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BIOMARKERS

POSTER PRESENTATIONS

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Neuroimaging / differential diagnosis

Relative contribution of white matter hyperintensity to amyloid and neurodegeneration in cognitive decline over time or clinical diagnoses in a diverse, community-based cohort of older adults

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Abstract

Background: The 2018 NIA-AA Alzheimer's disease (AD) research framework moves towards a multiple biomarker approach to explain AD development and progression more fully. This research framework has the flexibility to incorporate various biomarkers into a full or partial amyloid-tau-neurodegeneration (A/T/N) profile. The objective of this study was to determine the relative contribution of white matter hyperintensities (WMH) to amyloid and neurodegeneration on cognition in a diverse, community-based cohort of older adults.

Method: A subset of cognitively healthy participants (n=155; age=69-99yrs; 65% women, 30%/44%/26% Non-Hispanic White/Non-Hispanic Black/Hispanic) from the Washington Heights-Inwood Columbia Aging Project underwent baseline Florbetaben PET (amyloid SUVR), T1-weighted (cortical thickness[mm]) and T2-weighted FLAIR MRI (WMH volume[cm^3]), as well as subsequent neuropsychological assessments and consensus diagnoses every 1.5 years (up to 6 visits). Linear mixed effects models were used to test for change over time in language, memory, executive function, and visuospatial ability, while cox proportional hazard models were used to test for risk of developing MCI or AD. Biomarkers of interest included amyloid, cortical thickness, and WMH, adjusted for demographics (sex/gender, race/ethnicity, education). Interactions between biomarkers and time (e.g., slope differences) were evaluated as significant below 0.1.

Result: In A/N/V models, higher amyloid was associated with faster rates of decline in language (B [95%CI]: -0.08 [-0.13, -0.02]), memory (-0.13 [-0.21, -0.05]), and visuospatial ability (-0.05 [-0.12, 0.01]), higher WMH was associated with faster rates of decline in executive function (-0.05 [-0.11, 0.009]) and visuospatial ability (-0.02 [-0.05, 0.005]), and lower cortical thickness was associated with lower executive function scores (1.6 [0.10, 3.0]). Individuals were more likely to develop MCI or AD with higher amyloid

(Hazard Ratio=4.2, [1.1, 15.9]), but not with higher WMH (1.2 [0.83, 1.7]) or lower cortical thickness (0.03 [4E-4, 2]).

Conclusion: In this imaging subsample of older community-dwelling adults, cognitive decline is differentially associated by domain with amyloid or vascular burden, while broader, multi-domain cognitive impairment necessary for MCI or AD diagnoses is associated with amyloid, one of the hallmark AD pathologies. Results support the use of complementary information from biomarker profiles, including traditional AD, vascular, and neurodegenerative biomarkers, to investigate AD and related dementias.

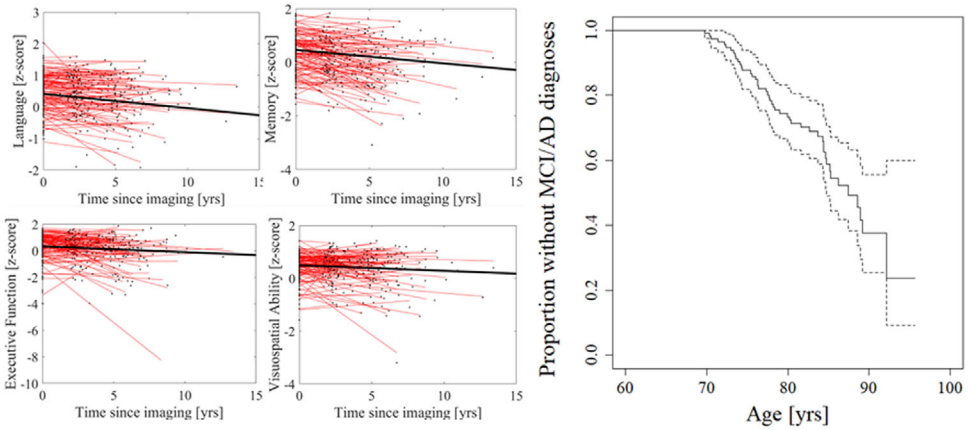

Figure 1. Cognitive trajectories over time and survival curve for MCI or AD diagnosis.

FIGURE 1