



Neuropathological profiles of Latin Americans living in the US and their associations with life course risk factors for Alzheimer's disease and related dementias



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1 Background

- Worldwide prevalence and incidence rates of Alzheimer's disease and other forms of dementia are higher in Latin Americans, suggesting a significant global burden.
- Despite this, less is known about their underlying neuro-pathological profiles or what may be associated with these profiles during life.
- While results from primarily clinic-based studies are emerging, we outline neuropathological profiles and their associations with life course risk factors in a non-clinical, US community-based sample of Latin American decedents.

2 Participants and Methods

	Max N=75
Age at death, mean(SD), years	83.0±11.2
Female, %	70%
Education, mean(SD), years	13.9±5.3
US-born, %	33%
Diagnosis at death, %	
Normal cognition	24.7%
Mild cognitive impairment	16.4%
Dementia including Alzheimer's dementia	50.0%
Post-mortem interval, mean (SD), hours	10.0±6.1

Quantified Neuropathologies (also pictured in Figure 1)

- Alzheimer's disease (AD)
 - NIA-AA diagnosis - *high or intermediate*
 - Cortical β -amyloid - *counts*
 - Tau tangles - *counts*
- Cerebrovascular disease (CVD)
 - Atherosclerosis - *moderate to severe*
 - Arteriosclerosis - *moderate to severe*
 - Cerebral amyloid angiopathy or CAA - *moderate to severe*
 - Macro-infarcts - *one or more*
 - Micro-infarcts - *one or more*
- Other non-AD neurodegenerative-related
 - LATE-NC - *moderate to severe*
 - Hippocampal sclerosis - *presence*
 - Lewy bodies - *presence*

Life Course Risk Factors for AD/ADRD

- Demographic – age at death, sex, education
- Cardiovascular – diabetes (ever), blood pressure, BP (slopes)
- Exposomic – Census-level neighborhood vulnerability

Statistical Methods

- Regression models investigated associations of life course risk factors including demographic, cardiovascular, and exposomic

3 Results

Neuropathological Profiles Overall and Individually

Figure 1. Neuropathologies quantified and number of decedents represented

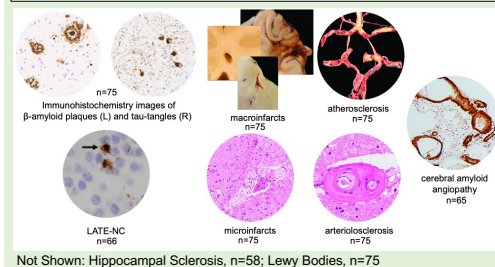
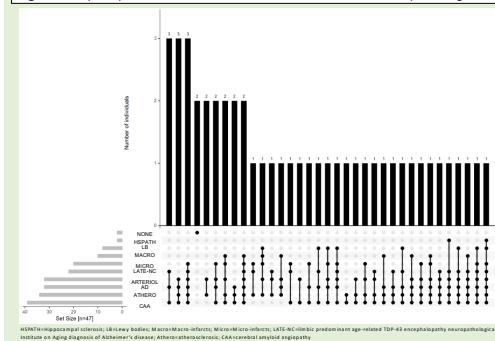


Figure 2. Upset plot of Latin American decedents with all neuropathologies



4 Conclusions

- Latin American decedents from non-clinical, US community-based cohorts exhibited a generally mixed neuropathological profile despite the majority having an intermediate/high likelihood of AD at autopsy
- As with other non Latin American studies, older age at death positively associated with cerebrovascular burden for both vessel disease and tissue damage
- Diabetes, a known and robust contributor to adverse cognitive aging and plasma-based biomarkers of dementia for Latin Americans living in the US, showed associations with AD- and CVD-related neuropathologies
- Neighborhood-level vulnerability differentially associated with individual neuropathologies but not always in the expected direction (e.g., LATE-NC)
- Given the small and varying analytic samples of this preliminary work, we are actively expanding the quantification of our named neuropathologies and life course risk factors to all Latin American decedents of the RADCC

5 Acknowledgements

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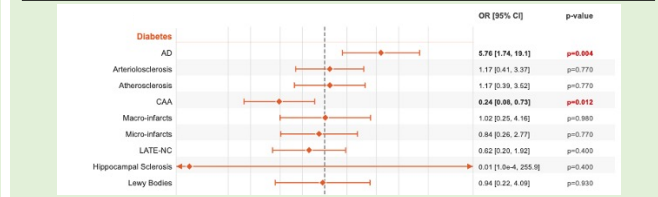
Associations with Life Course Risk Factors for AD/ADRD

Table 1. Associations of demographic risk factors and neuropathology

	AD (high or intermediate)	Arterio- sclerosis (mod to severe)	Athero- sclerosis (mod to severe)	CAA (mod to severe)	Macro- infarcts (one or more)	Micro- infarcts (one or more)	LATE-NC (mod to severe)	Hippocampal Sclerosis (presence)	Lewy Bodies (presence)
Age at death	n=75 1.006 [0.968, 1.046] p=0.75	n=75 1.186 [1.047, 1.348] p=0.0003	n=75 1.070 [1.024, 1.119] p=0.003	n=65 1.008 [0.965, 1.054] p=0.71	n=75 1.065 [0.990, 1.140] p=0.093	n=75 1.117 [1.037, 1.203] p=0.003	n=66 1.054 [0.987, 1.125] p=0.12	n=58 0.979 [0.905, 1.060] p=0.59	n=75 1.012 [0.963, 1.064] p=0.64
Sex (male)	n=75 1.110 [0.522, 2.272] p=0.57	n=75 0.452 [0.162, 1.261] p=0.13	n=75 0.868 [0.325, 2.317] p=0.78	n=65 0.648 [0.238, 1.764] p=0.40	n=75 2.260 [0.634, 8.053] p=0.21	n=75 1.090 [0.334, 3.537] p=0.89	n=66 1.781 [0.533, 5.953] p=0.35	n=58 1.611 [0.278, 9.328] p=0.59	n=75 2.383 [0.805, 7.060] p=0.11
Education	n=75 1.082 [0.998, 1.175] p=0.060	n=75 1.004 [0.923, 1.091] p=0.93	n=75 1.026 [0.942, 1.119] p=0.55	n=65 0.986 [0.908, 1.072] p=0.75	n=75 1.041 [0.930, 1.1645] p=0.49	n=75 0.976 [0.883, 1.079] p=0.63	n=66 0.995 [0.896, 1.103] p=0.92	n=58 0.962 [0.868, 1.144] p=0.66	n=75 0.970 [0.877, 1.072] p=0.55

Values are odds ratios (OR), 95% confidence intervals (CI) and p-values resulting from Cox Proportional Hazard models. Bold red box entries represent significance using 95% CI and a p<0.05 threshold. Italicized entries represent significance at 0.10 level. AD: Alzheimer's disease; Arteriosclerosis: Arteriosclerosis; CAA: Cerebral amyloid angiopathy; LATE-NC: Late-onset neurofibrillary tangle; Macroinfarcts: Macroinfarcts; Microinfarcts: Microinfarcts; Hippocampal Sclerosis: Hippocampal Sclerosis; Lewy Bodies: Lewy Bodies.

Figure 3. Forest plot of associations of cardiovascular risk factors and neuropathology



Neither systolic nor diastolic BP slopes associated with our quantified neuropathologies

Figure 4. Associations of exposomic (i.e., Social Vulnerability Index, SVI) and neuropathology

