Tracking changes in cognition in Mild Cognitive Impairment and Alzheimer's Disease over a 6-month period using a speech-based digital biomarker

Jessica Robin [1], William Simpson [1,2], Liam D Kaufman [1]

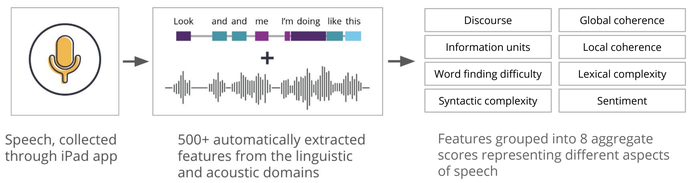
(1) Winterlight Labs, Toronto, ON, Canada, (2) Department of Psychiatry and Behavioural Neuroscience, McMaster University, Hamilton, ON, Canada

Background

A lack of precision in quantifying cognitive performance is a key pillar in the overwhelmingly negative results obtained from clinical trials in Alzheimer's Disease (AD). Language may provide sensitive insights into cognitive function and is a low-cost, non-invasive, naturalistic measure. In AD, changes have been reported in the acoustic and linguistic characteristics of speech, which may be detectable years before a clinical diagnosis is made *(1,2)*. The objective of this study was to compare how language and cognition changed over a 6-month period in a sample of individuals with mild cognitive impairment (MCI) and mild AD, using a novel speech-based digital biomarker and current gold standard cognitive assessments.

Methods

- Participants were 24 individuals with MCI or mild AD (aged 64-87 years, mean age at baseline = 76.5 years) recruited at clinical sites in Canada.
- N = 15 participants completed a tablet-based speech assessment which included two picture description tasks at Baseline and 6-month timepoints.
- Verbal responses to the picture description task were recorded, transcribed and analyzed to produce more than 500 individual speech and language markers.
- From these markers, 8 aggregate scores (expressed as z-scores from healthy norms), chosen for their previous association to AD *(1)*, were produced describing: discourse, information units, word finding difficulty, syntax, coherence (global and local), lexical complexity and sentiment.
- At baseline and 6 months, participants also completed a neuropsychological assessment including:
  - Montreal Cognitive Assessment (MoCA)
  - Alzheimer's Disease Assessment Scale - cognitive subscale (ADAS-Cog)
  - Digit Span tests (forward and backward)
  - Hopkins Verbal Learning Test (HVLT)
  - Symbol Digit Modalities Test (SDMT)
  - Judgment of Line Orientation test (JLO)
- Baseline to endpoint changes were evaluated using non-parametric, within-subjects t-tests. Threshold p-values were set using a Bonferroni correction.



Speech, collected through iPad app

500+ automatically extracted features from the linguistic and acoustic domains

Features grouped into 8 aggregate scores representing different aspects of speech

Figure 1: Baseline to endpoint change in aggregate markers of speech and language capability

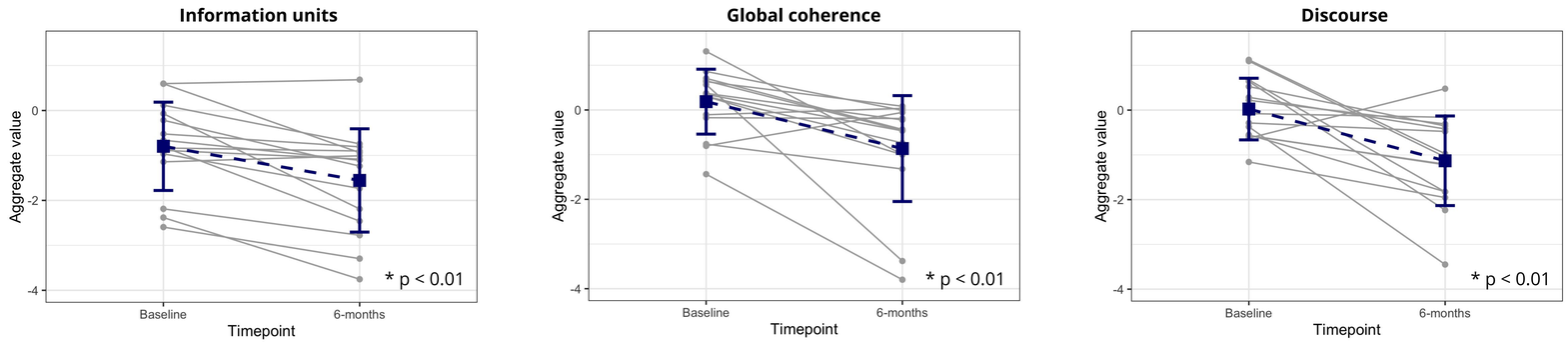


Figure 2: Baseline to endpoint change in neuropsychological assessment scores

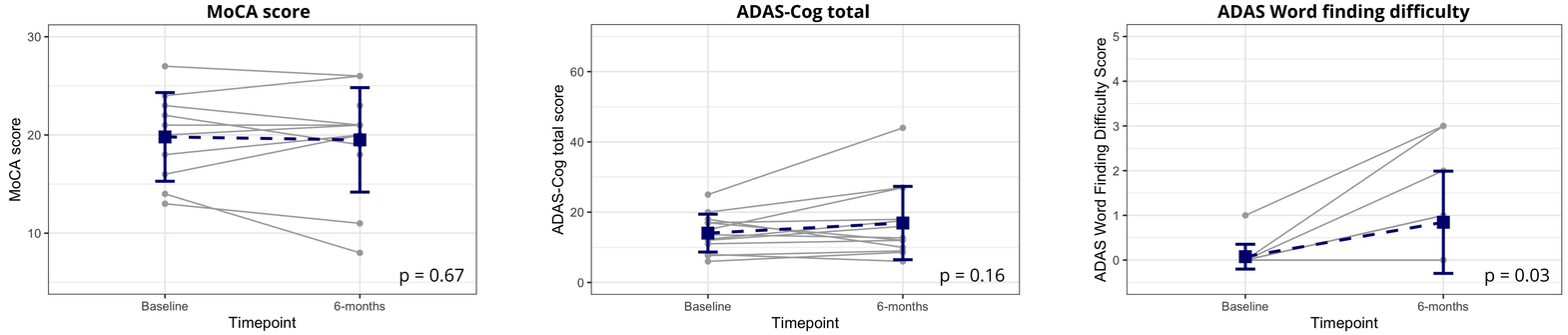


Table 1: Non-parametric, within-subjects t-test results

Speech Aggregate	p-val.	Effect size
Discourse	0.002*	-1.34
Information Units	0.0006*	-0.69
Word Finding Difficulty	0.76	0.17
Syntactic Complexity	0.36	-0.18
Global Coherence	0.002*	-1.04
Local Coherence	0.72	-0.08
Lexical Complexity	0.39	-0.17
Sentiment	0.98	-0.11

Neuropsych Score	p-val.	Effect size
MoCA	0.67	-0.09
ADAS-Cog Total	0.16	0.27
ADAS Word Finding Difficulty	0.03	0.71
ADAS Spoken Language Ability	0.34	0.58
Digit Span (backward)	0.75	-0.03
HVLT (free recall)	0.86	-0.04
SDMT (total correct)	0.83	-0.13
JLO (total correct)	0.69	0.21

* Statistically significant with Bonferroni correction

Conclusions

- Three speech and language aggregates showed significant declines from baseline to endpoint, consistent with previous results in healthy, older adults *(3)*.
- Some neuropsychological measures show numerical decline over six months, but none were significant after Bonferroni correction.
- These results suggest that speech measures may be more sensitive to changes over six months than traditional neuropsychological tools.
- Speech-based biomarkers show promise as sensitive measures of cognitive change in MCI and AD patients.

References

(1) Slegers, A., Filiou, R.-P., Montembeault, M. & Brambati, S. M. Connected Speech Features from Picture Description in Alzheimer's Disease: A Systematic Review. *J. Alzheimers. Dis.* 65, 519–542 (2018).

(2) Ahmed, S., Haigh, A.-M. F., de Jager, C. A. & Garrard, P. Connected speech as a marker of disease progression in autopsy-proven Alzheimer's disease. *Brain* 136, 3727–3737 (2013).

(3) Simpson, W., Balagopalan, A., Kaufman, L.D., Yancheva, M. Comparing a speech-based digital biomarker to the Montreal Cognitive Assessment (MoCA) for tracking cognition over a 6-month period in a naturalistic cohort of older adults. *CTAD Conference* (2019).

Presented at ISCTM 16th Annual Scientific Meeting, Washington, DC, USA. February 19-21, 2020