

Diabetes mellitus is associated with attenuated tau pathology and cognitive decline in Alzheimer’s disease

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INTRODUCTION

Diabetes mellitus is a known risk factor for dementia, but whether it promotes cognitive decline through classical Alzheimer’s disease pathology remains unclear.

We examined whether diabetes modifies amyloid- β , tau pathology, plasma p-tau217–tau coupling, tau propagation, and tau-related cognitive decline across three independent cohorts.

METHODS

2,784 participants from three cohorts:
CPAS: n = 734
ADNI: n = 835
HABS-HD: n = 1,215

Biomarkers:
Amyloid PET, tau PET, plasma p-tau217, plasma GFAP

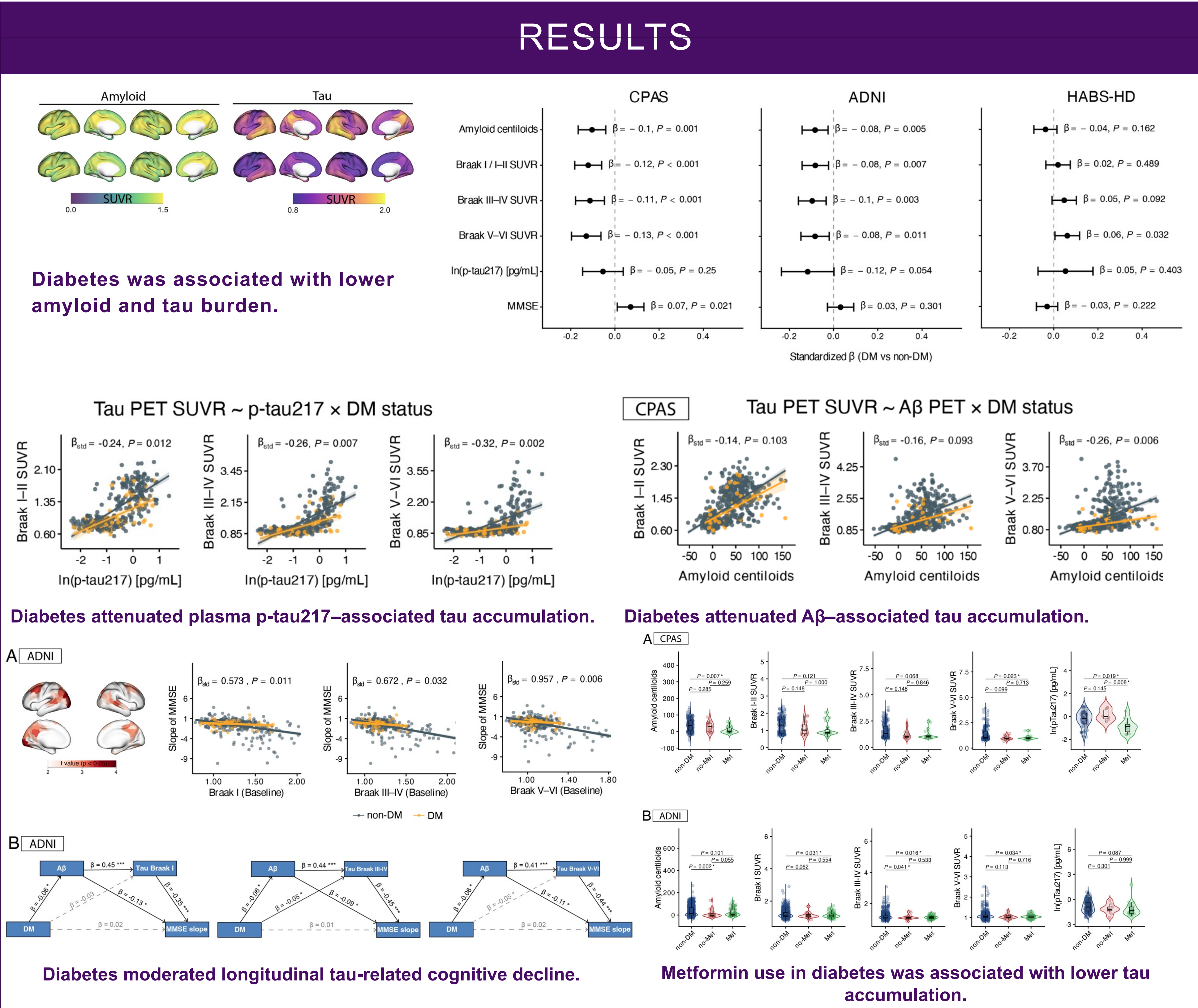
Cross-sectional biomarker association:
DM $\rightarrow$ amyloid PET, tau PET, plasma p-tau217, MMSE

Interaction analyses:
DM $\times$ plasma p-tau217 $\rightarrow$ tau PET
DM $\times$ amyloid PET $\rightarrow$ tau PET

Longitudinal analysis in ADNI:
DM $\times$ baseline tau PET $\rightarrow$ MMSE slope

Exploratory analysis:
Metformin use $\rightarrow$ amyloid and tau burden

Models adjusted for age, sex, education, cognitive status, and APOE $\epsilon 4$.



CONCLUSION

Diabetes mellitus was not associated with accelerated classical AD pathology. Instead, diabetes was associated with lower tau burden, weaker amyloid/p-tau217–tau coupling, reduced tau propagation, and slower tau-related cognitive decline.

Dementia risk in diabetes may involve non-AD pathways and that diabetes management may modify AD-related pathological progression.

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