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

William Simpson, PhD [1,2] , Aparna Balagopalan, MSc [2], Liam D Kaufman, MSc [2], Maria Yancheva, MSc [2]

(1) Department of Psychiatry and Behavioural Neuroscience, McMaster University, Hamilton, ON, Canada, (2) Winterlight Labs, Toronto, 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). For example, both the ADAS-Cog (1) and MMSE (2) have well established limitations, including floor/ceiling effects, practice effects and poorer psychometric properties for milder forms of impairment. This can lead to masking of clinically relevant treatment effects particularly within the short time frame of a clinical trial. Computerized cognitive assessment batteries have ameliorated some issues but are also far from perfect (3). Speech represents an excellent, novel input for a digital biomarker. It has a stable, linear association with AD severity (4) and is simple to collect, requiring minimal equipment and rater training. Speech-based digital biomarkers developed using natural language processing and machine learning could significantly reduce measurement variance by producing objective, consistent estimates, thereby yielding greater precision and greater sensitivity to change compared to existing gold standards. The objective of this study was to compare how cognition changed over a 6 month period in a naturalistic cohort of older adults when measured via a gold standard brief cognitive assessment and speech-based digital biomarker.

Methods

- Participants were 111 older adults (aged 55-90), recruited from the community and independent living facilities in Canada and the US.
- Participants completed a tablet-based speech assessment which included two picture description tasks at Baseline, 1 month and 6 month timepoints.
- At baseline and 6 months, a MoCA was administered by a trained psychometrist.
- 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 (5), were produced describing: discourse, information units, word finding difficulty, syntax, coherence (global and local), lexical complexity and sentiment.
- Baseline to endpoint changes were evaluated using non-parametric, within-subjects t-tests. Threshold p-values were set using a Bonferroni correction.

Results

- 58 individuals completed the baseline and 6 month assessments
- Mean MoCA scores and distribution of Baseline to 6-month change are depicted in Figure 1
- Longitudinal changes in individual feature aggregates are depicted in Figure 2 (**Statistically significant with Bonferroni correction)
- Results of non-parametric, baseline to 6-month within-subjects t-tests for each aggregate are summarized in Table 1. Correlations are summarized in Table 2.

Figure 1:
(A) Distribution of change scores (+ = improvement, - = worsening) for MoCA
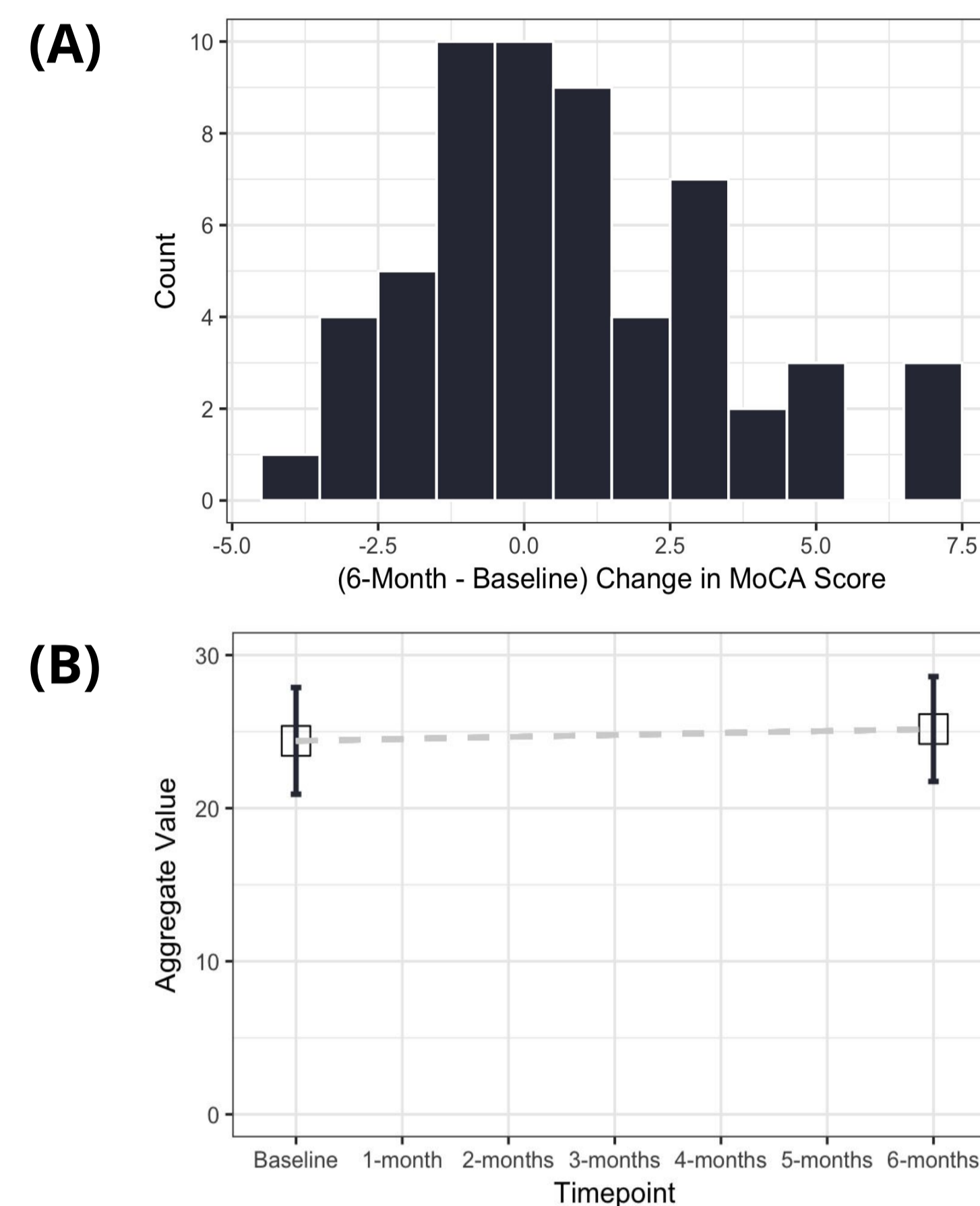(B) Group mean of MoCA scores at baseline and 6-months

(A)

(B)

Figure 2:
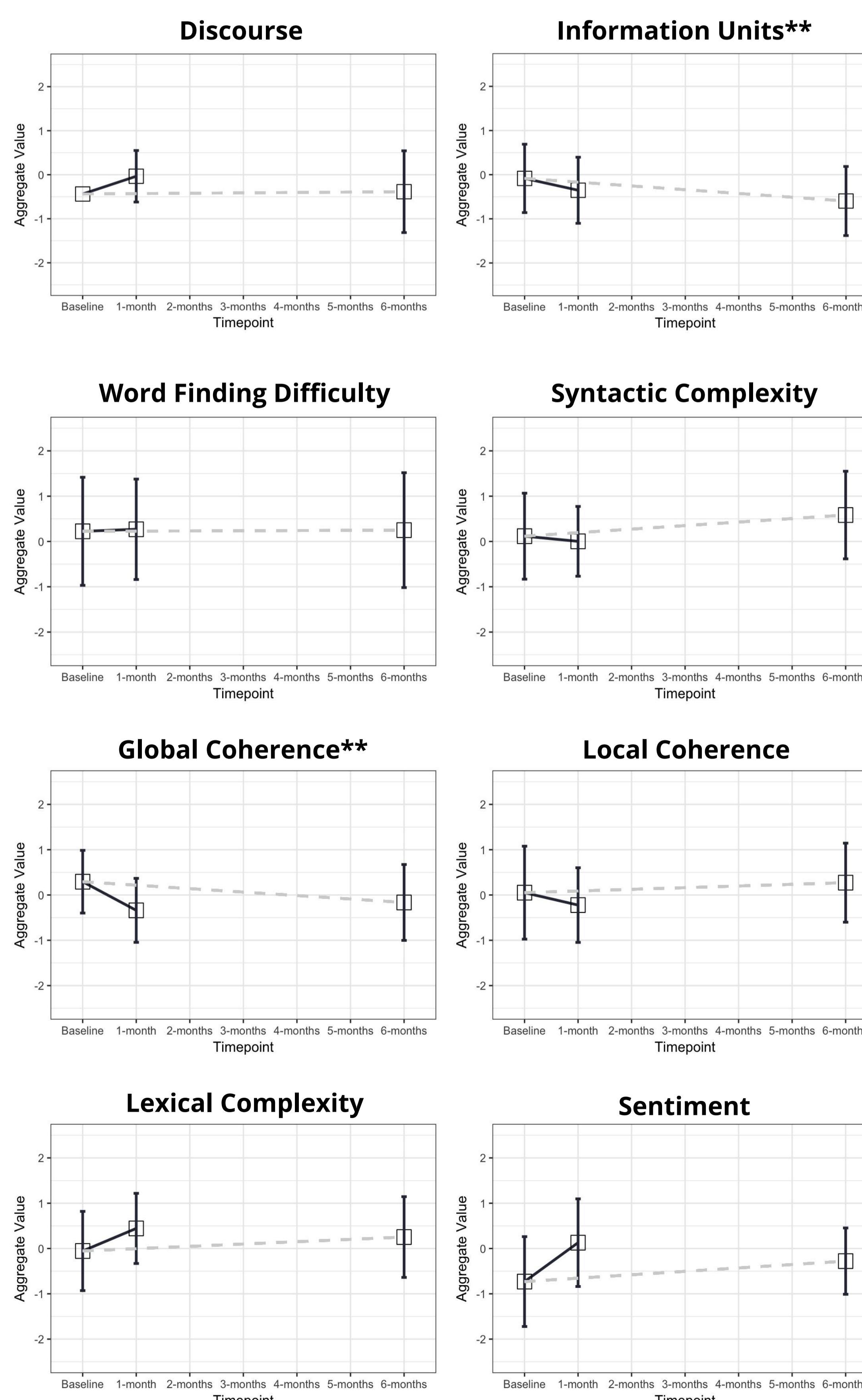Group level baseline to endpoint change in aggregate markers of speech and language capability

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

Aggregate	Mean Difference	p-value
Discourse	0.107	0.49
Information Units**	-0.495	0.00012**
Word Finding Difficulty	0.039	0.965
Syntactic Complexity	0.509	0.0055
Global Coherence**	-0.479	0.000059**
Local Coherence	0.230	0.118
Lexical Complexity	0.278	0.0059
Sentiment	0.473	0.0068

Table 2:
Spearman correlations between aggregate and MoCA score

Aggregate	rho
Discourse	0.016
Information Units	0.248
Word Finding Difficulty	-0.363
Syntactic Complexity	0.185
Global Coherence	0.119
Local Coherence	0.117
Lexical Complexity	0.343
Sentiment	0.026

Conclusions

This preliminary study highlights statistically significant reductions in two components of language previously associated with AD severity (coherence and information units) over a 6 month period, with no accompanying reductions in cognitive status as measured by the MoCA. These data provide preliminary support for the use of speech-based digital biomarkers as sensitive tools for detecting subtle changes in cognition within clinical trials. Replication with larger cohorts, followed for >6 months is required.

References

(1) Cano, S. J. et al. The ADAS-cog in Alzheimer's disease clinical trials: psychometric evaluation of the sum and its parts. J. Neurol. Neurosurg. Psychiatry 81, 1363–1368 (2010).
(2) Nieuwenhuis-Mark, R. E. The death knoll for the MMSE: has it outlived its purpose? J. Geriatr. Psychiatry Neurol. 23, 151–157 (2010).
(3) Lenehan, M. E., Summers, M. J., Saunders, N. L., Summers, J. J. & Vickers, J. C. Does the Cambridge Automated Neuropsychological Test Battery (CANTAB) Distinguish Between Cognitive Domains in Healthy Older Adults? Assessment 23, 163–172 (2016).
(4) 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).
(5) 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).