Speech characteristics and their association with neuroimaging and CSF biomarkers of AD pathology

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Background

- Digital speech assessment shows promise as an objective and low burden measure of progressive speech and language changes in Alzheimer's disease (AD).
- Although associations with clinical endpoints are well established, less is known about how computational speech features align with biomarkers of AD pathology.
- **Objective:** The current analysis sought to examine associations between speech and AD biomarkers, both cross-sectionally and longitudinally.

Methods

- Participants were 427 English-speaking individuals with mild-to-moderate AD from a Phase 2/3 clinical trial (placebo group *n* = 145; treatment group *n* = 282).
- Clinical assessments (CDR, ADAS-Cog, MMSE) and speech assessments (two picture description tasks) were completed at baseline, and at 3-month, 6-month, and 12-month follow-up.
- Biomarkers, including neuroimaging markers (cortical thickness and volume) and CSF measures (Aβ40/42, tau, p-tau), were obtained at baseline and at month 12.
- Nine speech features (3 acoustic, 6 linguistic) comprising our previously published speech-based digital biomarker (Robin et al., 2023; *Alzheimer's & Dementia: DA&DM*, doi: 10.1002/dad2.12445) were extracted for each participant from the transcribed speech recordings of the picture description tasks.
- Participants were grouped into terciles (lower, middle, and upper thirds) based on each imaging and CSF biomarker, and tercile group differences in speech characteristics and clinical endpoints at baseline were assessed. Associations were also examined using a correlational approach.
- Sensitivity to change was also explored by examining whether baseline to 12-month changes in speech and clinical endpoints were correlated with changes in biomarker values.

AD biomarkers

Imaging
- Bilateral whole brain volume
- Right hippocampal volume
- Left hippocampal volume
- Mayo AD-signature cortical thickness*

CSF
- Aβ40/42
- Tau
- Phosphorylated tau (p-tau)

*Meta region of interest (ROI) comprising entorhinal, inferior temporal, middle temporal, and fusiform cortex

Speech features

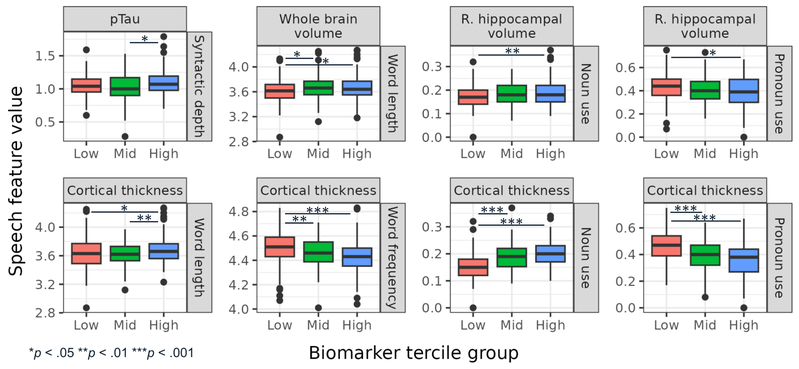
Linguistic
- Word length
- Syntactic depth
- Word frequency
- Noun use
- Particle use
- Pronoun use

Acoustic
- MFCC 11 mean
- MFCC 25 variance
- MFCC 26 variance

Results: baseline biomarker tercile comparisons

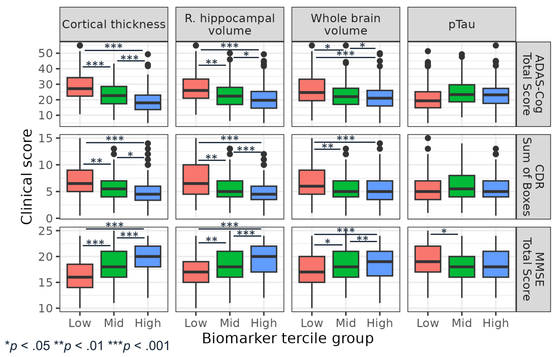
Speech feature differences among tercile groups

- Speech significantly differed among biomarker tercile groups, particularly cortical thickness and hippocampal volume, where word length, noun use, and pronoun use showed progression across terciles.



Clinical severity differences among tercile groups

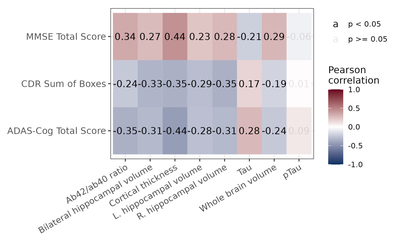
- A similar, stepwise association with biomarker terciles was observed across all three clinical endpoints.



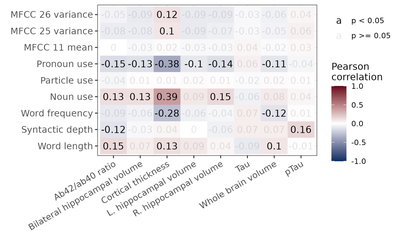
Results: baseline correlations

- At baseline, clinical endpoints were significantly associated with all biomarkers except for p-tau.
- Baseline correlations between speech and biomarkers were more variable. The most robust findings were the association between pronoun use and most biomarkers, and between cortical thickness and most speech features.

Correlations with clinical endpoints



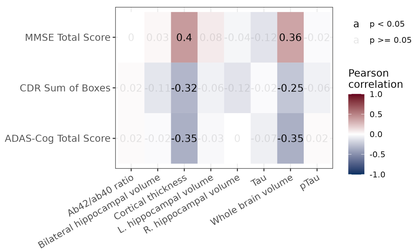
Correlations with speech features



Results: longitudinal associations

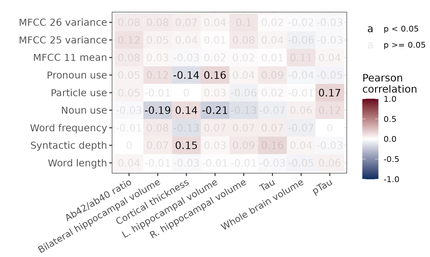
- For all clinical endpoints, longitudinal change scores were significantly correlated with change in whole brain volume and cortical thickness.

Correlations with clinical endpoints



- Longitudinally, several change score correlations between biomarkers and speech characteristics were significant but weaker in magnitude, with most significant findings observed for imaging biomarkers.

Correlations with speech features



Conclusions

- We found converging evidence for stepwise associations between neuroimaging markers and speech features previously shown to track clinical progression in AD.
- Associations with speech were generally weaker than associations with clinical endpoints, consistent with the different level of specificity of each measure (speech vs. general cognition and function).
- Results highlight a disease-level association between speech parameters and neuroimaging markers of AD. Future work will help understand how these findings can be leveraged in screening and monitoring settings.

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