PROSPECT-AD: Population-based screening over speech for clinical trials in AD

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Introduction

Language and speech impairments are an early feature of neurodegenerative dementias. Consequently, digital biomarkers of language and speech performance can be promising tools for early diagnosis. The current "new era of Alzheimer's disease (AD) clinical trials" suggests a shift to very early identification of people at risk. To this end, digital markers of language and speech could be employed for screening at-risk populations at a prodromal stage of AD. In combination with advanced machine learning longitudinal modelling, we conceived a pre-screening battery consisting of speech-based neurocognitive tests, enabling automated first-line pre-screening to be performed remotely using a telephone.

This large pre-clinical cohort study - PROSPECT-AD aims at building and validating speech-based machine learning models for the detection of the relevant phenotype through testing the gold-standard phenotyped cohorts. Specifically, based on information extracted from the participant's speech, to investigate the predictive potential (sensitivity/specificity) for differential/prognostic diagnosis, and its usability for remote pre-screening and monitoring will be examined.

Method

Participants:
From four existing cohorts:
EPAD Scotland (UK), DESCRIBE (Germany), INSIGHT-preAD II (France) and BioFINDER (Sweden)

Participants at preclinical stages are recruited to form a 'probability-spectrum' population covering the entire continuum of anticipated probability for Alzheimer's dementia development.

- 1200 participants
- ≥50 yr, CDR 0, 0.5 or 1
- SCI / MCI & Amyloid +/- & Tau +/-

Remote speech protocol:
- 18-month longitudinal study (see Fig 1. Study protocol)
- Pre-screening battery of speech-based neurocognitive tests remote, decentralized, automated via telephone

ki:e SB-C (ki:elements remote speech biomarker for cognition):
- 10-15 Word List Encoding & Retrieval [Learning & Memory]
- Semantic Verbal Fluency [Executive Functions]

\+ Spontaneous free speech [Psychological and/or behavioral symptoms]

Analysis

Speech data will be compared to neuropsychological evaluations, genetic profiles, biomarkers (Tau & Aβ), neuroimaging data and family history

Speech feature extraction:
- Automatically calculated test scores (e.g. number of correct items)
- Acoustic features
- Prosodic features (pitch, energy) and speech rate
- Voice features: F0, spectral flux, ACF, cepstrum, pitch, onset, beats, energy, voice quality, intensity, vocalisation rhythms
- Content features: sentiment analysis, words, lexical and semantic content

Based on the analysis of vocal performances, advanced machine learning and different computational techniques will be employed to identify the most significant speech markers which could represent an early indicator for a pre-screening scenario.

Timeline

This is an ongoing pre-clinical AD study. At the time of CTAD 2021, data acquisition has started. An interim analysis is expected in Q3 2022 and the final analysis in Q3 2023.

Impact of the expected outcome

The current study should make a major impact on the improvement of drug development research methodology by providing a validated telemedical solution for neurocognitive pre-screening and monitoring of participants of early AD clinical trials.

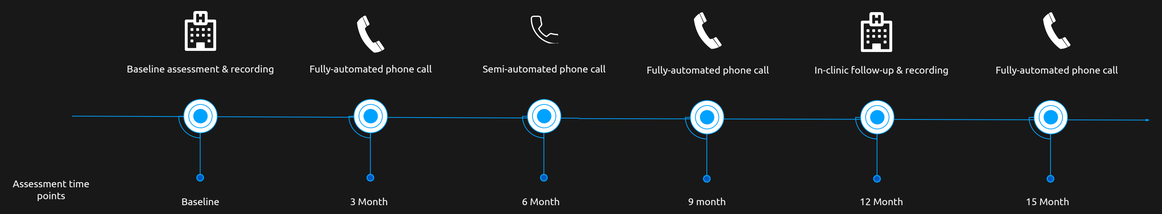

Fig. 1. Study protocol

funded by Alzheimer's Drug Discovery Foundation