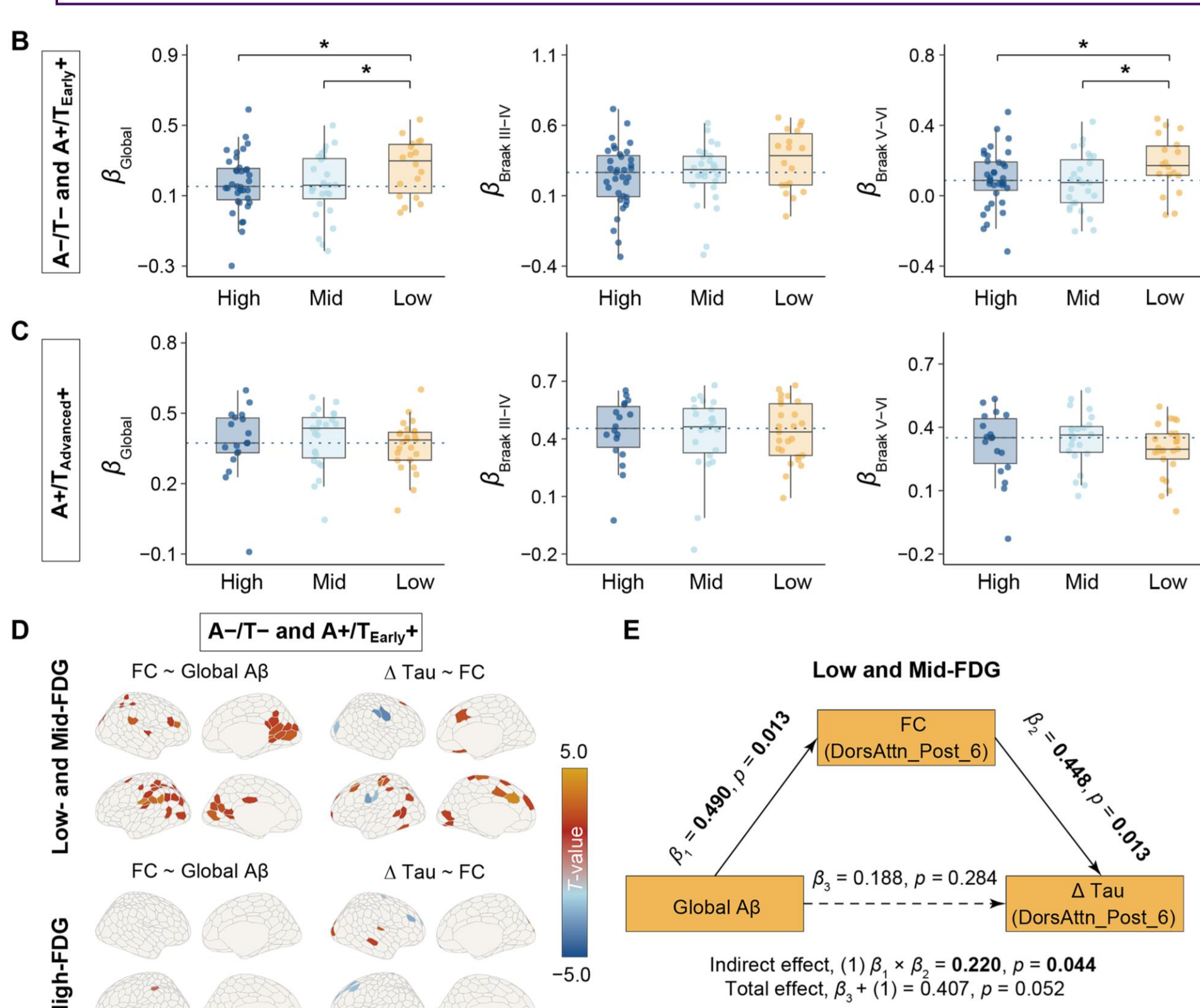


Fig.3. Low MTL FDG is associated with faster connectivity-associated tau spread and increased FC.