Longitudinal Speech-based Cognitive Trajectories Of Csf Biomarker-positive Versus Biomarker-negative Individuals

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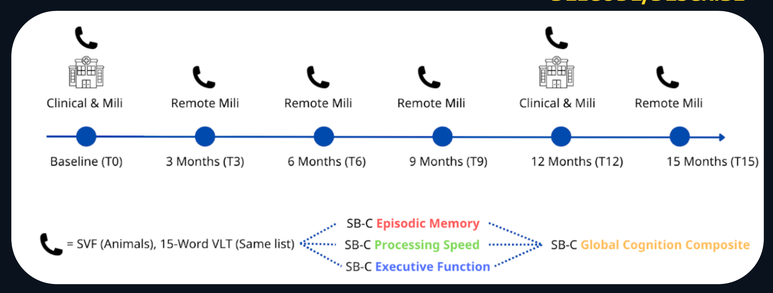
Introduction

Cerebrospinal fluid (CSF) biomarkers provide evidence of Alzheimer's disease (AD) pathology, yet their relationship to cognitive change captured by digital tools remains unclear. Speech-based digital cognitive measures are sensitive to early impairment[1]. Yet, whether they capture distinct longitudinal trajectories in biomarker-positive versus biomarker-negative individuals is unknown. Here, we examined whether **a speech-based global cognitive composite (SB-C) and its domain scores** captures longitudinal change as a function of CSF biomarker status.

Methods



Participants: *N* = 50 participants at baseline divided into biomarker positive (*N* = 15) and biomarker negative (*N* = 35) based on **CSF Aβ42/P-tau 181.**

Statistics: Linear mixed-effects models examined longitudinal SB-C trajectories adjusting for covariates and participant-specific random effects. Estimated slopes and marginal means changes from baseline were derived. CSF was collected prior to speech; all biomarker-positive participants were included, while biomarker-negative participants were restricted to a CSF-to-baseline-speech gap ≤2.5 years.

Results

Longitudinally, there was a significant interaction between CSF-biomarker status x time for the **SB-C global** (p = 0.03) **and memory scores** (p = 0.05). **Biomarker-negative individuals improved faster over time** indicating **learning-related gains (Fig.1).** No significant interaction was found for the SB-C executive function (p = 0.16) and processing speed scores (p = 0.10)

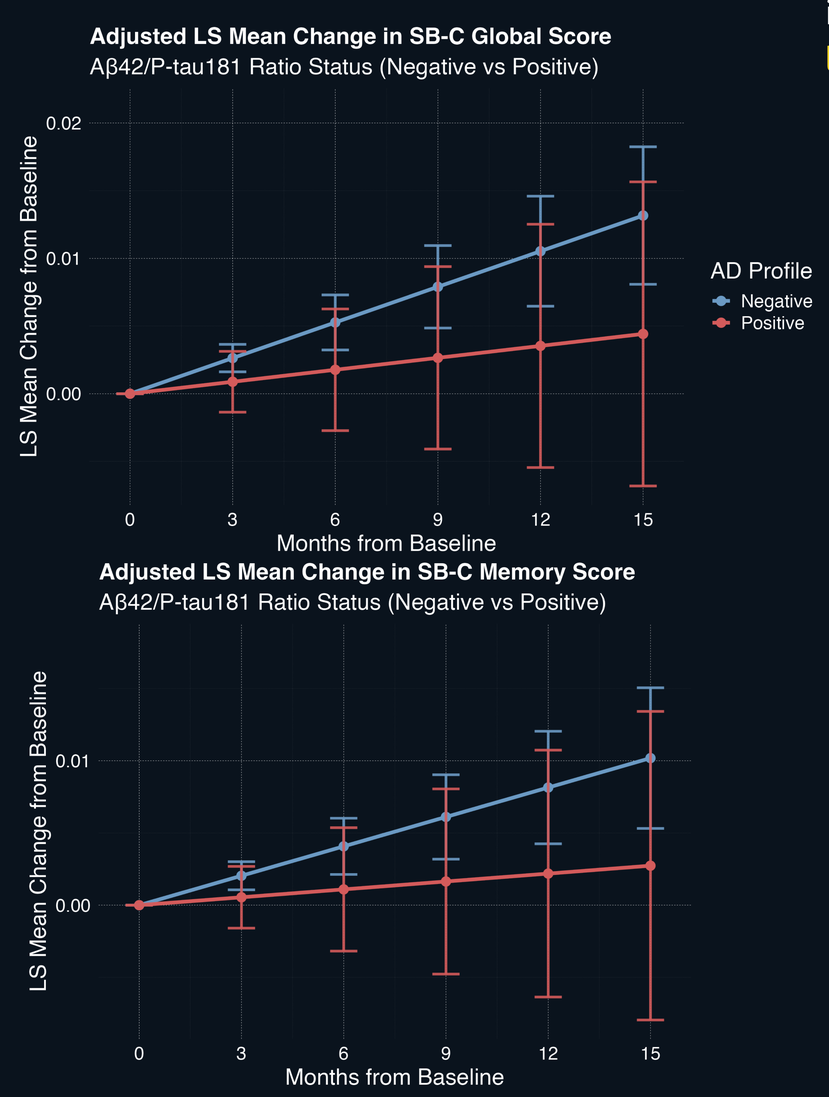


Figure 1. Adjusted LS Mean Changes from Baseline in SB-C Scores

Conclusion

Despite modest sample size and temporal separation between CSF collection and speech, **SB-C captured longitudinal patterns by CSF biomarker status.** Improvement confined to biomarker-negative individuals, potentially reflecting preserved learning/practice-related gains. Findings highlight the potential of speech-based markers in complementing biomarker-informed stratification and improving **longitudinal monitoring**.

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References

1. König, A., Tröger, J., Mallick, E., et al. Speech-based digital cognitive assessment for clinical trials: Detecting cognitive impairment stages and AD biomarker relations across European cohorts. ***Alzheimer's & Dementia. 2026; 22***(5), e71462. doi: https://doi.org/10.1002/alz.71462
2. König A, Linz N, Baykara E, et al. Screening over Speech in Unselected Populations for Clinical Trials in AD (PROSPECT-AD): Study Design and Protocol. ***J Prev Alzheimers Dis.*** 2023;10(2):314-321. doi:10.14283/jpad.2023.11