

in older adults. Higher plasma pTau-181 was associated with increased odds of MCI diagnosis. Detection of pTau-181 in plasma allows a novel, non-invasive method to detect burden of one form of AD pathology. These findings lend support to the use of plasma pTau-181 as a valuable marker in detecting even early cognitive changes prior to the development of AD. Additional longitudinal studies are warranted to explore the prognostic value of plasma pTau-181 over time.

Categories: Dementia (Alzheimer's Disease)

Keyword 1: cognitive functioning

Keyword 2: dementia - Alzheimer's disease

Keyword 3: mild cognitive impairment

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33 Associations Between Long-Term Forgetting and Slow Wave Activity in Autosomal-Dominant Alzheimer's Disease: Findings from the Colombia-Boston (COLBOS) Biomarker Study

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Objective: Sleep contributes to memory retention and recall. Alzheimer's disease (AD) patients experience decreased slow wave activity (SWA) during sleep. This decrease in SWA is associated with impaired memory consolidation (Lee et al., 2020). Long-term forgetting (LTF) over days or weeks has been linked to memory consolidation deficits and has been suggested as an early marker of AD that could be useful for identifying at-risk individuals for preclinical AD trials (Weston et al., 2018). Here, we examined associations between LTF and SWA in a sample of Presenilin-1 (PSEN1)

E280A mutation carriers with autosomal dominant Alzheimer's disease and non-carrier family members. Carriers of this mutation usually develop dementia in their forties (Fuller et al., 2019).

Participants and Methods: Fourteen cognitively unimpaired PSEN1-E280A mutation carriers and sixteen age-matched non-carriers (mean age: 34.2 years) from the Colombia-Boston (COLBOS) biomarker study were included. Participants completed an overnight polysomnogram (PSG) and memory testing (NEUROPSI Word List) at 3-time points: 1) the night before PSG: immediate recall (Day1-ImmRecall) and a 20-minute delayed recall (Day1-DelayedRecall), 2) recall the following day (Day2-recall), and 3) recall one week later (Day7-recall). SWA was measured as the ratio 0.6-1Hz/0.6-4Hz in frontopolar and frontotemporal regions and was calculated for sleep stages N2+N3 (slow wave sleep) based on an automated staging algorithm. Each participant's LTF was calculated as the percent retention between Day 1 immediate recall and Day 7 recall (Butler, 2009). Mann-Whitney U tests were used to compare differences in recall, SWA, and LTF between groups. Spearman's correlation was used to examine the associations between memory recall at different time points and SWA, as well as between LTF and SWA.

Results: On Day 1, carriers had lower performance in immediate recall ($p=0.02$), compared to non-carriers, but there were no group differences in the 20-minute delayed recall. Carriers also recalled fewer words on Day 2 ($p=0.03$) and Day 7 ($p=0.009$) and had greater LTF ($p=0.03$). There were no group differences in SWA. In our overall sample, worse performance on word list delayed recall on Day 1, Day 2, and Day 7 was associated with less SWA across both frontotemporal (Day1: $p=0.04$, Day2: $p=0.02$, Day7: $p=0.02$) and frontopolar (all $P<0.01$) regions. In carriers, only worse performance on Day 1 delayed recall was associated with lower SWA in the frontopolar region ($r=0.535$; $p=0.049$). Memory recall on other days was not associated with SWA in any brain regions. Additionally, greater LTF was associated with less SWA across both frontopolar ($r=0.507$; $p=0.005$) and frontotemporal regions ($r=0.463$; $p=0.01$).

Conclusions: Preliminary findings suggest that long-term forgetting is associated with less slow-wave activity in preclinical autosomal dominant Alzheimer's disease. These results also suggest

that SWA may be related to pre-sleep learning and subsequent overnight memory consolidation processes. LTF testing may be useful in selecting individuals for preclinical AD trials. Future research on the impact of slow wave activity on LTF may be useful in identifying ways to enhance short- and long-term memory consolidation in individuals at greater risk for dementia.

Categories: Dementia (Alzheimer's Disease)

Keyword 1: dementia - Alzheimer's disease

Keyword 2: sleep

Keyword 3: neuropsychological assessment

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34 Machine Learning Predicts Time to Dementia Conversion in Cognitively Normal Subjects

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Objective: Identification of pre-clinical Alzheimer's disease (AD) is necessary for the development of future disease-modifying treatments, which would ideally target pre-clinical stages to mitigate functional loss. Despite advanced in biomarker development, clinical trials are still without a non-invasive and cost-effective means of identifying pre-symptomatic subjects who are at high risk for eventual conversion to AD. In previous work, we developed a machine learning algorithm using neuropsychological test scores and health history to identify subjects at high risk for eventual conversion. Here, we examine the performance of a similar algorithm in predicting the timing of that conversion in years.

Participants and Methods: Data were obtained from the National Alzheimer's Coordination Center (NACC) Uniform Data Set (UDS) version 3.0. Subjects with normal cognition at baseline were used to train a multi-class Random Forest classifier to predict conversion to AD. Each subject could be classified as a short-, mid-, or long-term converter (0-3 years, 4 to 6 years, and 7 to 9 years, respectively) or as a non-converter,

if no dementia diagnosis was given within ten years of baseline. Predictors included baseline demographics, basic medical history, and neuropsychological test results. Algorithms were evaluated using standard, cross-validated performance metrics.

Results: Multi-class Matthews correlation coefficient between predicted time to diagnosis and the ground truth averaged 0.26 +/- 0.06 across 100 cross validation splits. Prediction accuracy exceeded 0.67 in all cases, when computed for each class individually, and was greatest for the short-term (0.75) and non-converter (0.78) classes.

Conclusions: Machine-learning algorithms applied to neuropsychological, demographic, and medical history information were able to predict the eventual timing of conversion to dementia in cognitively healthy adults significantly better than chance. Results were most accurate when predicting shorter time to conversion. Results illustrate the potential of this data analytic approach for targeted recruitment in clinical trials.

Categories: Dementia (Alzheimer's Disease)

Keyword 1: dementia - Alzheimer's disease

Keyword 2: neuropsychological assessment

Keyword 3: technology

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35 The Effect of Diagnostic Method on Racial Disparities in Mild Cognitive Impairment and Dementia Diagnosis Using the NACC Database.

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