Evaluation of speech-based digital biomarkers for Alzheimer's disease

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Background

Non-invasive, low-cost digital biomarkers for Alzheimer's disease (AD) would represent a major advance for dementia research. Digital biomarkers could facilitate more efficient screening and treatment of disease, and provide more sensitive endpoints for research studies and clinical trials. Speech changes in AD have emerged as an exciting area of research and a promising potential digital biomarker.[1-6] Rigorous validation is needed to better understand what speech features are affected by disease, the time course of speech changes, and how these novel measures compare to current clinical standards.

Objectives:

- Outline a framework for clinical validation of digital biomarkers.
- With reference to this framework, provide evidence on the development of speech-based biomarkers for detecting and monitoring AD.
- Demonstrate what aspects of speech are useful for AD screening and symptom tracking, and present directions for future research and further validation.

Methods

Winterlight uses an automated, natural language processing pipeline to extract >500 acoustic and linguistic variables from speech samples. We developed recommendations for clinical validation and apply them to our novel speech-based digital measures.[7,8] We provide evidence from a series of studies examining the relationship between features extracted from automated speech processing and the presence and severity of cognitive impairment in mild cognitive impairment (MCI) and AD.

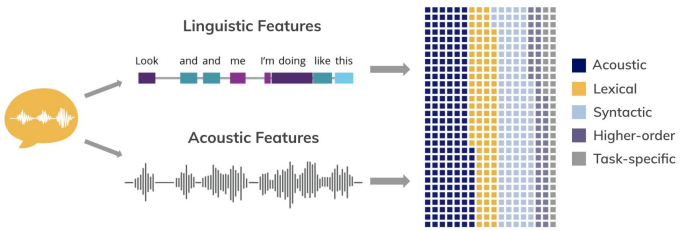


Figure 1: Clinical validation framework for digital biomarkers

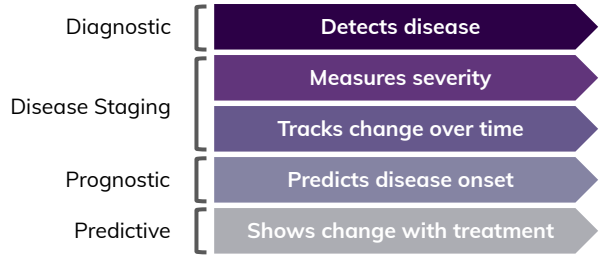
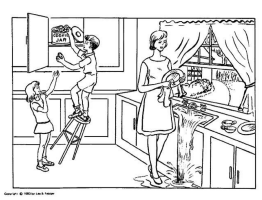


Figure 2: Classification of Alzheimer's Disease based on speech

Detects disease



Picture description task

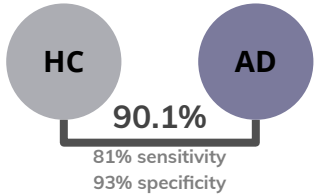


Figure 3: Prediction of MoCA scores based on speech variables

Measures severity

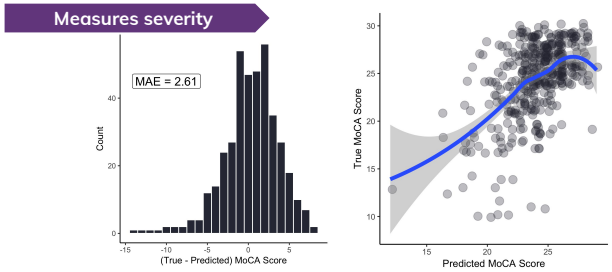
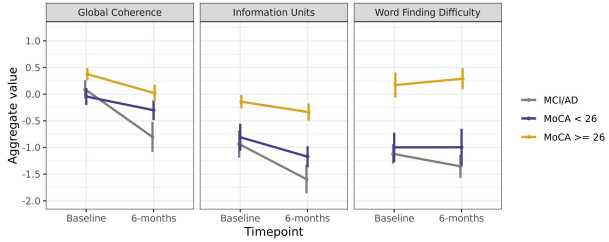


Figure 4: Longitudinal changes in speech in controls & MCI/AD

Tracks change over time



Results

We present a framework for clinical validation for novel digital measures relevant to MCI and AD (Figure 1). Our research shows evidence for speech measures in three aspects of clinical validation:

- **Disease detection**: Our machine-learning models based on picture description speech samples have 90% accuracy when differentiating healthy controls from cases of AD, with high sensitivity (82%) and specificity (91%). (Figure 2)
- **Measuring severity**: We show that speech features can be used to predict scores on clinical measures. In this study, we used speech variables to predict scores on the Montreal Cognitive Assessment (MoCA), within an average of 2.6 points of true values. (Figure 3)
- **Tracking change over time**: We assessed speech in a longitudinal study of community-dwelling older adults, grouped according to MoCA scores, and those with diagnoses of MCI or early MCI. We identified measures that differ between groups and show declines over time, including exploratory composite scores relating to the information content and coherence of speech. (Figure 4)

Conclusions

Together, these studies show how speech represents a promising potential biomarker for AD by demonstrating diagnostic specificity, change with disease progression and correlation with current clinical tools. Collection of speech is naturalistic, low-cost and requires little training, making it a flexible tool for clinicians and researchers. Future work will continue to develop and refine speech-based biomarkers for identifying and tracking AD onset and progression. In addition, more work is needed to demonstrate how speech measures can be used to predict disease before onset and measure response to effective treatment.

References

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