

A real-world, longitudinal observational study in patients with Alzheimer's Disease dementia and healthy controls, using frequent repeated digital measurements performed at-home on the Cumulus Platform: a preliminary report

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Cumulus Real-World Neurophysiology and Cognitive Testing Platform



Developed in collaboration with leading pharma companies (below) and KOLs Cumulus provides full service:

- Protocol/study/SAP design
- On-site training, off-site support
- Full data package
- Reporting and custom analytics

Key characteristics of the Cumulus Platform:

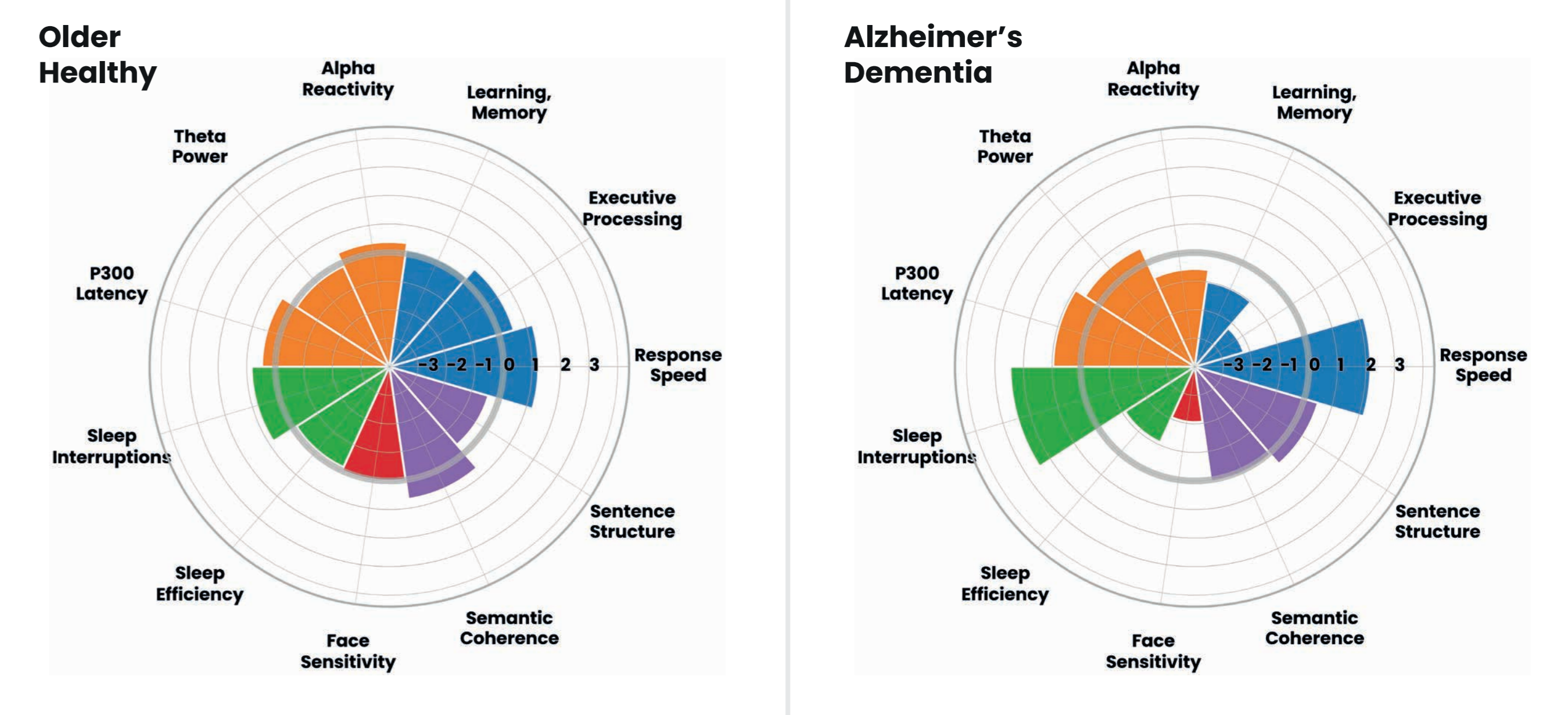
- Wireless dry sensor EEG headset, synchronized to mobile tablet with gamified apps for ease of patient use
- Designed for and with patients and clinicians, deployed in Phase 0-Ib CNS trials
- Secure automatic upload and QC
- Real-time dashboard monitoring of decentralized and home-based data collection
- Audit ready including FDA 510(k), UKCA, HIPAA, GDPR, ISO13485

Cumulus cognitive tests are designed to be highly repeatable, with large banks of non-repeating stimuli.

- Objectively administered and automatically scored
- Results available in moments, enabling remote monitoring
- Suitable for detecting change over time



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)
- Language**
 - Vocabulary, language, organisation, prosody
- Mood**
 - Facial emotion recognition task
- Sleep**
 - Sleep quality metrics

Introduction

- Conventional tools that measure cognitive decline give an infrequent 'snapshot' in an atypical environment and are costly to administer
- Home-based technology gives the opportunity for repeated sampling in a natural environment, combined with AI/data analytics techniques that extract more discriminatory power from multiplex data
- The Cumulus Platform is designed specifically to realize this potential with longitudinal measurement of electrophysiology, cognition, and behaviorally-relevant symptoms within a single unified platform, that participants can use at home
- Here we describe a real-world study of the feasibility of Cumulus to measure neurocognitive function at-home in people with Alzheimer's Disease and healthy adult controls

Methods

Study protocol

- N = 119 (59 AD, 60 matched controls) enrolled in a 52-week study in the UK
- Repeated 30-minute sessions at-home, consisting of behavioral tasks (memory, executive function, affective processing and language), while synchronized EEG was recorded using a self-applied dry sensor headset
- Conventional neurocognitive paper-and-pen assessments (including ADAS-Cog, and subtests from WMS-IV and WAIS-IV) were conducted at baseline, 26 and 52 weeks
- Preliminary analyses are presented here, focusing on cross-sectional analysis during the initial burst period, and usability/feasibility to-date

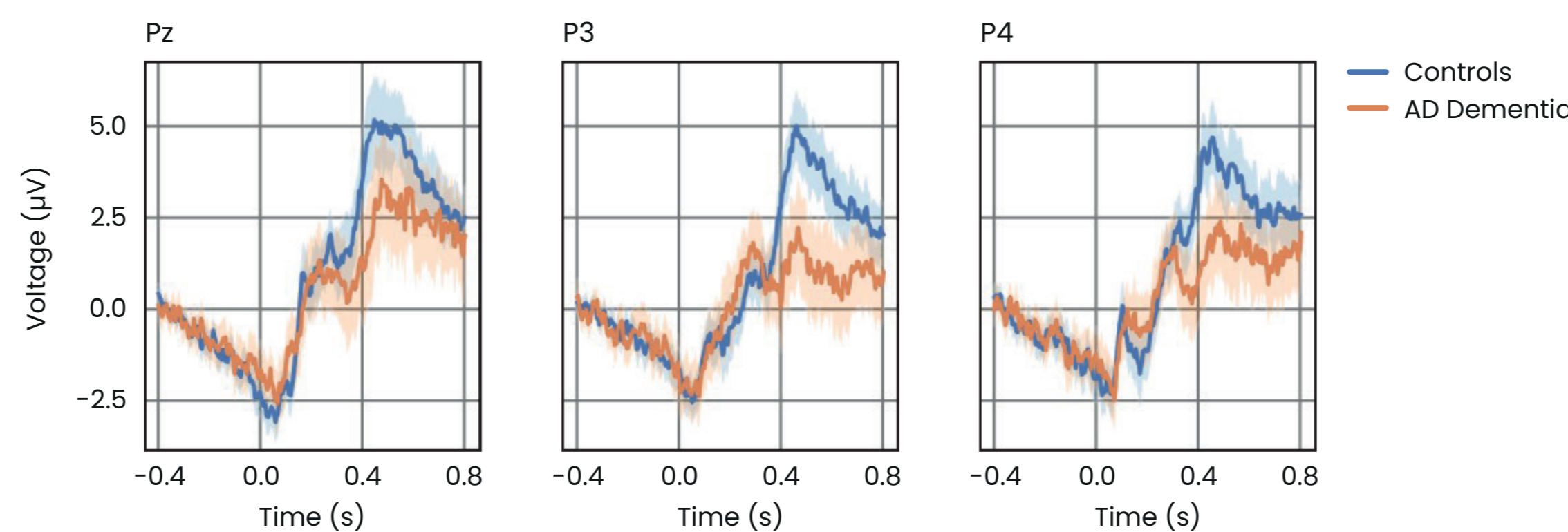
Results

Demographics, assessments and adherence

Variable	Control	AD Dementia	Statistical test	Sig.
Demographics				
N	60	59		
Age	71.1 (SD 7.2)	73.7 (SD 6.2)	t(117) = -2.02, p=0.0452	*
Sex (N)	31 Females 29 Males	22 Females 37 Males	χ ² (1) = 1.94, p=0.1635	n.s.
Education (N)			χ ² (5) = 9.03, p=0.108	n.s.
Left formal education by 18 (3 levels)	25	30		
Undergraduate or equivalent	25	14		
Master degree or PhD or equivalent (2 levels)	10	15		
Assessments				
ADAS Cog 13	9.1 (SD 7.2)	25.1 (SD 7.9)	t(117) = -13.55, p=9.7e-26	***
Coding (DSST)	56.7 (SD 14.4)	37.8 (SD 14.7)	t(117) = 7.1, p=1e-10	***
VPA	26.35 (SD 6.5)	12.2 (SD 6.0)	t(117) 12.34, p=6.4e-23	***
NART	41.4 (SD 4.8)	36.2 (SD 9.02)	t(117) = 3.94, p=1.4e-4	***
AMI	1.2 (SD 0.4)	1.6 (SD 0.4)	t(111) = -4.41, p=2.4e-5	***
GDS	1.1 (SD 1.7)	3.5 (SD 3.4)	t(112) = -4.83, p=4.45e-6	***
SCI	3.5 (SD 0.7)	3.1 (SD 1.1)	t(111) = 2.28, p=0.0259	*
DASS (Depression)	3.4 (SD 4.3)	6.9 (SD 6.5)	t(110) = -3.35, p=1.1e-3	**
DASS (Anxiety)	3.2 (SD 4.1)	5.3 (SD 5.7)	t(110) = -2.27, p=0.0249	*
DASS (Stress)	6.3 (SD 5.5)	9.6 (SD 7.5)	t(110) = -2.64, p=9.4e-3	**
SUS	63.8 (SD 19.6)	54.5 (SD 13.6)	t(91) = 2.58, p=0.0115	*
CL (past)	8.0 (SD 1.1)	7.1 (SD 2.1)	t(110) = 2.77, p=6.67e-3	**
CL (present)	7.7 (SD 1.9)	7.9 (SD 1.9)	t(110) = -0.57, p=0.573	n.s.
CL (future)	7.5 (SD 1.8)	6.0 (SD 2.7)	t(110) = 3.52, p=6.4e-4	***
FBS score (how confident do you feel)	2.6 (SD 1.1)	2.0 (SD 1.0)	t(113) = 3.05, p=2.9e-3	**
FBS score (how difficult was it to learn)	2.8 (SD 1.0)	2.0 (SD 1.0)	t(113) = 4.17, p=6.0e-5	***
Adherence to-date (2023/08)				
Withdrawals (N)	4	15		
N	56	44		
Session adherence	88.5 (SD 15.5)	82.8 (SD 19.3)	t(98) = 1.62, p=0.109	n.s.

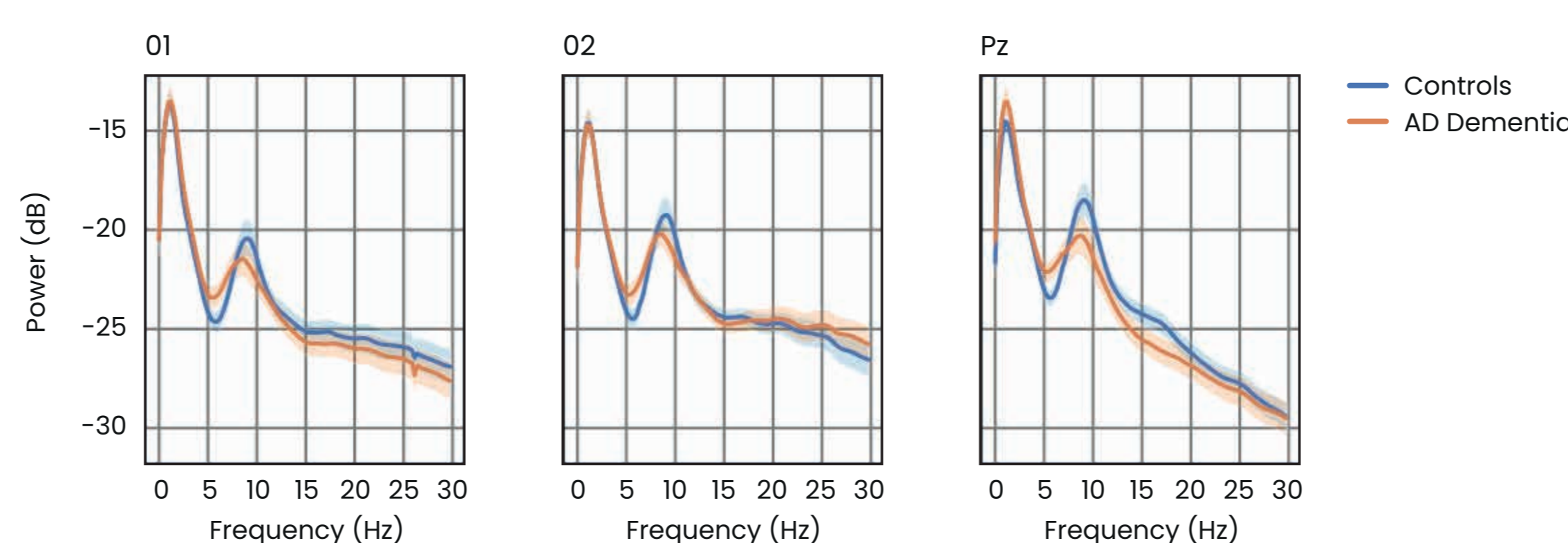
Demographics of participants. Means and standard deviations (SD) of demographics and assessments per group. Non-paired t-tests were run for continuous variables, and χ² tests were run for categorical variables. ADAS Cog: Alzheimer's Disease Assessment Scale - Cognitive Subscale; AMI: Apathy Motivation Index; CL: Cantril's Ladder; DASS: Depression, Anxiety and Stress Scale; DSST: Digit Symbol Substitution Test; FBS: Feedback Survey; GDS: Geriatric Depression Scale; NART: National Adult Reading Test; SCI: Sleep Condition Indicator; SUS: System Usability Scale; VPA: Verbal Paired Associates Assessment. * p<0.05; ** p<0.01; *** p<0.001; n.s.: non-significant.

Group EEG estimates



Group estimates from mixed models of the Target condition of channels Pz, P3 and P4.

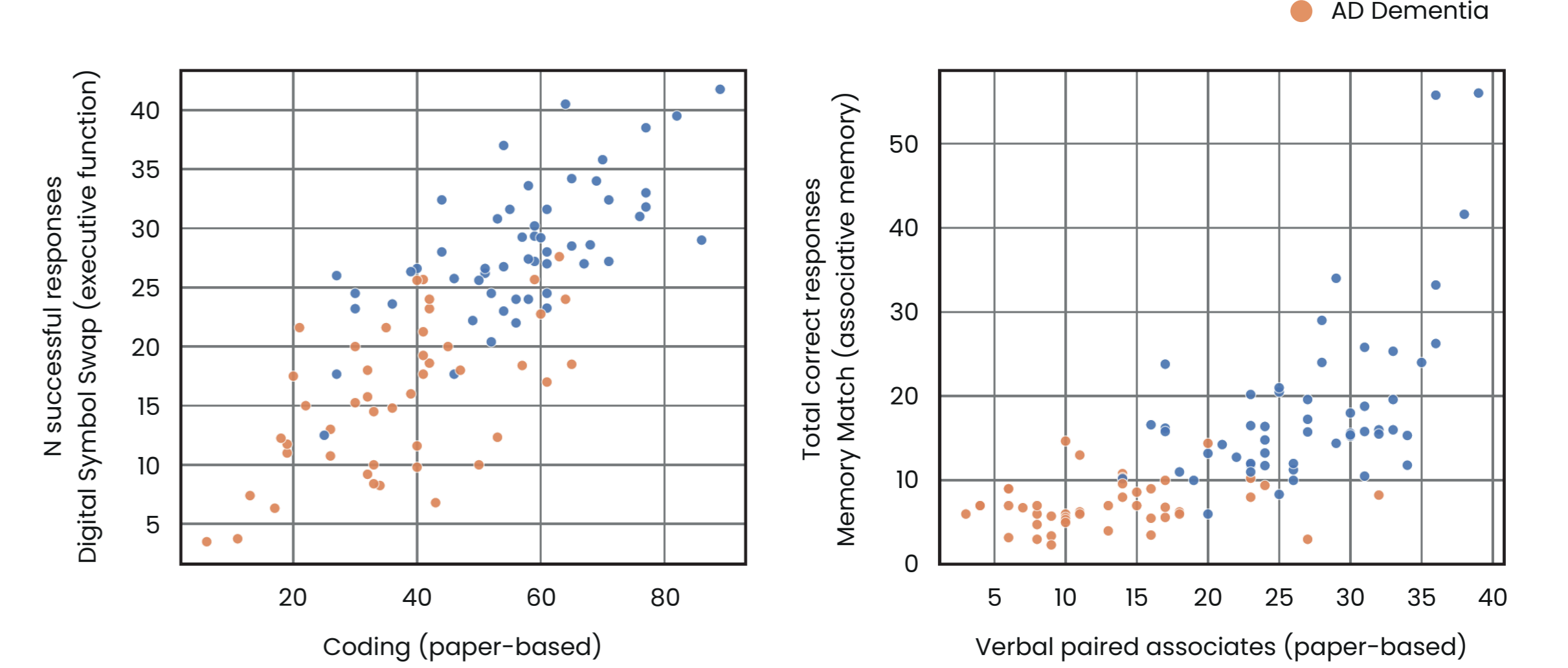
The Target condition of the visual oddball task elicited a P300 over channel Pz, with a lower amplitude in the group with dementia compared to the control group. 95% confidence intervals were obtained from the models' standard errors.



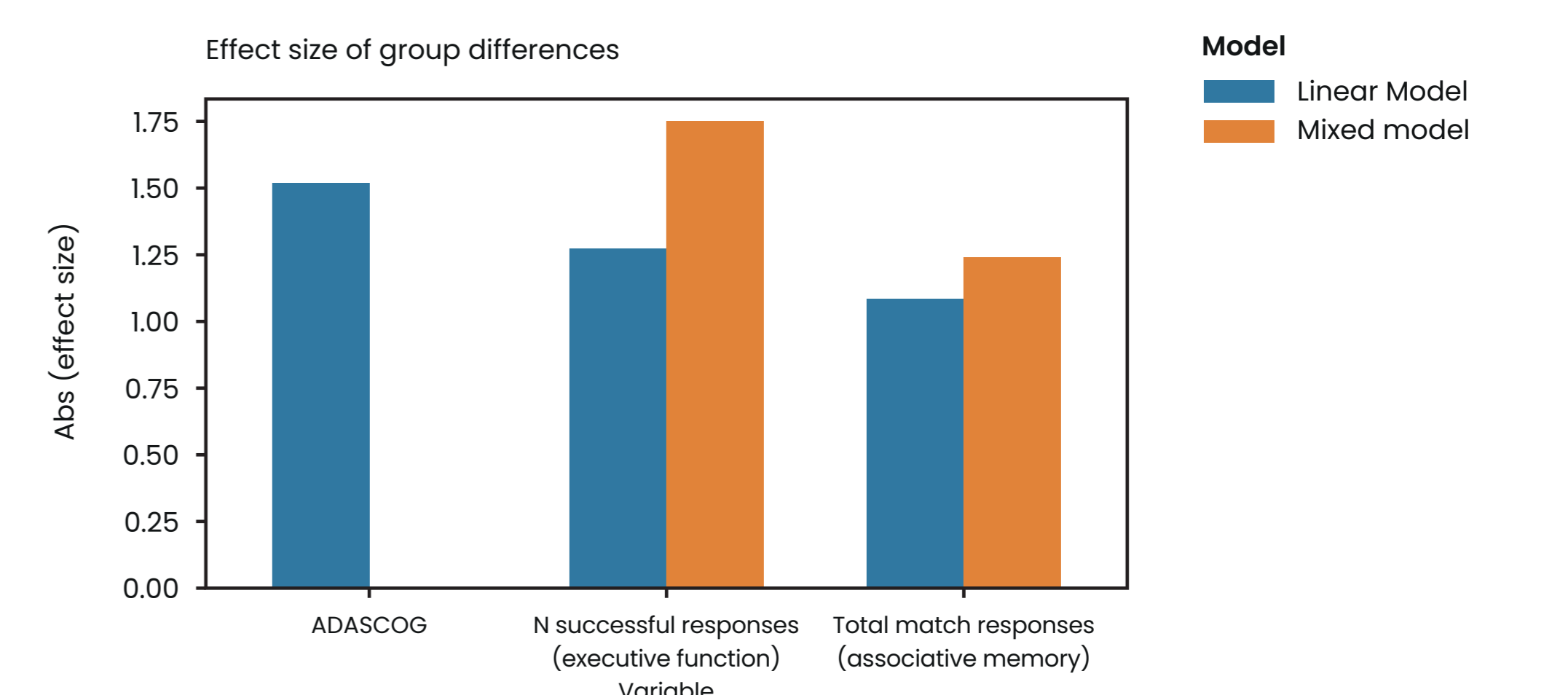
Group estimates from mixed models of the PSDs of channels O1, O2 and Pz during eyes closed.

The alpha peak is reduced and slowed down, and the theta band is increased in the group with dementia when compared to the control group. 95% confidence intervals were obtained from the models' standard errors.

Correlations with benchmarks and effect size comparison



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=5e-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 effect size of selected Cumulus variables and the ADAS Cog 13. Using the average of Cumulus sessions results in a lower effect size than the one obtained from the ADAS Cog. With mixed models, we exploit the within-user variability and obtain an effect size higher than the ADAS Cog.

Conclusions

- Based on the data to-date, digital assessments through the Cumulus Platform can be frequently used by people with mild symptomatic AD at-home.
- Preliminary analysis of the burst stage indicates these types of digital technology have construct validity, distinguishing groups, correlating with conventional benchmarks, and confirming EEG predictions.
- We propose the Cumulus Platform as feasible to provide objective, frequent and patient-centered tracking of functional neurophysiology, facilitating future use of these digital biomarkers in tracking decline or treatment response.

Analysis

- Demographics and pen-and-paper assessments summarized per group
- Session adherence to-date calculated per participant and summarized per group
- Spearman's correlations calculated between selected behavioral Cumulus variables and paper-based benchmarks
- Group effect sizes of selected behavioral Cumulus variables were compared to the ADAS Cog
- Preprocessed and epoched data from the Visual oddball task (Target condition) and the Resting State (2-min eyes close condition)
- Group estimates were obtained from robust mixed models with random intercept representing between-user variance. Models were fitted respectively per timepoint or frequency bin to the session level ERPs or power spectral density (RS)



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