Characterizing progressive speech changes in prodromal-to-mild Alzheimer's disease using natural language processing

Jessica Robin[1], Mengdan Xu[1], Aparna Balagopalan[1], Jekaterina Novikova[1], Laura Kahn,[2] Abdi Oday,[2] Mohsen Hejrati,[2] Somaye Hashemifar,[2] Mohammadreza Negahdar,[2] William Simpson,[1] Edmond Teng[2]

[1]Winterlight Labs, Inc., Toronto, Ontario, Canada; [2]Early Clinical Development, Genentech, Inc, South San Francisco, CA, USA

Background

- Novel automated tools for analyzing speech and language may provide new insights into Alzheimer's disease (AD).
- Recent studies have focussed on identifying the presence of AD based on speech, using natural language processing and machine learning models.[1-4]
- Less is known about the longitudinal progression of speech changes in AD and how these may be useful for monitoring disease over time.[5-7]
- Current clinical assessments to monitor speech and language symptoms can be burdensome and may have limited sensitivity to detect changes.
- Through automated analyses of open-ended naturalistic speech collected from a standardized clinical interview, we developed a novel measure to characterize progressive speech changes in AD.

Methods

- We analyzed Clinical Dementia Rating (CDR) recordings from a subset of 101 English-speaking, US-based participants (58F, 43M, mean age = 69 years, SD = 7) from the Tauriel trial of semorinemab in prodromal-to-mild AD (NCT03289143). All participants were grouped together since no effects of treatment group were detected on clinical outcome measures.[8]
- CDR recordings were collected at the baseline, 6-month, 12-month and 18-month timepoints.
- Recordings were segmented, diarized, and transcribed to identify the participant's responses to the recent experience section of the clinical interview.
- Speech samples were analyzed using the Winterlight speech analysis platform which generates >500 acoustic and linguistic features from the audio recording and text transcript of each sample.
- Controlling for age, sex and level of education, we identified multiple features that had significant linear effects of time (indicating progressive longitudinal change) from baseline to 18-months.
- Selected speech features were combined into an unweighted composite speech score to measure multimodal speech changes, and compared with other clinical endpoints from the trial.

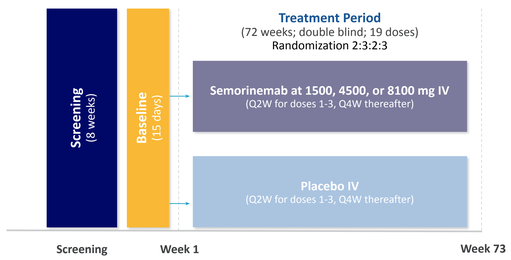

Figure 1: Development of speech composite score for tracking longitudinal change in early AD

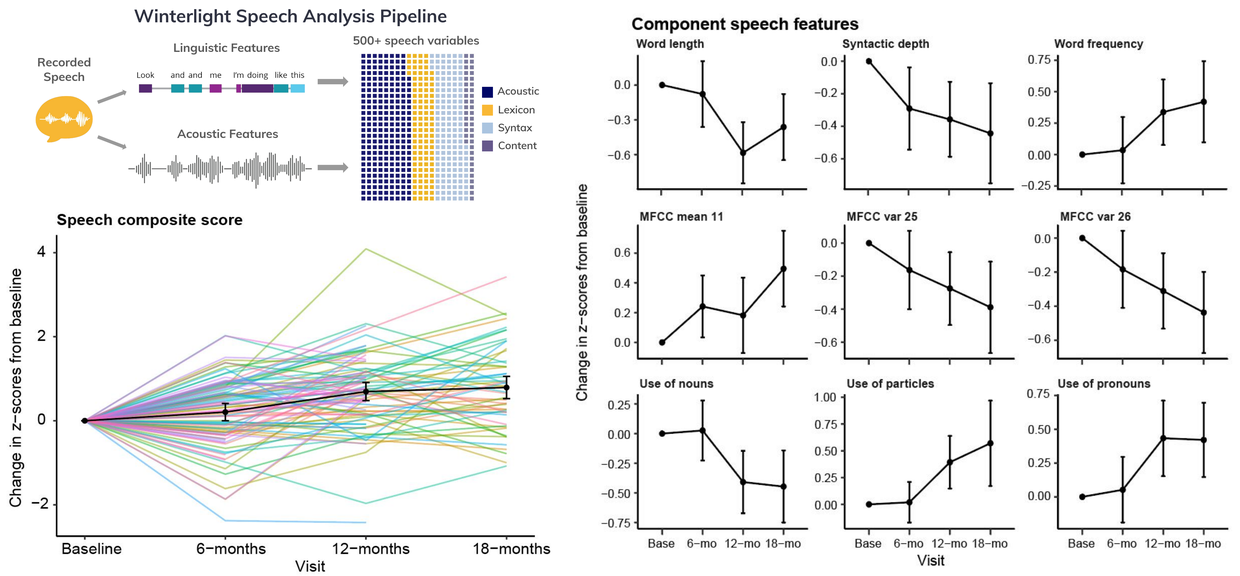

Figure 2: Comparison of novel speech composite score to clinical and language scales

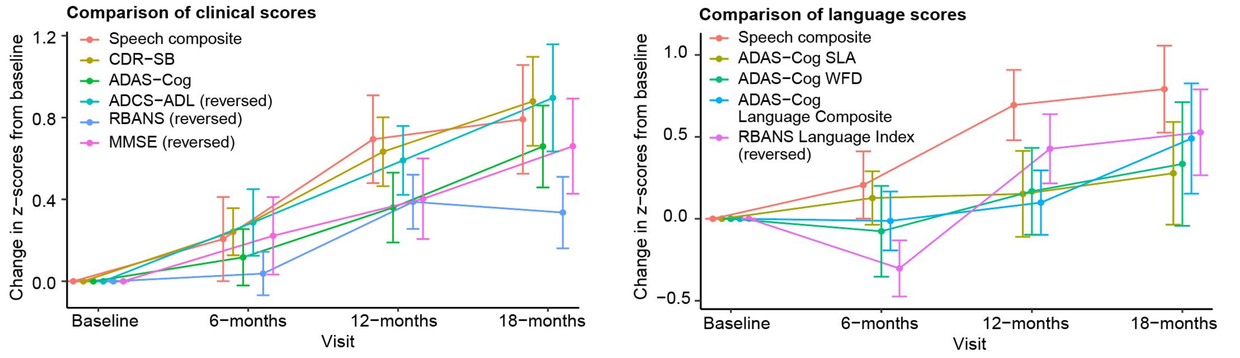

Figure 3: Replication in held-out dataset

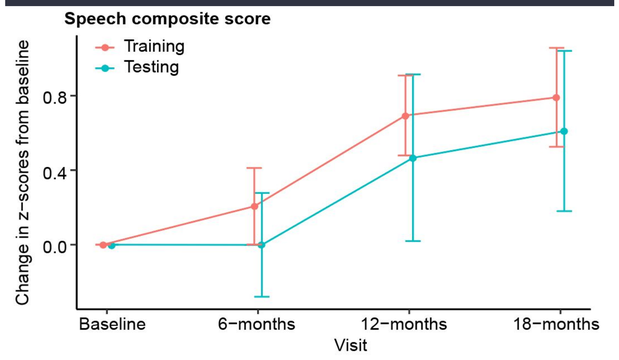

Table 1: Standardized change from baseline by score

Score	Effect size
CDR	.30
ADCS-ADL	-.30
Speech composite	**.29**
Speech composite (replication)	**.26**
MMSE	-.23
ADAS-Cog	.22
RBANS	-.19
RBANS language index	-.15
ADAS-Cog language composite	.16
ADAS-Cog word finding difficulty	.12
ADAS-Cog spoken language ability	.09

Results

- We developed a novel speech composite score that showed significant longitudinal change from baseline to trial endpoint (18 months).
- The composite score included six linguistic features and three acoustic features, relating to word length, word frequency, syntactic depth, use of nouns, pronouns and particles, and acoustic characteristics based on the power spectrum of the voice (Figure 1).
- When standardized and compared with clinical endpoints (Figure 2; Table 1), the speech composite had a similar or greater effect size for detecting longitudinal change compared to standard assessments of cognition and function including the CDR, ADAS-Cog, and RBANS, and language subscales of the ADAS-Cog and RBANS.[9]
- To test the generalizability and replicability of the speech composite, we computed the composite score in a held-out test data set (n = 26) from the same trial, and found similar longitudinal progression (Figure 3).

Conclusions

- Progressive speech changes are detectable in early AD and measurable via automated language processing tools.
- Using open-ended speech samples from a standard clinical interview, this study developed a novel speech-based composite score to characterize changes in speech and language in prodromal-to-mild AD and monitor them over time.
- Speech-based scores can be computed in an automated, objective way, and have the potential to be sensitive measures of disease progression and/or treatment response for speech-related symptoms in AD, without contributing to additional patient burden.
- These results represent a promising prototype, but further validation is needed to replicate these findings and confirm the clinical and neuropathological relevance of this novel measure.

References

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Contact: jessica@winterlightlabs.com