

Machine-learning signatures of brain aging and Alzheimer’s disease show distinct associations with plasma biomarkers



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Introduction

- Cerebral atrophy is driven by the culmination of multiple neuropathological and age-related processes.
- Machine-learning algorithms may improve diagnostic specificity by capturing regionally-specific morphological alterations associated with aging (SPARE-BA¹) and AD (SPARE-AD^{2,3}), respectively.
- This study examined whether SPARE-BA and SPARE-AD map onto specific ADRD blood-based biomarker (BBMs) profiles.

Participants (N = 1,297)

71 yrs

Mean age

42%

Female

29%

Amyloid PET positivity

70%

Cognitively unimpaired

Cohort

51%
HABS-HD

35%
ADNI

STAC

Race/Ethnicity

21%
Black

27%
Hispanic

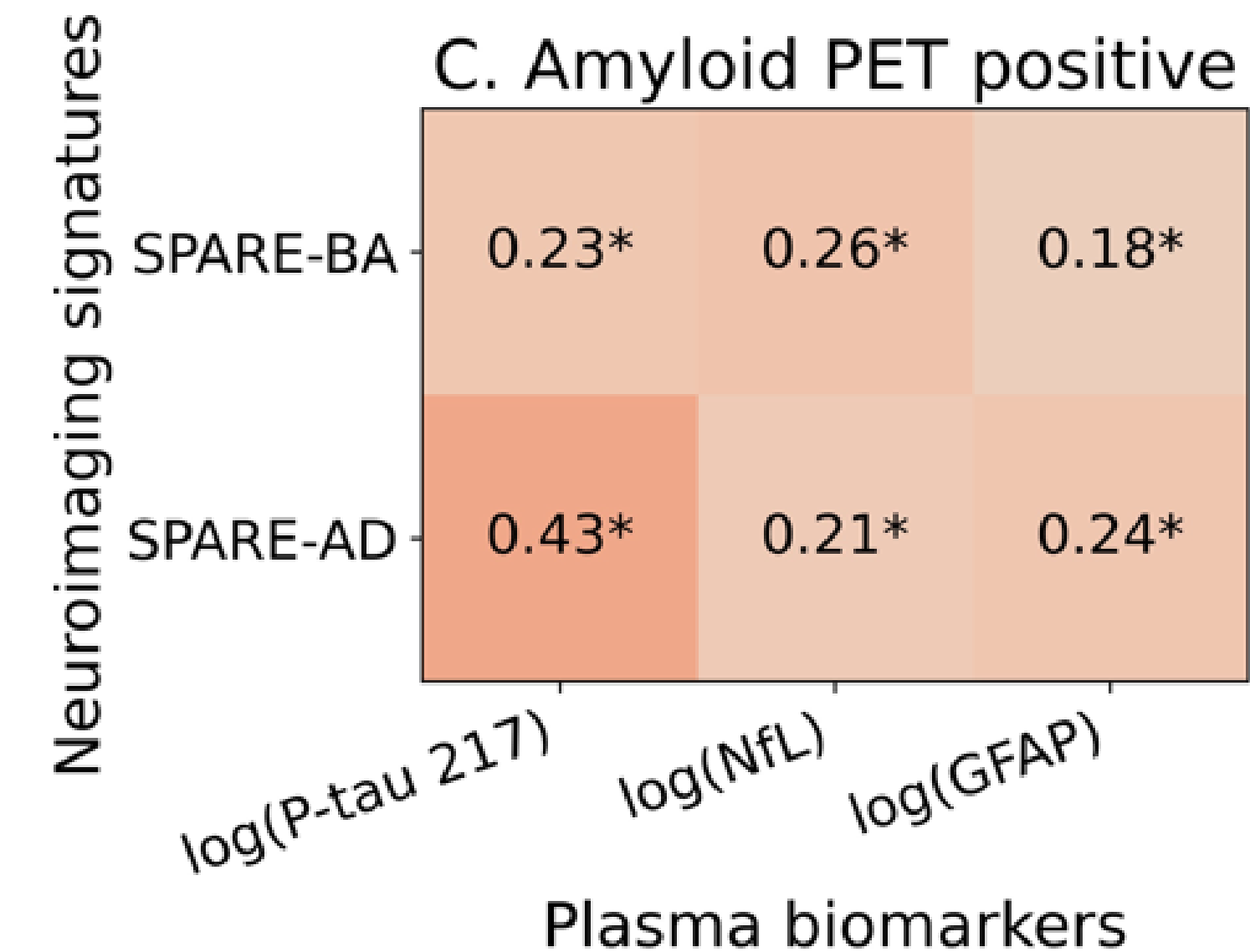
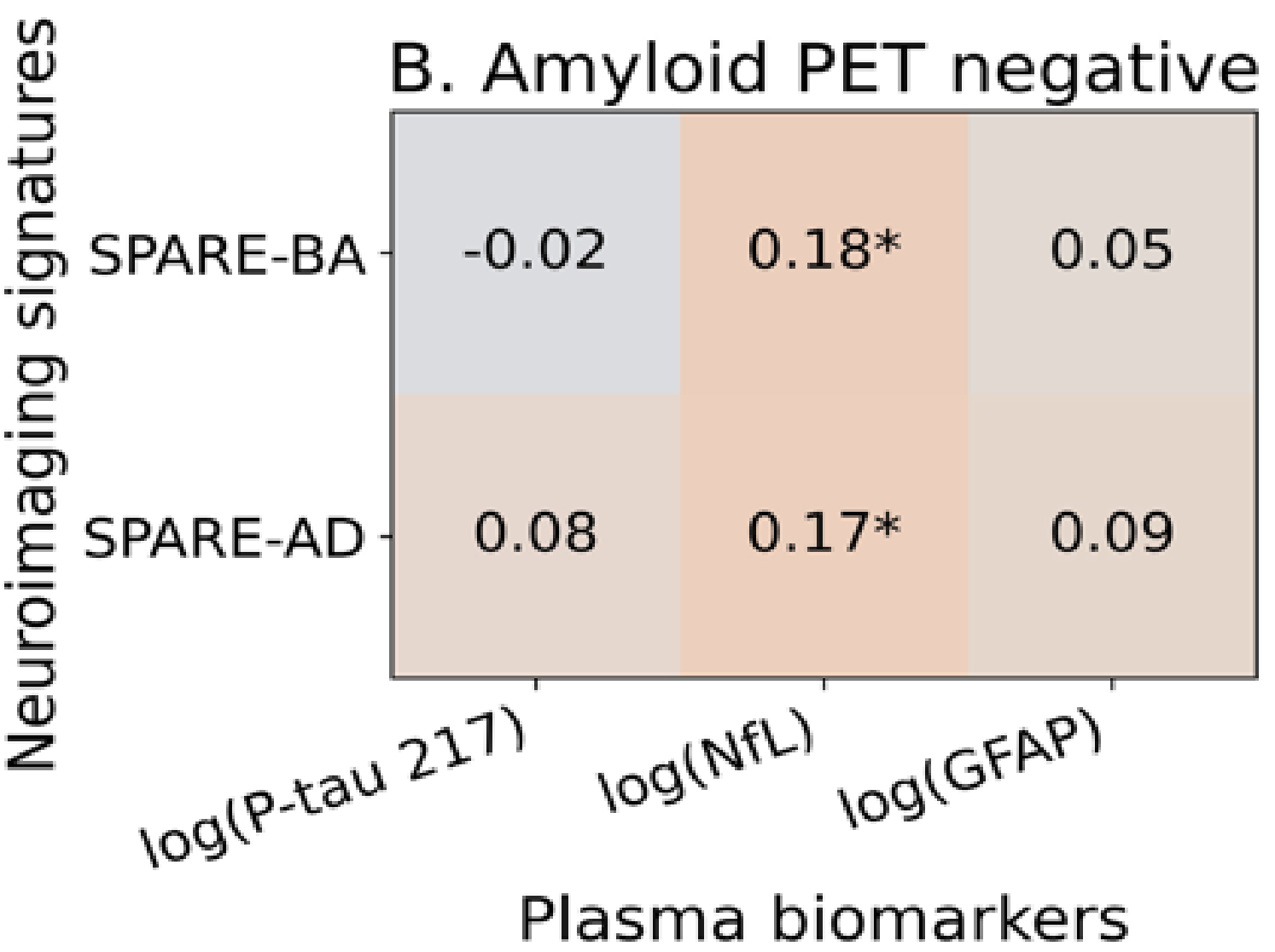
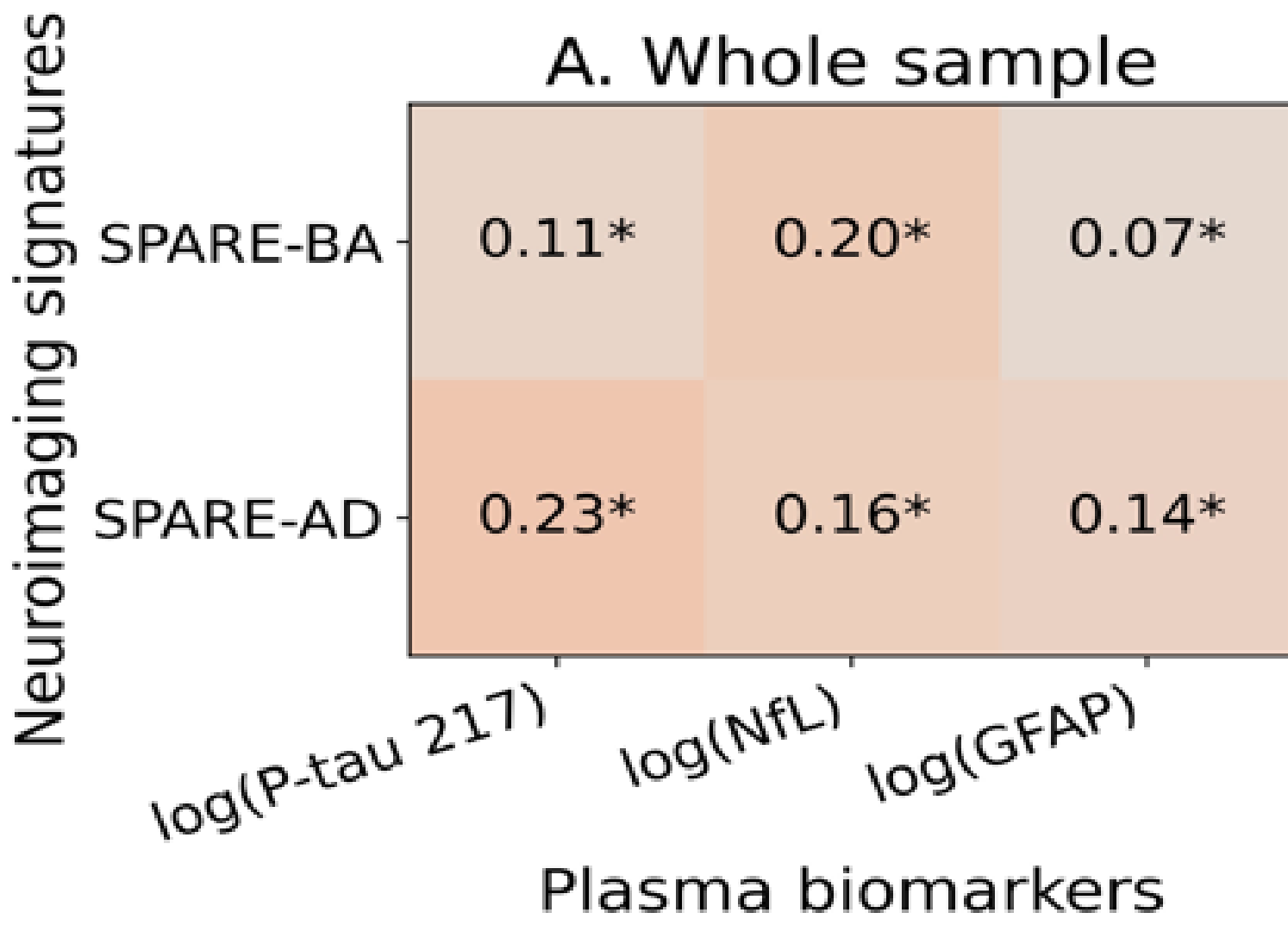
47%
White

Methods

- SPARE-BA, SPARE-AD, hippocampal (HV), and whole brain (WBV) were derived on 2,238 HABS-HD participants, ages ≥ 60 years
- Plasma p-tau 217, NFL, and GFAP were quantified using the Quanterix HD-X. and log-transformed.
- Associations between neuroimaging measures and BBMs were evaluated with linear regression adjusting for age, sex, and education
- Results were stratified by amyloid (aβ) PET positivity.

Results

Neuroimaging & plasma biomarker correlations



Conclusions

- 1 SPARE-AD and plasma p-tau 217 demonstrated the strongest partial correlation, which was further amplified in Aβ PET positive participants.
- 2 The results highlight the improved capability of SPARE-AD, relative to SPARE-BA, for detecting atrophy patterns associated with AD pathology.
- 3 SPARE-BA and SPARE-AD had modest correlations with plasma GFAP and NFL, suggesting they capture related but distinct aspects of aging and ADRD
- 4 Among Aβ negative participants, SPARE-BA and SPARE-AD were solely associated with plasma NFL, a marker of neuro-axonal injury

References & Acknowledgments

- 1) Habes et al. *Brain* 139.4 (2016): 1164-1179.
 - 2) Davatzikos et al. *Brain* 132.8 (2009): 2026-2035.
 - 3) Davatzikos, et al. *Neurobiology of Aging* 32.12 (2011): 2322-e19
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