

Electrophysiological Correlates of a Ketamine Infusion Captured via the Portable Cumulus Neurocognitive Platform Using Repeated Sampling from the Clinic and the Home

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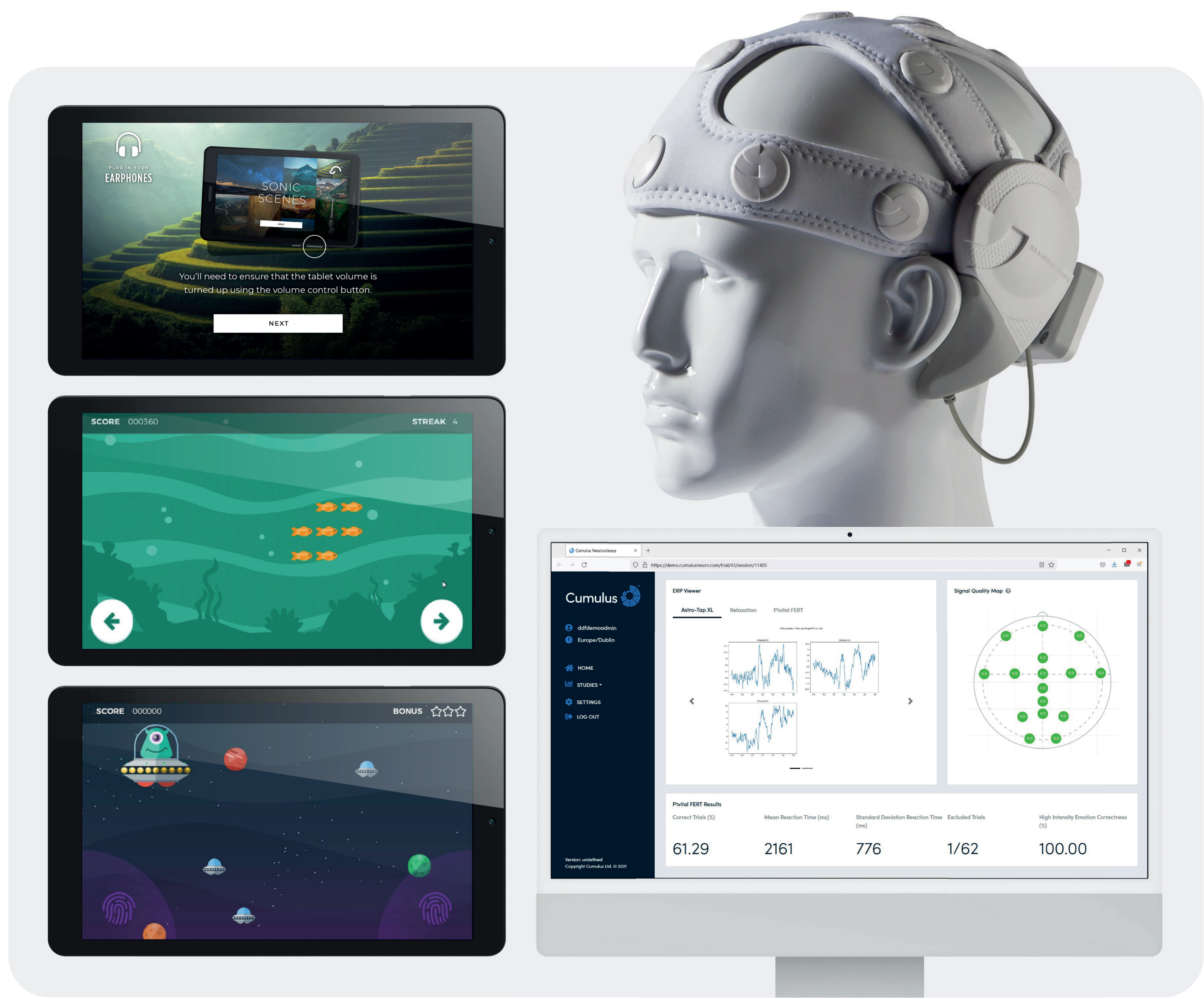


Fig 1. The Cumulus Platform. Left (from top to bottom): Screenshots of the gamified MMN, Flanker and Oddball tasks. Right (from top to bottom): The Cumulus 16-channel dry EEG headset, and the online dashboard for remote study monitoring.

Motivation

- There is a critical need for valid, reliable and broadly usable biomarkers for monitoring target engagement and drug efficacy in neuropsychiatric and other CNS clinical trials.
- Real world assessments should include both direct measures of neurophysiological mechanisms, and of the higher functions which are impacted by CNS conditions.
- To validate the Cumulus platform, we evaluated the well-known effects of ketamine using objective measures of a range of domains including EEG that are user-friendly and suitable for frequent sampling – either in clinic or over longer periods of time in the home.

Method

- Double blind cross over design: racemic ketamine (0.5 mg/kg) vs. saline.
- 16-channel dry EEG Cumulus headset.
- EEG paradigms: 20-min eyes-closed resting state recordings, gamified 12-min visual Oddball, 7-min Flanker and 15-min MMN tasks.
- In-lab recordings: before, 1h-post and 24h-post infusions.
- Remote at home recordings for a week before and after infusions.

Results

- In-lab, we observed robust enhancement of gamma band activity (>25Hz) during infusion, primarily in the parietal lobe.
- In the MMN during infusion, hypothesized trends were seen in reduction of amplitude and increase of latency.
- Robust changes were not seen in the ERN and the P300
- Real-world feasibility was confirmed with adherence of 83% to scheduled at-home sessions (19.1 sessions out of 23 requested, SD=2.33, range: 13-22) – see Figure 2.

Demographics

Number of participants	30 males
Age in years [mean, (std)]	25.57 (3.74)
MADRS at baseline [mean, (std)] (non-depressed cohort)	0.27 (0.69)

Sessions

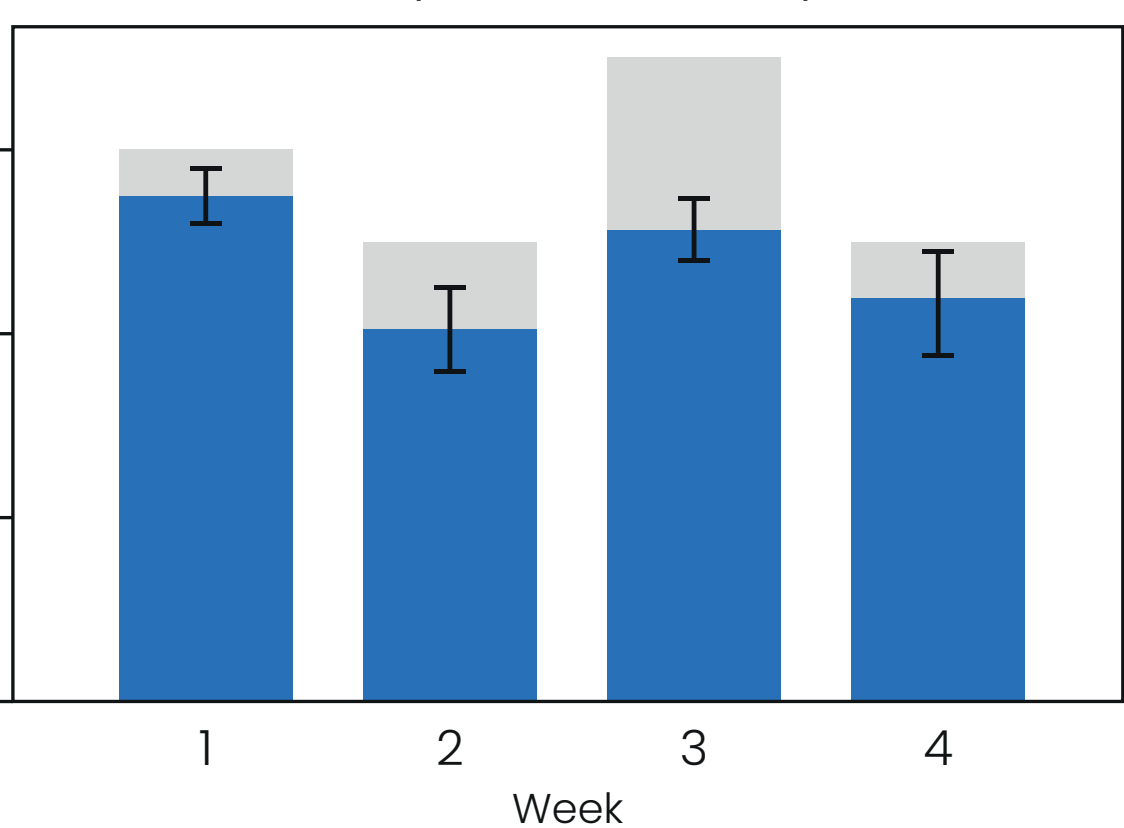


Fig 2. Mean number of at home sessions per participant.

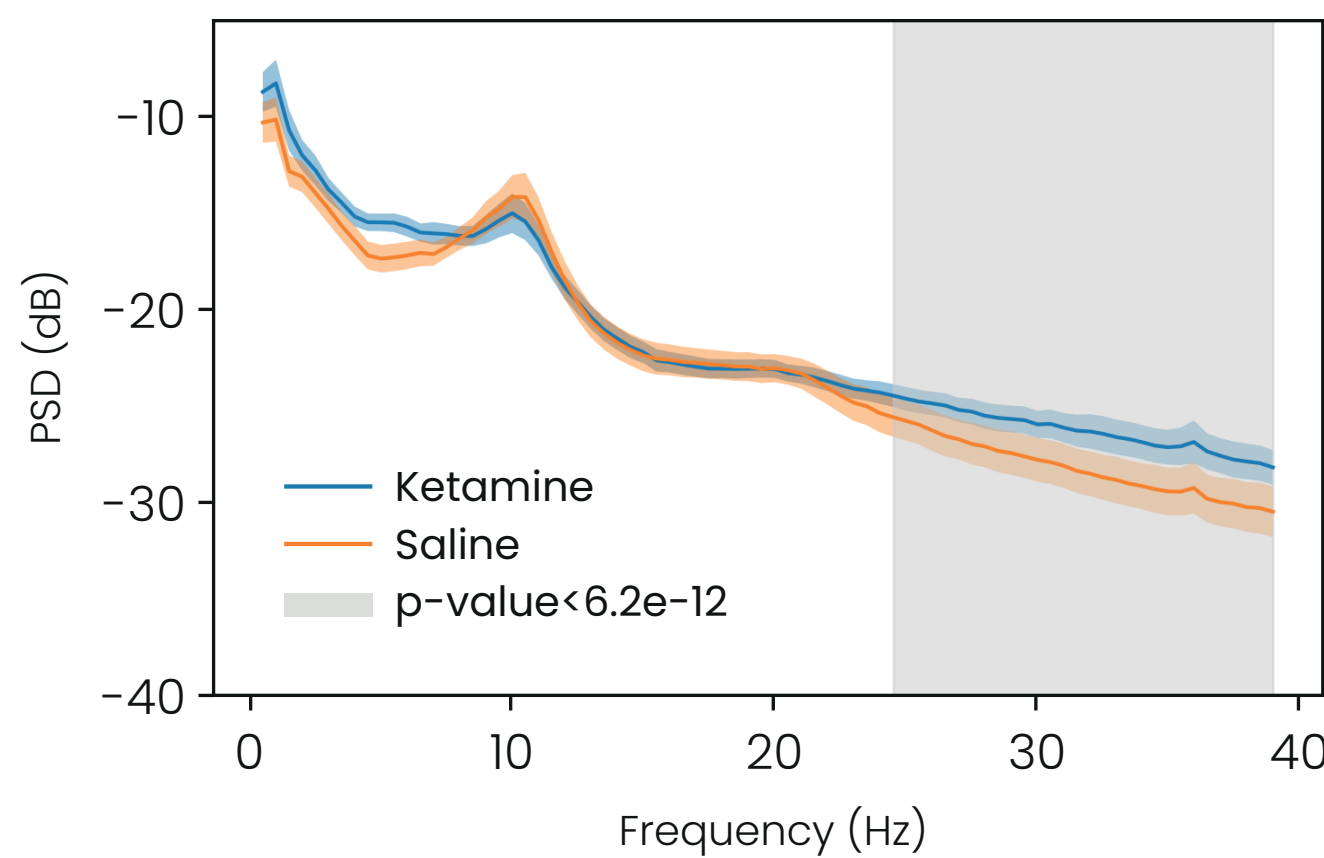


Fig 3. Power Spectrum Density collected during the 2nd half of the ketamine infusion at channel Fz.

Mismatch Negativity (MMN)

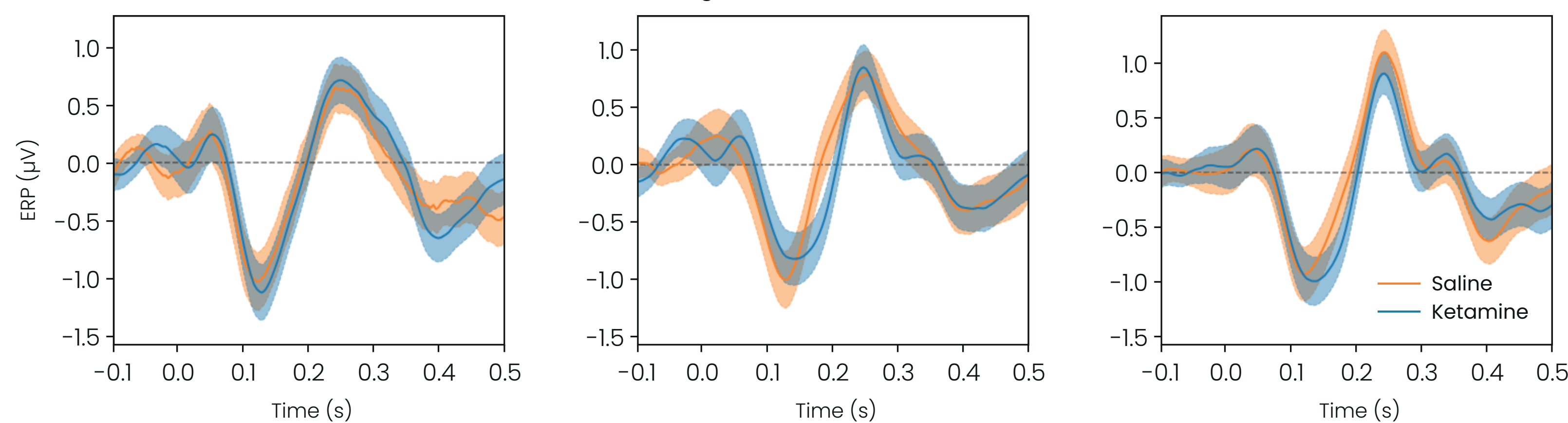


Fig 4. (above) Event related potential of the MMN difference wave extracted from the passive auditory oddball task at channel Fz.

Target P300

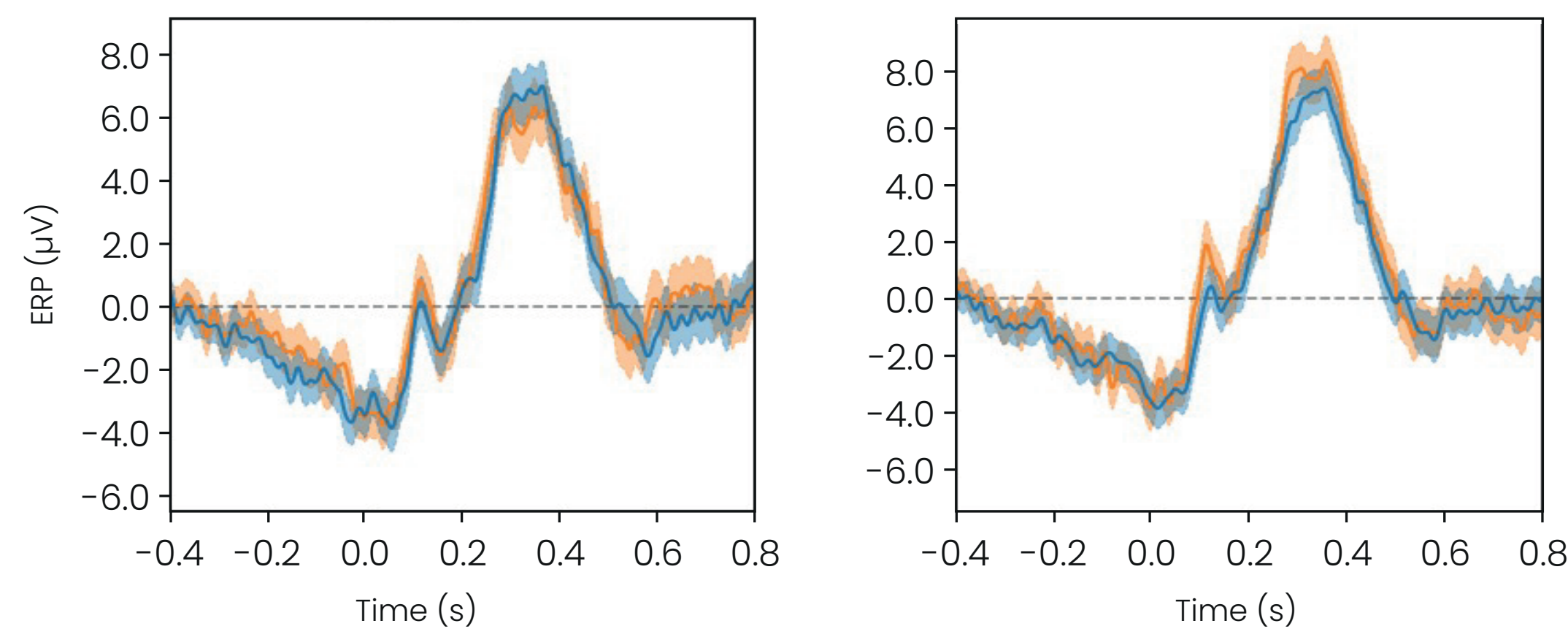
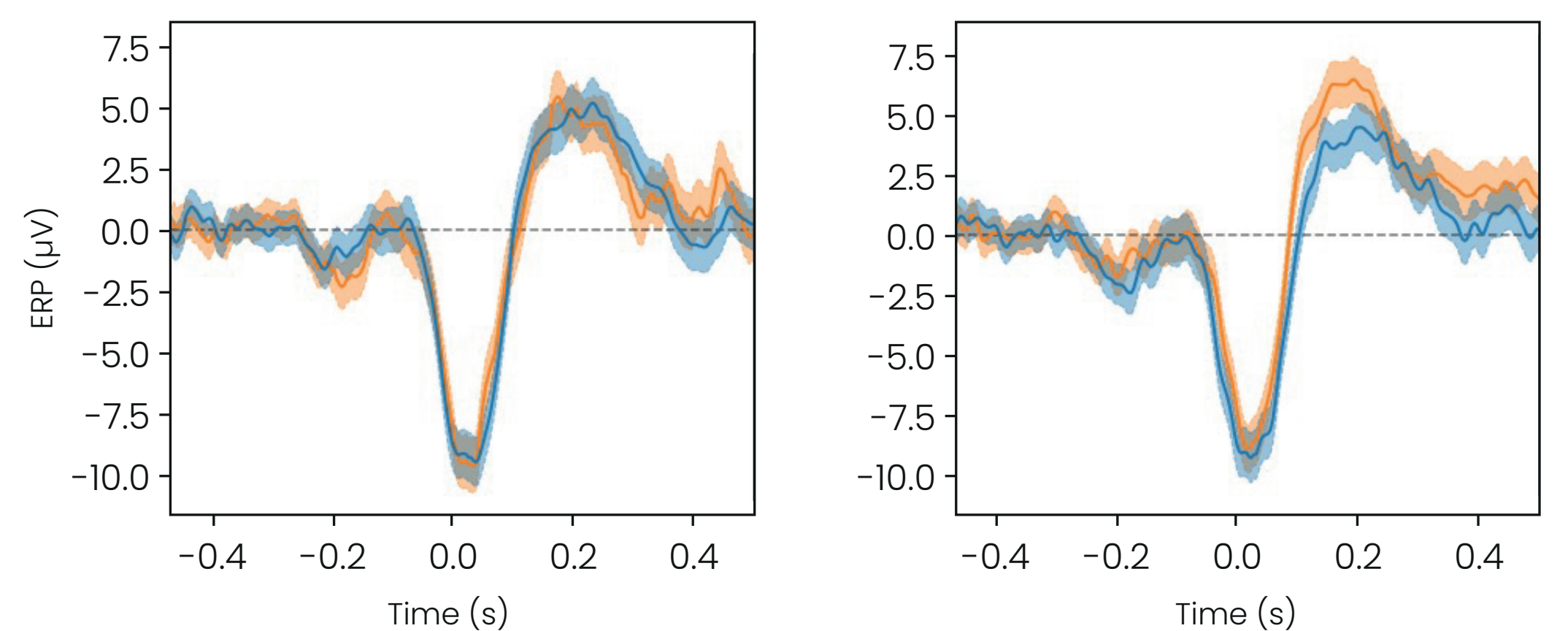


Fig 5. (left) Event related potentials collected before and 1h after infusion. Top: Target trials extracted from the gamified Oddball task at channel Pz.

Error Related Negativity (ERN)



Bottom: Error Related Negativity extracted from the gamified Flanker task at channel FCz.

Conclusions

Lab-based measurement demonstrated sensitivity to pharmacologic intervention

- Clear enhancement of gamma power during ketamine infusion
- Apparent trends toward effects on evoked response measures (MMN)
- P300 and ERN collected after infusion, effects less clear using traditional analysis.

Successful integration of the technology in the lab and in the home

- ERPs elicited in the home are consistent with baseline lab-based measures
- Excellent adherence to at-home test schedule.

Neuropharmacological effects can be observed with easy-to-use dry EEG technology, both in the laboratory, and over longer baseline and post-administration periods in the home, opening new possibilities in psychiatric clinical research, particularly in mood related disorders, where gamma-band alterations have been described.

