

# Scalable and Translational Neurophysiology Biomarkers for Measuring Drug Target Engagement in Clinical Trials in Neuropsychiatry

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## 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 0-2 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.**

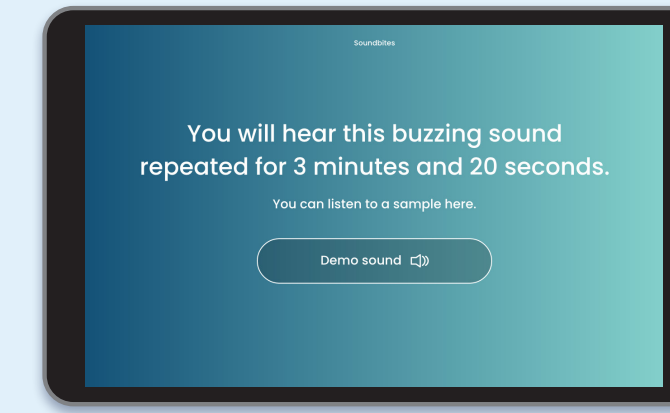
- Objectively administered and automatically scored
- Results (including EEG metrics) available in minutes, enabling remote monitoring and QC
- Suitable for detecting change over time



**Symbol Swap:** Digit symbol substitution/coding task



**Go with the Flow:** Flanker task



**Soundbites:** Auditory steady state response at 40Hz



**Relaxation:** Resting State EEG



## Introduction

- There is a critical need for scalable translational biomarkers which potentially could transform the low success rate (6.7%) from preclinical discovery to therapeutic benefit in CNS trials (Sertkaya et al., 2024)
- A consortium of 10 pharma companies (listed above) came together with Cumulus to design a solution for frequent, objective, real-world measurement across a range of domains relevant for CNS trials: the NeuLogiq® Platform
- A core domain measurement of NeuLogiq® is neurophysiology, providing mechanistic EEG tasks for translational bridging from preclinical work to studies with healthy volunteers and patients
- Two different studies are presented in this poster to illustrate the potential for capturing frequent objective and scalable measurement of cognition, and active and passive EEG, using NeuLogiq®

## Study 1 Electrophysiological Correlates of Ketamine

### Methods

- Double blind cross over design: sub-anaesthetic infusion of racemic ketamine (0.5 mg/kg) vs. saline control
- 30 healthy male adults (mean age=25.6 years)
- EEG paradigms: 20-min eyes-closed resting state recordings, and gamified ERP tasks
- In-lab recordings: before, during, 1 hour post and 24 hours post infusions
- Remote at home recordings for a week before and after infusions

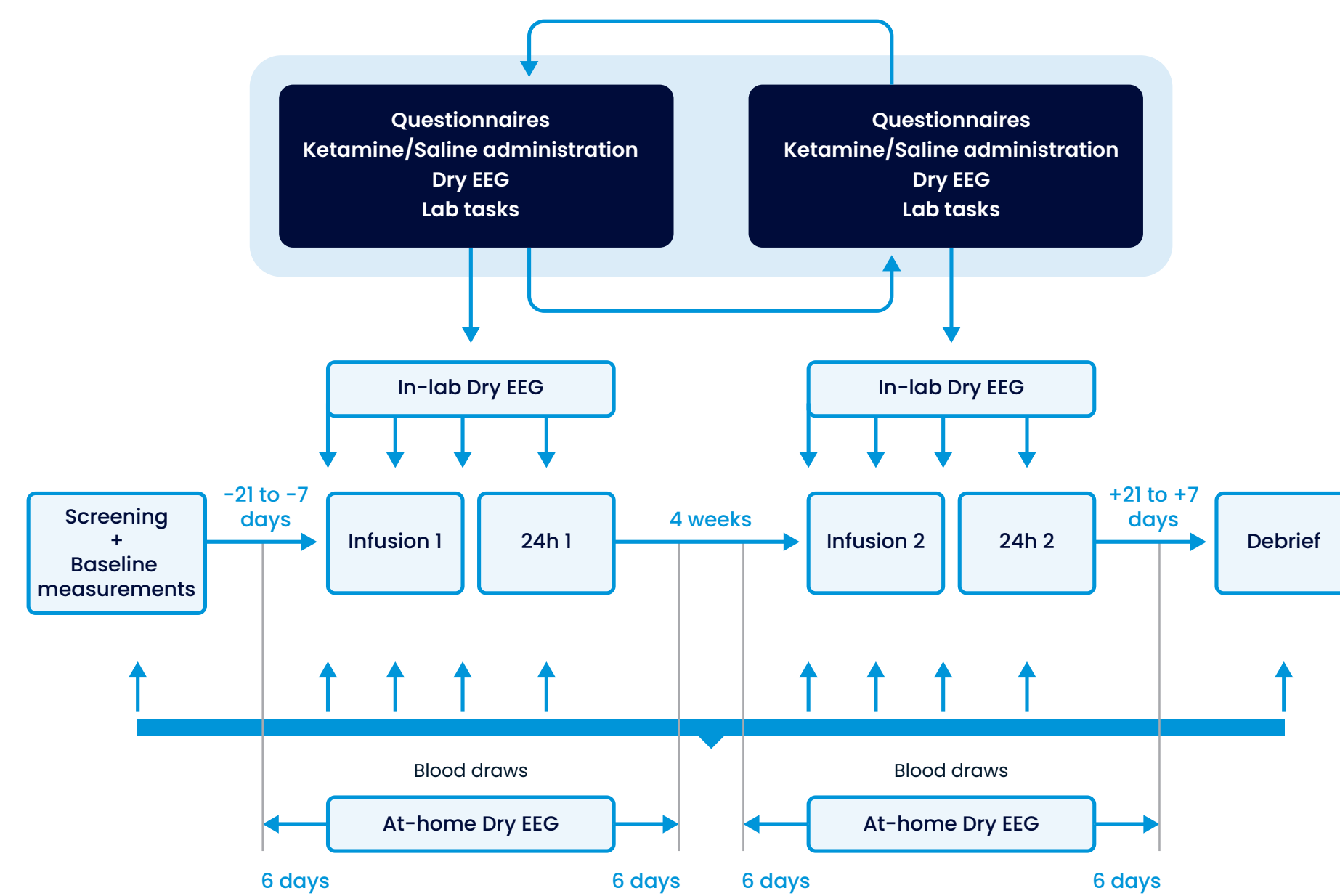


Figure 1: Ketamine study design

## Results

### PSDs During Infusion

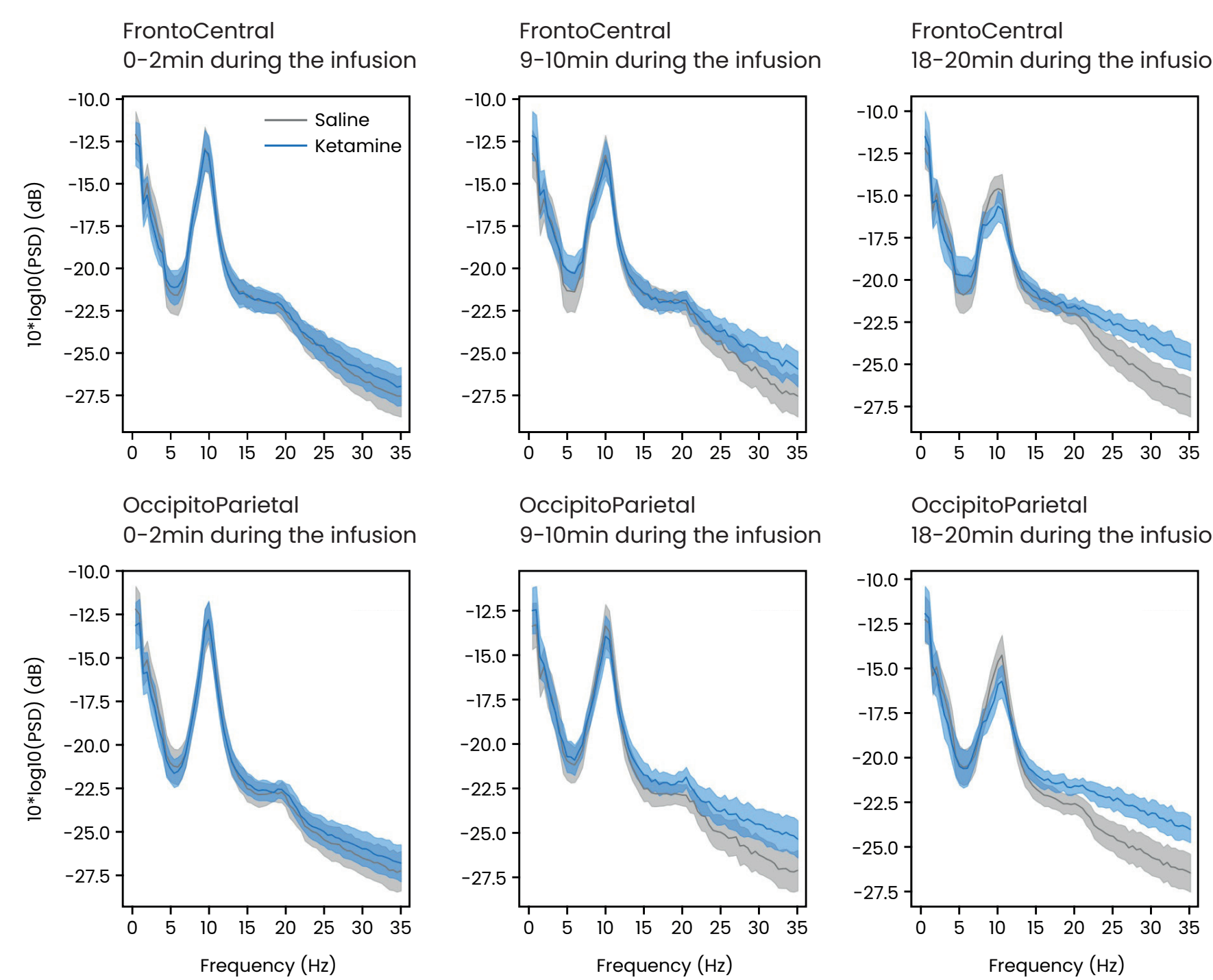
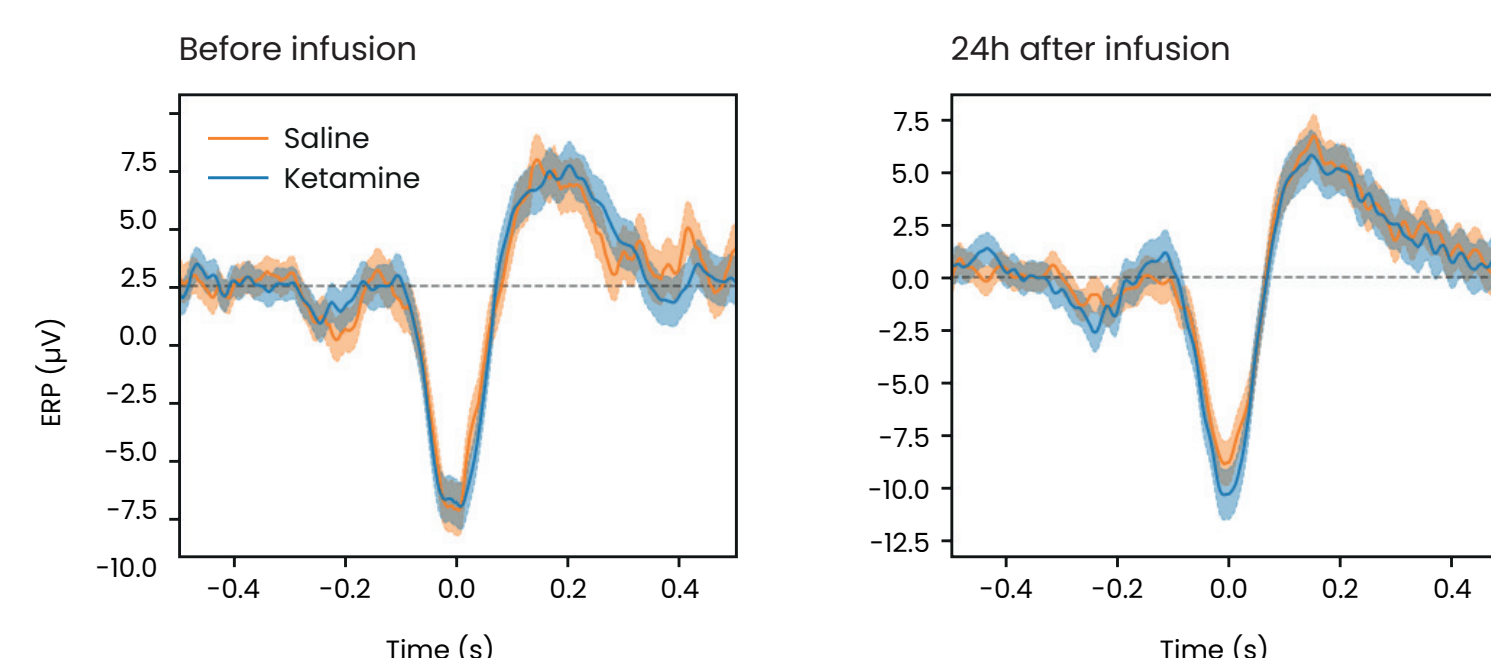


Figure 2: Power spectral density plots over the time-course of infusion

### Error Related Negativity (ERN) Plot



### Test-Retest Reliability

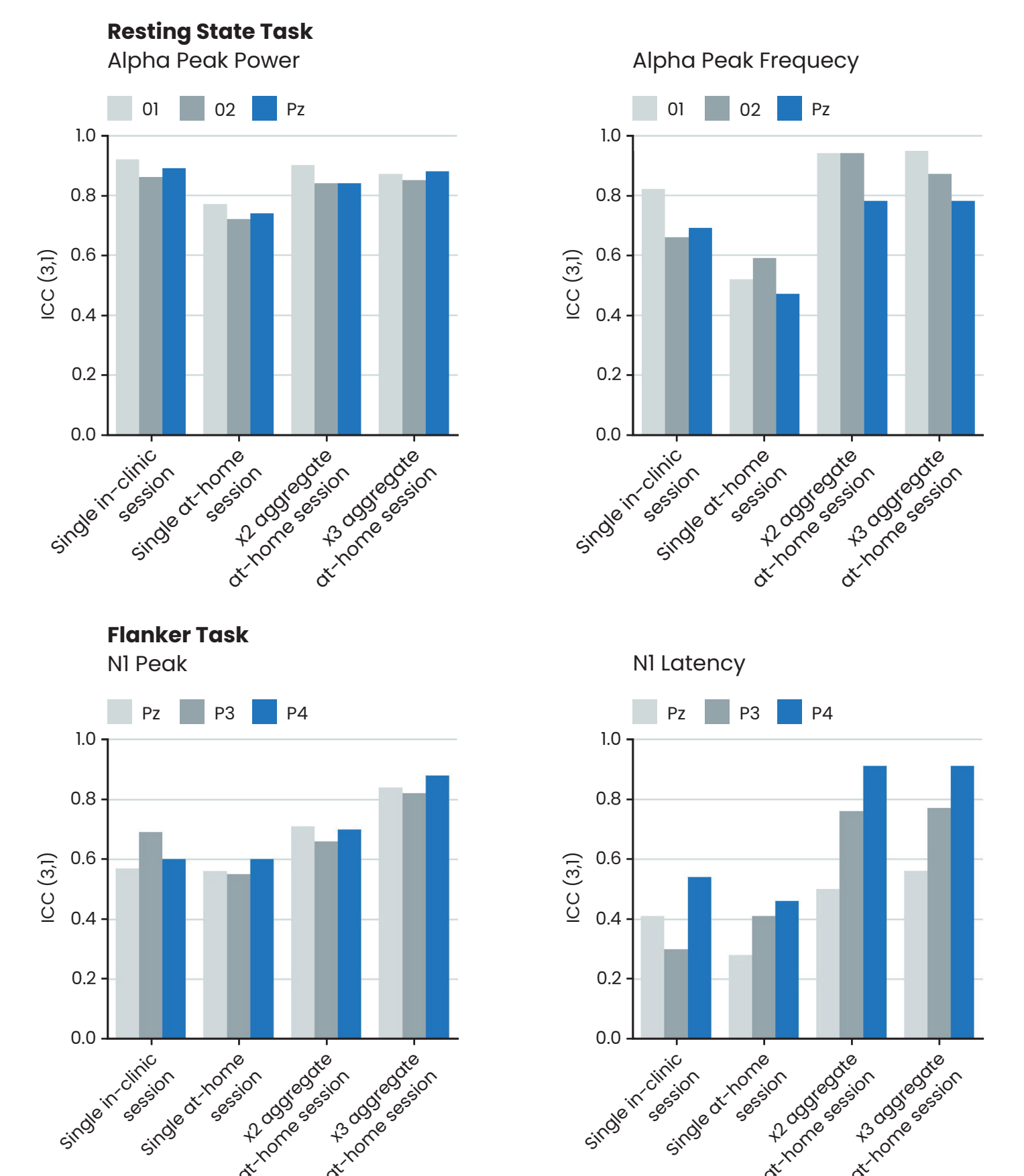


Figure 3: (Left) Grand average plotted from gamified Flanker task showing typical morphology and topography: Difference wave ERN between the correct and incorrect response ERPs at channel FCz.

Figure 4: (Above) Reliability results from a two-way mixed effect model, single-measure consistency ICC. Data used for these ICC analysis are restricted to baseline data, collected at home and in clinic, prior to drug administration.

## Study 2 Electrophysiological and Cognitive Correlates of a Novel Neuroplastogen

### Methods

- Here, we report on interim data from the first 9 participants (Cohort A). Results from Cohort B will be presented at future conferences
- A dose-blinded, single centre, phase 1b study in people with major depressive disorder (MDD), with Cohort A receiving daily dosing (Days 1-7, n=9) of DLX-001, a non-hallucinogenic, non-dissociative, neuroplastogen in an in-patient trial unit
- EEG paradigms included: resting state EEG, eyes-open (90s) and eyes-closed (210s); and a 4-min 40Hz auditory steady-state response (ASSR)
- Cognitive paradigms included digit symbol substitution task (DSST - Symbol Swap) - a digital adaptation of symbol coding repeated up to twice daily, capturing range of cognitive domains relevant for executive function. Outcome measure = number of boxes correctly completed within 90 seconds

## Conclusions

- Effects of known dissociative ketamine observed using NeuLogiq® were consistent with the literature (Herzog et al., 2024)
- Effects of a novel non-dissociative neuroplastogen measured using NeuLogiq® (Cohort A data from a Ph1b study) were consistent with a previous Phase 1 healthy volunteer study, and corroborated findings using a traditional wet electrode 64-channel EEG acquisition system (Koenig et al., 2025)
- NeuLogiq® is a suitable tool for objective, frequent and patient-centred tracking of functional neurophysiology, providing translatable and scalable biomarkers for use in evaluating target engagement for clinical trials in neuropsychiatry

## Results

### Resting state theta band trended upwards after first dose of DLX-001

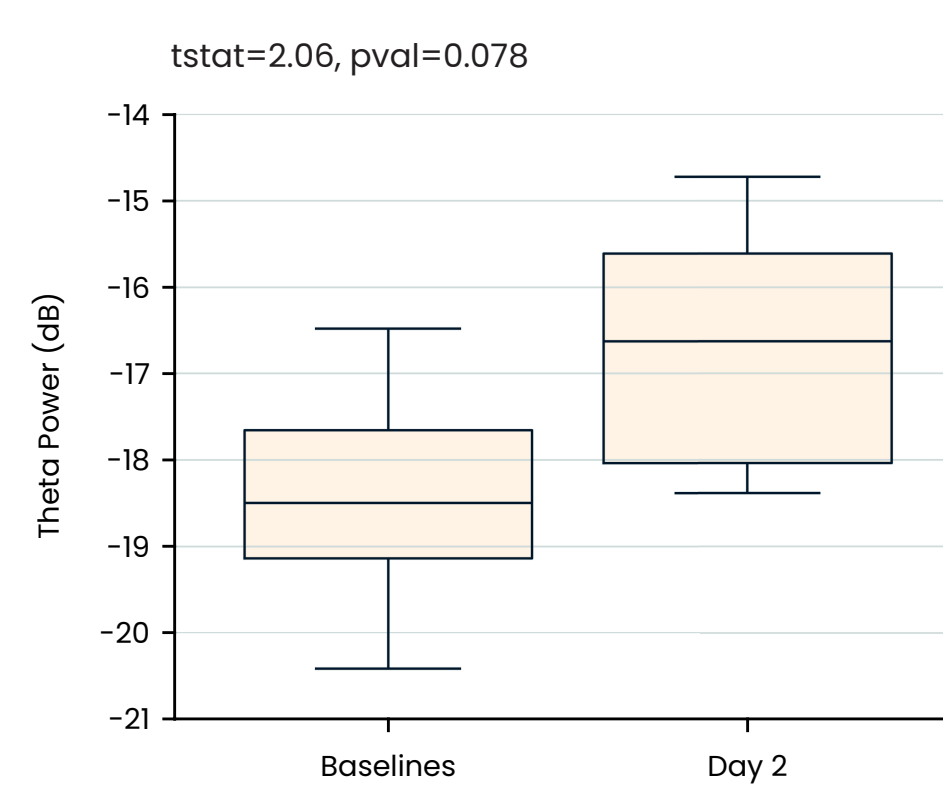


Figure 5: Boxplots of mean fronto-central theta power (6-8.5Hz). The baseline boxplot includes data averaged within participants across the two baseline timepoints. Paired t-test results including t-statistics and p-values are displayed at the top of the figures. The data presented include 8 patients who contributed a total of 23 sessions.

### Digital symbol swap task showed no measurable impairment of executive function following administration of DLX-001

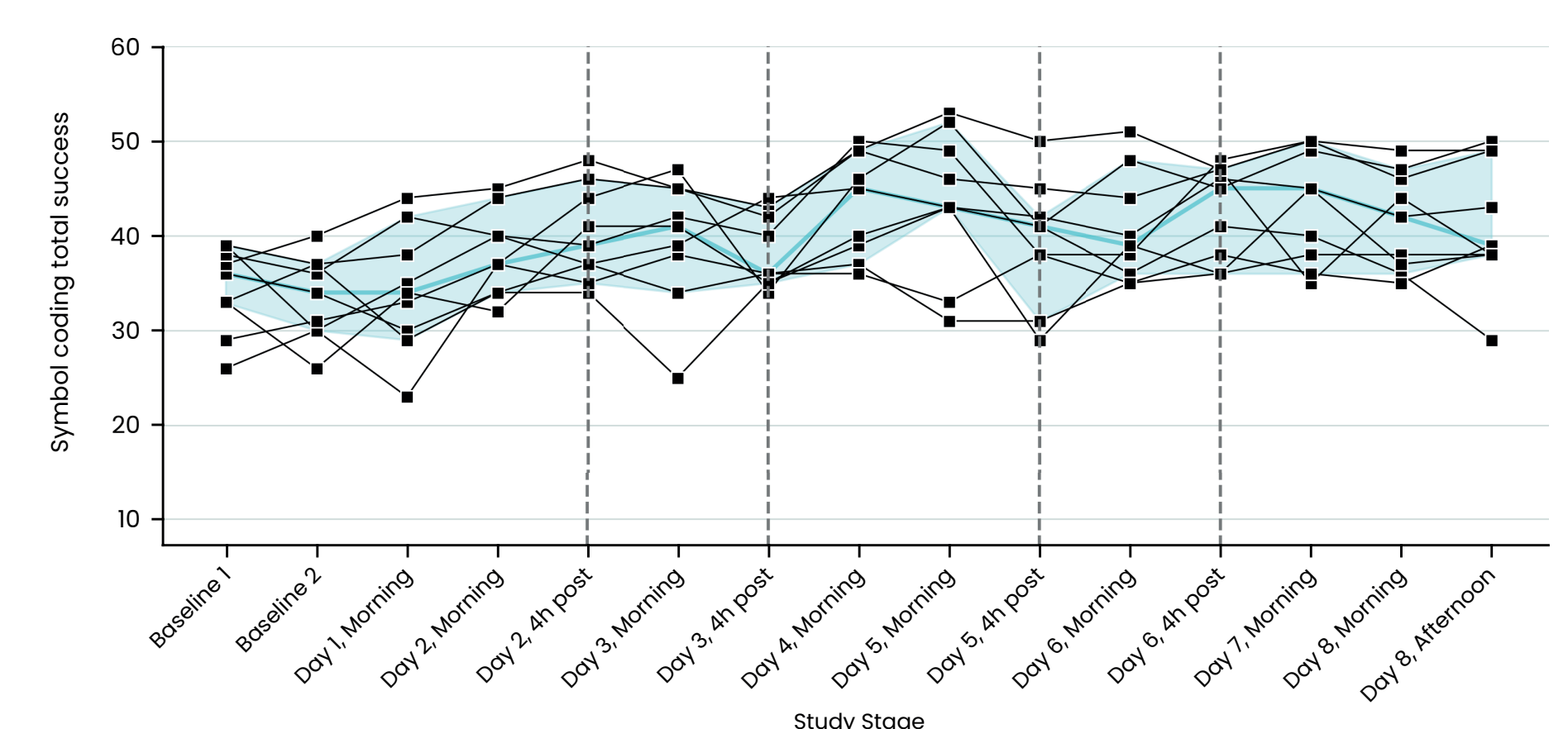


Figure 6: Individual trajectories of the number of correct answers in the digital DSST. The vertical dotted lines indicated the acute 4hr post-dose timepoints. The blue line represents the median across all participants. The blue shaded area represents the 95% confidence interval. The data presented include 9 patients who each contributed 15 sessions.

### Auditory steady-state response task showed inter-trial coherence (ITC) rose acutely after DLX-001 administration

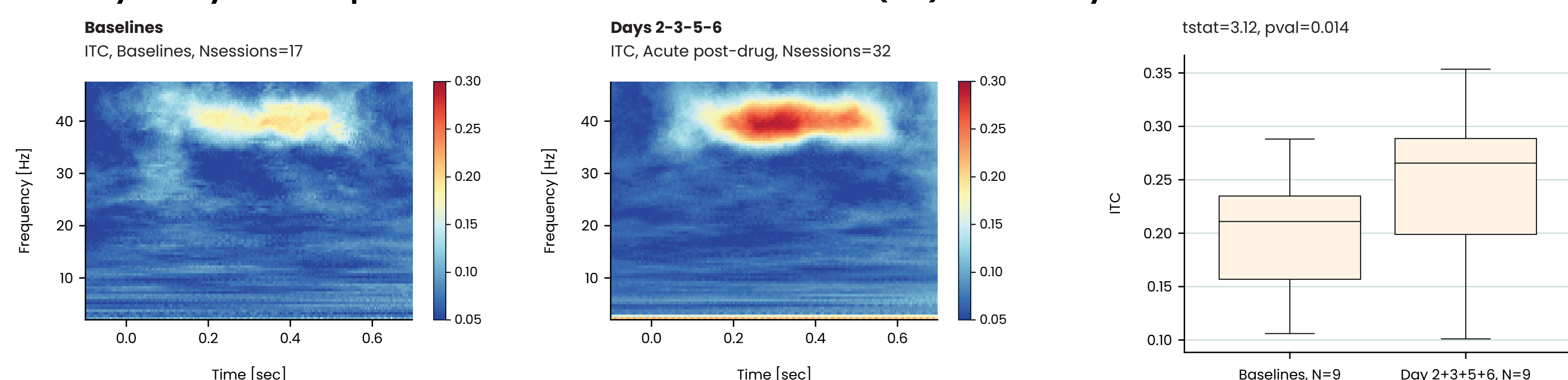


Figure 7: Left & centre: Heatmaps of the ITC averaged over the two Baselines (left), and over Days 2, 3, 5 and 6 (centre). Right: Boxplots of the mean ITC averaged over the two baseline days compared to the average of Days 2, 3, 5 and 6. Paired t-test results including t-statistics and p-values are displayed at the top of the figure.

## References

- Sertkaya A, Beleche T, Jessup A, et al. Costs of Drug Development and Research and Development Intensity in the US, 2000-2018. *JAMA Netw Open*. 2024;7(6):e2415445.  
 Herzog R, Barbey FM, Islam MN, et al. High-order brain interactions in ketamine during rest and task: a double-blinded cross-over design using portable EEG on male participants. *Transl Psychiatry*. 2024;14:310.  
 Koenig A, Tiessen R, Pelletier N, et al. A Phase 1b Study to Evaluate the Pharmacodynamics, Safety, and Tolerability of the Novel Neuroplastogen DLX-001 in Participants with Major Depressive Disorder: Interim Findings. *ASCP Poster 2025*.

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