

results among all patients, whereas BMI only influenced on the results among patients with SCD and MCI. Our findings do not support that BMI is associated with delayed recall of memory in AD.

Categories: Dementia (Alzheimer's Disease)

Keyword 1: mild cognitive impairment

Keyword 2: dementia - Alzheimer's disease

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3 Stricker Learning Span criterion validity: remote self-administration of a computer adaptive word list memory test shows similar ability to differentiate PET-defined biomarker groups as in-person Rey Auditory Verbal Learning Test performance in cognitively unimpaired individuals on the Alzheimer's continuum

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Objective: The Stricker Learning Span (SLS) is a computer-adaptive word list memory test specifically designed for remote assessment and self-administration on a web-based multi-device platform (Mayo Test Drive). Given recent evidence suggesting the prominence of learning impairment in preclinical Alzheimer's disease (AD), the SLS places greater emphasis on learning than delayed memory compared to traditional word list memory tests (see Stricker et al., *Neuropsychology* in press for review and test details). The primary study aim was to establish criterion validity of the SLS by comparing the ability of the remotely-administered SLS and in-person administered Rey Auditory Verbal Learning Test (AVLT) to differentiate biomarker-

defined groups in cognitively unimpaired (CU) individuals on the Alzheimer's continuum.

Participants and Methods: Mayo Clinic Study of Aging CU participants (N=319; mean age=71, SD=11; mean education=16, SD=2; 47% female) completed a brief remote cognitive assessment (~0.5 months from in-person visit). Brain amyloid and brain tau PET scans were available within 3 years. Overlapping groups were formed for 1) those on the Alzheimer's disease (AD) continuum (A+, n=110) or not (A-, n=209), and for 2) those with biological AD (A+T+, n=43) vs no evidence of AD pathology (A-T-, n=181). Primary neuropsychological outcome variables were sum of trials for both the SLS and AVLT. Secondary outcome variables examined comparability of learning (1-5 total) and delay performances. Linear model ANOVAs were used to investigate biomarker subgroup differences and Hedge's G effect sizes were derived, with and without adjusting for demographic variables (age, education, sex).

Results: Both SLS and AVLT performances were worse in the biomarker positive relative to biomarker negative groups (unadjusted p's<.05). Because biomarker positive groups were significantly older than biomarker negative groups, group differences were attenuated after adjusting for demographic variables, but SLS remained significant for A+ vs A- and for A+T+ vs A-T- comparisons (adjusted p's<.05) and AVLT approached significance (p's .05-.10). The effect sizes for the SLS were slightly better (qualitatively, no statistical comparison) for separating biomarker-defined CU groups in comparison to AVLT. For A+ vs A- and A+T+ vs A-T- comparisons, unadjusted effect sizes for SLS were -0.53 and -0.81 and for AVLT were -0.47 and -0.61, respectively; adjusted effect sizes for SLS were -0.25 and -0.42 and for AVLT were -0.19 and -0.26, respectively. In secondary analyses, learning and delay variables were similar in terms of ability to separate biomarker groups. For example, unadjusted effect sizes for SLS learning (-.80) was similar to SLS delay (-.76), and AVLT learning (-.58) was similar to AVLT 30-minute delay (-.55) for the A+T+ vs A-T- comparison.

Conclusions: Remotely administered SLS performed similarly to the in-person-administered AVLT in its ability to separate biomarker-defined groups in CU individuals, providing evidence of criterion validity. The SLS showed significantly worse performance in A+ and A+T+ groups (relative to A- and A-T- groups) in this CU sample after demographic

adjustment, suggesting potential sensitivity to detecting transitional cognitive decline in preclinical AD. Measures emphasizing learning should be given equal consideration as measures of delayed memory in AD-focused studies, particularly in the preclinical phase.

Categories: Dementia (Alzheimer's Disease)

Keyword 1: computerized neuropsychological testing

Keyword 2: technology

Keyword 3: memory disorders

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4 Evaluating Plasma GFAP for the Detection of Alzheimer's Disease Dementia

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Objective: Blood-based biomarkers represent a scalable and accessible approach for the detection and monitoring of Alzheimer's disease (AD). Plasma phosphorylated tau (p-tau) and neurofilament light (NfL) are validated biomarkers for the detection of tau and neurodegenerative brain changes in AD, respectively. There is now emphasis to expand beyond these markers to detect and provide insight into the pathophysiological processes of AD. To this end, a reactive astrocytic marker, namely plasma glial fibrillary acidic protein (GFAP), has been of interest. Yet, little is known about the relationship between plasma GFAP and AD. Here, we examined the association

between plasma GFAP, diagnostic status, and neuropsychological test performance. Diagnostic accuracy of plasma GFAP was compared with plasma measures of p-tau₁₈₁ and NfL.

Participants and Methods: This sample included 567 participants from the Boston University (BU) Alzheimer's Disease Research Center (ADRC) Longitudinal Clinical Core Registry, including individuals with normal cognition (n=234), mild cognitive impairment (MCI) (n=180), and AD dementia (n=153). The sample included all participants who had a blood draw. Participants completed a comprehensive neuropsychological battery (sample sizes across tests varied due to missingness). Diagnoses were adjudicated during multidisciplinary diagnostic consensus conferences. Plasma samples were analyzed using the Simoa platform. Binary logistic regression analyses tested the association between GFAP levels and diagnostic status (i.e., cognitively impaired due to AD versus unimpaired), controlling for age, sex, race, education, and APOE *e4* status. Area under the curve (AUC) statistics from receiver operating characteristics (ROC) using predicted probabilities from binary logistic regression examined the ability of plasma GFAP to discriminate diagnostic groups compared with plasma p-tau₁₈₁ and NfL. Linear regression models tested the association between plasma GFAP and neuropsychological test performance, accounting for the above covariates.

Results: The mean (SD) age of the sample was 74.34 (7.54), 319 (56.3%) were female, 75 (13.2%) were Black, and 223 (39.3%) were APOE *e4* carriers. Higher GFAP concentrations were associated with increased odds for having cognitive impairment (GFAP z-score transformed: OR=2.233, 95% CI [1.609, 3.099], p<0.001; non-z-transformed: OR=1.004, 95% CI [1.002, 1.006], p<0.001). ROC analyses, comprising of GFAP and the above covariates, showed plasma GFAP discriminated the cognitively impaired from unimpaired (AUC=0.75) and was similar, but slightly superior, to plasma p-tau₁₈₁ (AUC=0.74) and plasma NfL (AUC=0.74). A joint panel of the plasma markers had greatest discrimination accuracy (AUC=0.76). Linear regression analyses showed that higher GFAP levels were associated with worse performance on neuropsychological tests assessing global cognition, attention, executive functioning, episodic memory, and language abilities (ps<0.001) as well as higher CDR Sum of Boxes (p<0.001).