

Background

- Alzheimer's disease (AD) and cerebrovascular disease (CVD) often coexist in aging, but clinical diagnosis alone may miss mixed biological pathology.
- CSF and PET identify AD biology but their cost and invasiveness make large-scale screening difficult.
- Combining blood-based biomarkers (BBMs) with MRI vascular markers can support practical biological classification.

Methods

Participants: N = 321 from UNM MarkVCID¹ + NM ADRC.
AD Factor (ADF): pTau217, pTau181, pTau217/Aβ42.
VD Factor (VDF): mean free water (mFW), peak width of skeletonized mean diffusivity (PSMD), white matter hyperintensity (WMH) volume.

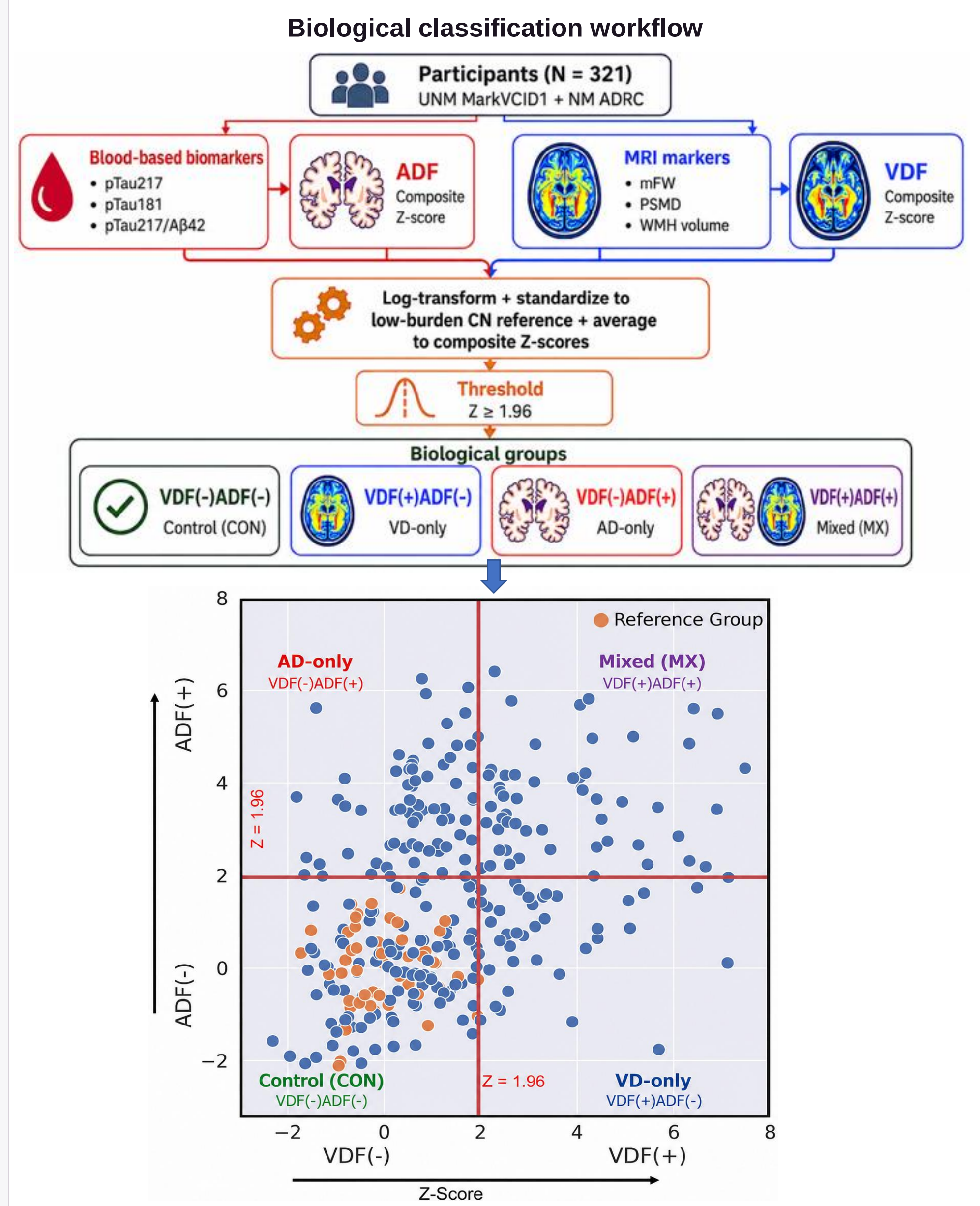


Figure 1. Biological classification workflow using a double-dichotomy framework². Participants were classified into four biological groups: CON n=155, VD n=41, AD n=70, and MX n=55.

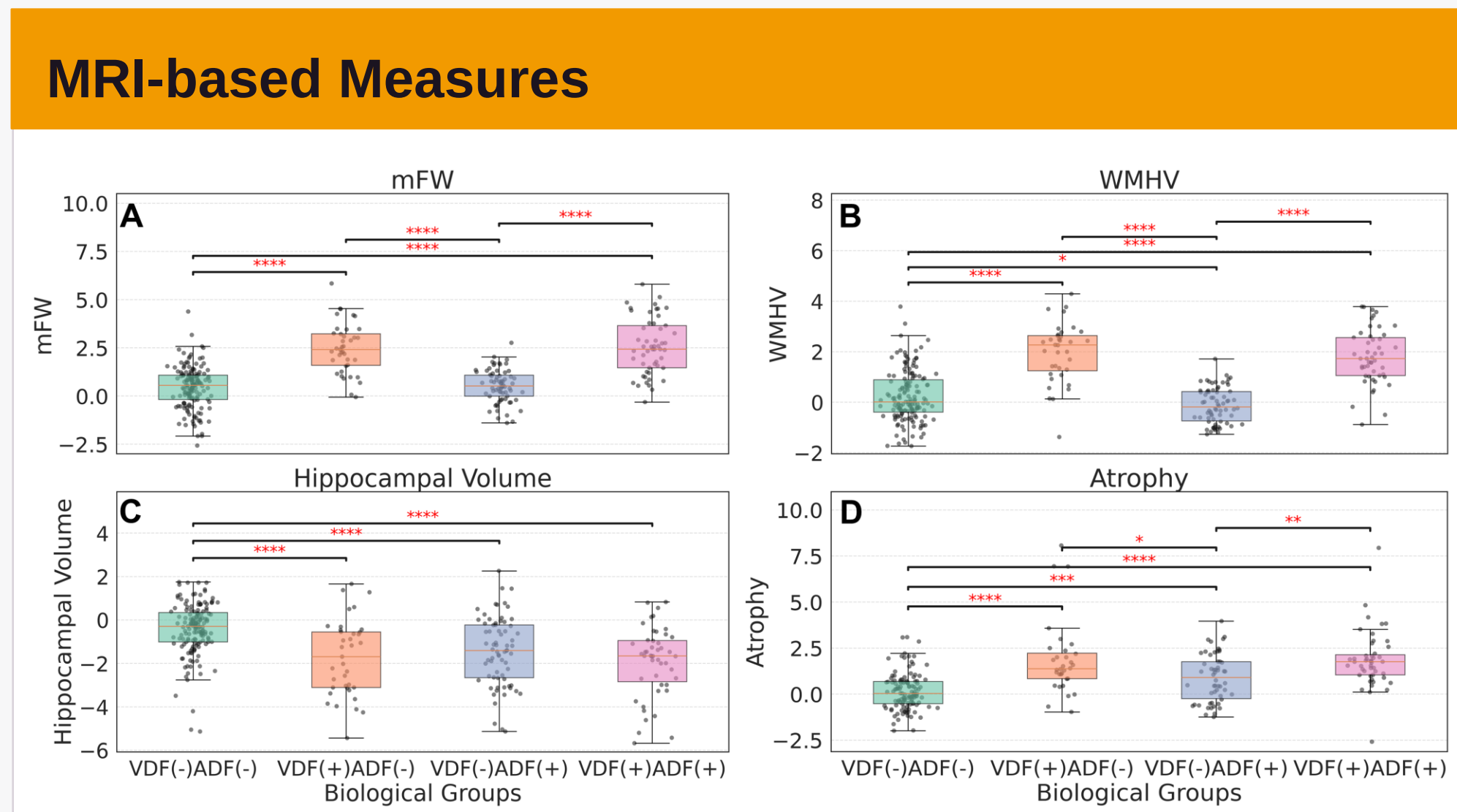


Figure 2. Neuroimaging measures across biological groups. Age- and sex-adjusted Z-scores are shown for (A) mFW, (B) WMHV, (C) hippocampal volume, and (D) brain atrophy. Boxplots show median/IQR with individual data points; stars indicate pairwise significance.

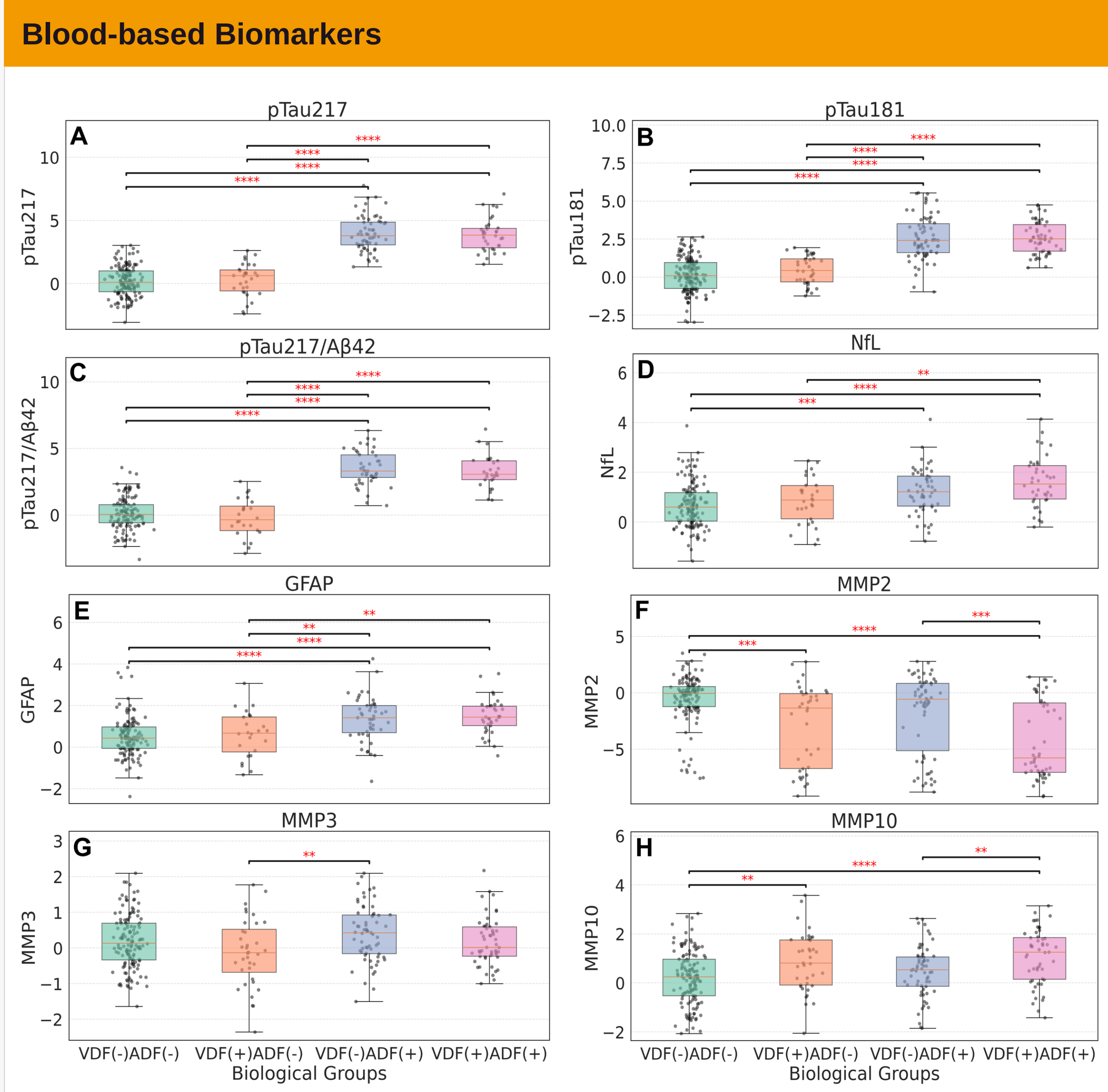


Figure 3. Blood-based biomarkers across biological groups. Age- and sex-adjusted Z-scores are shown for (A) pTau217, (B) pTau181, (C) pTau217/Aβ42, (D) NfL, (E) GFAP, (F) MMP2, (G) MMP3, and (H) MMP10. Boxplots show median/IQR with individual data points; stars indicate pairwise significance.

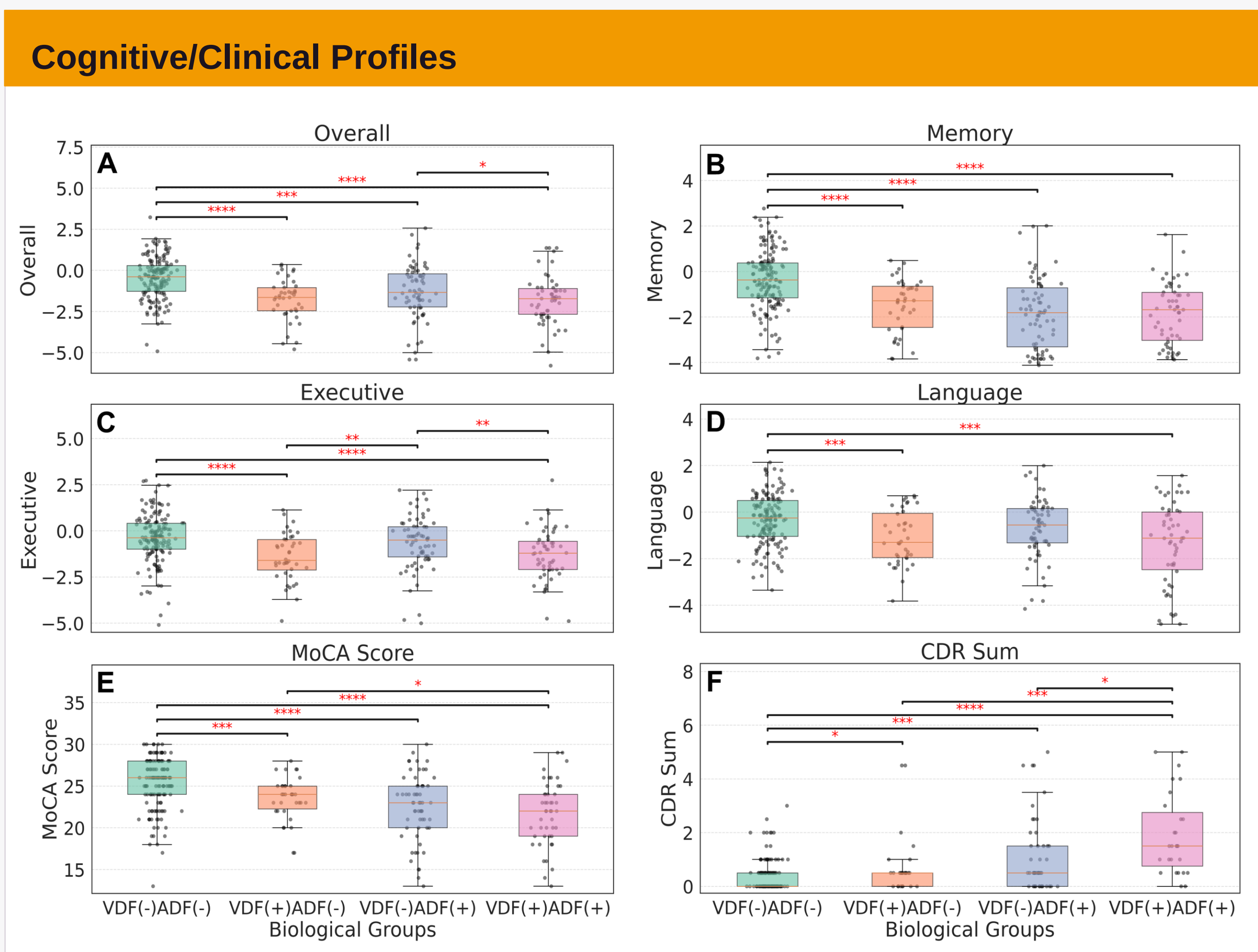


Figure 4. Cognitive and clinical measures across biological groups. Boxplots show (A) overall cognition, (B) memory, (C) executive function, (D) language, (E) MoCA, and (F) CDR Sum; stars indicate pairwise significance.

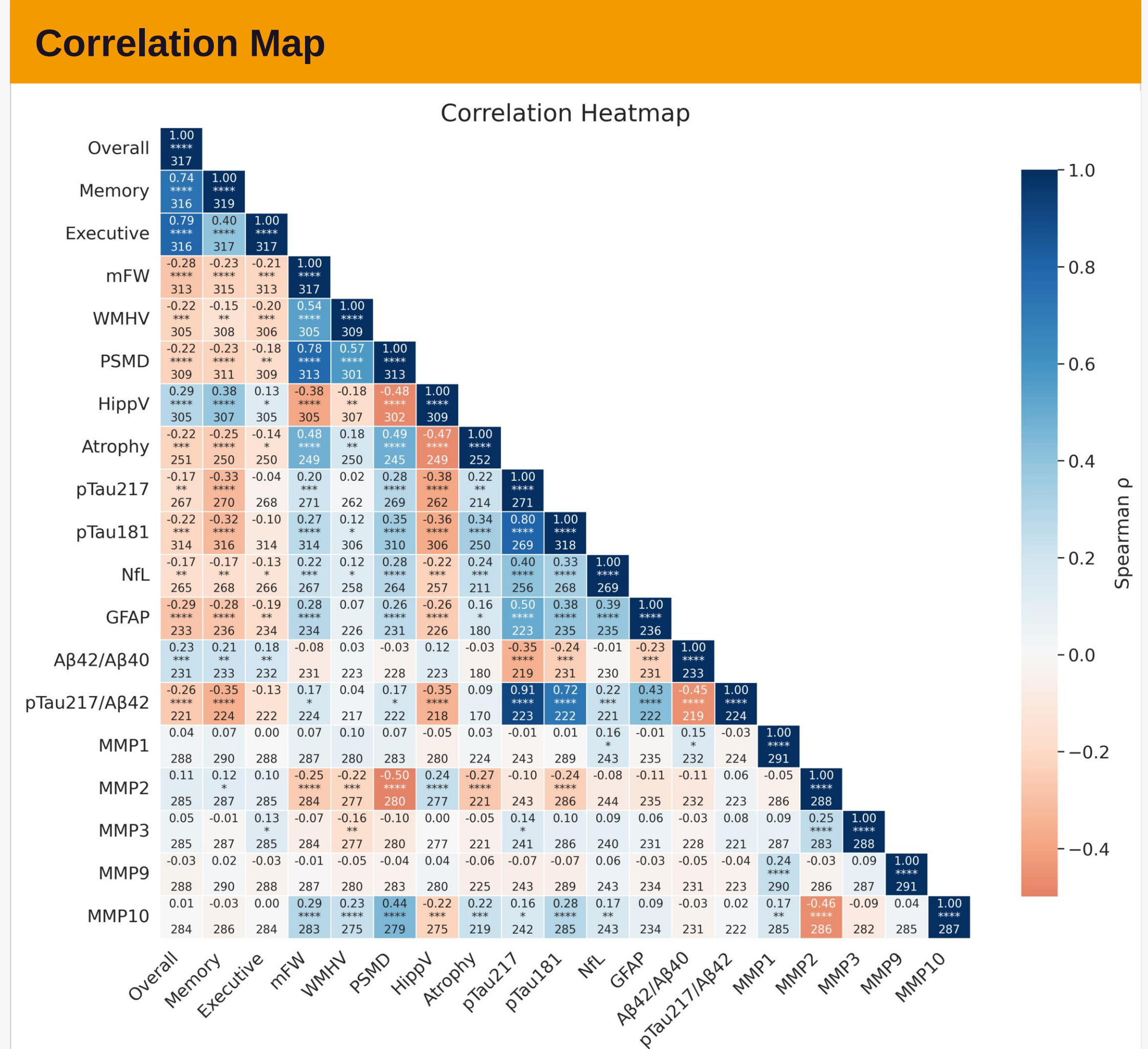


Figure 5. Spearman correlations across cognition, MRI measures, and blood-based biomarkers.

Key Findings

- Mixed pathology was common: 55/321 (17.1%).
- ADF+ groups showed higher AD biomarkers including NfL and GFAP.
- VDF+ groups showed greater vascular markers including Hippocampal volume and atrophy.
- AD profiles aligned with memory decline; vascular profiles aligned with executive/language dysfunction.

Take-home Message

Non-invasive blood-based biomarkers combined with MRI measures provide a framework to identify AD, VD, and mixed pathology.

Conclusions

- Multimodal BBM + MRI classification gives biologically interpretable dementia groups.
- Mixed pathology showed the highest overall burden across several MRI, blood, and clinical measures.
- This scalable approach may improve screening and participant classification, but independent validation is required before clinical use.

References

- Maillard, Pauline, et al. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring* 14.1 (2022): e12261.
- Caprihan, Arvind, et al. *Cerebral circulation-cognition and behavior* 2 (2021): 100011.

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