explore the value of psychophysical olfactory assessment as biomarker measure in preclinical AD studies and drug trials by investigating its relationships with structural measures of the hippocampus.
Participants and Methods: A sample consisted of non-demented older adults (age ≥75), recruited from the UCSD Alzheimer's Disease Research Center as part of a ongoing olfactory biomarker study. Participants completed the AD Assessment Scale-Cognitive Subscale-13 (ADAS-Cog-13), San Diego Odor Identification Test (SDOIT), tests of odor recognition memory (ORMem) and odor associative memory (OAM), and MRI derived hippocampal volumes and average hippocampal occupancy (Avg HOC). Left and right hippocampal volumes were adjusted for each participant's estimated intracranial volume. Bivariate correlations were calculated for ADAS-Cog-13 and SDOIT total scores, performance scores for odor recognition and odor associative memory tests, and the three hippocampal measures (bilateral volumes and average occupancy).
Results: ADAS-Cog-13 score did not show significant correlations with either hippocampal measure at the .05 level. SDOIT scores were significantly correlated with the measure of Avg HOC (p<.05). ORMem false positive responses were significantly correlated with Avg HOC (p<.01) and right hippocampal volume (p<.05). ORMem miss responses and OAM errors were both correlated with left (p<.05) and right (p<.01) hippocampal volumes.
Conclusions: These results demonstrate that psychophysical assessments of odor identification and odor memory can better reflect the integrity of the hippocampus in nondemented older adults, compared to the neuropsychological ADAS-Cog-13. This is congruent with olfactory dysfunction preceding cognitive-memory decline in AD cases and provides support for the utility of psychophysical olfactory assessment along with other established AD biomarkers in research and drug trials in preclinical populations.
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Categories: Dementia (Alzheimer's Disease)
Keyword 1: olfaction
Keyword 2: hippocampus
Keyword 3: dementia - Alzheimer's disease
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4 Association Between Plasma Neurofilament Light Chain (NfL) and Non-Verbal Abstract Reasoning in a Colombian Cohort with Autosomal Dominant Alzheimer's Disease

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Objective: Neurofilament light chain (NfL), a plasma-based biomarker for neurodegeneration, is a promising marker for early Alzheimer disease (AD) detection in individuals at increased risk. We previously reported that Presenilin1 (PSEN1) E280A carriers have increased levels of plasma NfL relative to non-carrier family members twenty years before the onset of clinical symptoms. Abstract reasoning is one of the first cognitive abilities to deteriorate in AD. Here, we examined whether levels of plasma NfL were associated with non-verbal abstract reasoning performance in non-demented PSEN1-E280A carriers and non-carriers.
Participants and Methods: A total of 798 members of the Colombian kindred with the PSEN1 E280A mutation (462 cognitively-unimpaired and 336 non-carriers; mean age= 34.02 (10.53), mean education= 8.23(4.60), 57% females and 43% males) were included in the study. Participants completed the Raven's Progressive Matrices (RPM), Mini Mental State Examination (MMSE), and underwent blood sampling. Plasma NfL concentrations were measured with a single molecule array (Simoa) method. Mann-Whitney U test and education-adjusted Spearman partial correlation were used to examine group differences and associations between abstract reasoning performance and NfL levels.
Results: Non-carriers were older (p<.001) and had higher levels of education than carriers

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(p=.025). Compared to non-carriers, carriers had higher levels of NfL (p=.014), lower performance on the MMSE (p<.001) and on the RPM (p=.001). In the whole sample, performance on the RPM was significantly associated with age (r= -.144, p<.001), and MMSE score (r=.198, p<.001). In carriers only, performance on the RPM was negatively associated with NfL levels (r=-.121, p=.009). This association was not significant in non-carriers.
Conclusions: Our findings support the hypothesis that plasma NfL levels may be indicators of disease progression and early cognitive dysfunction in autosomal dominant AD. Future work with NfL, abstract reasoning and memory with larger samples across the preclinical/prodromal spectrum will allow a more comprehensive examination of these associations.

Categories: Dementia (Alzheimer's Disease)
Keyword 1: dementia - Alzheimer's disease
Keyword 2: cognitive functioning
Keyword 3: visuospatial functions
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5 Intraindividual Variability in Processing Speed on Digital Cognitive Assessments Differs by Amyloidosis Status in Cognitively Normal Older Adults

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Objective: Intraindividual variability (IIV) is defined as fluctuations in an individual's cognitive performance over time1. IIV has been identified as a marker of neurobiological disturbance making it a useful method for detecting changes in cognition among cognitively healthy individuals as well as those with prodromal syndromes2. IIV on laboratory-based computerized tasks has been linked with cognitive decline and conversion to mild cognitive impairment (MCI) and/or dementia (Haynes et al., 2017). Associations between IIV and AD risk factors including apolipoprotein (APOE) ε4 carrier status, neurodegeneration seen on brain imaging, and amyloid (Aβ) Positron emission tomography (PET) scan status have also been observed1. Recent studies have demonstrated that evaluating IIV on smartphone-based digital cognitive assessments is feasible, has the capacity to differentiate between cognitively normal (CN) and MCI individuals, and may reduce barriers to cognitive assessment3. This study sought to evaluate whether such differences could be detected in CN participants with and without elevated AD risk.
Participants and Methods: Participants (n=57) were cognitively normal older adults who previously received an Aβ PET scan through the Butler Hospital Memory and Aging Program. The sample consisted of primarily non-Hispanic (n=49, 86.0%), White (n=52, 91.2%), college-educated (M=16.65 years), females (n=39, 68.4%). The average age of the sample was 68 years old. Approximately 42% of the sample (n=24) received a positive PET scan result. Participants completed brief cognitive assessments (i.e., 3-4 minutes) three times per day for eight days (i.e., 24 sessions) using the Mobile Monitoring of Cognitive Change (M2C2) application, a mobile app-based cognitive testing platform developed as part of the National Institute of Aging's Mobile Toolbox initiative (Sliwinski et al., 2018). Participants completed visual working memory, processing speed, and episodic memory tasks on the M2C2 platform. Intraindividual standard deviations (ISDs) across trials were computed for each person at each time point (Hultsch et al., 2000). Higher ISD values indicate more variability in performance. Linear mixed effects models were utilized to examine whether differences in IIV existed based on PET scan status while controlling for age, sex at birth, and years of education.
Results: n interaction between PET status and time was observed on the processing speed task such that Aβ- individuals were less variable over the eight assessment days compared to Aβ

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