Using connectome harmonic decomposition to characterize brain activity during states of unconsciousness and altered consciousness

Andrea Luppi et al., 2023

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18.04.24
Neuro-club

UCSF University of California San Francisco
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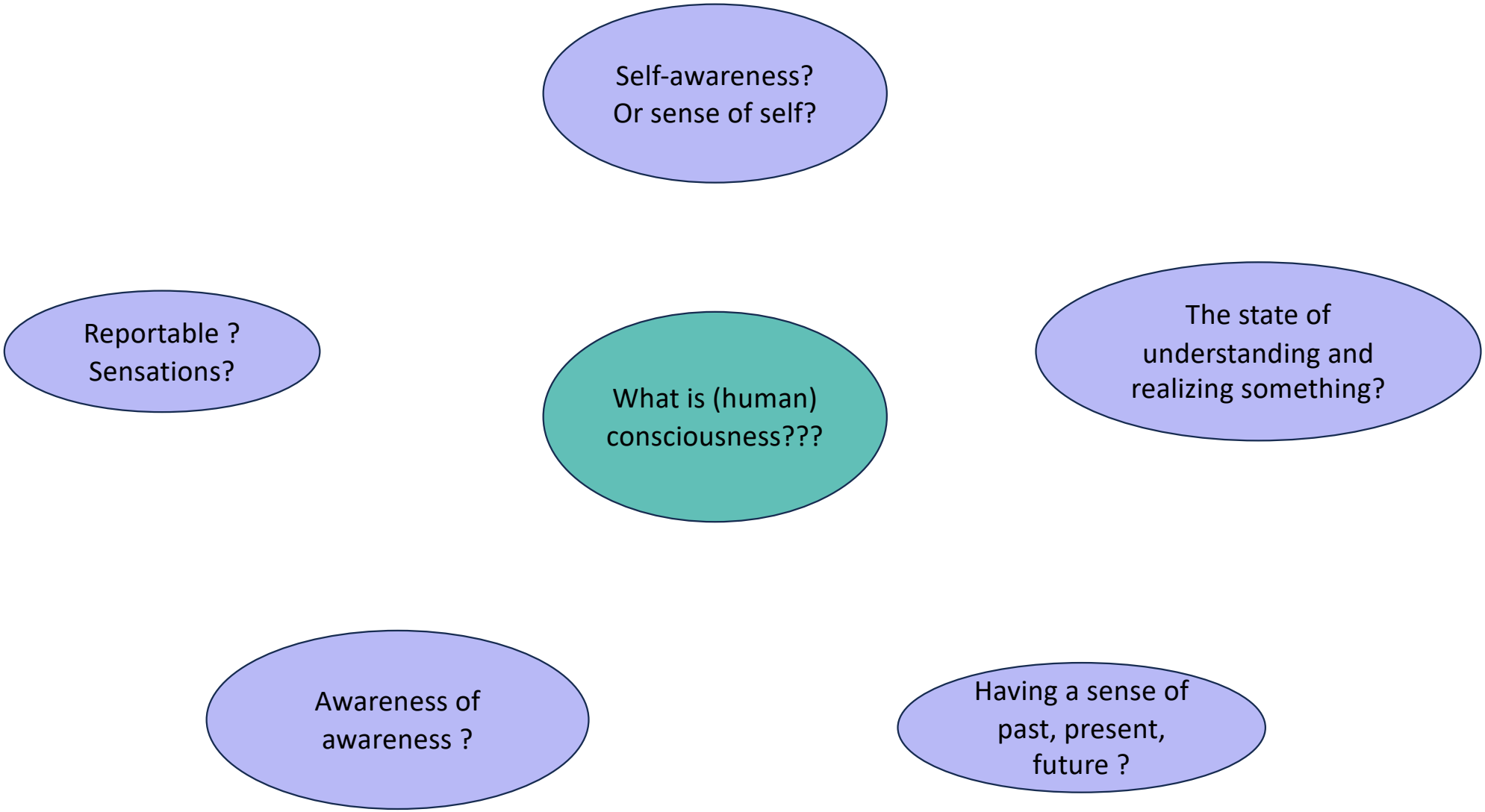
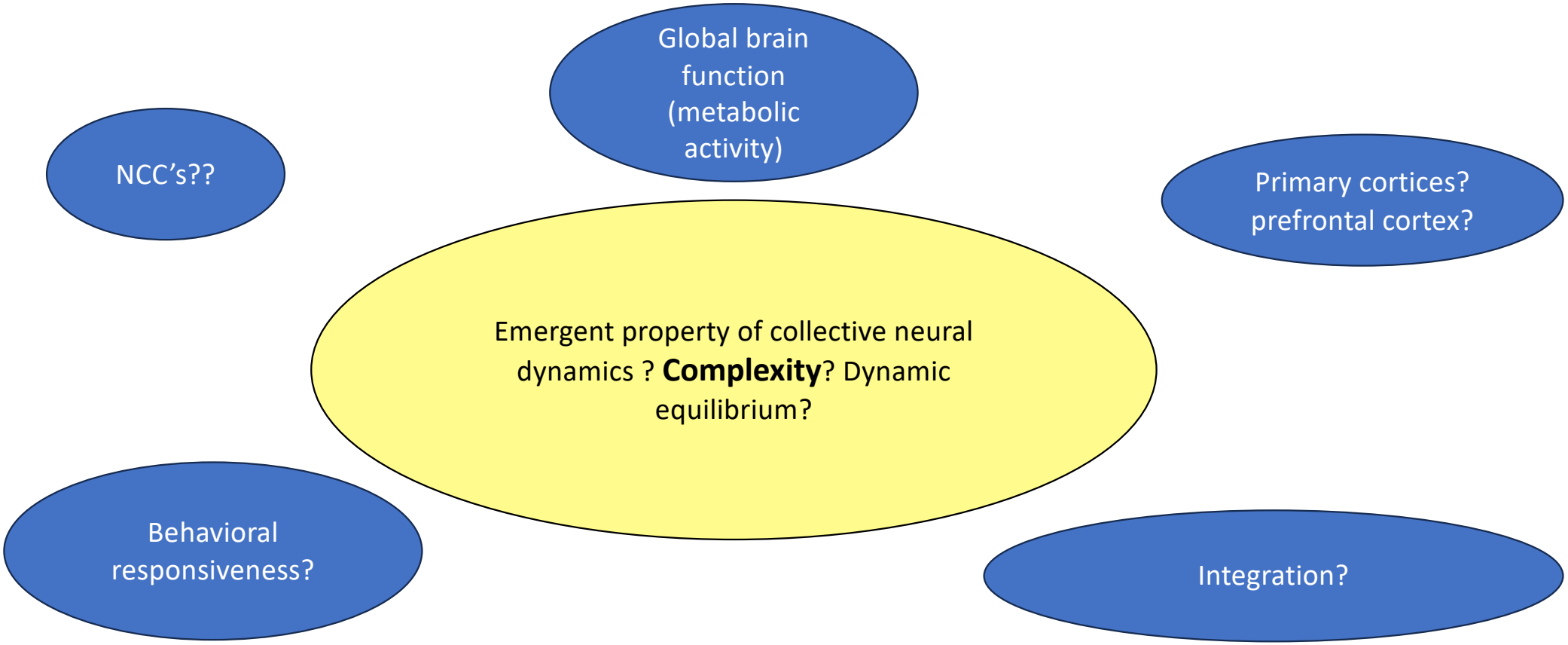
AARHUS UNIVERSITY
Imperial College London
USC University of Southern California
UNIVERSITY OF CAMBRIDGE


Self-awareness?
Or sense of self?
Reportable ?
Sensations?
What is (human)
consciousness???
The state of
understanding and
realizing something?
Awareness of
awareness ?
Having a sense of
past, present,
future ?

An organism has conscious mental states if and only if there is something that it is like to be that organism—something it is like for the organism – Thomas Nagel

Is consciousness localized in a part of the brain? How can we recognize it?



Clinical relevance of studying consciousness ?

Disorders of consciousness

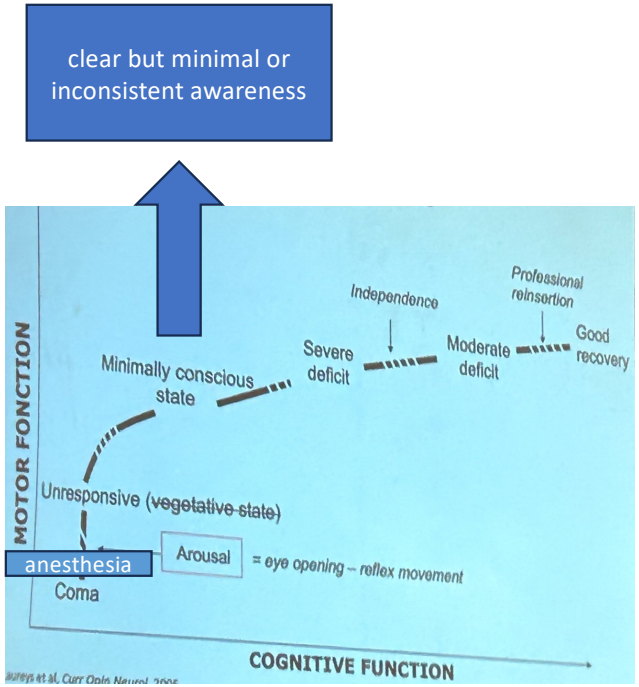
- 38% of people in MCS misdiagnosed as unresponsive (Wang et al., 2020)

Psychiatry

- 1/8 people are living with a mental health disorder (WHO, 2022)
- Treatments no better than 50 years ago (Paul et al., 2024) → not getting to the cause

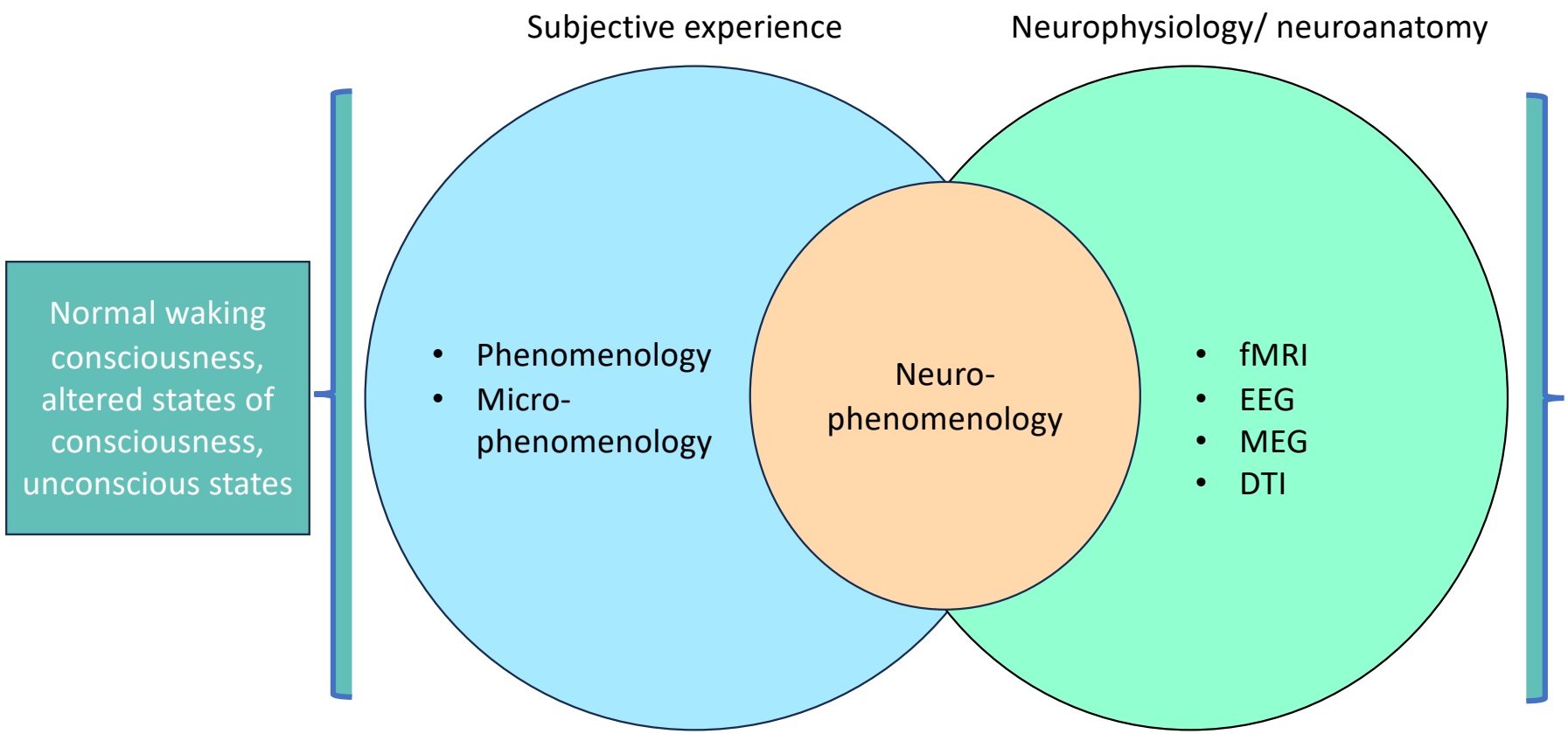
BUT also because:

- **Absolutely fascinating**- it is what enables us to love, feel joy and sadness, make meaning, have intentionality
- **AI?**



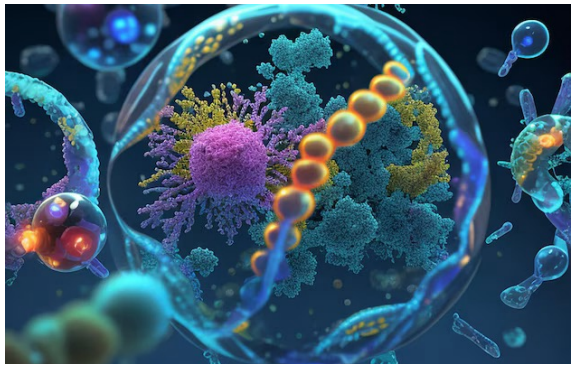
Laureys et al., 2005

Methods for studying consciousness



What is this study contributing to the field ?

- **But how can the brain architecture support, or enable consciousness to emerge?**
  - Structure, function, and subjective experience
- **Previous studies:** Multi-scale analysis? Asymmetry?
- **Anesthesia:** unknown process + errors
- **DOC:** unreliable diagnosis + prognosis
  - Effects of lesions?
- **Psychedelics:** altered states of consciousness + treatment for mental health conditions



How much is the structural organization of the connectome contributing to a given brain state across spatial granularities ?

Do altered states of consciousness and unconscious states have specific and detectable patterns brain activity associated with their state? And how do they compare?

Effect of global neuronal inhibition vs excitation (anesthesia vs ketamine)

Definitions

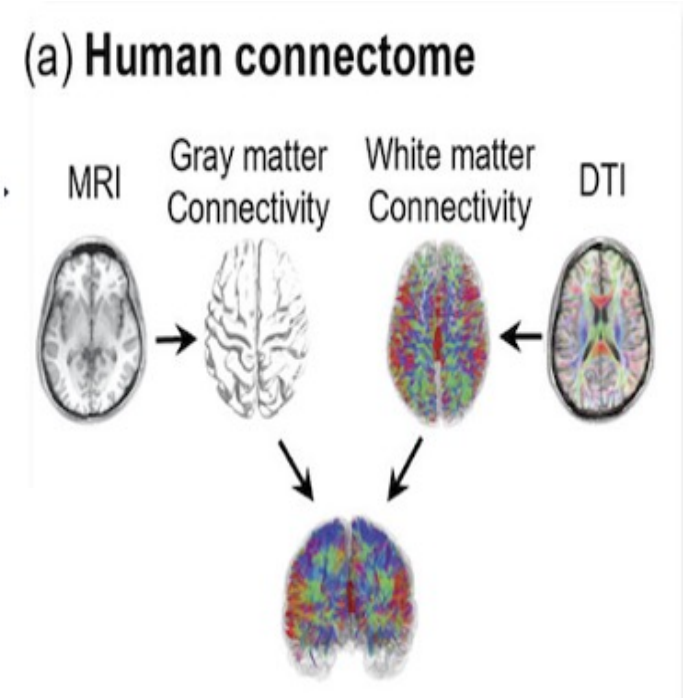
Connectome: a comprehensive map of neural connections (Advaith Veturi, UCL)

Structural connectome: the brain's physical connections

- DTI : architecture of white matter tracts
- MRI: cortical surface

Functional connectome: The collective set of functional connections in the brain

- fMRI



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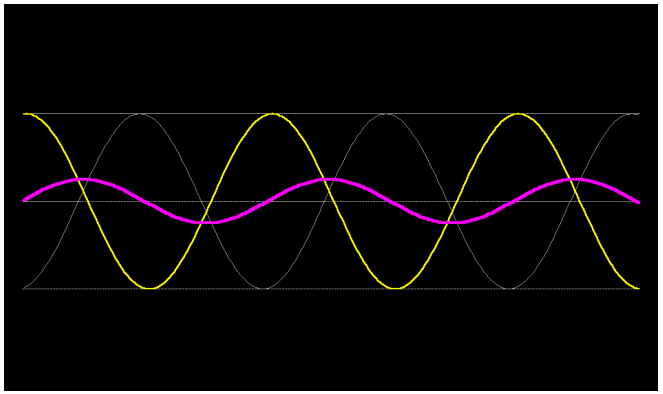
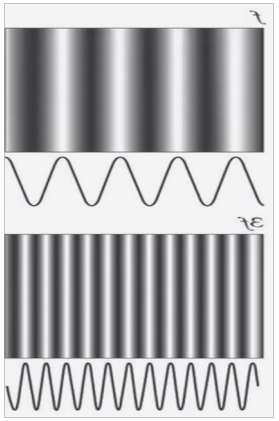


Standing waves: what allows us to hear music !

Harmonics: all set of possible standing wave patterns

Connectome Harmonics: The patterns of brain activity arising from the brain geometry at specific spatial frequencies

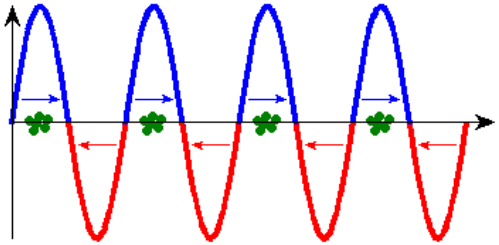
- Spatial patterns of synchronous/ harmonious oscillations

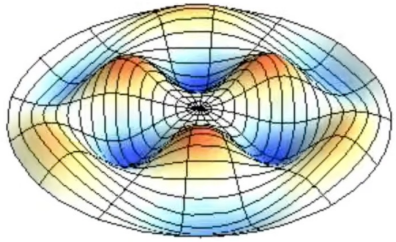


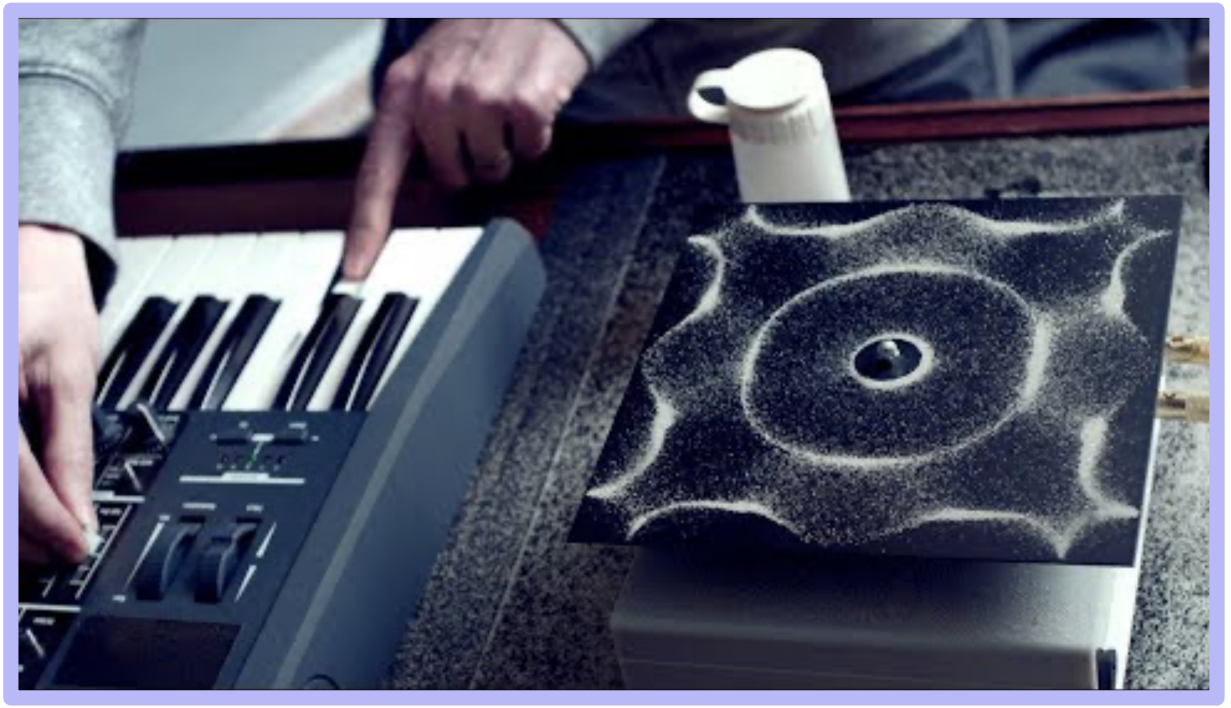
Spatial frequencies: coarse-grained to fine-grained

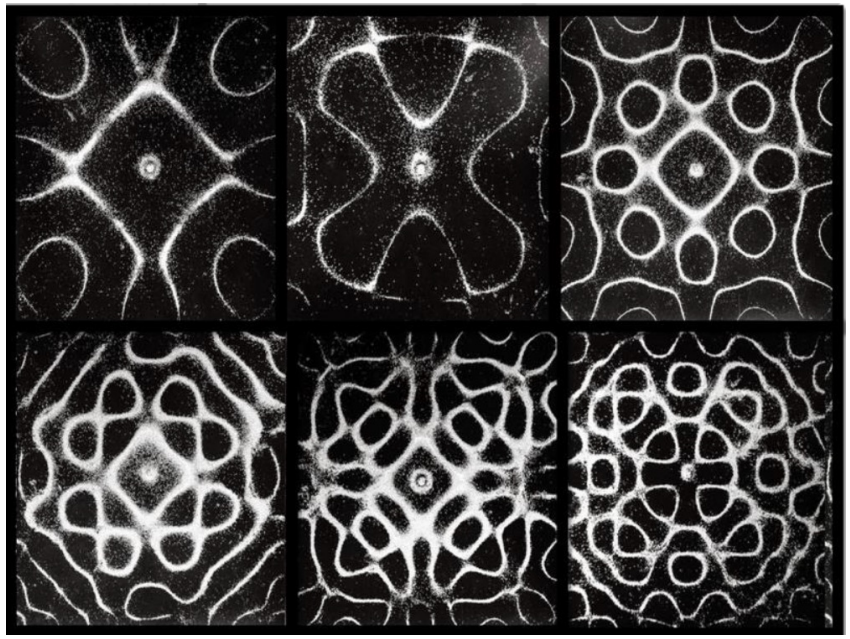
Helmholtz equation: describes electromagnetic wave propagation, music, morphogenesis, electron orbitals… etc

Emerging patterns from musical notes- what kind of music is your brain playing in different states?

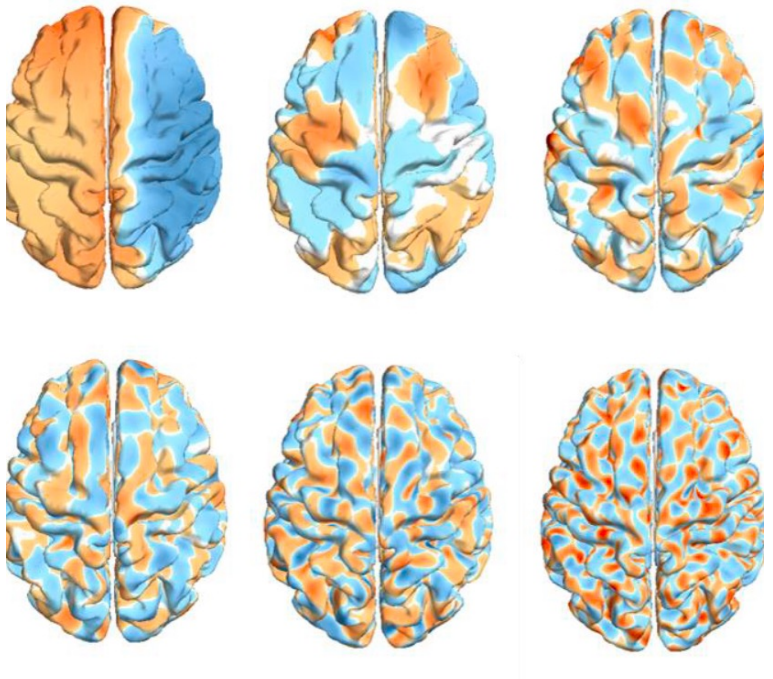






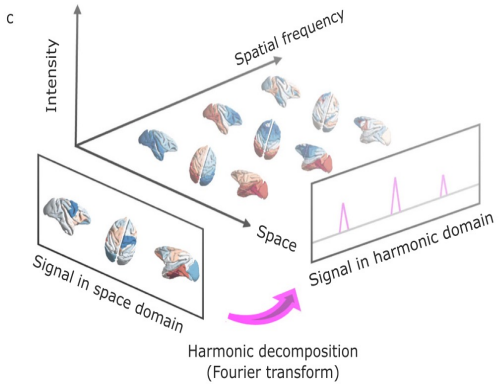


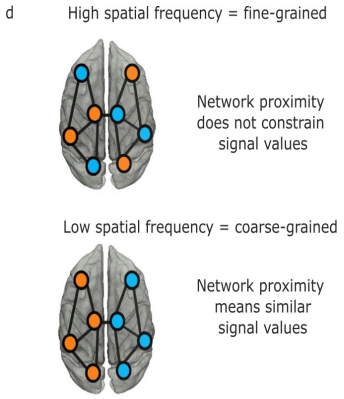
Coarse-grained



Fine-grained

What does high or low frequency really mean?





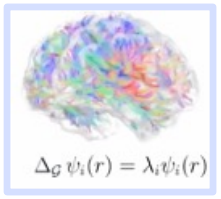
Neurons that wire together DO NOT necessarily fire together !!

Straying from expectations?

Translating the Laplace Operator + **Helmholtz equation** to the brain

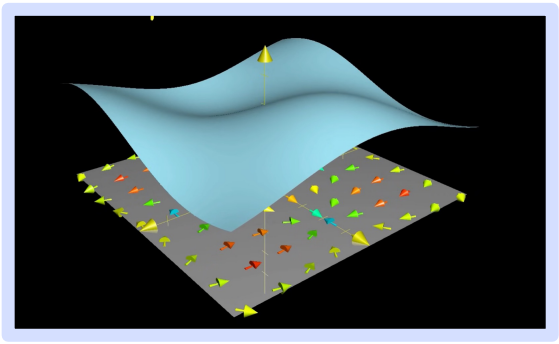
Harmonic patterns

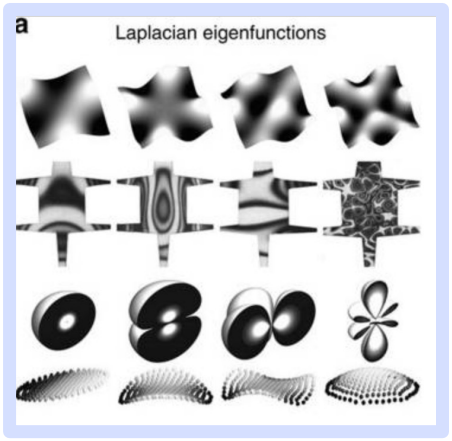
Natural frequencies



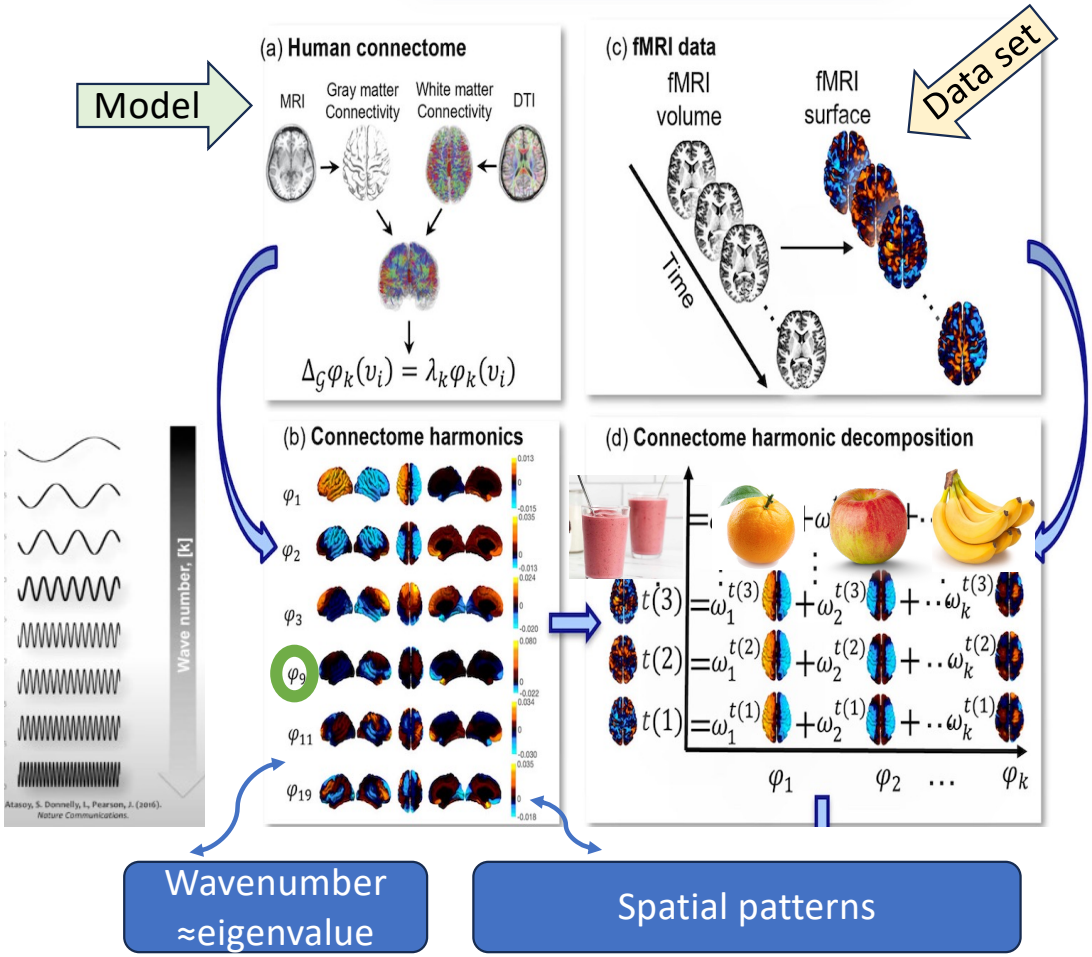
$$\Delta_{\mathcal{G}}\,\psi_i(r) = \lambda_i \psi_i(r)$$

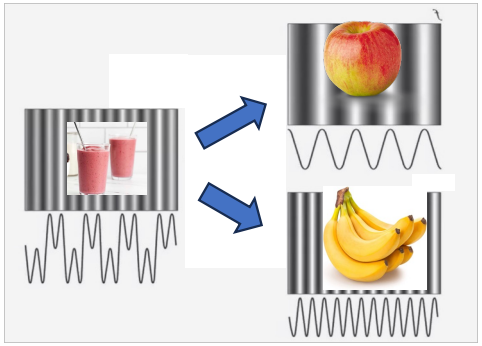
Helmholtz equation





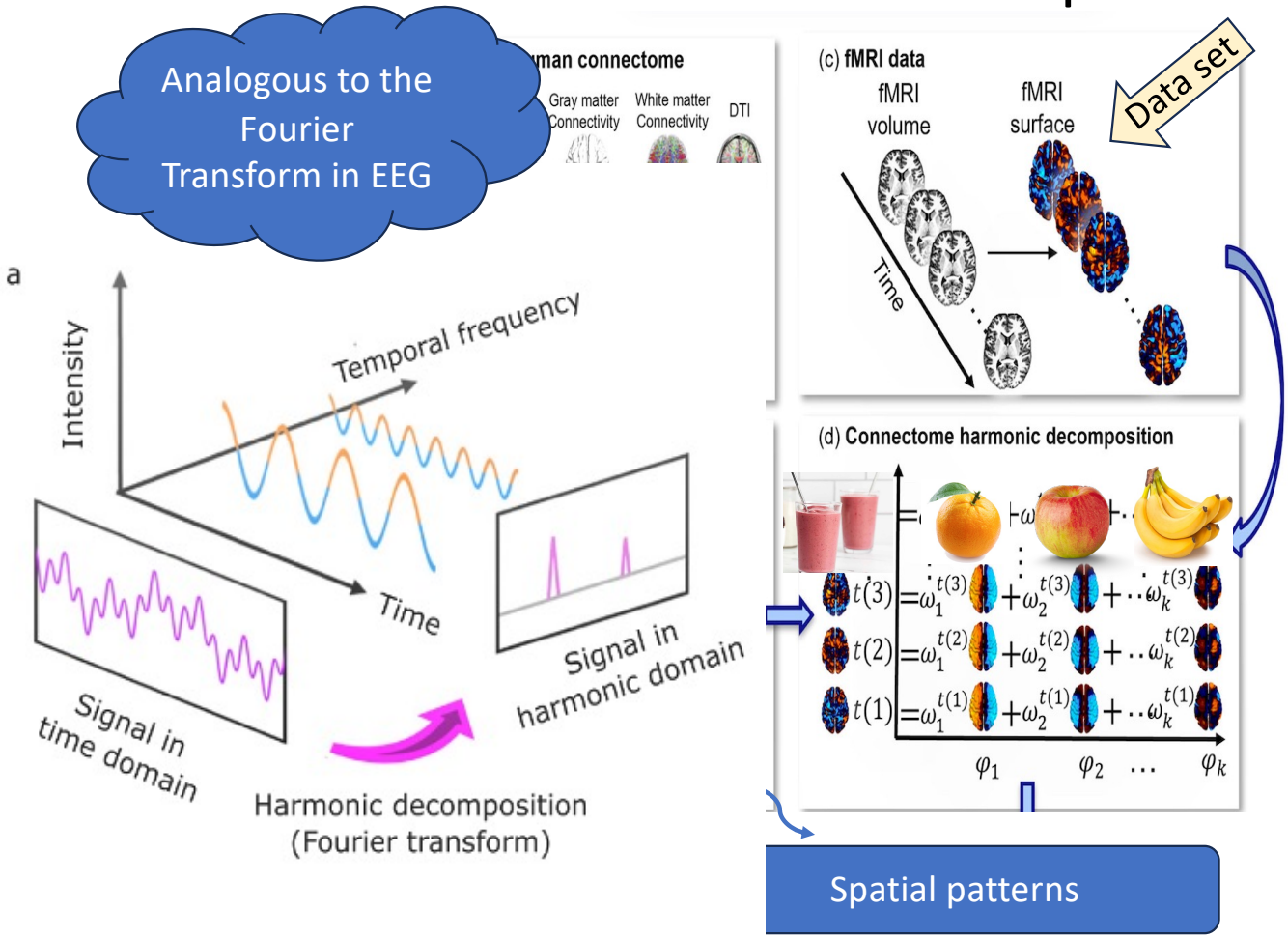
Connectome Harmonic Decomposition

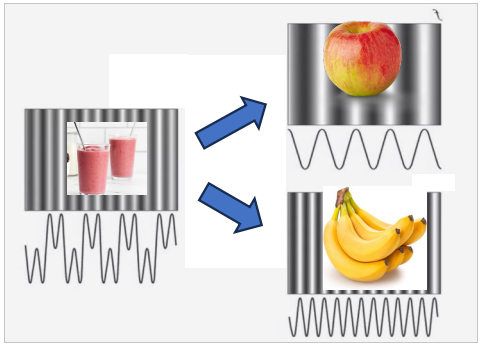




Selen Atasoy et al., 2016
Luppi et al., 2019

Connectome Harmonic Decomposition

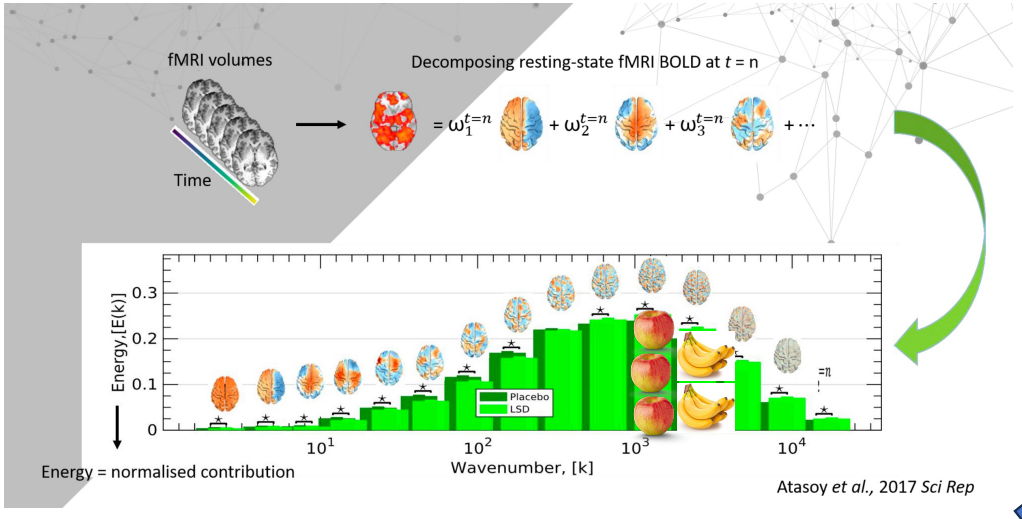




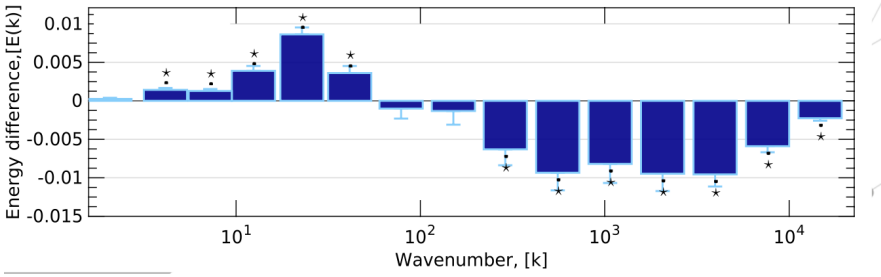
Selen
Lu

Power, energy and entropy

How many of each fruit in the smoothie (power)

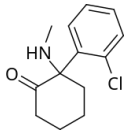


Atasoy *et al.*, 2017 *Sci Rep*

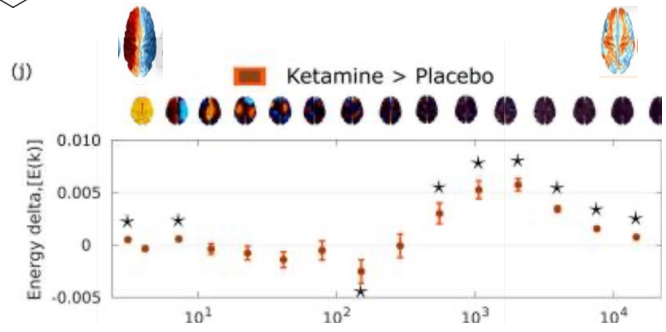


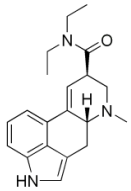
"Do we need a wide or restricted repertoire of connectome harmonics to build the brain activity we observed?"

Signatures of altered states of consciousness/ phenomenally rich experiences?

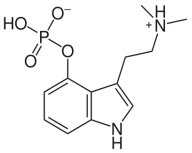


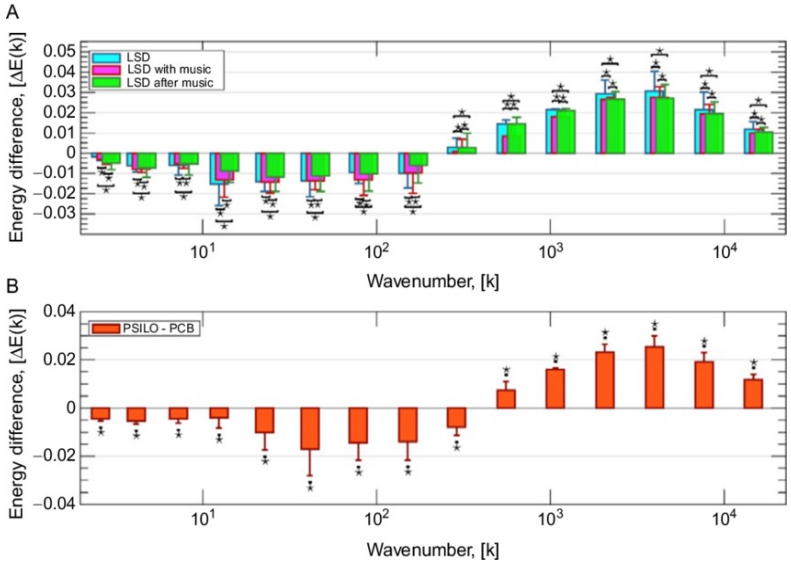
Ketamine





LSD and Psilocybin





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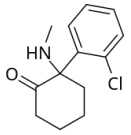
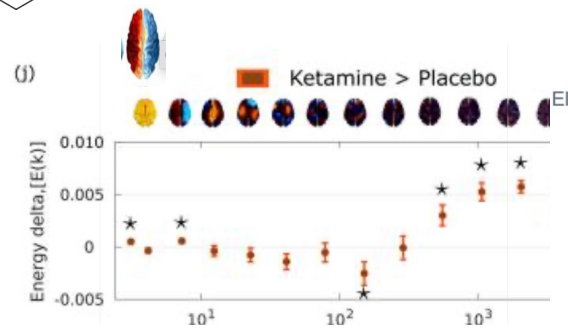
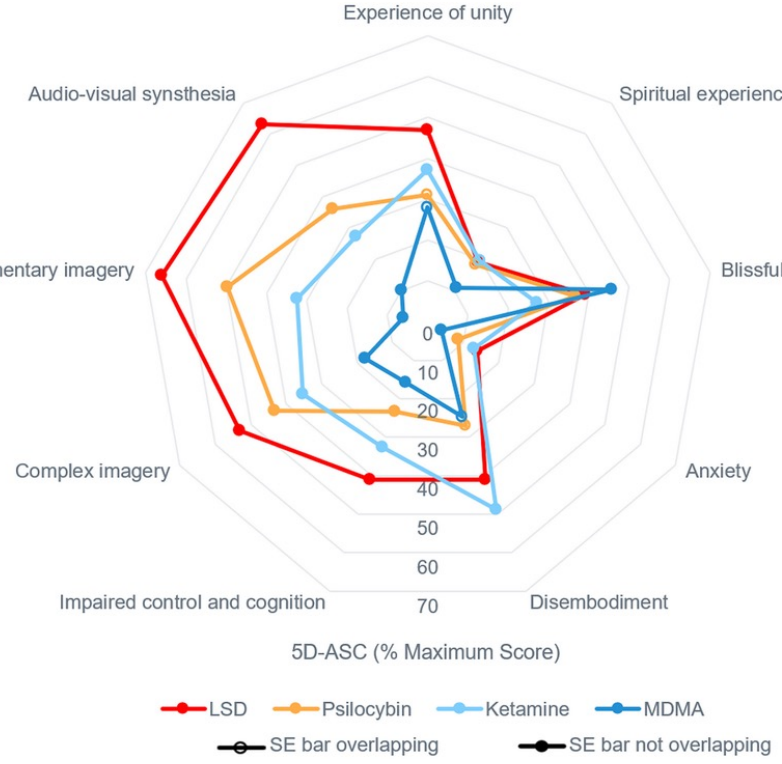
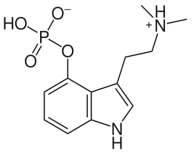


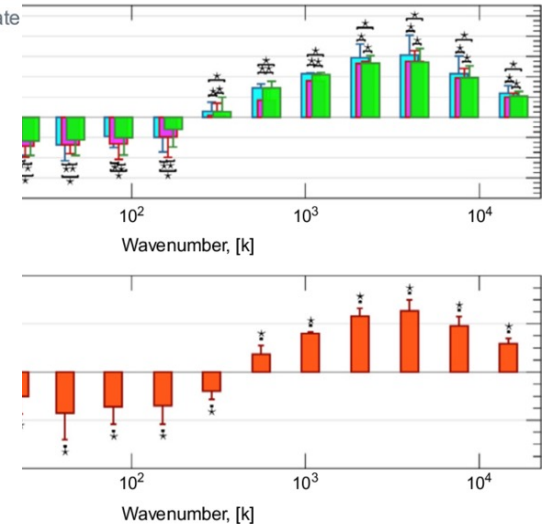
Ketamine



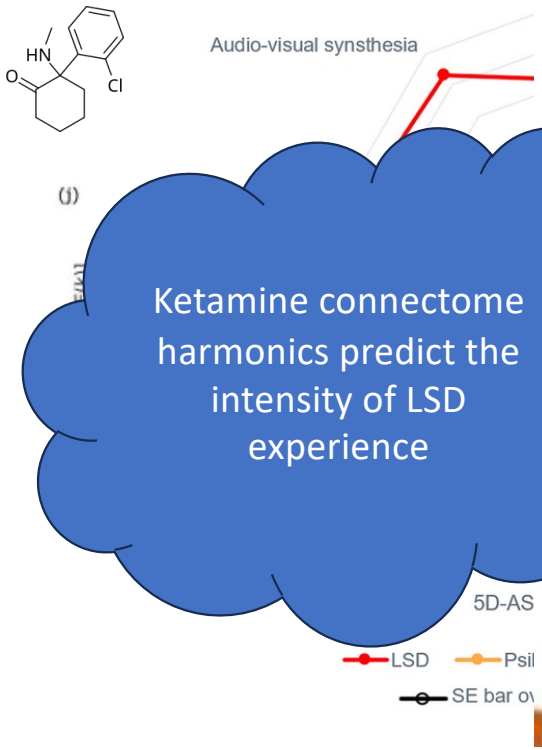


d Psilocybin

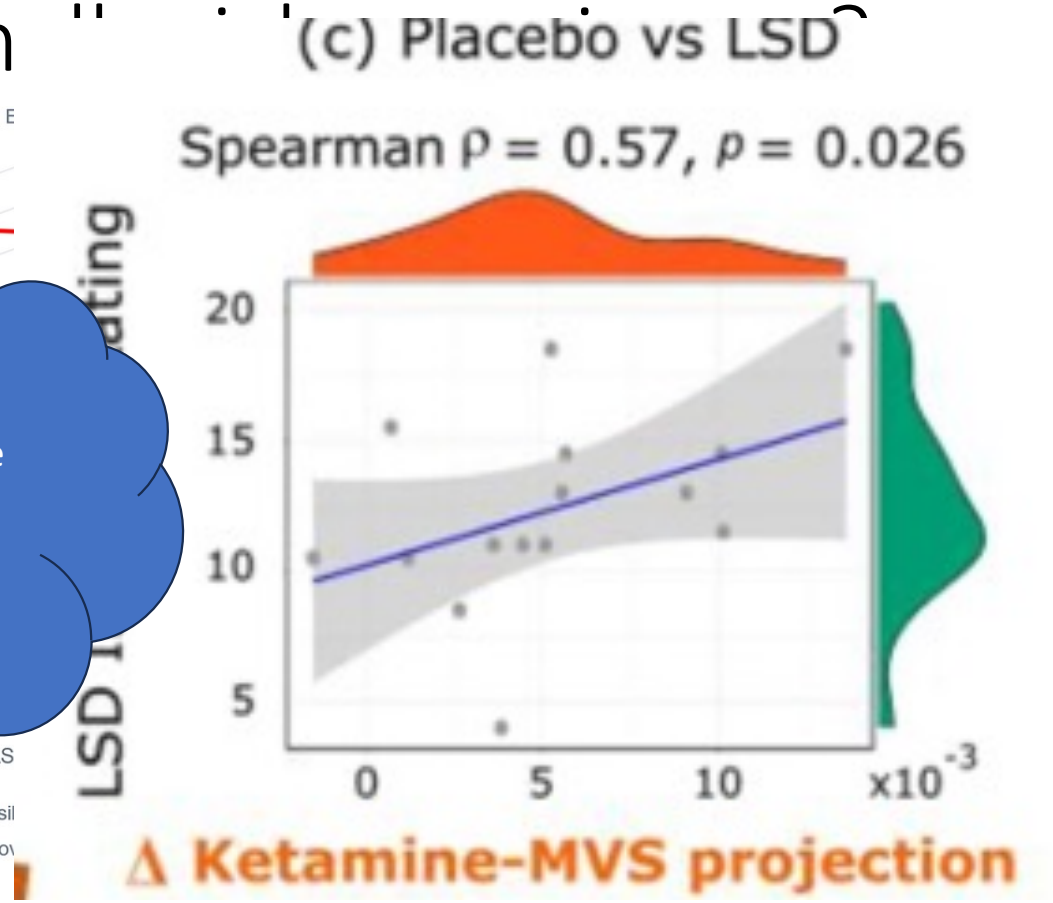




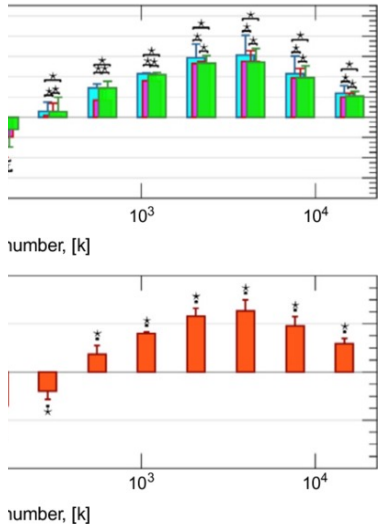
Signatures of altered states of consciousness/ phenomen



Ketamine connectome harmonics predict the intensity of LSD experience



ilocybin



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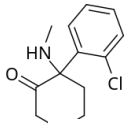
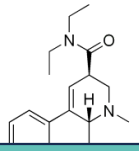
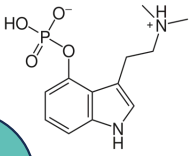
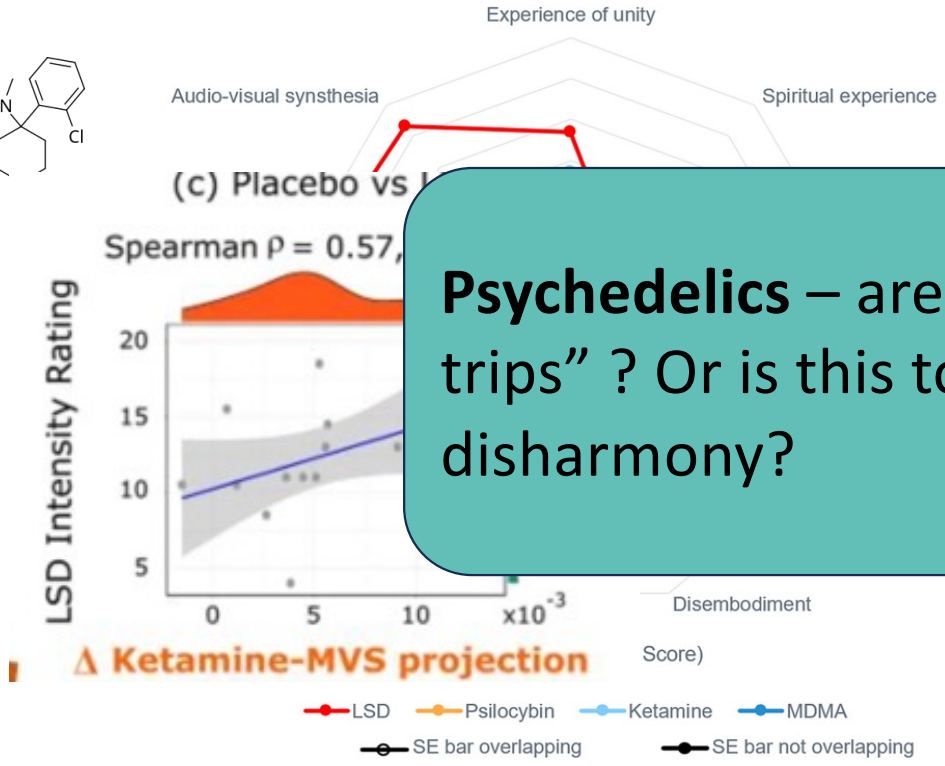


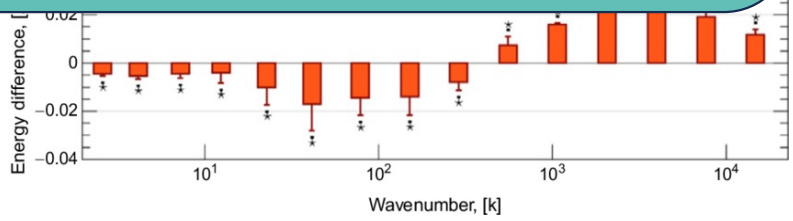


LSD and Psilocybin

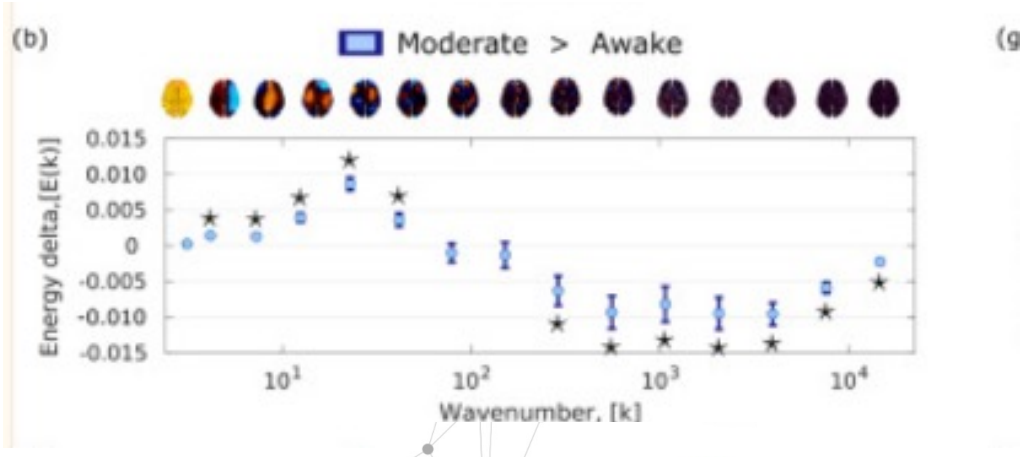


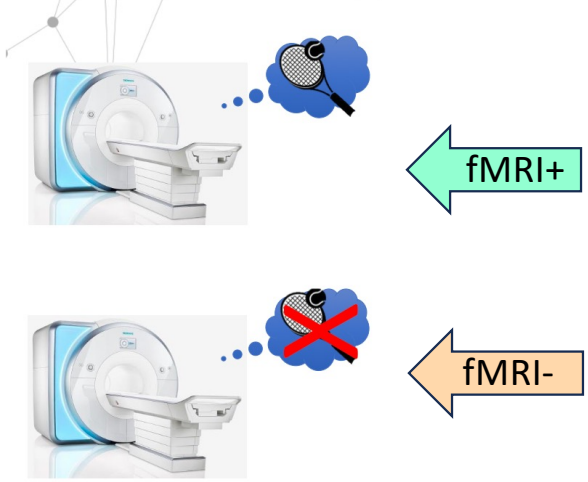
Psychedelics – are there signatures of “good” vs “bad trips” ? Or is this too macroscale? Harmony vs disharmony?

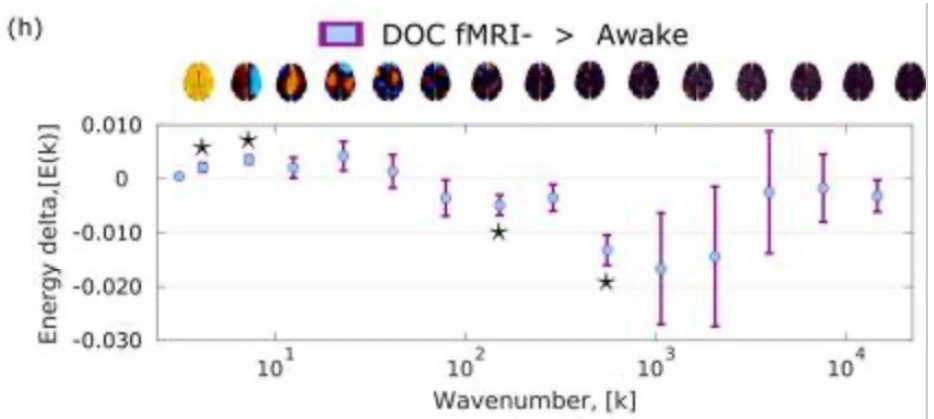


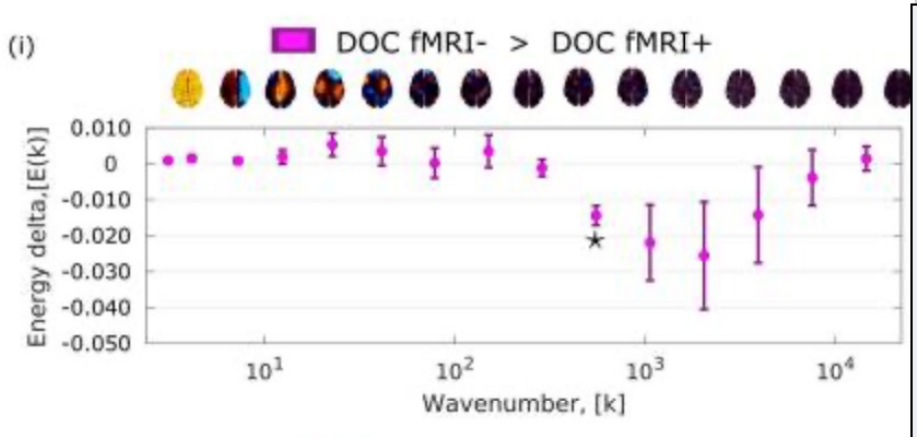


Signatures of unconscious states

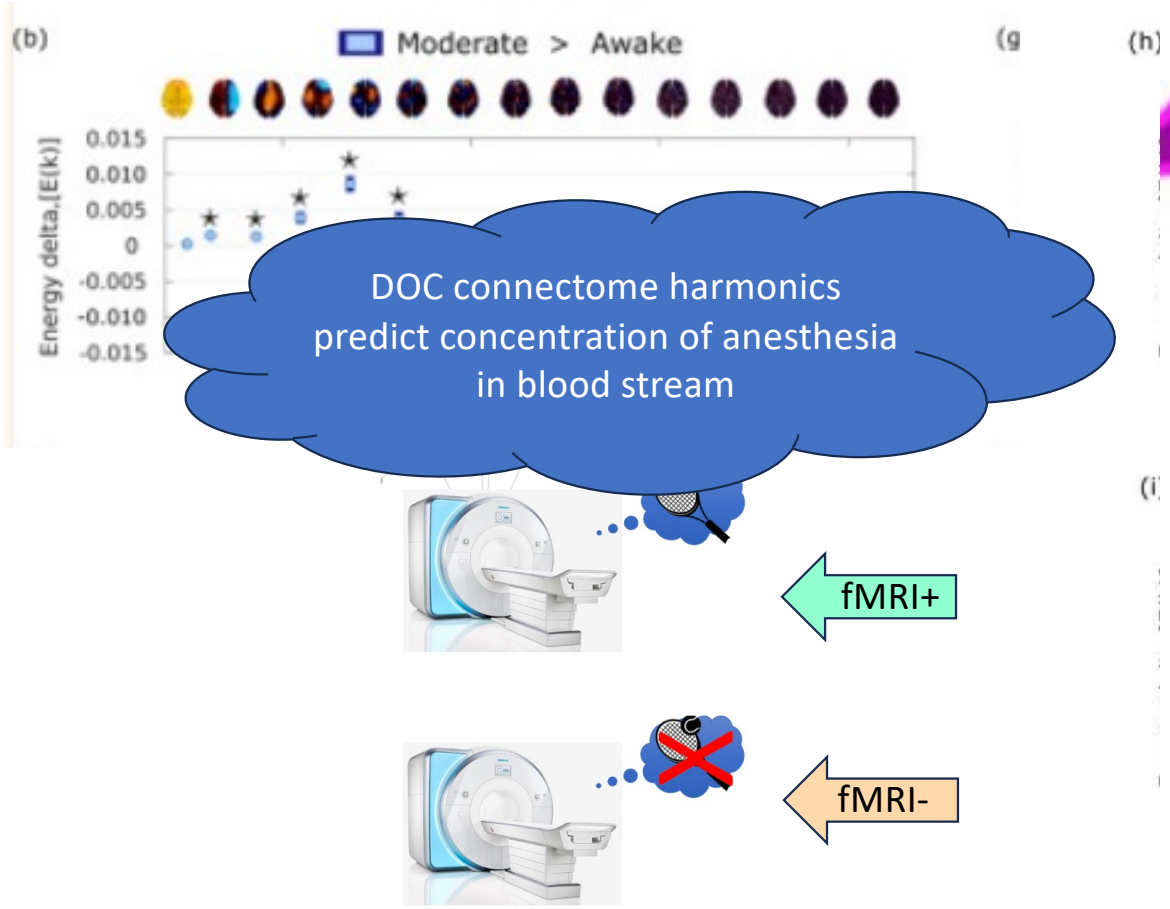


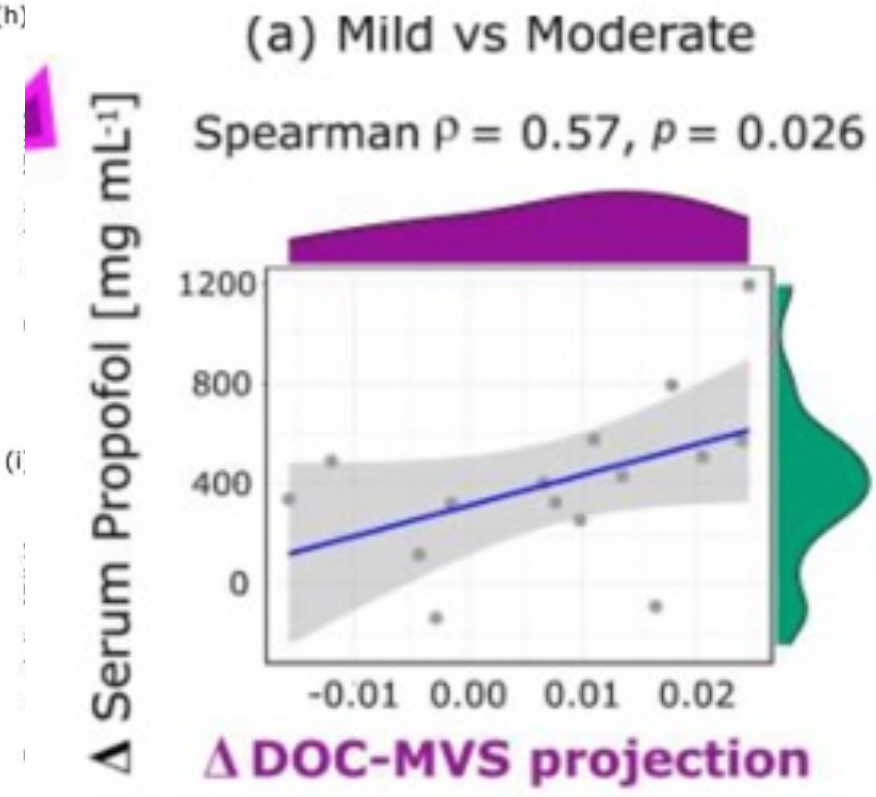




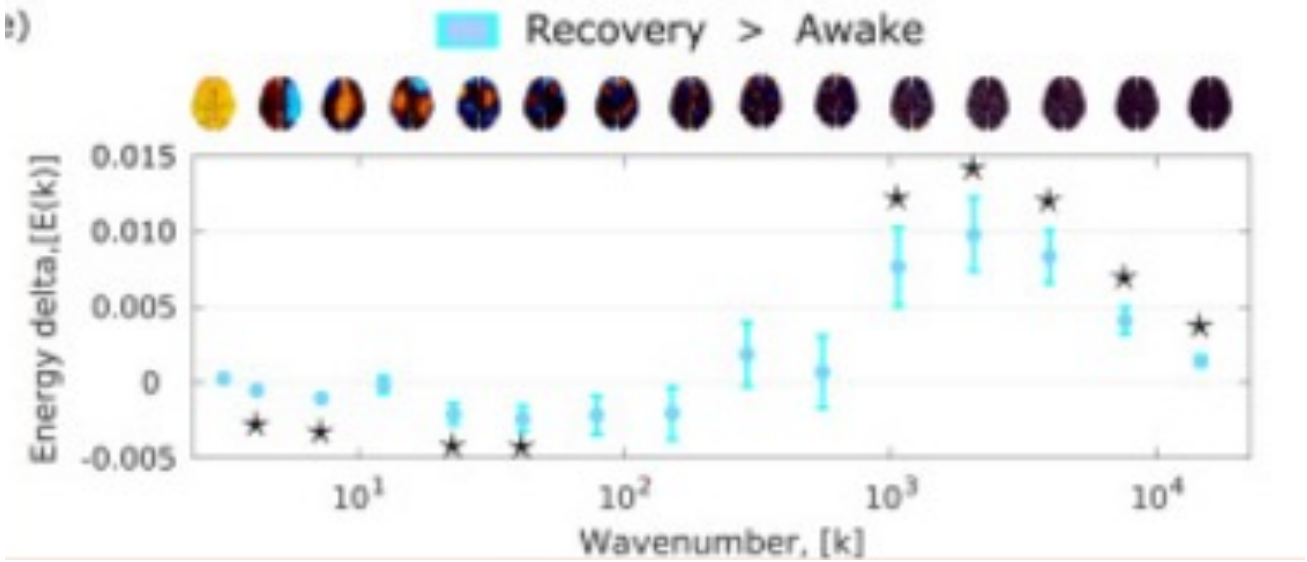


Signatures of unconscious states

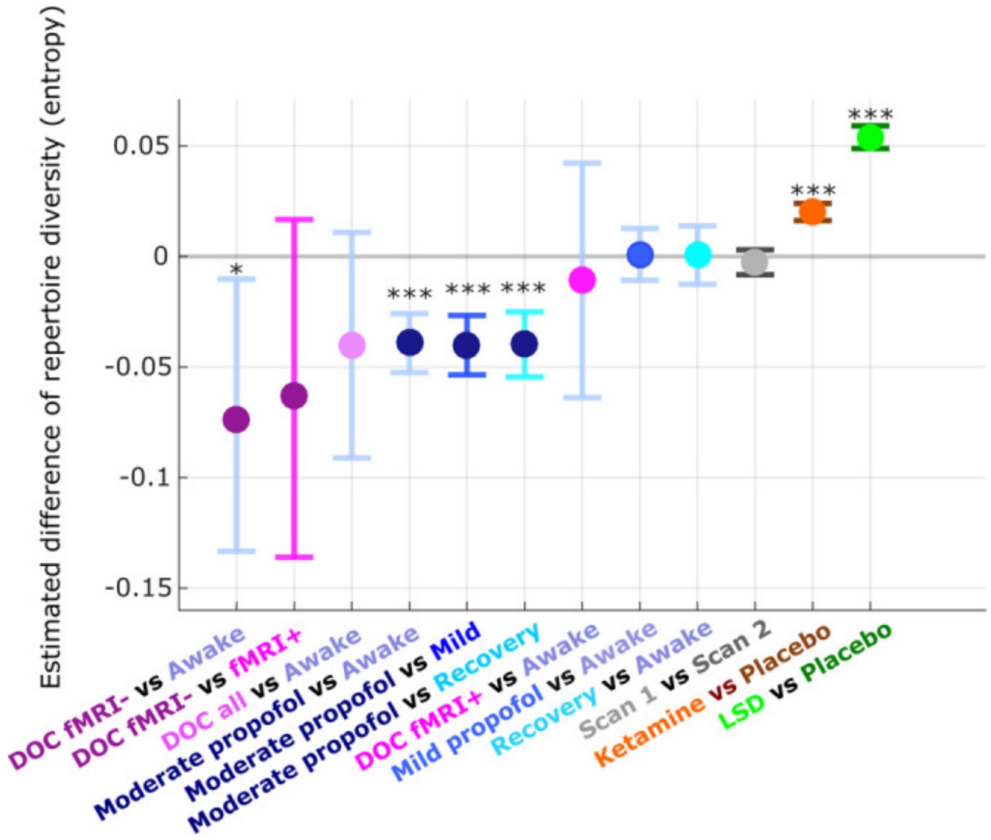




How about recovery from anesthesia?



Entropy



Do we need a wide or restricted repertoire of connectome harmonics to build the brain activity we observed?

↓

Is your brain improvising more? Hallucinations?

↓

The number of musical notes played during improvisation is significantly higher compared with memorized play of the same piece

Main points, limitations, and future

Contribution of high-frequencies to phenomenally rich states?

- A wider repertoire of brain activity feeding subjective experience?

Synergy in the brain (+ music) → dynamic equilibrium

- Anesthesia
- DOC
- Psychedelics – decreased gating, increase excitation?

Depression: rigid expectations?

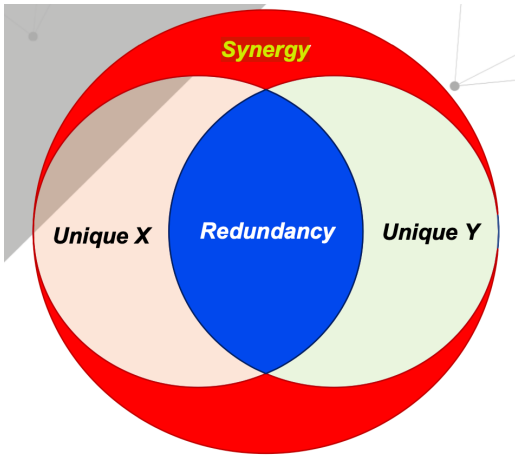
Schizophrenia?

- Too many high frequencies ? Too much disorder? No synergy?

Zolpidem GABA agonist → awakes SOME people with DOC's

- Individualized analysis

Anesthesia : actually unconscious? Clinical definition



Luppi et al., 2022

ALL MODELS ARE WRONG!!!!! Maybe this is all bs ☺

Data sets

Ketamine

- 20 participants, healthy
- 100 ng/ml continuous intravenous infusion or placebo
- Siemens Trio 3T scanner: fMRI + MRI
- 2 scans, 1 week apart, resting state, eyes closed

DOC

- 22 unresponsive wakefulness syndrome/ vegetative state or minimally conscious state
- Tennis task: fMRI - or fMRI +
  - •Motor Cognitive Dissociation
- Siemens Trio 3T scanner: fMRI and MRI
- Resting state fMRI

Propofol

- 25 participants, healthy
- No drug, 0.6 mg/ml (Mild), 1.2 mg/ml (Moderate)
- Siemens Trio 3T scanner: fMRI + MRI
- Resting-state fMRI acquired at each stage, including recovery.

LSD

- 15 participants, healthy, previous psychedelic use
- 75 µg intravenous or placebo
- 3T GE HDx system: fMRI + MRI
- 2 scans, 14 days apart, resting state, fMRI eyes closed
- 11-D altered states of consciousness questionnaire (ASC)

Re-test

- 18 right-handed participants
- Nothing
- Siemens Trio 3T scanner: fMRI and MRI
- 2 scan, 2-4 weeks apart