Within-session Learning of an Object Identification Task Predicts Elevated Brain Aβ and Future Task Performance

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BACKGROUND

Slight impairments on neuropsychological testing are evident in the preclinical stages of AD, but performance is still well within healthy ranges. This has been demonstrated using pen-and-paper and computerized assessments.

Within-session practice effects—improving on a task through its course—have been found to be a strong predictor of future performance. Computerized tests such as the Computer-Administered Neuropsychological Screen for MCI (CANS) can capture item-level response times which may be imperceptibly but detectably slower in the preclinical stage of AD.

OBJECTIVES

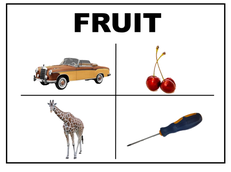
This study explored within-session learning and AD biomarkers. We operationalized learning as item response time slope through a self-administered, computerized object identification test on the CANS. In other words, participants should respond faster within the course of a simple task as they learn its nature.

METHODS

Participants were cognitively intact older adults who consented to lumbar puncture and completing the CANS. CSF collection and analysis are described elsewhere. CSF Aβ ≤ 250pg/ml was used as cutoff for likely preclinical AD (Aβ+) or not (Aβ-). All procedures approved by UK IRB.

The CANS Word-to-Picture Matching subtest was used; see Figure 1. Participants were instructed to touch the image that matched the word, as fast as they could. There were 14 trials. Depression was measured using the 10-item GDS.

Figure 1.



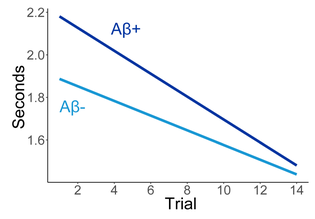
A linear mixed model (LMM) with response times from correct-trials as the dependent variable had standard covariates and trial as fixed effects. Participant was a random effect. Slopes were extracted and used to predict Aβ status and future performance.

RESULTS

Of 96 participants, 57 were Aβ- and 39 were Aβ+. The groups were not statistically different in sex, education, GDS score, or prior CANS administrations, ps > 0.33. The Aβ+ group (76.6y) was slightly older than Aβ- (73.9y), $p = 0.05$.

A LMM was initially computed with a trial × Aβ status term. It was anticipated that the Aβ+ group would simply perform slower throughout the task. However, the estimated marginal means in Figure 2 show the Aβ+ group started significantly slower but was responding as fast as the Aβ- group by the end of the task.

Figure 2.



To examine how learning was related to future performance, Aβ status was dropped. Response times decreased significantly by trial. Plotted in Figure 3 are the LMM coefficients with 95% CIs; point size is scaled to η².

Figure 3.

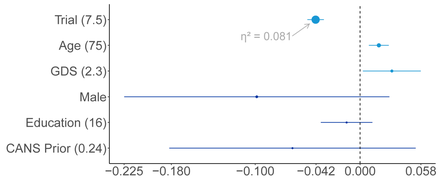
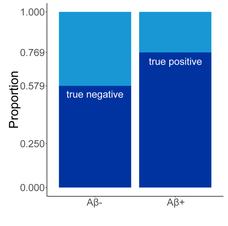


Figure 4.



Participant slopes for response time were extracted from the LMM. A logistic regression with age, GDS, and slopes as covariates was used to predict Aβ status. ROC was used to find the optimal cutoff, *AUC* = 0.69. Classification of Aβ status is presented in Figure 4.

42 Aβ- participants and 26 Aβ+ had a CANS administration 6 months later. They were binned into groups based on completing the Matching subtest faster or slower/same rate (i.e., performance worsened) at follow-up. Logistic regression was used to predict slower performance with an interaction between slope and Aβ status, with age and GDS as covariates.

RESULTS cont.

Aβ status × slope, slope, and Aβ status were all significant predictors of not faster at follow-up (*p*s < 0.05). Age and GDS were non-significant (*p*s > 0.38). Estimated marginal mean probabilities of not faster at follow-up at the quartiles of slope are shown in Figure 5, by Aβ status. Although it is a smaller sample, as shown in Figure 6, a slope × not faster-follow-up term predicts Aβ status more accurately, AUC = 0.82.

Figure 5.

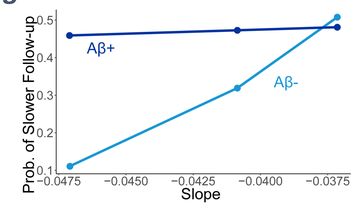
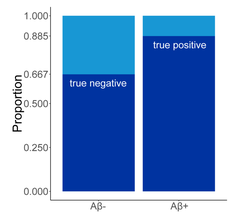


Figure 6.



CONCLUSIONS

- Steeper slopes seen in the Aβ+ group may reflect early retrieval delays and subsequent compensatory recruitment of additional brain regions or neuronal hyperactivation
  - This hypothesis could be examined with fMRI
- The study also adds to the growing literature on within-session practice effects (i.e., slope) as a predictor of future performance

- On CANS Word-to-Picture Matching, a steeper learning slope at baseline and no improvement at 6-month follow-up are indicators of elevated brain Aβ and possible preclinical AD
  - This is useful given the widespread clinical use of the CANS and routine administrations

REFERENCES