Home-based closed-loop auditory stimulation in chronic insomnia: preliminary effects on subjective sleep quality and overnight declarative memory consolidation

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INTRODUCTION

Closed-loop auditory stimulation (CLAS) is a promising non-invasive method for studying and enhancing sleep, yet its potential to alleviate the symptoms of chronic insomnia remains unclear. We present preliminary results on whether a home-based CLAS affects subjective sleep quality and declarative memory consolidation in chronic insomnia.

AIMS

1. Does CLAS alter subjective sleep quality in insomnia?
2. Does CLAS alter overnight declarative memory consolidation?

METHODS

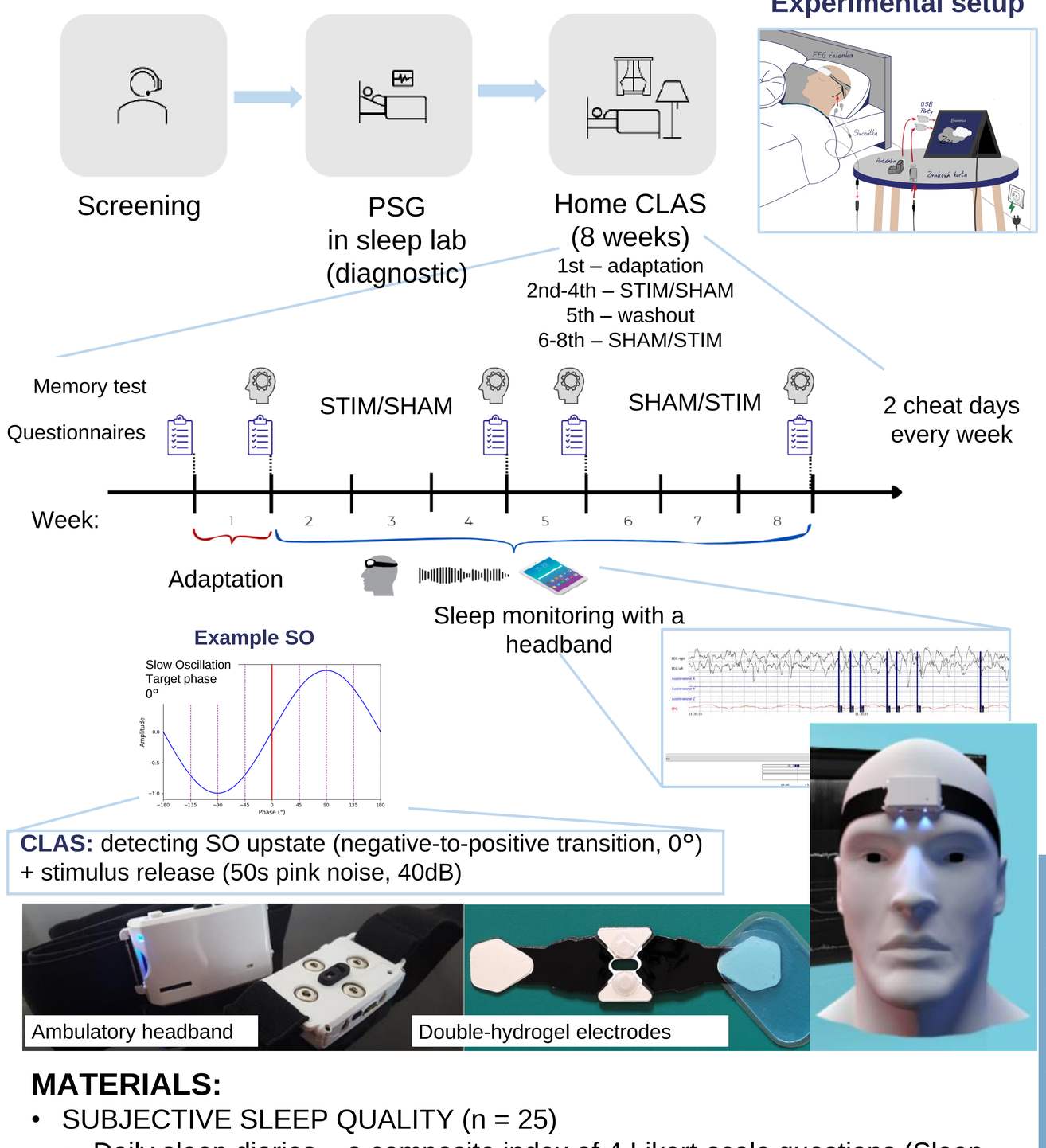
PARTICIPANTS:

- N = 25 patients with insomnia (17 w, aged 21-45, M_{age} = 34.68, SD_{age} = 7.71)

DESIGN:

- Within-subject, randomised crossover (slow-oscillation stimulation vs. sham), 8 weeks total. Up to 30 nights of EEG recordings per individual.

PROCEDURE:

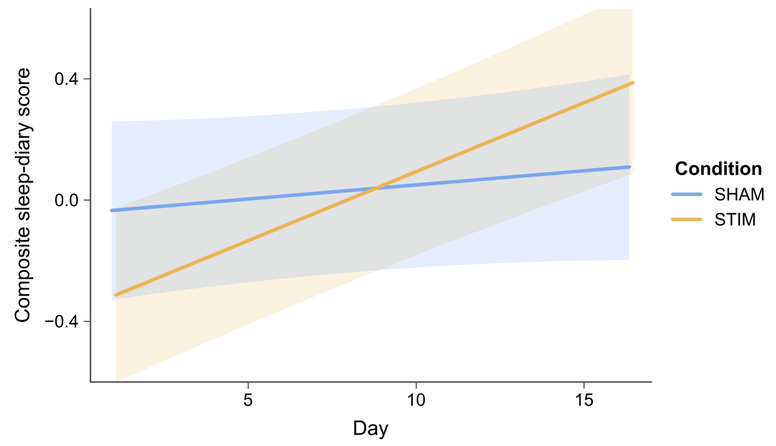


MATERIALS:

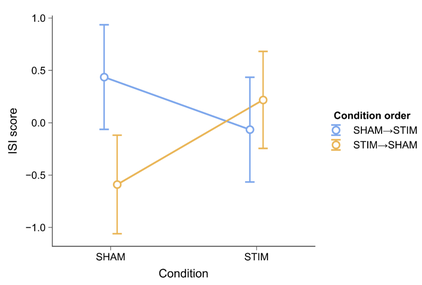
- SUBJECTIVE SLEEP QUALITY (n = 25)
  - Daily sleep diaries – a composite index of 4 Likert-scale questions (Sleep Depth, Restfulness, Quality, Sleepiness in the morning)
  - Insomnia Severity Index (ISI)
  - Pittsburgh Sleep Quality Index (PSQI)
- SLEEP-DEPENDENT MEMORY CONSOLIDATION (n = 24)
  - Paired-associate word task (% retention)
    - after 1st night (acute) + end of block (15th and 30th night – long-term)

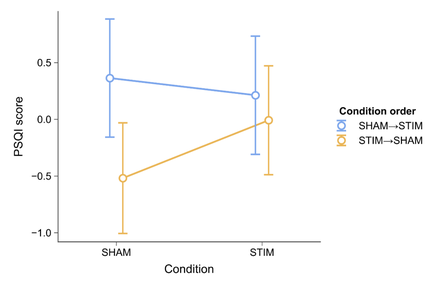
RESULTS

SUBJECTIVE SLEEP QUALITY – SLEEP DIARIES: For sleep diaries composite score, the condition main effect was non-significant (b=−0.03, p=.621), but a condition-by-day interaction (b=0.04, p=.007) indicated that composite sleep-quality scores improved across days under STIM (b=0.05, p<.001) but not SHAM (p=.326).



SUBJECTIVE SLEEP QUALITY – PSQI + ISI: ISI and PSQI showed no CLAS main effect; PSQI improved from pre to post irrespective of condition (b=−0.35, p=.016), and both questionnaires showed order-dependent condition-by-order interactions (p<.001; p=.020).





MEMORY: CLAS produced no main effect on memory retention (F(1,58.9)=0.13, p=.717); retention declined with time since encoding (F(1,65.8)=222.82, p<.001) regardless of condition, with no acute or long-term benefit.

DISCUSSION

These preliminary findings, from a small and still-growing sample, show no enhancement of overnight declarative memory consolidation and no consistent main effect on subjective sleep quality with home-based CLAS. However, sleep-diary trajectories improved more under active stimulation, suggesting possible time-dependent subjective sleep quality benefits. Results should be interpreted with caution and await confirmation in the full, higher powered sample.

KEY TAKEAWAYS

- **Long-term home CLAS in chronic insomnia is feasible.**
- **Ambulatory recordings allow to study insomnia across multiple nights – 30 nights were possible.**
- **No changes found in sleep-dependent memory consolidation**
- **No changes in subjective sleep quality (PSQI) and insomnia severity (ISI)**
- **Sleep diaries showed that subjective sleep quality increased after stimulation (at trend level) – should be taken with caution, need for larger, better powered sample**

Conflict of interest statement: Authors Filip Černý, Stefan Jongejan and Lucia Talamini are currently employed by Deep Sleep Technologies BV, Netherlands. DST had no involvement in the design, analysis, interpretation, or reporting of this study but was involved in conduct of the study for the detection of sleep oscillations. The study was conducted entirely at the National Institute of Mental Health, Czechia. All other authors declare that they have no conflicting interests.

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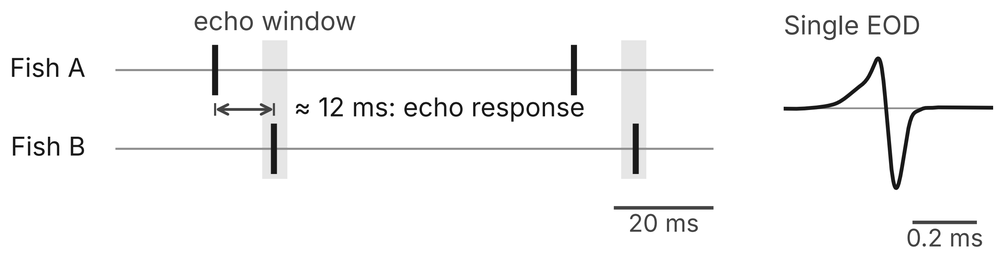
Ketamine alters dyadic electrocommunication in a novel model of schizophrenia based on weakly electric fish

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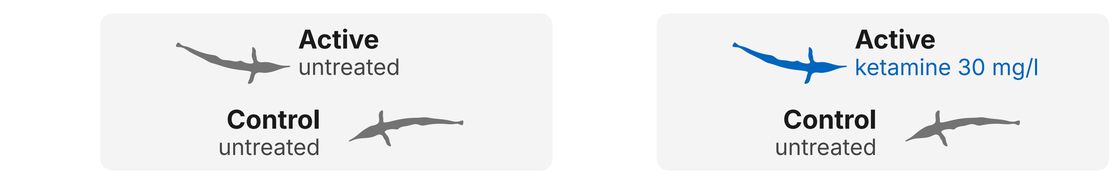
BACKGROUND

- Disorganised speech and disrupted social reciprocity are core symptoms of schizophrenia yet remain challenging to quantify in animal models.
- The weakly electric fish *Gnathonemus petersii* communicates with electric organ discharges (EODs).
- One of the simplest forms of interaction is the **echo response**, in which a fish discharges about 12 ms after its partner.



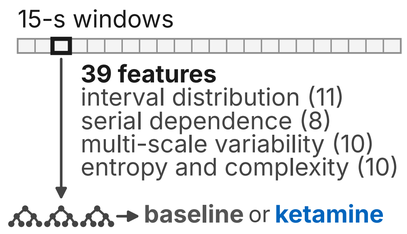
How does ketamine affect the discharge pattern of the treated fish and its electric interaction with an untreated partner?

METHODS



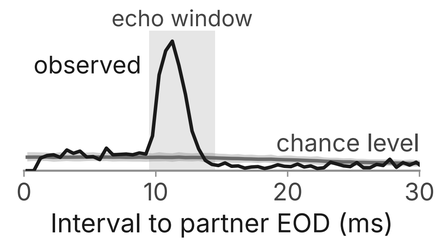
11 dyads with 12-min baseline and ketamine sessions, EODs separated as in [1].

Classifier (Random Forest)



Leave-one-fish-out: each fish is classified by a model trained on the other 10.

Echo response



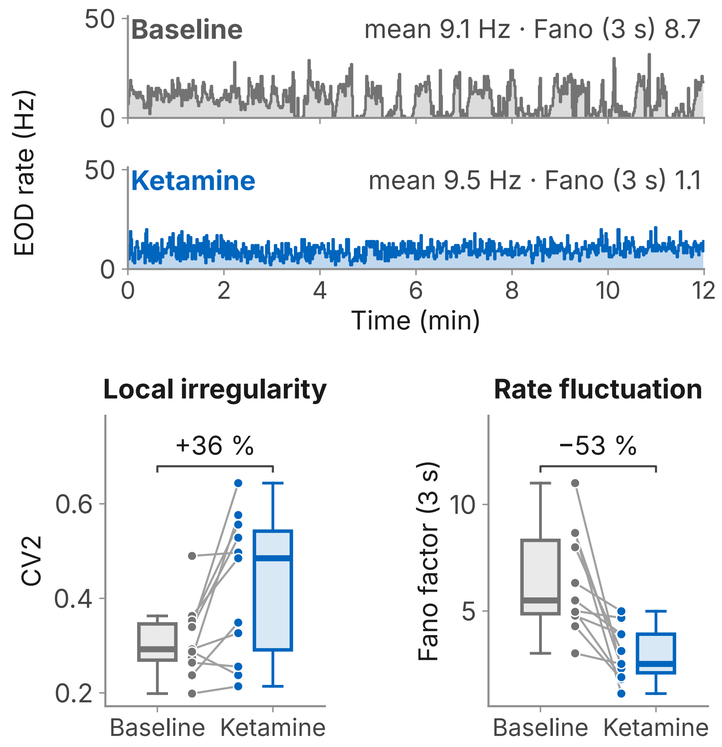
$$\text{Echo fraction} = \frac{\text{echoes observed}}{\text{echoes expected by chance}}$$

RESULTS

1 Ketamine alters the discharge pattern of the treated fish

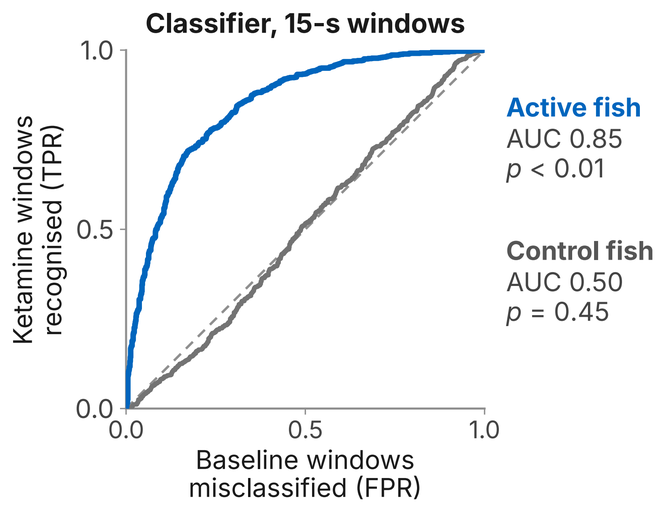
Interval statistics

- **Higher local irregularity:** CV2 +36 %
- **Lower rate fluctuation over seconds:** Fano factor −53 %



Window-level classification

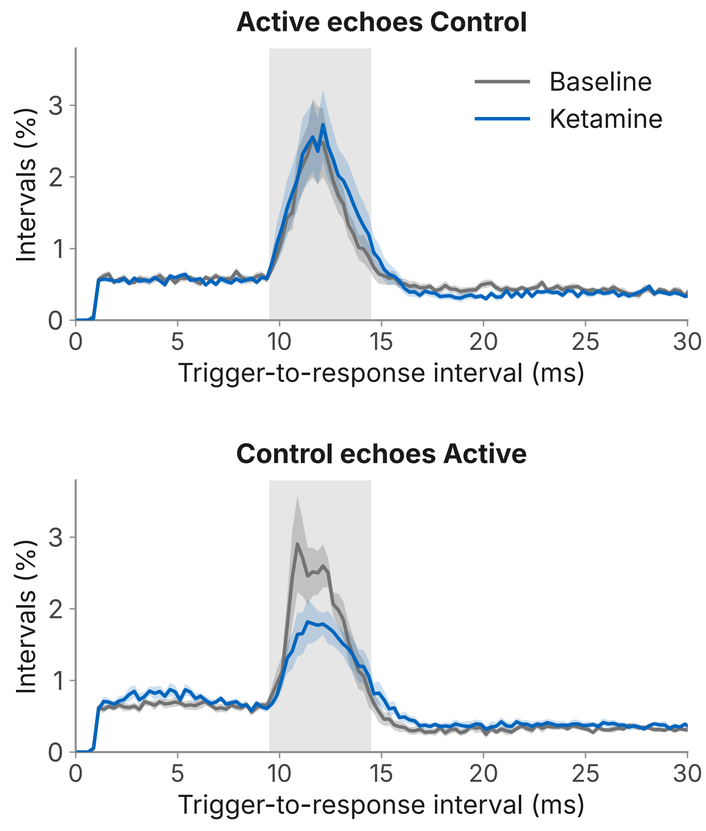
- **Active fish:** AUC 0.85 ($p < 0.01$), all 22 sessions classified correctly.
- **Control fish:** chance level (AUC 0.50, $p = 0.45$).
- **Most informative features:** sample and permutation entropy of the interval sequence (its unpredictability), then CV2 and local variation, all higher under ketamine in most fish.

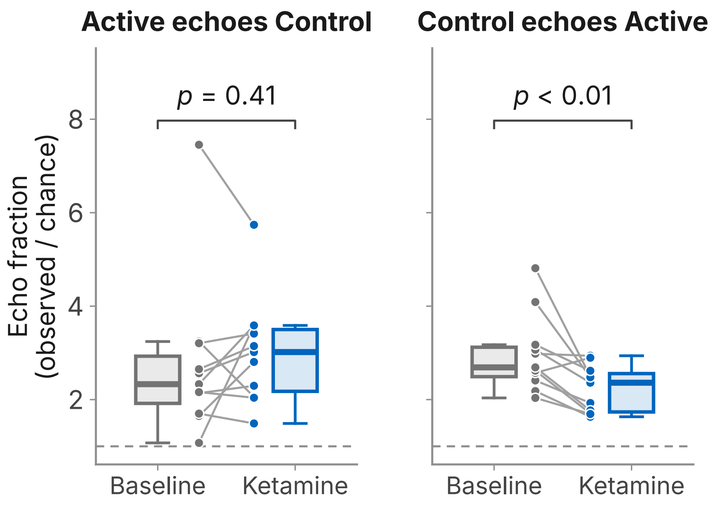


Box plots show session means of CV2 and the Fano factor in all 11 Active fish, with lines connecting the two sessions of each fish. These two complementary measures describe variability at different time scales, between neighbouring intervals and in 3-s pulse counts, and rank among the largest changes of the 39 features. The example fish shows reduced slow fluctuations of the discharge rate at a similar mean rate. The classifier operates on single 15-s windows, and its *p*-value was obtained with a permutation test.

2 The untreated partner echoes less often

- **Active echoes Control:** no significant change in echo fraction ($p = 0.41$).
- **Control echoes Active:** echo fraction −25 % ($p < 0.01$).
- **Latency:** no significant change in either direction.





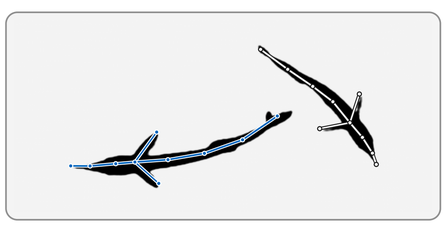
Histograms show the mean ± SEM over 11 dyads in 0.25-ms bins. In the box plots, the dashed line marks chance. Wilcoxon signed-rank tests, FDR-corrected.

DISCUSSION

- **Ketamine reshapes the discharge pattern of the treated fish.** Beyond disrupting the coupling between EODs and locomotion [1,2], it changes the temporal structure of the signal itself.
- **The effect propagates to the untreated partner.** The untreated fish responded to the treated fish with fewer echoes, whereas its own discharge pattern showed no detectable change.
- **The echo response may provide a quantitative readout of disturbed social communication.** Based solely on EOD timing, it measures how one fish responds to another and can be used to assess changes in electrocommunication in pharmacological studies.
- **Limitations.** 11 dyads and a single dose. Whether the weaker echo reflects the treated fish's altered signal, its altered behaviour or a change in their coupling remains open.

NEXT STEPS

- **Antipsychotics:** To test whether antipsychotic treatment normalises these changes.
- **Behaviour:** Pose tracking of both fish (DeepLabCut) to link EOD patterns to social behaviour.



DeepLabCut pose estimation.

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[1] Chrtkova I, et al. Unsupervised electric signal separation for linking behavior and electrocommunication in *Gnathonemus petersii*. Sci Rep. 2025;15(1):33542. doi:10.1038/s41598-025-18291-5
[2] Langova V, et al. Ketamine disrupts locomotion and electrolocation in a novel model of schizophrenia, *Gnathonemus petersii* fish. J Neurosci Res. 2023;101(7):1098-106. doi:10.1002/jnr.25186

Symptom-Domain Outcomes and Pretreatment EEG Biomarkers of Antidepressant Response in Major Depressive Disorder

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Background

- Major depressive disorder (MDD) is clinically heterogeneous: patients with similar overall depression severity may have different symptom profiles and patterns of improvement.
- Although a ≥50% reduction in total score provides a conventional measure of treatment response, it does not indicate which symptom domains improved.
- Domain-specific outcomes may therefore provide clinically relevant information that is obscured by an aggregate score.

Objective

To determine whether pretreatment resting-state EEG features predict antidepressant response within clinically defined MADRS symptom domains, and to compare domain-specific prediction with conventional MADRS total-score prediction.

1. Evaluate pretreatment EEG biomarkers as predictors of response in four MADRS symptom domains.
2. Compare domain-specific predictive performance with prediction of conventional MADRS total-score response.

- **Rationale:** domain-level outcomes may reveal neurophysiological associations that are obscured when heterogeneous depressive symptoms are aggregated into a single score.

Methods | EEG Measures

Pretreatment resting-state EEG predictors

EEG was summarized as 90 features spanning five families of measures: Lempel–Ziv complexity (LZC), the aperiodic exponent, alpha peak frequency, frontal alpha asymmetry, and spectral power in six bands (delta, theta, alpha, beta, gamma1, gamma2).

Methods | Clinical Outcome Definition

MADRS total score and four clinically defined symptom domains

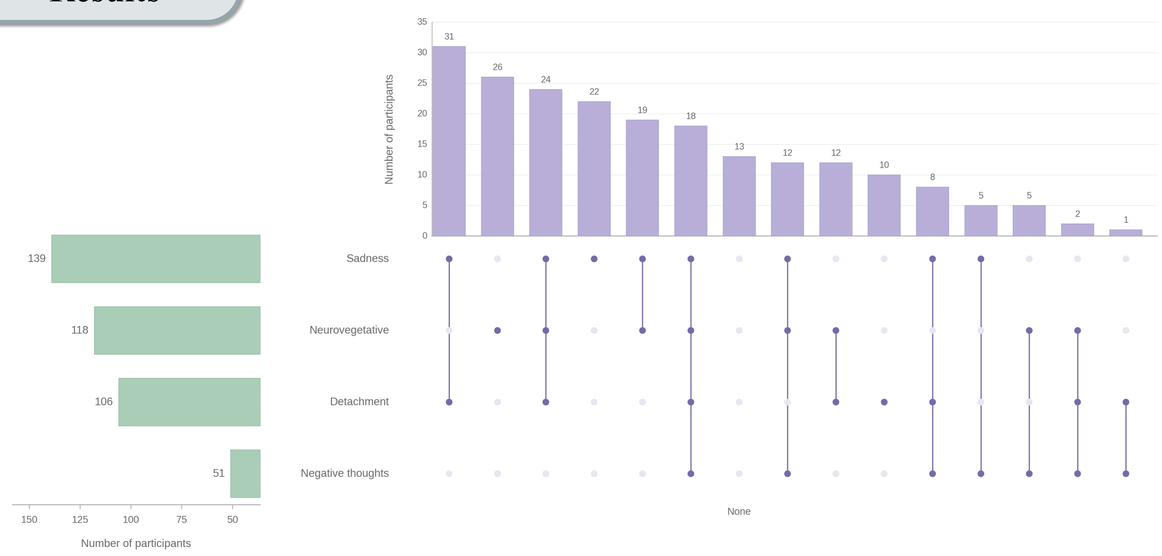
Prediction target	Constituent MADRS items	n	R	NR
MADRS Total:	All 10 MADRS items	146	71	75
Sadness:	Apparent sadness; Reported sadness	91	44	47
Negative Thoughts:	Pessimistic thoughts; Suicidal thoughts	40	24	16
Detachment:	Concentration difficulties; Lassitude; Inability to feel	75	35	40
Neurovegetative:	Inner tension; Reduced sleep; Reduced appetite	91	43	48

- **Response** – ≥ 50% reduction from baseline to the study-specific endpoint, in the total score or in the corresponding domain sum score.
- **Baseline domain positivity** – Sadness / Negative Thoughts: both items ≥ 3; Detachment: all three items ≥ 3; Neurovegetative: ≥ 2 items ≥ 3 with reduced appetite ≥ 2. Domain analyses include only positive participants.

Methods | Pretreatment EEG Predictors

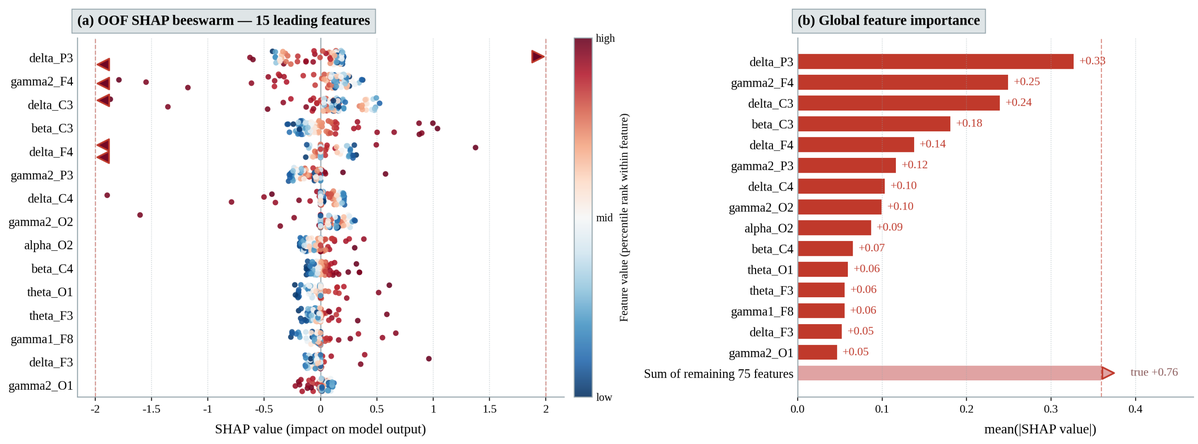
- **Cohorts and Endpoints** – week 8 (CAN-BIND-1); week 12 (Ottawa).
- **Classifiers** – elastic-net logistic regression, linear support vector machine, random forest, XGBoost.
- **Validation** – nested stratified cross-validation: 5 outer folds for out-of-fold evaluation, 4 inner folds for hyperparameter tuning (subject to feasible class counts). Outer-fold assignments are shared by all models within a target; inner-loop selection uses ROC AUC.
- **Performance** – estimated from pooled out-of-fold probabilities at a 0.50 threshold; accuracy, balanced accuracy, precision, sensitivity, specificity and F1 are also reported.
- **Inference** – 2,000 stratified bootstrap samples for the 95% CI of OOF AUC; 200 permutations repeating the complete nested cross-validation; coefficient or feature-importance magnitude and feature stability summarized across the five outer folds.

Results



Overlap among baseline symptom\-domain phenotypes. *The UpSet plot shows the set sizes and intersections of four prespecified symptom\-domain phenotype definitions: sadness, neurovegetative symptoms, detachment, and negative thoughts. Horizontal bars show the number of participants meeting each phenotype definition. Filled circles and connecting lines indicate the phenotypes included in each exact intersection, while vertical bars show the number of participants exhibiting each intersection pattern. Fourteen non\-empty exact phenotype combinations were observed, of which 13 included at least two participants. An additional 13 participants did not meet the criteria for any of the four phenotype definitions and are represented by the "None" intersection column.*

The elastic-net logistic regression model predicted sadness-domain response above chance (AUC = 0.638, 95% CI: 0.524–0.750; permutation $p = 0.0299$; $n = 91$). After winsorizing all EEG features at the 1st and 99th percentiles to reduce the influence of extreme power values, predictive performance remained statistically significant (AUC = 0.639; permutation $p = 0.0149$).



Out-of-fold SHAP summary for the winsorized elastic-net logistic regression model. (a) Beeswarm of out-of-fold SHAP values for the 15 leading EEG power features, ordered by mean |SHAP|; each point is one participant (n = 91) and color encodes the within-feature percentile rank of that participant's feature value. SHAP values are the additive contributions to the log-odds of the Sadness classification and are clipped to ±2. (b) Global importance (mean |SHAP|) for the same 15 features, with the remaining 75 features summed (total 0.76; bar truncated at 0.36).

Discussion and Conclusion

Pretreatment resting-state EEG showed modest but statistically significant prediction of antidepressant response in the sadness domain. The association remained significant after winsorization, suggesting that the result was not explained solely by extreme EEG values.

These findings suggest that symptom-domain outcomes may reveal EEG associations that are obscured when treatment response is defined using only the MADRS total score. However, the predictive performance was modest and was evaluated in a relatively small sample. Replication in larger independent cohorts is required before these EEG features can be considered clinically useful biomarkers.

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Baseline Heartbeat-Evoked Potentials Are Associated with Subsequent Reversion from Mild Cognitive Impairment

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Background

- Mild cognitive impairment (MCI) has a heterogeneous course, with some individuals reverting to normal cognition.
- The neurophysiological characteristics associated with MCI reversion remain poorly understood.
- Heartbeat-evoked potentials (HEPs) reflect cortical processing of cardiac signals and have been linked to attention, perception, and cognitive functioning.
- Whether baseline HEPs are associated with subsequent cognitive reversion in MCI remains unclear.

Objectives

- To compare baseline HEPs between individuals with MCI who subsequently reverted to normal cognition and those with persistent MCI.
- To examine associations between baseline HEP amplitude and domain-specific reversion, as well as continuous cognitive performance at follow-up.

Methods

Cluster-based permutation tests: Whole-scalp HEP comparisons (200-600ms), adjusting for age, sex, and mean NN interval.
Bayesian hierarchical model: Associations with domain-specific reversion, adjusting for baseline severity.
Linear mixed-effects model: Associations with continuous follow-up cognition, adjusting for baseline cognitive score and cognitive domain.

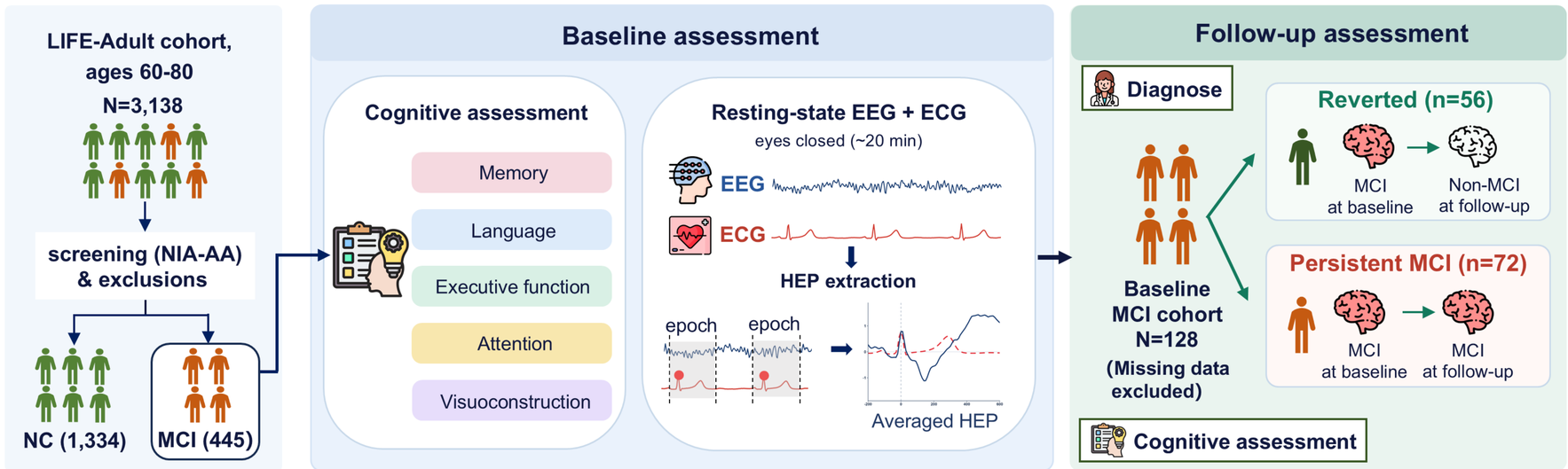
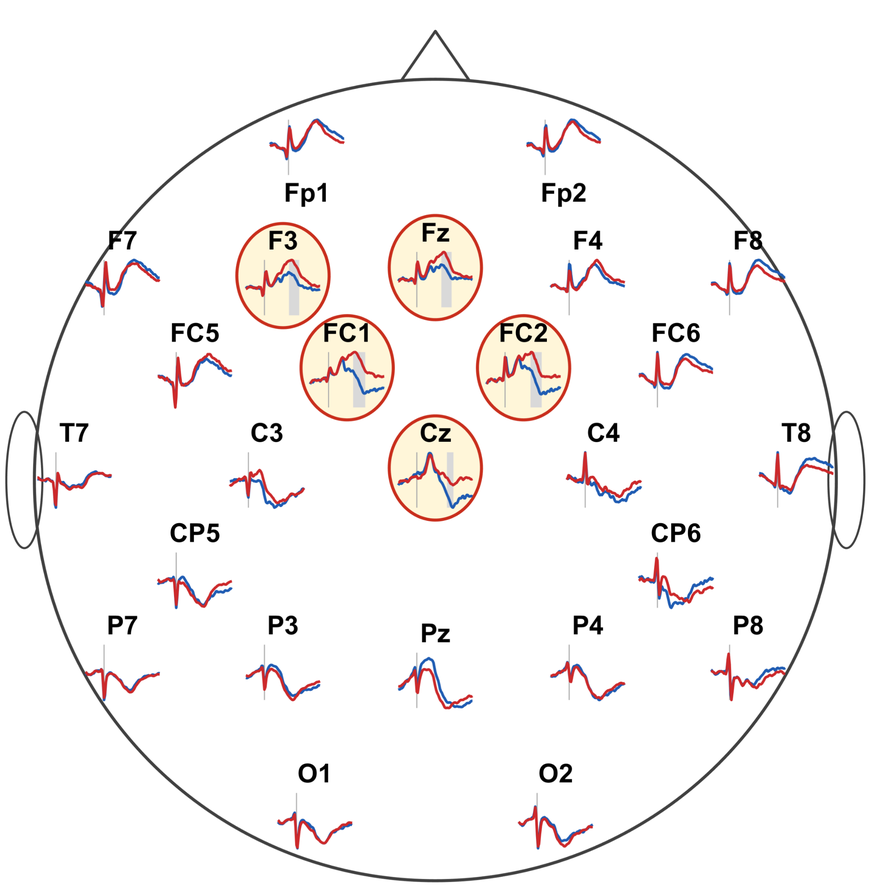


Figure. Study design

Results



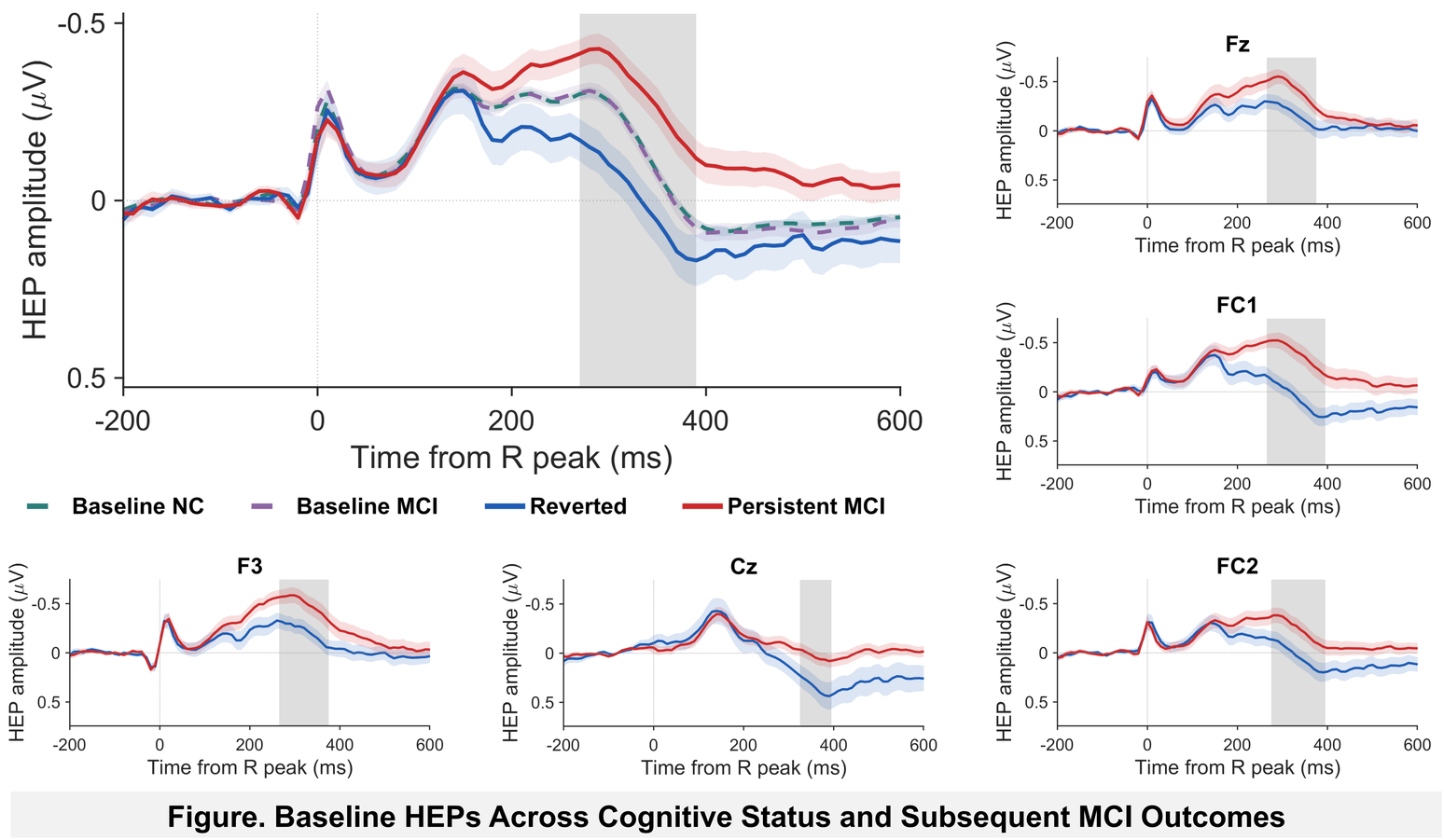
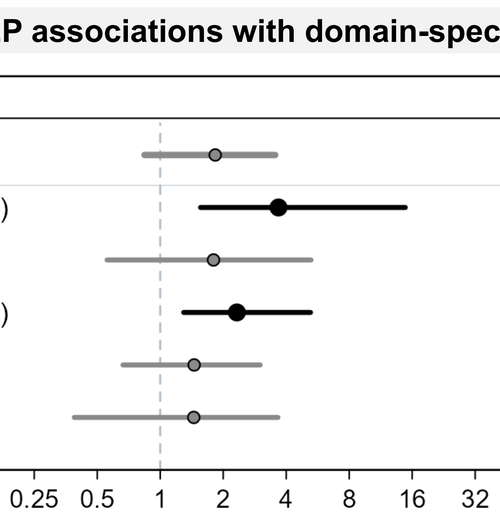


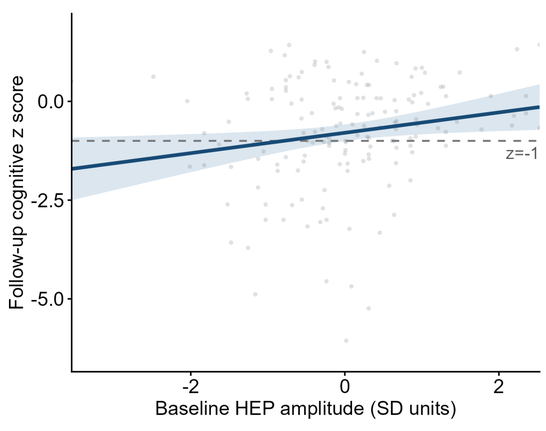
Figure. Baseline HEPs Across Cognitive Status and Subsequent MCI Outcomes

Reverted group showed higher baseline frontocentral HEP amplitudes at 270-390ms than Persistent MCI group (cluster-corrected p = 0.012). No significant HEP cluster was identified between baseline NC and MCI groups.

Table. HEP associations with domain-specific reversion

Domain	N (R/P)	OR (95% CrI)	P(OR > 1)
Overall	--	1.83 (0.84-3.55)	94.5%
Memory	46 (32/14)	3.67 (1.56-14.84)	99.98%
Language	11 (5/6)	1.80 (0.56-5.26)	86.2%
Executive	44 (24/20)	2.33 (1.29-5.23)	99.77%
Attention	40 (31/9)	1.45 (0.66-3.00)	82.2%
Visuoconstruction	15 (6/9)	1.45 (0.39-3.65)	73.5%





Higher baseline HEP amplitude was associated with better follow-up cognitive performance (β = 0.258, 95% CI: 0.041-0.474; p = 0.020).

Figure. Baseline HEPs and follow-up cognitive performance

Conclusion: Higher baseline frontocentral HEP amplitudes were associated with subsequent reversion from MCI to normal cognition and better follow-up cognitive performance. HEPs may reflect neurophysiological differences related to cognitive recovery in MCI, although independent validation is needed.

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Evaluation of Functional Networks from EEG data of subjects under the effects of Ayahuasca

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[3] Psychedelic Research Group, National Institute of Mental Health (NUDZ)

INTRODUCTION

Ayahuasca is an ancestral Amazonian that induces an altered stated of consciousness characterized by profound changes in perception, emotion and cognition[1]. Its effects arise from the decoction of the leaves of Psychotria Viridis, which contain the psychedelic compound N,N-DMT (dimethyltryptamine), with the liana Banisteriopsis Caapi, which contain MAO inhibitors that make DMT orally active. Although medical uses of Ayahuasca were known thousands of years ago by indigenous people of the Amazon and the Andes, it has recently been proven its therapeutical potential in treatment of depression, anxiety and addictions[2]. Therefore, understanding the neurobiology behind Ayahuasca is key to explaining its therapeutical effects. At the brain level, Ayahuasca changes neural activity, as shown by fMRI and EEG studies (Fig, 1).

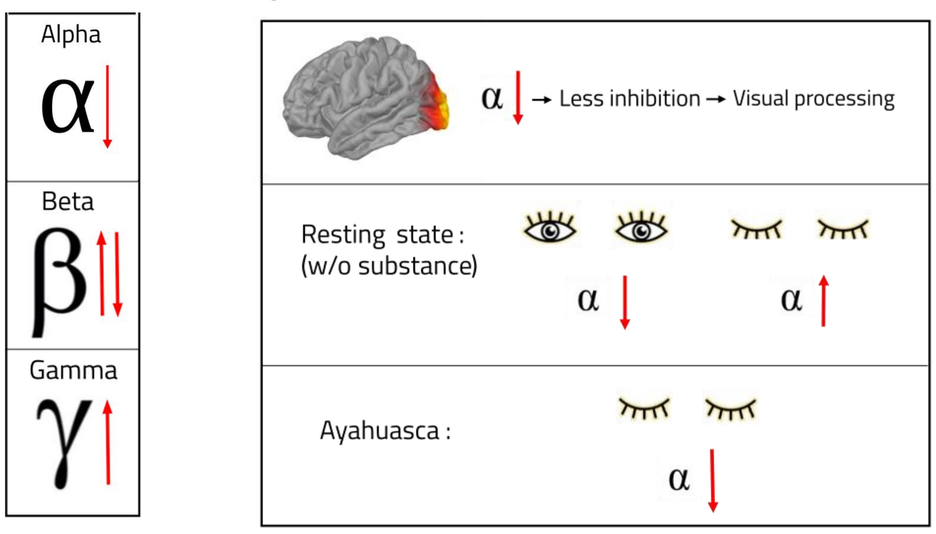


Figure 1. Known EEG effects of Ayahuasca. Left: Reported power changes by frequency band[3] . **Right:** Occipital alpha decreases even with eyes closed[3 4]

METHODS

Design

- Randomized, triple-blind, placebo-controlled
- N = 50 healthy participants (age 32 ± 10 years; 31% men)
- Single dose: ayahuasca (1 ml/kg) or placebo brew

EEG recording

- BrainProducts, 32 channels, 1 kHz
- Time points: 0h (baseline), 2h (acute effects), 4h (offset) post-intake
- Per time point: 4x [Eyes open (20 s) → Eyes closed (40 s)] = 4 minutes

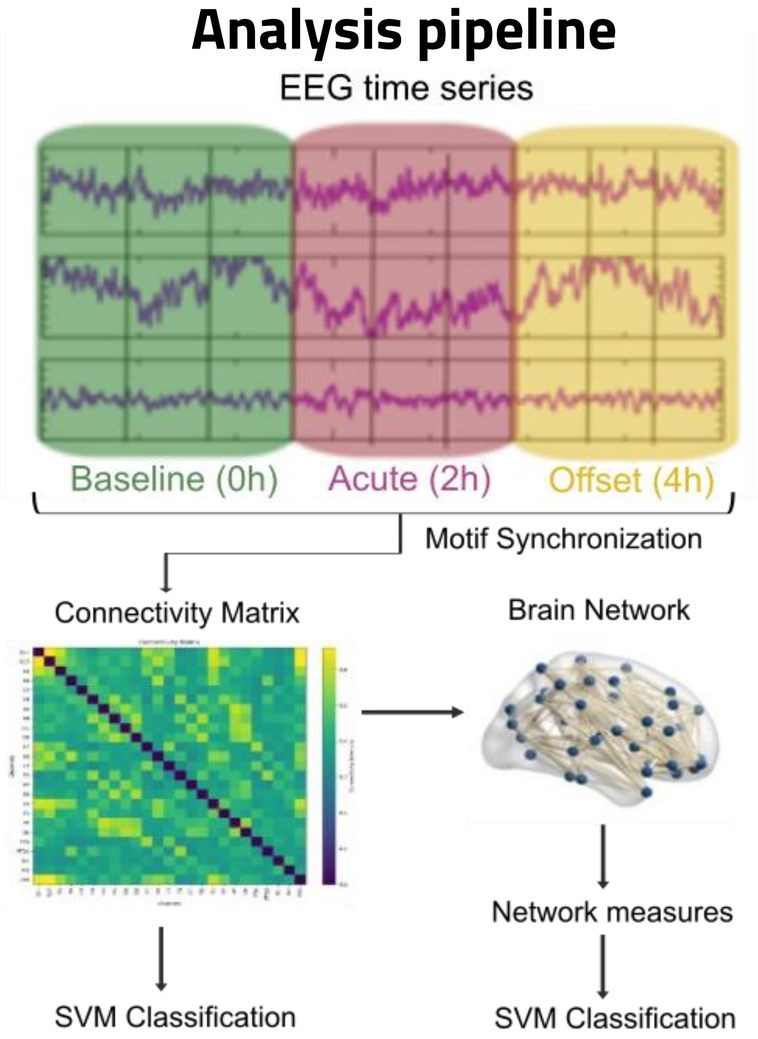


Figure 2. EEG time series (blue line) translation into a motif series[5]

RESULTS

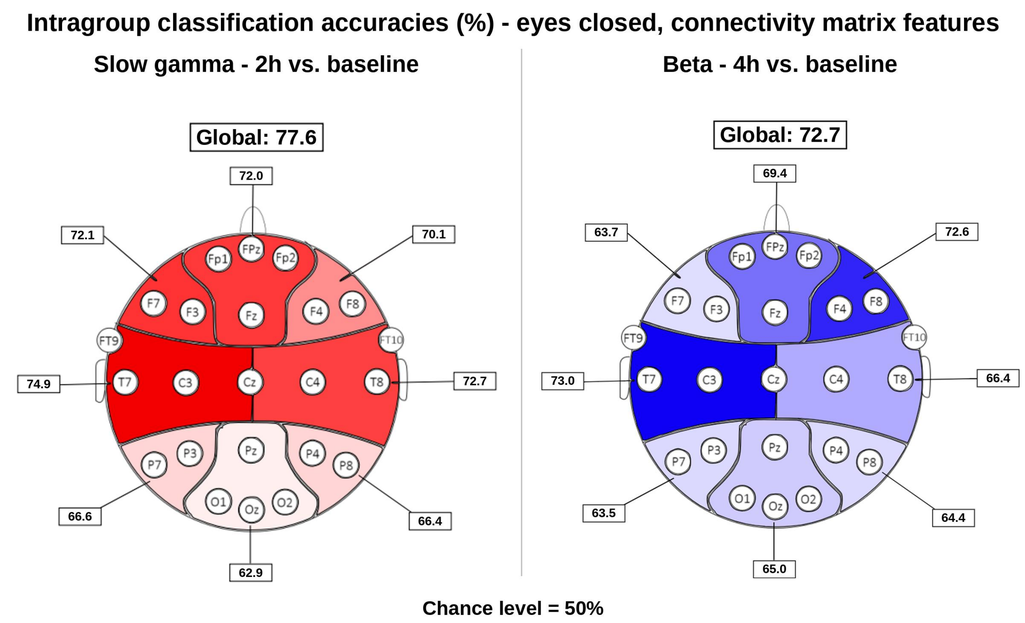
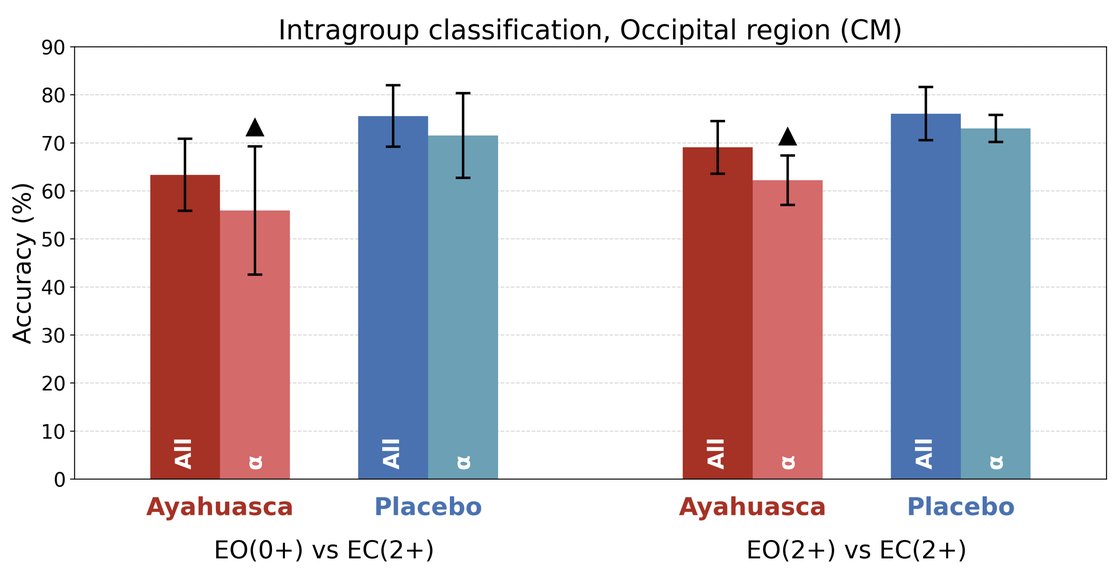


Figure 3. Intragroup Classification accuracies (eyes closed, connectivity matrix features). Left: Slow-gamma band: 2h vs baseline. **Right**: Beta band : 4h vs baseline



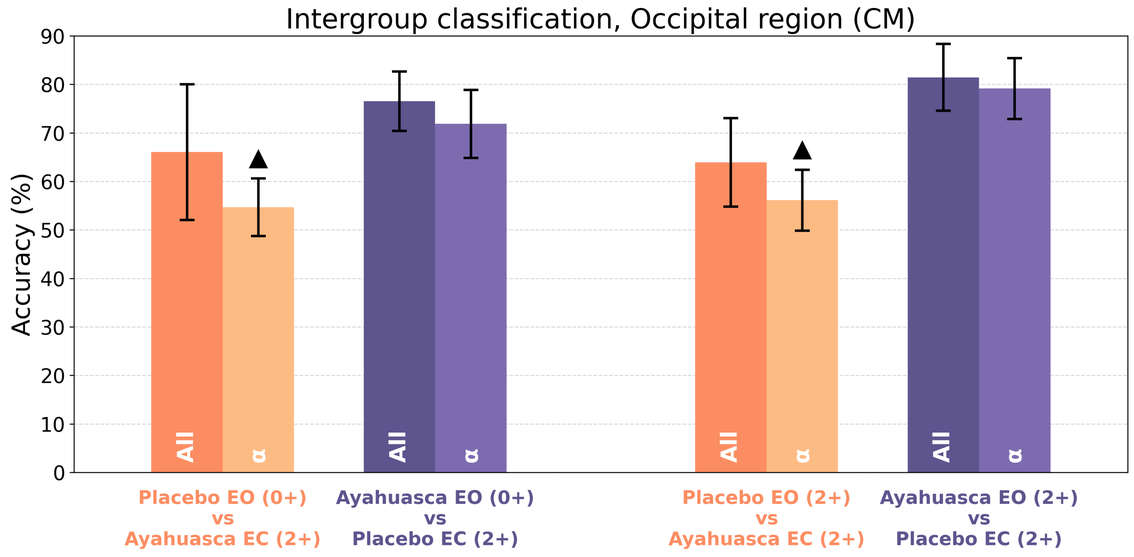


Figure 4. Classification comparison in Occipital region (connectivity matrix features). Top: Intragroup classification of eyes open (OA) vs. eyes closed (OF). **Bottom:** Intergroup classification of placebo vs. ayahuasca.

CONCLUSION

- Acute effects (2h): The most pronounced changes were in slow-gamma connectivity. This may reflect an introspective state similar to meditation or lucid dreaming in which memories are recalled and given meaning by mental imagery. This state is also related to information manipulation (working memory).

- Offset (4h): The most pronounced were in beta connectivity. Although beta findings under ayahuasca are mixed, an increased in right-hemisphere beta power has been linked to perceptual imagery in the relaxed-to-drowsy transition, which may point to similarities with hypnagogic states.

- Occipital Alpha band: Under ayahuasca, eyes-closed connectivity resembles the eyes-open connectivity pattern without the substance, suggesting visual processing as they were with the eyes open.

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Individualized Gamma Neurofeedback in Healthy Older Adults: Individual Gamma Frequency Modulation and Auditory Working Memory

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BACKGROUND

Gamma-band (>30 Hz) neural oscillations are implicated in sensory and cognitive functions and exhibit alterations in various neuropsychiatric conditions [1]. Gamma-based neurofeedback (NFB) represents a promising noninvasive neuromodulation approach [2]. Although neuromodulatory potential of rhythmic auditory stimulation has been studied before [3], NFB approaches incorporating periodic auditory stimulation are lacking. We developed an individualized EEG-NFB system based on gamma auditory steady-state responses (ASSR), targeting individual gamma frequency (IGF). The present study was aimed at testing the system in healthy older adults, assessing its potential effect on auditory working memory performance.

METHODS

26 healthy volunteers (69.5 ± 5.5 years, all F; 16 exp. / 10 ctrl. group). Experimental group received real visual feedback, while control condition consisted of sham visual feedback sequence obtained from a random NFB run recorded in a previous study.

NFB system was implemented in Python using:

- LabStreamingLayer for data acquisition
- PsychoPy for stimulus presentation
- MNE for online data analysis

EEG was recorded using a mobile Smarting Mobi device (mBrainTrain, Serbia) with saline-based electrodes.



Participants underwent **4 experimental sessions** which consisted of the following steps:

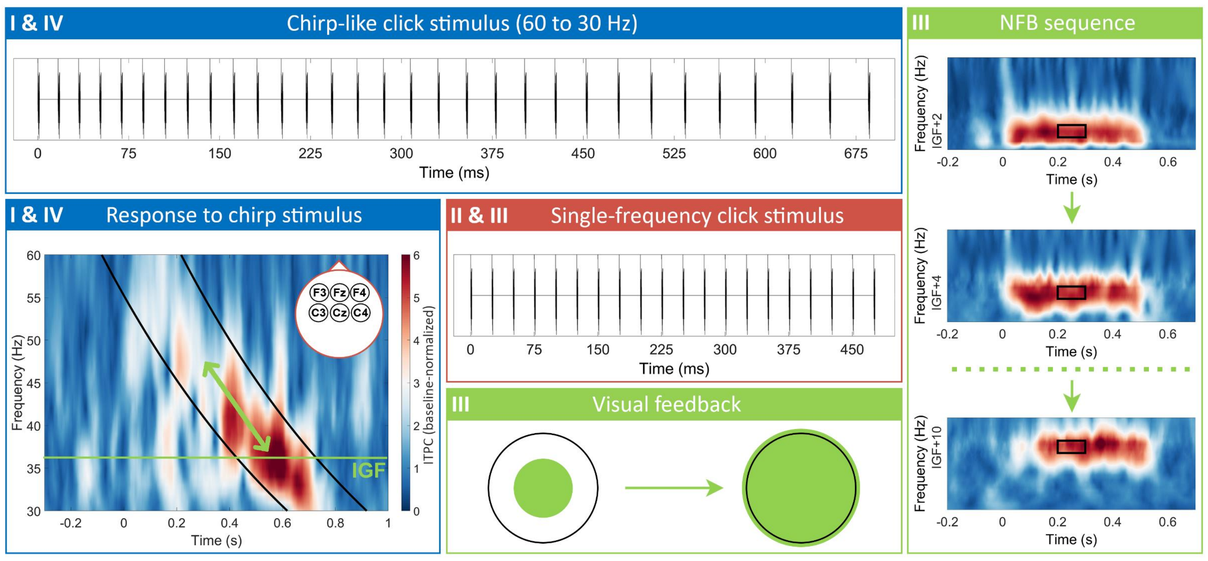
I. IGF estimation pre-NFB using chirp-like auditory click stimuli covering 30-60 Hz.

II. Reference **response at IGF estimation** for NFB calibration using single-frequency click stimulus at IGF.

III. 3 repetitions of **NFB training** with levels of auditory stimulation above IGF, with a maximum of IGF+10 Hz depending on NFB success.

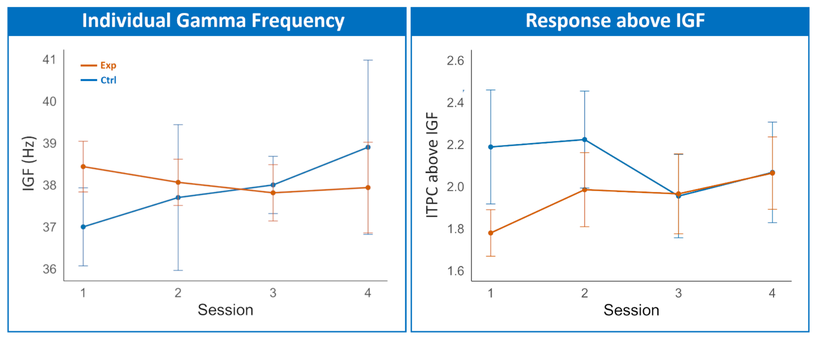
IV. IGF estimation post-NFB (same as step I).

EEG measures were estimated via time-frequency transformation (Morlet wavelet, 7 cycles), computing Inter-Trial Phase Coherence (ITPC).

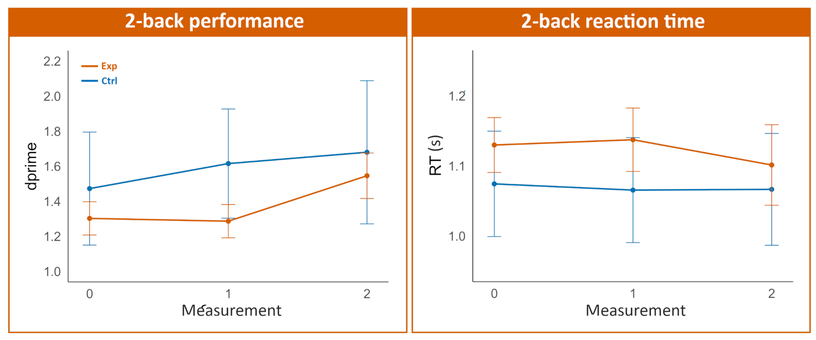


Auditory version of **2-back** working memory task consisting of 6 pure sine tones (300-2800 Hz, 500-Hz step) with different carrier frequency was performed at baseline, after completing Session 2 and Session 4.

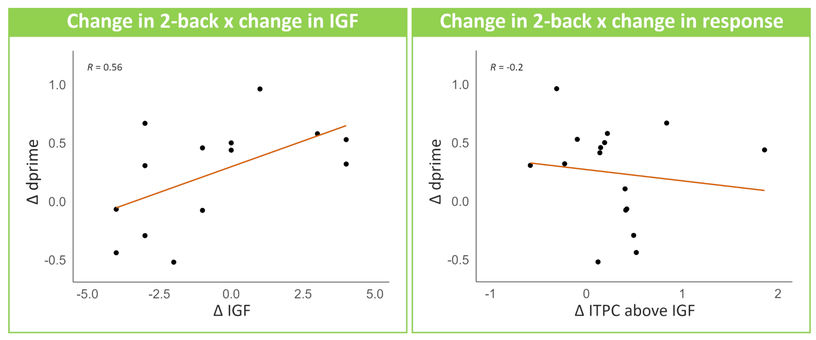
RESULTS



- No group, session, or group × session effects on IGF ($p > 0.18$).
- Significant session × NFB success rate effect on IGF ($\beta = 4.44$, $p = 0.01$) in experimental group.
- Significant group × session on response above IGF ($\beta = 0.14$, $p = 0.03$)



- No significant group, session, or group × session effects on 2-back dprime ($p > 0.15$).
- No significant group, session or group × session effects on 2-back reaction time ($p > 0.44$).



- Significant Group × Δ IGF interaction effect on 2-back Δ dprime ($\beta = 0.08$, $p = 0.03$).
- No significant group, Δ response above IGF or interaction effects on 2-back dprime.

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CONCLUSIONS

Although group-level changes in IGF and working memory performance were not observed, successful NFB training predicted subsequent increases in IGF, and greater IGF increases were associated with improvements in auditory working memory. This suggests that individualized gamma-ASSR-based NFB may facilitate neurophysiological changes linked to cognitive benefits in healthy older adults. However, substantial inter-individual variability highlights the importance of identifying individual factors contributing to NFB responsiveness.

Support for this study was received from Vilnius University Research Promotion Fund (MSF-JM-09/2025)

DOSE-ESCALATION STUDY · PHARMACO-EEG

Effects of intravenous N,N-DMT on EEG spectral power and Lempel-Ziv complexity: a placebo-controlled dose-escalation study

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(1) Centre for Psychedelic Research, Imperial College London, UK · (2) Centre for Consciousness Research, University College London, UK · (3) Cybin Ltd (now Helus Pharma), London, UK

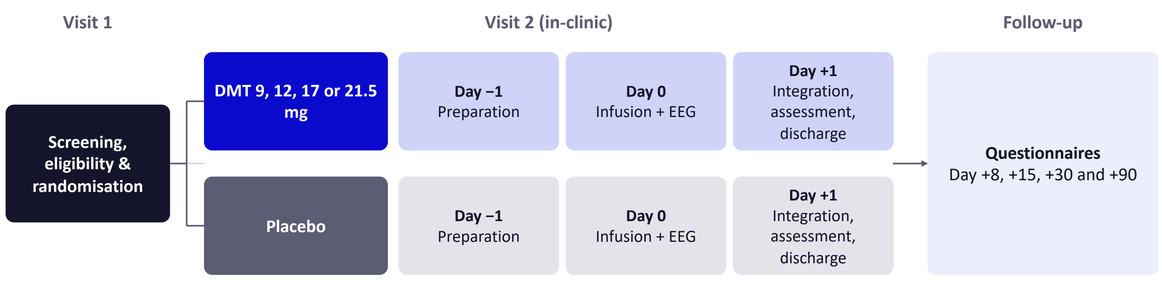
BACKGROUND

- **N,N-dimethyltryptamine (DMT)** is a short-acting serotonergic psychedelic that profoundly alters consciousness.[1]
- Classic psychedelics reduce oscillatory power, most reliably in the alpha band, and increase signal diversity.[2,3]
- Dose, subjective intensity and EEG signatures are candidate markers of response, yet the **dose-dependence of these EEG effects for continuous-infusion intravenous DMT is poorly characterised.**

Aim Test whether intravenous DMT changes EEG spectral power and Lempel-Ziv complexity relative to placebo, and whether these changes, and subjective effects, scale with dose.

METHODS

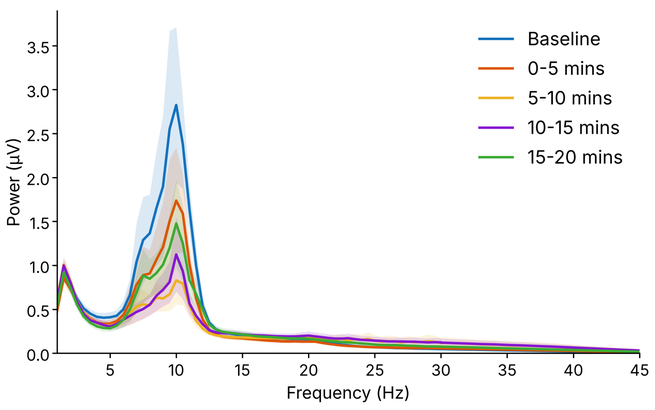
N = 32	4 doses	10 min	64-ch EEG	n = 29
healthy volunteers randomised, parallel groups	DMT 9, 12, 17 or 21.5 mg (n=6 each); placebo n=8	continuous intravenous infusion	sampled at 250 Hz	in EEG analysis (DMT n=23, placebo n=6)



- **A phase 1, double-blind, randomised, placebo-controlled, parallel-group, dose-escalation trial** in healthy volunteers.
- **EEG features:** spectral power (1-45 Hz) and Lempel-Ziv complexity (LZC) over 25 min: pre-infusion baseline, 10-min infusion and 10-min post-infusion, in 5-min windows.
- **Statistics:** change from baseline tested at channel level with cluster-based permutation tests; dose relationships within DMT assessed by rank correlation (ρ).
- **Subjective effects:** Mystical Experience Questionnaire (MEQ), % of maximum score.

RESULTS · SPECTRAL POWER

Alpha and theta power fell with DMT



−50%
alpha power vs baseline, p<0.001

−25%
theta power vs baseline, p<0.001

Fig. 1 Mean power spectra (1–45 Hz) at baseline and in successive 5-min windows from infusion start. Participants given DMT (n=23).

- Mean changes are -36% (0-5 mins), -60% (5-10), -56% (10-15) and -43% (15-20) in alpha. The effect sizes (dz: -0.9 to -1.5).

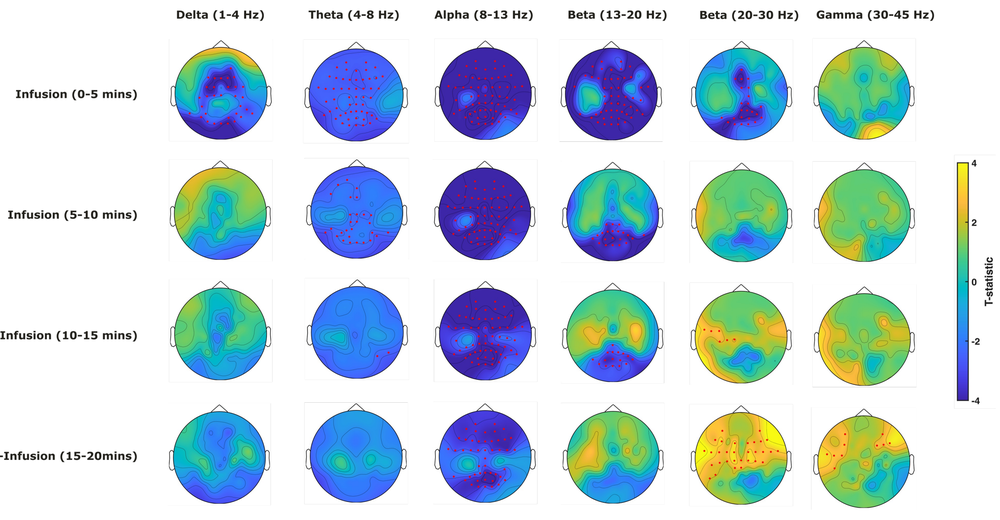


Fig. 2 Change in band power vs baseline (t-statistic) by frequency band and time window. Red dots: channels in significant clusters.

- **Alpha reductions were the most extensive,** spanning frontal, central and parietal channels in every window.
- Alpha and theta reductions did not scale significantly with dose (ρ = −0.15 to −0.22, p ≥ 0.30).
- **Exploratory:** early delta decreases; high-beta shifts from decrease to increase after infusion; gamma increases late.

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RESULTS · SIGNAL COMPLEXITY

DMT increased signal complexity; placebo did not

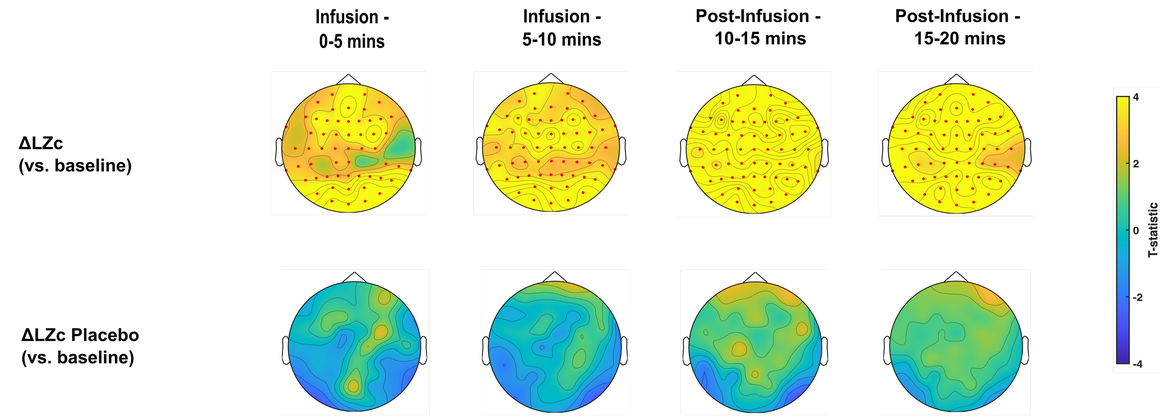


Fig. 3 Change in LZC vs baseline (t-statistic) in 5-min windows. Top row: pooled DMT doses (n=23). Bottom row: placebo (n=6). Red dots: significant channels.

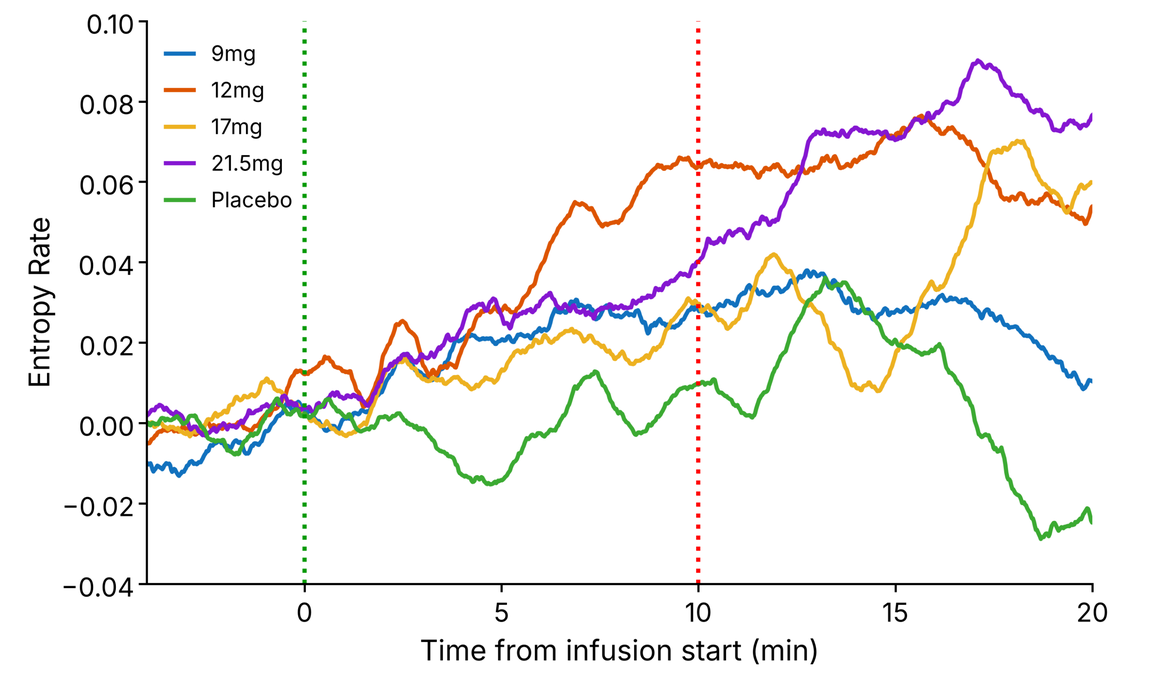


Fig. 4 Group-mean entropy rate (change from baseline) over time by dose group. Dashed lines: infusion start (green) and end (red).

- **LZC was higher with DMT than placebo (p = 0.048).**
- Increases were widespread: significant at most channels throughout infusion and for 10 min afterwards. No channel reached significance with placebo.
- Group-mean LZC peaked approximately 3-8 min after the end of infusion.
- Entropy-rate time-courses separate from placebo but are not ordered by dose; within DMT, LZC did not differ significantly by dose (ρ = 0.11, p = 0.62).

RESULTS · DOSE & SUBJECTIVE EFFECTS

No graded dose-response from 9 to 21.5 mg

60% vs 3%
median MEQ (% of maximum), DMT vs placebo
p<0.001, primary study[4]

Within DMT, vs dose	ρ	p
LZC	0.11	0.62
Alpha & theta power	−0.15 to −0.22	≥ 0.30
MEQ	0.21	0.34

None significant. MEQ analysis: n=22 DMT, n=8 placebo.

CONCLUSIONS

More complexity, less alpha and theta, but no clear dose gradient

- Continuous intravenous infusion of DMT increased signal complexity and reduced alpha and theta power, consistent with previous studies.
- Complexity was higher with DMT than placebo; however, graded dose-dependence was not evident in this small sample.
- **Findings are preliminary.** Next: relating EEG features to acute subjective effects and post-acute psychometric measures.

FUNDING & CONTACT

Funding: This study was funded by Cybin (now Helus Pharma).
Corresponding author: Joseph Peill, joseph.peill18@imperial.ac.uk
Keywords: DMT; psychedelics; pharmaco-EEG; Lempel-Ziv complexity; dose-escalation

HELUS PHARMA

UNIVERSITÀ DI PADOVA
Centro di Ateneo
Padova Neuroscience
Center - PNC

EEG Microstate Temporal Parameters and Transition Structure Characterise Cognitive Impairment in Parkinson's Disease

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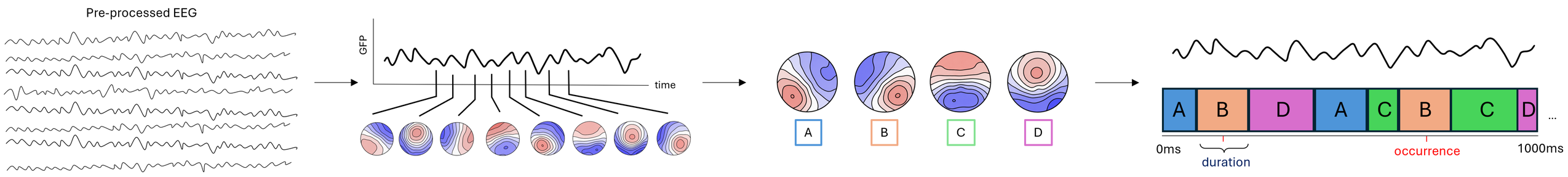
[1] *Padua Neuroscience Center (PNC) University of Padua*
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BACKGROUND: Cognitive impairment is a major non-motor symptom of Parkinson's disease (PD), with growing evidence linking decline to alterations in large-scale brain network dynamics[1]. Electroencephalographic (EEG) microstates are brief, recurring periods of quasi-stable scalp topography, and may provide a means of investigating the rapid organisation of such activity[2]. However, how microstate temporal properties and sequential structure may vary with level of cognitive impairment in PD remains incompletely understood.

OBJECTIVE: To compare differences in EEG microstate temporal parameters and transition structure among healthy controls and PD patients with normal cognition (PD-NC), mild cognitive impairment (PD-MCI) or dementia (PDD).

DATA: 59 PD subjects {17 PD-NC; 27 PD-MCI; 15 PDD} · 19 HC | Resting-state EEG: 5 min, eyes-closed (64 channels)

METHODS

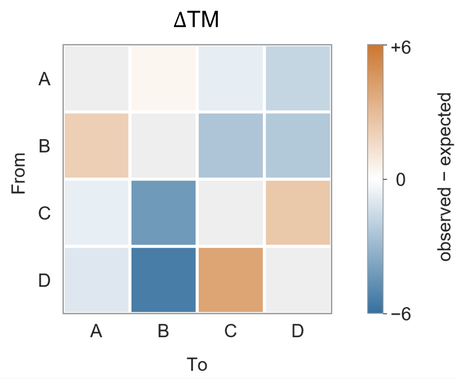


Global field power (GFP), reflecting the spatial standard deviation of scalp potentials at each time point, was calculated from pre-processed EEG signals (1-30 Hz).

Scalp topographies were extracted at local GFP maxima and subjected to polarity-invariant modified k-means clustering to identify representative microstate maps for each participant.

Individual maps were subsequently clustered to derive group-mean maps, which were combined to obtain a common grand-mean solution comprising four microstate classes (A-D).

The grand-mean templates were backfitted to each participant's EEG at GFP peaks, with labels subsequently assigned to intervening time points to obtain a continuous microstate sequence from which temporal parameters (**duration, occurrence, coverage**) and **transition dynamics** were extracted.

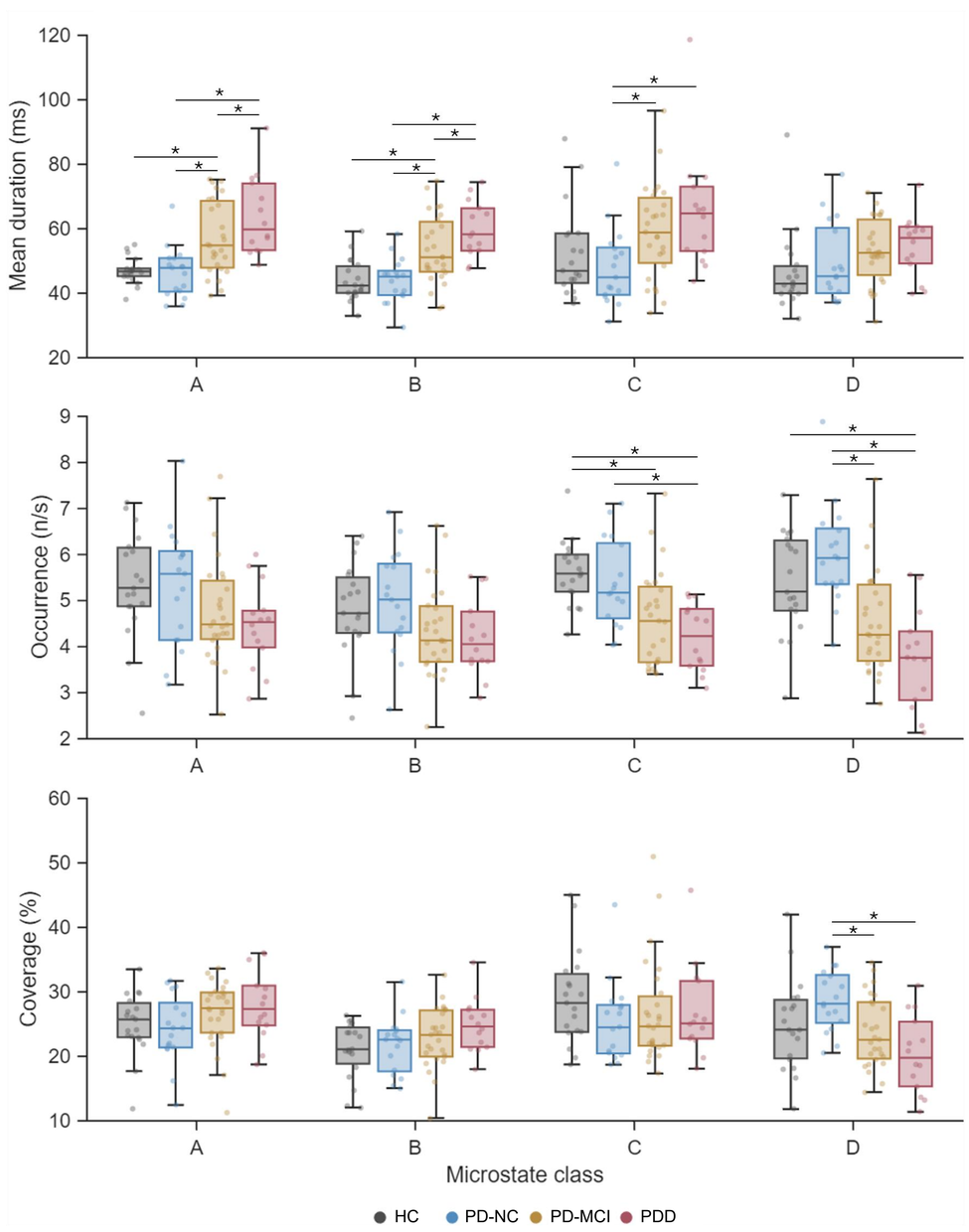


Transition deviation (ΔTM) values quantify the percentage deviation between observed and expected probabilities (positive = more frequent than expected; negative = less frequent than expected).

Expected transition probabilities were derived from relative microstate occurrences under random sequencing, excluding self-transitions.

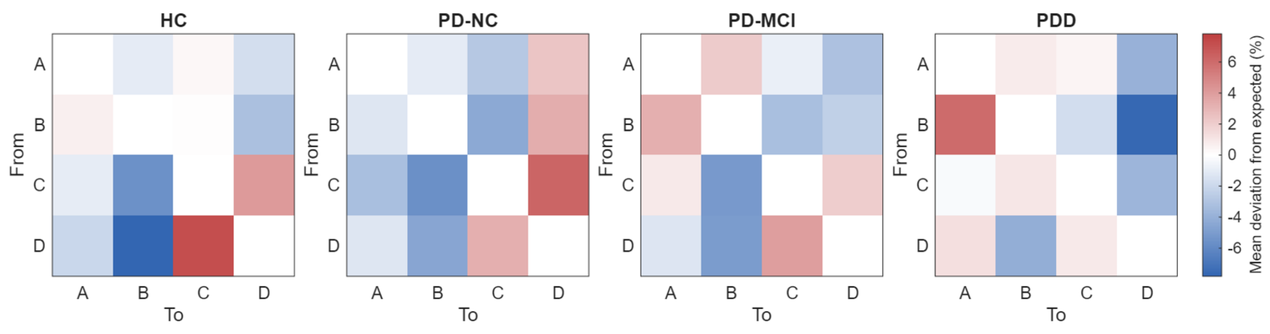
RESULTS

Prolonged microstate duration and reduced occurrence characterise cognitive impairment



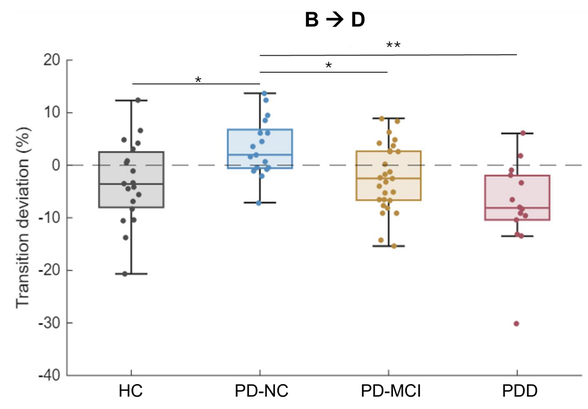
Mean microstate durations showed a visually graded increase with cognitive impairment. Classes A and B exhibited significantly longer durations in PD-MCI and PDD than in HC and PD-NC, while class C duration was longer in PDD and PD-MCI than in PD-NC.
The opposite pattern was observed for state frequency, where the occurrence of microstate C was significantly lower in both cognitively impaired groups compared to HC, and in PDD compared to PD-NC. Class D occurrence was lower in both cognitively impaired groups compared to PD-NC, and in PDD relative to HC. A higher proportion of the overall recording time was also occupied by class D in PD-NC relative to those with cognitive impairment.

Distinctive transition organisation in cognitively preserved PD



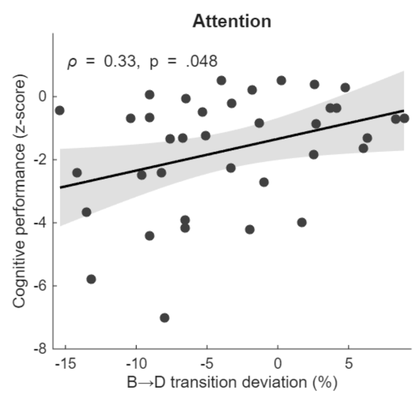
Microstate sequencing deviated significantly from random expectation in all four groups (χ^2 distance; all $p < .001$).

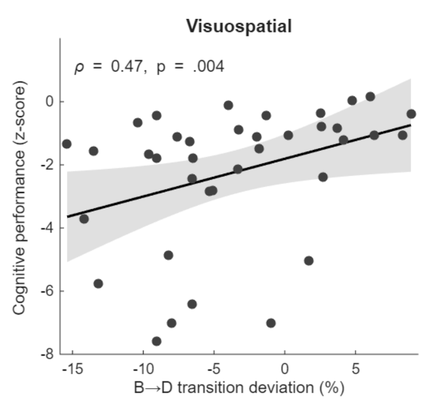
The B→D transition deviation was significantly greater in cognitively preserved PD patients than in all other groups. Moreover, mean deviations were positive in PD-NC and negative in HC, PD-MCI and PDD, indicating that, on average, B→D transitions occurred more frequently than expected in PD-NC and less frequently than expected in all other groups.



B→D deviation correlates with visuospatial and attentional performance

Across PD participants, greater B→D transition deviation was positively associated with performance on neuropsychological tests of visuospatial function and attention.





CONCLUSIONS

Altered microstate dynamics are evident already in PD-MCI. Prolonged A-B durations and reduced C-D occurrence suggest a **shift in the balance between persistence and recurrence** of distinct microstate configurations, potentially reflecting **altered flexibility** in switching between functional brain states.

Reduced class D occurrence and coverage may reflect **altered dynamics of attention-related networks**, consistent with the proposed association of microstate D with dorsal attention systems and the prominent attentional-executive deficits in PD-related cognitive impairment.

The distinctive B→D transition pattern in PD-NC may represent a form of **functional reorganisation associated with cognitive preservation**. Its positive associations with visuospatial and attentional performance are consistent with the proposed involvement of microstates B and D in visual processing and dorsal attention networks, respectively. Notably, both cognitive domains are vulnerable to impairment in PD, with visuospatial deficits often particularly informative of subsequent cognitive decline. Whether this reorganisation serves a compensatory function remains to be established with longitudinal investigation.

Cognitive impairment in PD is associated with altered microstate temporal dynamics, while cognitively preserved patients exhibit a distinctive pattern of microstate sequencing potentially relevant to the maintenance of cognitive function. Together, these findings highlight the potential value of examining both temporal parameters and transition structure to characterise PD-related cognitive dysfunction.

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NATIONAL INSTITUTE OF MENTAL HEALTH

BRAIN Team FBME
Biosignal Recognition & Artificial Inteligence in Neuroscience

FACULTY OF BIOMEDICAL ENGINEERING CTU IN PRAGUE

Test-retest reliability: reliability of repeated measurements in EEG project

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[1]Faculty of Biomedical Engineering, CTU in Prague; [2]National Institute of Mental Health, Klecany; [3]Third Faculty of Medicine, Charles University, Prague

Introduction

In longitudinal EEG designs, test-retest reliability analysis is often underestimated. It determines whether EEG recordings are stable when the same subjects are recorded under the same conditions. Stability is a key issue in the New Psychoactive Substances project, in which EEG is recorded in rats over 10 weeks with electrodes implanted before the first recording, which may degrade over time.

Aim

The aim of this study is to analyse the test-retest reliability of baseline EEG recordings in the New Psychoactive Substances project and to determine whether the time of recording (electrode age) can affect the project outputs.

Methods

EEG was recorded at the National Institute of Mental Health across 7 cohorts. Every week for 10 weeks, each rat underwent a baseline (resting-state) recording followed by a recording after administration of a psychoactive substance or placebo in randomised order; the one-week interval ensured washout. The implanted electrodes remained the same for all 10 weeks. The analysis included the **59 rats** measured so far with a baseline recording in each of the 10 weeks and without a technically failed recording. EEG power was analysed in the theta (0.5–6 Hz), alpha (6.5–12 Hz), beta 1 (12.5–25 Hz) and beta 2 (25.5–30 Hz) bands. Only baseline recordings were compared, so the effect of baseline correction was not addressed in this first phase.

The effect of the week of recording was tested by the Friedman test with Bonferroni correction and further quantified by a linear mixed-effects model for repeated measurements (log-transformed power, week as a continuous predictor, cohort and arena as covariates, random intercept and slope for each rat). Test-retest reliability was quantified by the intraclass correlation coefficient for absolute agreement of single measurements, ICC(A,1), from a two-way random-effects model [1]:

$$\mathrm{ICC(A,1)} = \frac{\sigma_r^2}{\sigma_r^2 + \sigma_w^2 + \sigma_e^2}, \tag{1}$$

where σ_r^2 is the between-rat variance, σ_w^2 the variance between weeks (a systematic shift of the whole group, e.g. electrode ageing) and σ_e^2 the residual variance. ICC was computed across all weeks ($\mathrm{ICC_{all}}$), for weeks 1 and 2 ($\mathrm{ICC_{1–2}}$, short-term) and weeks 1 and 10 ($\mathrm{ICC_{1–10}}$, long-term), and for every pair of weeks 1–9 weeks apart, averaged over pairs with the same interval. Reliability was rated as poor (< 0.5), moderate (0.5–0.75), good (0.75–0.9) or excellent (> 0.9) [2].

Results

Box plots show EEG power for the individual weeks; as the design is within-subject, power is centred for visualisation only.

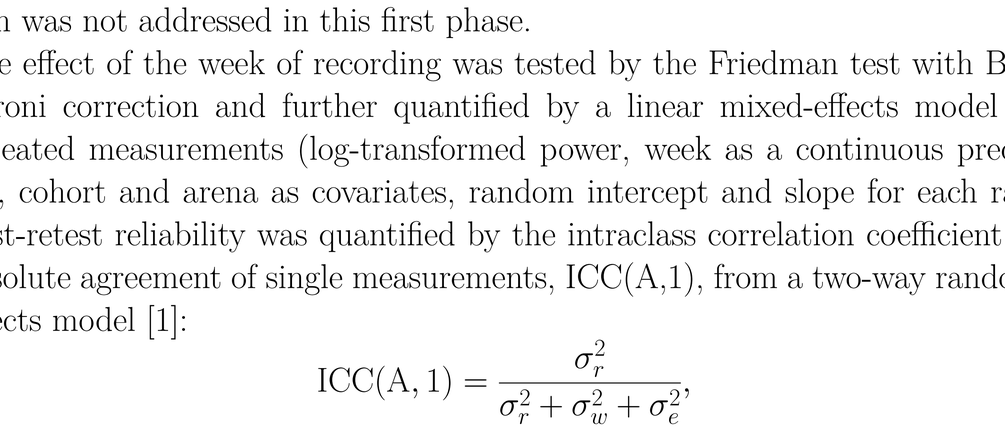


Figure 1:Baseline EEG power in the theta (left) and alpha (right) bands over 10 weeks ($n = 59$ rats). Data are centred for visualisation of the longitudinal comparison (the within-subject mean was subtracted). Two theta outliers above 300 $\mu\mathrm{V}^2/\mathrm{Hz}$ are not shown.

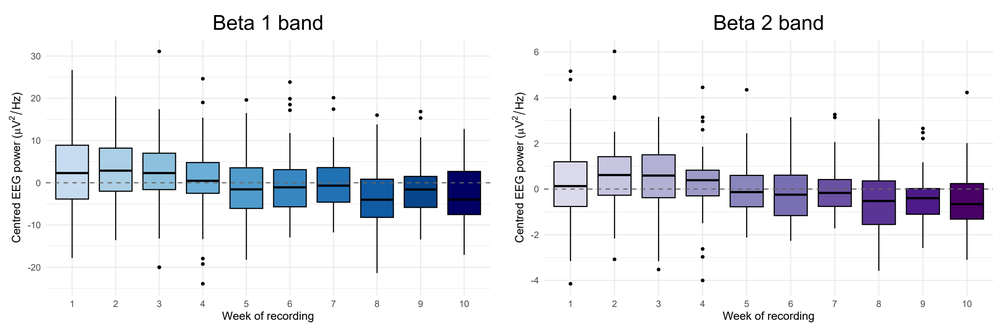


Figure 2:Baseline EEG power in the beta 1 (left) and beta 2 (right) bands over 10 weeks ($n = 59$ rats). Data are centred for visualisation of the longitudinal comparison (the within-subject mean was subtracted).

The mixed-effects model confirmed a decrease in power over time in all bands, by 1.9 % (theta), 2.4 % (alpha), 1.9 % (beta 1) and 2.0 % (beta 2) per week (all $p < 0.001$ after Bonferroni correction).

Frequency band	p-value	$\mathrm{ICC_{1–2}}$	$\mathrm{ICC_{1–10}}$	$\mathrm{ICC_{all}}$
Theta	3.1×10^{-5}	0.410	0.372	0.433
Alpha	2.4×10^{-5}	0.486	0.281	0.551
Beta 1	3.5×10^{-4}	0.551	0.384	0.583
Beta 2	7.6×10^{-7}	0.476	0.340	0.621

Table 1:p-values of the Friedman test after Bonferroni correction, ICC(A,1) for short-term stability ($\mathrm{ICC_{1–2}}$), long-term stability ($\mathrm{ICC_{1–10}}$) and across all weeks ($\mathrm{ICC_{all}}$), for each frequency band ($n = 59$ rats).

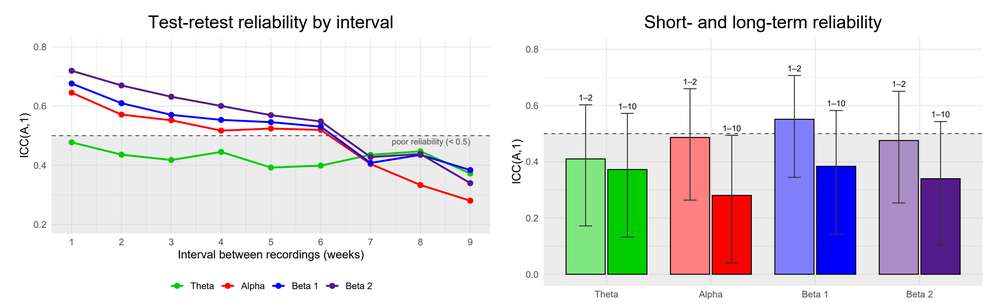


Figure 3:Left: ICC(A,1) as a function of the interval between recordings. Each point is the mean ICC(A,1) over all pairs of weeks separated by the given interval. Right: ICC(A,1) for weeks 1–2 (light) and 1–10 (dark) with 95 % CI. Shaded: poor reliability.

Conclusion

Baseline EEG power differed significantly across the 10 weeks in all bands and gradually decreased over time by approximately 2 % per week. In the alpha and beta bands, reliability decreased with increasing interval, from moderate (0.65–0.72) for consecutive weeks to poor or borderline for intervals of 7 or more weeks. Theta showed poor reliability (ICC 0.37–0.48) regardless of the interval. The time of recording thus affects EEG power and may reduce measurement stability over longer intervals. Future work will test whether normalising the markers to baseline suppresses this effect.

Acknowledgements

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Rhythm, background and artefact: dissecting the resting-state EEG response to ketamine in depression

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TAKE-HOME **Ketamine removes the alpha rhythm, not the aperiodic background, and that loss accounts for most of the apparent change in alpha burst dynamics.**

1 Background

Subanaesthetic ketamine acts as a rapid antidepressant and profoundly alters the resting EEG. Band power, however, mixes oscillatory rhythms with the aperiodic background and with muscle activity, and a rhythm that merely weakens also changes its burst and scaling statistics, because its signal-to-noise ratio (SNR) falls.

Aim: to separate these contributions before relating EEG changes to the antidepressant response.

2 Methods

Design

Pre-infusion	Start of infusion	End of infusion
10 min	0.27 mg/kg, 10 min	0.27 mg/kg, 20 min

One EEG per period. Ketamine 0.54 mg/kg i.v. over 30 min; MADRS 24 h later. Single-blind, fixed sequence with a placebo infusion one week earlier[4]; EudraCT 2013-000952-17.

Participants and EEG

- 24 patients with major depressive disorder (21 treatment-resistant); age 44 ± 13 years, baseline MADRS 27 ± 5
- 20 scalp channels (10–20), 1000 Hz, eyes closed, average reference; 71 recordings
- First 10 min of artefact-free 4-s windows in every recording
- Outcomes: MADRS change at 24 h; responders 12 of 24 (study classification)

Four controls

Rhythm vs background
Periodic power is the excess over a fitted aperiodic line[1].

Muscle
Sub-band gradient, topography and 65–95 Hz power as covariate.

Signal-to-noise
Simulations of each patient's own loss of periodic power, timing unchanged[2].

Direction
Fronto-parietal theta dPTE, corrected by time reversal[3].

Measures

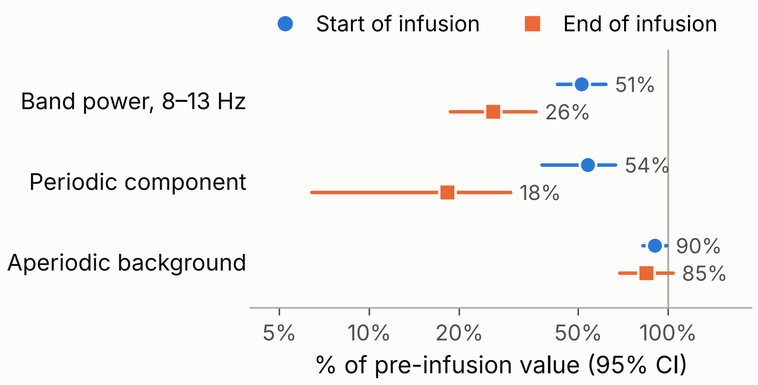
- Aperiodic line fitted in log–log space between anchor ranges (alpha: 2.5–5.5 and 17–30 Hz); periodic power is the signed mean excess, so an absent rhythm counts as about zero
- A peak counts as detected when its maximum lies inside the search range, at least 3 standard errors above the line
- Bursts: envelope above 1.5 × its median for at least one cycle; DFA of amplitude envelopes over 0.5–20 s

Statistics

Paired ratios of geometric means with 95% CI (periodic power: ratio of means, Fieller CI); Spearman ρ and Mann–Whitney tests; Benjamini–Hochberg FDR within tables; sensitivity analyses without 6 flagged recordings. All clinical associations are exploratory.

3 The alpha rhythm goes, the background stays

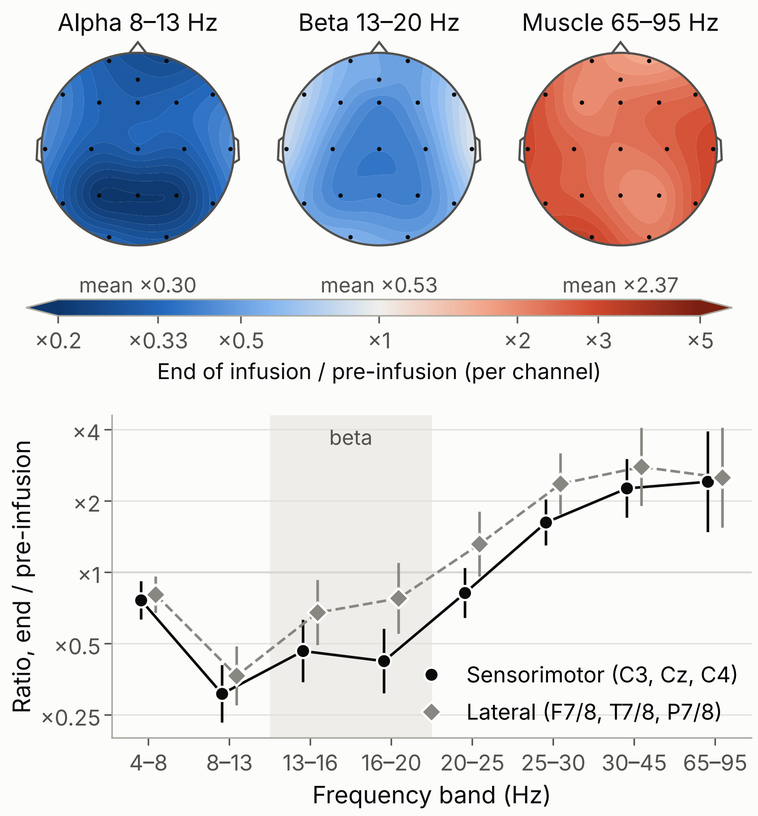
Posterior alpha power fell to 51% of baseline at the start and to 26% at the end of infusion. The loss was carried by the periodic component, whereas the aperiodic background did not change significantly, and an alpha peak remained detectable in only 14 of 23 patients (22 of 24 before infusion). Peak frequency did not shift (−0.4 Hz, 95% CI −1.2 to 0.4).



Posterior channels (O1, O2, P3, Pz, P4, P7, P8); periodic component and background at 6–14 Hz. n = 24 at the start, 23 at the end of infusion.

4 Beta falls, muscle rises: two processes

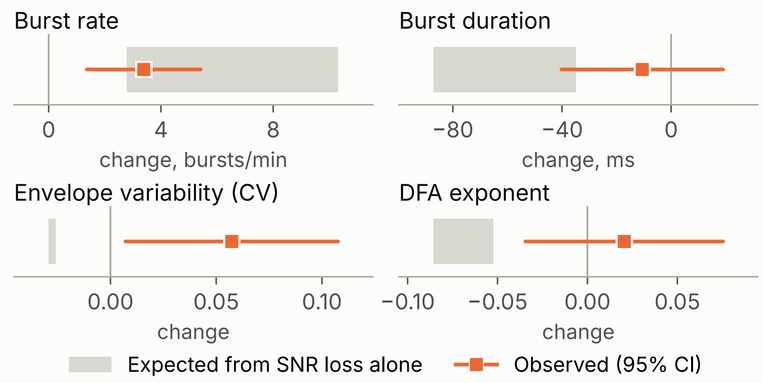
Sensorimotor beta (13–20 Hz) fell to 44%, most over the midline, where muscle is weakest. Across sub-bands, power fell below 20 Hz and rose above 25 Hz: a decrease that added muscle cannot produce. Power above 30 Hz rose 2.1- to 2.8-fold (at 65–95 Hz most at T7, T8 and O1), reflecting muscle, gamma activity or both.



End of infusion vs pre-infusion, n = 23. Maps: per-channel ratios, significant at 20/20 channels for alpha and muscle and 16/20 for beta (FDR q < 0.05). Lower panel: ratios with 95% CI.

5 Burst dynamics: mostly signal-to-noise

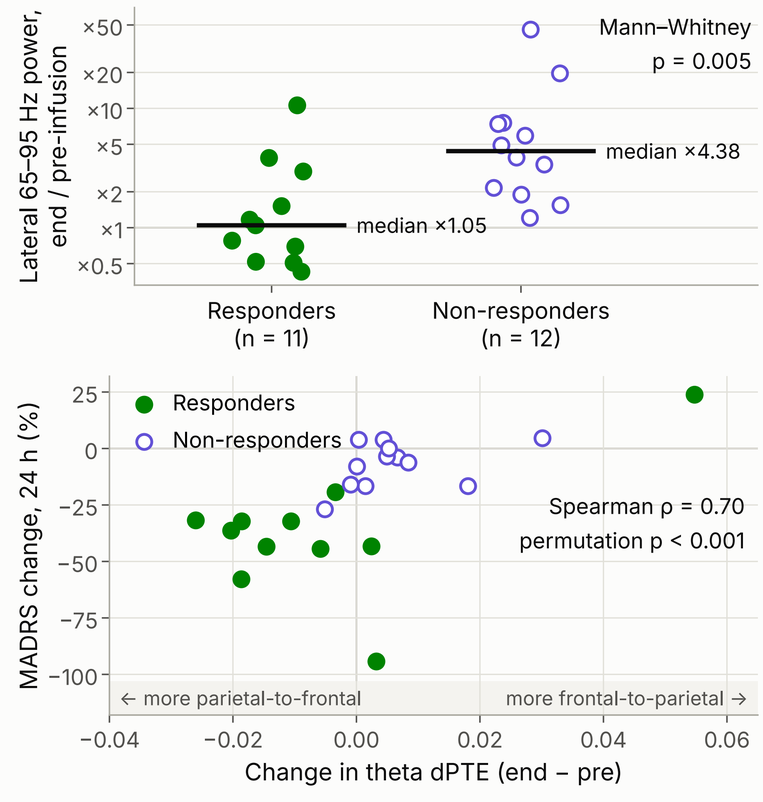
Long-range temporal correlations were present in every band (DFA 0.67–0.75 against 0.50 after shuffling). Alpha burst rate and duration changed as SNR loss alone predicted. The envelope, however, became more variable instead of less, and its DFA exponent did not decline: the remaining alpha appears more intermittent. Theta matched the SNR expectation in 6 of 7 measures.



Posterior alpha, end of infusion vs pre-infusion, n = 23. Grey: range expected from SNR loss alone across three model bandwidths. The model failed validation for beta, which is therefore not tested.

6 Early correlates of response

Muscle power rose 4.4-fold in non-responders but not in responders, robust to leaving out any patient. Theta dPTE showed a weak parietal-to-frontal predominance (0.487) that did not change on average, yet its change tracked MADRS change (ρ = 0.70, 95% CI 0.35–0.87; 0.65 after adjustment for muscle).



Upper: lateral 65–95 Hz power (F7/8, T7/8, P7/8), median over clean windows; bars are medians. Lower: theta dPTE, F3, Fz, F4 against P3, Pz, P4; negative MADRS change is improvement.

Conclusions

1
Ketamine abolishes the posterior alpha rhythm rather than broadband activity: periodic power falls by 82%, the aperiodic background is preserved.

2
The beta decrease is not muscular. The rise above 30 Hz cannot be read as gamma until muscle has been removed.

3
Most apparent changes in alpha burst dynamics follow from SNR loss: dynamic measures need an SNR control.

4
Muscle activation and a shift in theta directionality are exploratory markers of non-response and response that require replication.

Limitations: 24 patients; single-blind, fixed-sequence design; clinical associations exploratory and not corrected across analyses; muscle and gamma not yet separated by blind-source cleaning.

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