NÁRODNÍ ÚSTAV DUŠEVNÍHO ZDRAVÍ

Národní Ústav Duševního Zdraví (NUDZ)

Témata zapojení studentů do výzkumu

BIODEN, 24. 5. 2024

Fakulta elektrotechnická,
České vysoké učení technické v Praze

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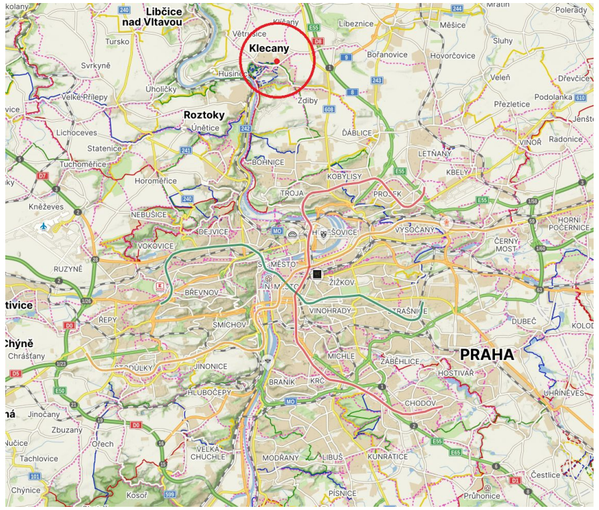
Úvod: o NÚDZ

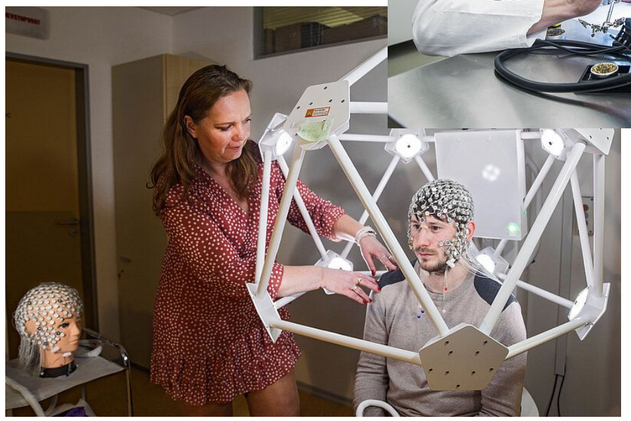
NÚDZ

Základní info

- Veřejná výzkumná instituce
- Spadá pod Ministerstvo Zdravotnictví ČR
- Vznikl 1.1.2015 (financováno EU/ OP VaVPI)
- Navazuje na Psychiatrické centrum Praha
- Sídlí v Klecanech u Prahy
- 15 min bus z Kobylis
- www.nudz.cz



ROLE NÚDZ



1 **Výzkumná činnost**

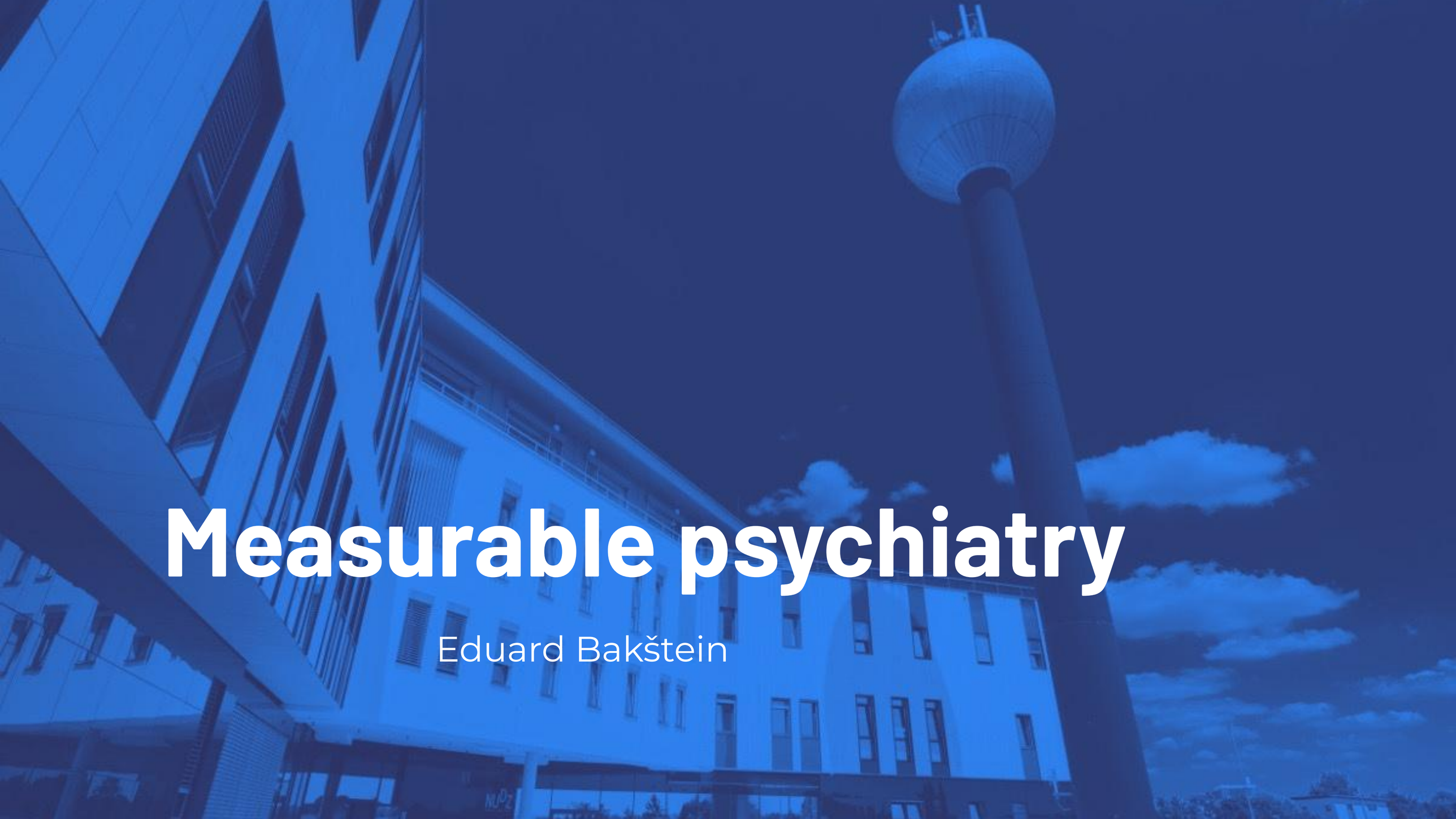
- Od **preklinického** výzkumu (animální modely, laboratoře), přes **klinický** (MRI, hdEEG, polysomnografie, farmakologie), až po epidemiologii, výzkum služeb a aplikovaný výzkum

2 **Klinická péče**

- Psychiatrická ambulance
- 3 lůžková oddělení (úzkostné, poruchy nálady a psychotické poruchy)
- Denní stacionáře

3 **Výuka**

- Zejm. studenti 3.LF UK, Celoživotní vzdělávání lékařů
- Přednášky, konference, odborné semináře a workshopy



Measurable psychiatry

Eduard Bakštein

Goals

Development of objective biomarkers and tools for clinical decision making and therapy in psychiatry

Example problems

- **Prediction of functional outcome** in first-episode schizophrenia
- Long-term clinical status monitoring in bipolar disorder using actigraphy and self-assessment

ESO Study

Early-stage Schizophrenia Outcome

- Longitudinal study, 3 visits
- First-episode schizophrenia patients

~500, **260** and **70** patients at each visit

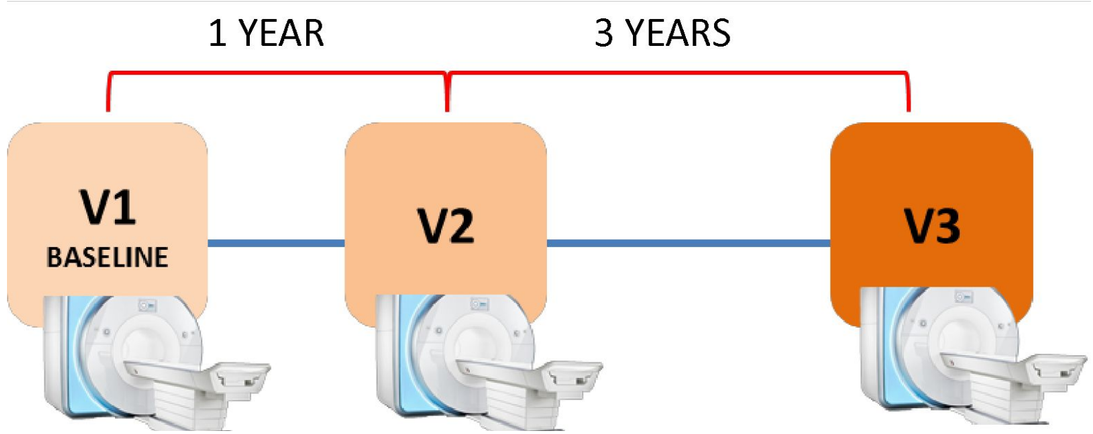
~300 Healthy controls

Hundreds of variables, Multiple modalities

MRI (structural, fMRI, DWI),

Sociodemography, Clinical scales

Laboratory measurements



Main aims

1. Understanding clinical heterogeneity of schizophrenia (phenotyping)
2. Development of tools for clinical decision-making
3. Integrated care center for patients with first episode of schizophrenia

Clinical episode prediction

Bipolar disorder:

- Study AKTIBIPO: 369 patients,
- follow-up 18+ months
- wrist-worn actigraphy and self-assessments in a mobile application
- (collaboration with a startup Mindpax)

Schizophrenia:

- Digital monitoring with self-assessments
- Automatic alerts sent to psychiatrist
- ILIA multi-centric RCT study starting in Q3/2024 in Germany (PI prof. Stefan Leucht), 60+60 patients

Contact us

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Eduard.Bakstein@**fel.cvut**.cz

http://neuro.felk.cvut.cz

Time Perception

Tereza Nekovářová

Time perception

One "internal clock" vs. Several timers

Structures dedicated purely for timekeeping vs. secondary functions

Time receptors

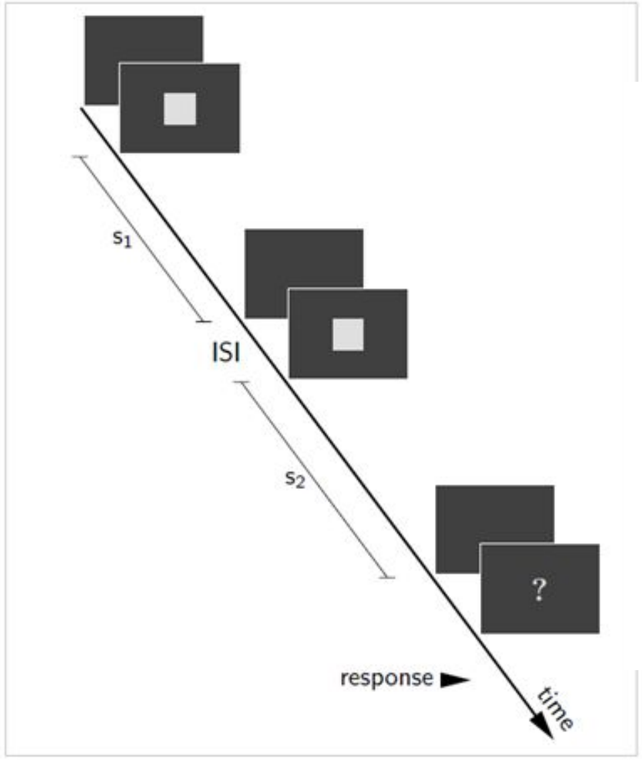
Time on different scales

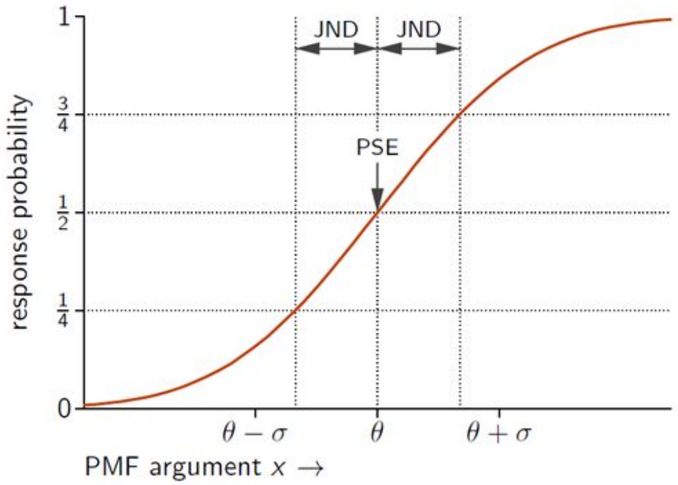
Different neurobiological and cognitive mechanisms

Interval timing

Time perception

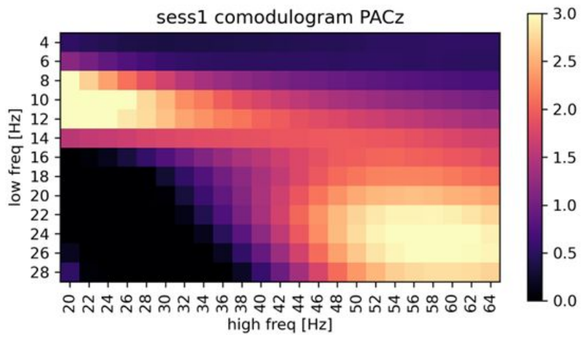
Intrinsic oscillatory brain activity as a basis for time perception

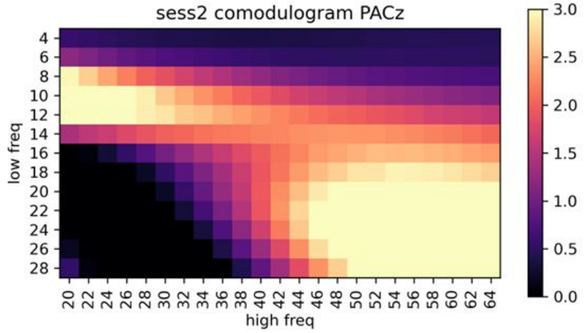


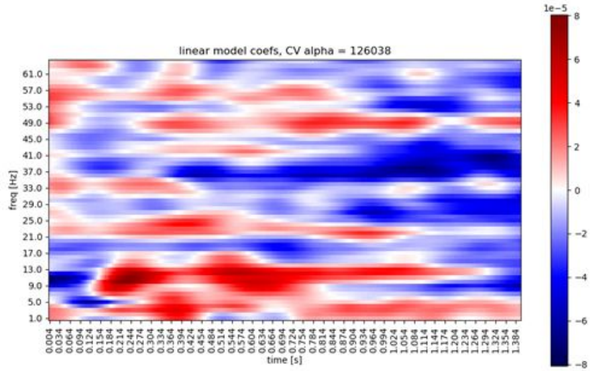


Θ: Point of subjective equality ("accuracy")
σ: a measure of the "unsharpness" of the discrimination ("precision"/"acuity")

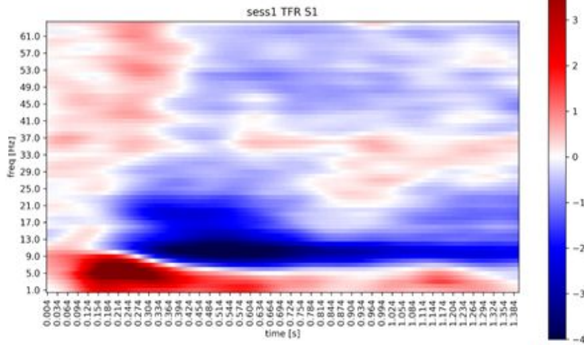
Time perception

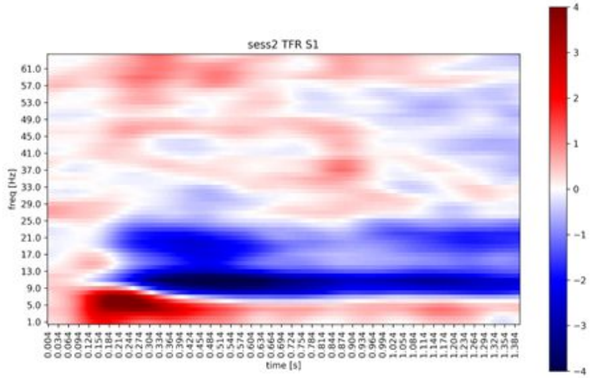


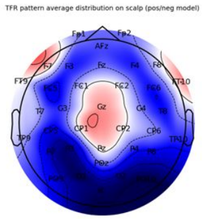




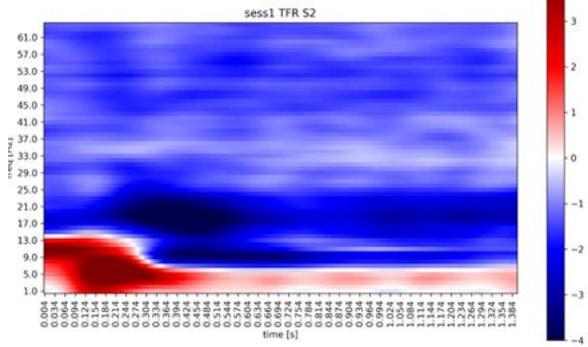
Stimulus 1

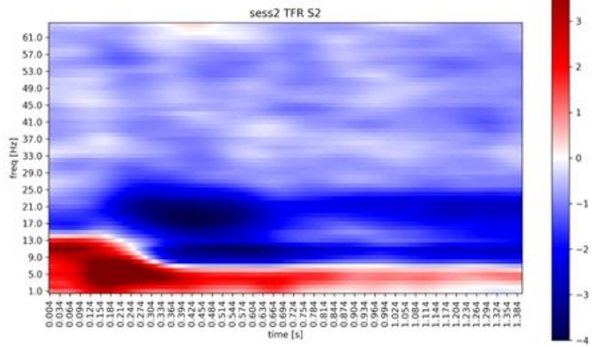


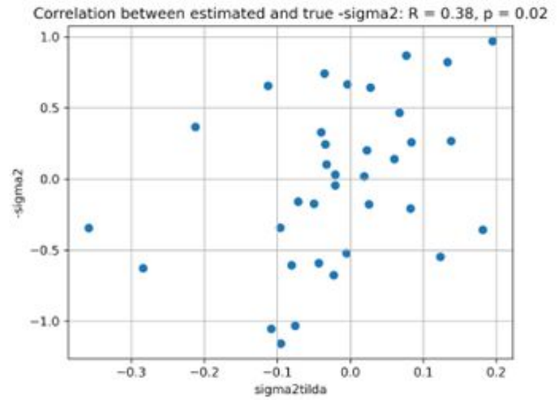




Stimulus 2







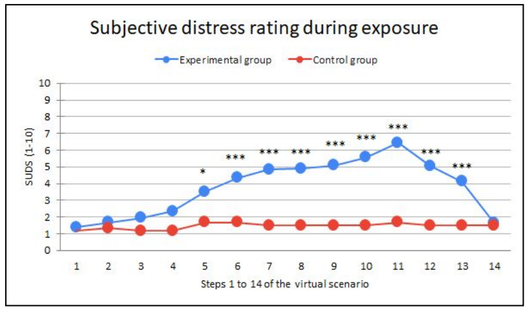
Virtual Reality

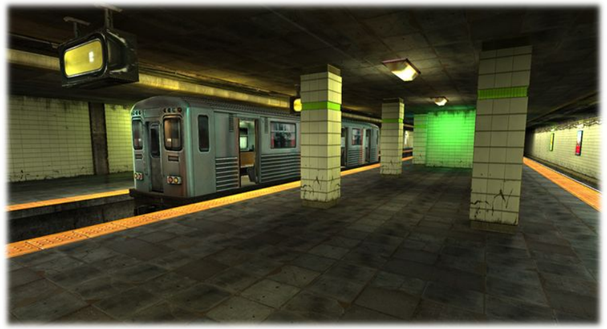
Iveta Fajnerová

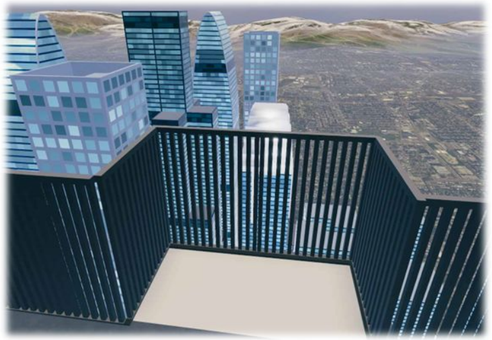
Exploring the link between objective physiological measures (ECG,EDA) & subjective anxiety ratings during VRET in phobias

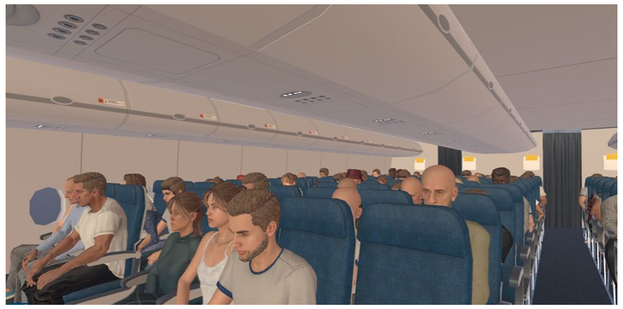
VRET - Exposure therapy in VR

- exposure to feared stimulus
- **Various exposure scenarios**
- **Increasing intensity**
- **subjective ratings**





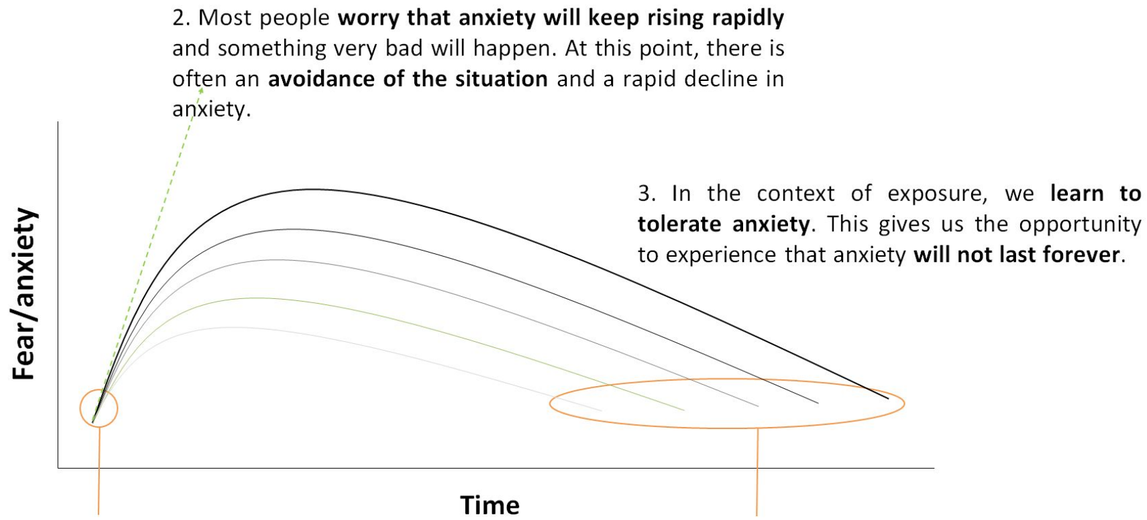




Exploring the link between objective physiological measures (ECG,EDA) & subjective anxiety ratings during VRET in phobias

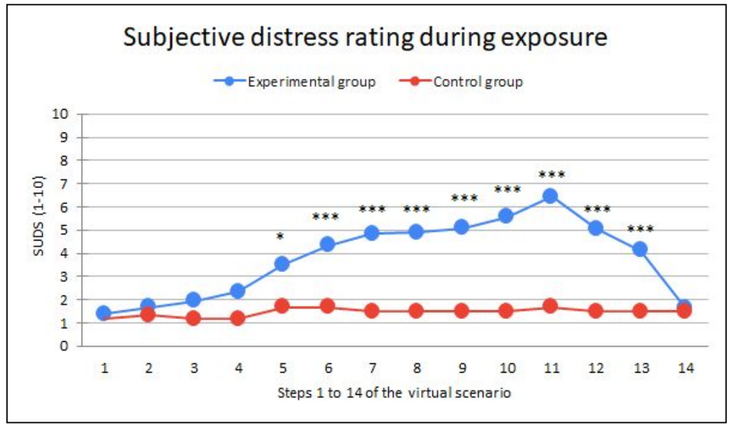
VRET - Exposure therapy in VR

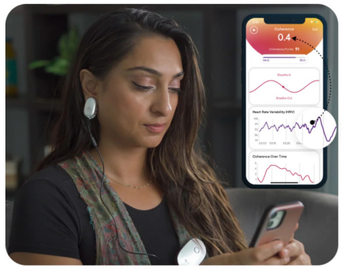
- **Various exposure scenarios**
- **Increasing intensity <u>within/between sessions</u>**
- **subjective ratings in specific events**
- **recording of position/orientation and all interactions in VR**



Physiological response during VR exposure

- Indicators of cognitive load (stress response).
- CL assessment using HRV, EDA….
- AI methods for **Artifacts removal** and automatic detection/**identification of the targeted events** provoking fear response
- **Comparing subjective and objective responses**





Behavioral activity during virtual exposure in obsessive-compulsive disorder (heatmaps, position tracking, interactions in VR environments)

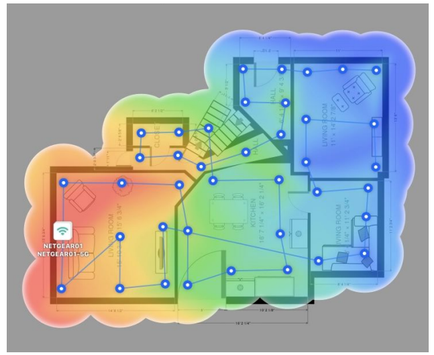
„fear-of-harm/ checking“

“hoarding”

“contamination/ cleaning”

“symmetry”

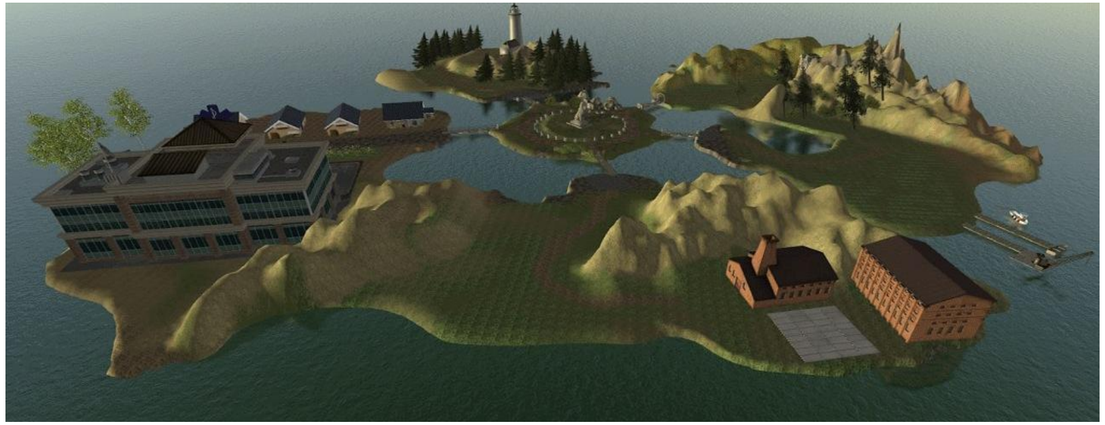
Fajnerová, I., Francová, A., Taranzová, K. *et al.*. *Virtual Reality* **27**, 2691–2701 (2023)



Behavioral analysis & Heatmaps>

- position based
- interactions with virtual objects
- reactivity to individual stimuli (attention, vs. interactions)
- time spent in compulsive activity, number of repetitions

Neural correlates of episodic memory retrieval: MRI-based functional connectivity



- Healthy and schizophrenic subjects

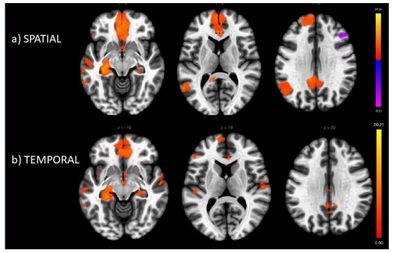
Training in 3-5 islands (collecting 5 objects per island)

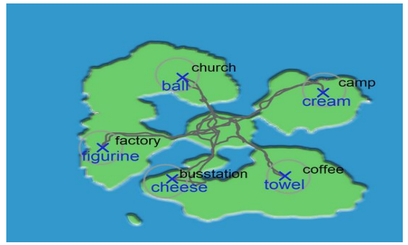
Functional connectivity (fMRI) during memory retrieval

1. object selection

2. selection of location (original order)

3. object placed in the original position





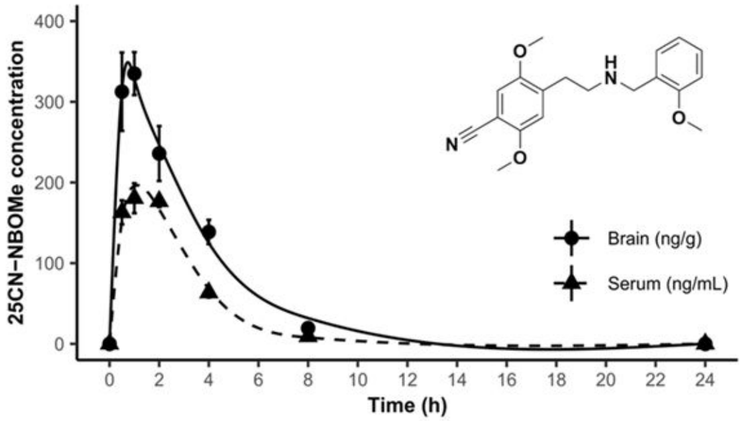
Design combining events and blocks of activity (decision making, movement, interactions)

Preclinical Research

Čestmír Vejmola

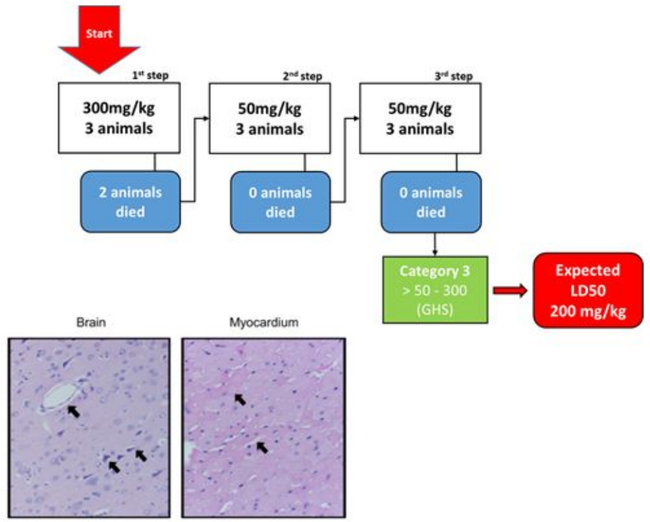
Novel psychoactive drugs

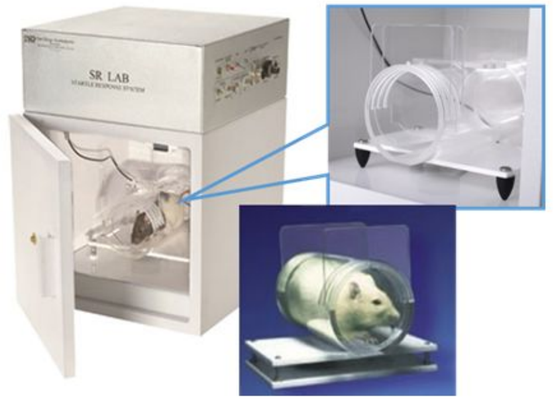
Pharmacokinetic profile

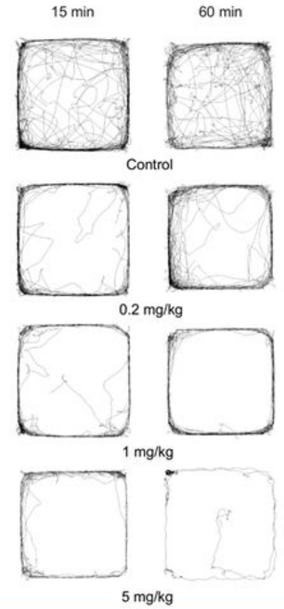


EEG

Acute toxicity

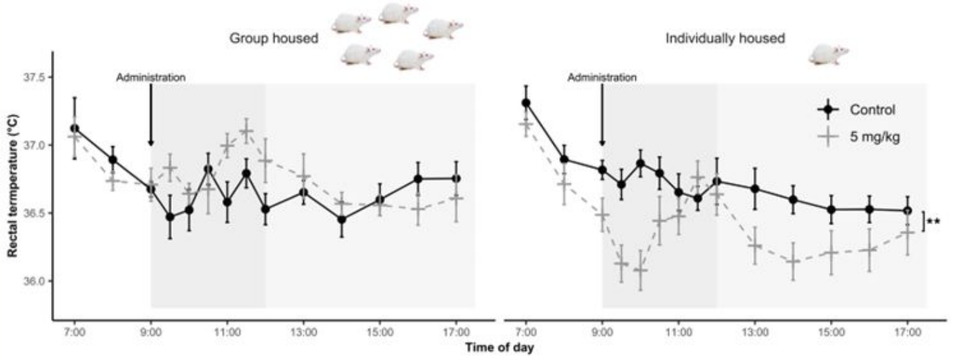






Behavioral effects - OFT and PPI

Thermoregulation changes



OPIODS

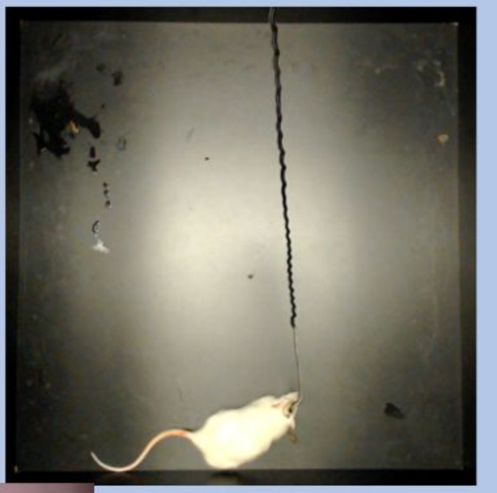
heroin

PLACEBO

VEH, VEHET

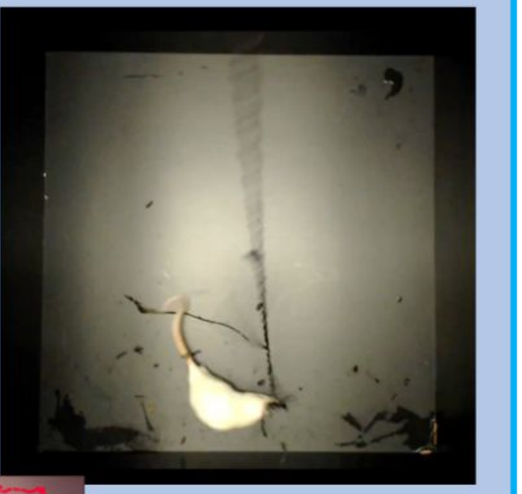
PSYCHEDELICS

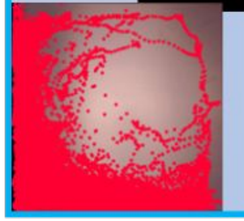
psilocybin



STIMULANTS - DAT

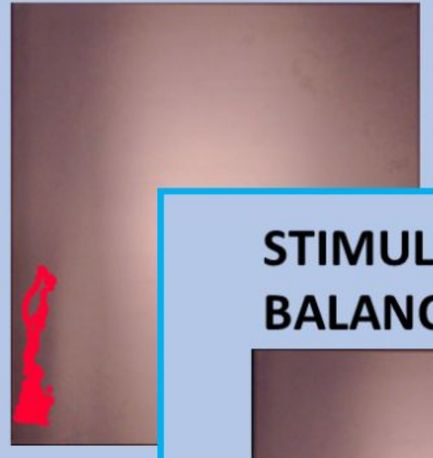
MDPV





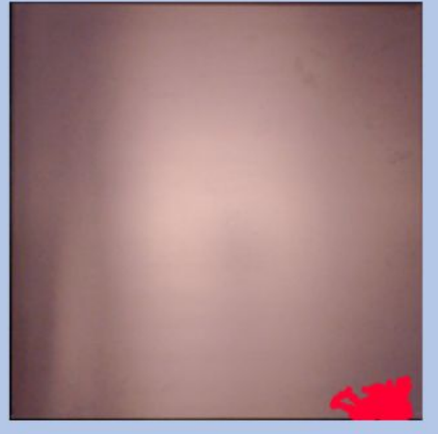
CANNABINOIDS

CBD



STIMULANTS – BALANCED

cocaine



CANNABINOIDS

HHC

DISSOCIATIVES

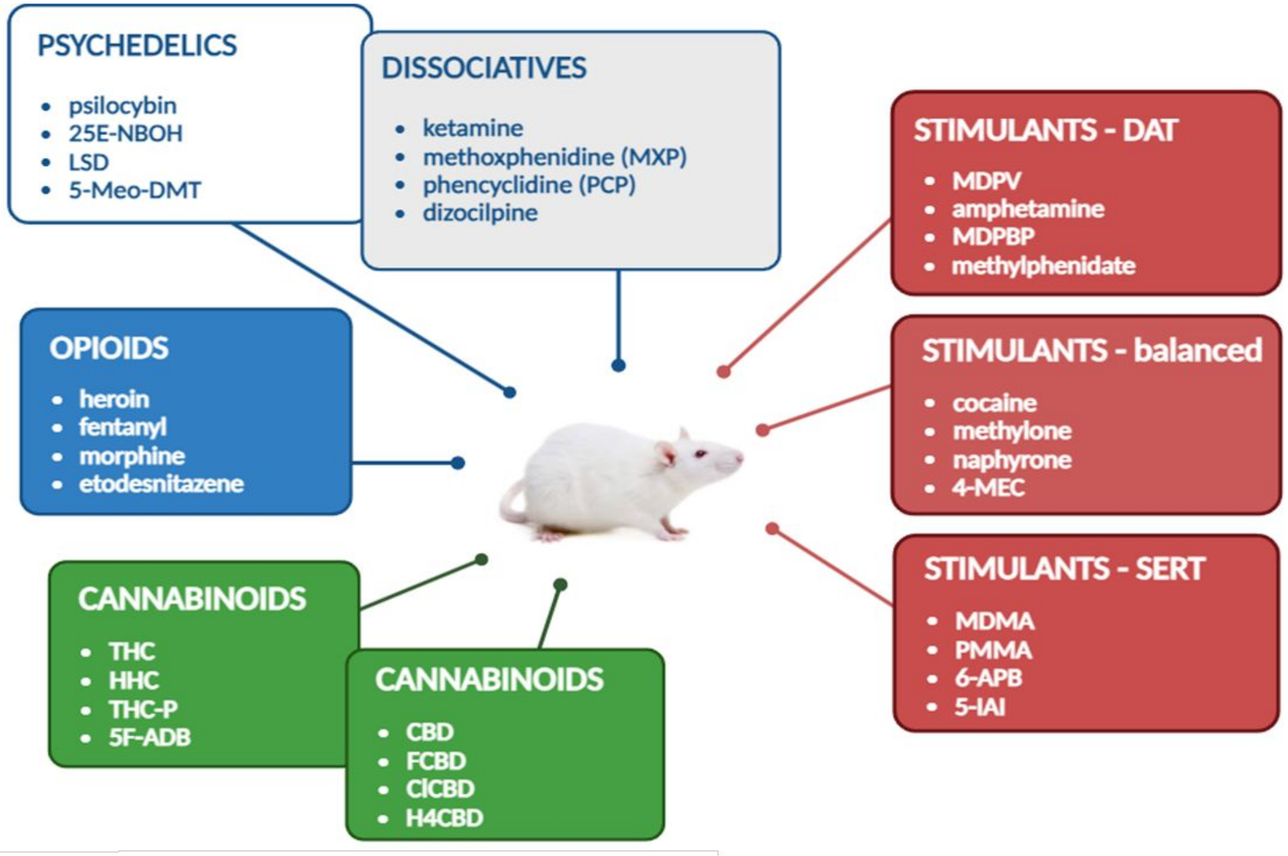
MXP

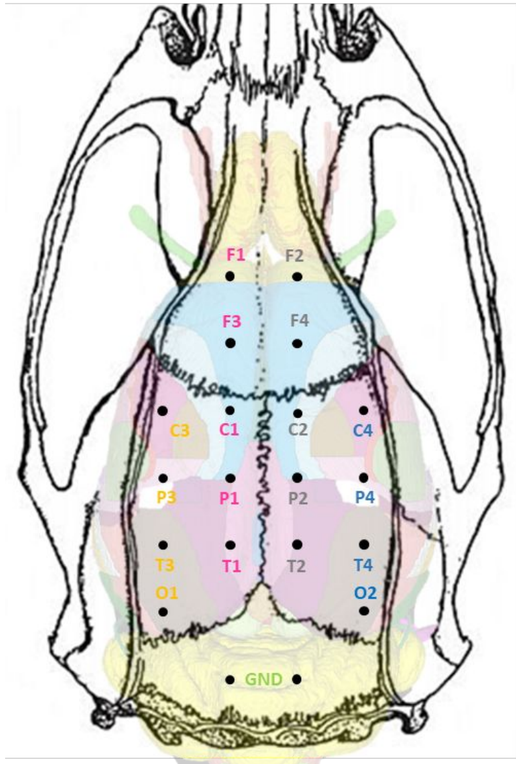
STIMULANTS – SERT

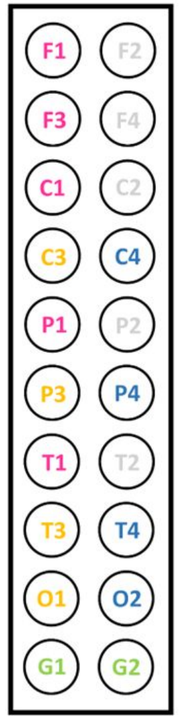
MDMA

Creating database

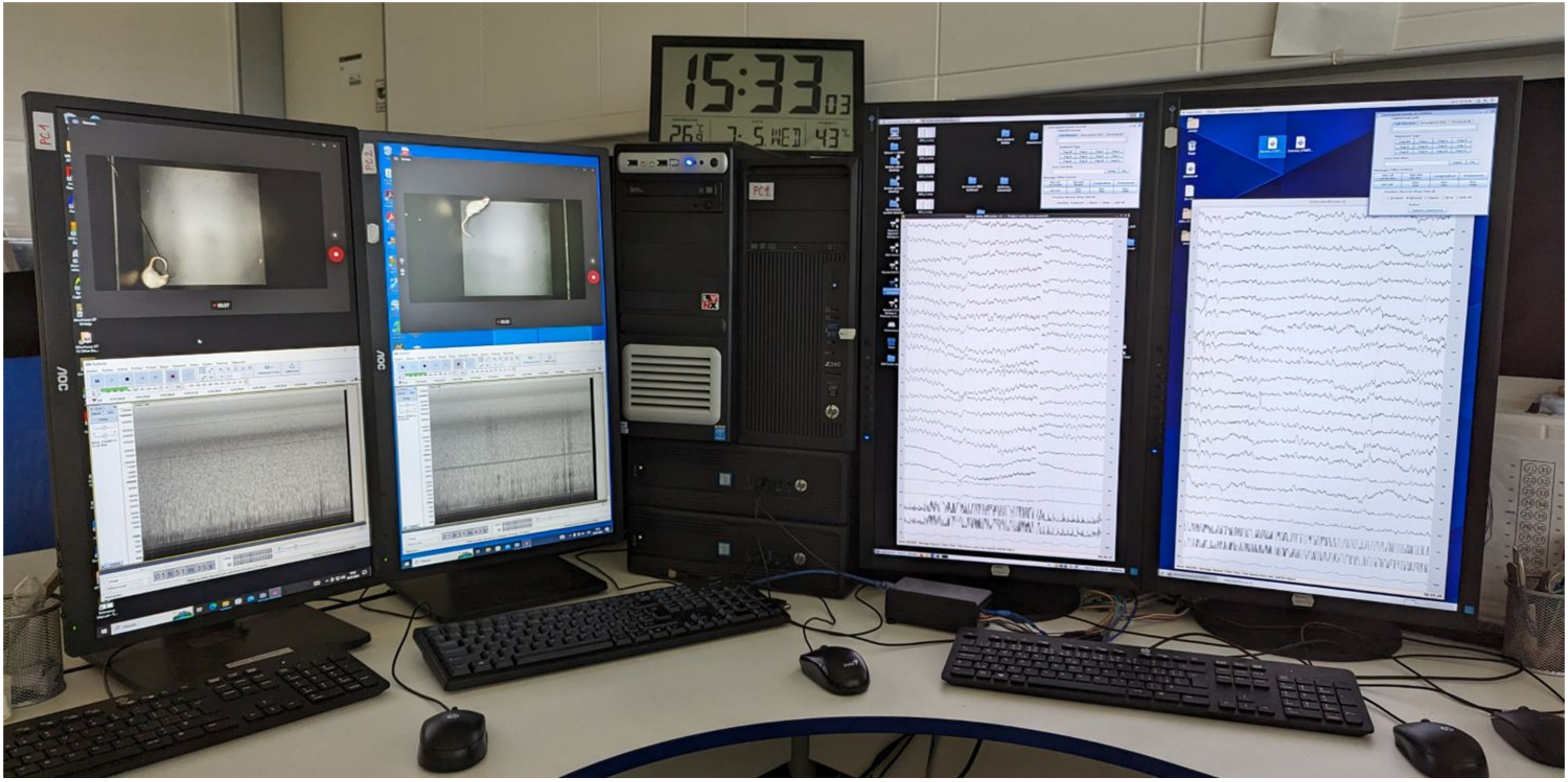
	RUN 1		RUN 2		RUN 3	
GROUP	TREATMENT	dose mg/kg	TREATMENT	dose mg/kg	TREATMENT	dose mg/kg
VEH	SAL+deionized	x	SAL+deionized	x	SAL+deionized	x
VEHET	SAL+eth+Tween	x	SAL+eth+Tween	x	SAL+eth+Tween	x
psychedelics	psilocybin	5	25E-NBOH	5	psilocybin	0,5/2
SERT	MDMA	5	PMMA	20	MDMA	2,5/10
BALANCED	cocaine	20	methylone	10	cocaine	5/10
DAT	MDPV	2	apmhetamine	5	MDPV	1/4
dissociatives	MXP	20	ketamin	30	MXP	10/40
opioids	heroin	0,25	fentanyl	20ug	heroin	0,05/2
CB1 antagonist	CBD	10	FCBD	10	CBD	1/5
CB1 agonist	HHC	10	THC	10	HHC	1/5



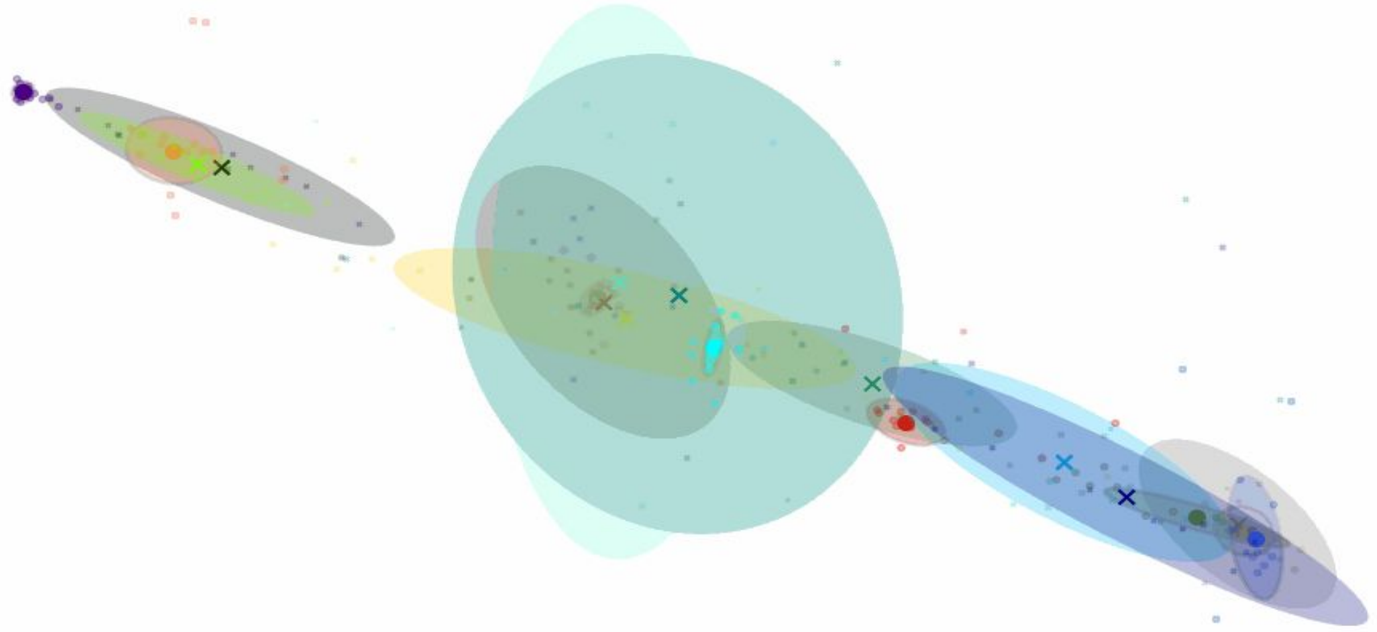


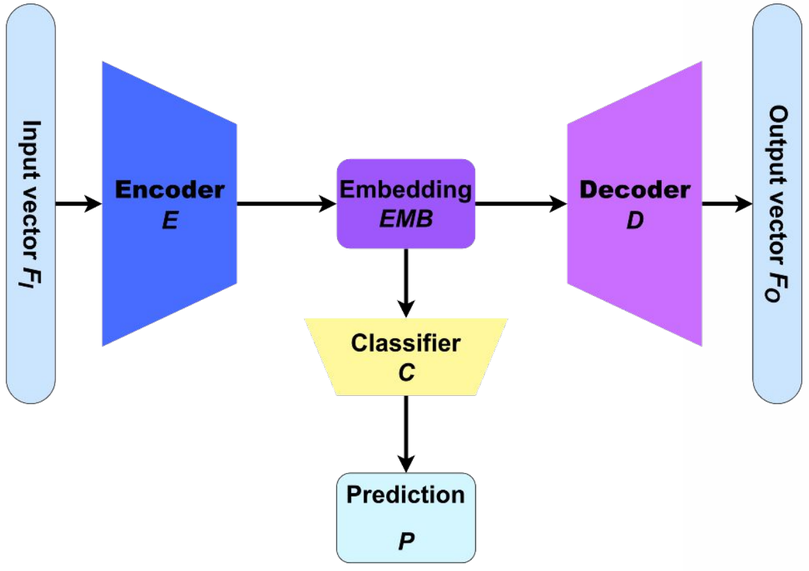


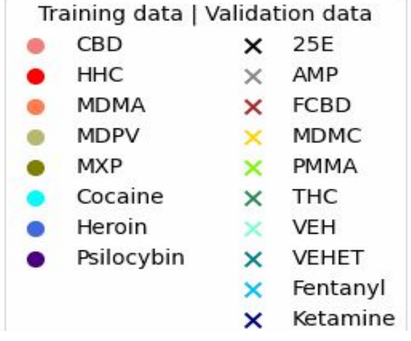
1	F1	frontal association cortex
11	F2	
2	F3	secondary motor cortex
12	F4	
3	C1	primary motor cortex
13	C2	
4	C3	primary somatosensory
14	C4	cortex, forelimb area
5	P1	medial parietal association
15	P2	cortex
6	P3	primary somatosensory
16	P4	cortex, trunk area
7	T1	secondary visual cortex,
17	T2	mediomedial area
8	T3	primary visual cortex,
18	T4	binocular area
9	O1	primary visual cortex,
19	O2	binocular area
10		GND
20		


15:33 03
WED
43%
PC1
PC2

Neural network clustering of drugs based on EEG

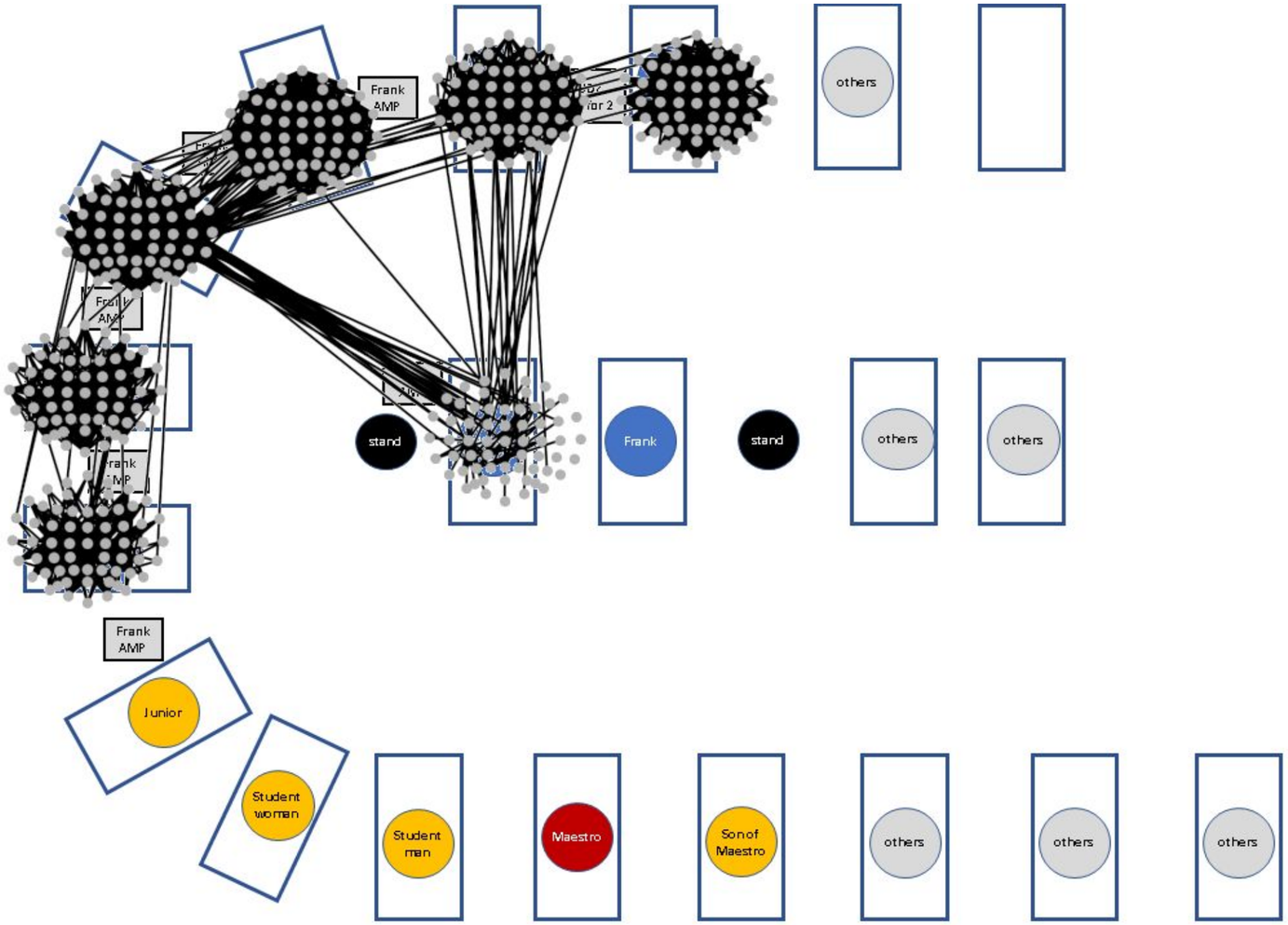


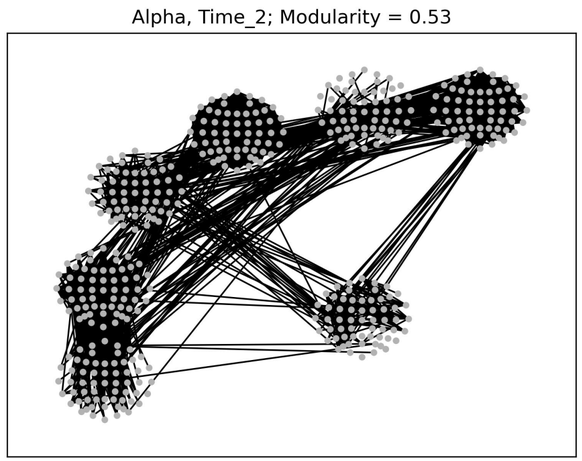


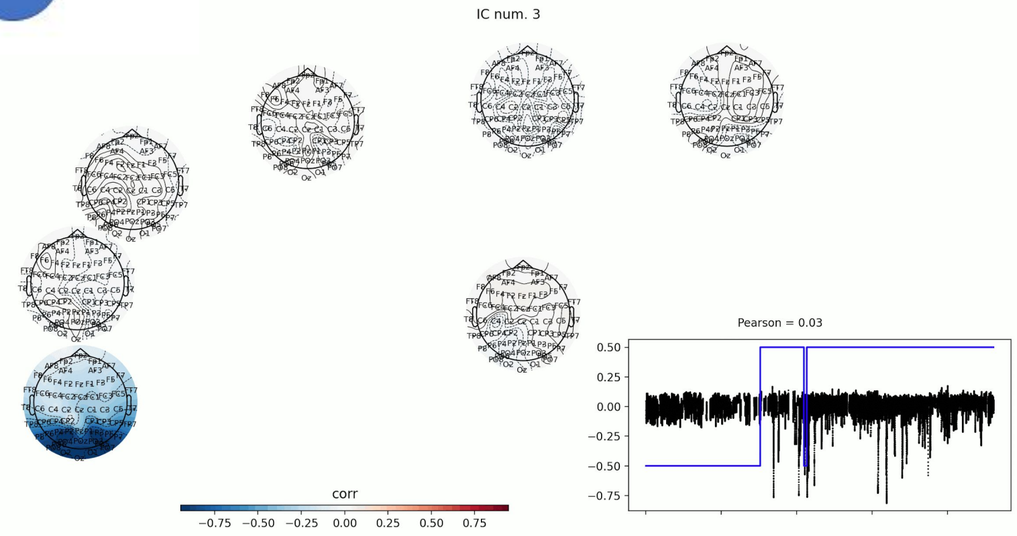


Rat brains synchrony

1st session

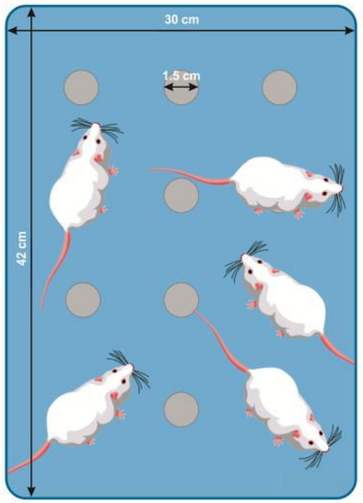


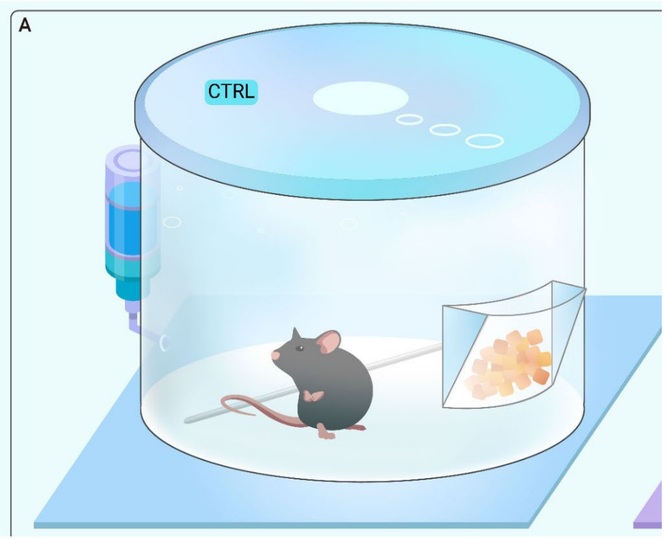


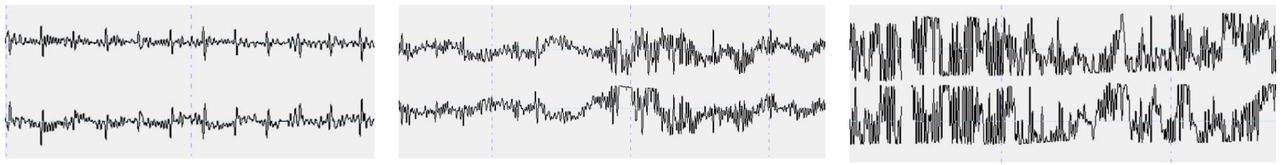


Automated accelerometer-vibration-based method for rat sleep deprivation

- Currently available procedures for sleep deprivation in rodents:
- gentle handling and forced locomotion
- gentle handling is not very standardized and its practical applicability and effectiveness over prolonged periods of sleep deprivation are limited; rats manage to sleep, e.g. 6% of the time (Deboer et al., 2007)
- Protocols that are used for forced locomotion are standardized within laboratories but may induce high levels of locomotor activity while still allowing for brief naps in between periods of forced activity (e.g. Gong et al., 2004; GuzmanMarin et al., 2005, 2006).



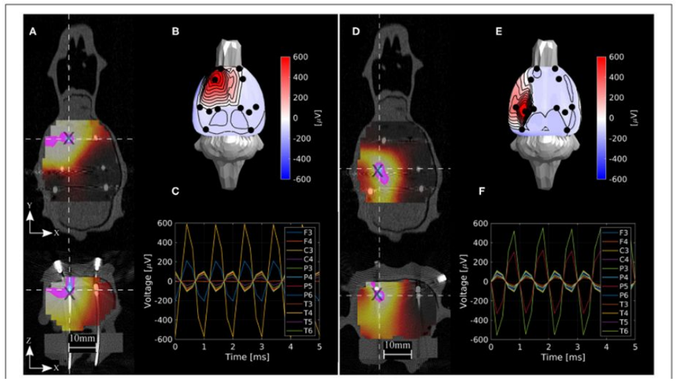


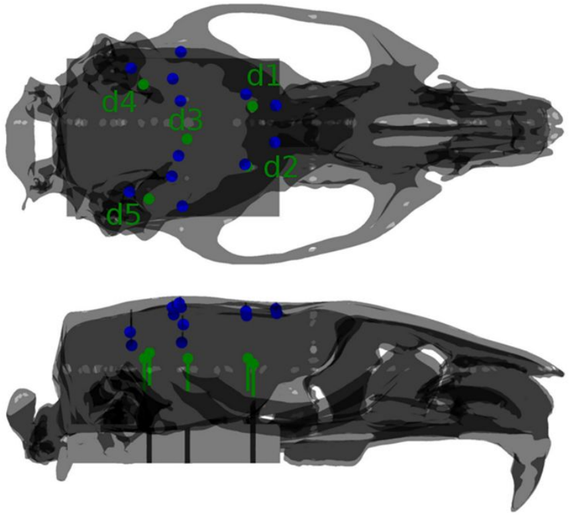


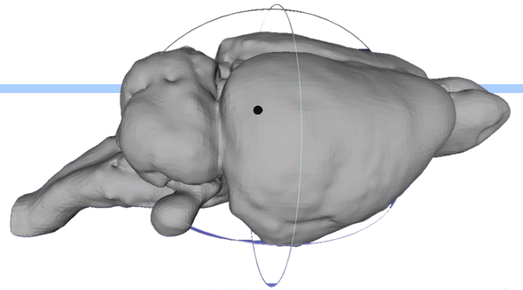
sleep head waving walking

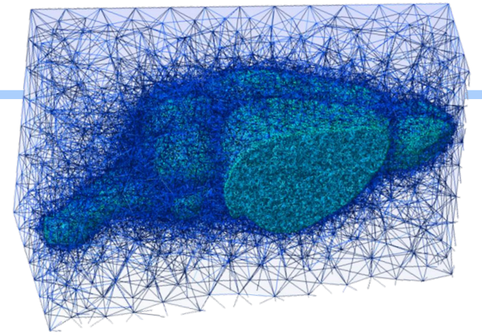
NÁRODNÍ ÚSTAV DUŠEVNÍHO ZDRAVÍ

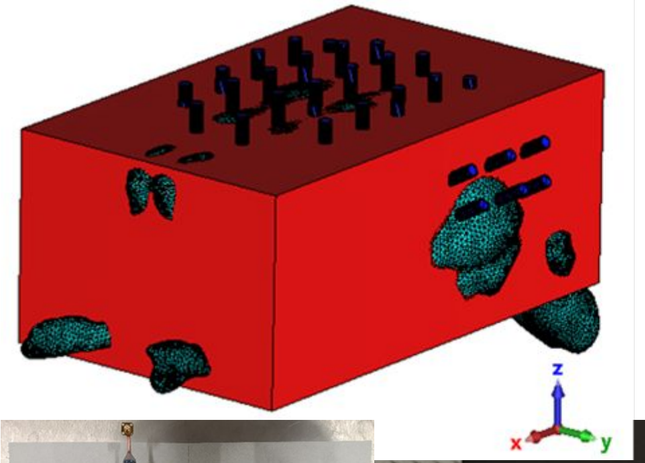
RatCon

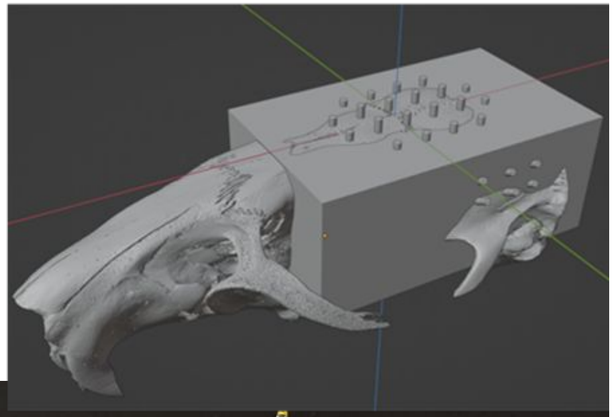


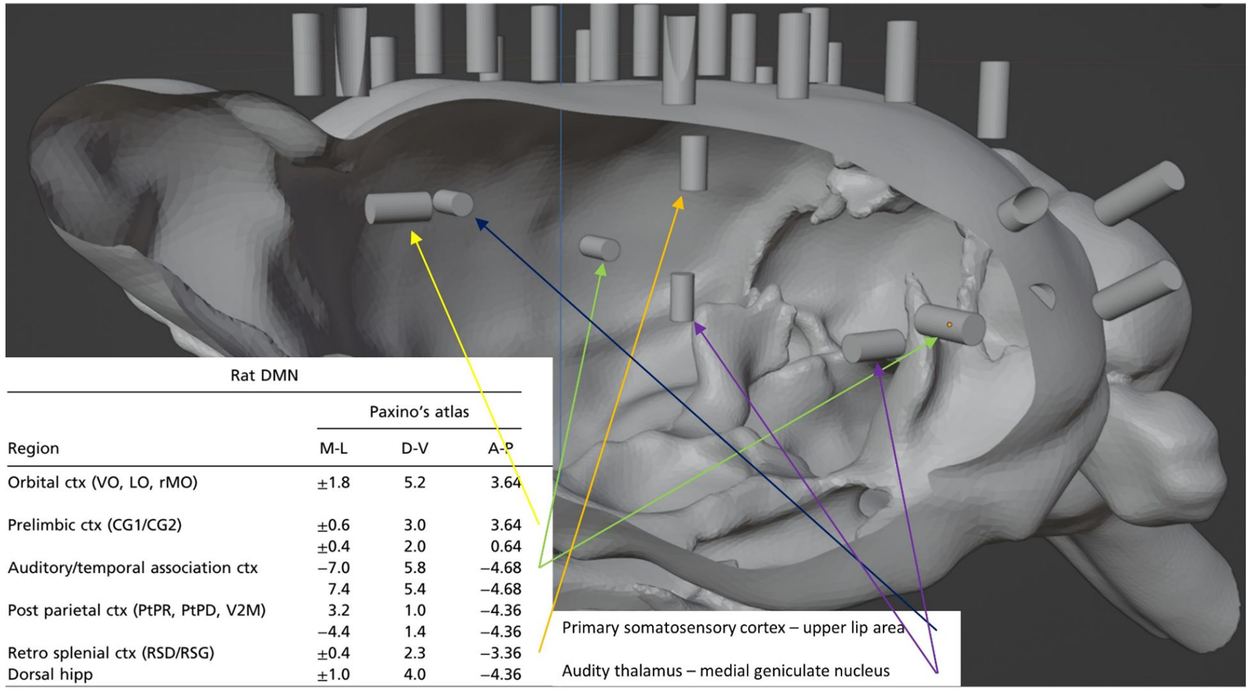










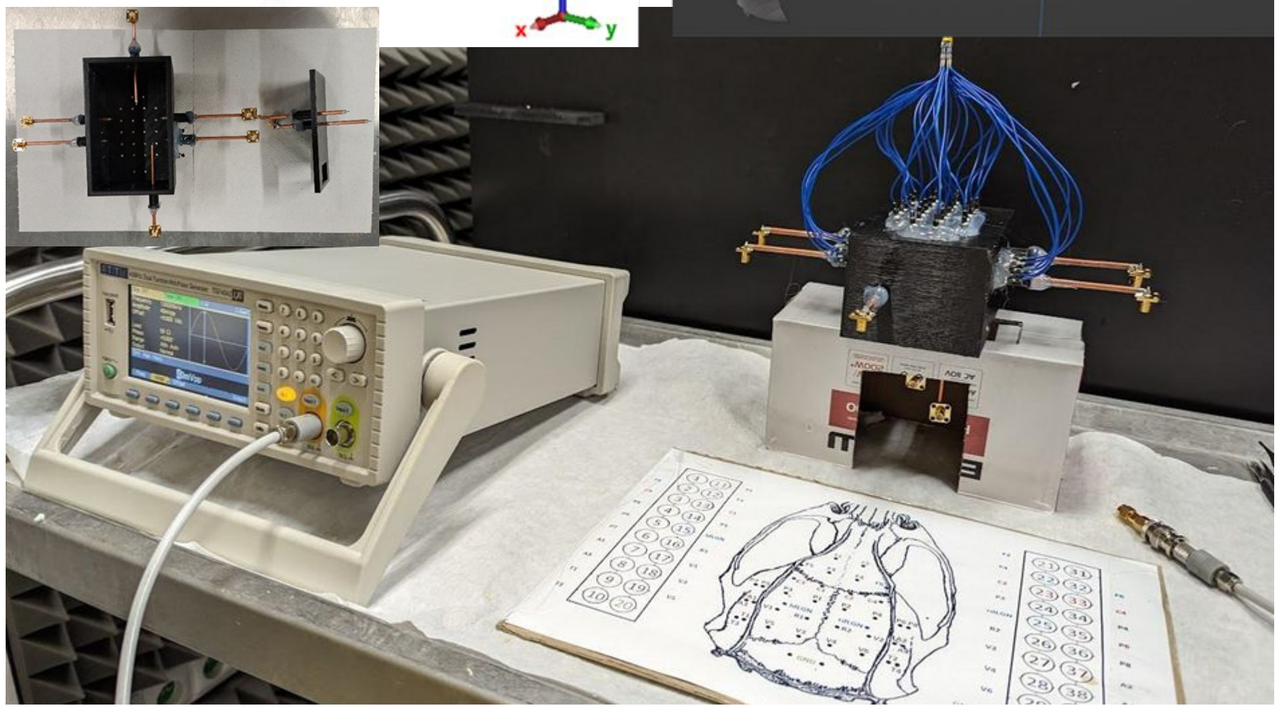


Rat DMN

Region	Paxino's atlas M-L	D-V	A-P
Orbital ctx (VO, LO, rMO)	±1.8	5.2	3.64
Prelimbic ctx (CG1/CG2)	±0.6	3.0	3.64
	±0.4	2.0	0.64
Auditory/temporal association ctx	−7.0	5.8	−4.68
	7.4	5.4	−4.68
Post parietal ctx (PtPR, PtPD, V2M)	3.2	1.0	−4.36
	−4.4	1.4	−4.36
Retro splenial ctx (RSD/RSG)	±0.4	2.3	−3.36
Dorsal hipp	±1.0	4.0	−4.36

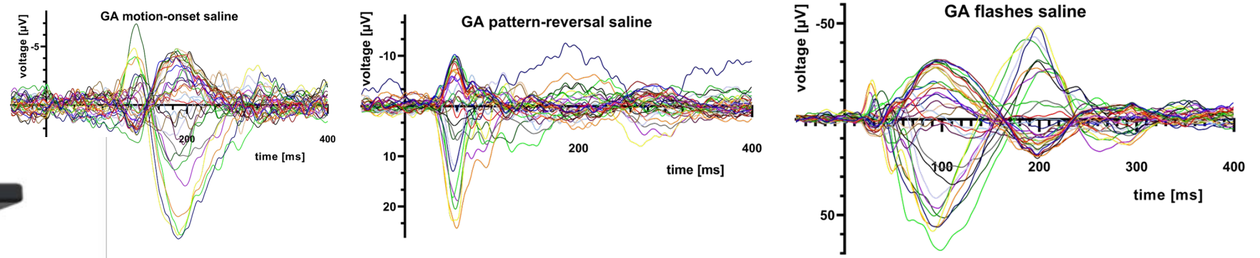
Primary somatosensory cortex – upper lip area

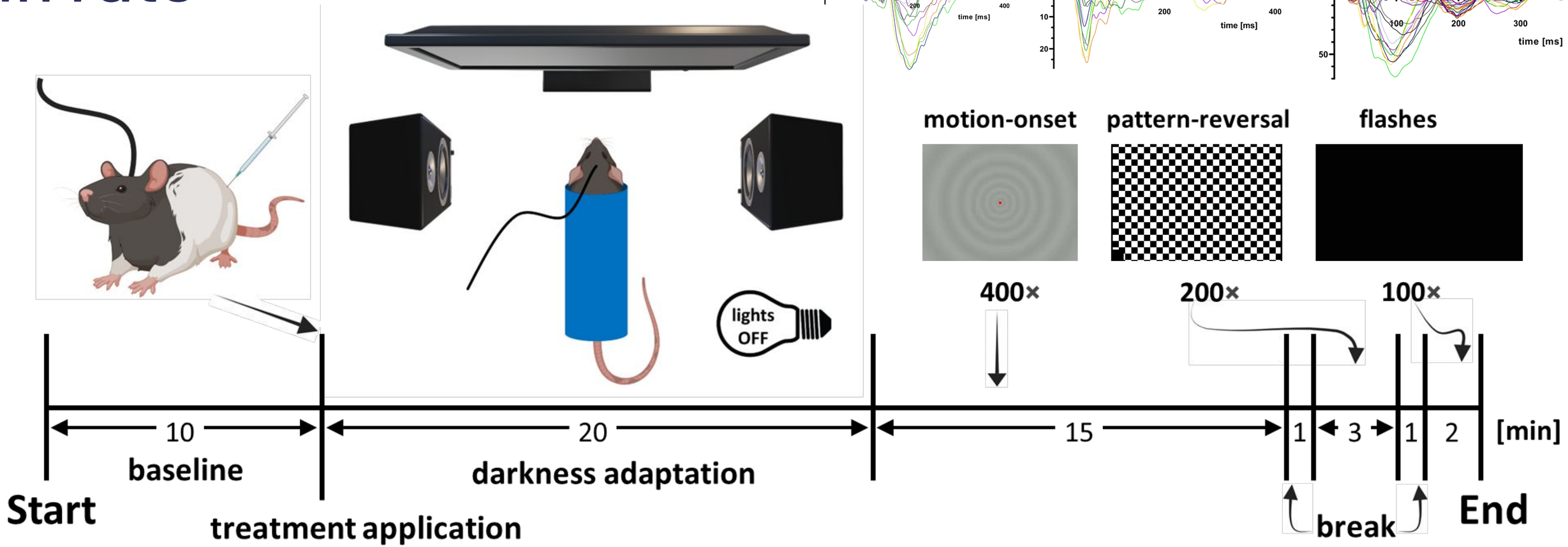
Audity thalamus – medial geniculate nucleus



Drug-induced visual alterations in rats

- Generating stimuli for VEP paradigms
- Can we track evoked potential from retina up to the visual cortices?
- Analyzing VEP parameters





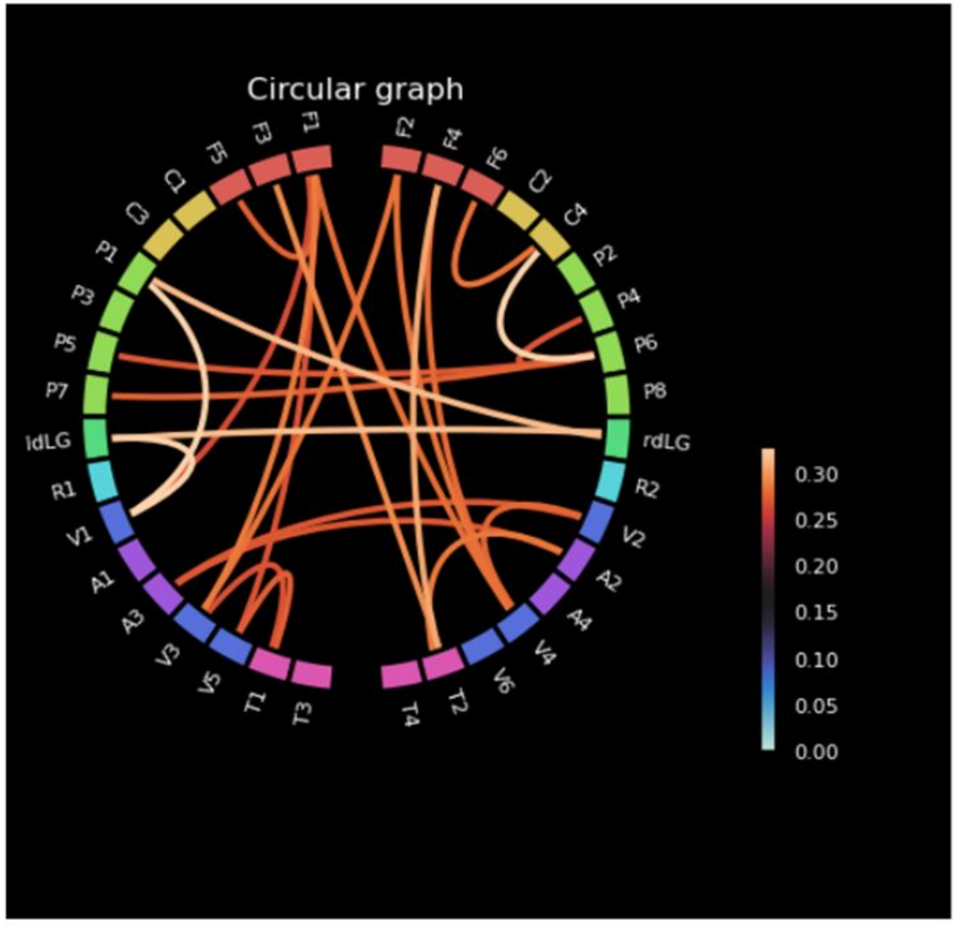
Drug: Saline

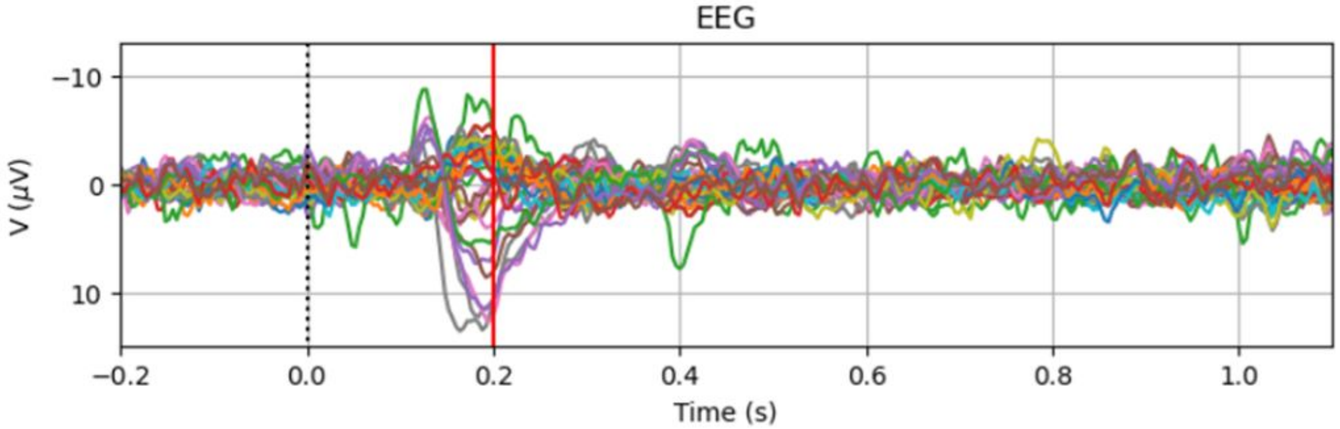
Connections: 25

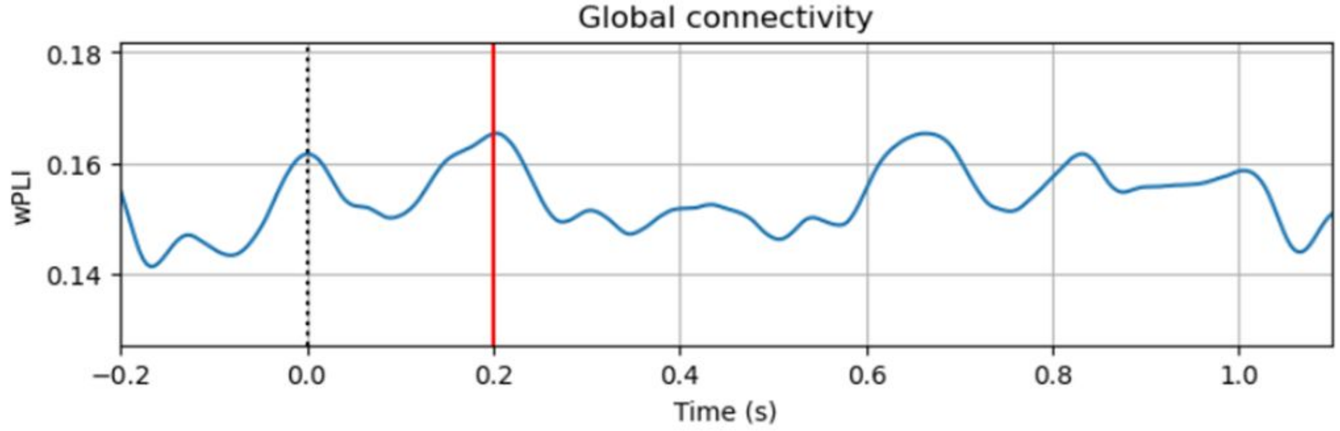
Frequency range: 10 – 13

Time: 0.20

- [ ] Connectivity baseline correction (z-score)
- [ ] VEP baseline correction (z-score)
- [ ] Display connectivity matrix
- [ ] Show layout



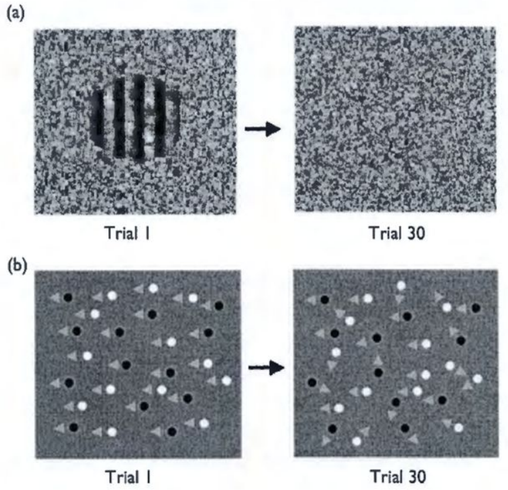


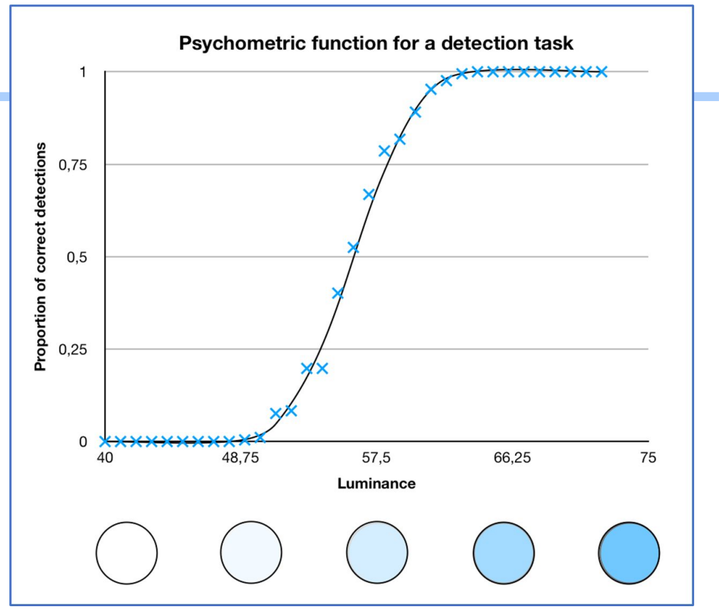


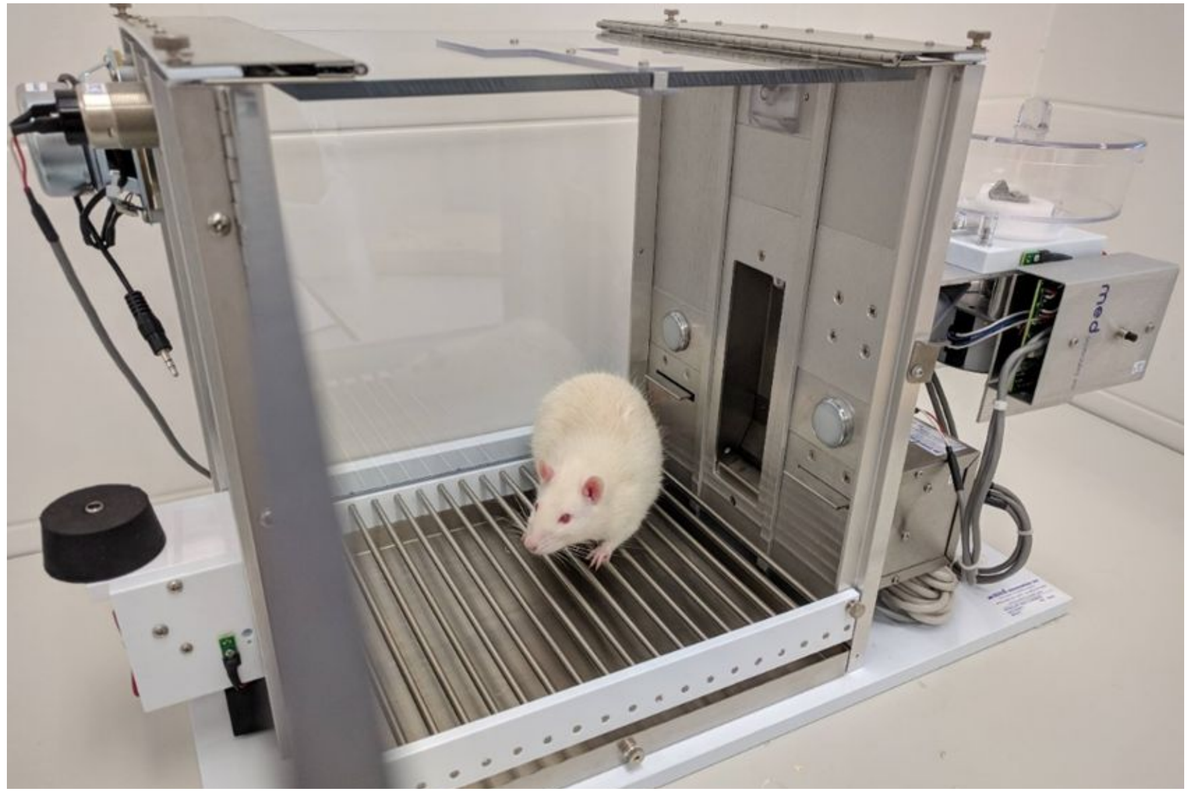
NÁRODNÍ ÚSTAV DUŠEVNÍHO ZDRAVÍ

Drug-induced visual alterations in rats

- Implementing behavioral testing in skinner boxes







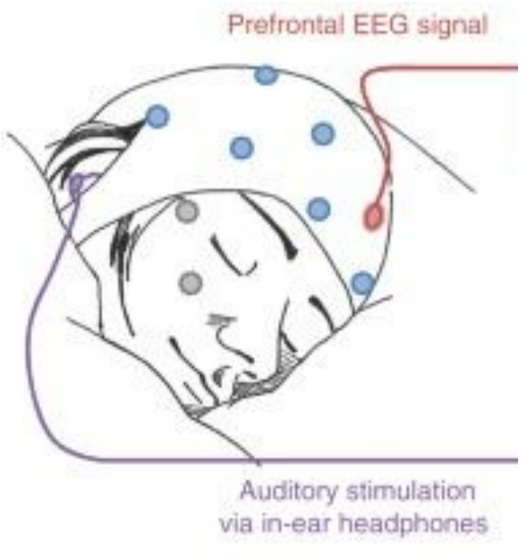
Sleep Research

Filip Černý

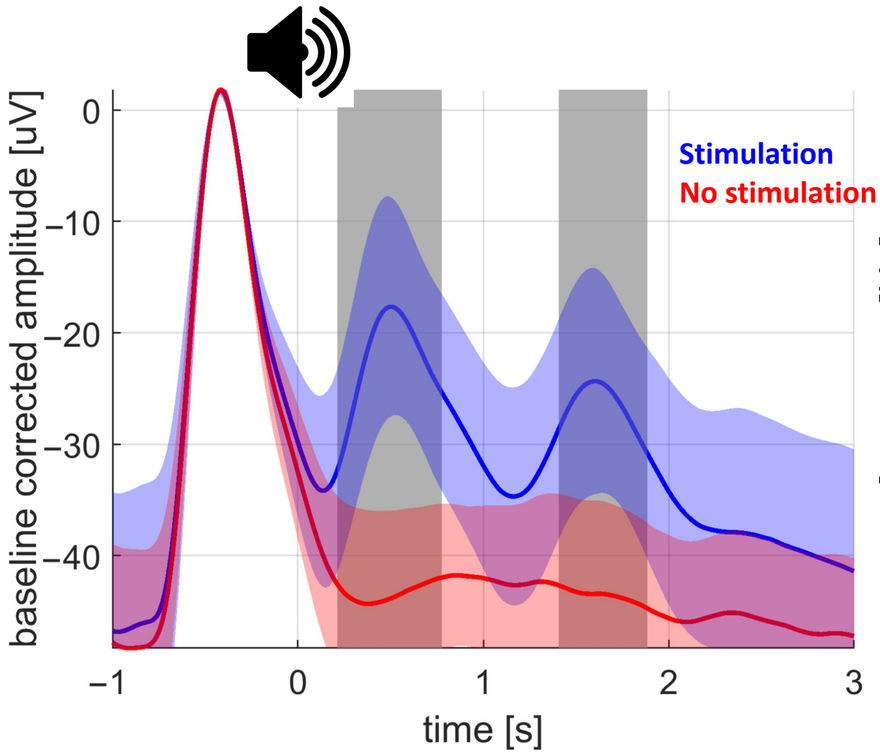
Sleep Research

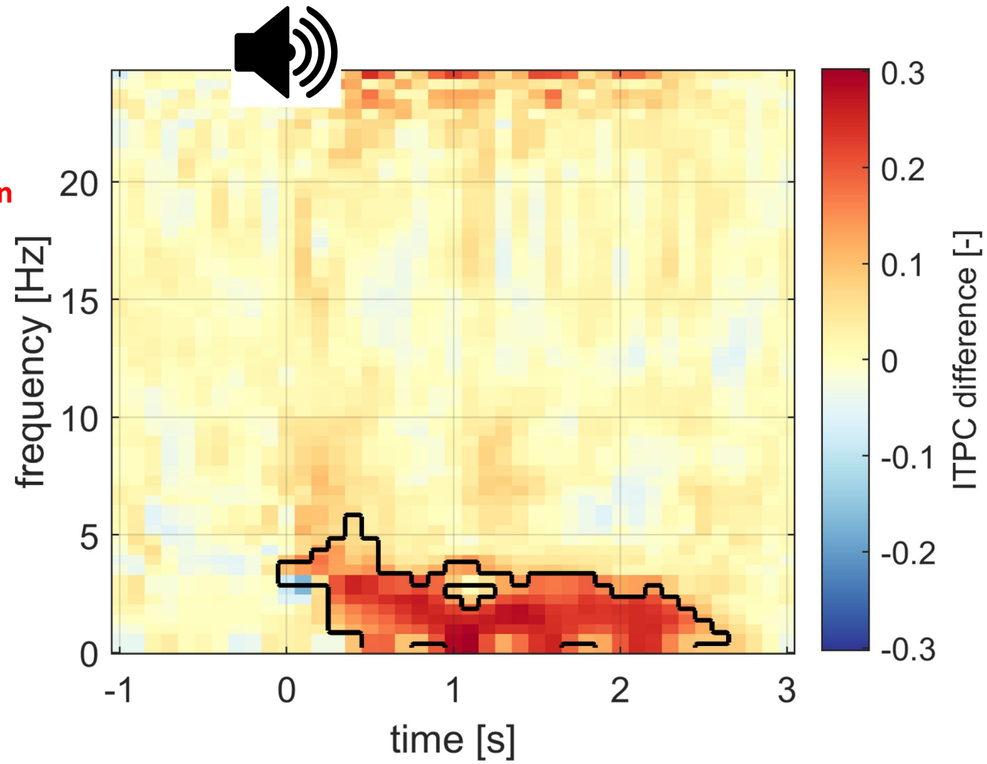
CLAS - closed loop acoustic stimulation of deep sleep

- Memory consolidation
- Sleep deepening
- Effect of the phase of stimulation
- Different length of sounds



Real-time EEG evaluation

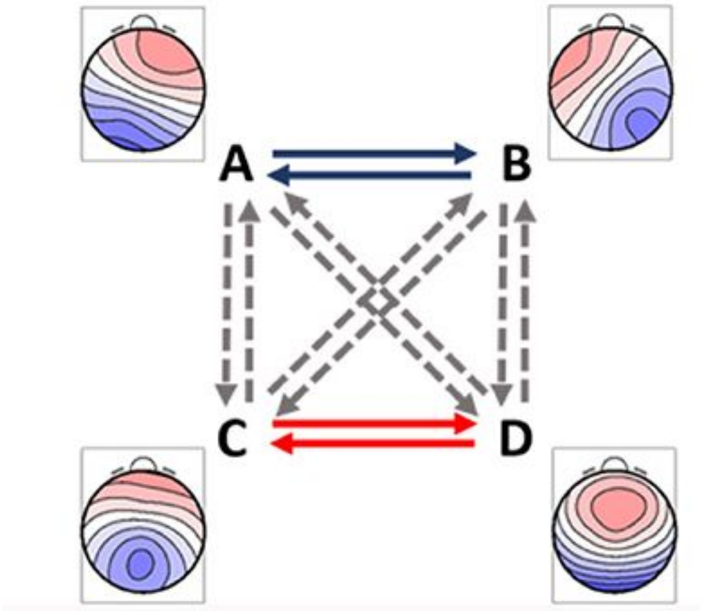


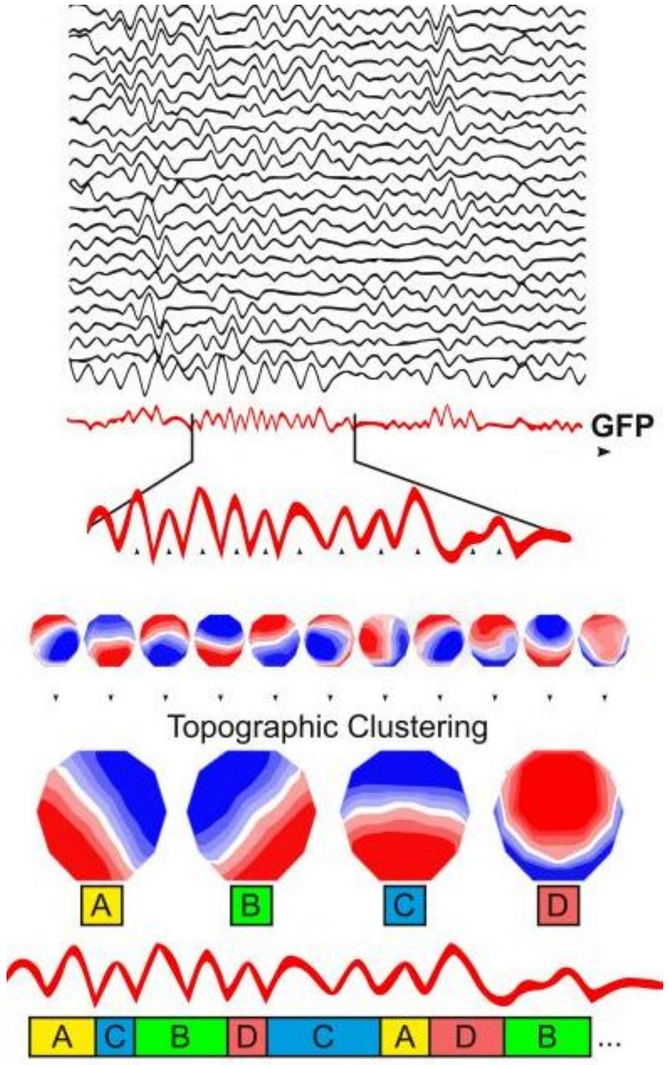


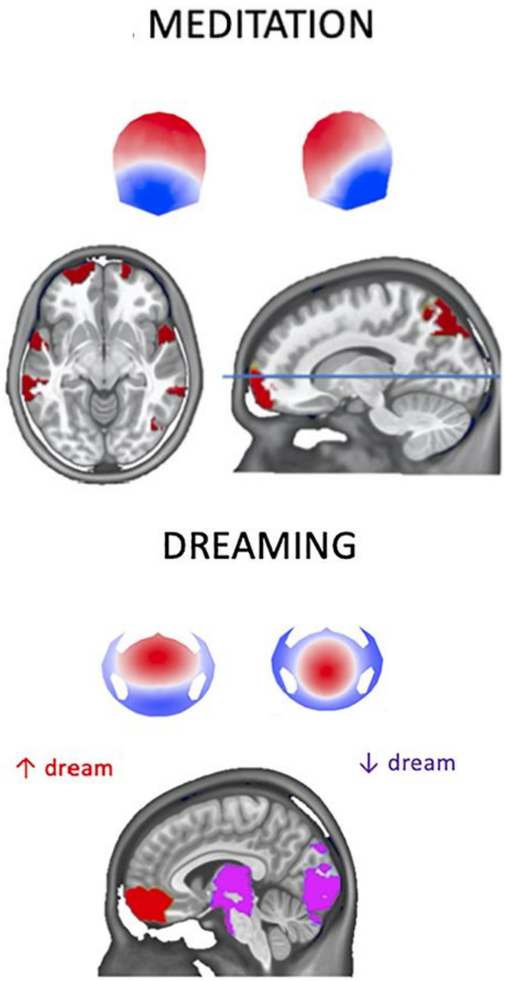
Sleep Research

EEG Microstates analysis

- Clustering of EEG into several topographies
- Descriptions/diagnostic?



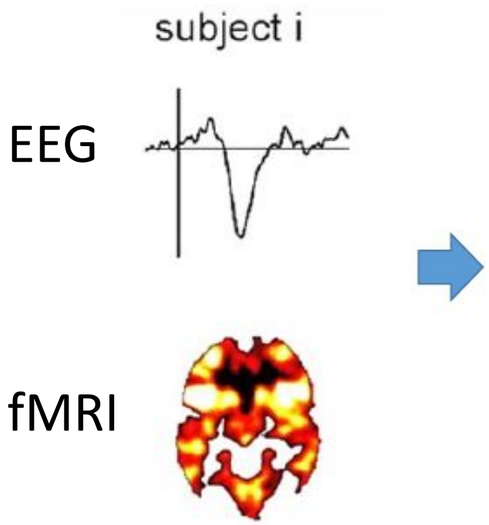


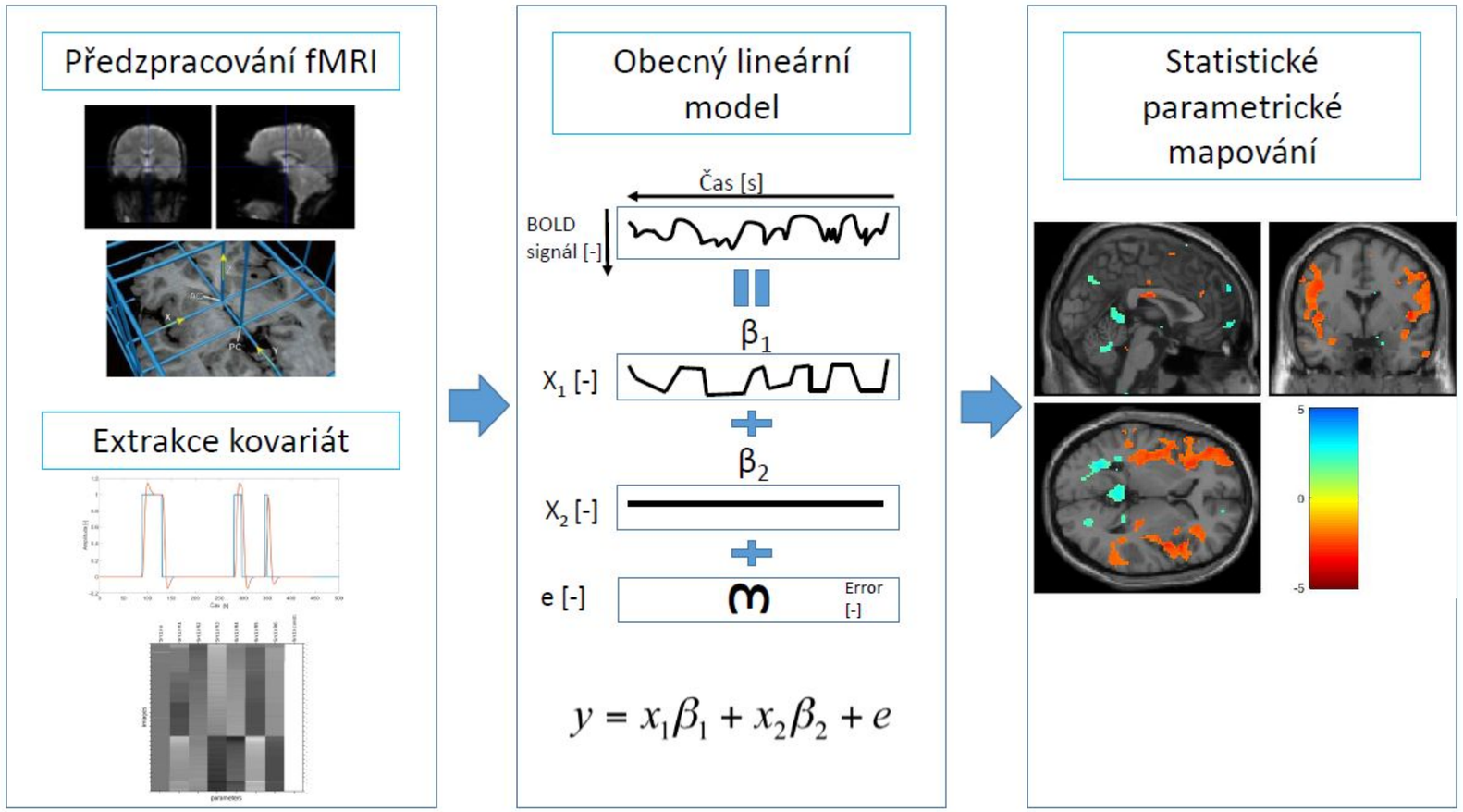


Sleep Research

Simultaneous EEG-fMRI

- High temporal and spatial resolution
- Asymmetric integration
- Artifact removal
- Parameter extraction





Brain Dynamics

Jaroslav Hlinka

COBRA ve tvářích

BMW a COBRA

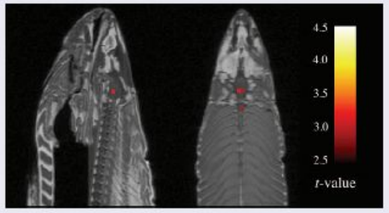
Jaroslav Hlinka, hlinka@cs.cas.cz

https://cobra.cs.cas.cz

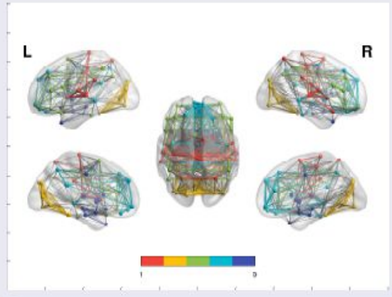
COBRA v obrazech

Šílené experimenty

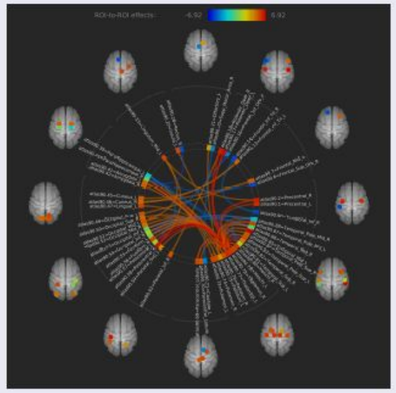
Záhady a mystéria



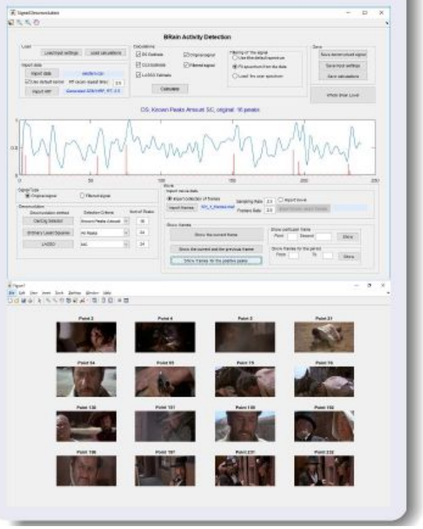
Internety mozku



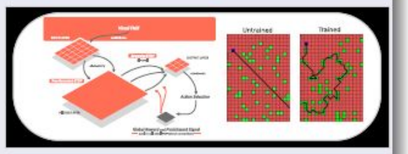
Porozumění nemocem



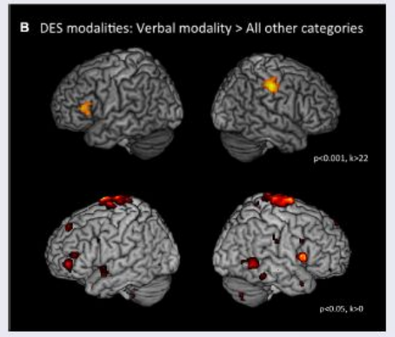
Čtení mysli



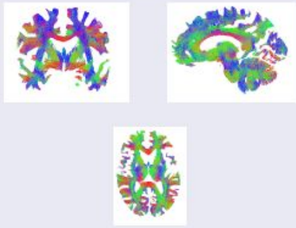
Mozek jako lego



Kreslení map



Hledání cest

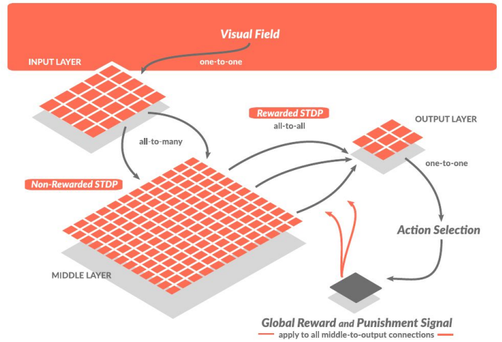


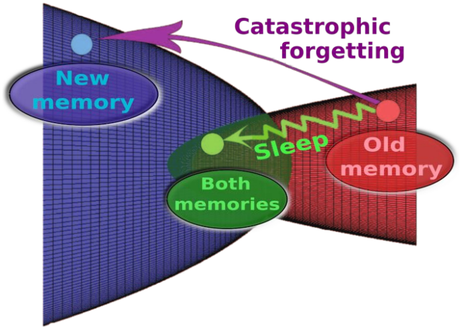
COBRA ve slovech

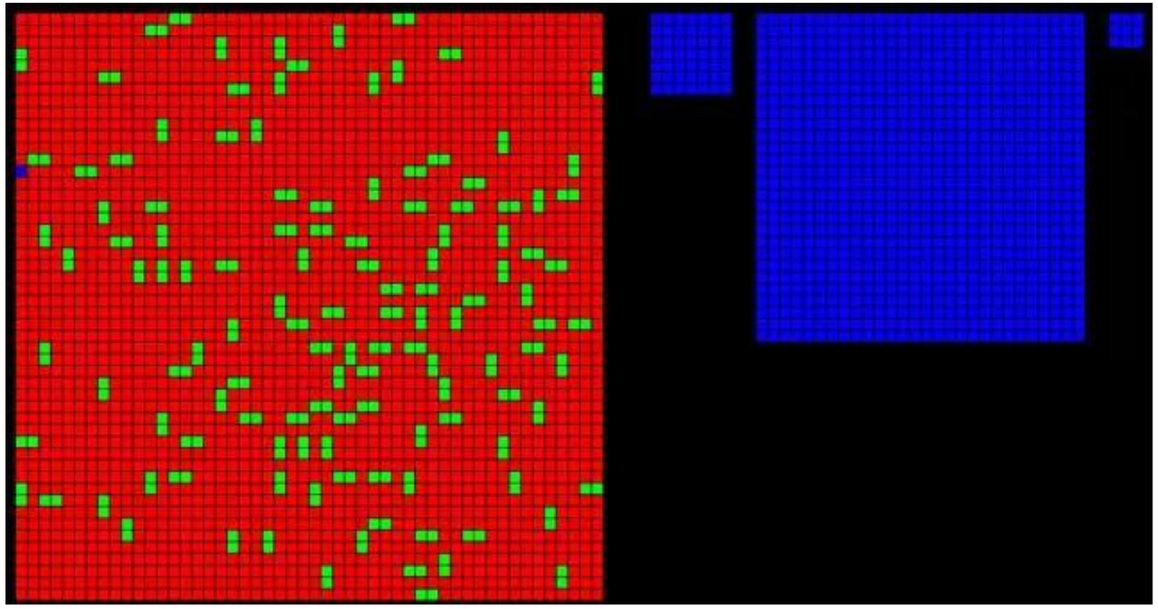
- Brain networks
  - Neuroimaging data analysis (Pidnebesna, Buckova, Jiricek, Jajcay, Dallmer-Zerbe, Kopal, Billings, Jajcay, Jajcay)
  - Brain dynamics modelling (Sanda, Schmidt, Jajcay)
- Causal interaction inference
  - Causality and information flow inference (Korenek, Pidnebesna, Jajcay)
  - Nonlinearity and nonstationarity (Korenek, Tani Raffaeli, Hartman)
- Complex network analysis - development/optimization/**application**
  - Graph theory (Hartman, Korenek, Billings, Jajcay, Cinardi)
  - Machine learning and multivariate statistics (Pidnebesna, Buckova, Jiricek, Jajcay)
  - Application in neuroscience, climate research, economics, . . . ALL

COBRA v simulacích

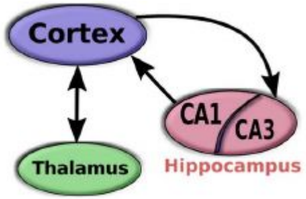
Decision making and memory consolidation

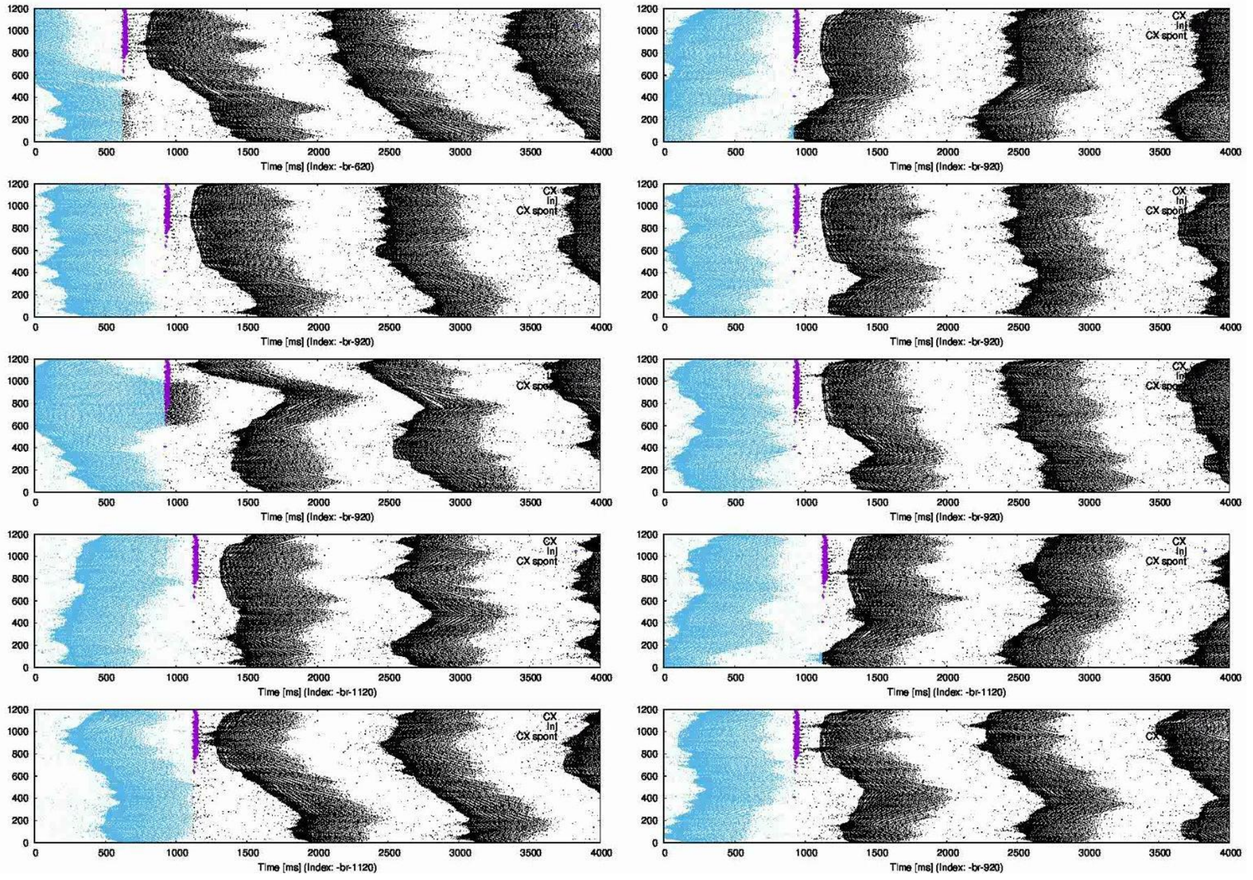






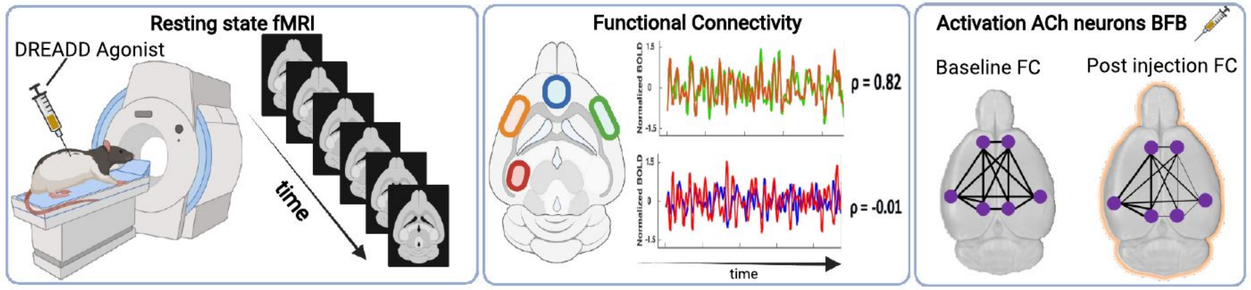
Sleep oscillations

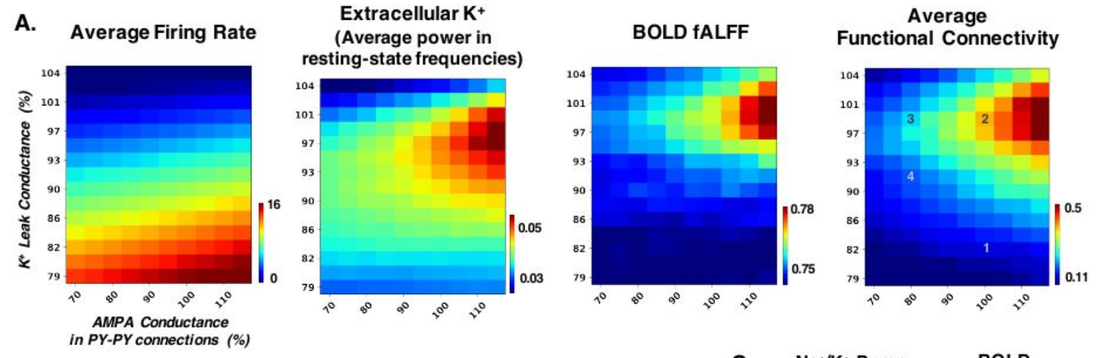


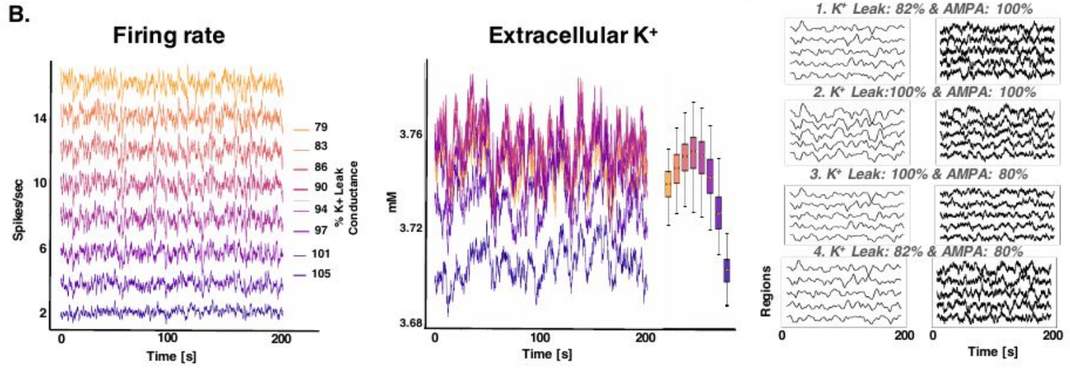


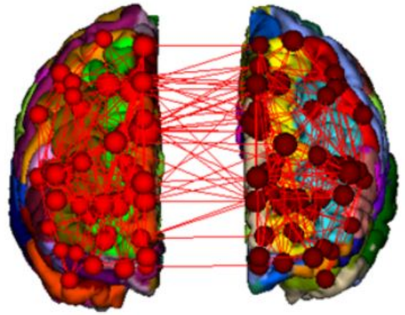
COBRA v MRI a simulacích

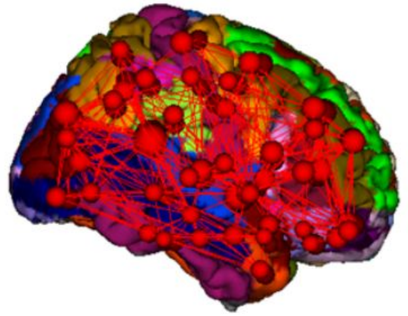
Neuromodulation of resting state activity

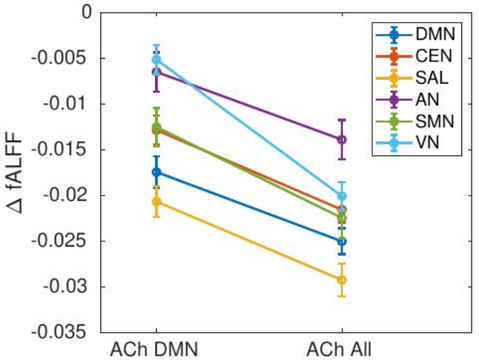


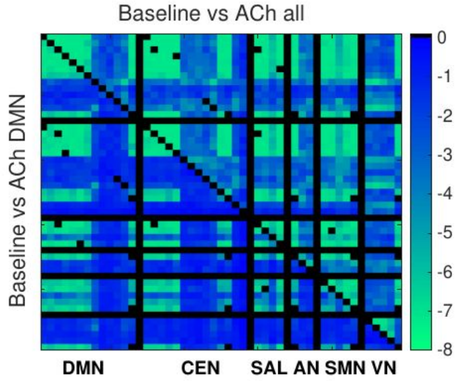












Laboratory Innovation

Jan Hubený

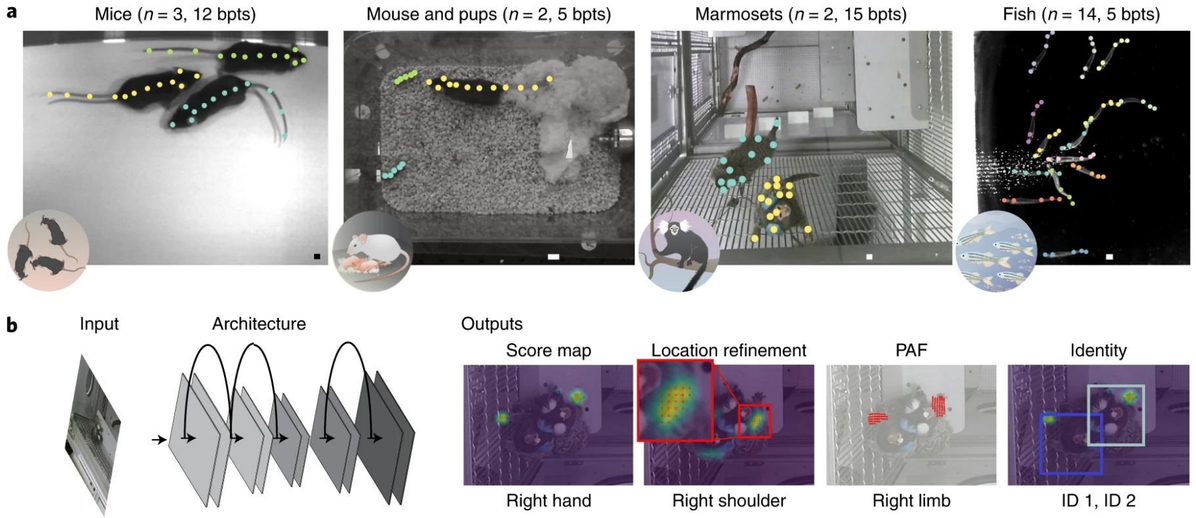
Téma 1

Hodnocení lokomoce potkana/ryby z videozáznamu pomocí open source toolboxu DeepLabCut™

Kvantifikace chování má zásadní význam pro mnoho aplikací v neurovědách, etologii, genetice, medicíně a biologii. Videografie poskytuje snadné metody pro pozorování a záznam chování zvířat v různých prostředích, avšak extrakce určitých aspektů chování pro další analýzu může být časově velmi náročná. DeepLabCut nabízí efektivní metodu pro 3D odhadování polohy bez markerů založenou na učení s hlubokými neuronovými sítěmi, která dosahuje vynikajících výsledků s minimem trénovacích dat (typicky 50-200 snímků). Balíček má otevřený zdrojový kód, je rychlý, robustní a lze jej použít k výpočtu odhadů 3D polohy. Cílem práce je optimalizovat a implementovat DeepLabCut toolbox pro videozáznamy sesbírané v průběhu animálních EEG studií.

1. A. Mathis et al., “DeepLabCut: markerless pose estimation of user-defined body parts with deep learning,” Nat. Neurosci., vol. 21, no. 9, pp. 1281–1289, 2018, doi: 10.1038/s41593-018-0209-y.

Téma 1

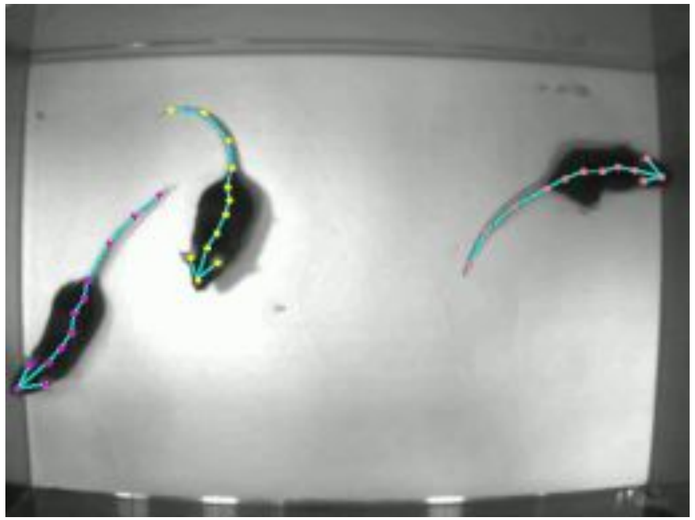


DeepLabCut: a software package for animal pose estimation

DLC GUI

use our Project Manager GUI, Jupyter Notebooks, Google Colab, or terminal!

Create a project, extract frames, + GUIs to label your data → Select + Train your deep neural network → Evaluate network performance (active learning + GUIs if improvement needed) → Run inference on new videos, create labeled videos, + plot your results!



Lauer, J., Zhou, M., Ye, S. *et al.* Multi-animal pose estimation, identification and tracking with DeepLabCut. *Nat Methods* 19, 496–504 (2022). https://doi.org/10.1038/s41592-022-01443-0

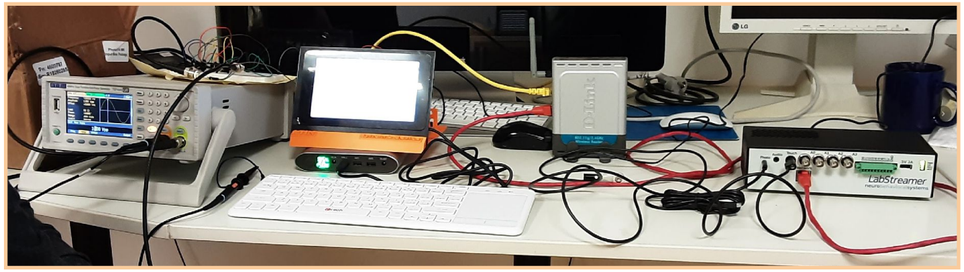
Téma 2

Embedded řešení pro synchronizaci biosignálů metodou lab streaming layer

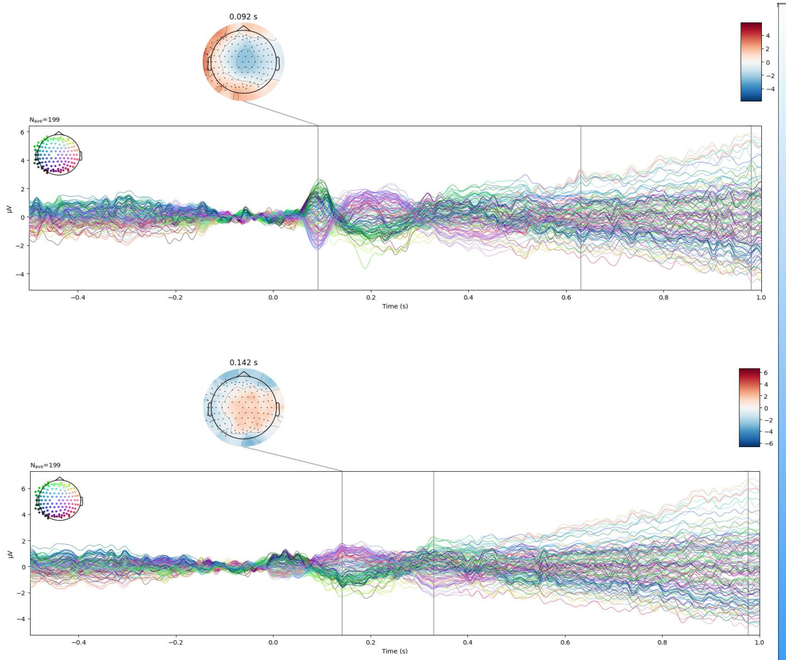
V současném výzkumu mozku sílí potřeba simultánního nahrávání neurofyziologických a dalších biosignálů signálů v jednom okamžiku. Typickým příkladem může být kombinace signálů EEG, EKG, EMG, EYETRACKER a fMRI. S přibývající složitostí experimentů vzrůstá chyba způsobená nepřesnou synchronizací všech signálů. Lab streaming layer (LSL) protokol je určen k přesné synchronizaci toku různých biosignálů a je založen na fyzické vrstvě ethernet. Cílem bakalářské práce je implementovat LSL protokol na jednočipovou vývojovou desku Teensy 4.1, otestovat synchronizaci za pomocí generátoru, osciloskopu a zařízení LabStreamer a validovat na jednoduchém EEG experimentu na dobrovolníkovi v Národním Ústavu Duševního Zdraví.

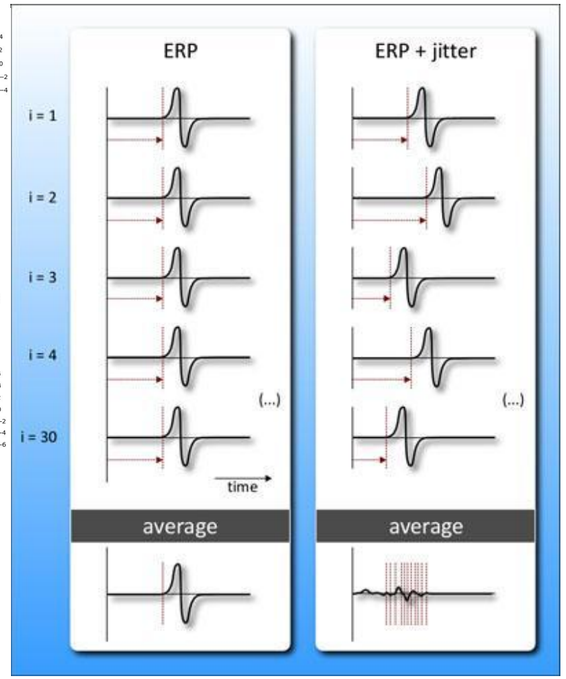
1. https://labstreaminglayer.readthedocs.io/info/intro.html
2. MOULI, Surej; PALANIAPPAN, Ramaswamy. DIY hybrid SSVEP-P300 LED stimuli for BCI platform using EMOTIV EEG headset. *HardwareX*, 2020, 8: e00113.

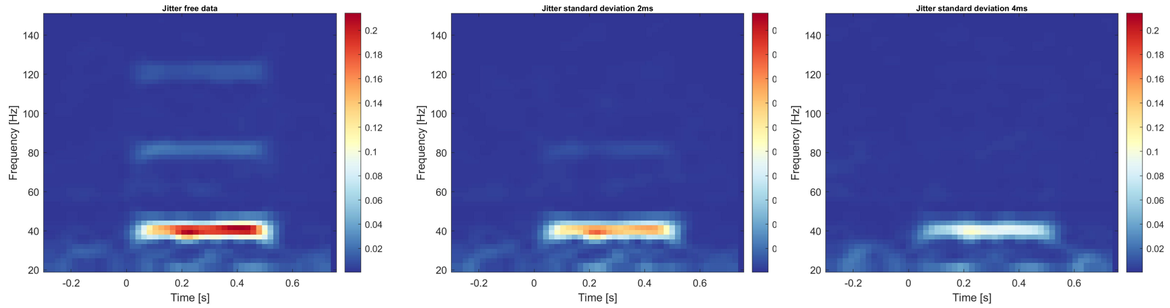
Téma 2


LabStreamer


Syncbox device


0.092 s
0.142 s
Time (s)


ERP
ERP + jitter
i = 1
i = 2
i = 3
i = 4
i = 30
(...)
time
average
average


Jitter free data
Jitter standard deviation 2ms
Jitter standard deviation 4ms
Frequency [Hz]
Time [s]

Téma 3

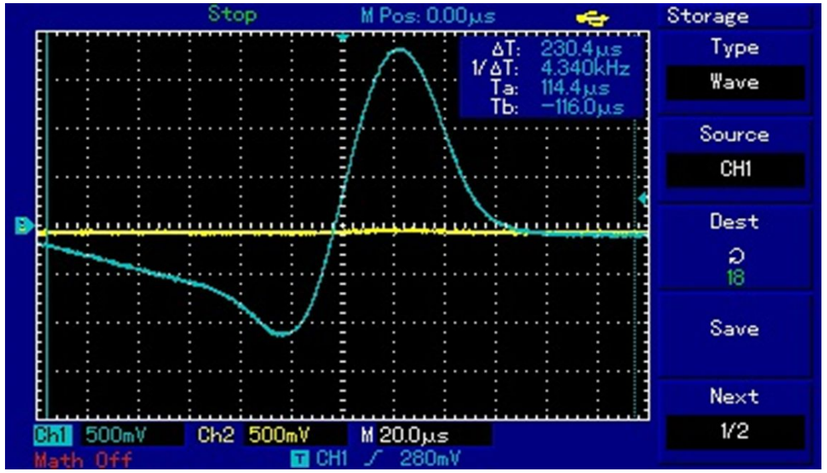
Metody pro zvýšení kvality snímaného signálu EOD u Gnathonemus petersii a optimalizace procesu akvizice dat

Gnathonemus petersii se vyznačuje unikátní schopností geneze elektrického signálu EOD (electric organ discharge) za účelem geolokace ale také i komunikace se svým druhem. Gnathonemus petersii má potenciál přinést inovační vhled do návrhu a aplikace animálních modelů v kontextu výzkumu duševního zdraví. Cílem práce je stanovit metodiku nahrávání EOD u Gnathonemus petersii a navrhnout a implementovat vlastní řešení. Součástí práce je také validace a ověření výsledků se stávající měřící aparaturou.

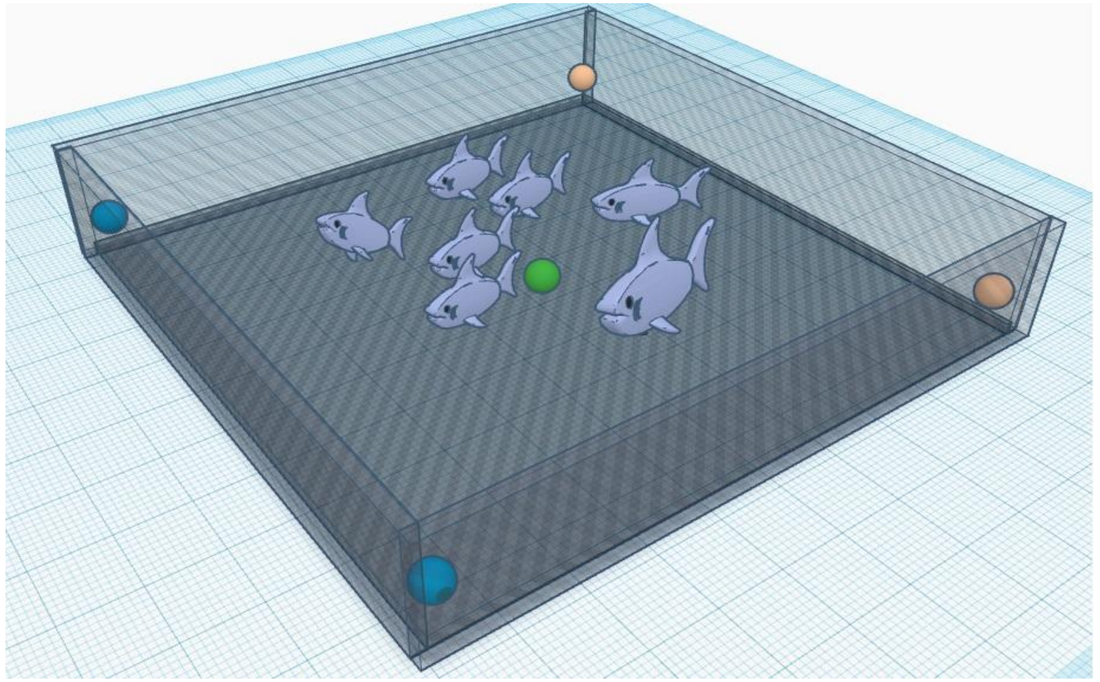
1. Langova, V., Horka, P., Hubeny, J., Novak, T., Vales, K., Adamek, P., Holubova, K., & Horacek, J. (2023). Ketamine disrupts locomotion and electrolocation in a novel model of schizophrenia, *Gnathonemus petersii* fish. *Journal of Neuroscience Research*, 101, 1098–1106. https://doi.org/10.1002/jnr.25186
2. Andrea Scapin. Electrocommunication for weakly electric fish. *Inverse Problems and Imaging*, 2020, 14(1): 97-115. doi: 10.3934/ipi.2019065

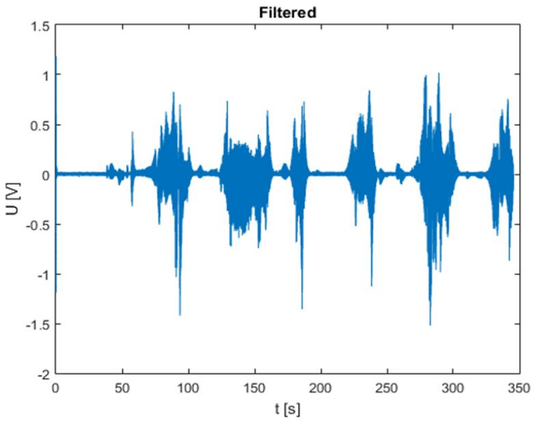
Existující řešení

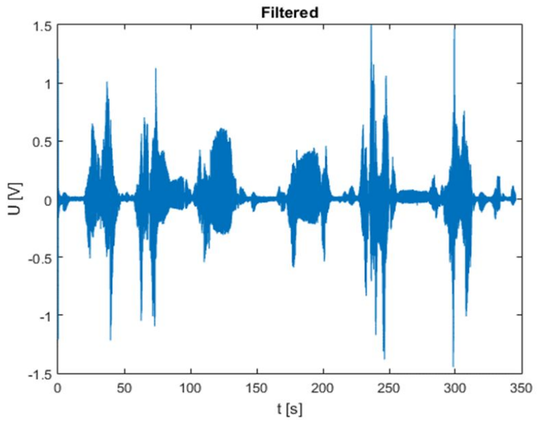
- 4 měřící elektrody -> 2 kanály
- 16 bit (kv. krok 0.3 mV), 50Khz, bipolární zapojení
- Synchronizace s videem
- NI USB 6003



Téma 3

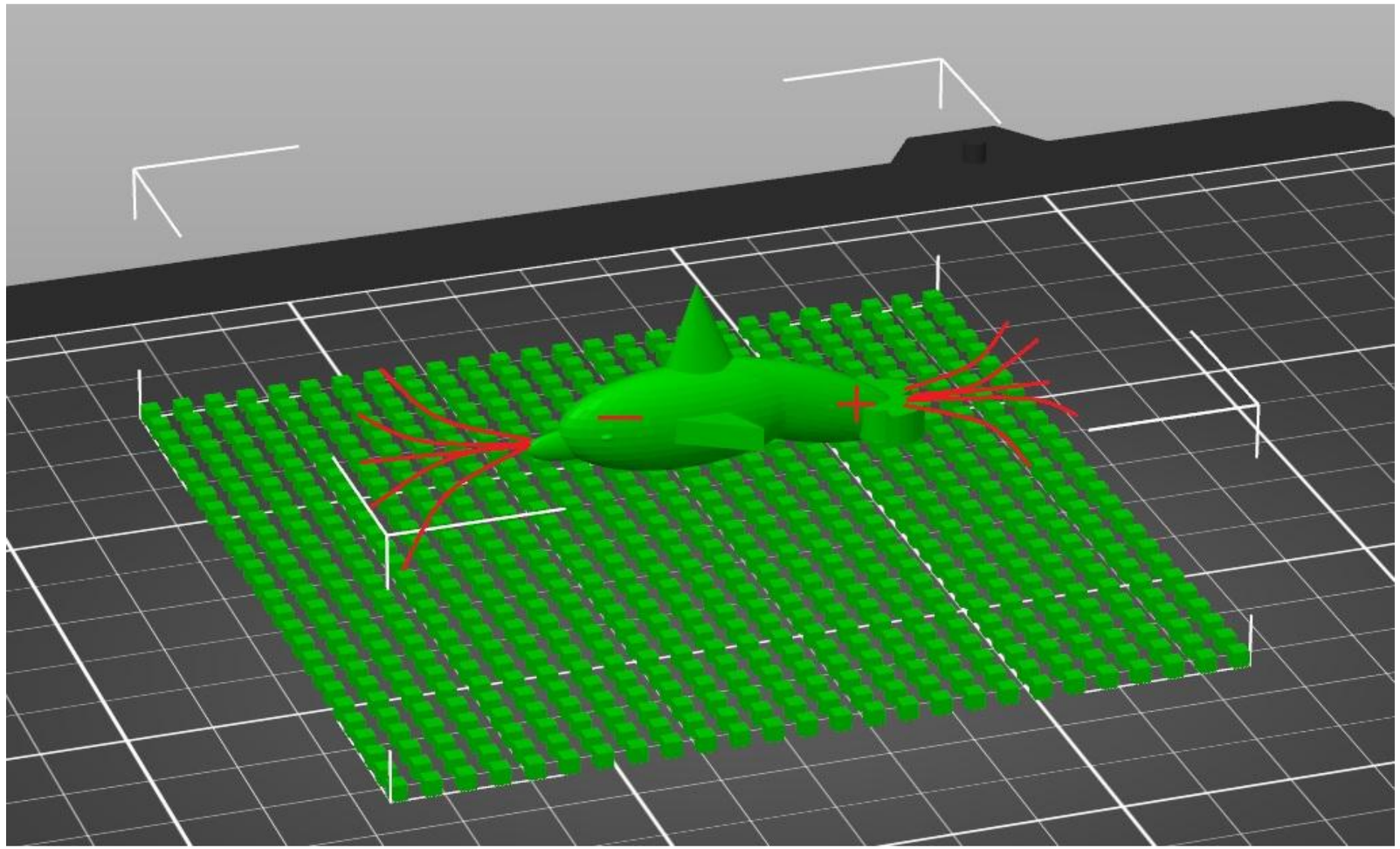






Koncept elektrodového pole

Téma 3



Psychedelics

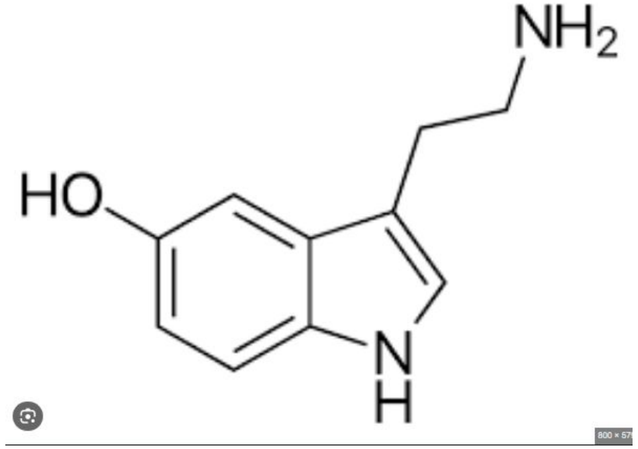
Marek Nikolič

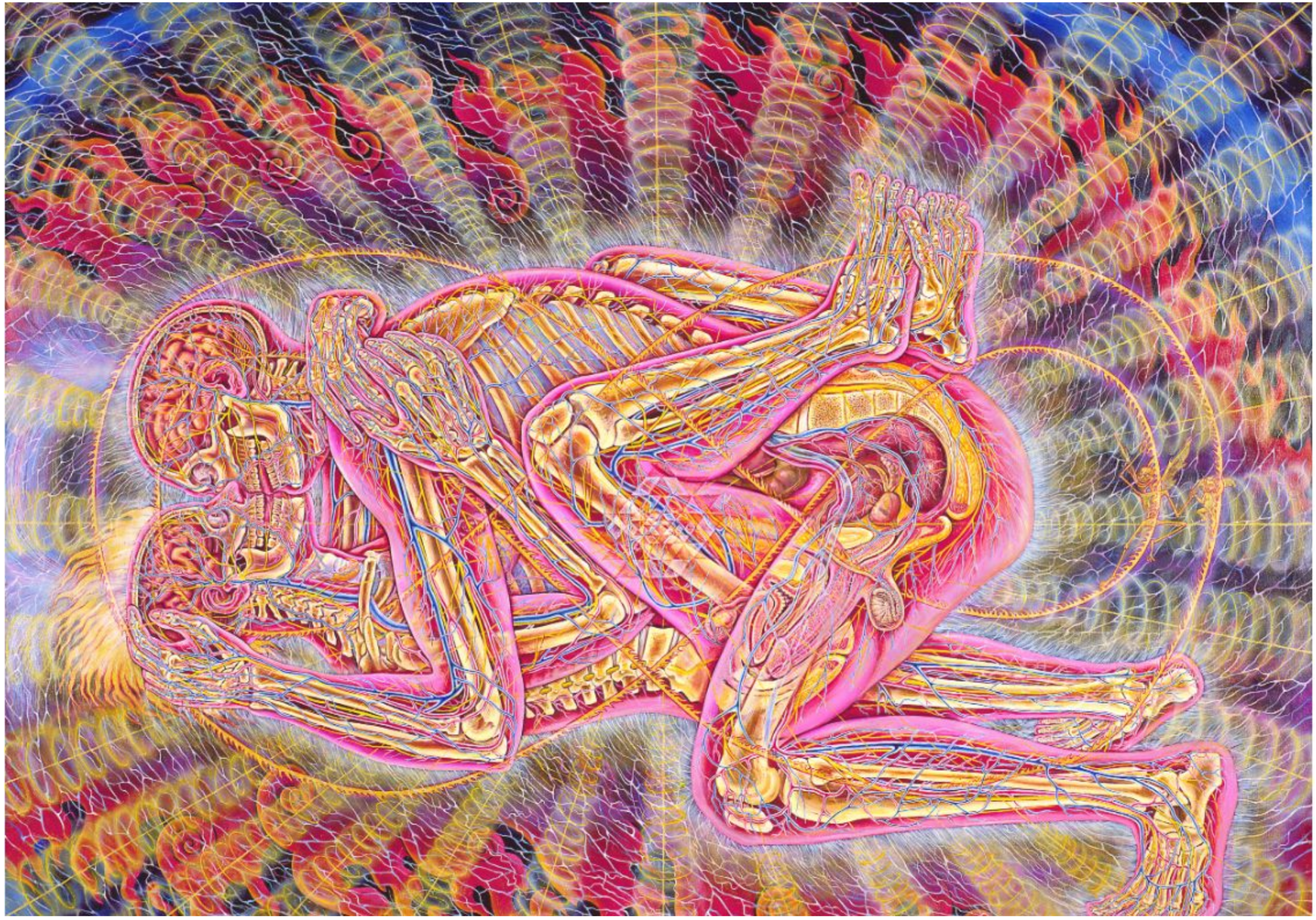
Téma 1

Multivariátní analýza prediktorů antidepresivní odpovědi na Psychedelika


CALYPSOL®
10 ml i.m., i.v.
Ketaminum 500 mg
29078620


DEA


NH2
HO
NH



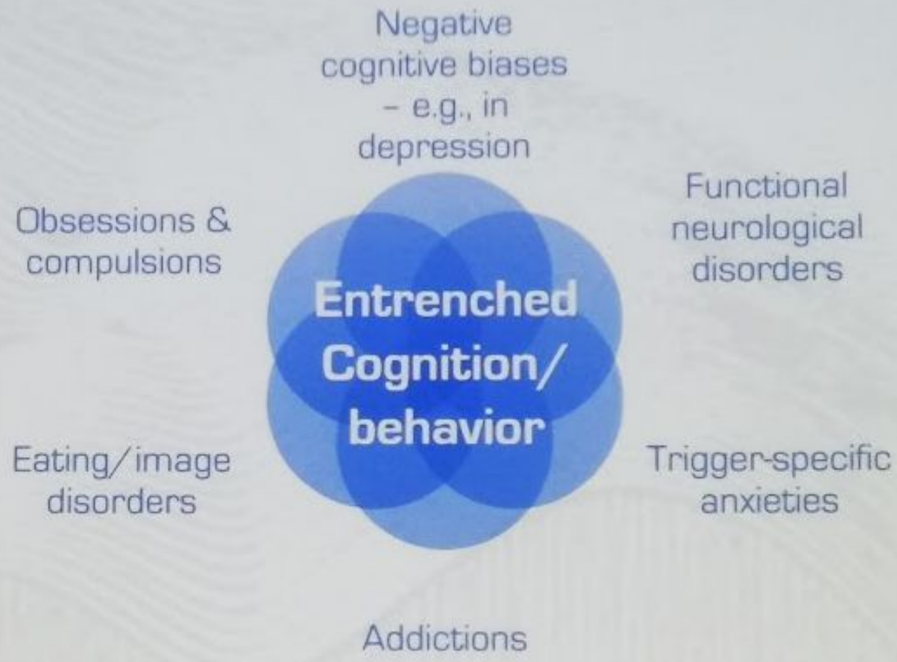
Alex Grey, Copulation

Deviantart

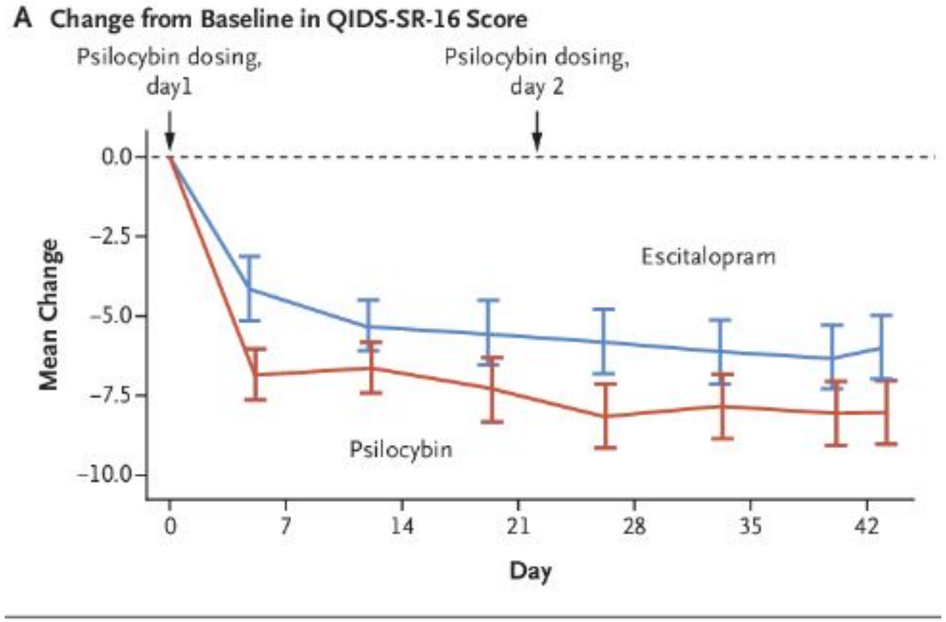

KOMU TÍM PROSPĚJETE, CO?!

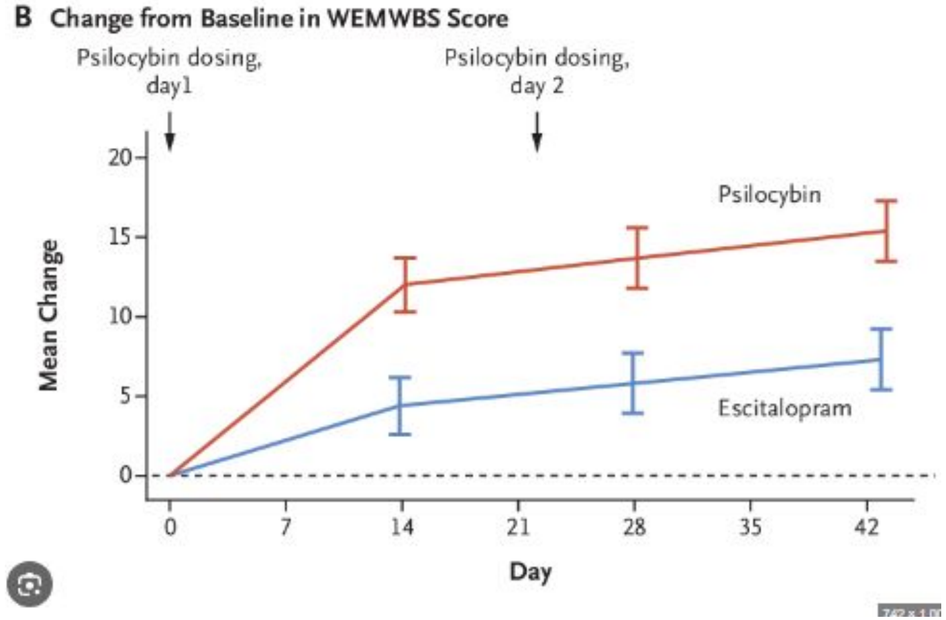
'Canalization'

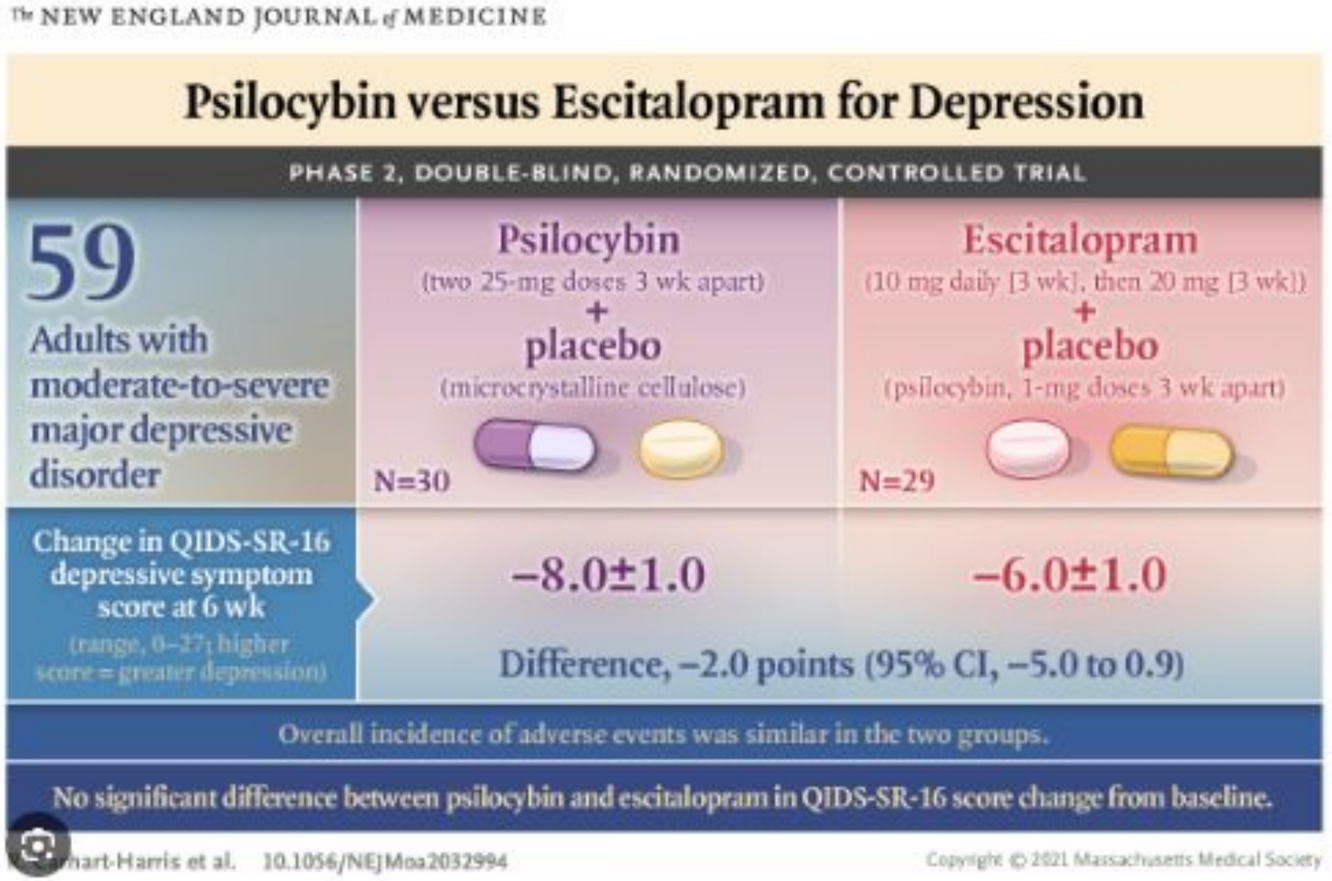
#1 component of psychopathology?



*CH et al. 23 – 'Canalization & plasticity in psychopathology'. Frontiers in Pharmacology.







Carhart-Harris, R.L., Giribaldi, B., Watts, R., Baker-Jones, M., Murphy-Beiner, A., Murphy, R., Martell, J., Blemings, A., Erritzoe, D., & Nutt, D.J. (2021). Trial of Psilocybin versus Escitalopram for Depression. *The New England journal of medicine, 384 15*, 1402-1411 .


God: *makes psychedelic plants*
Humans: *make psychedelic plants illegal*
God:
1,024 × 767

Image from a study of healthy subs treated with psilocybin

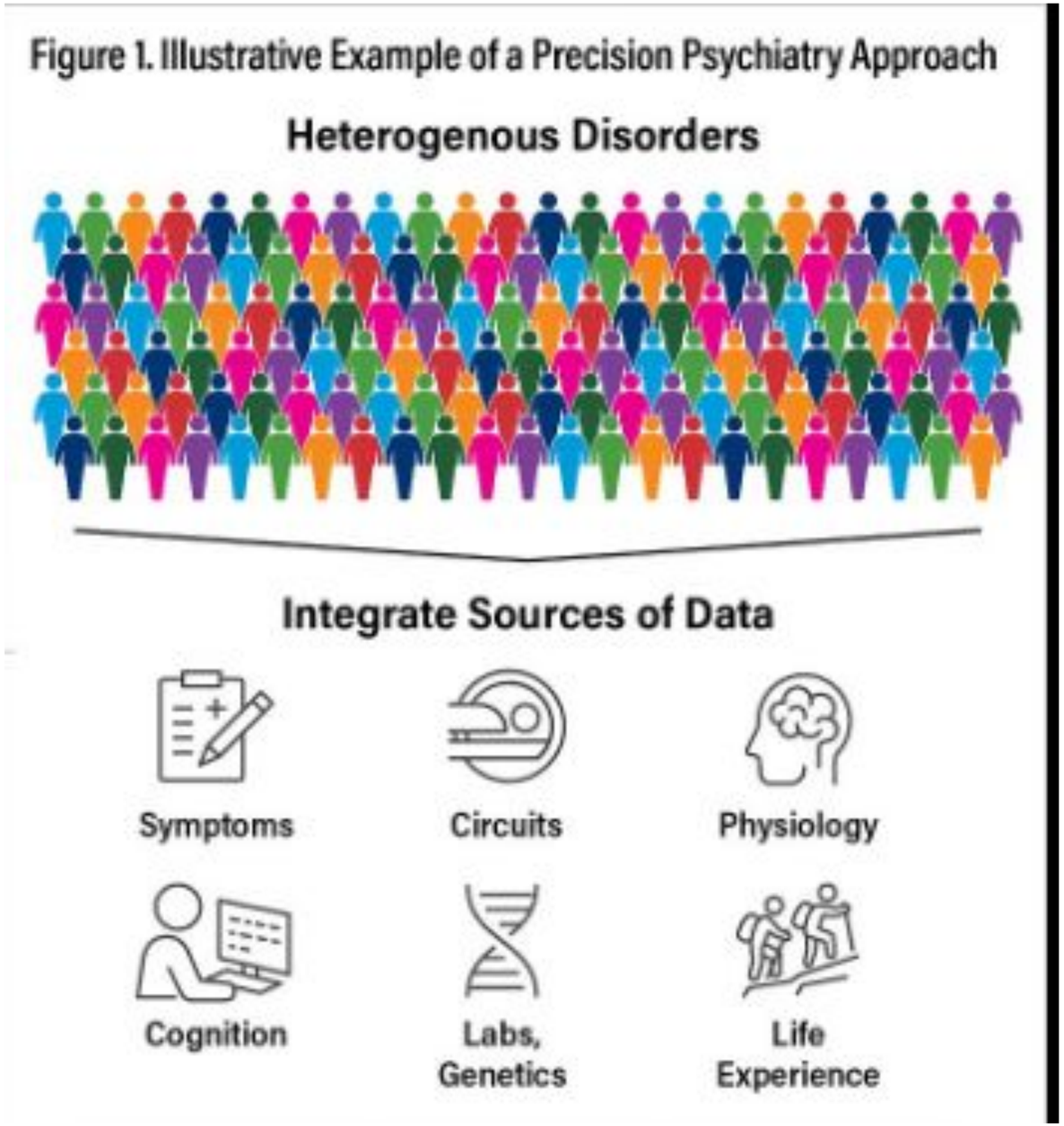


Figure 1. Illustrative Example of a Precision Psychiatry Approach
Heterogenous Disorders
Integrate Sources of Data
Symptoms
Circuits
Physiology
Cognition
Labs, Genetics
Life Experience

Výhody:

malé N

Noisy data

Spousty dostupných neotestovaných metod a modelů

Black-box modely s limitovanou interpretabilitou

NÁRODNÍ ÚSTAV
DUŠEVNÍHO ZDRAVÍ

Děkuji za pozornost

email@nudz.cz