Speech measures enhance the prediction of Alzheimer's disease biomarkers

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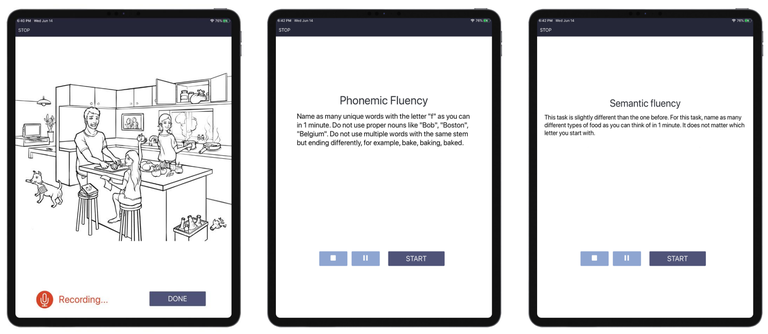
CAMBRIDGE COGNITION

Background

- Speech and language characteristics change in mild cognitive impairment (MCI) and Alzheimer's disease (AD).[1,2]
- Digital voice-based assessments offer scalable, low-burden ways to measure these changes, which could enhance sensitivity to disease-related changes.[3]
- Voice assessments could be used as a screening tool for MCI/AD, to help identify patients early in healthcare and clinical research settings.
- We tested whether voice-based measures enhanced the prediction of AD biomarkers, including Aβ42/40 ratio, CSF total tau and cortical thickness in participants with mild-to-moderate AD.

Objective: Determine which speech features and tasks are most strongly related to AD biomarkers, and whether these can be used to improve predictive models of biomarkers in AD.

Figure 1. Winterlight Speech Assessment.



Methods

- Participants included 429 English-speaking individuals with clinically-confirmed mild-to-moderate AD, who participated in a Phase 2/3 clinical trial (see Table 1 for demographic summary).
- At baseline, participants completed a voice-based assessment including picture description, letter (phonemic) fluency and category (semantic) fluency tasks (Figure 1) in-clinic via the Winterlight Speech Assessment app.
- Speech recordings were manually transcribed and checked for audio quality, and speech measures were extracted via the automated Winterlight speech processing pipeline.
- AD biomarkers included Aβ42/40 ratio and levels of total tau (t-tau), assessed via CSF assay, and cortical thickness, assessed via MRI in an AD-specific region of interest (ROI) including: entorhinal, inferior temporal, middle temporal and fusiform cortex.[4]
- We assessed the relationships between speech measures and AD biomarkers using Pearson partial correlations, controlling for participant age and sex.
- We used LASSO regression to select speech measures to predict AD biomarkers. We compared linear models predicting AD biomarkers based on age, sex and MMSE score (base models) to those also including selected speech features (speech models).

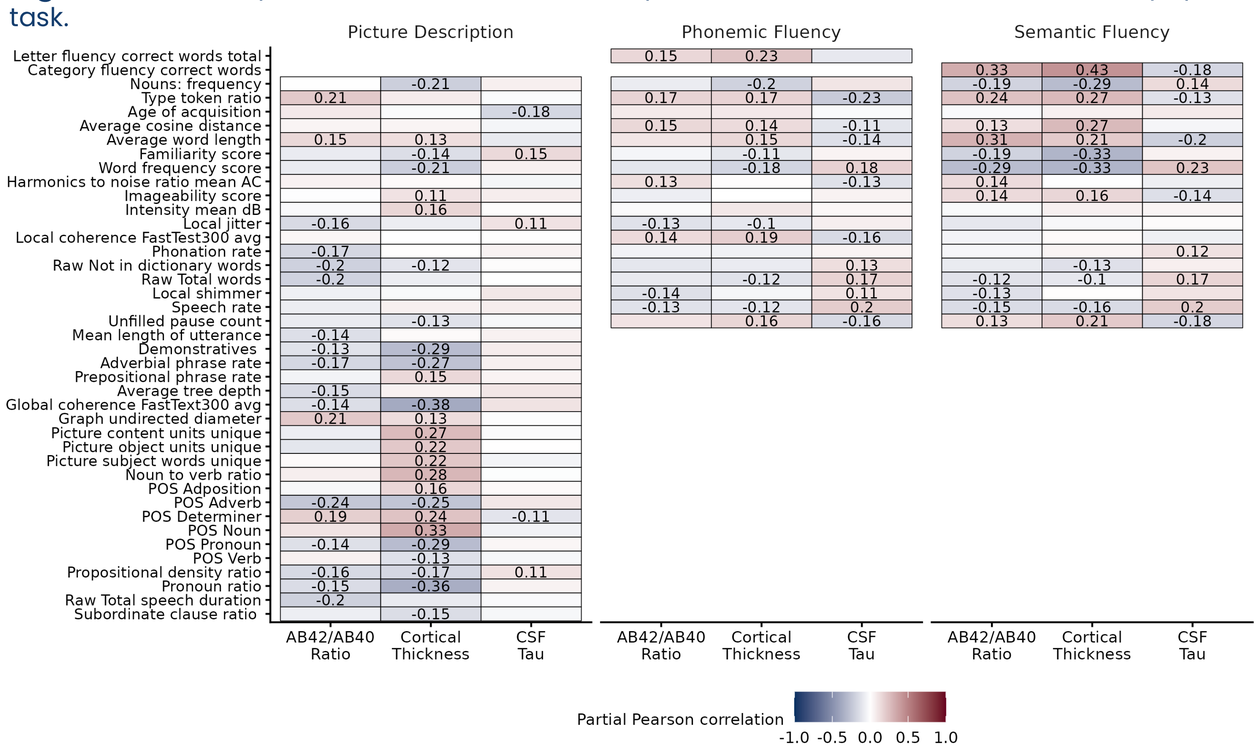
Table 1. Participant demographics.

Baseline characteristics	
N	429
Age (*M, SD*)	69.5 (6.77)
Sex (n, %)	
Female	186 (43%)
Male	243 (57%)
MMSE Total (*M, SD*)	18.1 (3.07)

Results: Correlations between speech measures and AD biomarkers

- The strongest correlations between speech measures and AD biomarkers were with cortical thickness in the AD-relevant ROI, followed by Aβ42/40 ratio, and levels of CSF tau (Figure 2).
- Measures from the category fluency task and the picture description task had the strongest correlations with AD biomarkers, while letter fluency measures had weaker correlations overall.
- The strongest correlations were with measures relating to word types (e.g. use of nouns, pronouns, adverbs), information content (e.g. how many items were correctly described in the picture), fluency scores (e.g. number of correct words listed for the given letter or category) and vocabulary (e.g. familiarity and frequency of words used).
- All speech measures with significant correlations with AD biomarkers ($p < 0.05$, uncorrected, see Figure 2 for correlation coefficients) were included in the LASSO regression analysis (see next section).

Figure 2. Pearson partial correlations between speech measures and AD biomarkers, by speech task.



Results: Predicting AD biomarkers using selected speech measures

- We compared linear models including age, sex and MMSE scores (base models) to linear models including age, sex, MMSE scores and speech measures selected via LASSO regression (speech models).
- In all cases, the speech models significantly improved prediction of AD biomarkers compared to the base models ($p < 0.05$; Figures 3, 4, 5).
- The cortical thickness speech model achieved the highest prediction accuracy ($R^2 = 0.35$).

Figure 3. Regression models predicting cortical thickness in AD-relevant ROI.

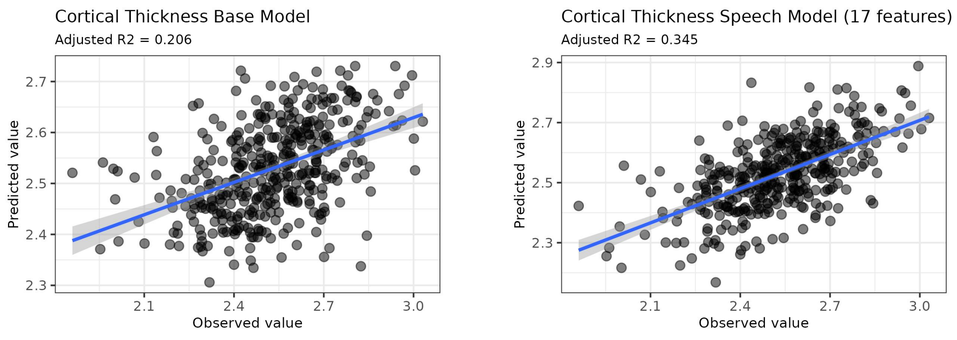


Figure 4. Regression models predicting CSF Aβ42/40 ratio.

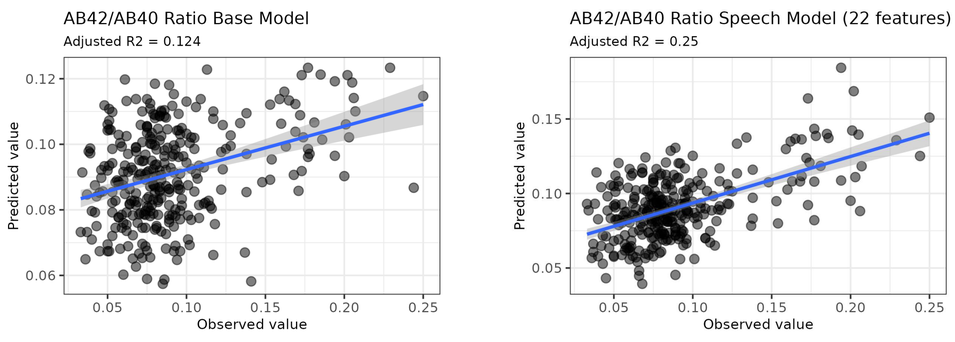
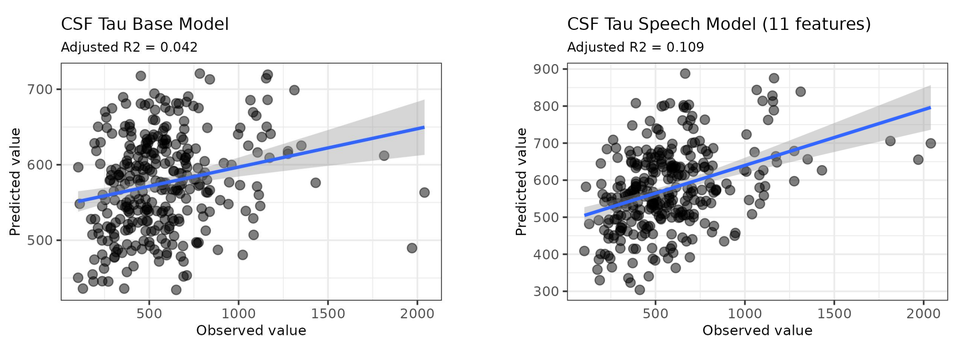


Figure 5. Regression models predicting CSF t-tau levels.



Conclusions

- The results of this study demonstrate the potential utility for voice-based assessments in screening and early identification of MCI/AD.
- The baseline speech assessment, which took approximately 5 minutes to complete, resulted in higher accuracy predictions of the level of AD biomarkers compared to demographics and standard screening tools.
- The present results suggest that cortical thickness in AD-related areas of the brain, indicative of current neurodegeneration, may be more closely related to speech characteristics than CSF biomarker levels.
- Future work can build on this study to examine other AD biomarkers including blood-based biomarkers.

References

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