Two Year Cognitive and Biomarker Change in a Racially Diverse, Middle-aged, Cohort at Risk for Alzheimer's Disease

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Background
Alzheimer's disease (AD) incidence among Black/African Americans (B/AA) is 64% higher than non-Hispanic Whites (NHW). Studies show CSF total and phosphorylated tau are lower in cognitively unimpaired middle-aged B/AAs compared to NHWs. Cognitive changes in B/AA adults are associated with smaller increases in CSF tau. We examined rate of cognitive and CSF AD biomarker change, over two years, in a cognitively unimpaired, racially diverse, middle-aged cohort with a parental history of AD.

Methods
Cognitive tests (MOCA, Trails B, Digit Span, Benson Delay, Buschke Delay, and MINT) were collected at baseline (BL), 1 year (Y1), and 2 years (Y2). CSF was collected at BL and Y2 for AD biomarkers (Aβ and tau) and sPDGFRβ, an index of blood brain barrier damage. Analyses controlled for age, sex, race, education, and APOE4.

Results
Participants (N=80) were mostly female (69%), highly educated (81% ≥college), and 34% B/AA. B/AAs exhibited lower levels of p-tau, t-tau, and sPDGFRβ at BL and Y2 compared to NHWs ($p \leq 0.02$). P-tau increased from BL to Y2 for all participants ($p < 0.01$). NHWs outperformed B/AAs in 7/7 cognitive tests at baseline and 6/7 at Y2. Digit Span improved from BL to Y2 ($p = 0.014$) for all participants. Analyses by race demonstrated improvements for MOCA and Buschke Delay among B/AAs, and improvements for Trails B and Benson Delay among NHWs. There was a difference in rate of change over time by race in Benson Delay ($F = 8.22$, $p = 0.0055$). Linear models showed positive associations between Trails B and p-tau and sPDGFRβ ($p \leq 0.05$). Negative associations were found between Benson Delay and p-tau and t-tau ($p \leq 0.04$), between MINT and sPDGFRβ, p-tau, and t-tau ($p = 0.04$), and between Buschke Delay and sPDGFRβ ($p = 0.03$).

Conclusions
While cognitive scores changed over time, group analyses showed improvements among B/AA participants in verbal memory and global cognition, while NHW participants improved in tests of processing speed and visuospatial memory. CSF p-tau increased over 2 years. As CSF AD biomarkers were predictive of cognitive function scores, AD pathologic processes may begin earlier in at-risk adults. Further study of race-associated differences in AD biomarkers is needed, as these differences may contribute to AD-related health disparities.