

Suchita Ganesan¹, Victoria R. Tennant¹, Koral V. Wheeler¹, Amariyllis A. Tsiknia¹, Noelle Lee¹, Maxwell W. Hand¹, Arthur W. Toga¹, Kristine Yaffe², Meredith N. Braskie¹ for the HABS-HD study team
1. USC Stevens Neuroimaging and Informatics Inst., USC, Los Angeles, CA; 2. Dept. of Psychiatry, Neurology, and Epidemiology and Biostatistics, Univ. of California San Francisco, San Francisco, CA

Rationale and Aims

- Plasma phosphorylated tau-217 (pTau217) is a FDA approved core-1 biomarker for Alzheimer's disease (AD) with high accuracy for predicting amyloid- β (A β) accumulation¹.
- However, the relationships between plasma pTau217 and regional tau-PET, and the potential modifying effect of A β positivity, remain underexplored in ethnoracially diverse samples²⁻⁴.

Methods

Cohort

- We studied 530 cognitively unimpaired (CU) older adults enrolled in the Health and Aging Brain Study–Health Disparities (HABS-HD) cohort (Table 1).

Imaging and Fluid Biomarkers

- Plasma pTau217 concentrations were quantified using the Quanterix Simoa platform.
- Tau burden was assessed using [¹⁸F]-PI-2620 PET scans, and standardized uptake value ratio (SUVR) images were generated using the inferior cerebellar gray matter as the reference region. SUVR images were normalized to MNI space and smoothed with a 4-mm Gaussian kernel.
- Amyloid burden was assessed using [¹⁸F]-florbetaben (FBB) PET scans, with SUVR images referenced against the whole cerebellum; A β positivity was defined as a global FBB SUVR > 1.08. All continuous variables were standardized prior to analysis.

Statistics

- Voxelwise linear regression analyses were conducted in SPM12, with an eroded cortical gray matter mask applied to minimize the influence of meningeal off-target binding on voxelwise correlations.
- All models were adjusted for age, sex, education, ethnicity, APOE- ϵ 4, A β -PET status, and scanner effects.
- We separately tested interactions between plasma pTau217 and A β -PET status, APOE- ϵ 4 status, sex, and ethnoracial group.
- Statistical significance was assessed using a voxel-level threshold of $p < 0.001$ in conjunction with cluster-level family-wise error (FWE) correction at $p < 0.05$.
- We performed a sensitivity analysis of our voxelwise results by running robust regressions between pTau217 and the mean SUVR in the FWE-surviving cluster (using the Imrob package in R).

	Non-Hispanic White (N=228)	Hispanic (N=136)	Non-Hispanic Black (N=166)	Overall (N=530)
Plasma pTau217 (pg/ml)	0.49 $\pm$ 0.33	0.39 $\pm$ 0.39	0.33 $\pm$ 0.17	0.41 $\pm$ 0.31
Age	69 $\pm$ 8.0	63 $\pm$ 7.2	62 $\pm$ 7.2	65 $\pm$ 8.1
Years of Education	16 $\pm$ 2.3	11 $\pm$ 4.2	15 $\pm$ 2.7	14 $\pm$ 3.6
Gender (Male/Female)	88/140	38/98	47/119	173/357
APOE Status (ϵ 4-/ ϵ 4+)	153/75	109/27	106/60	368/162
Amyloid Status (A β -/A β +))	174/54	116/20	144/22	434/96
Centiloids	17.9 $\pm$ 29.0	10.9 $\pm$ 16.3	9.3 $\pm$ 15.8	13.4 $\pm$ 22.8

Table 1. Demographic information for cognitively unimpaired participants of the HABS-HD cohort.

Results

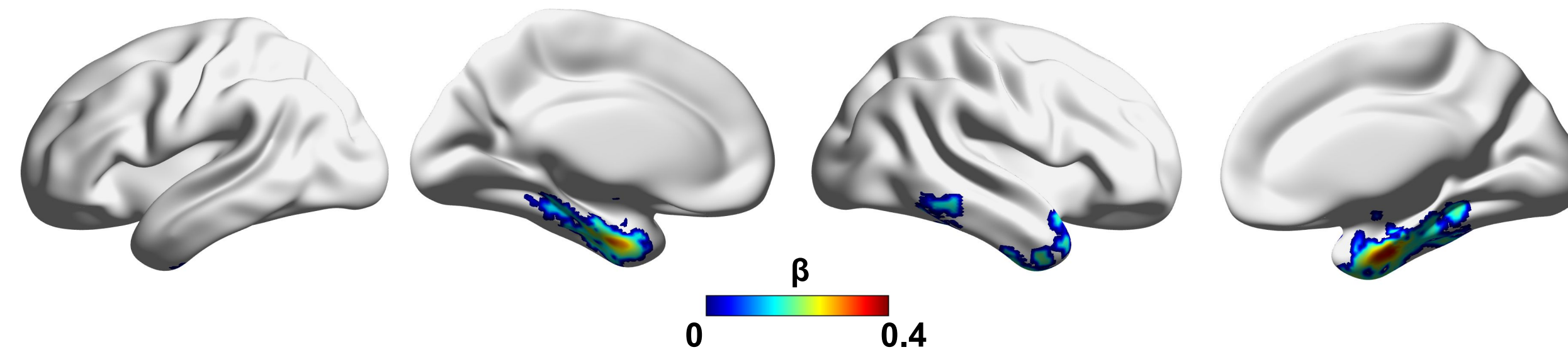


Figure 1. FWE-corrected ($p < 0.05$) effect size map showing the association between plasma pTau217 and PI-2620 SUVR.

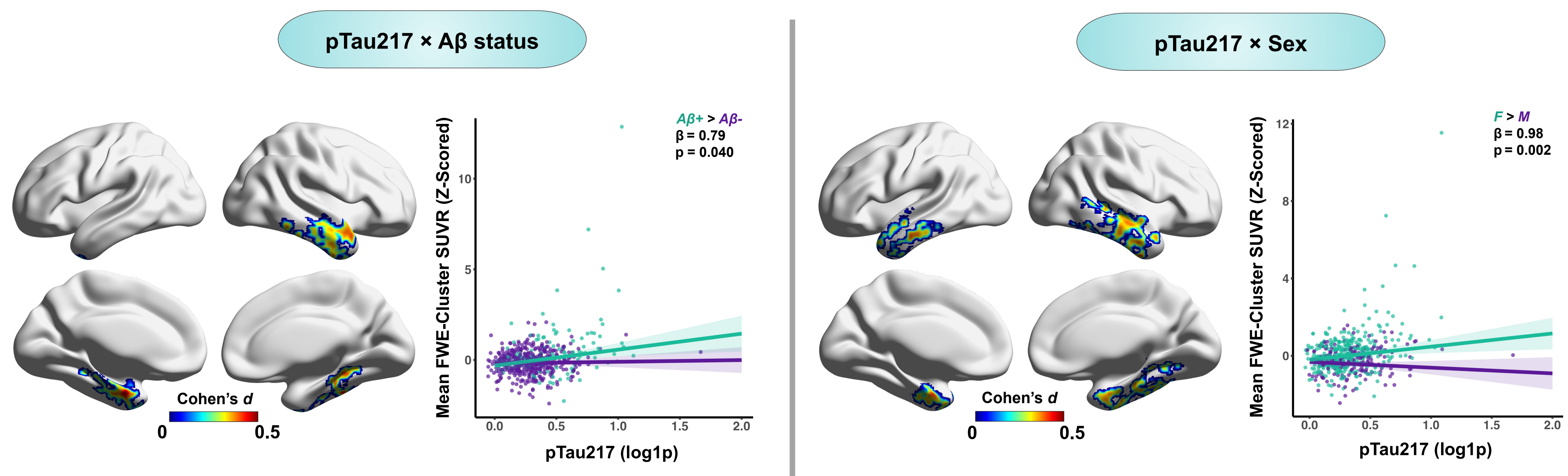


Figure 2. Interactions of pTau217 with A β status and sex. FWE-corrected ($p < 0.05$) Cohens'd maps show the difference between groups. All models survived sensitivity analysis (robust regressions shown on the right).

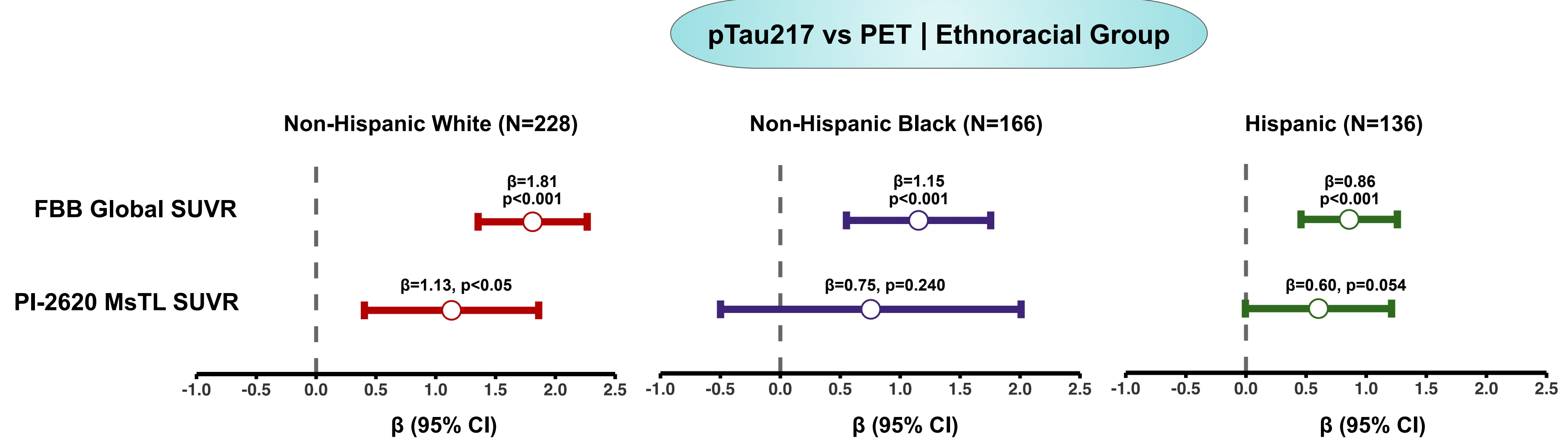


Figure 3. Robust regressions stratified by ethnoracial group: Standardized regression coefficient showing the association between pTau217 and PET SUVR outcomes: FBB Global SUVR and PI-2620 Mesial Temporal (MsTL) SUVR.

- The interaction between pTau217 and ethnicity on Tau-PET was not significant at the voxelwise or ROI level.
- Stratified models showed robust pTau217-PET associations amongst NWH participants.
- Within NHB participants, pTau217 was related to amyloid but not MsTL tau.

Conclusion

- Plasma pTau217 levels capture tau-PET uptake in MTL regions, with stronger associations in A β + vs A β - individuals and women compared with men.
- There are no significant differences across ethnoracial groups and larger samples will be needed to validate our observations at the stratified level.
- Longitudinal analyses will be needed to examine whether pTau217 trajectories predict tau-PET progression in this cohort.

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