

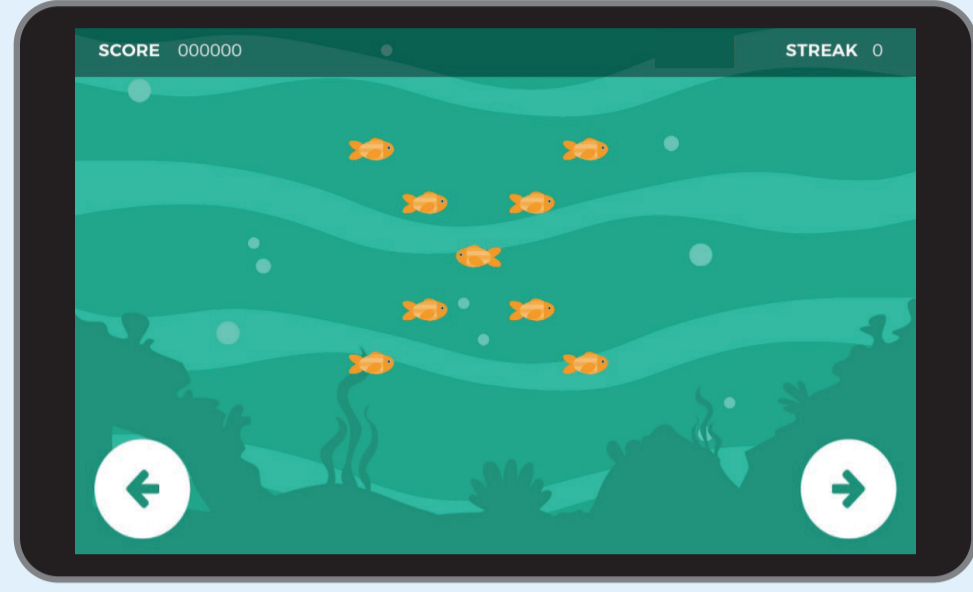
# Scalable tools for the non-invasive measurement of neuroplasticity in clinical trials of CNS therapies

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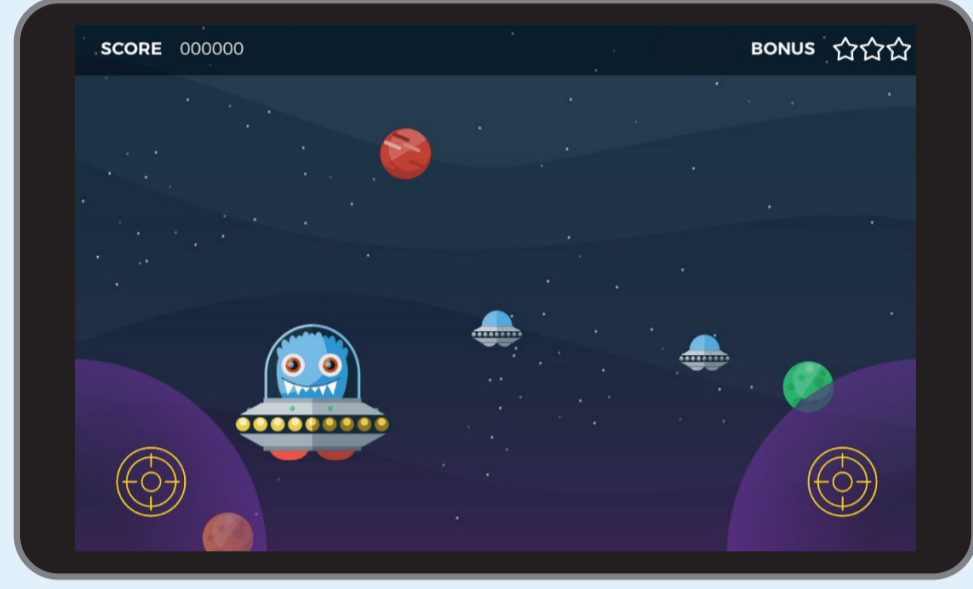
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## Cumulus NeuLogiq® Platform for cognitive and EEG data collection at scale



**Go with the Flow:** Gamified Flanker ERN



**AstroTap:** Gamified P300 visual oddball

### Developed in collaboration with leading pharma companies and KOLs (below)

Cumulus provides full service:

- Protocol/study/statistical 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 0-2 CNS trials.

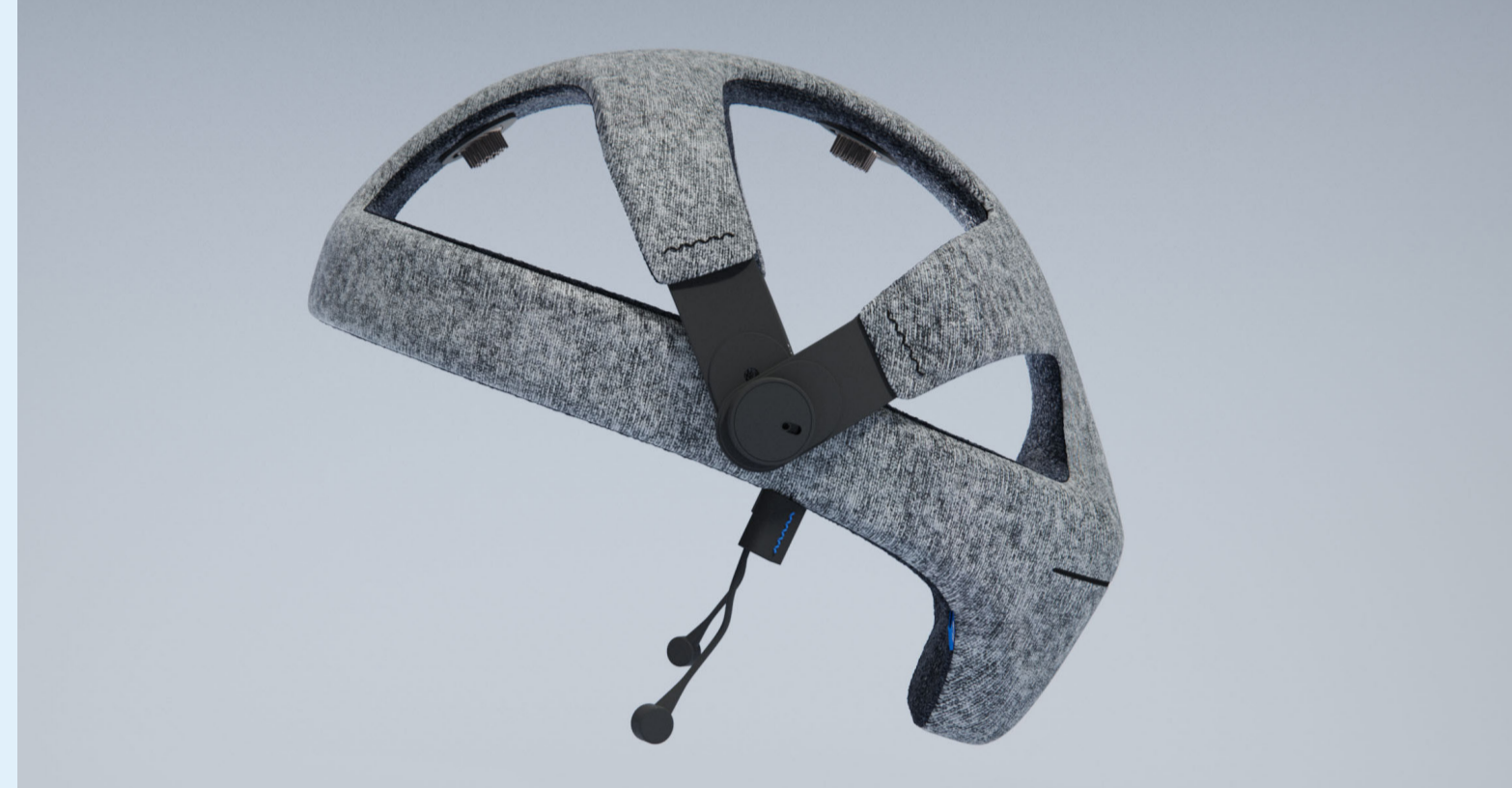
Used for "burst" and longitudinal sampling in clinics and in patients' homes.

Secure automatic upload and quality control.

Real-time dashboard monitoring of decentralized and remote data collection.

### Cumulus cognitive-EEG tests are designed to be highly repeatable, quick to run and low-burden for participants.

- Objectively administered and automatically scored
- Results, including Event Related Potentials, available in minutes, enabling remote monitoring
- Tasks designed to be approachable and low burden vs. classical ERP paradigms



## Introduction

- Neuroplasticity is a key mechanism in healthy cognition, in CNS disorders, and in pharmacological and device-based therapies (e.g. Volk et al 2015)
- Clinical trials would benefit from an objective non-invasive measure of functional and structural neuroplasticity
- The Visual Evoked Potential – Long Term Potentiation task (VEP-LTP) is a non-invasive correlate of invasive LTP (Cooke & Bear 2010)
- It is used in academic clinical research to measure functional neuroplasticity (Teyler et al 2005, Normann et al 2007, Valstad et al 2020), but requires more time for montage and collection than is practical in many clinical trials
- Cumulus Neuroscience partnered with Sumitomo Pharma America to develop a streamlined version of the task, and validated it in clinical trials



**Fig 1 Hardware setup:** NeuLogiq platform headset (16 flexible dry pin sensors) and wirelessly synchronised tablet stimulus.

## Dry-EEG headset designed for lab, home and hybrid trials

### Case study 1: Timesaver in the lab

Comparison with traditional, wet-gel lab-based alternative



<30 minutes for a typical EEG session (multi-domain, EEG and cognitive assessment)  
Dry sensor design penetrates hair with no need for wet gel  
Can be applied by non-technical users in low-support environments

90 minutes minimum session duration is typical  
Hair washing required after each session  
Requires staff who are expert EEG technicians

### Impact

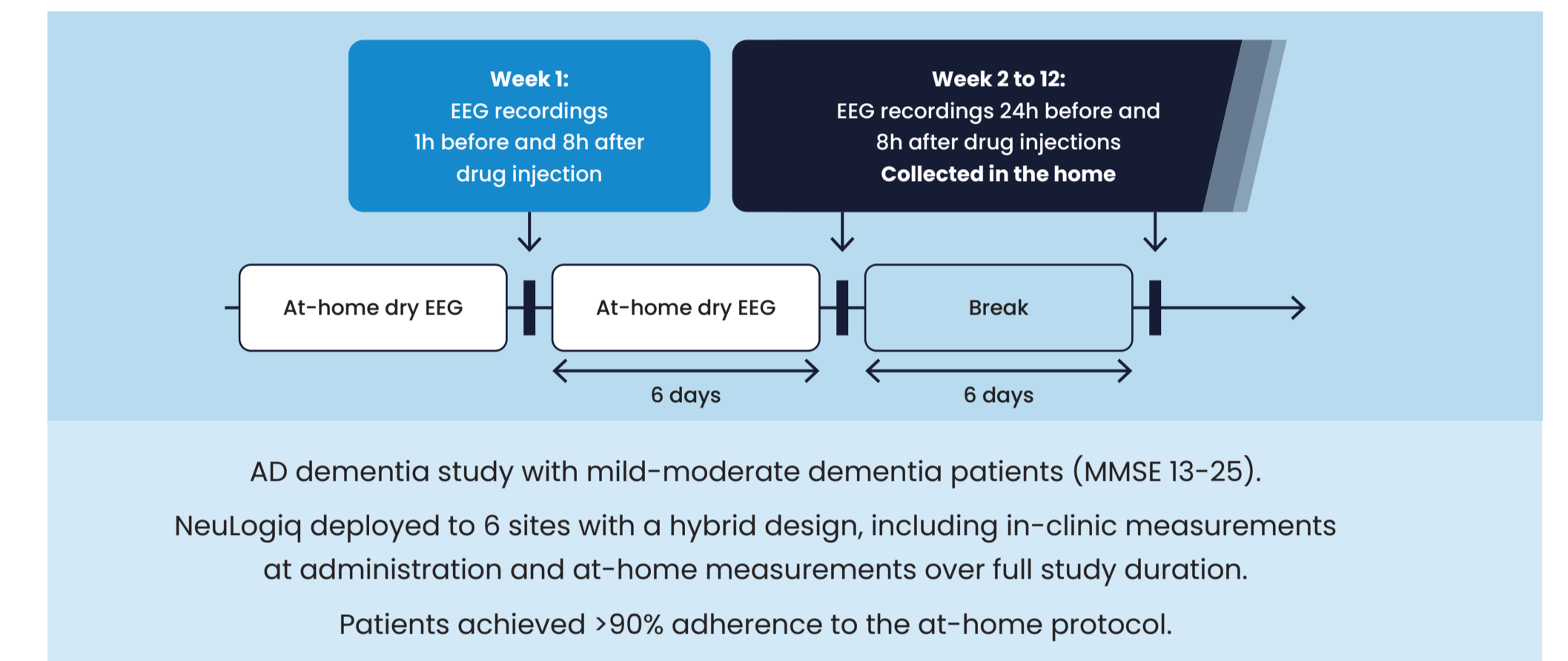
Phase 1 inpatient clinical trial setting was made possible with acceptable user burden, **reducing conventional VEP-LTP paradigm time by ~75%.**

Reported that use of Cumulus made it feasible to collect in **low-support environments.**

Milanovic et al, ECNP 2023

### Case study 2: Hybrid home and lab multisite deployment

Late addition to an ongoing trial in Australia, during Covid-19 pandemic

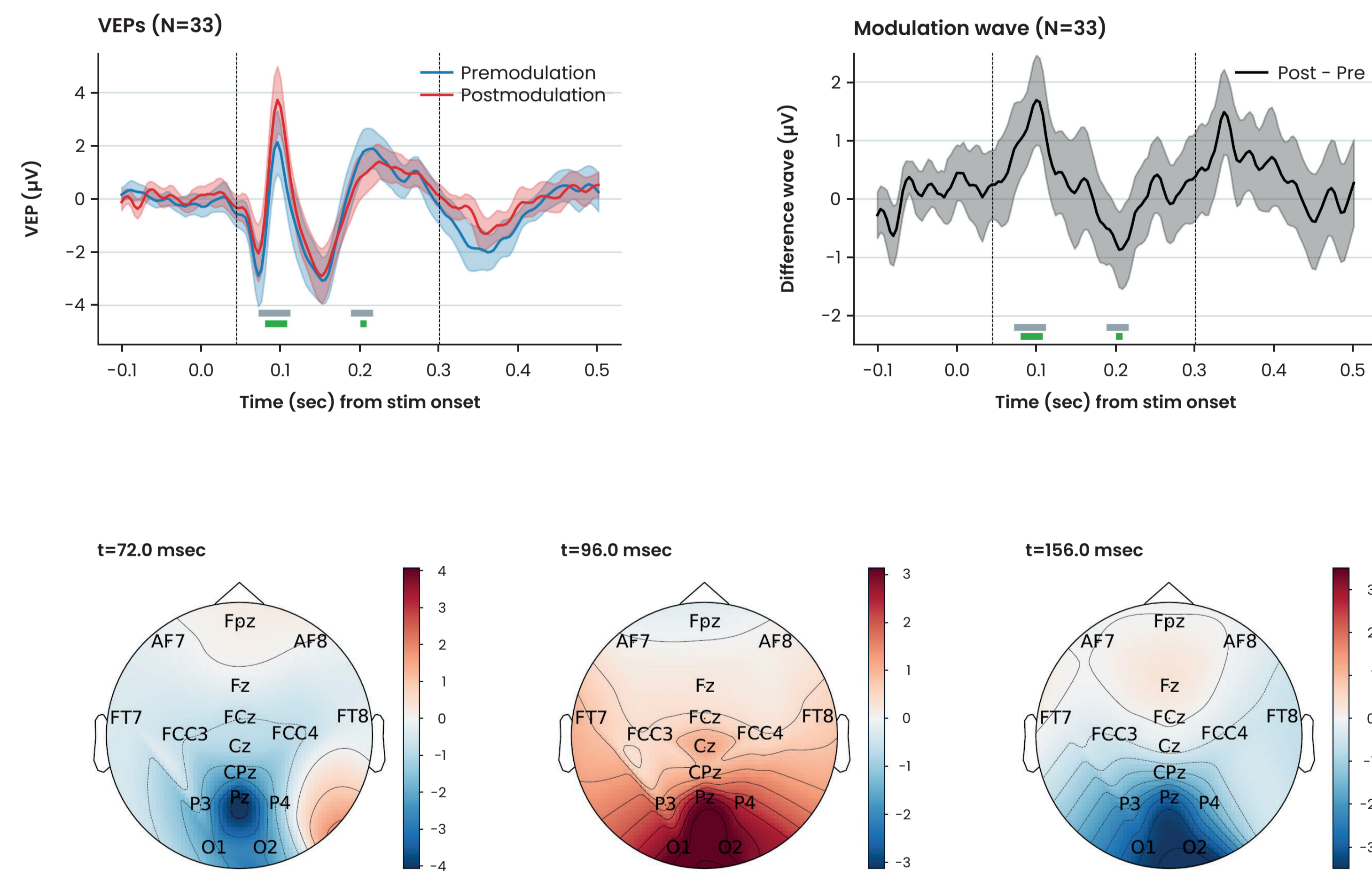


### Impact

A hybrid-remote clinical trial during the height of lockdown was made possible, accommodating vulnerable patients who were reluctant to travel to clinical sites.

Significant improvement in EEG markers of brain function following drug infusion was found.

Barbey et al., CTAD 2023



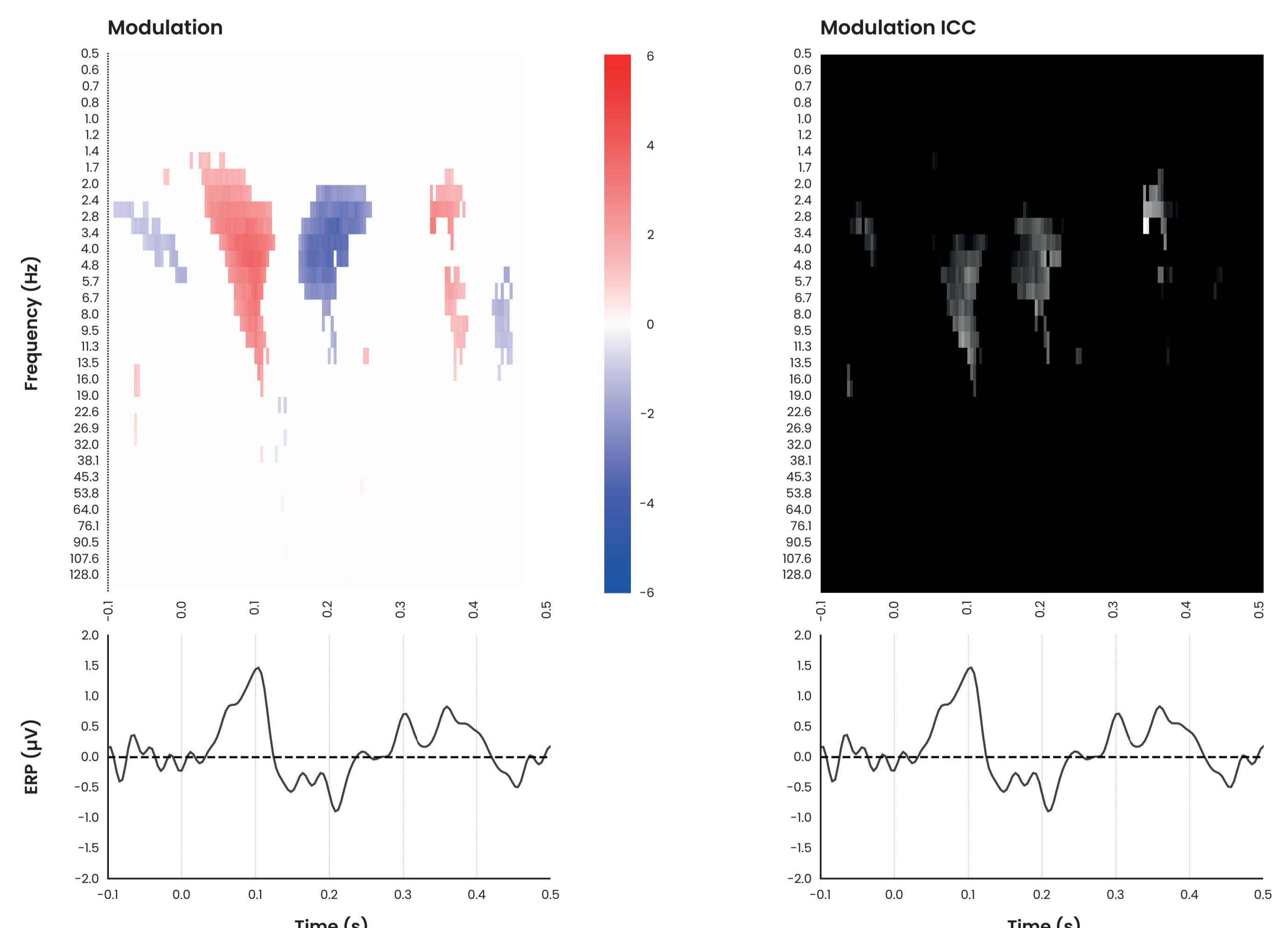
**Fig 2 Modulation effect, N=33:** Group analysis of first session per participant. Time windows of significant difference (p-values uncorrected for multiple comparisons) are indicated by grey bars; time windows of significant difference following correction of p-values are indicated by green bars (false discovery rate correction [FDR; Benjamini & Hochberg, 1995]). Error bars SEM; Luck et al 2021.

## Methods

- The abbreviated VEP-LTP task lasts 11 minutes in total, and is presented on a secured tablet, while EEG is recorded with a 16-channel wireless dry-EEG headset (Fig 1)
- Data was collected during clinical trials of experimental therapies at CenExel sites in California and New Jersey
- N=198 participants were evaluated during screening, including n=59 African American individuals
- All data presented here is from off-drug sessions with N=33 neurotypical participants
- Test-retest results (one-way random-effect model-based estimation of the variance components) are given for the subset of N=16 participants with between 2 and 6 off-drug sessions, comparing features from a conventional time-domain VEP and a frequency domain wavelet transform

## Results

- The shortened task was deployed successfully to clinical trials sites, with a typical session duration of <30 minutes and with tolerance/sensor connectedness/placement issues for fewer than 10% of participants
- VEP morphology and topography (Fig 2) compared well to the literature and strong group level effects were seen on the P1 component (Cohen's d=0.78) and the N1b component (Cohen's d=-0.52)
- Reliability of the time-domain VEP was low with test-retest ICC<0.3
- Test-retest reliability for wavelet analysis reached levels ICC>0.5



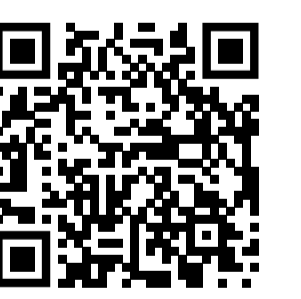
**Fig 3 Reliability of modulation, N=16:** Scaleograms of 2nd derivative Gaussian wavelet transformation of the VEP. Masked to hide regions where the modulation response was non-significant (p>0.01 after correction for multiple comparisons).

## Discussion

- The abbreviated VEP-LTP task is suitable for real-world use in clinical trials, easy to deploy at sites with ethnically diverse cohorts
- Group level modulation effects are strong, proving validity of the approach
- Test-retest for individual sessions is more modest, but could be improved upon with repeated assessment (Barbey et al 2022)
- This raises promise of use as a stratification, target engagement or dosing end-point in trials, with future potential as companion diagnostic and precision neuropsychiatry tool
- Complementary markers in resting EEG (Snipes et al 2023) and sleep EEG (Tononi 2014) could provide a broader picture of functional and structural plasticity

## References

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