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.

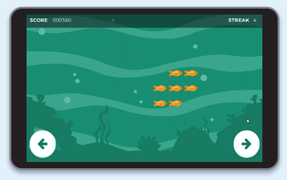
Secure automatic upload and QC.

Real-time dashboard monitoring of decentralized and home-based data collection.

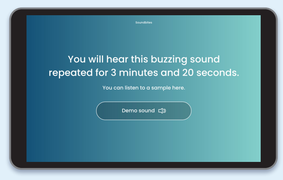
Cumulus cognitive and EEG / ERP tests are designed to be highly repeatable, with large banks of non-repeating stimuli.
- Objectively administered and automatically scored
- Results (including EEG metrics) available in minutes, enabling remote monitoring and QC
- Suitable for detecting change over time

Biogen · Boehringer Ingelheim · Bristol Myers Squibb · GSK · J&J · Lilly · MSD · Pfizer · Roche · Takeda

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, l hour post and 24 hours post infusions
- Remote at home recordings for a week before and after infusions

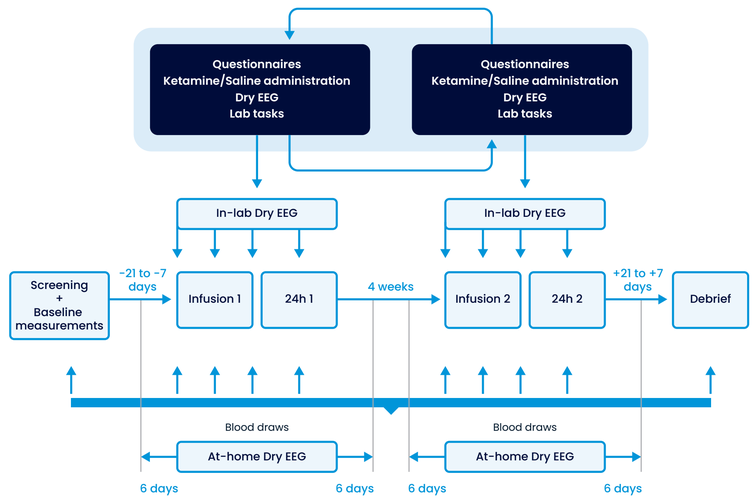


Figure 1: Ketamine study design

Results

PSDs During Infusion

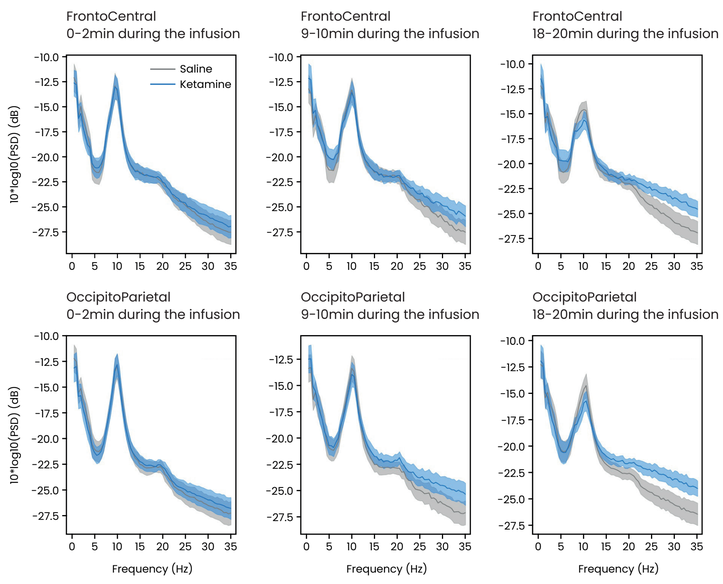
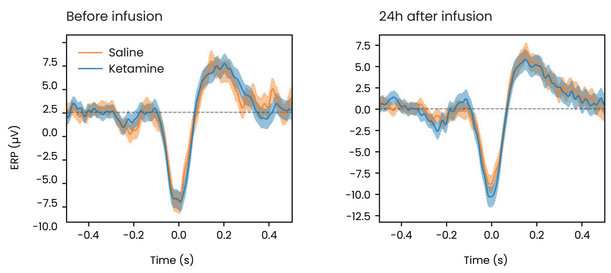


Figure 2: Power spectral density plots over the time-course of infusion

Error Related Negativity (ERN) Plot



Test-Retest Reliability

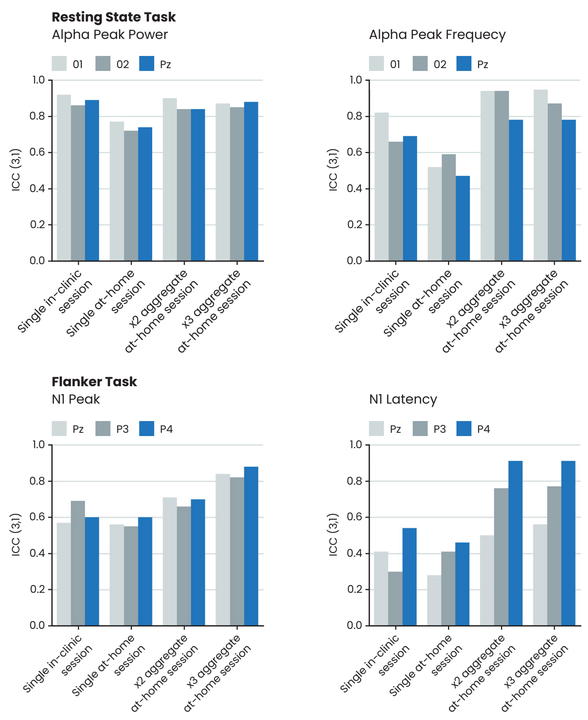


Figure 3 : (Left) Grand average plotted from gamified Flanker task showing typical morphology and topography: Difference wave ERN between the correct and incorrect response ERPs at channel FCz.

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 repeated up to twice daily, capturing range of cognitive domains relevant for executive function. Outcome measure = number of boxes correctly completed within 90 seconds

Results

Resting State EEG (theta power)

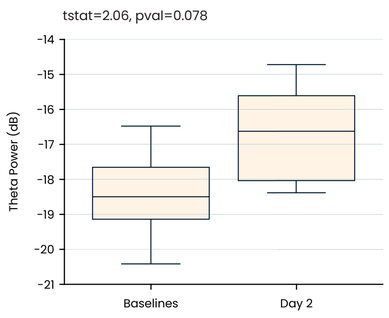


Figure 5: Boxplot of mean fronto-central theta power (6-8.5Hz). The baselines boxplots include data averaged within participant across the two baseline timepoints. Paired t-test results including t-statistics and p-value are displayed at the top of the figures. The data presented includes 8 patients who contributed to a total of23 sessions.

Cognition (Symbol Swap / DSST)

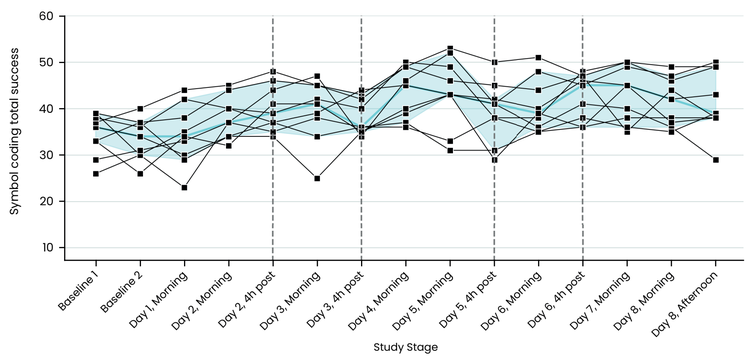


Figure 6: Individual trajectories of the number of correct answers in the digital DSST. The vertical dotted lines indicated the acute 4hr post-dose timepoints. The blue line represents the median across all participants. The blue shaded area represents the 95% confidence interval. The data presented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

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

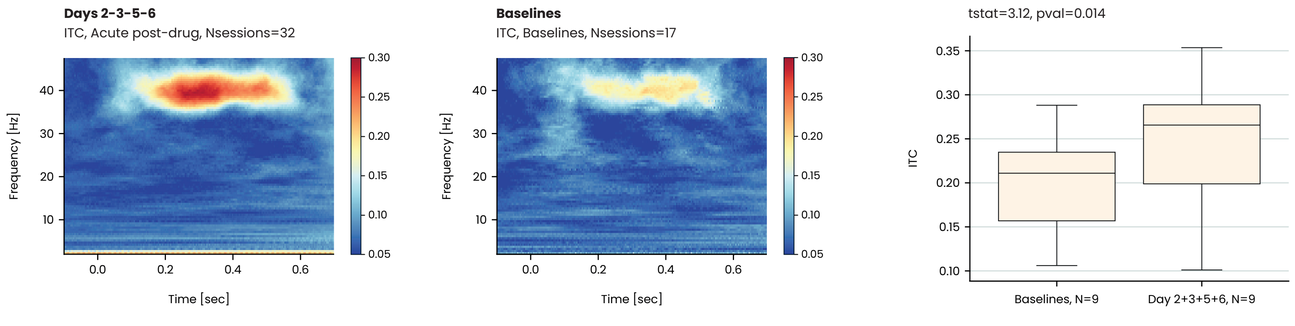


Figure 7: Left & centre: Heatmaps of the ITC averaged over Days 2, 3, 5 and 6 (left), and over the two Baselines (centre). Right: Boxplot of the mean ITC averaged over the two baseline days compared to the average of Days 2, 3, 5 and 6. Paired t-test results including t-statistics and p-value are displayed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

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

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 Ib 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.