

BACKGROUND

- Alzheimer’s disease (AD) biomarkers vary across sociodemographic groups.
- Unclear how gender/sex, racialization, and neighborhood deprivation jointly pattern AD-related neuroimaging biomarkers.
- Objective: Examine the intersectional variation in AD neuroimaging biomarkers across strata defined by gender/sex, racialization, and neighborhood deprivation.

METHODS

- Data: Connectomics in Brain Aging (CoBrA) study of community-dwelling older adults.
- Intersectional strata: Defined by gender/sex (men/women), racialization (White/Black), and neighborhood deprivation measured by Area Deprivation Index (ADI; low/high).
- Neuroimaging biomarkers: global amyloid burden (A); lobar unhealthy white matter connectivity (UWMC; V); AD signature cortical thickness (N).
- Statistical Analysis: Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (MAIHDA) to characterize differences in neuroimaging biomarkers across intersectional strata. All models adjusted for age; models for amyloid burden additionally adjusted for *APOE4* status.

KEY RESULTS

- N=196.
- Distinct intersectional stratum-level patterns relative to the group mean:
 - Global amyloid burden: lower among high-ADI Black women; higher among high-ADI White men.
 - Frontal UWMC: lower among low-ADI White men; higher among high-ADI Black/White women.
 - Occipital UWMC: lower among low- and high-ADI Black women; higher among high-ADI White men.
 - Cortical thickness: lower (NS) among Black men and women in both low- and high-ADI.
- Between-stratum heterogeneity was low to modest across all biomarkers (VPC: 2.1%-13.5%).
- Little evidence of excess intersectional heterogeneity beyond additive effects.

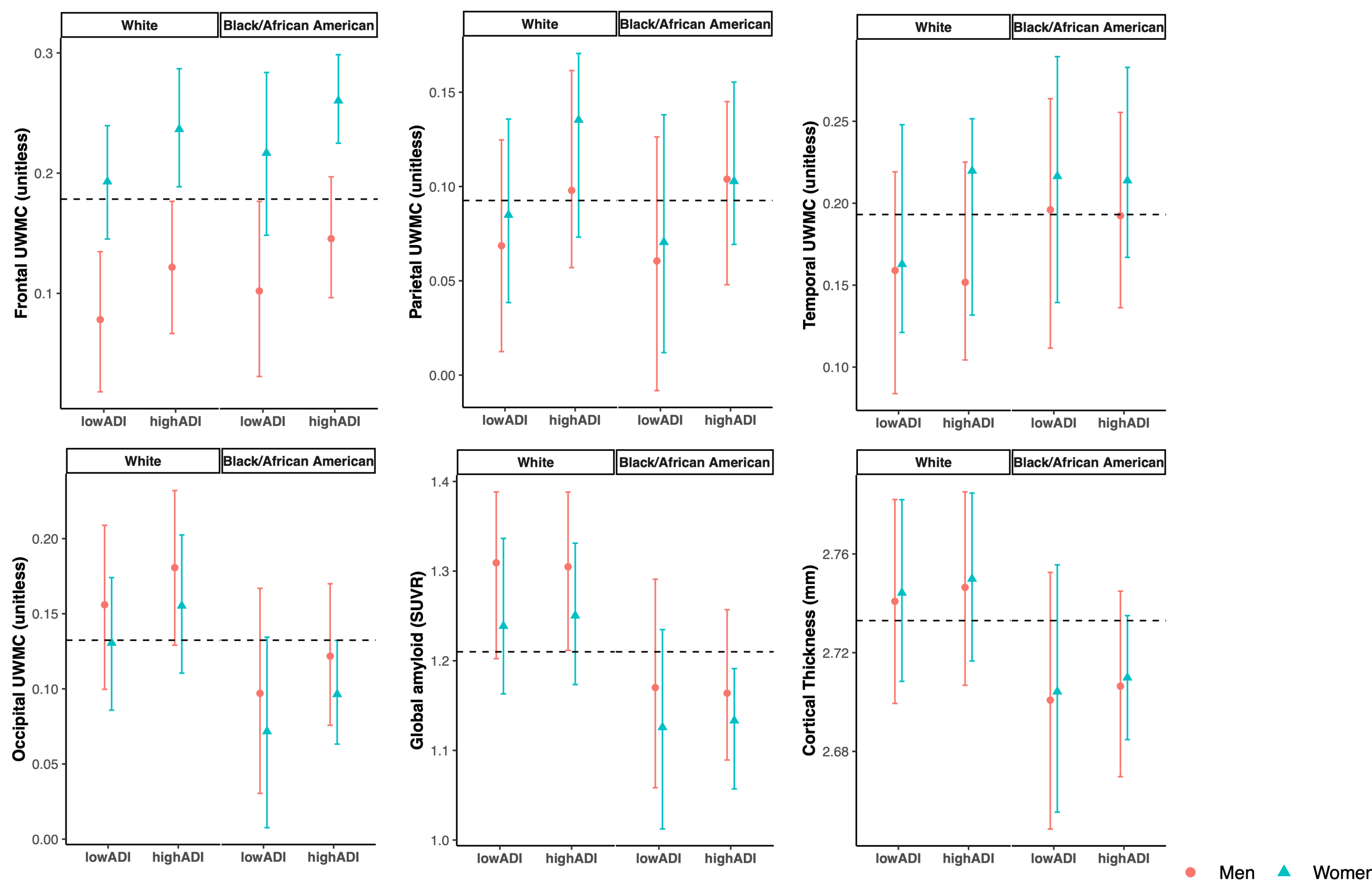
RESULTS

Table 1. Participant Characteristics at Time of Neuroimaging Visit by Intersectional Strata

	Overall	Low ADI- White -Men	Low ADI- White- Women	High ADI- White-Men	High ADI- White- Women	Low ADI- Black-Men	Low ADI- Black- Women	High ADI- Black-Men	High ADI- Black- Women
	N=196	N=16 (8.2%)	N=31 (15.8%)	N=20 (10.2%)	N=32 (16.3%)	N=5 (2.6%)	N=7 (3.6%)	N=24 (12.2%)	N=61 (31.1%)
Age, years	62.0 (57.0, 70.0)	67.0 (64.0, 74.2)	69.0 (58.5, 73.0)	60.0 (58.2, 74.0)	62.0 (57.0, 70.2)	62.0 (59.0, 69.0)	58.0 (56.5, 60.0)	62.5 (56.0, 67.0)	60.0 (55.0, 66.0)
Education, years	14.0 (12.0, 16.0)	17.0 (14.0, 18.0)	14.0 (12.0, 18.0)	12.5 (12.0, 14.2)	14.0 (12.0, 16.0)	16.0 (16.0, 16.0)	14.0 (12.5, 16.0)	14.0 (12.0, 16.0)	14.0 (12.0, 16.0)
<i>APOE4</i> +, N(%)	62 (31.6)	7 (43.8)	5 (16.1)	9 (45.0)	7 (21.9)	1 (20.0)	0 (0.0)	8 (33.3)	25 (41.0)
Hypertension, N(%)	75 (38.3)	6 (37.5)	6 (19.4)	8 (40.0)	9 (28.1)	3 (60.0)	5 (71.4)	11 (45.8)	27 (44.3)
Diabetes, N(%)	32 (16.3)	2 (12.5)	3 (9.7)	3 (15.0)	2 (6.2)	3 (60.0)	1 (14.3)	4 (16.7)	14 (23.0)
High cholesterol, N(%)	67 (34.2)	6 (37.5)	11 (35.5)	7 (35.0)	12 (37.5)	3 (60.0)	2 (28.6)	5 (20.8)	21 (34.4)
MoCA score	25.0 (23.0, 27.0)	27.0 (25.8, 28.0)	27.0 (23.5, 28.0)	25.0 (22.8, 27.0)	27.0 (25.5, 28.2)	24.0 (23.0, 26.0)	26.0 (24.0, 28.0)	23.0 (22.0, 25.0)	24.0 (23.0, 26.0)
Cognitively impaired, N(%)	53 (27.0)	5 (31.2)	9 (29.0)	4 (20.0)	6 (18.8)	1 (20.0)	2 (28.6)	9 (37.5)	17 (27.9)

N (%) for categorical variables; median (IQR) for continuous variables. ADI, Area Deprivation Index. MoCA, Montreal Cognitive Assessment

Figure. MAIHDA-based Predicted AD-related Neuroimaging Biomarkers across Strata



RESULTS

Table 2. MAIHDA Model Estimates and Variance Components for AD-related Neuroimaging Biomarkers

	Random Effects		Summary Statistics	
	Stratum-level Variance	Individual-level Variance	Variance Partition Coefficient (VPC)	Proportional Change in Variance (PCV)
Frontal UWMC				
Null model	0.0036	0.0260	12.2%	
Additive model	0	0.0257	0%	100%
Parietal UWMC				
Null model	0.0003	0.0148	2.0%	
Additive model	0.0003	0.0148	2.0%	0%
Temporal UWMC				
Null model	0.0007	0.0134	5.0%	
Additive model	0.0008	0.0134	5.6%	-14.3%
Occipital UWMC				
Null model	0.0005	0.0226	2.2%	
Additive model	0	0.0226	0%	100%
Amyloid burden				
Null model	0.0047	0.0478	9.0%	
Additive model	0.0008	0.0477	1.6%	83.0%
Cortical Thickness				
Null model	0.0004	0.0119	3.3%	
Additive model	0	0.0120	0%	100%
MoCA				
Null model	0.8249	9.8917	7.7%	
Additive model	0	9.8190	0%	100%

UWMC, Unhealthy White Matter Connectivity. MoCA, Montreal Cognitive Assessment

CONCLUSIONS

- AD neuroimaging biomarkers varied across intersectional strata defined by gender/sex, racialization, and neighborhood deprivation, notably for frontal UWMC and global amyloid burden.
- Low between-stratum variance and limited excess intersectional heterogeneity suggest that most biomarker variability occurred within, rather than between, intersectional strata.
- Given the modest sample size and exploratory nature of these analyses, observed stratum-level patterns should be interpreted cautiously and viewed as hypothesis-generating.
- Future studies with larger and more diverse populations should further examine how individual-, social-, and structural-level factors contribute to disparities in AD neuroimaging biomarkers and downstream dementia risk.

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Yan Wang, ScM YAW171@pitt.edu

FUNDING SUPPORT

Grant Numbers:
UF1AG051197
R01AG072641
K01AG071849