

Distribution of amyloid, vascular, and neurodegeneration biomarker profiles by cognition in the oldest-old: The LifeAfter90 Study

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OBJECTIVES

- The A/T/N framework, which classifies Alzheimer's disease (AD) pathophysiology based on markers of amyloid (A), tau (T), and neurodegeneration (N).
- This framework has been useful to characterize AD risk, prevalence, and progression.
- Vascular injury is currently not viewed to be a core biomarker of AD pathology in the ATN framework.

OBJECTIVE: Here, we implemented a similar approach, but including markers of amyloid-beta (A), vascular injury (V), and neurodegeneration (N). We assessed whether A/V/N biomarker profiles would be differentially distributed by cognitive function in oldest-old individuals.

METHODS

- Participants from LifeAfter90, an ongoing cohort of diverse adults aged 90+ years.

MEASURES

Neuropsychological assessment:

- Verbal episodic memory and executive function domain scores were derived using the Spanish and English Neuropsychological Assessment Scales and dichotomized at the median.

Neuroimaging:

- Amyloid-beta (A β): measured with amyloid-PET imaging with AV45; amyloid positivity at SUVR>1.1.
- T1 and FLAIR images from 3T MRI quantified white matter hyperintensity (WMH) volume as a marker of vascular injury (V).
- Total hippocampal volume, residualized for intracranial volume, indicated neurodegeneration (N).
- WMH and hippocampal volumes were dichotomized at the median.
- Markers were combined to create A/V/N biomarker profiles: high (+) vs. low (-) burden of A β (A), vascular injury (V), and neurodegeneration (N).

STATISTICAL ANALYSIS

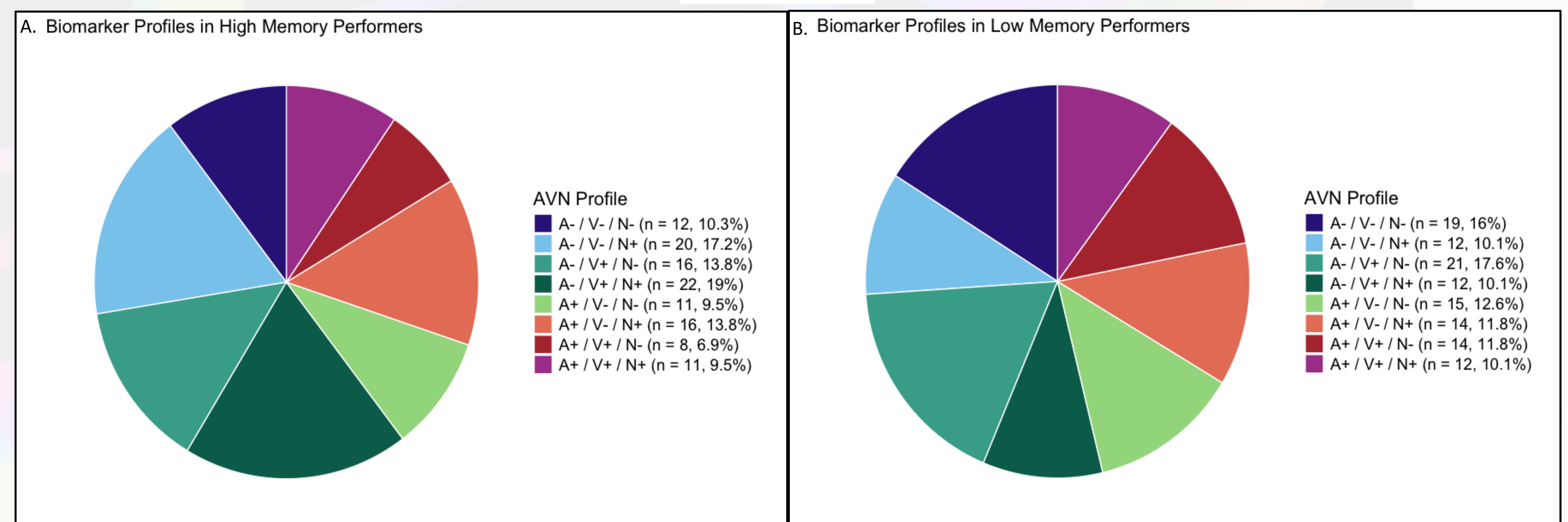
- Distributions of A/V/N profiles were compared between high and low memory groups and executive function groups using Chi-square tests.

RESULTS

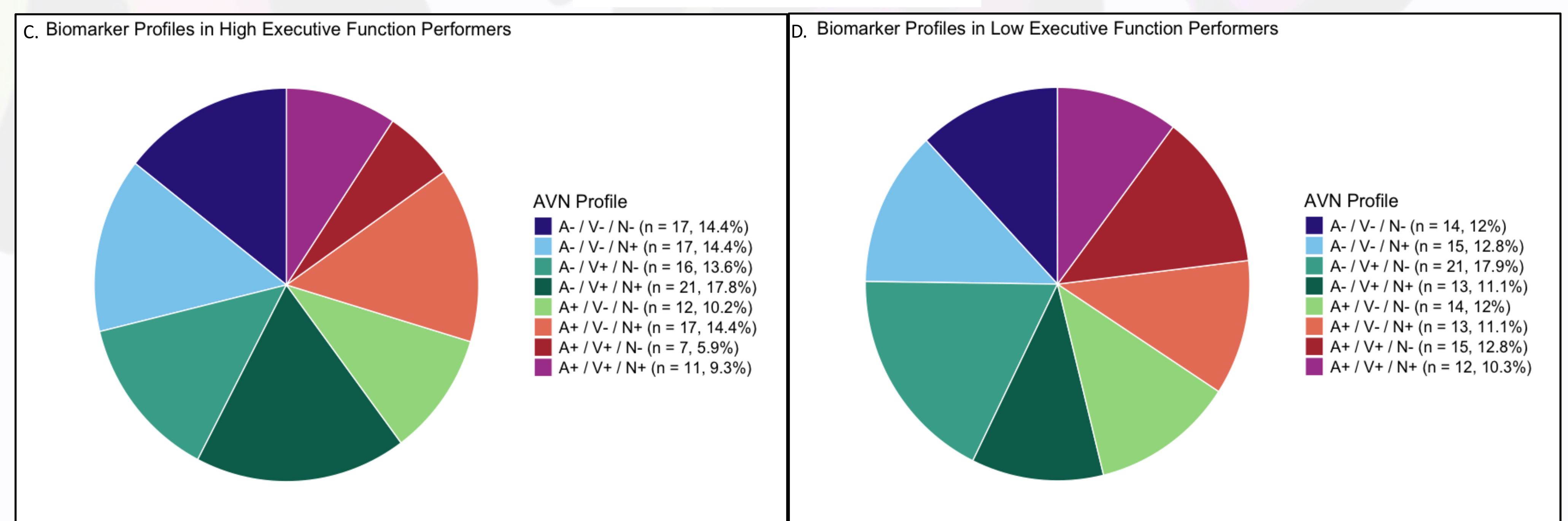
Participant Demographics: N=235, mean age of 93.32 $\pm$ 2.2 years (range: 90.1-101.1)

- 54% were women, 24% Asian, 21% Black, 20% Latinx, 8% Multiracial/Other, and 26% White.
- Biomarker profiles did not differ between high and low memory ($X^2(7)=9.59;p=0.21$) or between high and low executive function ($X^2(7)=6.61;p=0.47$) groups.

Memory



Executive Function



- Among high memory performers and high executive function performers, the A-/V+/N+ profile was most frequent at 19% and 18%, respectively.
- Among low memory and executive function performers, the A-/V+/N- profile was most frequent at 18% in both groups.

DISCUSSION

The distributions of A/V/N profiles were similar across high and low cognitive performers in this limited sample of the oldest-old. These findings suggest that other factors contribute to differential cognition in the oldest-old beyond amyloid-beta, vascular, and neurodegenerative pathologies.

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