

Scalable Digital Endpoints Improve Sensitivity to Cognitive Change and Can Drive Efficiencies in CNS Clinical Trials

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Introduction

- CNS clinical trials are long, costly and burdensome for patients
- One driver for this is the limited statistical power of conventional endpoints, which are not easily repeatable or scalable
- Digital cognitive assessments can measure the same constructs more conveniently for patients and efficiently for trial sponsors
- With frequent administration, digital endpoints also increase statistical power (Sliwinsky, 2008; Tackney et al., 2024)
- Here we compare sensitivity of digital and conventional endpoints in an at-home observational study over 1 year with dementia patients
- We quantify study power, and potential savings in clinical trial duration, cohort size, and costs

Methods

- Data was gathered using the Cumulus NeuLogiq[®] Platform (McWilliams et al., 2021) in a large, precompetitive, observational study of dementia (Rueda-Delgado et al., 2024 – see Figure 1)
- Mild dementia patients (n=59) and controls (n=60) were recruited at 7 UK sites, as a model of placebo and treated groups, respectively
- ADAS-Cog 13, a registered clinical composite endpoint, was collected at months 0, 6, 12
- Wake EEG, synchronous assessments in memory, executive function, affective processing and language, and sleep EEG were collected repeatedly in the home

Cumulus NeuLogiq[®] Platform for Use in Real-World Settings

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

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

Audit ready including FDA 510(k), UKCA, HIPAA, GDPR, ISO13485.
Designed for and with patients and clinicians, deployed in Phase 0-1b CNS trials.
Secure automatic upload and QC.
Real-time dashboard monitoring of decentralized and home-based data collection.

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

- Objectively administered and automatically scored
- Results (including EEG metrics) available in minutes, enabling remote monitoring and QC
- Suitable for detecting change over time



Results

1. At-home digital endpoints sensitively track progression of dementia, relative to the ADAS-Cog registered endpoint

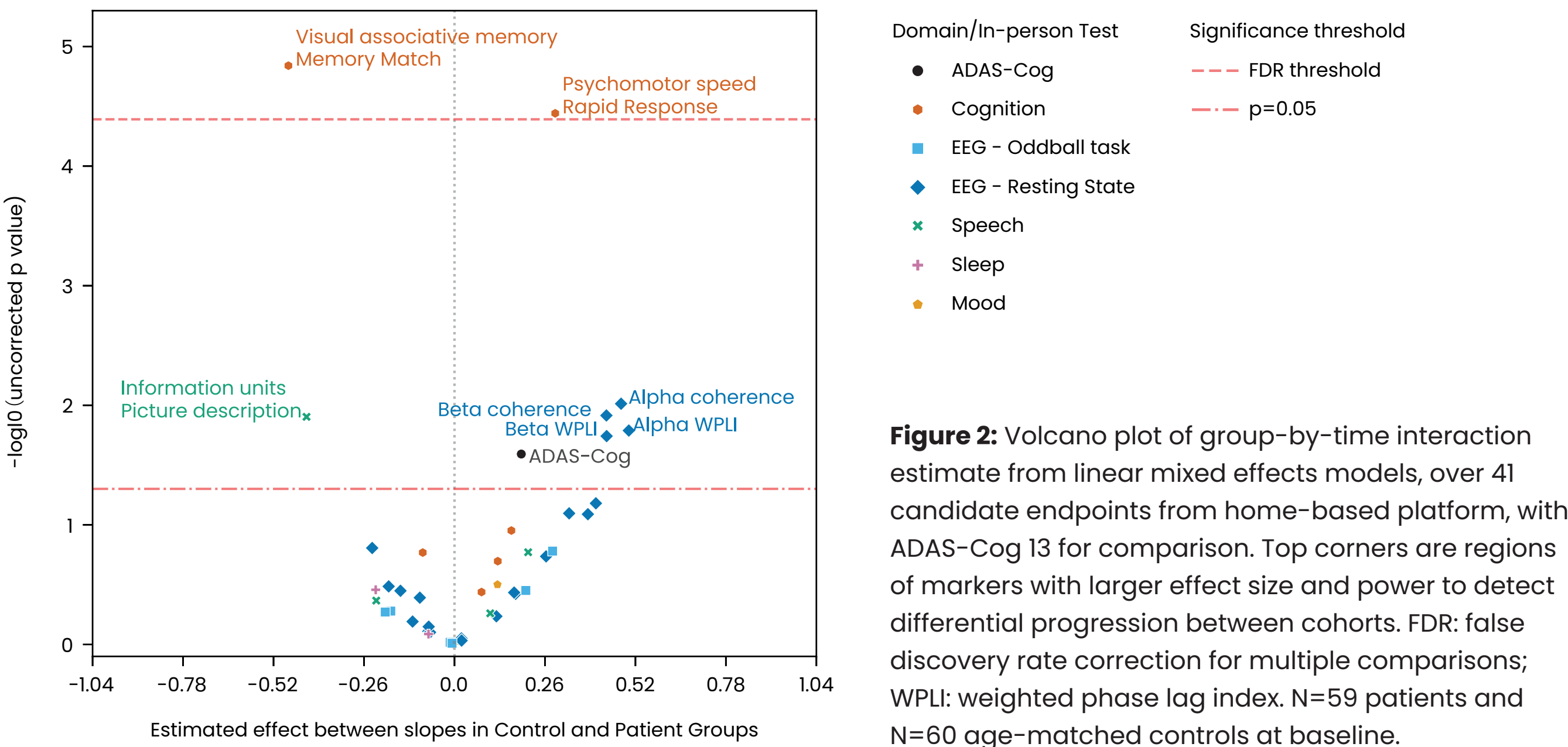


Figure 2: Volcano plot of group-by-time interaction estimate from linear mixed effects models, over 41 candidate endpoints from home-based platform, with ADAS-Cog 13 for comparison. Top corners are regions of markers with larger effect size and power to detect differential progression between cohorts. FDR: false discovery rate correction for multiple comparisons; WPLI: weighted phase lag index. N=59 patients and N=60 age-matched controls at baseline.

2. At-home digital endpoints provide higher statistical power, enabling leaner study designs with smaller cohorts

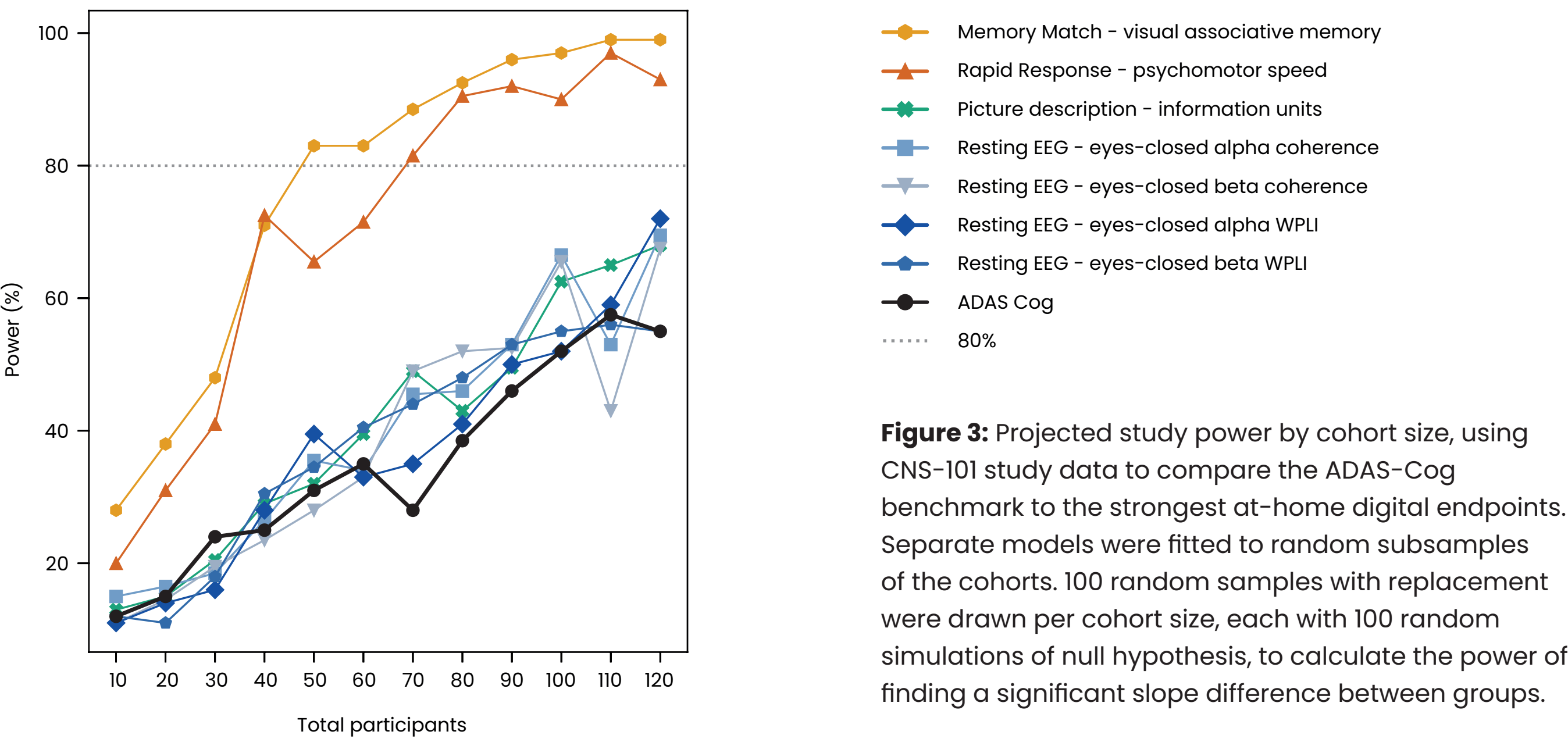


Figure 3: Projected study power by cohort size, using CNS-101 study data to compare the ADAS-Cog benchmark to the strongest at-home digital endpoints. Separate models were fitted to random subsamples of the cohorts. 100 random samples with replacement were drawn per cohort size, each with 100 random simulations of null hypothesis, to calculate the power of finding a significant slope difference between groups.

3. At-home digital endpoints provide higher statistical power, enabling leaner study designs with shorter protocols

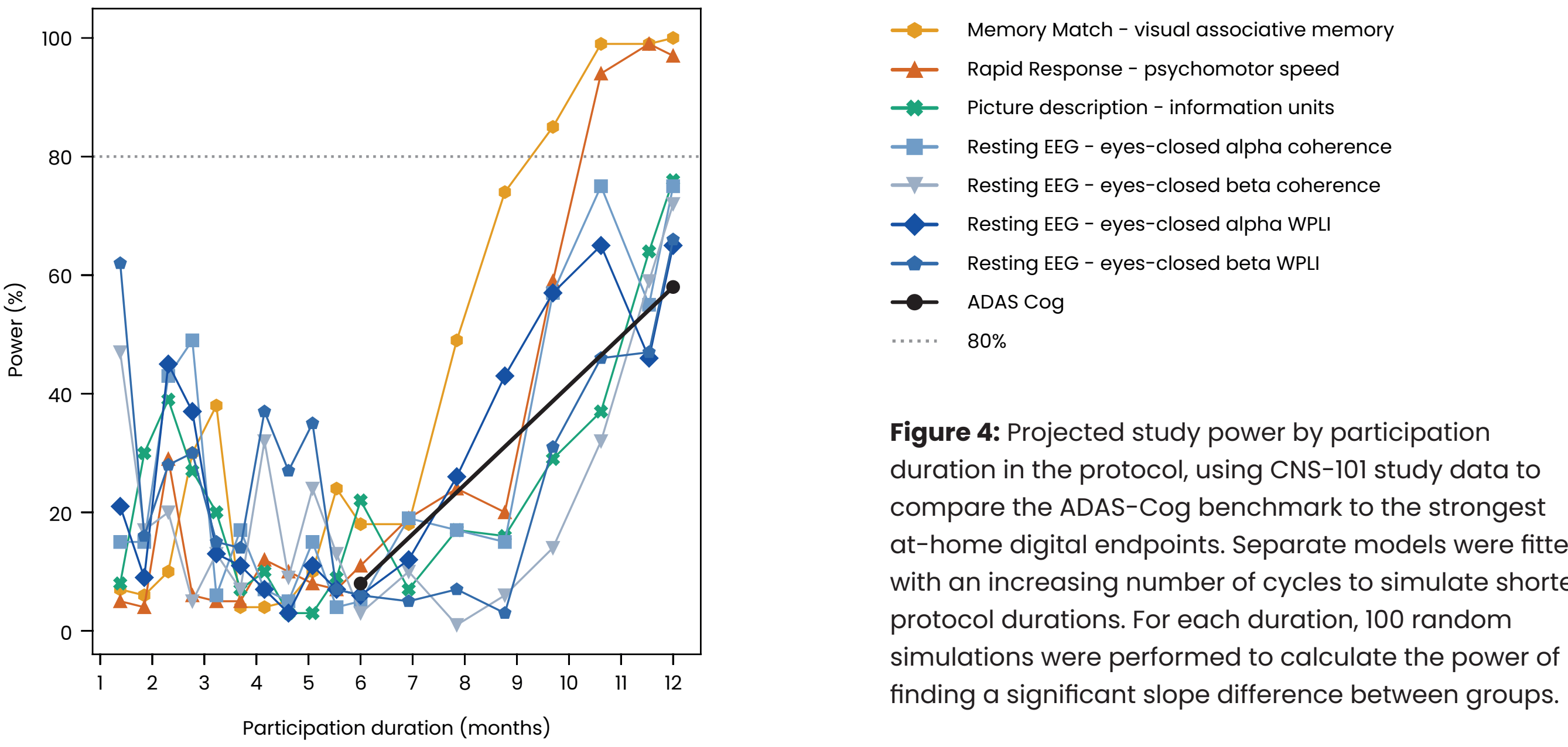


Figure 4: Projected study power by participation duration in the protocol, using CNS-101 study data to compare the ADAS-Cog benchmark to the strongest at-home digital endpoints. Separate models were fitted with an increasing number of cycles to simulate shorter protocol durations. For each duration, 100 random simulations were performed to calculate the power of finding a significant slope difference between groups.

4. A smaller cohort, supported by the inclusion of digital endpoints, can yield more savings than a shorter protocol, with ROI of up to 90%

	Phase 2 Case Study	25% Shorter Protocol	50% Smaller Cohort
Input variables			
number of participants (n)	370	370	185
duration of participation (years)	0.15	0.12	0.15
recruitment rate (n/year)	200	200	200
annual cost per patient per year	\$57.2k	\$57.2k	\$57.2k
total cost per patient	\$114.4k	\$114.4k	\$114.4k
Estimated costs			
recruitment duration FPI to LPI (years)	1.85	1.85	0.92
total duration (FPI to results) (years)	2.0	1.96	1.08
cost of ph2 (annual pt cost basis)	\$42.3m	\$41.5m	\$11.4m
cost of ph2 (per-head pt basis)	\$42.3m	\$42.3m	\$21.2m
Savings			
study duration in years		0.04	0.92
study cost (annual patient cost basis)		\$-2.6m	\$27.5m
study cost (per-head patient cost basis)		\$-3.4m	\$17.7m

Table 1: Time and cost savings when shortening the participation duration by 25% or reducing the cohort size by 50%. Two types of cost basis were calculated: i) annual cost per patient per year; and ii) fixed per-head costs per patient. FPI: first patient in; LPI: last patient in. Estimated cost of implementing digital measures are included at \$3.4m (DiMasi et al., 2024; DiMe, 2025). ROI calculation based on DiMe tool (DiMe, 2025).

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Conclusion

- Brief but repeated home-based digital cognitive endpoints are more sensitive to change than the ADAS-Cog 13 composite benchmark
- Passive EEG markers and naturalistic language based markers are similarly powerful to ADAS-Cog 13 (which takes ~45 minutes of clinician time to administer)
- Individual digital endpoints can enable streamlined study designs
- Reducing cohort sizes brings compounding benefits, as recruitment timelines are shortened – with lower overall costs and accelerated results
- Digital cognitive endpoints provide complementary evidence, and may support interim futility analyses and adaptive trial designs, for earlier go/no-go decisions, especially in phase 2

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Disclosures

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