Validation of an objective, speech-based object content score for measuring disease progression in AD

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Background

- Speech and language changes are well known to occur in Alzheimer's disease (AD), with patients frequently described as having "empty speech" lacking in information content.[1,2,3]
- Novel tools to objectively measure speech and language content can help to quantify this clinical symptom and provide measures of disease severity and progression.[4,5]
- By using a picture description task and natural language processing analyses, we developed an object content score to measure the information provided when describing a picture.
- In this study, we collected brief picture description speech assessments over the course of a 48-week AD clinical trial, which were administered via a tablet and took less than five minutes to complete.
- Our objective was to assess the validity of the object content score by examining its progression within the placebo arm of the 48 week study period and correlations with other clinical scores.

Methods

- 148 English-speaking participants with mild-to-moderate AD were randomized into the placebo arm of a clinical trial.
- Participants completed the Winterlight Speech Assesment at basline and follow up assessments at 12 weeks (n = 128), 24 weeks (n = 125) and 48 weeks (n = 98). Speech assessments were administered by a trained rater during each clinical visit.
- Each speech assessment included two picture description tasks: open-ended speech tasks in which participants are shown a line drawing of a scene and asked to describe it. Participants use their own words to describe the picture and have no time limit or feedback.
- Speech recordings were captured by the device's microphone and processed using the Winterlight speech analysis platform.
- Text transcripts were generated for every recording and objective measures of information content were automatically computed based on custom natural language processing algorithms.
- Object content scores measure the proportion of items in the pictures that are correctly named in the participant's description. Object content scores were averaged across the two pictures at each assessment.
- To test the sensitivity of object content scores to longitudinal change in untreated mild-to-moderate AD, we used a linear mixed model to estimate the slope of change over 48 weeks.
- To validate the object content score, we calculated correlations between it and other trial endpoints, including the ADAS-Cog, CDR-SB, MMSE and ADCS-ADL, both at baseline and in terms of baseline to endpoint change.
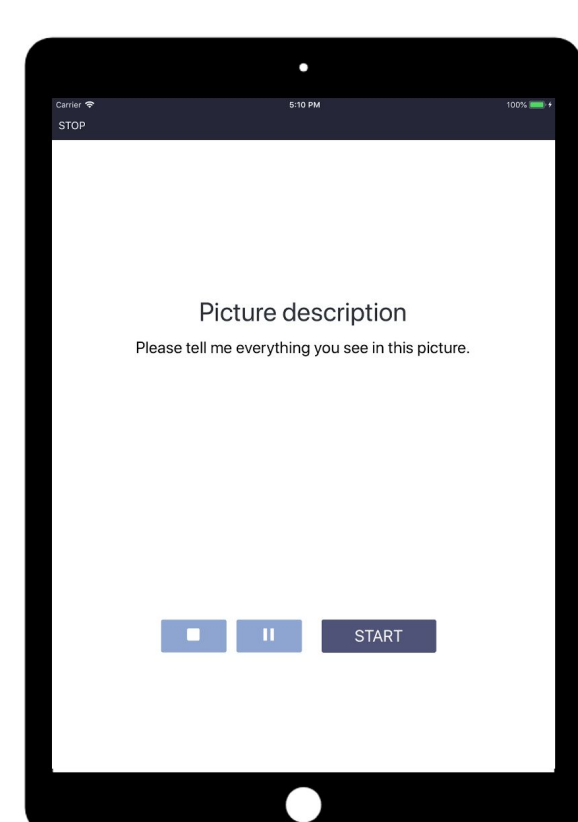
... there's a girl sitting on a stool, holding a tomato. The dog has a spatula and is heading toward the tv...

Object content score = proportion of correctly named objects in the picture

Figure 1: Mean change from baseline (CFB) in object content scores, at 12-, 24- and 48- weeks
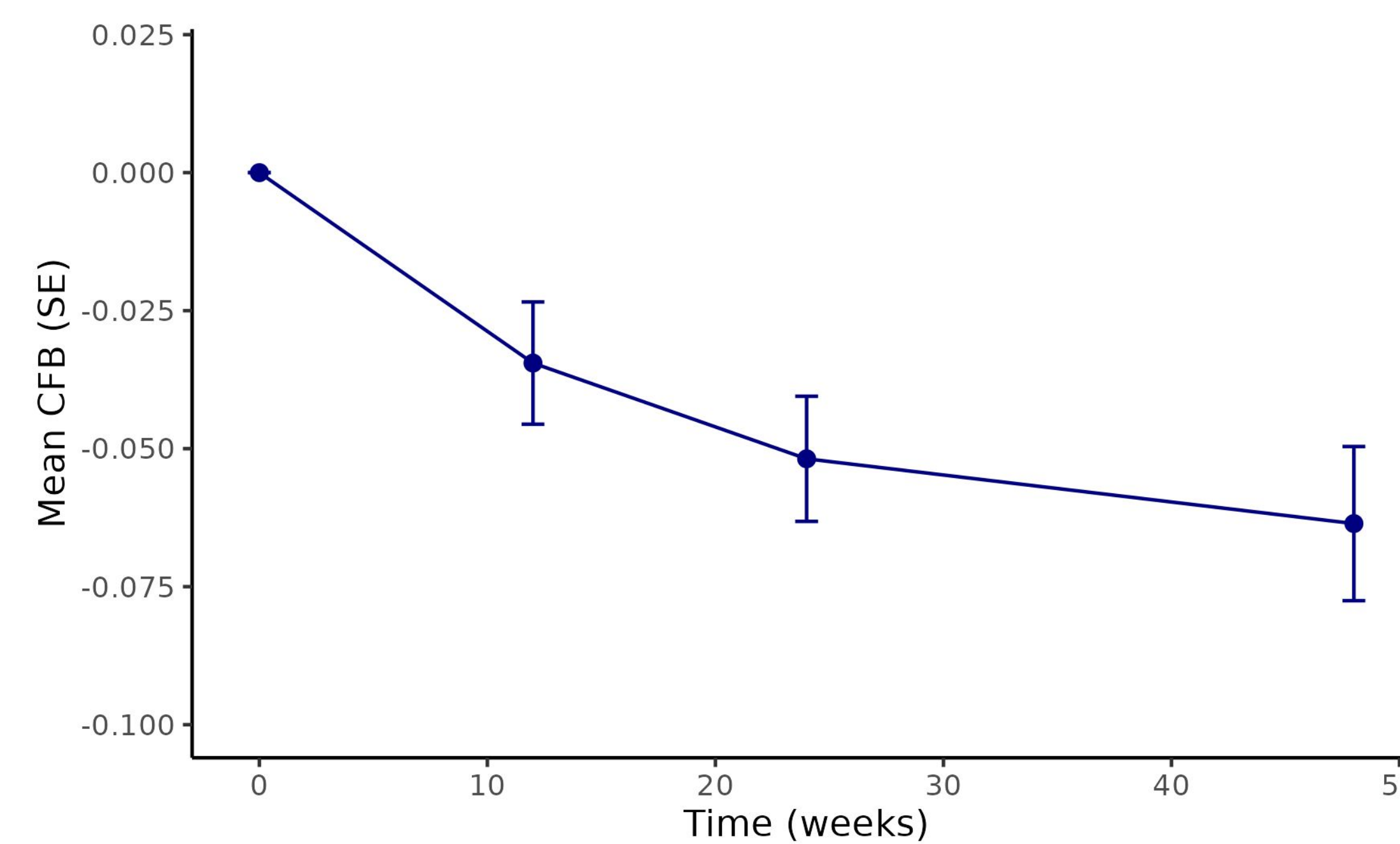

Figure 2: Change from baseline in object content scores, subgrouped based on change in ADAS-Cog total scores
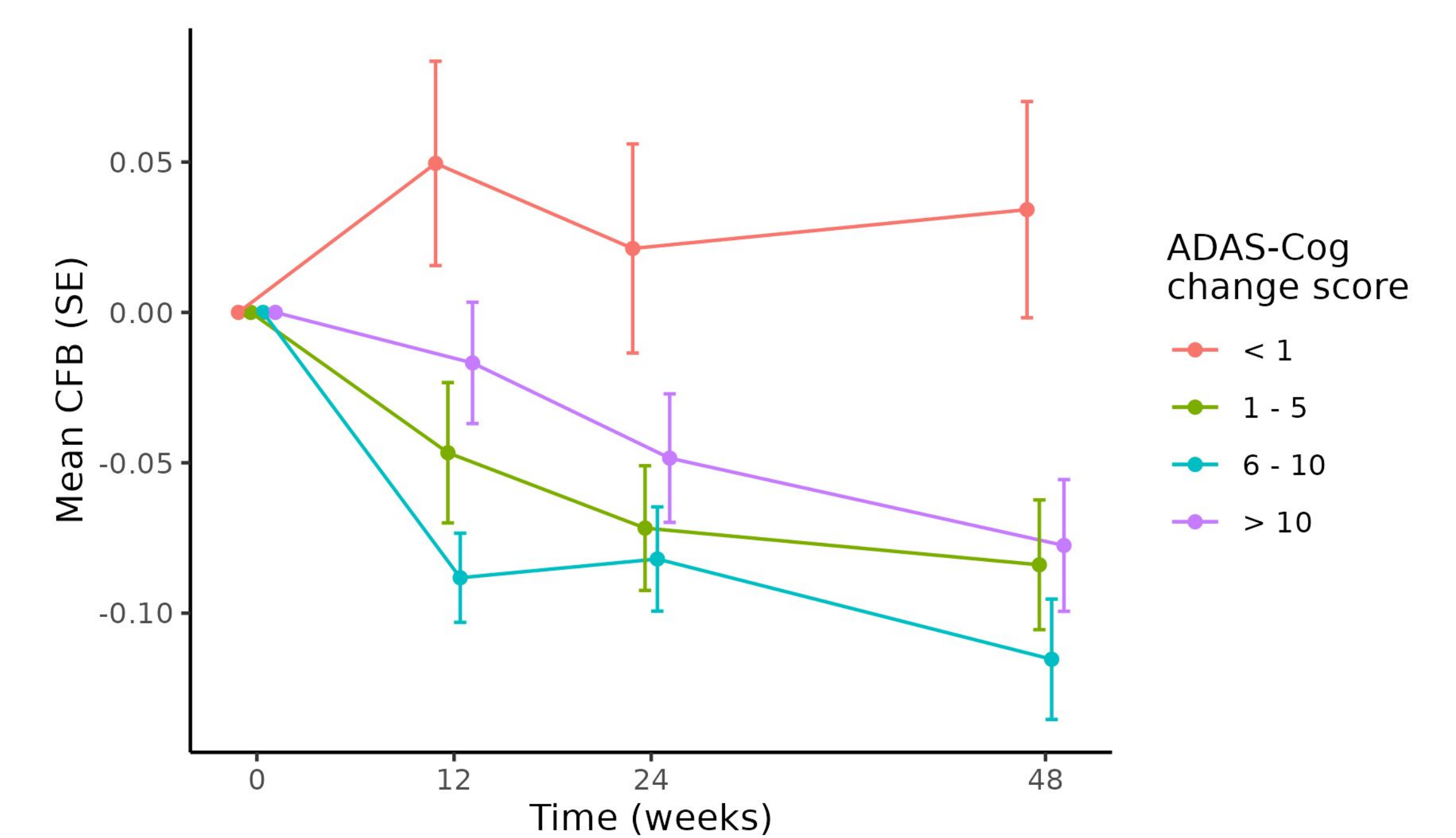

Figure 3: Correlations between object content scores and ADAS-Cog total scores, for baseline and change from baseline
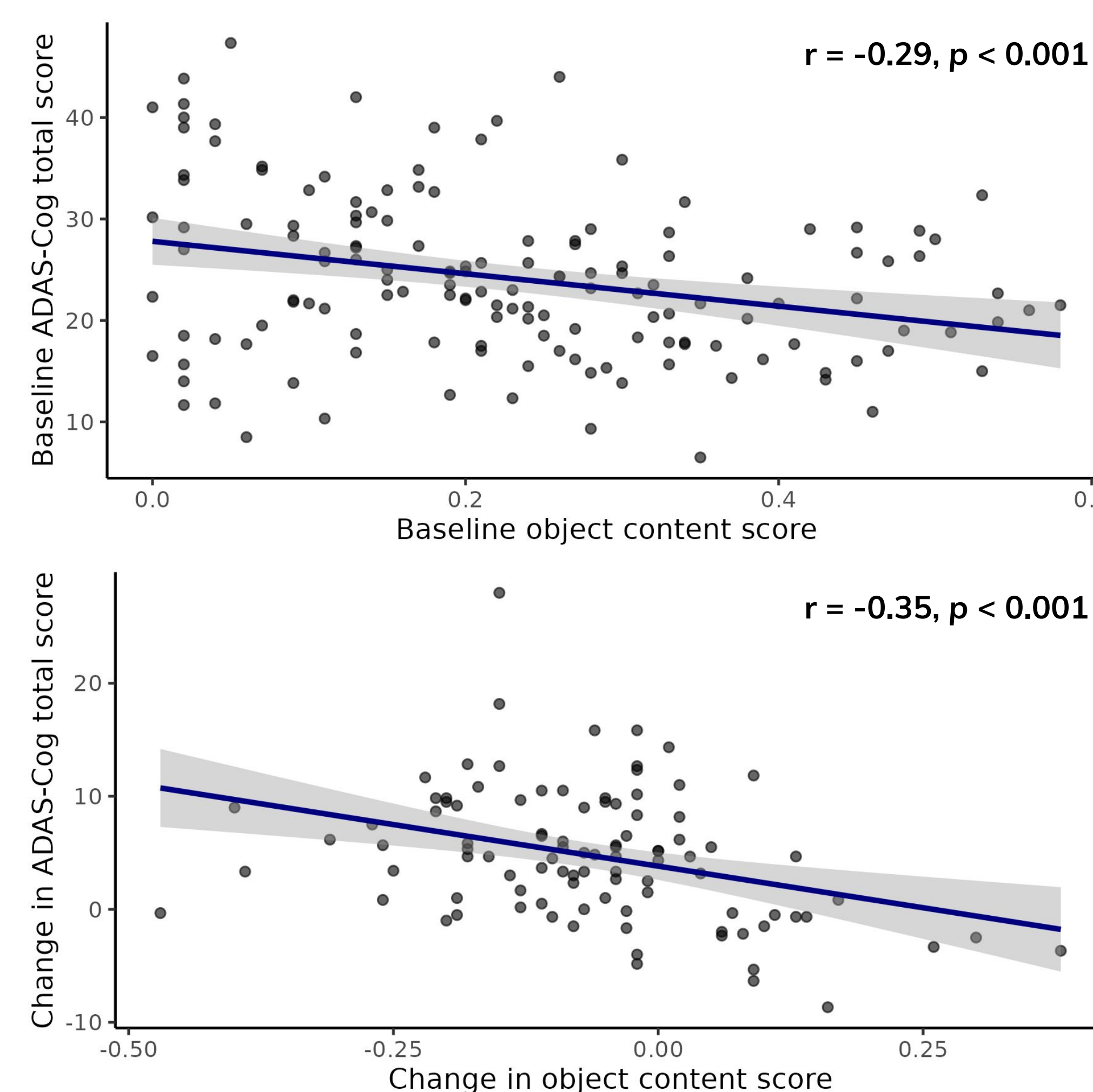

r = -0.29, p < 0.001

r = -0.35, p < 0.001

Table 1: Pearson correlations between baseline object content scores and baseline clinical scores

BASELINE	n	Correlation coefficient	p value
ADAS-Cog Score	148	-0.29	<0.001
ADCS-ADL Score	148	0.23	0.005
CDR-SB Score	148	-0.16	0.06
MMSE Score	148	0.24	0.003

Table 2: Pearson correlations between baseline-endpoint change in object content scores and change in clinical scores

CHANGE FROM BASELINE	n	Correlation coefficient	P value
ADAS-Cog Score	98	-0.35	<0.001
ADCS-ADL Score	98	0.29	0.004
CDR-SB Score	98	-0.17	0.10
MMSE Score	98	0.36	<0.001

Results

- Object content scores were found to show significant decline in the placebo group over the 48 week trial period, consistent with disease progression and decreased information content in speech (estimated slope of change = -0.05, t = -4.63, p < 0.001, Figure 1).
- Baseline object content scores had significant correlations with baseline scores of cognition and function (Table 1 and Figure 3), including the ADAS-Cog, MMSE and ADCS-ADL, but not CDR-SB.
- Baseline to endpoint (48-weeks) change in object content scores was significantly correlated with change in clinical scores (Table 2 and Figure 3), including the ADAS-Cog, MMSE and ADCS-ADL, but not CDR-SB.
- When participants were grouped based on change in ADAS-Cog from baseline to trial endpoint, those whose ADAS-Cog scores increased (indicating increasing cognitive impairment) had overall declines on object content scores (Figure 2). In contrast, in those whose ADAS-Cog scores improved, there was no decline in object content scores.

Conclusions

- This study provides initial validation of a speech-based, objective measure of information content as a measure of disease severity in mild-to-moderate AD.
- We found that in a placebo group of individuals with mild-to-moderate AD, object content scores showed significant decline over 48 weeks, consistent with disease progression.
- Object content scores had moderate correlations with standard trial endpoints measuring cognition and function.
- Notably, the strongest correlations were with the cognitive scales (ADAS-Cog and MMSE), suggesting that object content scores are more closely related to measures of cognition.
- In contrast to standard clinical assessments, object content scores are derived from an app-based speech assessment, which takes less than 5 minutes to complete and requires minimal instruction or training.
- Digital speech-based measures have the potential to reduce patient burden and improve sensitivity in assessing language and cognition in future AD trials.

References

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