EXPLORING SLEEP SPINDLES IN CHILDREN WITH AUTISM SPECTRUM DISORDERS: ANALYSIS OF SLEEP EEG RECORDINGS AND IMPLICATIONS FOR TARGETED NEUROFEEDBACK THERAPY.

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Introduction:

Sleep disturbances affect approximately 50% to 80% of children with autism spectrum disorders (ASD), significantly impacting cognitive performance and neuroplasticity.

Aim:

Building upon findings of resting-state EEG abnormalities, this study aimed to extend electroencephalographic investigations to non-rapid eye movement (NREM) sleep recordings. Specifically, the objective was to examine sleep spindle parameters in children with ASD compared to a control group to better understand brain bioelectrical dynamics and inform personalized neurofeedback approaches.

Material and methods:

This preliminary analysis was conducted on a pilot cohort of 55 subjects. The study evaluated sleep EEG recordings to assess characteristics of sleep spindles—namely dominant frequency, duration, and occurrence—in children with ASD compared to a typically developing (TD) comparison group .

Results:

Preliminary analyses revealed significant differences in sleep spindle parameters between children with ASD and the control group. Specifically, notable variations were identified in the dominant frequency, density, and occurrence of sleep spindles during NREM sleep.

Conclusion:

These findings advance the understanding of sleep spindle dynamics in pediatric ASD, highlighting the intricate relationship between sleep microarchitecture and developmental disorders. Furthermore, these insights support the development of tailored neurofeedback interventions designed to normalize brain activity, mitigate the effects of sleep disturbances, and improve overall cognitive functioning and quality of life for children with ASD and their families.

Keywords: ASD, QEEG, children, sleep spindles

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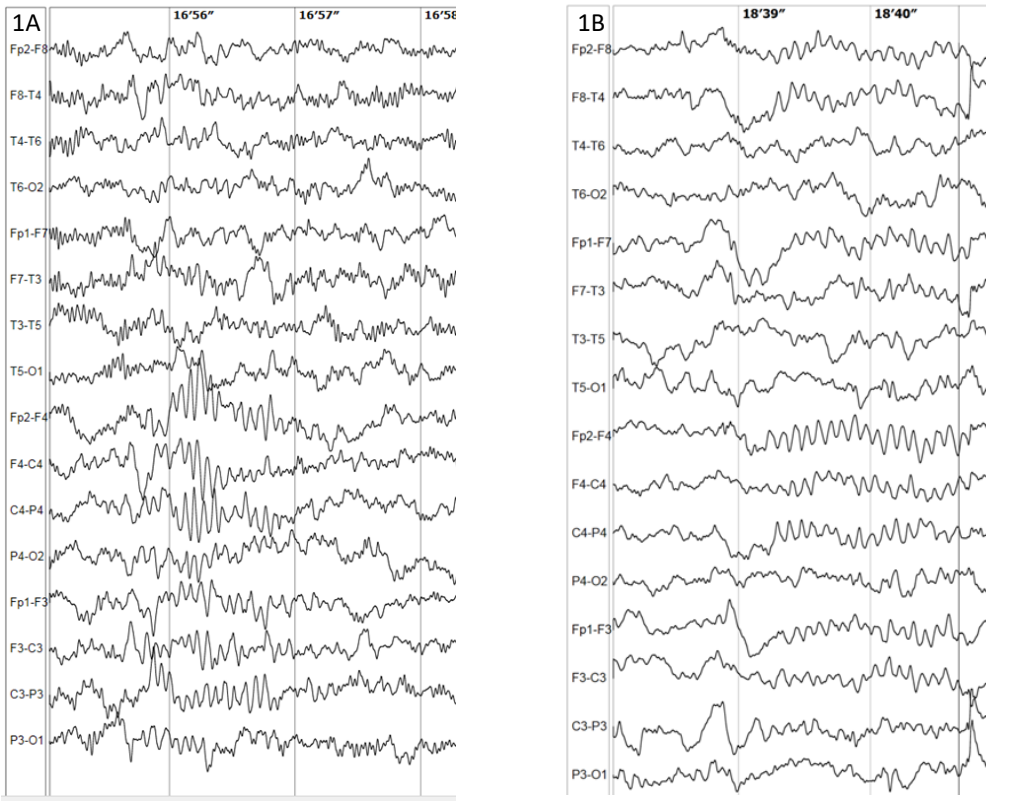


Figure 1. Representative N2 sleep EEG epochs illustrating group differences in sleep spindle morphology. (A) In a typically developing (TD) child, prominent, symmetrical, and synchronous sleep spindles with a dominant frequency of ~14 Hz are maximally expressed over frontal and central regions. **(B)** In a child with autism spectrum disorder (ASD), sleep spindles demonstrate a slower dominant frequency (~11 Hz) accompanied by attenuated amplitude and decreased occurrence density.

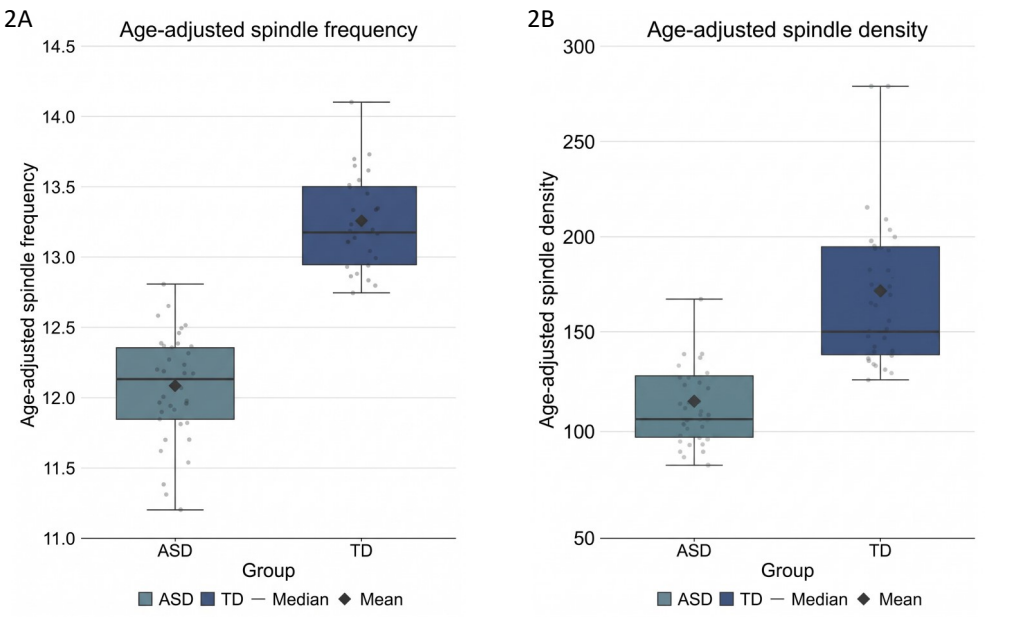
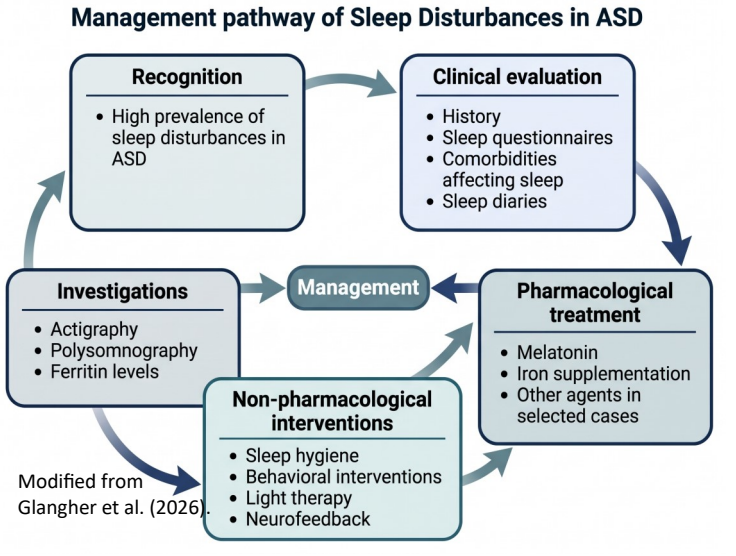


Figure 2A, B. Comparison of age-adjusted sleep spindle parameters between children with autism spectrum disorder (ASD; *n* = 33) and typically developing controls (TD; *n* = 22). (A) Age-adjusted spindle frequency and **(B)** age-adjusted spindle density. Children in the ASD group exhibited noticeably lower spindle density and slightly reduced spindle frequency with narrower interquartile dispersion compared to TD peers.



Beyond Predefined Frequency Bands: CoSupFormer, a Deep Learning Architecture for Preclinical Pharmaco-EEG Profiling

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CONTEXT

- CNS drug development remains challenging due to poor translation of preclinical efficacy to clinical outcomes [1].
- Quantitative pharmaco-EEG is one of the few functional measures that can be acquired in both rodents and humans, making it a promising translational reporter of target engagement and central drug effects [2], but conventional analyses often struggle to distinguish compounds with overlapping pharmacological profiles.
- To address this limitation, we built *MACO*, a standardized pharmaco-EEG database recorded on healthy mice, comprising over 30 reference compounds across 5 CNS therapeutic classes, and combined it with *CoSupFormer* [3], a deep-learning architecture trained directly on raw EEG signals.
- Here, we evaluate its ability to predict drugs pharmacological class on unseen subjects and, more stringently, on independent compounds absent from training, as a step toward a decision-support tool for compound prioritization, screening and repurposing.

AIMS

- **Drug therapeutic profile prediction.** Determine whether *CoSupFormer*, trained on raw EEG, separates antidepressants, antipsychotics, antiepileptics, anxiolytics, psychedelics and vehicle on the basis of their dominant central effect.
- **Reduction of noise impact in EEG-based analysis.** Learn meaningful patterns in raw EEG while discarding noisiest parts of the data.

DATASETS

METHODS

Cohorts of n=16 naïve mice (C57BL/6J, male)



Electrode implantation

- Parietal cortex [AP = -1.8, ML = +1.5 , DV = surface]
- Prefrontal cortex [AP = -1.8, ML = +1.5 , DV = surface]
- Hippocampus [AP = -2.4, ML = -1.5 , DV = -2.0]

Crossover design



DRUG CLASSES ENROLLED IN MACO DATASET

30+ *Reference compounds at different dose levels*

A Comprehensive Pharmacology Database

Vehicle	Antidepressant	Anxiolytic	Psychedelic	Antipsychotic	Antiepileptic
Control condition: vehicle solution with no active compound	Serotonin transporter – Inhibitor	GABA-A receptor – Positive allosteric modulator	5HT2A / 5HT2C receptors – Agonist	D2/D3/D4 receptors – Antagonist	Voltage-gated Sodium channel – Inhibitor
	Noradrenaline transporter – Inhibitor	5HT1A receptor – Agonist	NMDA receptor – Antagonist	5HT2A / 5HT2C receptors – Antagonist	Voltage-gated Calcium channel – Inhibitor
	Dopamin transporter – Inhibitor	H1 receptor – Antagonist			Potassium channel Kv7 – Modulator
	Muscarinic ACh receptor – Antagonist				Synaptic Vesicle Protein 2A – Agonist
	Alpha2 adrenergic receptor – Antagonist				GAT 1 transporter – Agonist

PUBLIC DATASETS

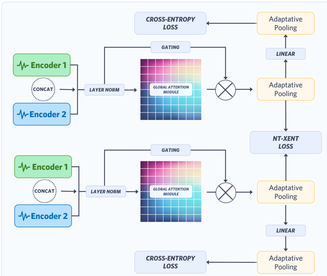
Dataset	Classes	n	Ch.	Segment	Added noise
TDBrain	Parkinson's, control	50	33	1 s	—
TDBrain+Noise	Parkinson's, control	50	33	1 s	Gaussian, 11 of 33 ch.
ADFTD	Alzheimer's, FTD, control	88	19	10 s	—
ADFTD+Noise	Alzheimer's, FTD, control	88	19	10 s	Gaussian, 6 of 19 ch.

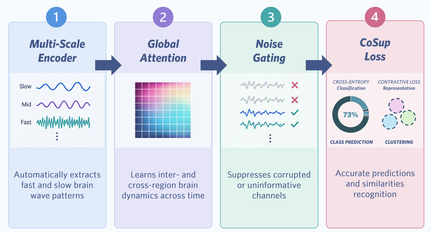
ADFTD [Miltiadous et al., 2023]. 36 patients with Alzheimer's disease, 23 with frontotemporal dementia (FTD), and 29 healthy controls.

TDBRAIN [van Dijk et al., 2022]. Balanced subset of 25 subjects with Parkinson's disease and 25 healthy controls.

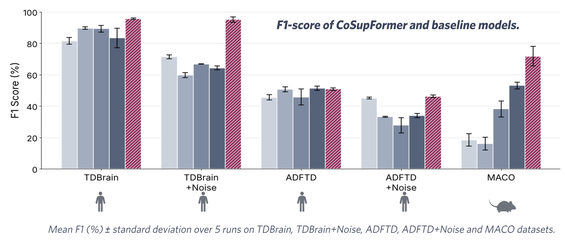
DEEP LEARNING MODEL : COSUPFORMER

1 ARCHITECTURE





2 PERFORMANCE



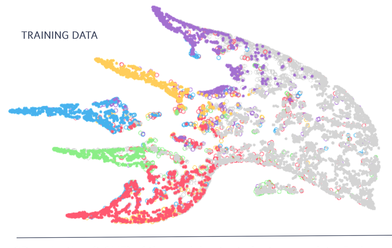
F1 Score: measures a classification model's accuracy by combining precision and recall into a single score.

Mean F1 (%) ± standard deviation over 5 runs on TDBrain, TDBrain+Noise, ADFTD, ADFTD+Noise and MACO datasets.

- ***BENCHMARKING:*** Under noisy conditions, *CoSupFormer* proved more robust than the baselines. While baseline F1-scores dropped by 10 to 30 points from TDBrain to TDBrain+Noise, *CoSupFormer* lost less than one point, consistent with its gating mechanism.
- ***GENERALIZATION:*** Across two clinical datasets (TDBrain, ADFTD) and one rodent pharmaco-EEG dataset (MACO), *CoSupFormer* matched or exceeded the best baselines, supporting a single architecture for both clinical diagnosis and preclinical drug profiling.
- ***CROSS-SPECIES***: On rodent EEG (MACO), *CoSupFormer* outperformed all baselines by a wide margin, demonstrating cross-species transfer. It also suggests resilience to real biological artifacts such as movement and muscle activity present in MACO.

3 INTERPRETABILITY

A - THERAPEUTIC CLASSES REPRESENTATION

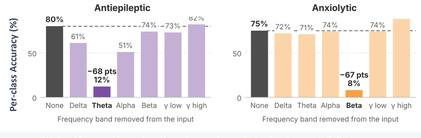


2D projection (t-SNE) of the model outputs for training data. Each point is one 10-min EEG segment, colored by its true drug class. Plain dots: correctly classified segments; Open dots: misclassified segments

- ***CLASS SEPARATION***
  Drug classes form **5 distinct clusters,** one per therapeutic class.
  This shows that *CoSupFormer* captures drug-specific EEG signatures. Misclassifications occur mainly as drug effects fade toward vehicle.
- ***PHARMACOLOGICAL GRADIENT***
  Each cluster extends from the vehicle toward a class-specific extreme, suggesting the embedding encodes both **drug class and effect strength**.

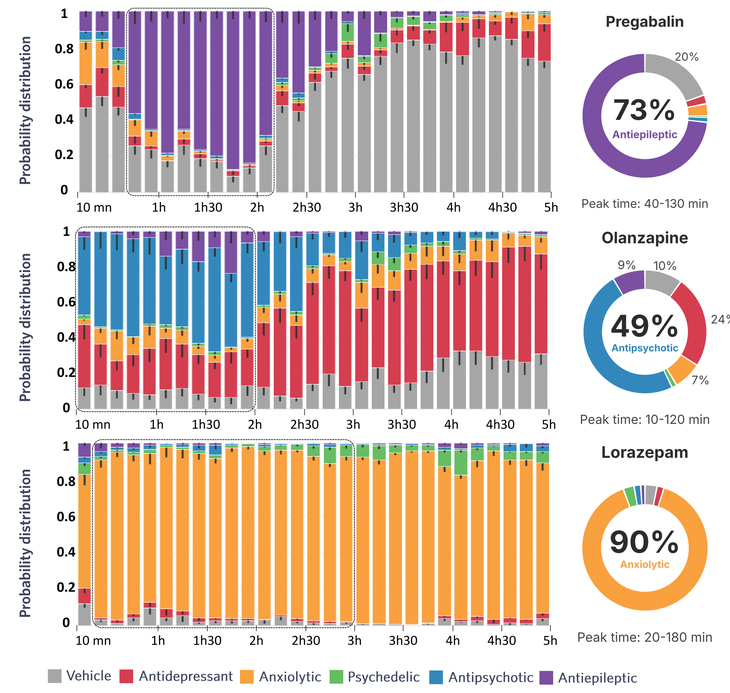
B - IMPACT OF FREQUENCY BANDS IN ANTIEPILEPTIC AND ANXIOLYTIC DRUGS CLASSES

- **Removing theta** collapses antiepileptic accuracy (80% → 12%)
- **Removing beta** collapses anxiolytic accuracy (75% → 8%).
- Other frequency bands have limited impact.



These class-specific bands can be linked to known pharmaco-EEG effects of antiepileptic and anxiolytic drugs [4,5].

COSUPFORMER PREDICTIONS ON UNSEEN DRUGS



Predicted therapeutic profile over time for three compounds unseen during training.
Each bar represents the mean class-probability distribution across animals (n = 16) for one 10-min block, from 10 min to 5 h after drug administration. Lower error bars show the SEM. Dashed box: peak-effect window. Donut: mean distribution over that window (shares below 5% are not labeled).

***CoSupFormer* correctly identified the main therapeutic class of unseen compounds and tracks their pharmacodynamic time course.**

- Pregabalin is predicted antiepileptic (73% at peak time, 40–130 min) before drifting back toward vehicle after about 3 h.
- Olanzapine is predicted antipsychotic (49% at peak time) during the first 2 h, then shifts to a mostly antidepressant profile.
- Lorazepam is predicted anxiolytic (90% at peak time) throughout the recording.

CONCLUSION

- ***DRUG PROFILE PREDICTION.*** *CoSupFormer* accurately classified unseen compounds based solely on their EEG profile, demonstrating its potential to predict pharmacological class early in development and to identify promising CNS candidates.
- ***A NEW READOUT OF DRUGS PHARMACODYNAMICS.*** Block-wise predictions over time provide a novel functional readout of drug action, capturing the evolution of therapeutic effects with a 10-minute resolution. This approach enables precise characterization of onset, peak activity, duration of action, and return toward baseline pharmacological states.
- ***EARLY DETECTION OF DRUGS WITH MIXED EFFECTS.*** Olanzapine's mixed profile prediction illustrate this point [6]. *CoSupFormer* revealed the complex pharmacological trajectory of olanzapine, initially expressing an antipsychotic-like profile before progressively exhibiting antidepressant-like characteristics. Such insights highlight the platform's ability to uncover hidden therapeutic dimensions and support drug repurposing opportunities.
- ***BIOLOGICALLY GROUNDED INSIGHTS.*** Frequency-band ablation analyses linked model predictions to established neurophysiological biomarkers, identifying theta oscillations as key drivers of antiepileptic classification and beta oscillations of anxiolytic classification. These findings strengthen the biological interpretability and translational relevance of the model as demonstrated in previous studies [4,5].
- ***TOWARD AN AI-POWERED COMPASS FOR CNS DRUG DISCOVERY.*** By transforming EEG data into actionable pharmacological insights, *CoSupFormer* provides a powerful decision-support framework for compound screening, candidate prioritization, mechanism-of-action assessment, drug repurposing and portfolio value creation across the CNS drug development pipeline.

References: **[1]** Pangalo et al., Nature Reviews Drug Discovery 6.7 (2007). **[2]** Drinkenburg et al., Neuropsychobiology 72.3-4 (2016). **[3]** Darankoum et al., arXiv preprint arXiv:2509.20489 (2025). **[4]** Kazmierska-Grebowska et al., International Journal of Molecular Sciences 22.24 (2021): 13604. **[5]** Christian Edward et al., Journal of neurophysiology 113.1 (2015): 116-131. **[6]** Shelton et al., Am J Psychiatry (2001).

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Auditory oddball event-related potentials during voluntary oral fentanyl intake and withdrawal in rats

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Chronic voluntary fentanyl intake did not detectably change the auditory oddball response, whereas psilocybin increased deviant-related theta power in control rats

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Introduction: The auditory oddball paradigm is a translational probe of sensory and attentional processing: the deviant-related evoked response (N1, P2, N2, P3) and its time-frequency correlate, mainly theta, can be recorded in rodents and humans. Opioid use disorder is linked to altered cortical processing; in humans, the P300 of the auditory oddball event-related potential (ERP) is reduced and delayed. ERPs and the event-related spectral perturbation (ERSP) are candidate translational biomarkers of drug effects and recovery. Psilocybin is studied as a treatment for addiction, but whether it changes sensory-evoked cortical activity after opioid exposure is unknown.

Aims: Q1: does chronic voluntary oral fentanyl intake change the deviant response? Q2: does psilocybin change it, and does the effect depend on fentanyl history?

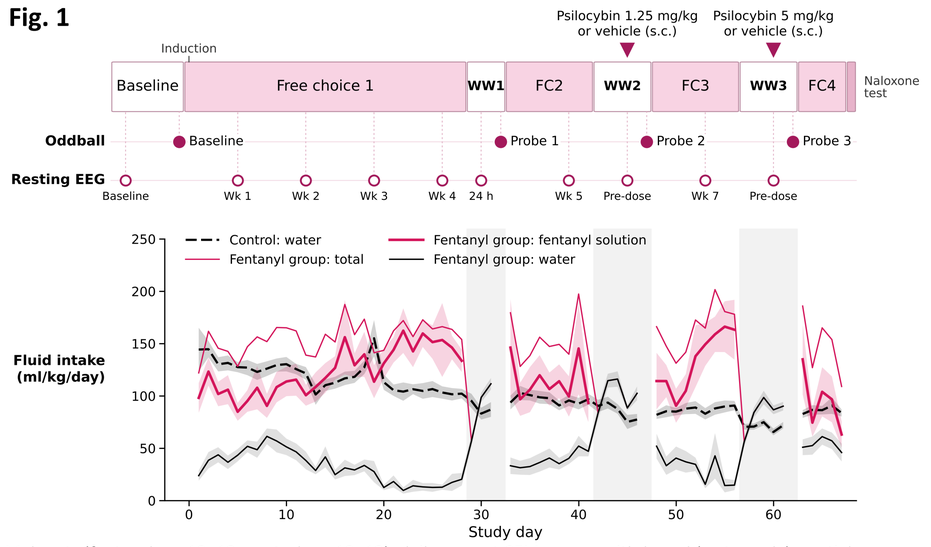
Methods: **Animals and design.** 30 Wistar rats (26 males, 4 females; 3 months old), single housed, two cohorts. Fentanyl rats (n = 15) had free choice of water and 5, 10 and 20 µg/ml fentanyl in four bottles (positions rotated weekly), interrupted by three withdrawal windows (Fig. 1); controls (n = 15) had four bottles of water. Intake was measured daily by bottle weighing (mg/kg/day). Psilocybin (1.25 and 5 mg/kg s.c.) or saline was given after 72 h of abstinence in the 2nd and 3rd withdrawal window; a final naloxone test (Fig. 1) is not analysed here. Two rats were lost before treatment (overdose; loose implant).

EEG and oddball. 18 gold-plated epidural electrodes and 2 stainless-steel screws over the cerebellum (ground); signals referenced to the common average), implanted before the drug-naive baseline; freely moving rats in an open-field arena with a loudspeaker above, sampled at 5 kHz. Standard 1 kHz / 70 dB (87%) and deviant 2 kHz / 80 dB (13%) tones, 50 ms, ISI 0.96–1.5 s, 30 min.

Preprocessing. ERP: 1–30 Hz, epochs −100 to 600 ms, automatic artefact rejection (AutoReject); measure = deviant − standard difference wave in the electrode pool C4 + P4 + T4 + O2, chosen on baseline data without group labels. ERSP: Morlet wavelets 4–100 Hz, dB relative to −400 to −100 ms. Only responders (baseline peak global field power ≥ 0.6 µV) were analysed: 23 of 28 rats, females included.

Measures and statistics. Peak-to-peak amplitudes (P1N1, N1P2, P2N2, N2P3) and latencies of P1–P3 (after Habelt et al., 2024); ERSP maximum, latency and frequency per band: 24 measures, Benjamini–Hochberg FDR (q). Q1: mixed model drug × session (baseline vs probe 1). Q2: psilocybin vs saline at probes 2 + 3, probe 1 as covariate, within each drug group. Hedges g with minimal detectable effect (MDE); cluster-based permutation test over the whole time-frequency plane (1000 permutations). Intake vs EEG: partial Spearman correlations (51 tests, FDR). Behaviour (male rats): repeated-measures ANOVA on log intake; including the four females gave the same results (escalation +70%, psilocybin/saline ratio 0.73).

Fig. 1

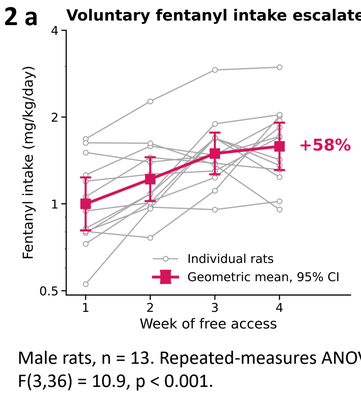


Male rats (fentanyl n = 12–13, control n = 12–13), daily mean ± SEM; grey = withdrawal (water only); partial re-access days omitted; cohort B aligned to cohort A.

Results – behaviour:

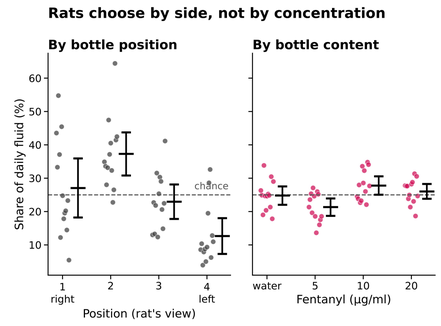
Intake escalated by 58% over four weeks (Fig. 2a; fentanyl share 70% → 91%; chance 75%); rats chose by side, not by concentration (Fig. 2b). Fentanyl rats drank more and grew more slowly (Fig. 2c); in withdrawal they drank water at control level, with no rebound after re-access (Fig. 2d). Psilocybin did not change intake (ratio 0.88, 95% CI 0.48–1.61).

Fig. 2 a Voluntary fentanyl intake escalates



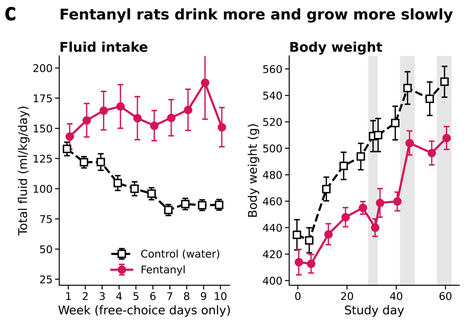
Male rats, n = 13. Repeated-measures ANOVA, F(3,36) = 10.9, p < 0.001.

b Rats choose by side, not by concentration



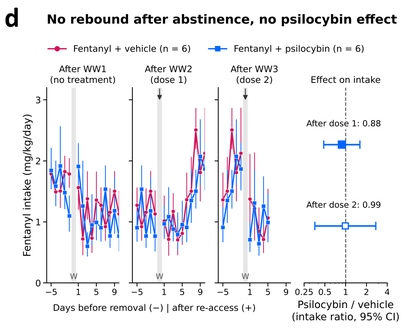
Position explains 16% of daily bottle choice, content 0.5% (male fentanyl rats, n = 13; dots = rats, bars = mean, 95% CI). The same side bias was present in control rats with four water bottles.

c Fentanyl rats drink more and grow more slowly



Male rats, n = 12–13 per group, mean ± SEM; grey = withdrawal. Fluid: +55% vs controls by week 4 (p < 0.001). Growth Days 0–40 (before treatment): 2.0% vs 3.5% per week (p = 0.005).

d No rebound after abstinence, no psilocybin effect

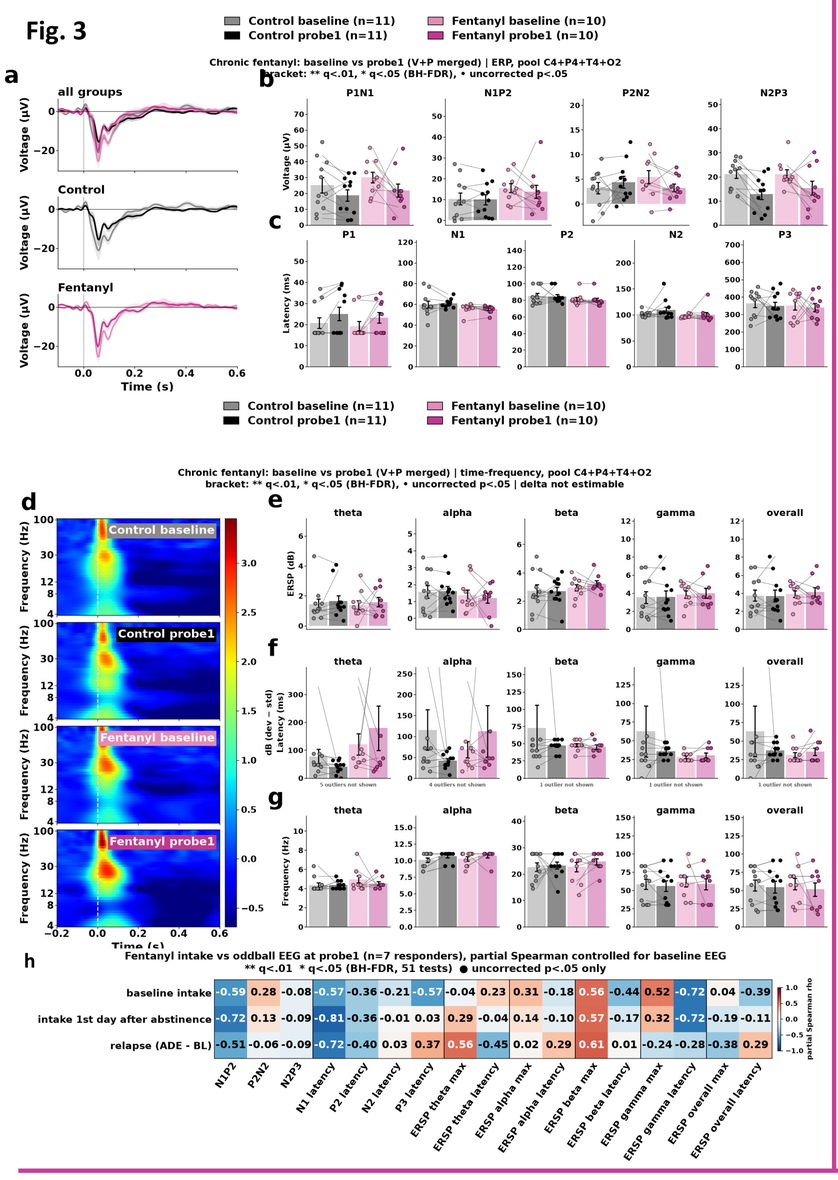


Male rats, geometric mean ± SEM; grey = bottle-free days, arrow = injection. Days 1–3 after re-access vs before removal: −45% (WW1, p = 0.01), −8% (WW2), −41% (WW3, p = 0.03). Ratio: ANCOVA adjusted for intake before treatment (dose 1 p = 0.65, dose 2 p = 0.98).

Q1 – Fentanyl: no change of the deviant response

Change from baseline to probe 1 did not differ between fentanyl (n = 9) and control rats (n = 10) in any ERP or ERSP measure (Fig. 3a–g; all q ≥ 0.79; cluster test p = 0.98, Fig. 5). P1 fell in fentanyl rats only (3.5 → 1.1 µV; uncorrected p = 0.006). No intake–EEG correlation survived FDR (Fig. 3h; 51 tests, n = 6–7).

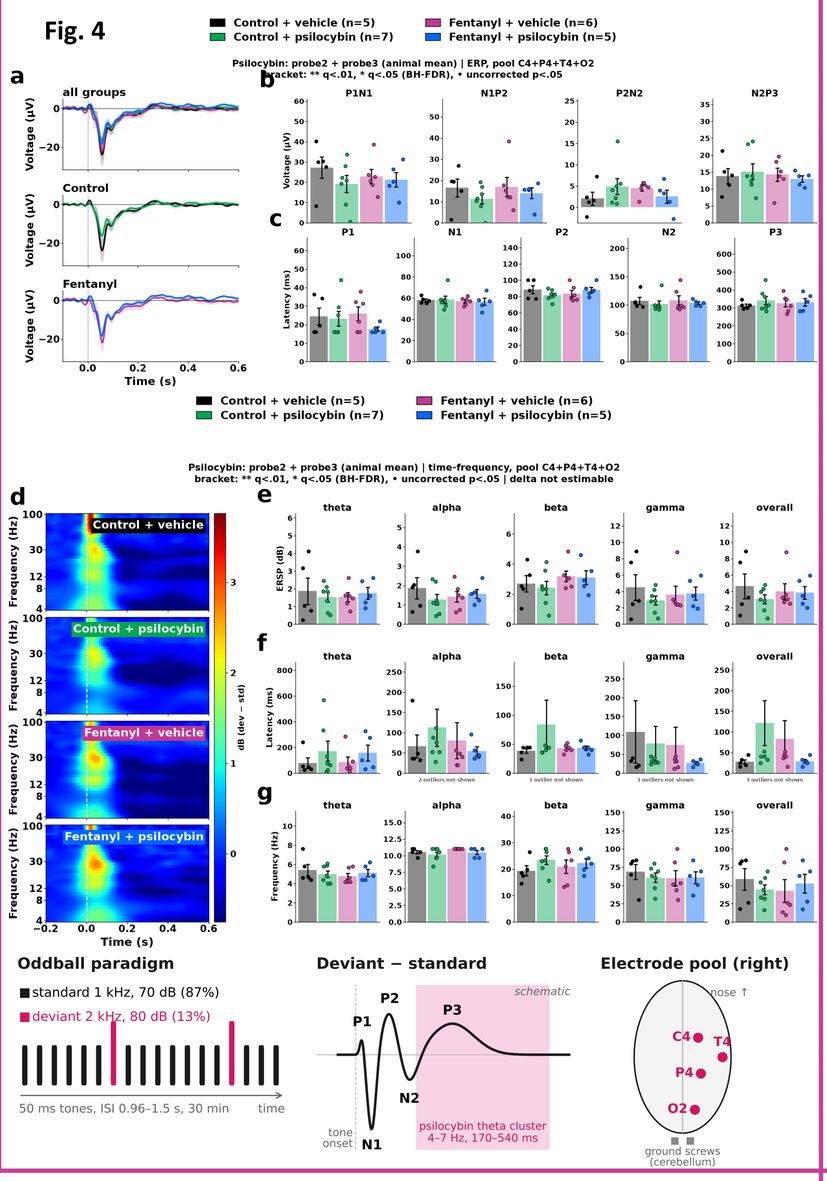
Fig. 3



Q2 – Psilocybin: ERP components unchanged

Psilocybin vs saline did not change any ERP measure or ERSP band measure, in control (n = 6 vs 5) or fentanyl rats (n = 5 vs 5) (Fig. 4a–g; all q ≥ 0.62). The theta maximum rose numerically in both groups (controls +0.68 dB, g = 1.00; fentanyl +0.65 dB, g = 0.64).

Fig. 4



Theta cluster after psilocybin; effect sizes

The cluster test found more deviant-related theta power (4–7 Hz, 170–540 ms, up to +1.5 dB) after psilocybin vs saline in control rats (Fig. 5; p = 0.013, n = 6 vs 5); same direction in fentanyl rats (p = 0.23, n = 4 vs 5) and pooled (exploratory, p ≈ 0.07). All Hedges g within the detectable range (Fig. 6; MDE ±1.3–1.9); all CIs included zero.

Fig. 5

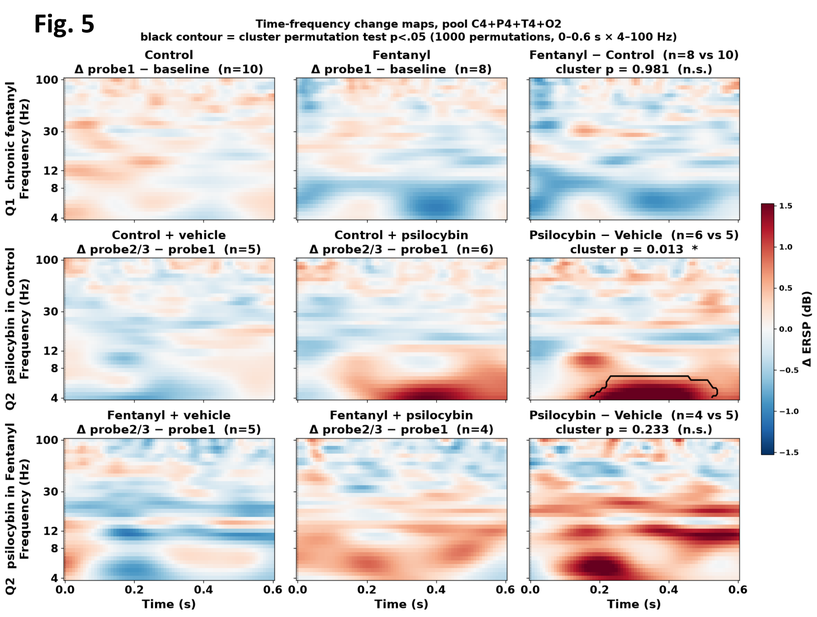
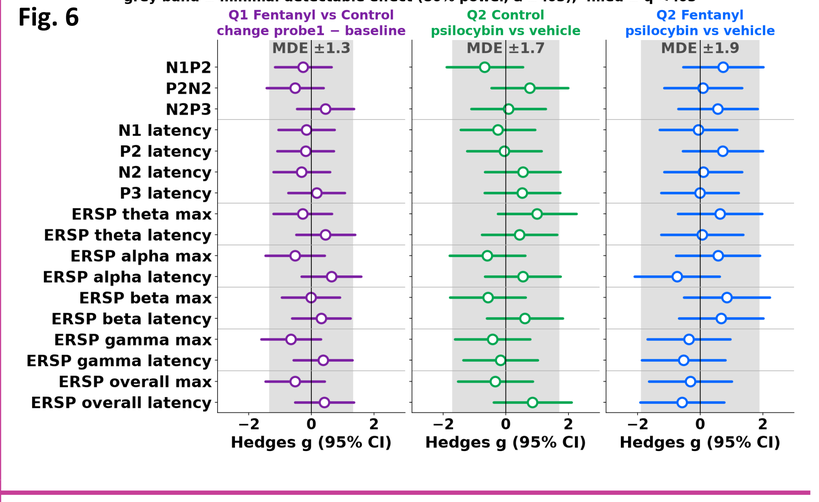


Fig. 6



Discussion

- Chronic voluntary fentanyl intake did not measurably alter the deviant response after four weeks of voluntary intake and a short withdrawal (probe 1, day 32). The conclusion is limited to large effects: with 9–10 animals per group, effects below about g = 1.3 cannot be excluded.
- Psilocybin increased deviant-related theta power, a frequency range that carries the evoked response in the oddball paradigm and is modulated by attention and expectation. The effect was seen in controls and pointed in the same direction after fentanyl, so it is not specific to drug history; it did not change the ERP amplitudes or latencies.
- Caution: the theta cluster rests on 6 vs. 5 animals, was one of three cluster tests (significant after Bonferroni correction at α = 0.017, but fragile), and the pooled test was proposed after inspecting the maps. The effects of a single injection may also reflect arousal or general drug state.
- Test-retest reliability of the measures was moderate for amplitudes and poor for latencies, and intake showed no robust association with EEG.
- Tone parameters followed the protocol of Habelt et al. (2024); because the deviant was also louder than the standard, the deviant response may partly reflect loudness as well as deviance.
- Limitations: small groups (EEG 4–10 rats per group); behaviour from males only, EEG from both sexes; responders only (23 of 28); no many-standards control.

Conclusions

1. Rats escalated voluntary oral fentanyl intake; bottle choice followed side rather than concentration.
2. Chronic voluntary oral fentanyl intake did not change the auditory oddball ERP or ERSP in this sample (23 responders, MDE g ≈ 1.3).
3. Psilocybin increased deviant-related theta ERSP in controls (cluster p = 0.013) and showed a similar trend after fentanyl; ERP components were unchanged.
4. The findings are preliminary: small groups, one significant cluster, moderate reliability of the measures; replication with larger groups is needed.

Ethics: All procedures complied with Act No. 246/1992 Coll. and Directive 2010/63/EU and were approved by the Ministry of Health of the Czech Republic (project PP112, No. 21/2026; MZDR 14897/2026-5/OVZ). References: Habelt BR et al. (2024) Transl Psychiatry 14:486. Maris E, Oostenveld R (2007) J Neurosci Methods 164:177–190. Funding: This work was supported by grants from Ministry of the Interior of the Czech Republic (project VK01010212 and VL01010008), Long-term conceptual development of research organization (RVO 00023752), ERDF-Project Brain dynamics, No. CZ.02.01.01/00/22_008/0004643, Charles University research program Cooperatio-Neurosciences and private funds obtained via PSYRES, Psychedelic Research Foundation, Charles University Grant Agency (GA UK), project No. 476726, and COST Action PSY-NET - Psychedelic renaissance: turn on, tune in and drop in (CA24130).

Longitudinal EEG changes in spindling excessive beta (SEB) after antidepressant treatment in MDD

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Background

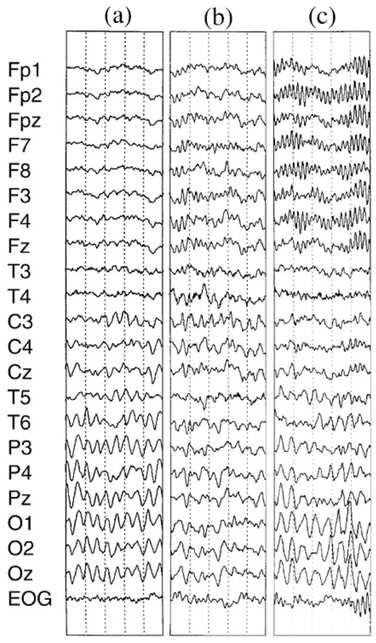


Figure 1. *Clarke et al., 2001 [3]*

- **Spindling excessive beta (SEB):** characterized as highly synchronous activity in the beta range with a spindle-like morphology [1].
- Observed in the frontocentral regions of the brain utilizing electroencephalography (EEG).
- Origin and function of this phenomenon remain unknown.
- Presence of SEB associated with:
  - ➢ A state of hypoarousal, often caused by sleep deprivation or the use of sedating drugs [2].
  - ➢ Psychopathology at a behavioral level for several psychiatric disorders [2], including major depressive disorder (MDD).

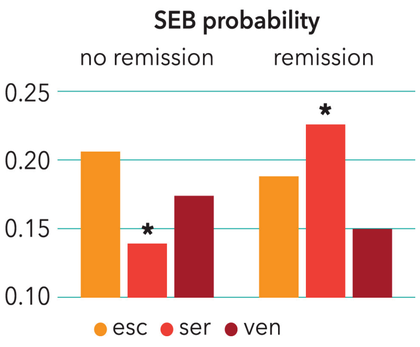


Figure 2. *Meijs et al., 2024 [4]*

- Interaction between antidepressant (AD) treatment effects and SEB in patients with MDD [4]:
  - ➢ Baseline SEB showed prognostic value for **sertraline** treatment, with higher values observed in **remitters** than non-remitters at baseline (**figure 2**).
  - ➢ A similar pattern was not observed for **escitalopram** or **venlafaxine**.

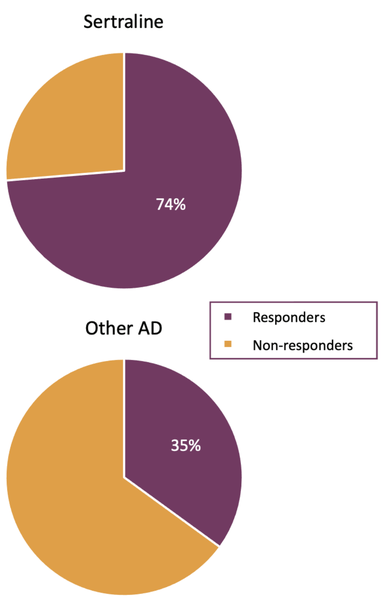


Figure 3. *Van der Vinne et al., 2017 [5]*

- The unique relationship between sertraline and SEB occurrence is consistent with findings on interactions between EEG abnormalities and ADs.
- EEG abnormalities (e.g., paroxysmal activity and EEG slowing) were reduced during an 8-week sertraline treatment in responders (**figure 3**) [5].

Hypothesis: similar to other EEG abnormalities, SEB occurrence is reduced following a successful 8-week sertraline depression treatment.

Materials and Methods

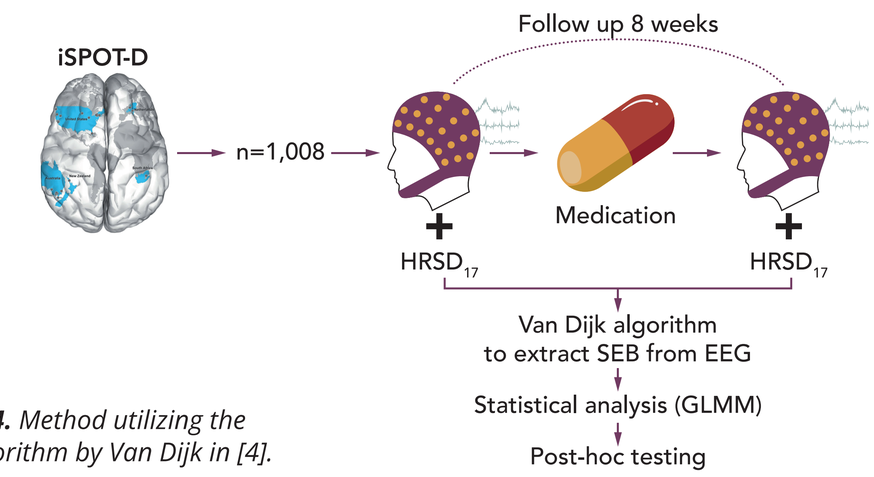
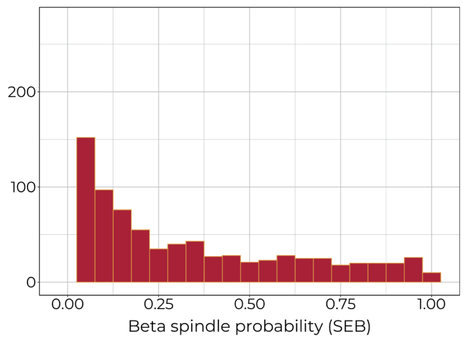


Figure 4. *Method utilizing the SEB algorithm by Van Dijk in [4].*

Results



The SEB data presents with a prominent right skew and is bound between 0-1, indicating the need for a GLMM with a beta distribution and logit-link.

Figure 5. *Distribution of SEB.*

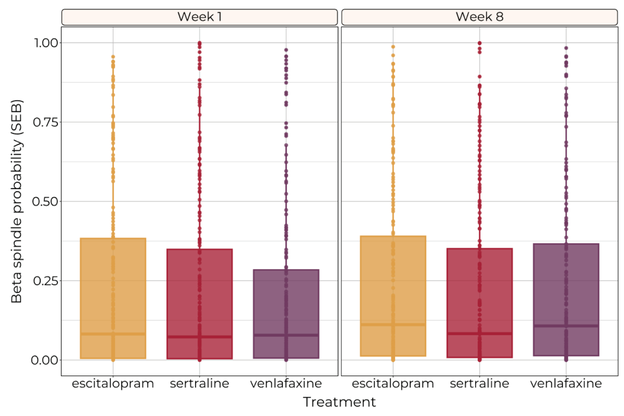


Figure 6. *Distribution of SEB per treatment condition and timepoint. Horizontal divider in boxplot = mean.*

- No significant SEB changes in **sertraline remitters** *(p* = .917*).*
- Significant SEB increase in **venlafaxine non-remitters** *(p* = .029*)*
- **Venlafaxine remitters** presented with lower SEB than **non-remitters** at week 8 *(p* = .008).

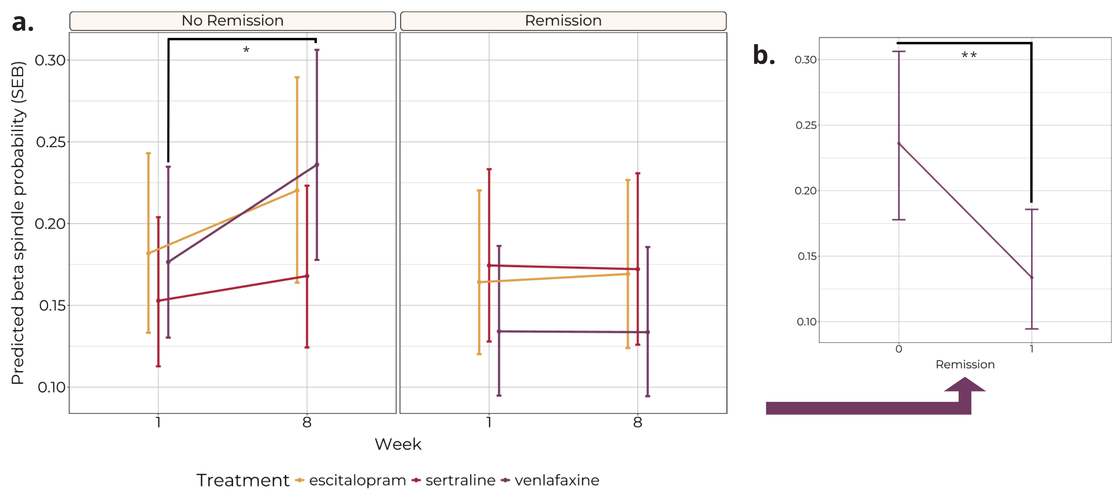


Figure 7. a) *Estimated marginal means extracted from fitted GLMM and log back-transformed. Significant SEB increase in venlafaxine non-remitters (OR = 1.44, 95% CI [1.09-1.90], p = .029),* ***b)*** *Venlafaxine only: week 8, split on remission. Venlafaxine remitters presented with lower SEB than non-remitters (OR = 0.50, 95% CI [0.29-0.87], p = .008).*

Discussion and conclusion

- SEB occurrence was not reduced following successful sertraline treatment.
- SEB occurrence increased following unsuccessful venlafaxine treatment.
  - A significant difference in SEB occurrence was observed between successful and unsuccessful venlafaxine treatment at week 8.

➢ Although SEB has been associated with various psychiatric disorders, no direct link was observed between changes in depressive symptom severity and changes in SEB probability.

➢ Previous research suggests that SEB may have value as a baseline prognostic biomarker. However, its occurrence does not appear to change in response to successful depression treatment.

1. Johnstone, J., Gunkelman, J., & Lunt, J. (2005). Clinical database development: Characterization of EEG phenotypes. Clinical EEG and Neuroscience, 36(2), 99-107.
2. Arns, M., Swatzyna, R. J., Gunkelman, J., & Olbrich, S. (2015). Sleep maintenance, spindling excessive beta and impulse control: an RDoC arousal and regulatory systems approach?. Neuropsychiatric Electrophysiology, 1(1), 5.
3. Clarke, A. R., Barry, R. J., McCarthy, R., & Selikowitz, M. (2001). EEG-defined subtypes of children with attention-deficit/hyperactivity disorder. Clinical Neurophysiology, 112(11), 2098-2105.
4. Meijs, H., Luykx, J. J., van der Vinne, N., Breteler, R., Gordon, E., Sack, A. T., ... & Arns, M. (2025). A deep Learning–Derived transdiagnostic signature indexing hypoarousal and impulse control: implications for treatment prediction in psychiatric disorders. Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 10(6), 587-596.
5. Van der Vinne, N., Vollebregt, M. A., Boutros, N. N., Fallahpour, K., van Putten, M. J., & Arns, M. (2019). Normalization of EEG in depression after antidepressant treatment with sertraline? A preliminary report. Journal of affective disorders, 259, 67-72

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Influence of cognitive workload and fatigue on the 40 Hz auditory steady-state response

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Introduction

Auditory steady-state response (ASSR) reflects the brain's ability to synchronize neural activity with periodic auditory stimulation [1]. ASSR is extensively researched for a variety of different biotechnology and medical applications, most prominently as a possible biomarker of neuropsychiatric diseases.

Cognitive workload and fatigue could potentially influence ASSR. However, the studies investigating these factors effects on ASSR are limited. Therefore, to use ASSR at its fullest potential, it is important to conduct research focused on the cognitive workload and fatigue's impact on ASSR.

Aim

The aim of this study was to investigate the effects of cognitive workload and fatigue on 40 Hz ASSR.

Methods

- ASSR was recorded using 24 channel EEG system in 28 (males = 14) healthy subjects. Mean age was 23.9±3.5 years.
- ASSR was evoked by using 1000Hz tone amplitude modulated at 40 Hz.
- N-back task was chosen to manipulate cognitive workload. Task performance was assessed using accuracy and reaction times.
- Subjective workload was evaluated using NASA-TLX.
- 40-Hz signal-to-noise ratio (SNR) was calculated at the Fz and Cz electrodes to quantify ASSR strength.

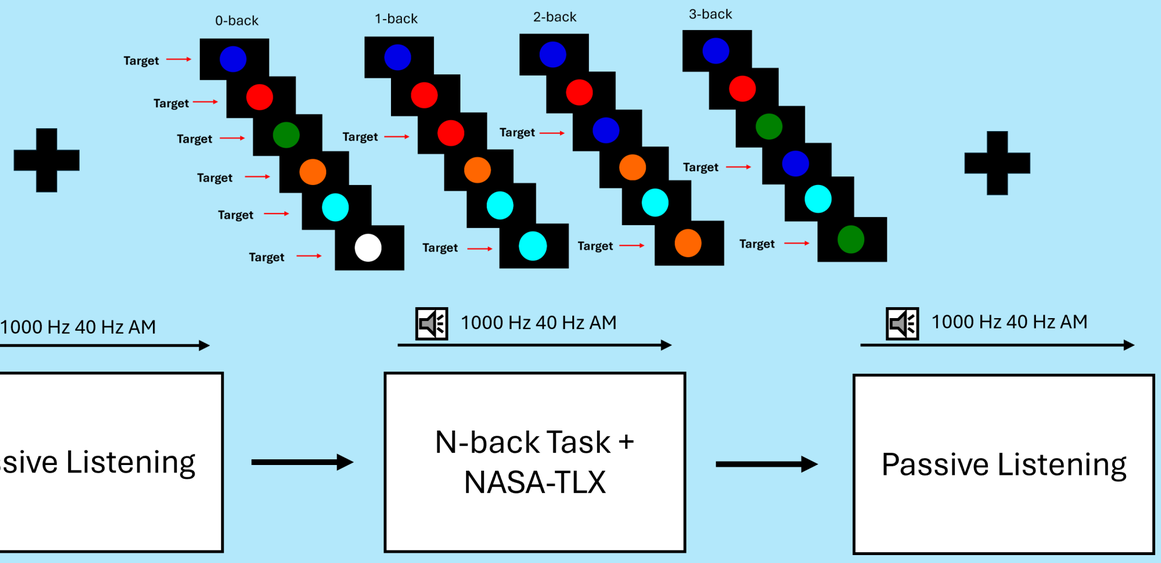


Fig. 1. The experimental design

Results

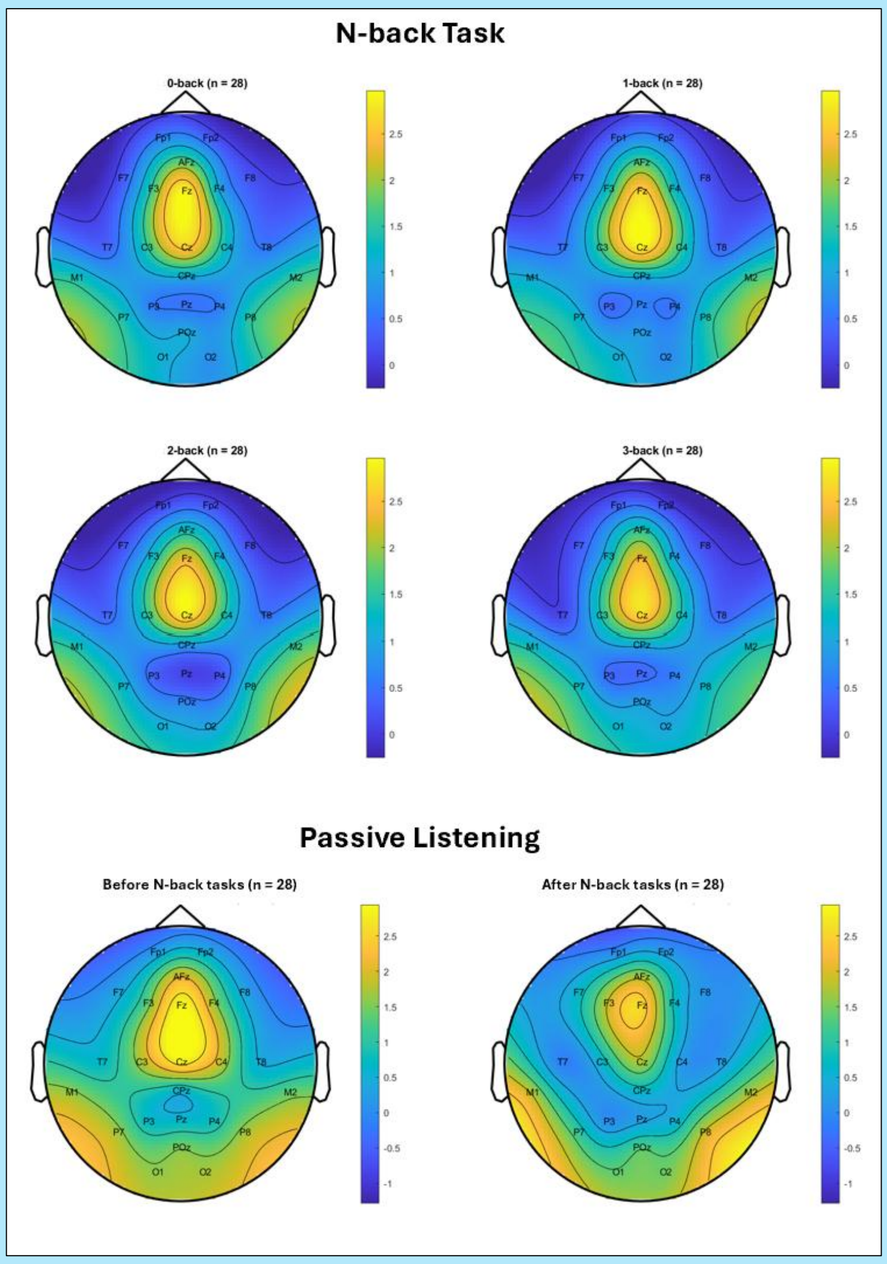


Fig. 2. Grand averaged 40 Hz SNR topographies of ASSR for N-back tasks (0-3 back) and passive listening before and after N-back task session.

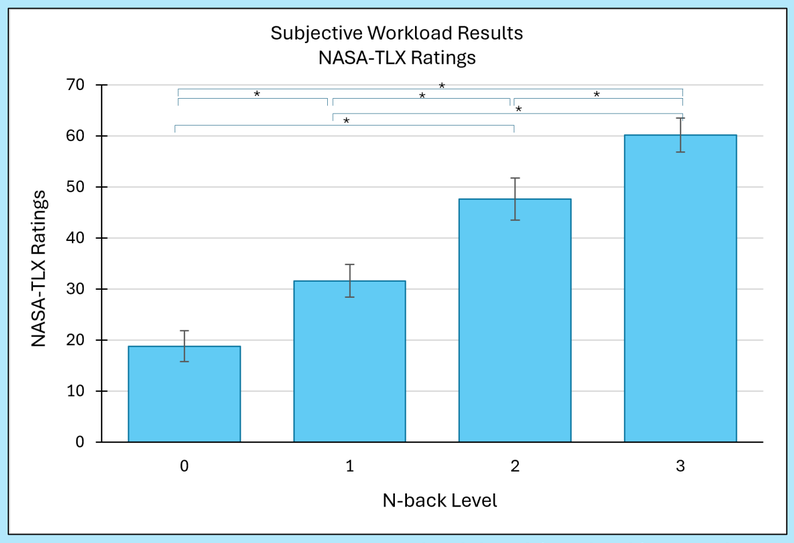


Fig. 3. Mean NASA-TLX ratings per N-back level (0-3 back). Error bars denote standard error of the mean across subjects. *p < 0.001

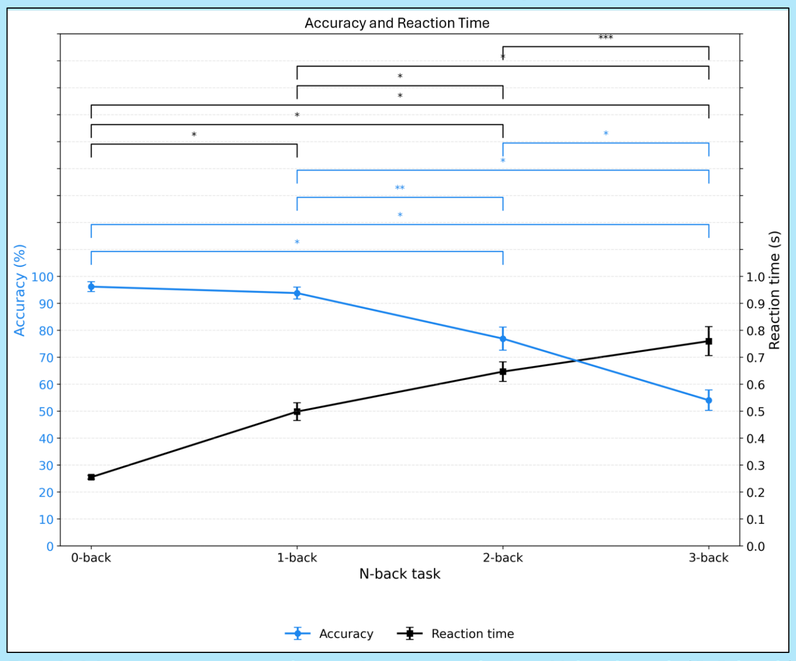


Fig. 4. Mean accuracy and reaction times during N-back task (0-3 back) performance. Error bars denote standard error of the mean across subjects. *p < 0.001,**p = 0.001, ***p < 0.009

- Statistical analysis revealed significant effects of N-back task on performance: reduced accuracy ($F(3, 81) = 48.29$, $p < 0.001$, $\eta^2 = 0.64$) and increased reaction times ($F(3, 81) = 65.04$, $p < 0.001$, $\eta^2 = 0.5$) were shown with increasing task difficulty.
- The ratings of NASA-TLX ($F(3, 81) = 59.09$, $p < 0.001$, $\eta^2 = 0.69$) representing subjective workload significantly increased as the task became more difficult.
- No effect of task difficulty on 40 Hz SNR ($F(3, 81) = 0.80$, $0 = 0.495$, $\eta^2 = 0.004$) was observed.
- A comparison of the pre- and post-N-back passive listening conditions revealed a trend towards lower 40 Hz SNR following the N-back task session ($p = 0.052$).

Conclusions

- Both task performance and subjective workload assessment were significantly affected by task difficulty.
- However, no effects of different task levels were shown for 40 Hz SNR as well as no differences and only a tendency was found between pre- and post-task ASSR measurements.

References

[1] Picton, T. W., John, M. J., Dimitrijevic, A., & Purcell, D. W. (2003). Human auditory steady-state responses: Respuestas auditivas de estado estable en humanos. International Journal of Audiology, 42(4), 177–219. https://doi.org/10.3109/14992020309101316