

Disparities in brain aging for aging and ADRD

Kacie Deters, PhD
ACT Research Symposium 2024
Assistant Professor
UCLA | Integrative Biology & Physiology
kdeters@g.ucla.edu
 @KcD_PhD



Terminology

- Health disparity = health difference linked with social, economic, or environmental disadvantage
- Latino, Hispanic, Latinx
- Black, African American, Black American
- Race (a social construct) vs groups that have been racialized
- Sex/gender

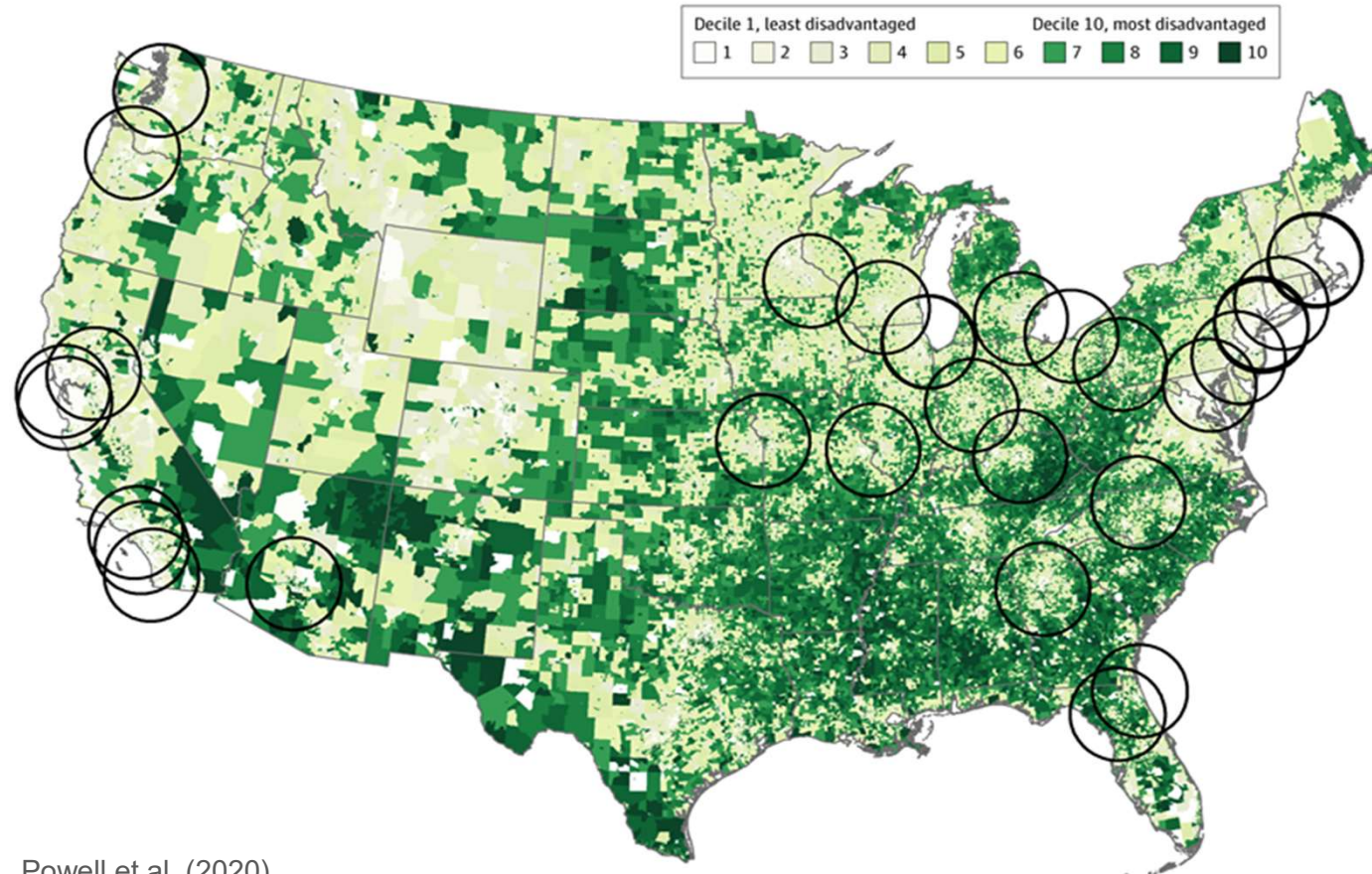
NIMHD Minority Health and Health Disparities Research Framework
Health Disparity Populations: Race/Ethnicity, Low SES, Rural, Sexual/Gender Minority
Other Fundamental Characteristics: Sex/Gender, Disability, Geographic Region

Domains of Influence	Levels	of	Influence	
	Individual	Interpersonal	Community	Societal
Biological	Biological Vulnerability and Mechanisms	Caregiver-Child Interaction Family Microbiome	Community Illness Exposure Herd Immunity	Sanitation Immunization Pathogen Exposure
Behavioral	Health Behaviors Coping Strategies	Family Functioning School/Work Functioning	Community Functioning	Policies and Laws
Physical/Built Environment	Personal Environment	Household Environment School/Work Environment	Community Environment Community Resources	Societal Structure
Sociocultural Environment	Sociodemographics Limited English Cultural Identity Response to Discrimination	Social Networks Family/Peer Norms Interpersonal Discrimination	Community Norms Local Structural Discrimination	Societal Norms Societal Structural Discrimination
Healthcare System	Insurance Coverage Health Literacy Treatment Preferences	Patient-Clinician Relationship Medical Decision-Making	Availability of Health Services Safety Net Services	Quality of Care HealthCare Policies
Health Outcomes	Individual Health	Family/Organizational Health	Community Health	Population Health



Disadvantaged neighborhoods

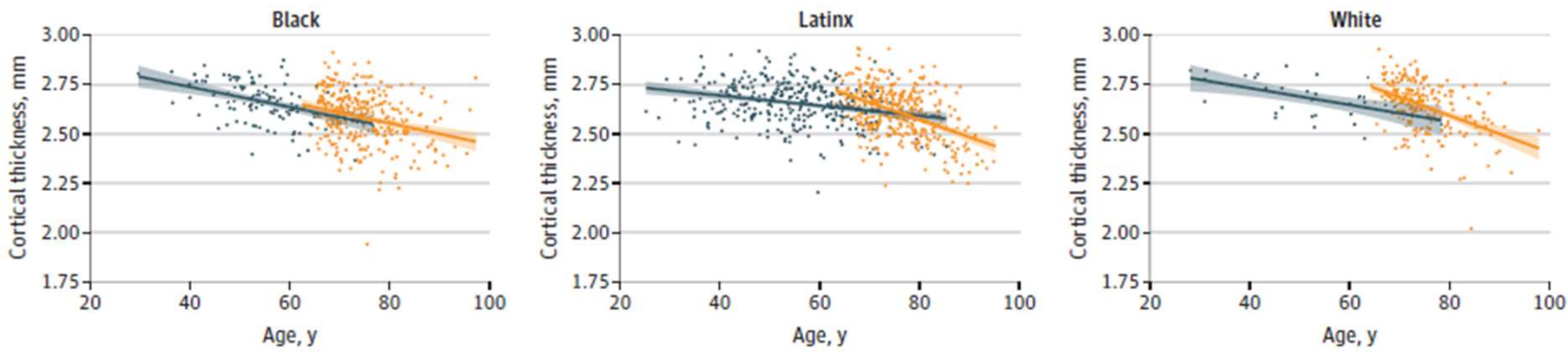
includes education level, income, housing, and employment characteristics



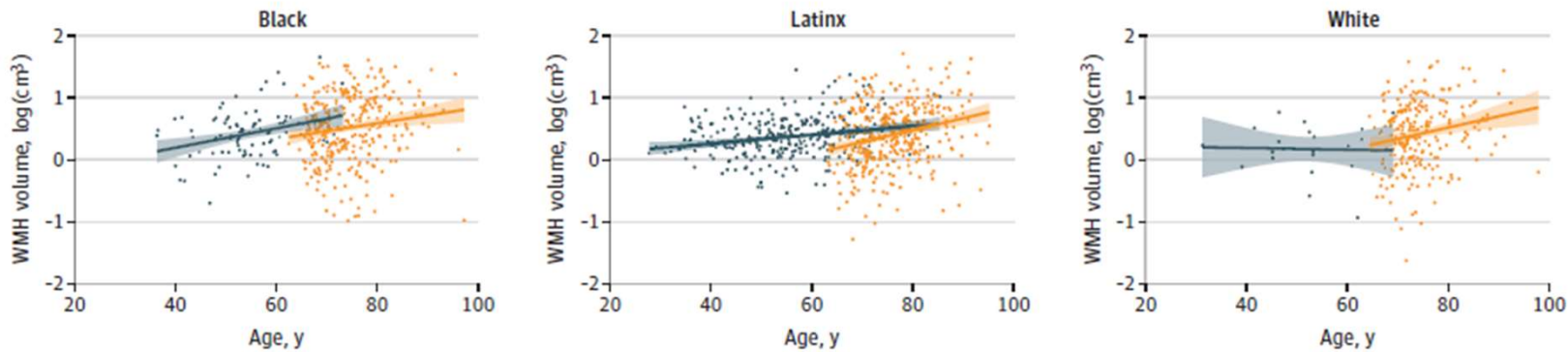
- Increased risk for dementia
- more AD neuropath
- lower brain and hippocampal volume
- poor memory performance

Brain integrity diminishes in middle-age for Black adults

A Age-related differences in CT by race and ethnicity



B Age-related differences in WMH volume by race and ethnicity

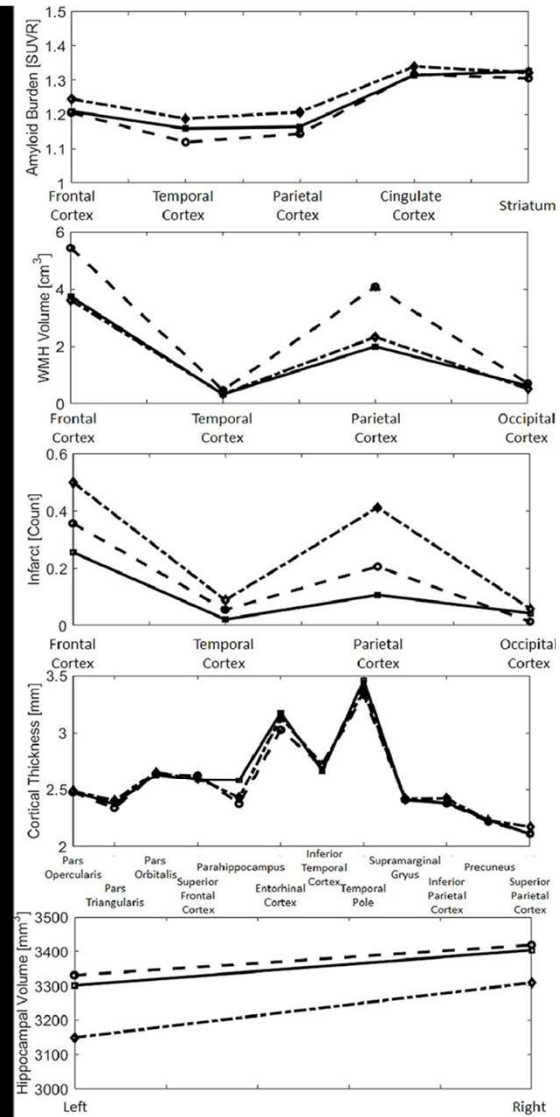
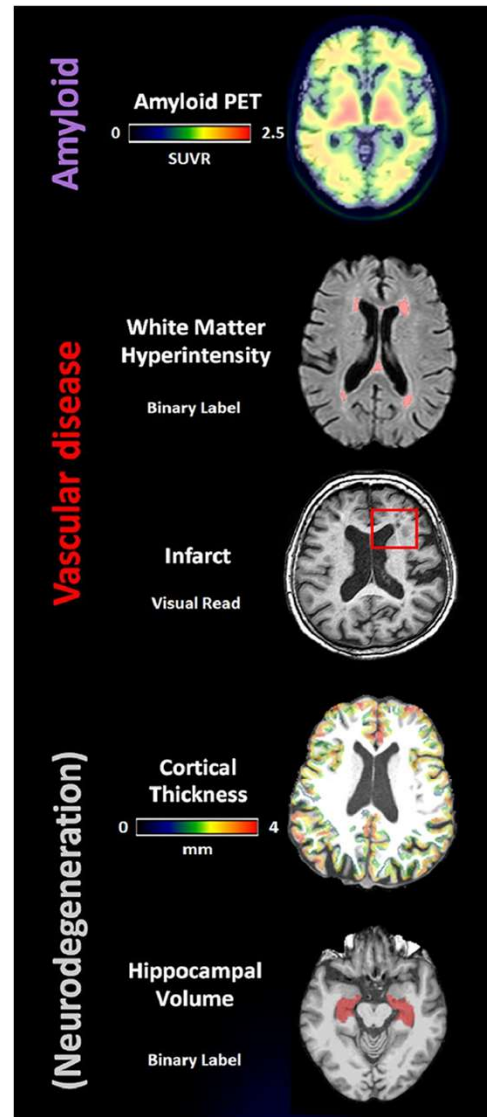


Turney et al., *JAMA Neuro.* 2022

Regional distribution of imaging biomarkers

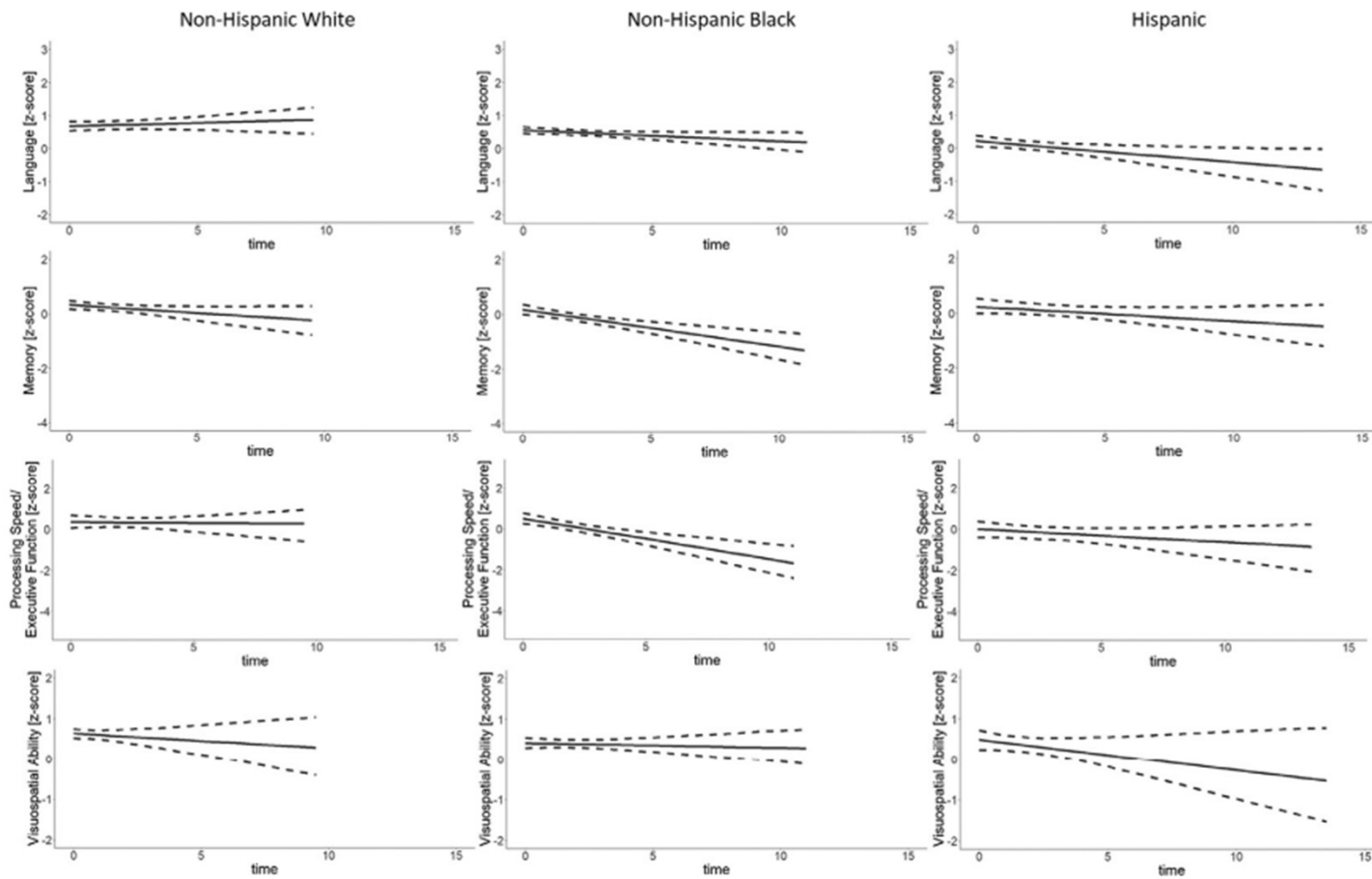


Lao et al., *Neurobi. Of Aging* 2022



■ Non-Hispanic White ● Non-Hispanic Black ◆ Hispanic

Cognitive trajectories adjusted for amyloid, WMH, and cortical thickness



Amyloid in Black individuals

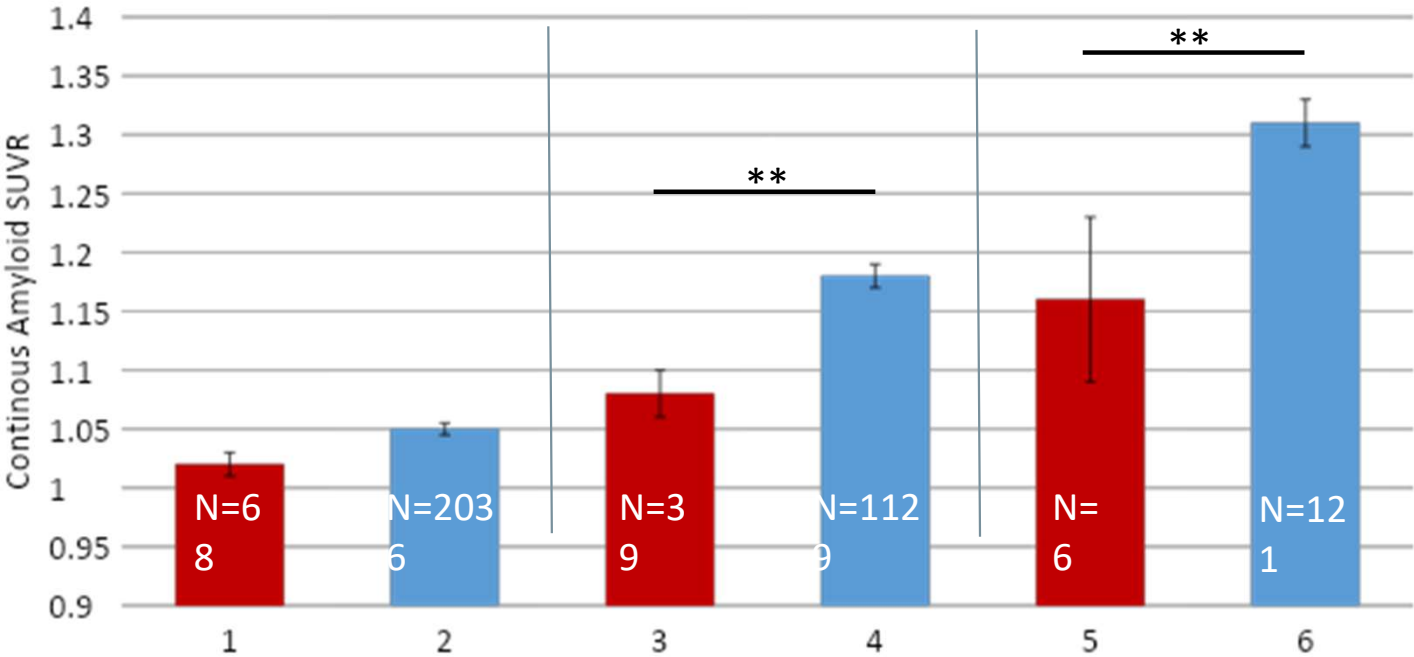
Increased cardiovascular burden in Black Americans...

→ Issues with amyloid-related imaging abnormalities (ARIA)?

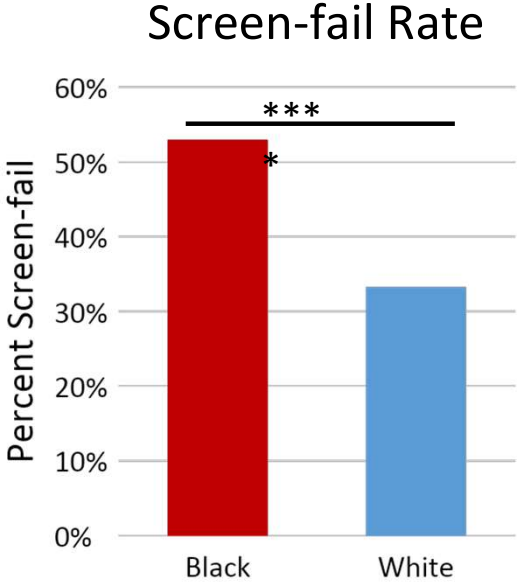
→ Are anti-amyloid drugs safe for Black Americans?

	Amyloid in older Black adults
Gu et al. 2015	No difference (PET)
Gottesman et al. 2016	Higher (PET)
Howell et al. 2017	No difference (CSF)
Garrett et al. 2019	No difference (CSF)
Morris et al. 2019	No difference (CSF)
Meeker et al. 2020	No difference (PET)
Kumar et al. 2020	No difference (CSF)
Brickman et al. 2021	No difference (PET, plasma)
Deters et al. 2021	Lower (PET)
Lao et al. 2022	No difference (PET)
Schindler et al. 2022	Lower (PET)
Ramanan et al. 2023	No difference (plasma)

Lower amyloid PET SUVR in Black E4 carriers



Higher screen-fail rate in Black participants



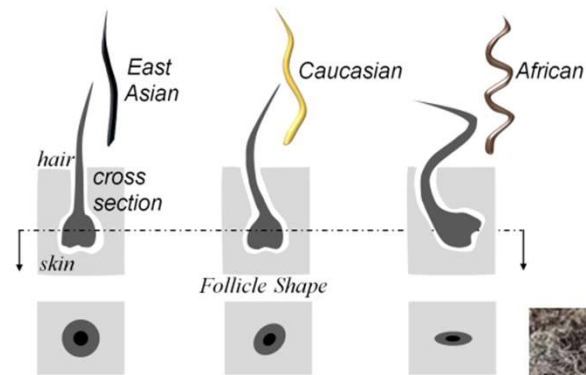
Racism in neuroscience tools and techniques

JA Ricard, TC Parker, et al. *Nature Neuroscience*. 2022



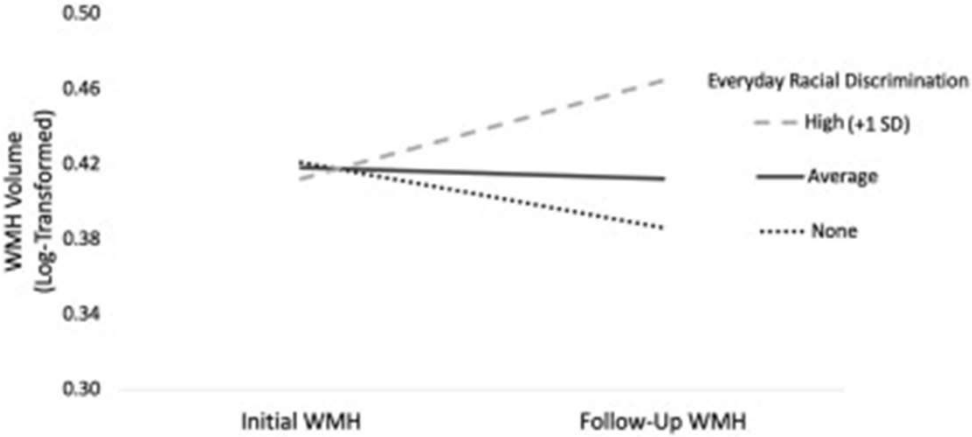
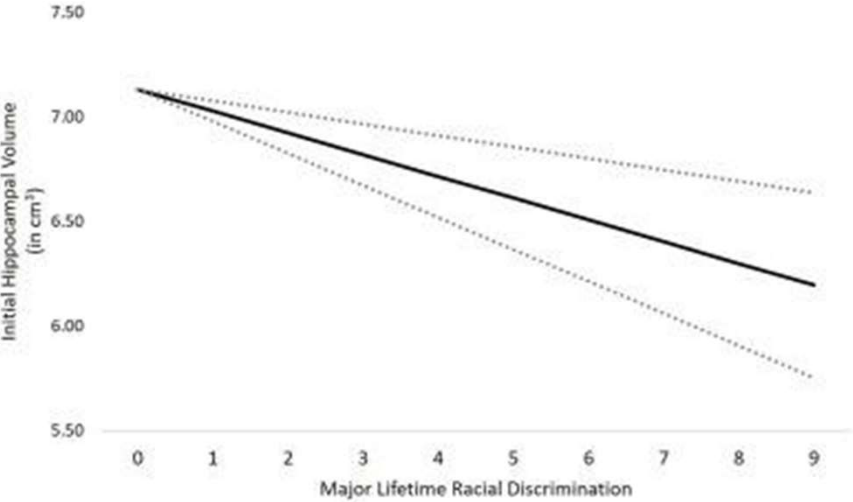
Hair styles

- Coarse and curly hair
- Afro-textured hair
- Dreadlocks
- Braids
- Sew-ins (metal tracks)
- Hair extensions (metal tracks)



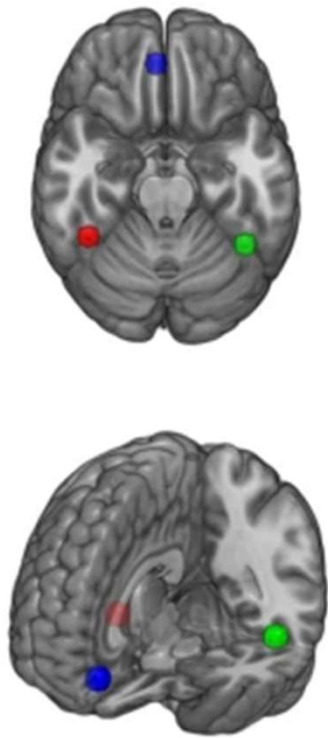
The Sevo clip
Etienne et al., *bioRxiv* 2020

Discrimination and MRI measures of brain aging

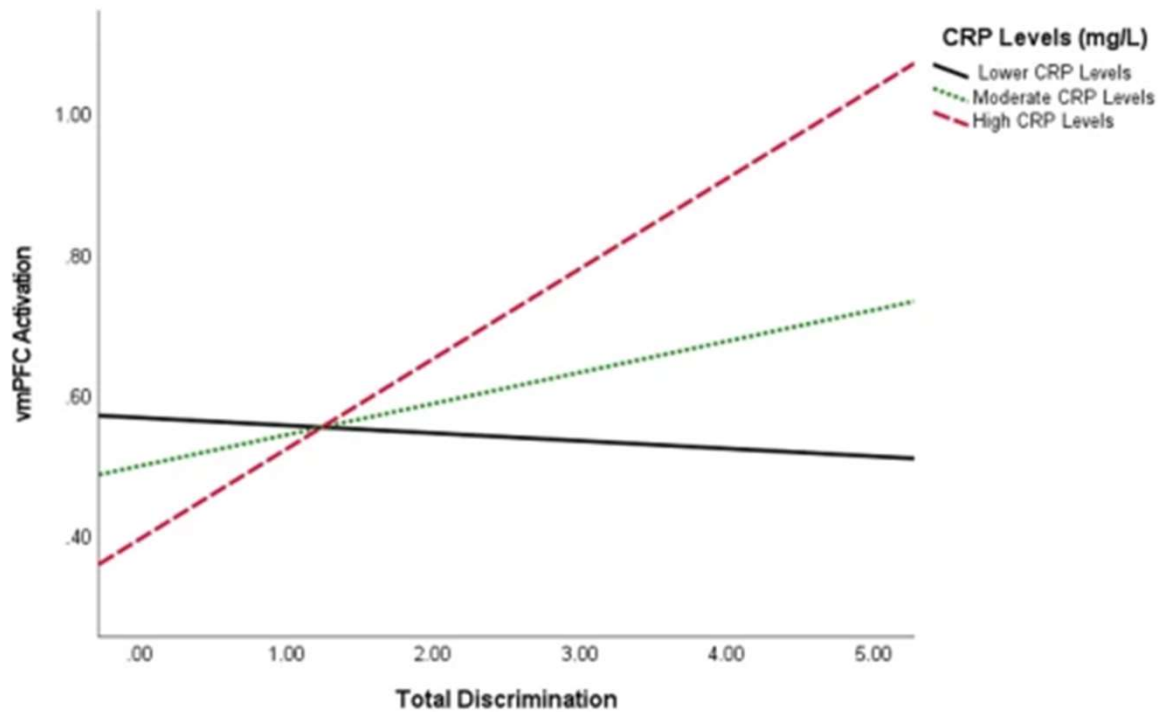


Zahodne et al., *Social Science & Medicine*. 2022

Biological mechanisms for how discrimination can increase vulnerability to brain health problems



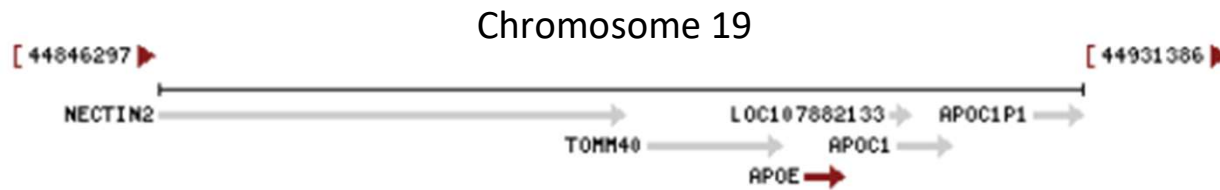
(a)



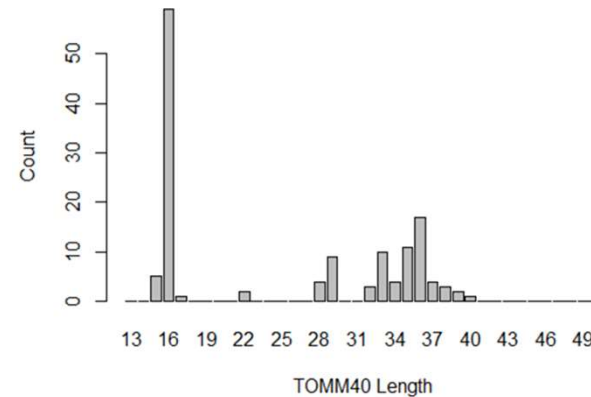
(b)

Elbasheir et al. (2024)
Neuropsychopharm.

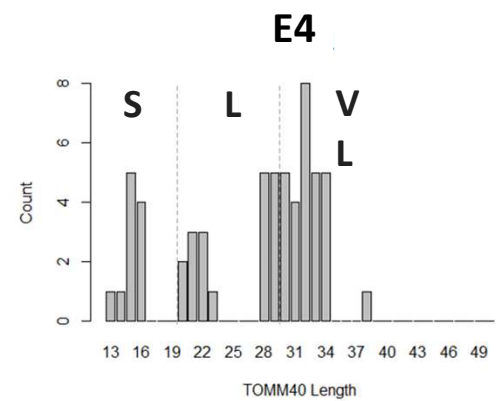
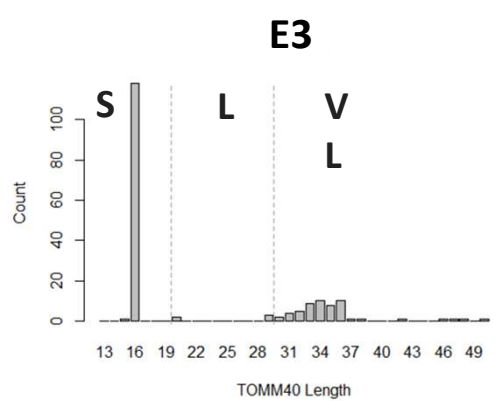
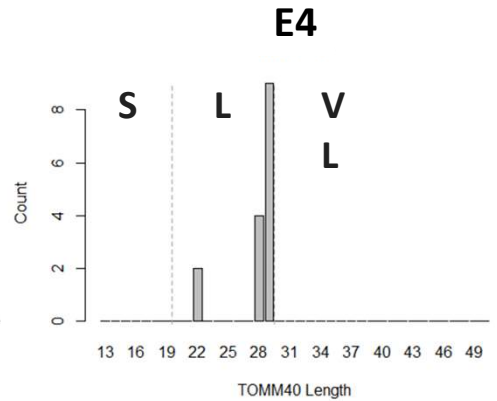
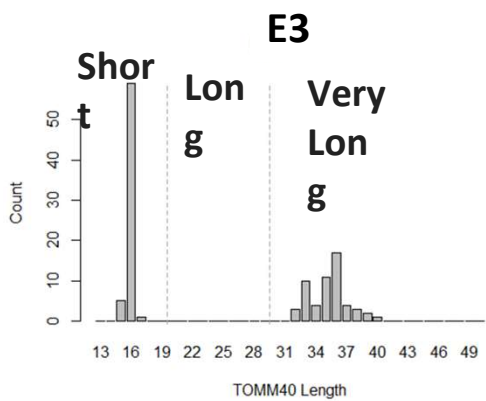
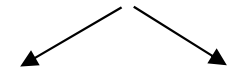
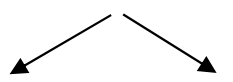
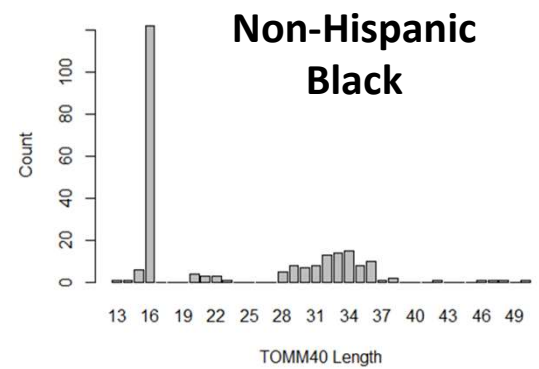
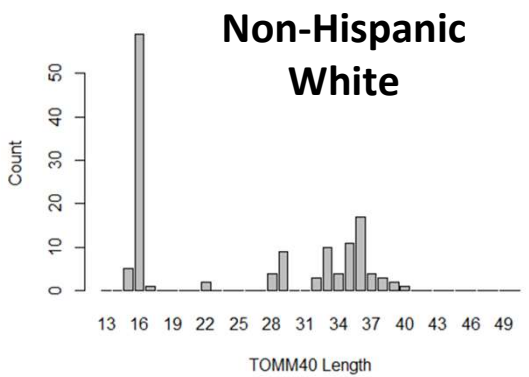
TOMM40 (translocase of outer mitochondrial membrane 40 homologue gene)



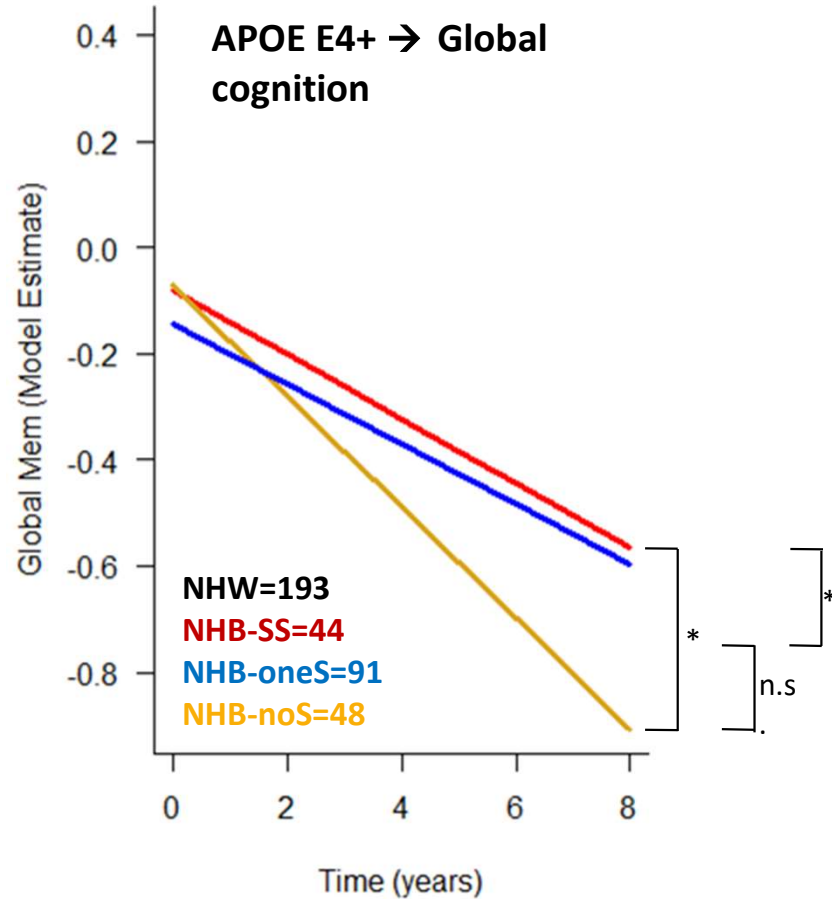
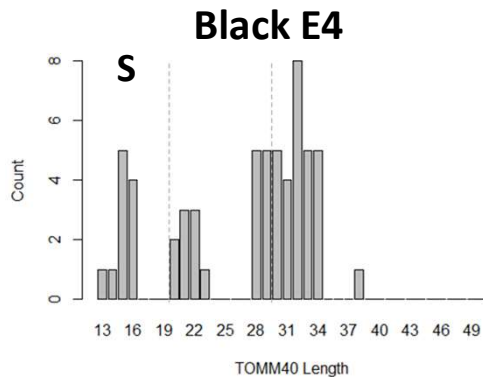
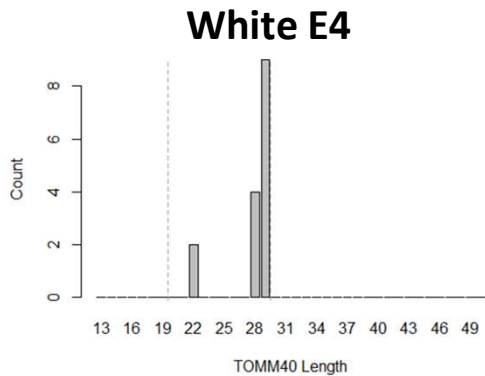
- The intronic poly-T repeat, rs10524523 ('523) associated with increased cognitive impairment and AD risk.
- In linkage disequilibrium (non-random association of alleles) with APOE.



APOE-TOMM40 '523 haplotypes



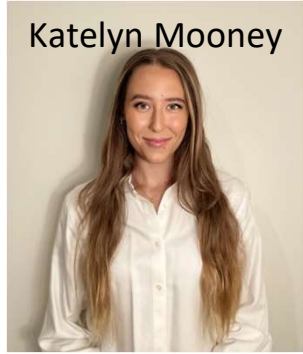
Is TOMM40 associated with cognitive decline in e4+?



S/S
 S/L
 S/VL > oneS
 L/L
 L/VL > noS
 VL/VL

Black E4 carriers with the TOMM40 Short allele present a potentially protected group against the detriments of E4.

Black E4 carriers with '523-S have better white matter integrity (dMRI)



White Matter Microstructure

Free-Water

(Random extracellular fluid movement in a voxel)

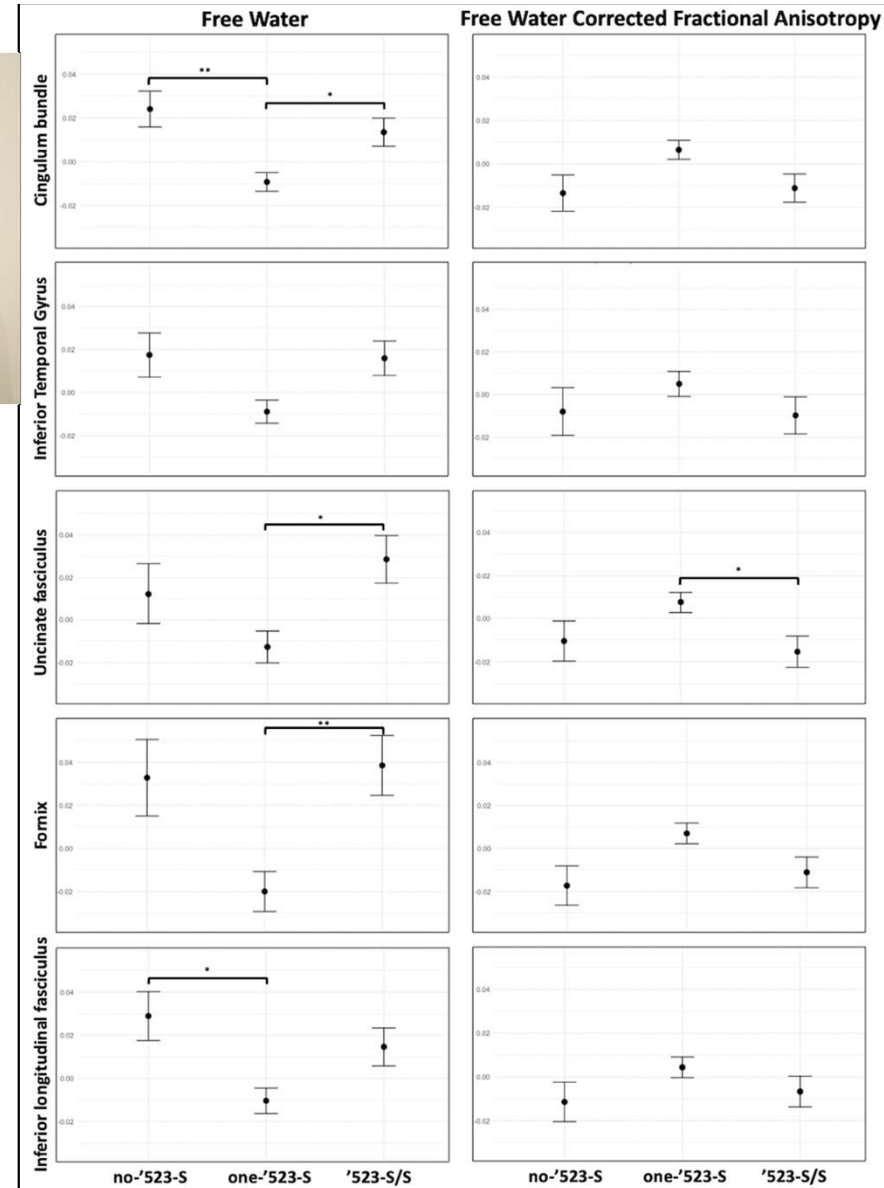
High Values = Abnormal

Free-Water Corrected Fractional Anisotropy

(Directional intracellular fluid movement with extracellular fluid removed)

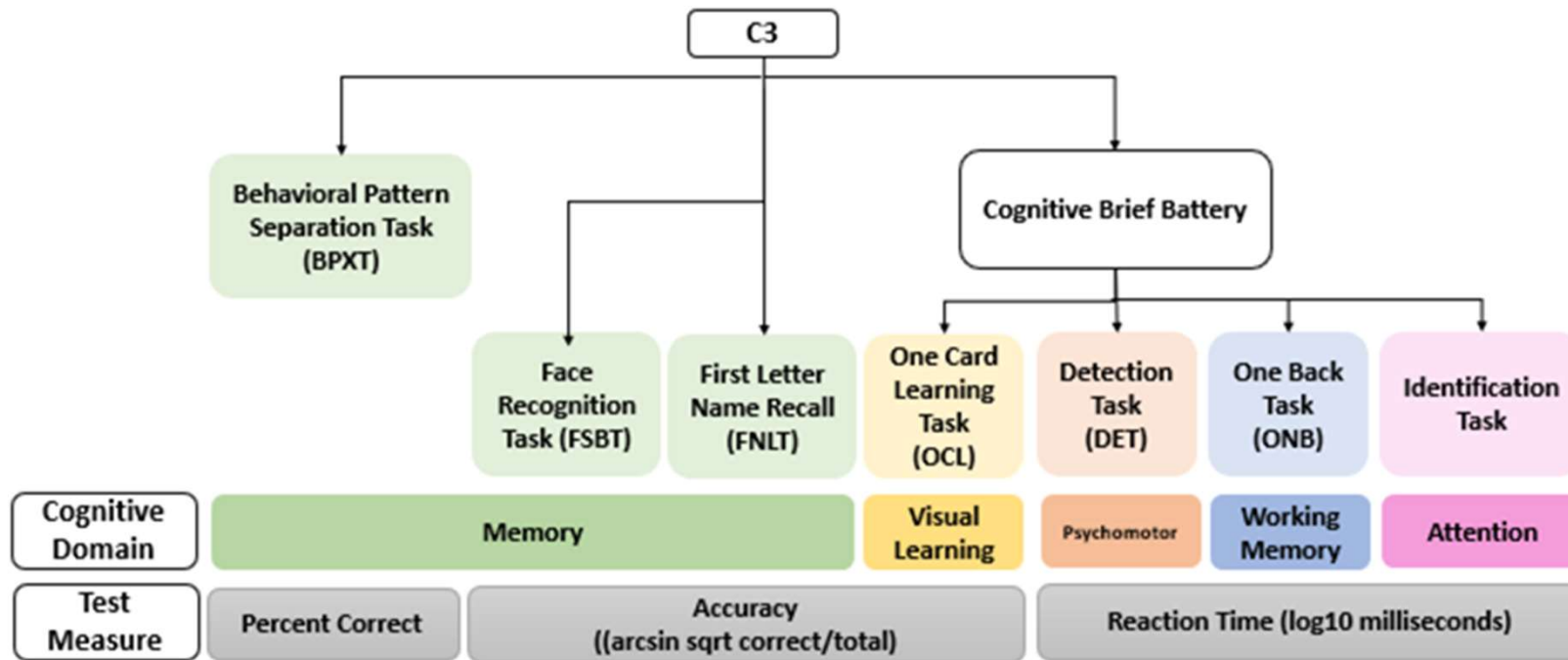
Low Values = Abnormal

Mooney et al. *In Prep*



Cogstate Computerized Cognitive Composite (C3) battery

accuracy → higher = better
 response time → higher = worse



Is C3 performance different across ethnic/racial groups?



Joy Stradford



Xinran Wang

Family history and amyloid



Phelan Glenn

	Model 1: amyloid ~ family history + demographics			Model 2: amyloid ~ family history + demographics + E4			
	β	SE	P	B	SE	P	
Non-Hispanic Black	Family History	0.032	0.23	0.13	0.031	0.240	0.144
	Age	0.033	0.22	0.11	0.004	0.002	0.046*
	Sex (Female)	-0.011	0.024	0.65	-0.003	0.023	0.882
	E4e4+	-	-	-	0.077	0.023	0.001**
Non-Hispanic White	Family History	0.028	0.006	<2e-05***	0.009	0.006	0.135
	Age	0.006	0.001	<2e-16***	0.008	0.001	<2e-16***
	Sex (Female)	0.011	0.006	0.096	0.013	0.006	0.032*
	E4e4+	-	-	-	0.154	0.006	<2e-16***
Latino/a	Family History	0.020	0.038	0.603	0.002	0.037	0.962
	Age	0.009	0.004	0.036*	0.007	0.004	0.066
	Sex (Female)	-0.007	0.038	0.845	0.031	0.038	0.412
	E4e4+	-	-	-	0.140	0.041	0.001**

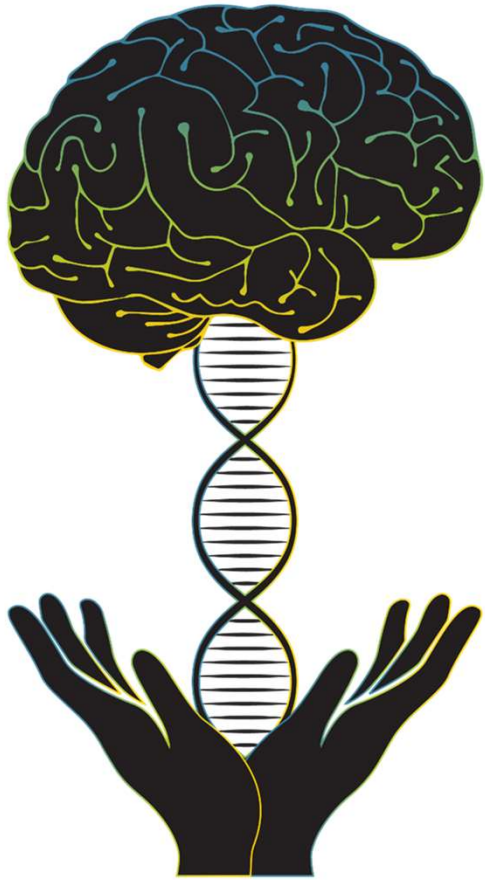
Barriers to PET scan in older Black and Latinos

Phase Two: Example Quotes Denoting Differences within each Overarching Theme for Older Black and Latino Adults.


	Older Black Adults	Older Latinos
Theme One: Knowledge Limitations	“No, because I don’t know if I wanna know. You know, if I’m not having any problems, and at my age, I don’t think I wanna know, uh, that something is getting ready to happen, and you can’t do nothing about it. Like, you know, I wouldn’t wanna have brain surgery at my age, so, uh—”	“Well, I’m under the impression that it’s a whole-body scan. Um, but nobody—I never really questioned it. I have, um, a relative that has cancer.”
Theme Two: Requirements for Consent	“I would have to know, uh, what—I would have to know more about what a PET scan is, and-and I would have to know what-what it does. And I would have to know what, um, what was the out—what would be the outcome, what are the risks, are there any risks in terms of your health, um, regarding taking the, um, brain PET scan. Um, and what are your goals, or why are you taking it. I mean, why would you be taking it. I would like to know that.”	“Well, not only—you know, I would like to know the immediate, you know, risk factors in terms of if it’s found- what contrast, if it’s the same kind of contrast that’s used with a CT scan. And, you know, um, I would wanna know if, you know, in the—if people, who have had brain PET scans, have had any ill after it. You know? Any bad side effects after completion of the-the brain scan.”
Theme Three: Motivators for Participation	“Yeah. I’d like to know. Um, there are things that I—that bothers me that I would like to know that once that PET scan is done that it would, uh, help me better understand my own brain. Or if there was something that might be lurkin’ somewhere in the brain that might be going to happen to me in the future, uh, I would like to, say, get ahead of it possibly with this scan.”	“I don’t—no, I don’t need-I-I don’t need anything in return. I mean, just as a study of, you know, to help, uh, the future.”
Theme Four: Social Networks	“I would, hopefully, be able to speak to somebody’s in the medical field, one, or certainly if there’s someone who’s also had a—who have had this, um, PET, uh, uh, PET scan, uh, what did they think about it, um. And I guess I would like to—I would have to do some research on my own. I would like to kn—I would like to know more about the PET scan itself.”	“I’m always eager to participate in a study that I know is not going to hurt me, you know, and only because my mother had Alzheimer’s, you know, she’s about this age, at my age now. And it’s just something I want to keep up with, and if I could do it for free, that would be great because you know how Medicare is nowadays.”



Glover et al. (2023) *J Alz Dis*



Thank you!

Kacie Deters, PhD
ACT Research Symposium 2024
Assistant Professor
UCLA | Integrative Biology & Physiology
kdeters@g.ucla.edu
 @KcD_PhD

UCLA College
Life Sciences

 **UCLA**
Integrative Biology
& Physiology



Mental Health and Academic Warriors

