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RCCN Workshop: Innovative Perspectives to Advance AD/ADRD Multidisciplinary Research

Discussion Topic I: Reimagining AD/ADRD risk and resilience

The need to identify risk factors for high-risk groups

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Acknowledgements

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Participants of the RADC Cohort Studies and Staff of the RADC

SOL Study of Latinos Hispanic Community Health Study

U.S. Department of Health and Human Services
National Institutes of Health

Lead Institute

National Heart Lung and Blood Institute

Six other Institutes contributed

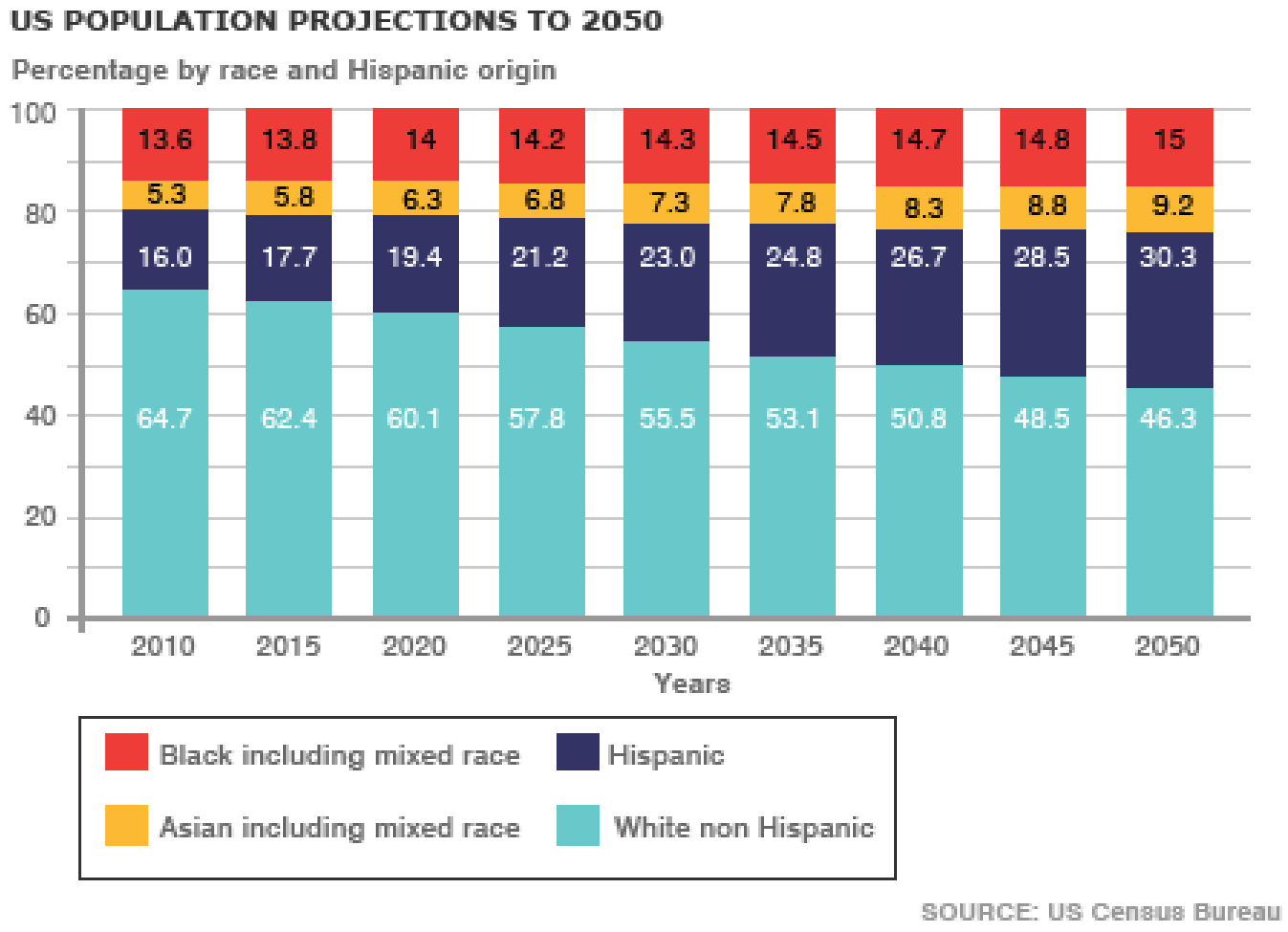
- National Institute of Diabetes and Digestive and Kidney Diseases
- National Institute of Neurological Disorders and Stroke
- National Institute of Deafness and Other Communication Disorders
- National Institute of Dental and Craniofacial Research
- National Institute of Minority Health and Health Disparities
- National Institute of Health-Office of Dietary Supplements

Outline / Objectives

1. Define the need
2. Describe a multi-disciplinary framework to identifying risk factors
3. Discuss gaps and opportunities for research in high-risk groups

No conflicts of interest

THE NEED: Representativeness & Generalizability



SOURCE: US Census Bureau

THE NEED: Population Differences

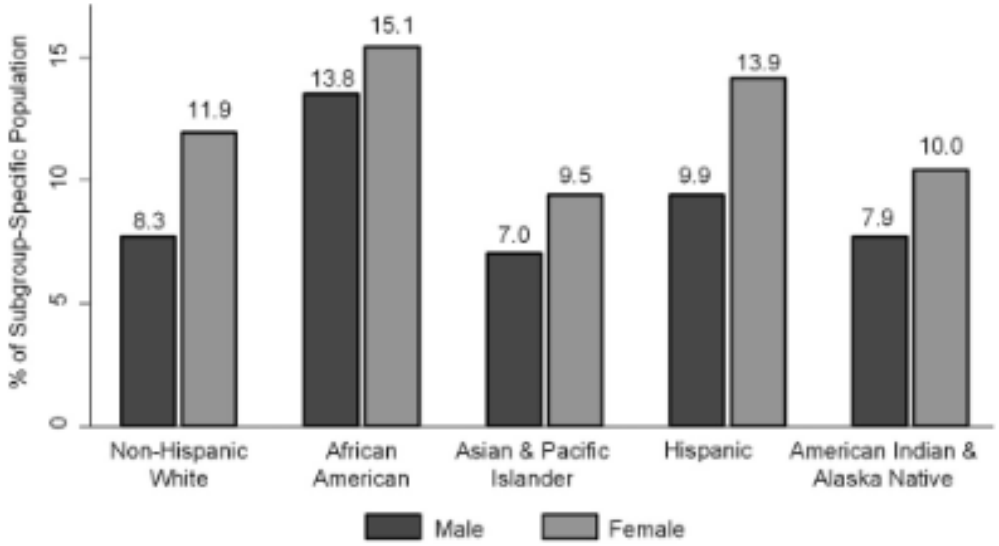
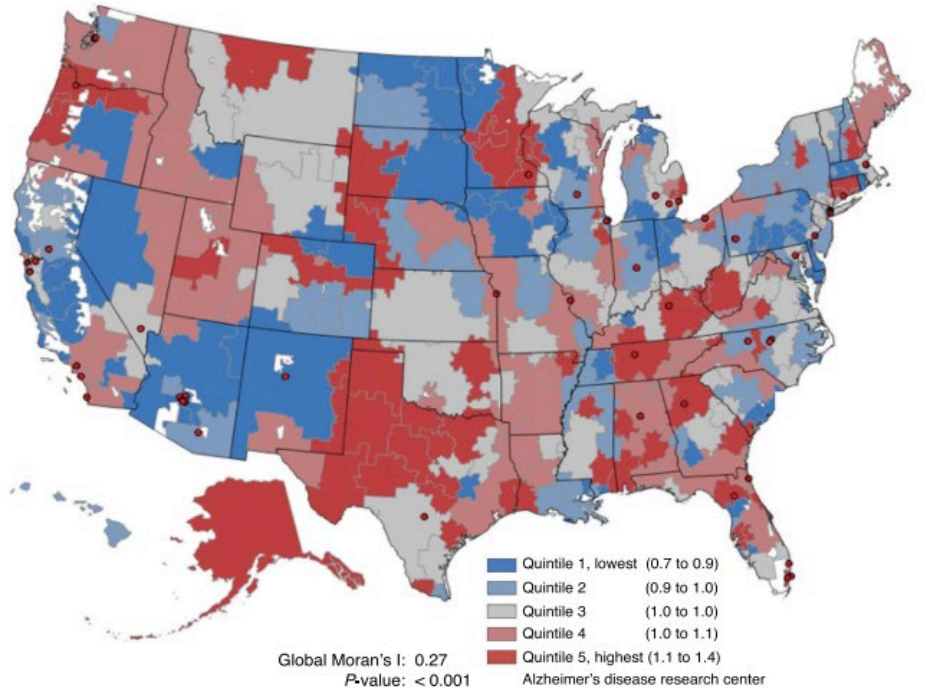


Fig. 2. Estimated prevalence of Alzheimer's disease and related dementias in the US Population aged ≥65 years, by sex and race and ethnicity; United States, 2014.

Matthews et al. Alzheimer's Dement, 2019;15:17-24.



Bynum et al. Alzheimer's Dement, 2024. 20:6755-6764

THE NEED: Disease Heterogeneity

- Traditional risk factors for AD/ADRD do not fully account for differences between Latino and non-Latino White adults
  - Disproportionate cardiovascular disease (CVD) risk factors[1] do not fully account for the difference[2,3]
  - APOE genotypes have not shown the same pattern of risk (e4) or protection (e2)[4]
  - APOE not related to cognitive decline[5] or amyloid load[6] in the same manner

[1]Pirzada et al. Curr Atheroscler Rep, 2023. 25(11):785-793; [2]Haan et al. JAGS, 2003. 51(2):169-177. [3]O'Bryant et al. Alzheimers Demen, 2013. 9(6):622-631. [4]Xiao et al. Alzheimers Demen, 2023. 19(11):5086-5094; [5]Chan et al. JINS, 2023. 29(2):126-135. [6]Duara et al. NeuroImage Clin, 2019. 22:101800.

IDENTIFYING RISK FACTORS using a Contextual Framework

a. ACCULTURATION

Adapting to a new environment and potentially adopting its values

ACCULTURATION IN CONTEXT

b. Exchange emerging from & reinforced by broader determinants

measured by **traditional acculturation factors** and
broader socioenvironmental contextual-related factors
including but not limited to:

Traditional Acculturation:	Socioenvironmental:	
	Individual-Level	*Neighborhood-level*
Language Preferences	Unfair Treatment	Crime, Access to
Years lived in the US	Social Isolation	Healthy/Unhealthy
Social Preferences	Family Stress	Food & Recreation

Lamar, Barnes & Marquez, 2023. In J Angel, F Andrade, S Mejia Arango & F Riosmena (Eds) *Aging in the Americas*. Switzerland: Springer Cham

Acculturation in Context: RADC Longitudinal Cohort

Rush Alzheimer's Disease Center

	N=199
Key Demographics	
Age (years)	69.7 (6.6)
Sex (male:female ratio)	38:161
Education (years)	10.8 (4.7)
Acculturation in Context	
Tested in Spanish (n,%)	140, 70.3
Nativity status (non-US; n,%)	161, 80.9
Parents' Nativity status (both non-US; n,%)	131, 92.9
Short Acculturation Scale for Hispanics (SASH)	2.1 (.76)
SASH language	1.9 (1.0)
SASH social	2.2 (.59)
The Sabogal Familism Score	20.9 (2.8)
Williams Everyday Discrimination Scale score	1.7 (2.0)
Social Network size	6.6 (5.1)
Jong-Gierveld Loneliness (Social Isolation) score	2.5 (.70)

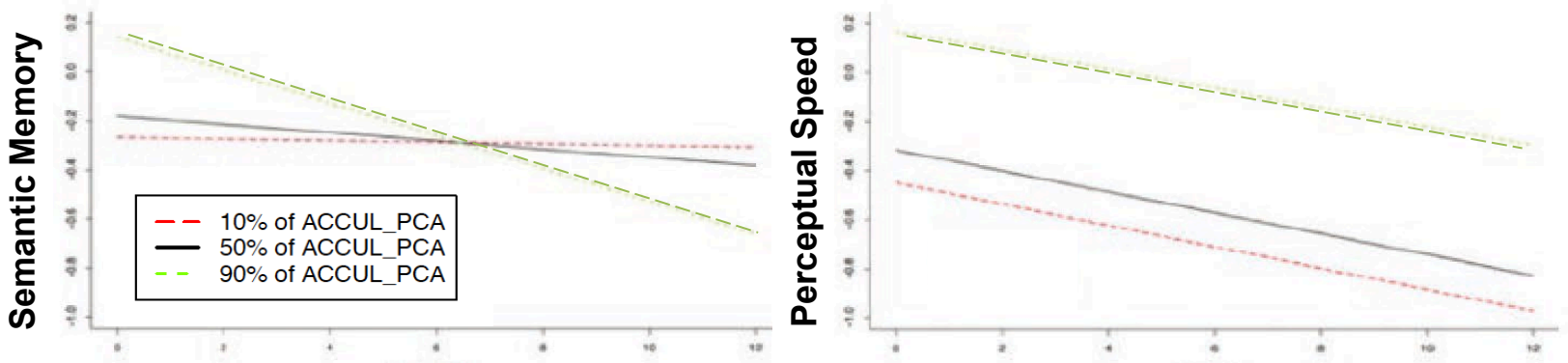
	FACTOR 1: Acculturation	FACTOR 2: SocioEnvirons	FACTOR 3: Familism
Tested in Spanish	0.894	–0.016	–0.002
Nativity status (non-US)	0.802	–0.127	–0.195
Parents' nativity status (both non-US)	0.563	–0.315	–0.356
SASH social	–0.695	–0.009	–0.070
SASH language	–0.953	–0.007	–0.006
SASH total	–0.967	–0.008	–0.025
Self-report of Unfair Treatment	0.004	0.665	0.101
Social network	0.011	–0.664	0.437
Social isolation	0.395	0.711	0.136
Familism	0.264	–0.014	0.839
Variance explained	43.136	15.083	10.957

Notes: SASH = Short Acculturation Scale for Hispanics. Factor loadings are unrotated with bold values representing the primary loading for each study variable.

Lamar et al. J Gerontol B Psychol Sci Soc Sci, 2021. 76:e129-e139.

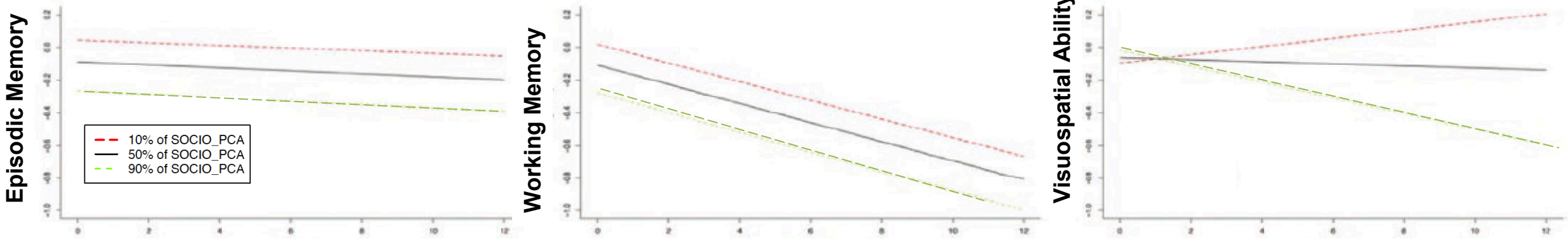
Acculturation in Context & Cognition: RADC Longitudinal Cohort

A



X-Axis: **Years in the study** (0 to 12 increments of 2)

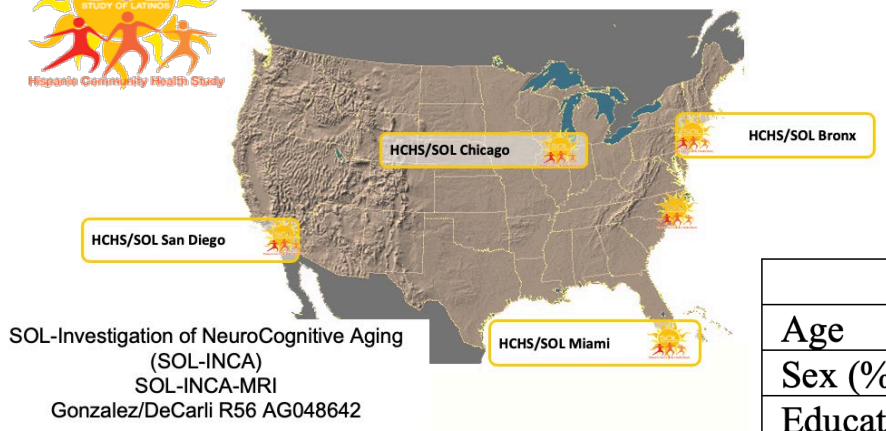
B



X-Axis: **Years in the study** (0 to 12 increments of 2)

Lamar et al. J Gerontol B Psychol Sci Soc Sci, 2021. 76:e129-e139.

Acculturation in Context: HCHS/SOL Visit 1



SOL-Investigation of NeuroCognitive Aging (SOL-INCA)
SOL-INCA-MRI
Gonzalez/DeCarli R56 AG048642

	n=8,476
Age	56.39 (9.91)
Sex (%, Female)	54.26 (0.71)
Education (%)	
<High School	39.76 (0.94)
High School	21.69 (0.76)
>High School	38.55 (0.97)
Background (%)	
Mexican	30.94 (1.68)
Puerto Rican	18.14 (1.05)
Cuban	26.98 (2.02)
Dominican	9.64 (0.77)
Central American	6.63 (0.44)
South American	5.41 (0.35)
Other/>1 background	2.26 (0.33)

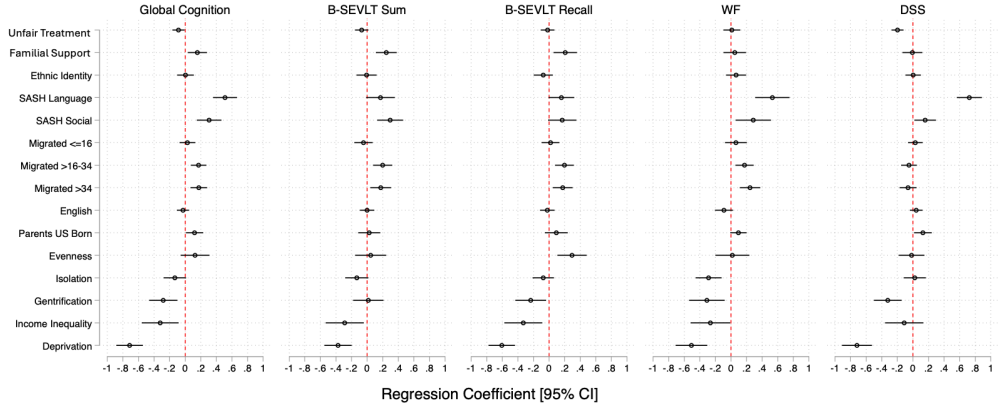
NOTE: %=percentage (standard error) for all variables but age which is mean (standard deviation)

		n=8,476
Acculturation-related	Language preference (% Spanish)	85.86 (0.87)
	SASH Language sub-score	1.75 (1.20)
	SASH Social sub-score	2.14 (0.74)
	Nativity/Age at Migration (%)	
	US Born	9.22 (0.60)
	<=16 years of age	10.89 (0.66)
	17-34 years of age	36.85 (0.94)
	35+ years of age	43.03 (1.39)
	Parental Nativity (% US born)	4.81 (0.38)
Individual-level	Ethnic Identity Index	3.22 (0.69)
	Unfair Treatment Score	3.51 (1.78)
	Familial Structural Support	2.12 (0.95)
Neighborhood-level	Census Level Evenness	0.39 (0.13)
	Census Level Isolation	0.77 (0.20)
	Gentrification	0.00 (0.02)
	Income Inequality	0.42 (0.07)
	Deprivation	-0.01 (0.13)

NOTE: %=percentage (standard error) for categorical variables, means (standard deviation) for continuous variables.
SASH = Short Acculturation Scale for Hispanics; US=50 United States and the District of Columbia; w/o=without; w/=with.

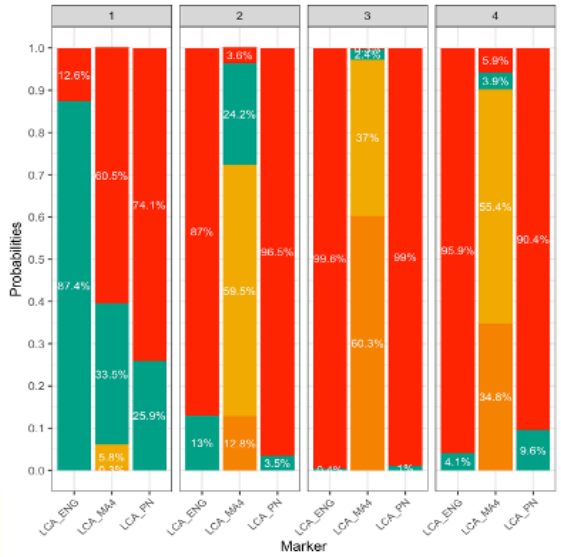
Lamar et al. under review.

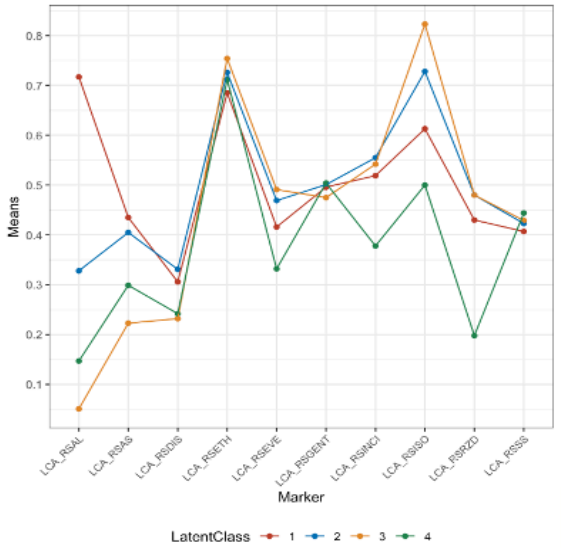
Acculturation in Context & Cognition: HCHS/SOL Visit 1



Note: SASH=Short Acculturation Scale for Hispanics. Regression coefficients for the acculturation in context variables represented in the forest plots are based on min-max rescaled variables (represent change in outcomes as a result of change from min to max in the exposure variable) except for categorical measures.

Lamar et al revise and resubmit





Lamar et al in progress

Latent Profiles

Class 1 – high acculturation lower neighborhood enclave

Class 2 – middle acculturation high neighborhood enclave

Class 3 – low acculturation high neighborhood enclave

Class 4 – low acculturation low neighborhood health

HIGH RISK GROUPS: Gaps & Opportunities

ACCULTURATION IN CONTEXT

Exchange emerging from & reinforced by broader determinants

measured by **traditional acculturation factors** and **broader socioenvironmental contextual-related factors** including but not limited to:

Traditional Acculturation:	Socioenvironmental:	
	Individual-Level	*Neighborhood-level*
Language Preferences	Unfair Treatment	Crime, Access to
Years lived in the US	Social Isolation	Healthy/Unhealthy
Social Preferences	Family Stress	Food & Recreation

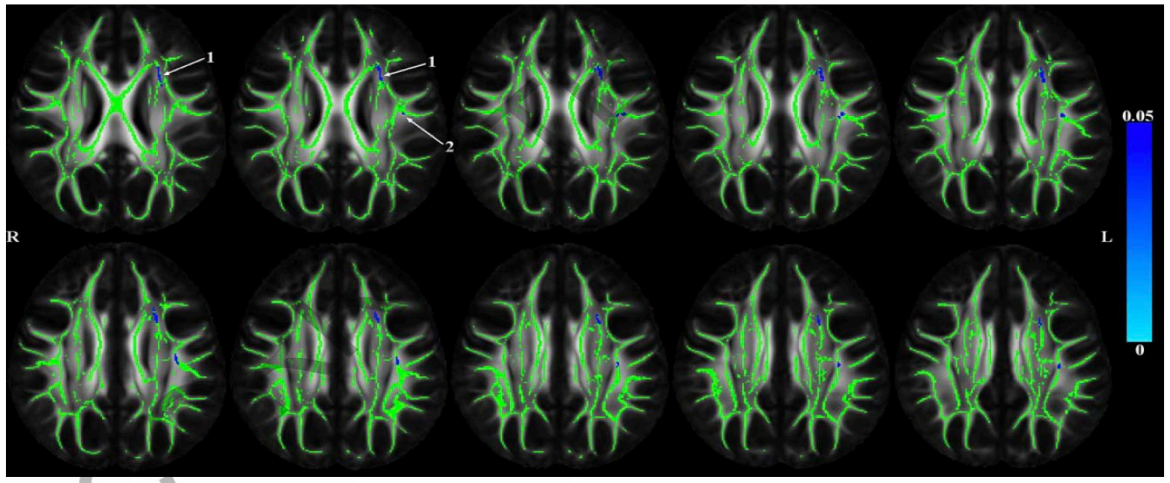
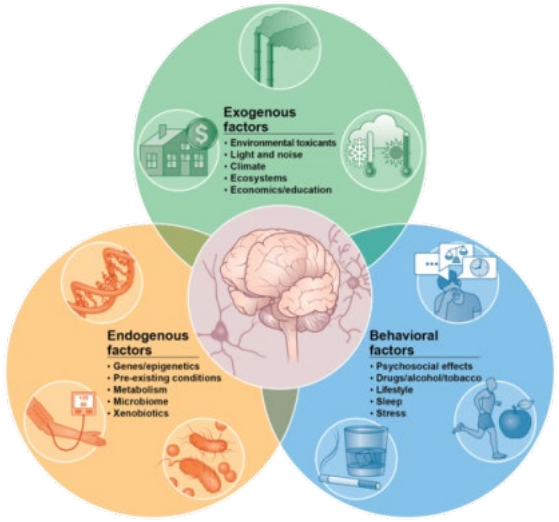


Fig. 1. *p*-value maps showing (in blue) white matter regions in which higher contextually-related socioenvironmental composite score is associated with lower DTI-derived fractional anisotropy adjusted for age, sex, education, scanner, and white matter hyperintensities (WMHs; voxelwise and total volumes normalized by intracranial volume). Results were TFCE and FWE corrected and represented $p < 0.05$. The arrows point to two significant clusters of probable white matter connections associated with the socioenvironmental composite.

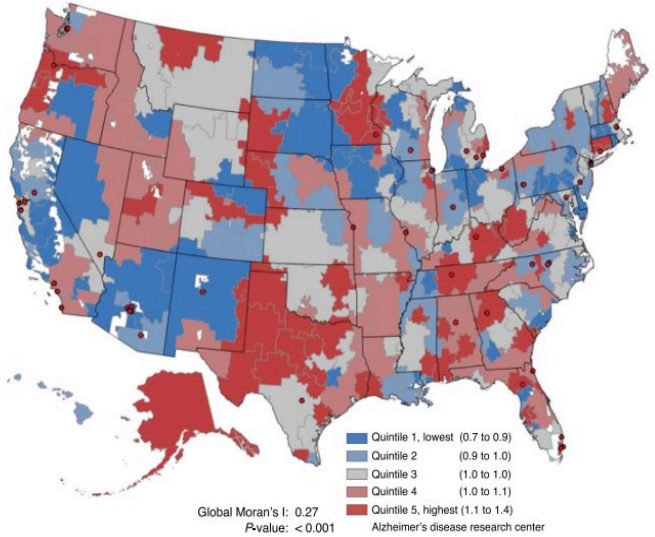
Fleischman et al. J Alz Dis, 2023. 95(4):1585-1595.



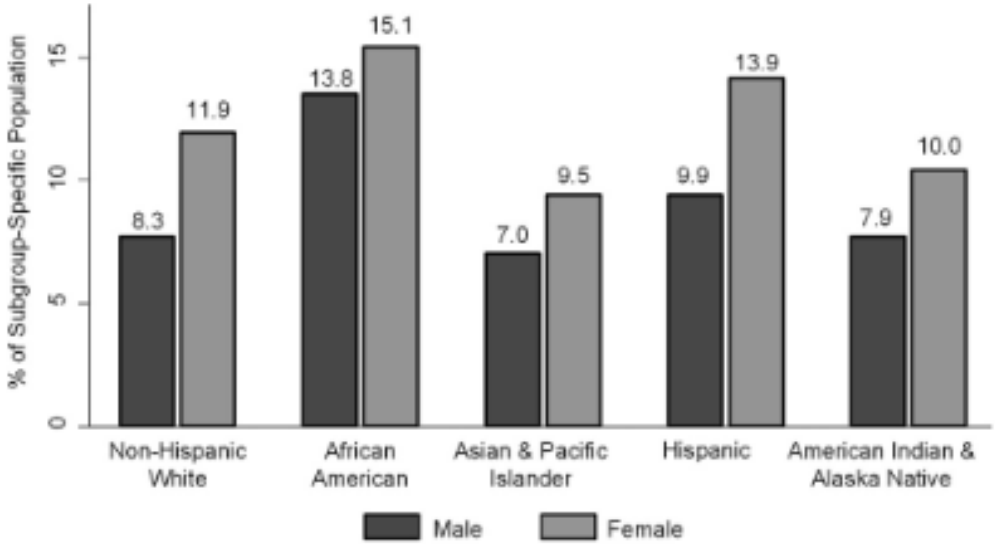
NINDS Neural Exposome

- Ultimately, the framework is flexible

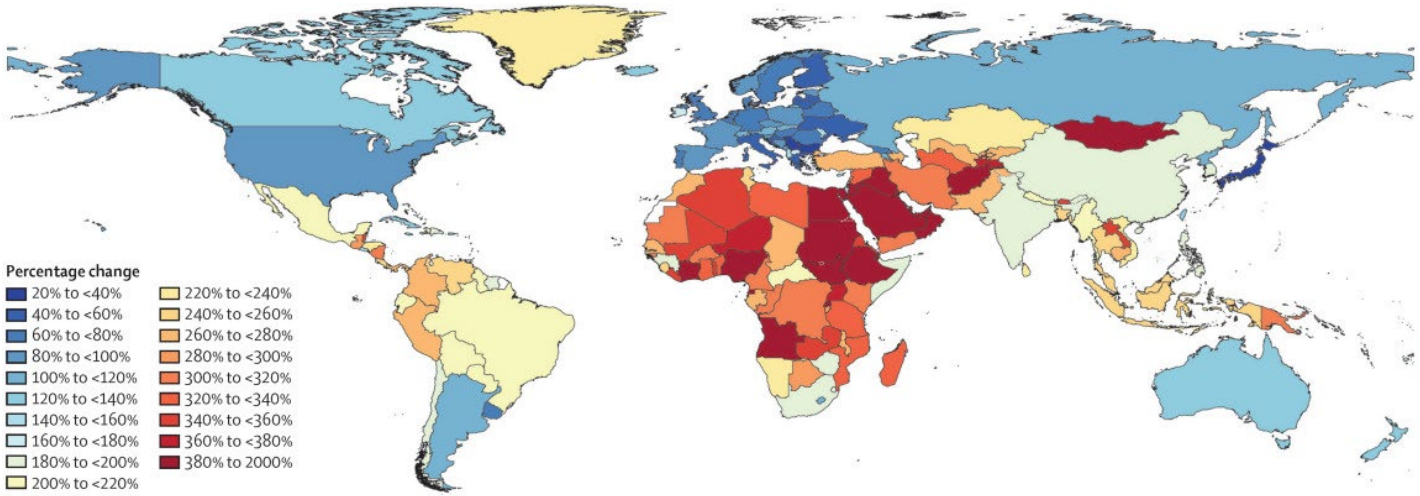
HIGH RISK GROUPS: Gaps & Opportunities



Bynum et al. Alzheimer's Dement, 2024. 20:6755-6764



Matthews et al. Alzheimer's Dement, 2019;15:17-24.



GBD 2019 Dementia Forecasting Collaborators The Lancet, 2022;7(2):E105-E125.

THANK YOU! ¡Y GRACIAS...

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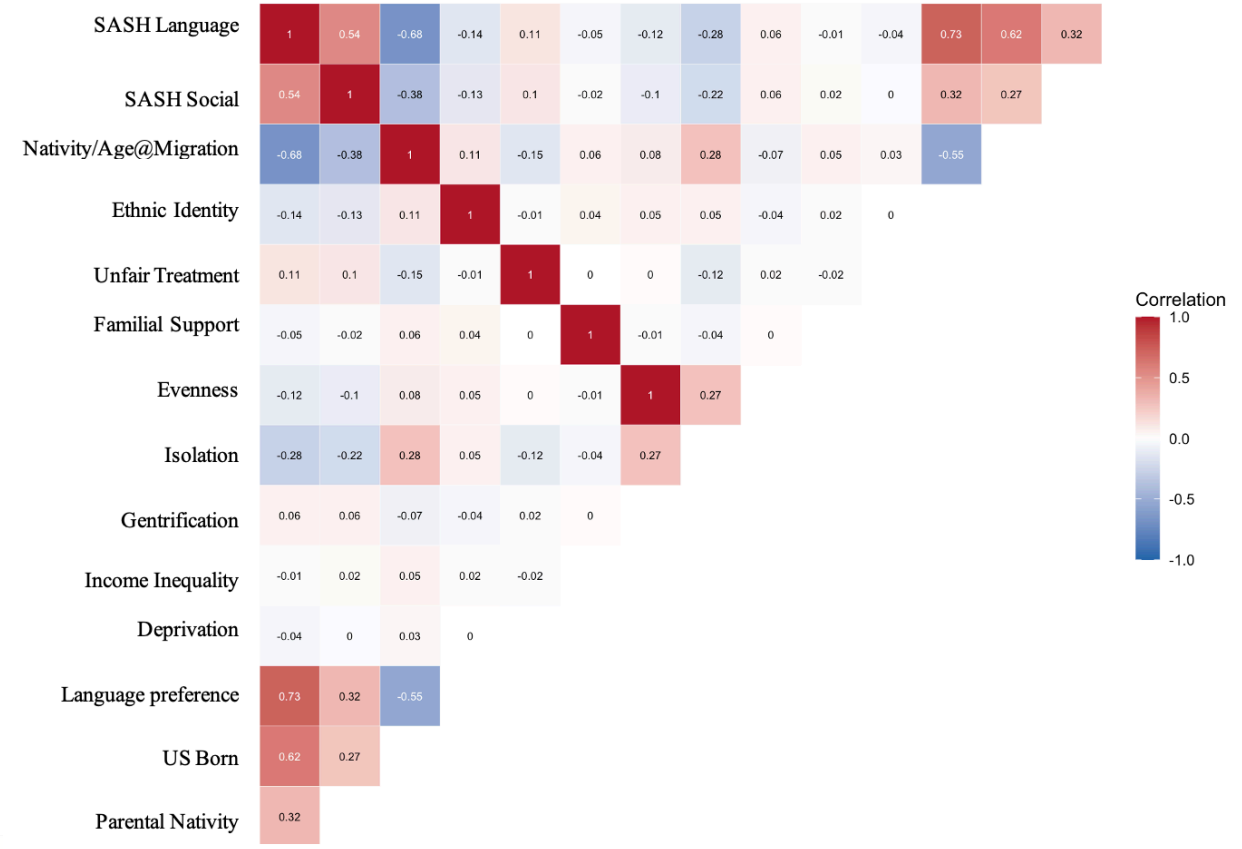
EXTRA SLIDES

Acculturation in Context: HCHS/SOL Visit 1



Lamar et al. under review.

Acculturation in Context: Next Steps @ HCHS/SOL

Latent Profiles

Class 1 – high acculturation lower neighborhood enclave

Class 2 – middle acculturation high neighborhood enclave

Class 3 – low acculturation high neighborhood enclave

Class 4 – low acculturation low neighborhood health

	Weighted					
	4-Class					
	C1	C2	C3	C4	Total	Test
N	242 (11.0%)	358 (16.7%)	1,403 (63.7%)	161 (8.6%)	2,164 (100.0%)	
Age at MRI scan (yrs)	63.867 (6.471)	67.605 (7.881)	68.451 (7.907)	68.758 (7.154)	67.832 (7.827)	<0.001
Sex: Male						
Female	143 (47.2%)	201 (45.5%)	1,016 (60.2%)	120 (67.5%)	1,480 (56.9%)	<0.001
Male	99 (52.8%)	157 (54.5%)	387 (39.8%)	41 (32.5%)	684 (43.1%)	
Education						
Less than HS	63 (24.6%)	103 (27.2%)	630 (41.2%)	52 (32.3%)	848 (36.3%)	<0.001
HS or Equivalent	53 (17.3%)	85 (23.6%)	296 (19.0%)	27 (11.6%)	461 (19.0%)	
More than HS	126 (58.1%)	170 (49.2%)	477 (39.8%)	82 (56.1%)	855 (44.8%)	
Latino Heritage						
Dominican	9 (2.5%)	30 (7.0%)	140 (10.4%)	5 (3.4%)	184 (8.3%)	<0.001
CA	6 (2.3%)	40 (8.6%)	199 (8.0%)	9 (4.3%)	254 (7.2%)	
Cuban	9 (7.4%)	22 (10.3%)	275 (39.3%)	1 (0.7%)	307 (27.7%)	
Mexican	62 (27.9%)	131 (27.0%)	530 (25.7%)	125 (74.9%)	848 (30.4%)	
PR	145 (56.2%)	100 (35.7%)	92 (6.7%)	7 (2.9%)	344 (16.7%)	
SA	3 (0.7%)	24 (5.7%)	144 (6.9%)	12 (10.7%)	183 (6.3%)	
Other	8 (3.0%)	11 (5.8%)	23 (2.9%)	2 (3.1%)	44 (3.4%)	

Lamar et al. in progress.

Acculturation in Context and SOL-INCA-MRI

Latent Profiles

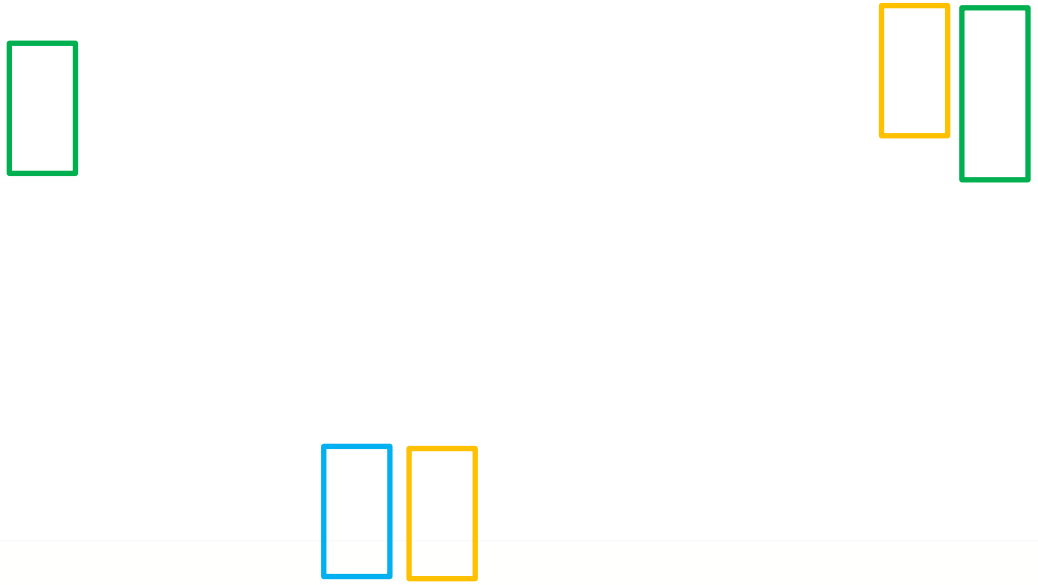
Class 1* – high acculturation
lower neighborhood enclave

Class 2 – middle acculturation
high neighborhood enclave

Class 3 – low acculturation
high neighborhood enclave

Class 4 – low acculturation
low neighborhood health

*reference group



Lamar et al. in progress.

Acculturation in Context: RADC Geospatial Additions

Acculturation		
	Tested in Spanish	67.7%
	US born/nativity	23%
	One or both parents US born/nativity	9.5%
SASH	Total acculturation (hi'er=more)	2.2±1.0
SASH	Language-based acculturation	2.1±1.2
SASH	Social-based acculturation	2.3±0.7
Individual-level SocioEnvironmental		
	Discrimination (hi'er=worse)	1.8±2.1
	Social Network Size (hi'er=larger)	6.6±5.0
	Social Isolation (hi'er=worse)	2.6±7.0
Individual Culturally Relevant		
	Familism (hi'er=more)	20.5±3.0
	Familial expectations sub-score	8.5±1.1
	Family as referent	12.0±2.8
	Acculturation Stress (hi'er=more)	1.7±2.2
Neighborhood-level SocioEnvironmental		
	½ mile count of Crime (hi'er=worse)	6.2±4.0
	½ mile presence of a Supermarket	28%
	½ mile count of Grocery Stores	3.7±3.6
	½ mile count of Convenience Stores	1.5±1.7
	CT count* full-service Restaurants	1.5±1.5
	CT count* Fast Food Restaurants	0.4±0.5
	CT count of Bars *per 1000 people	0.3±0.5
	½ mile count of Fitness Facility	0.3±0.5
	Walkability Score (hi'er=better)	80.0±37.7
	Distance to Nearest Park (in meters)	516
	Amount of Park Access (in acres)	3.1±7.7

NOTE: SASH=Short Acculturation Scale for Hispanics

Latinos participating in
RADC cohort studies N=385

Acculturation in Context: Conclusions To Date

- Acculturation- and contextually-related factors
  - differentiated from each other
  - differentially contributed to level > change in cognitive[12]
  - differentially contributed to change > level of cardiovascular health[13]

- Negative socioenvironmental contextually-related experiences
  - related to white matter integrity
  - may be the most robust white matter associate of the framework[14]
- Left hemisphere predominance consistent with other studies[14]
  - favored for higher-order social processes
  - self-other distinctions and perceived discrimination

[12]Lamar et al. J Gerontol B Psychol Sci Soc Sci, 2021. 76:e129-e139; [13]Lamar et al. J Amer Heart Assoc, 2023. 12(6):e027620; [14]Fleischman et al. J Alz Dis, 2023. 95(4):1585-1595.

Acculturation in Context: HCHS/SOL Conclusions

- Contextually-related factors in a larger, more diverse population
  - differentiated from each other
  - differentially contributed to levels of cognitive
  - showed select dose-response relationships with cardiovascular health

- Individual-level socioenvironmental experiences
  - did not coalesce into a latent factor
  - differences in ages and geographies may have contributed

Lamar et al. under review.

THANK YOU! ¡Y GRACIAS...

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