

Feasibility of real world end-points of functional neurophysiology in Alzheimer's disease dementia

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Introduction

Clinic-based biomarkers are effective in tracking disease progression in clinical research, but do not scale to support public health needs or large-scale real-world studies. Purely digital markers are scalable but lack the objectivity and neurobiological grounding of clinical measures. These first results of a real-world feasibility study demonstrate that objective measures of a range of domains (including EEG) are user-friendly and suitable for repeated at-home use by patients and older controls.

Methods

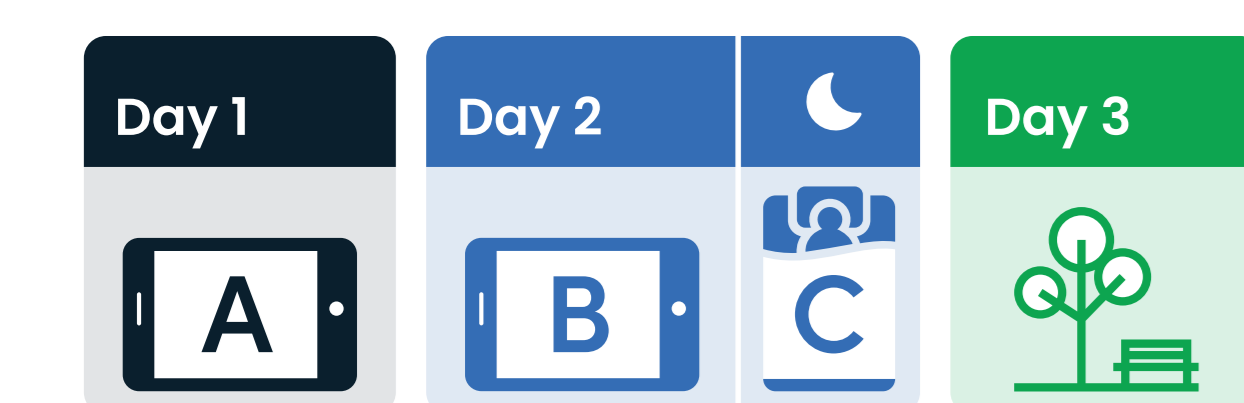
Participants

Patients with mild Alzheimer's type dementia (n=59) and controls (n=60) were recruited for a 1-year study in the UK.

Experimental design

- Participants were asked to complete repeated at-home sessions of ~30 minutes, consisting of behavioral tasks (memory, executive function, affective processing and language), while synchronized EEG was recorded using a self-applied dry-sensor headset.
- All participants have finished the initial 2-week burst sampling period. This is the focus here.

Cycle



A cycle is made up of 3 consecutive days:

- Day 1: Session A
- Day 2: Session B, Session C (overnight)
- Day 3: No Session

Sessions scheduled per cycle. In the 2-week burst stage, 5 cycles (15 sessions) are scheduled.

Analysis

- Session adherence of the burst stage calculated per participant and summarized per group.
- Spearman's correlations calculated between selected behavioral Cumulus variables and paper-based benchmarks.
- Preprocessed and epoched data from the Visual oddball task (Target condition) and the Resting State (2-min eyes close condition).
- Session ERPs and session power spectra (RS) were averaged per participant.

Results

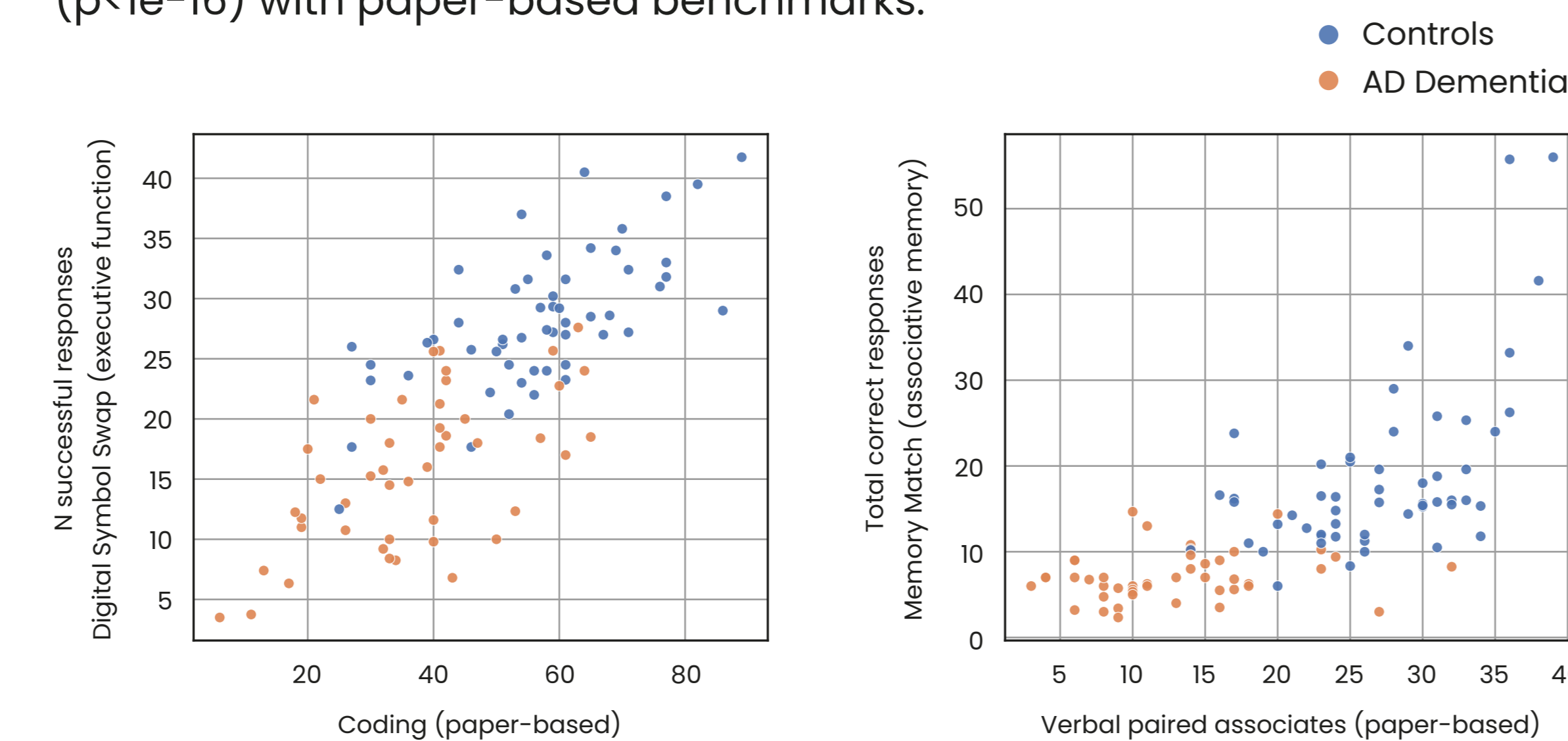
Demographics and adherence

| Variable | Control | AD dementia |
|------------------------------------|-------------------------|-------------------------|
| Demographics | | |
| N | 60 | 59 |
| Mean age | 71.1 (SD 7.2) | 73.7 (SD 6.7) |
| Sex | 31 females, 29 males | 22 females, 37 males |
| Mean ADAS Cog 13 | 9.1 (SD 5.1) | 25.1 (SD 7.9) |
| Mean NART score | 41.4 (SD 4.8) | 36.2 (SD 9.02) |
| Education (N) | | |
| Left formal education by age 18 | 25 | 30 |
| Undergraduate or equivalent | 25 | 14 |
| Master degree or PhD or equivalent | 10 | 15 |
| Withdrawals (N) | 4 | 12 |
| Adherence Burst stage | | |
| N | 56 | 47 |
| Mean session adherence | 83.3% (SD 20.6%) | 75.0% (SD 28.7%) |
| Mean number of sessions | 12.1 (SD 3.4) | 10.5 (SD 4.4) |

Demographics of participants. ADAS Cog: Alzheimer's Disease Assessment Scale – Cognitive Subscale; NART: National Adult Reading Test; SD: standard deviation.

Correlations with benchmarks

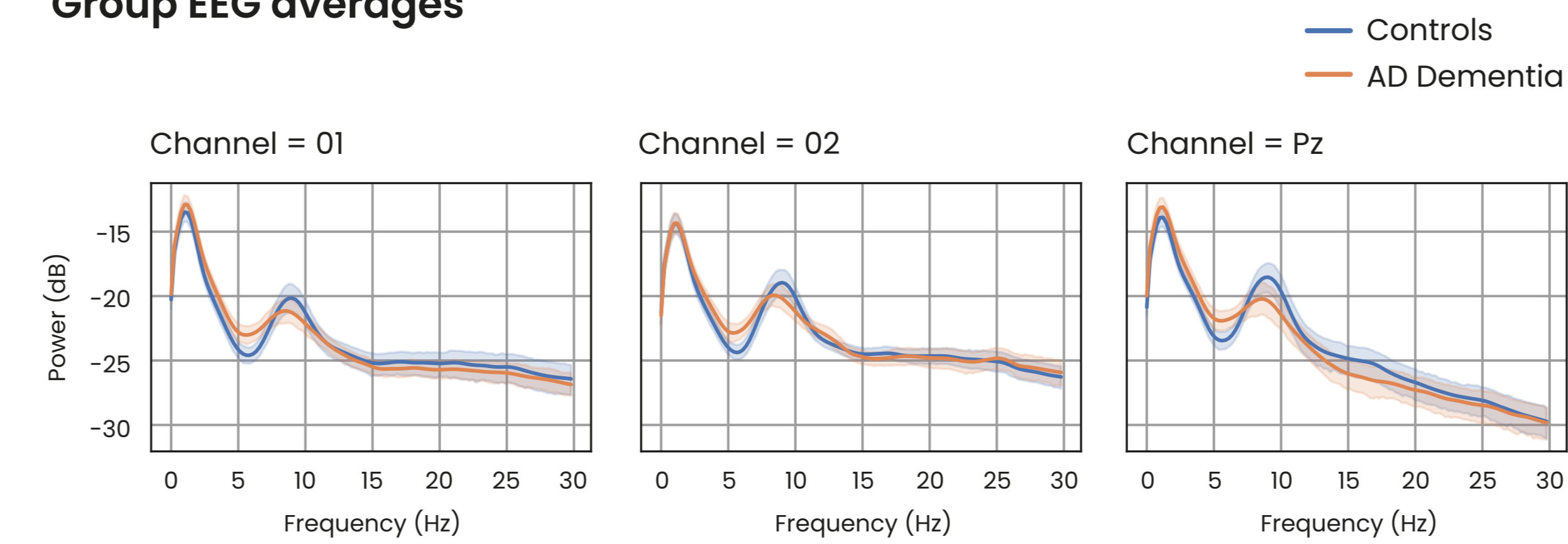
Behavioral Cumulus variables showed a strong correlation ($p < 1e-16$) with paper-based benchmarks.



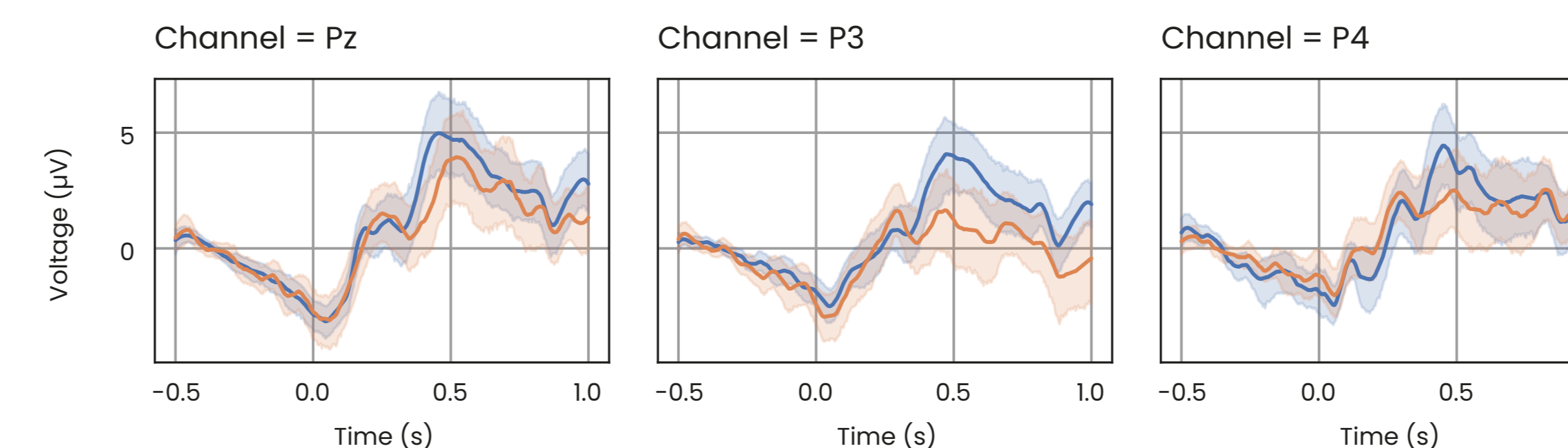
Scatterplots of Cumulus variables against paper-based benchmarks.

Left: The Cumulus' Digital Symbol Swap Test (DSST) showed a correlation with the Coding assessment of 0.76 ($p=4.6e-20$). Right: The Cumulus' Memory Match task showed a correlation with the Verbal paired associates (VPA) assessment of 0.75 ($p=6.2e-19$).

Group EEG averages



Group PSDs of channels O1, O2 and Pz during RS eyes close. The alpha peak is reduced and slowed down in the group with dementia when compared to the control group. The theta band is increased when compared to the control group. 95% confidence intervals were obtained with 1000 bootstrapped samples.



Group ERPs of the Target condition of channels Pz, P3, and P4. The Target condition of the visual oddball task elicited a P300 over channel Pz, with a smaller amplitude in the Dementia group compared to Controls. 95% confidence intervals were obtained with 1000 bootstrapped samples.

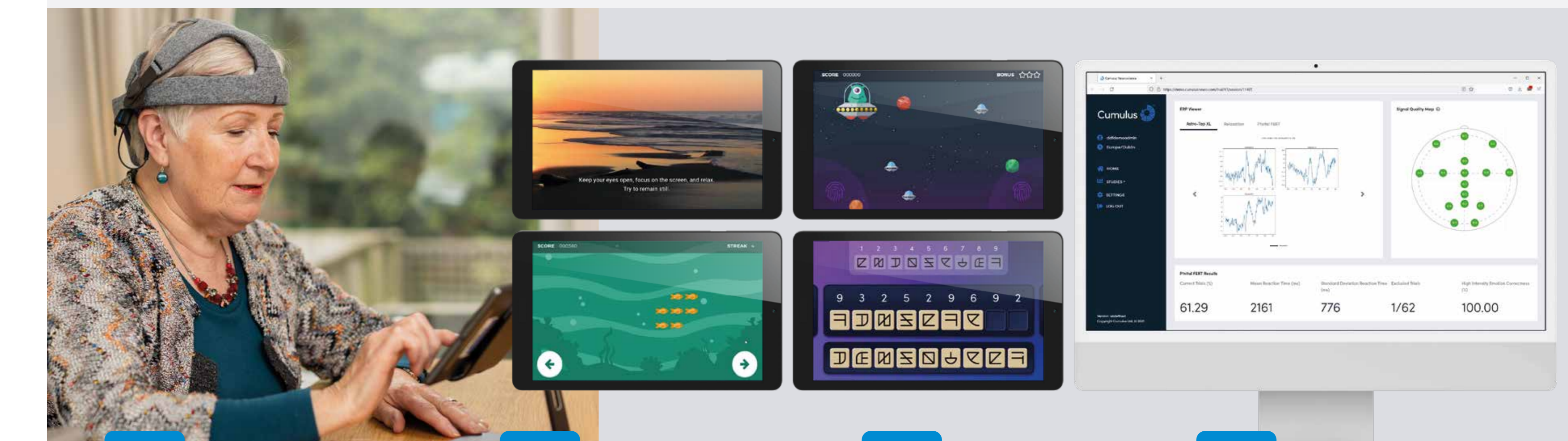
Discussion

- Interim data from this first-in-class study suggest that patients with mild Alzheimer's disease dementia are capable and willing to participate in intensive home-based functional neurophysiology studies, if technology is designed to be engaging and easy to use.
- Initial examination of the data aligns with established benchmarks, and with the literature on functional impairment in AD, constituting positive early evidence for construct validity and technical feasibility.

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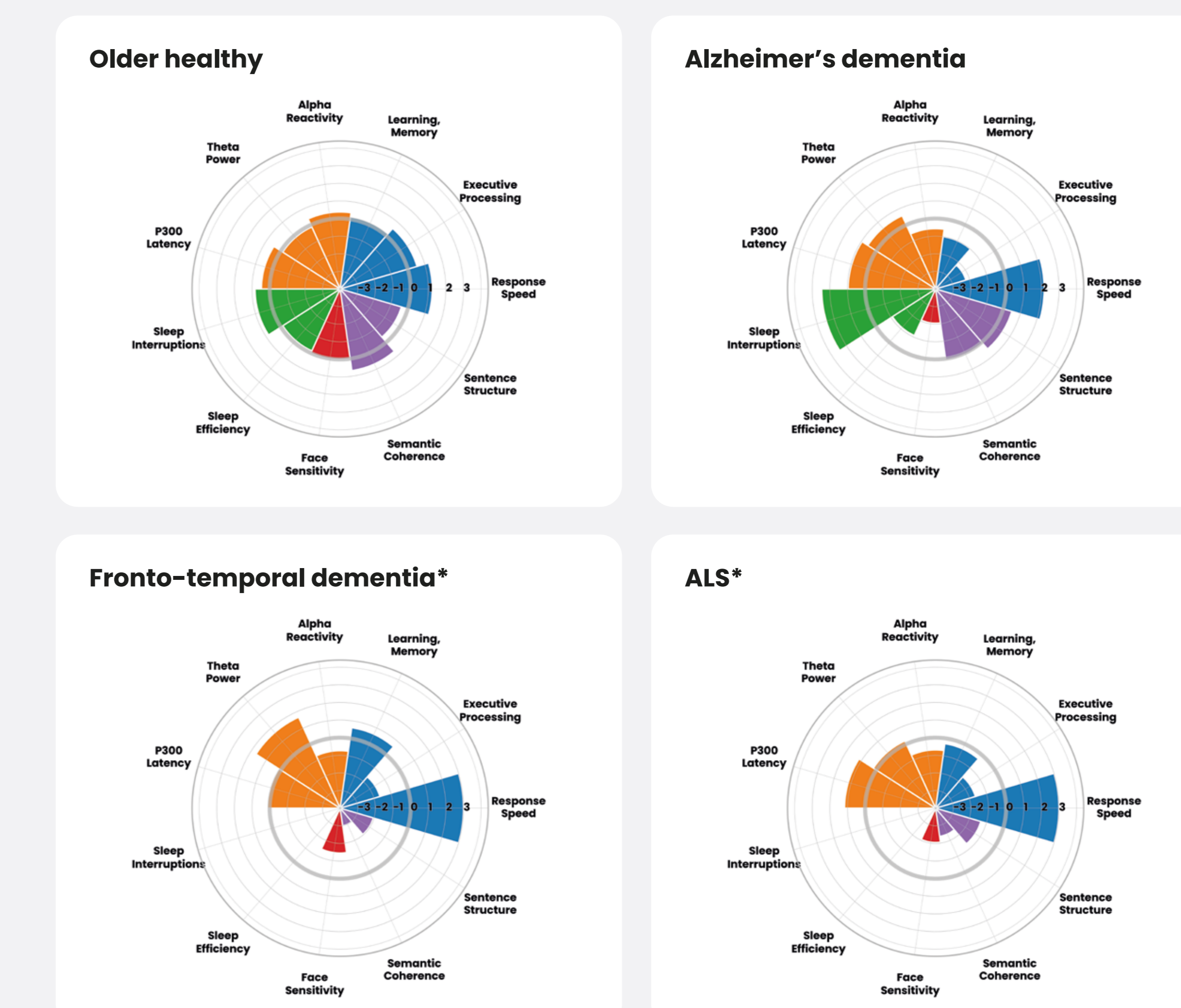


Cumulus Real-World Neurophysiology Platform



- Data Collection**
Clinical grade, easy to use. High engagement tasks with synchronised EEG. Real-time cloud uploads.
- Assessment**
Full-spectrum assessment in neurodegeneration and psychiatry.
- Analytics**
Powerful, proprietary ML analytics and cloud database to extract brain health insights.
- Database**
Large real-world database of annotated, longitudinal, matched data to provide new insight.

Examples of participants' radar plots obtained with Cumulus data



- Cognition**
 - Digital Symbol Swap Task (DSST)
 - Associative memory (Memory Match)
 - N-back task
 - Psychomotor task
- EEG**
 - Resting state
 - Visual oddball task (P300)
- Mood**
 - Facial emotion recognition task
- Language**
 - Vocabulary, language, organisation, prosody
- Sleep**
 - Sleep quality metrics

* Participants from a separate study with Trinity College Dublin and Beaumont Hospital. ALS: amyotrophic lateral sclerosis.