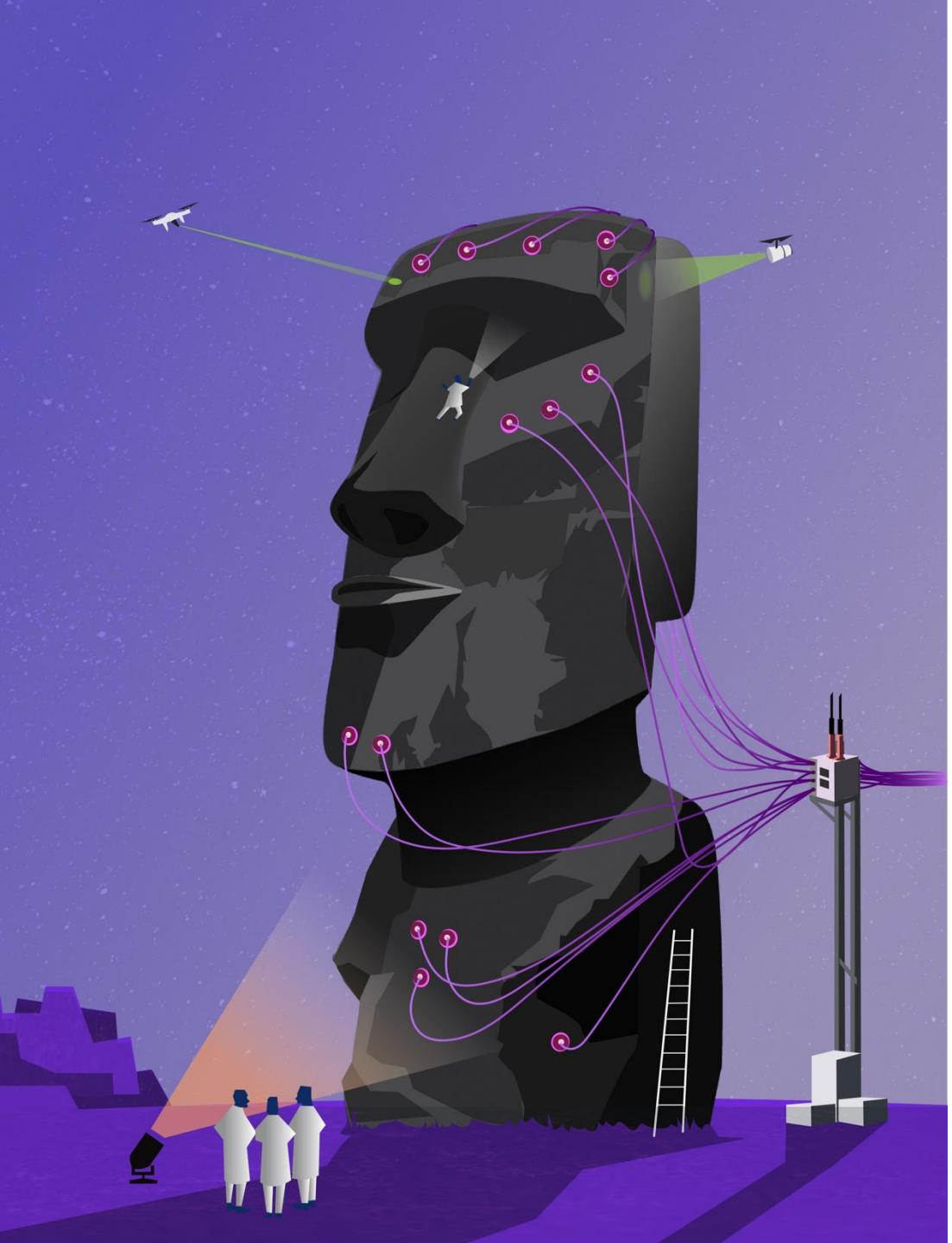


Paris Brain Institute ICM 15 YEARS

Inserm
La science pour la santé
From science to health

Latest developments in Neurophysiology of States of Consciousness: From Mechanistic Principles to Novel Diagnostic and Therapeutic Tools

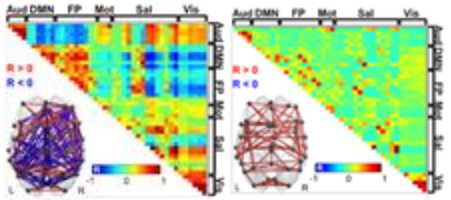
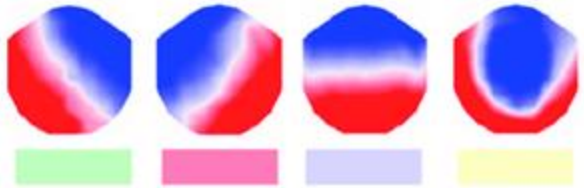
Jacobo Diego Sitt, MD, PhD
Paris Brain Institute, INSERM, France

Liege, May 19 2025

What drives the dynamics of subjective experience?

States of (un)consciousness ⟶ Responsiveness

			
Awake + aware	Sleep	Anesthesia	Disorder of consciousness (DOC)

Brain Dynamics		fMRI Dynamics		EEG Dynamics

What drives the dynamics of subjective experience?

States of (un)consciousness → Responsiveness

Awake + aware

Sleep

Anesthesia

Disorder of consciousness (DOC)

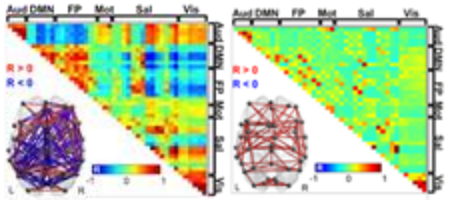
Conscious content → Report
(what's on your mind)

Perception

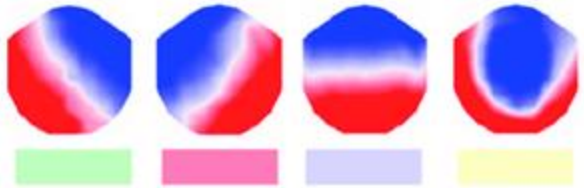
Metacognition

Other dimensions

Brain Dynamics

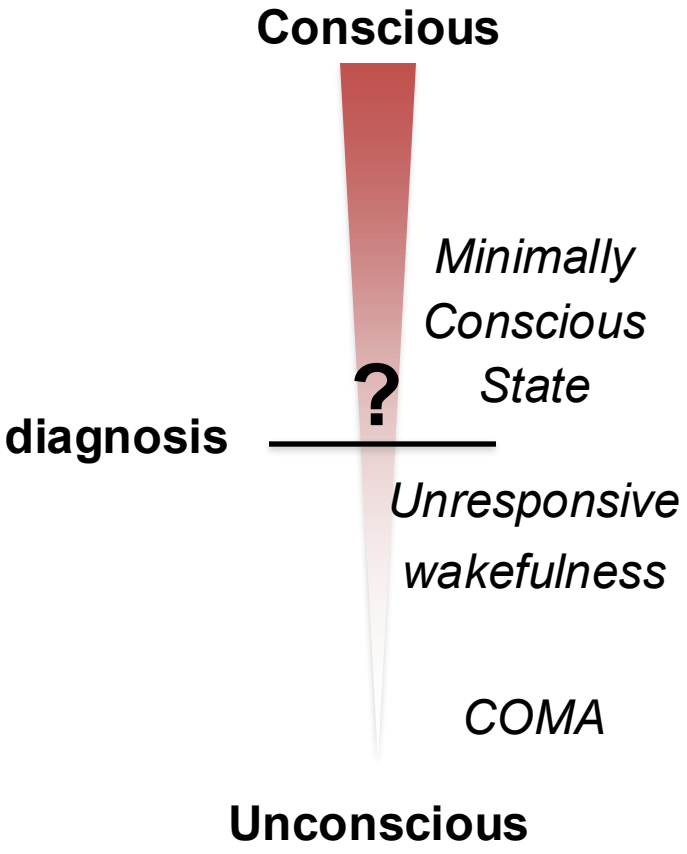


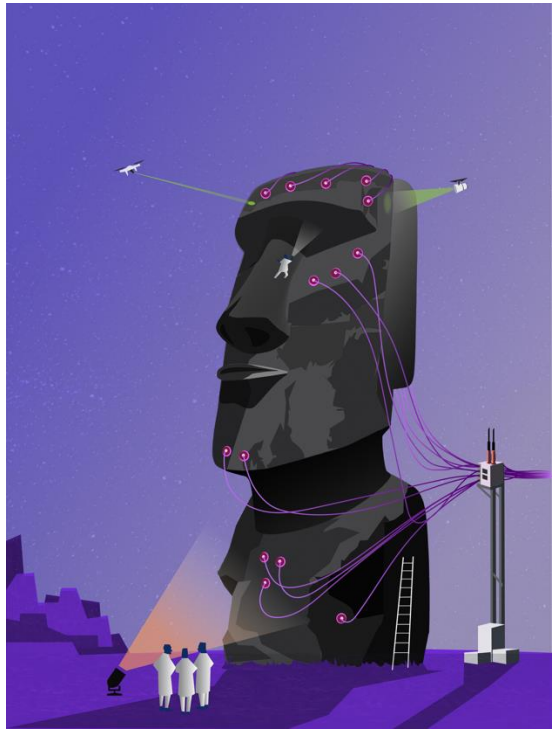
fMRI Dynamics



EEG Dynamics

State of Consciousness
a fundamental and translational project





State of Consciousness

a fundamental and translational project

The quest of neuronal markers

- ***Sleep***
  - *Strauss et al, PNAS 2015; Strauss et al, Neuroimage 2022*

- ***Anesthesia***
  - *Barttfeld* et al, PNAS 2015; Uhrig* et al, Anesthesiology 2018*
  - *Tasseries et al, Science advances 2022*

- ***Disorders of consciousness***
  - *King* et al, Cur. Bio. 2013*
  - *Sitt* et al, Brain 2014*
  - *Schurger et al, PNAS 2015*
  - *Raimondo et al, Ann of Neuro 2017*
  - *Perez et al, Cell Reports 2021*
  - *-Engemann* et al, Brain 2018*
  - *-Demertzi* et al, Science Advances 2019*
  - *-Hermann et al, Sci Rep 2020*
  - *-Flo et al, PNAS Nexus 2024*
  - *-Rohaut et al, Nature Medicine 2024*

EEG
M/EEG
fMRI
tDCS/DBS
Brain-Body
Multimodal

Research lines

Neurophysiological signatures of consciousness-state

Non-invasive stimulation

Brain-body interactions

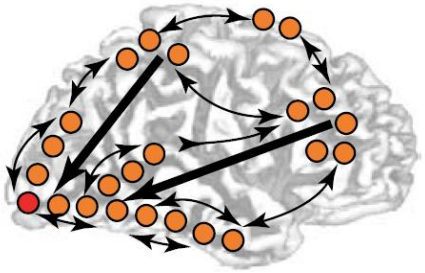
fMRI Dynamics

Computational Modeling

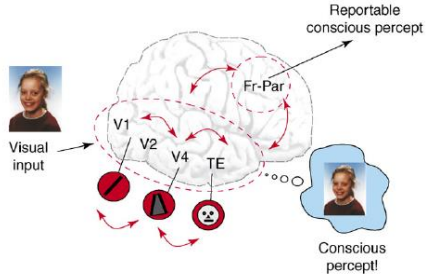
States biomarkers <-> content of consciousness dynamics

Deriving markers from theories of consciousness predictions

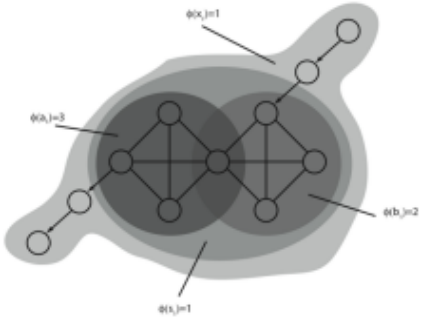
Distributed architecture theories of consciousness



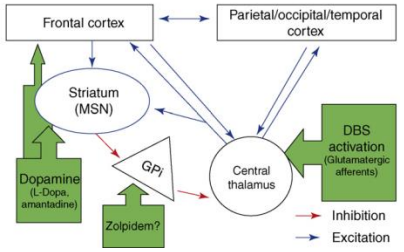
Global neuronal workspace theory
Dehaene et. al.



Recurrent processing theory
Lamme et. al.



Integrated Information theory
Tononi et. al.



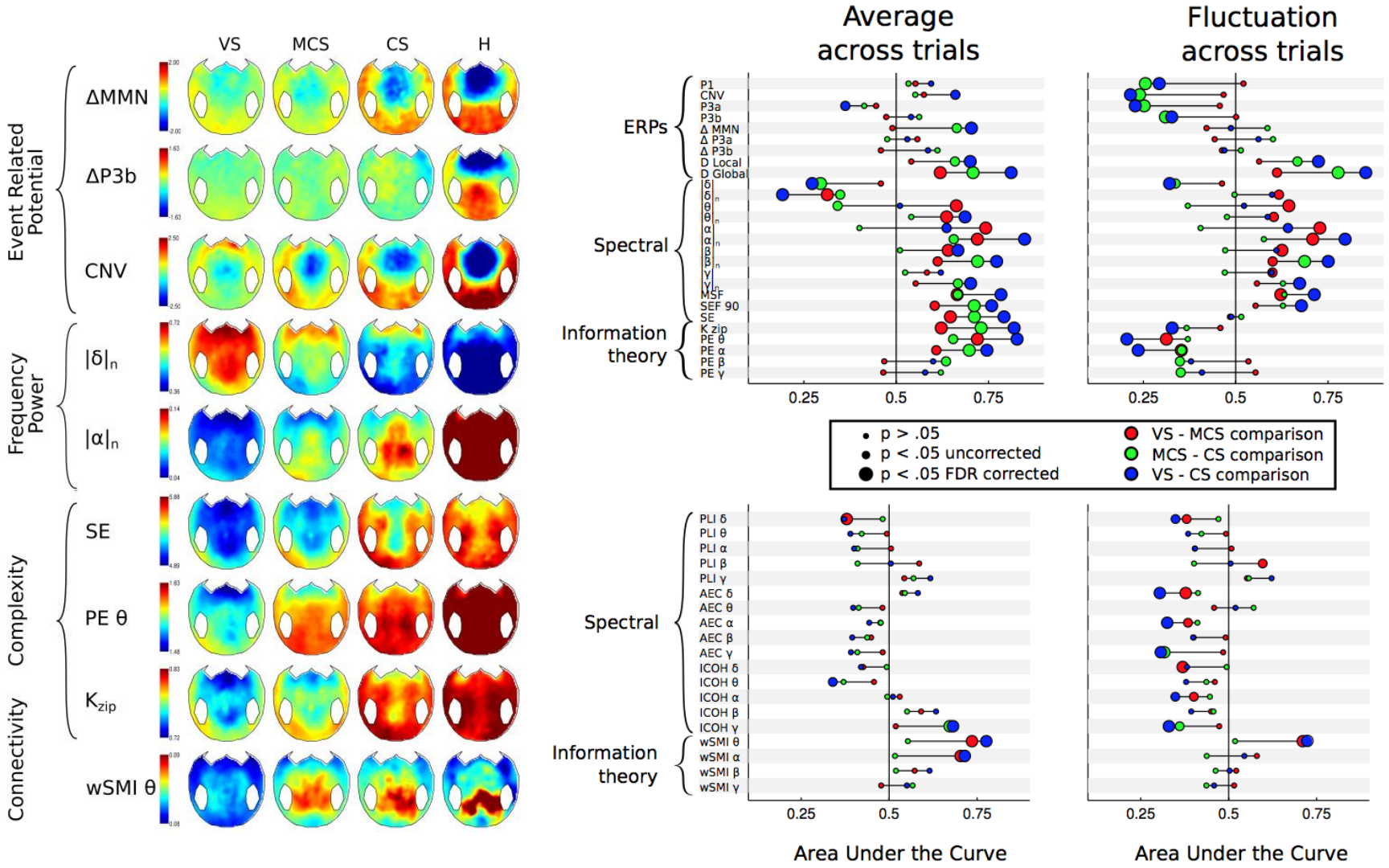
Meso-circuit theory

Schiff et. al.

Common Predictions

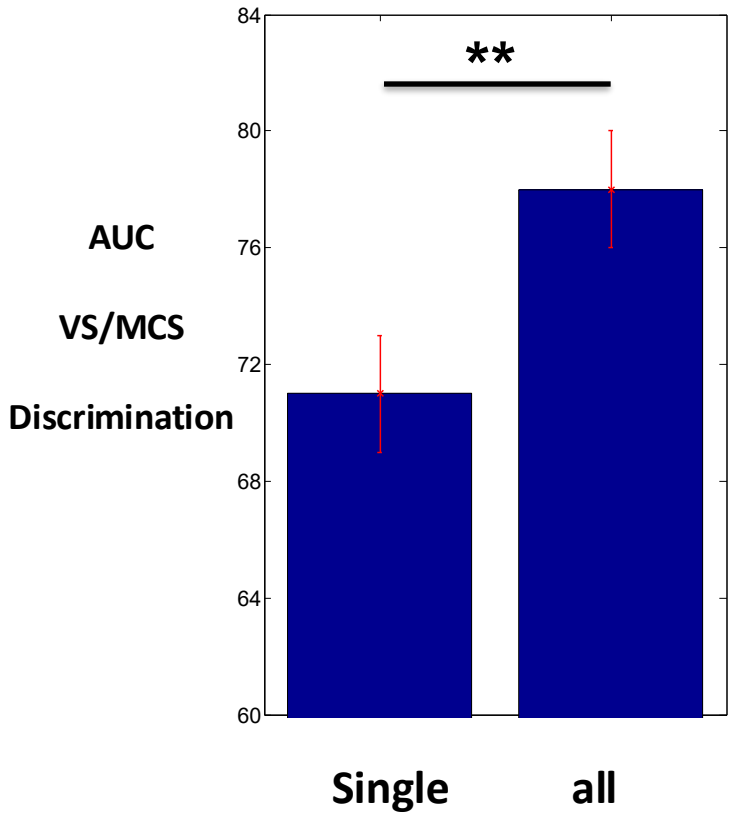
I. Information sha ng across brain regions
II. Information ty
III. Information ma tenance
IV. Relevant frequency bands

Going beyond single markers
Comparing and combining signatures

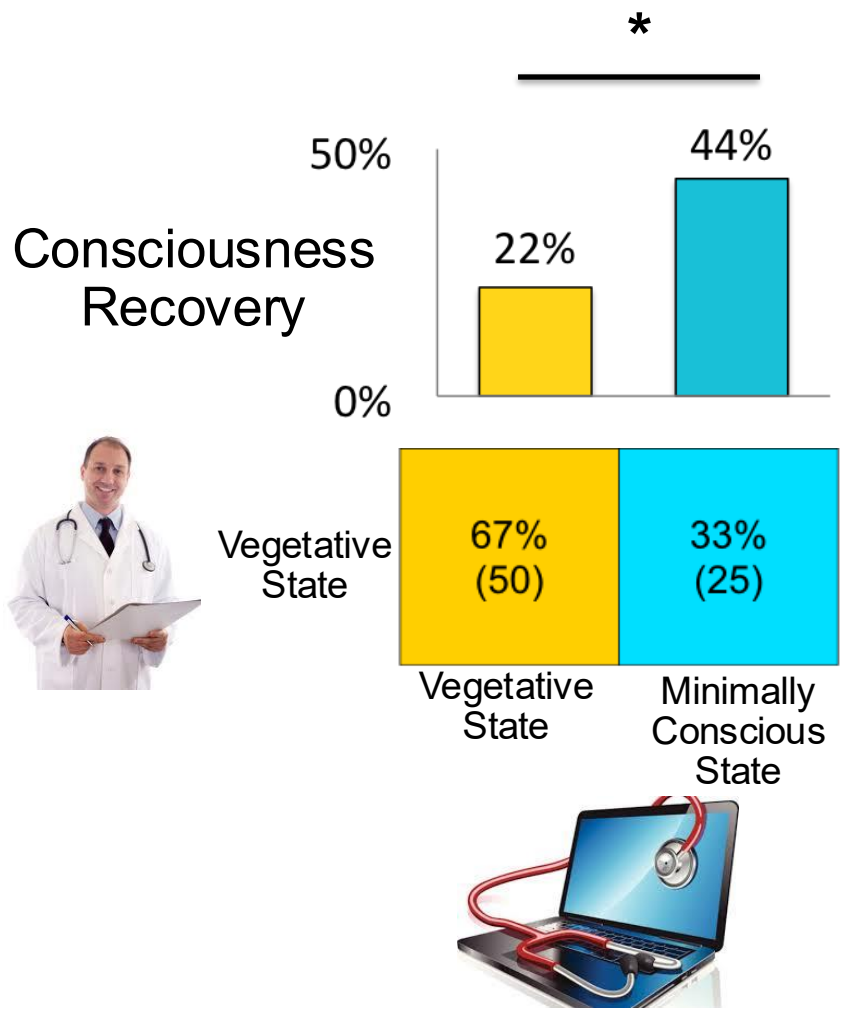


Sitt, King*,et al. Brain (2014)*

More is better ?
Combining using MVPA

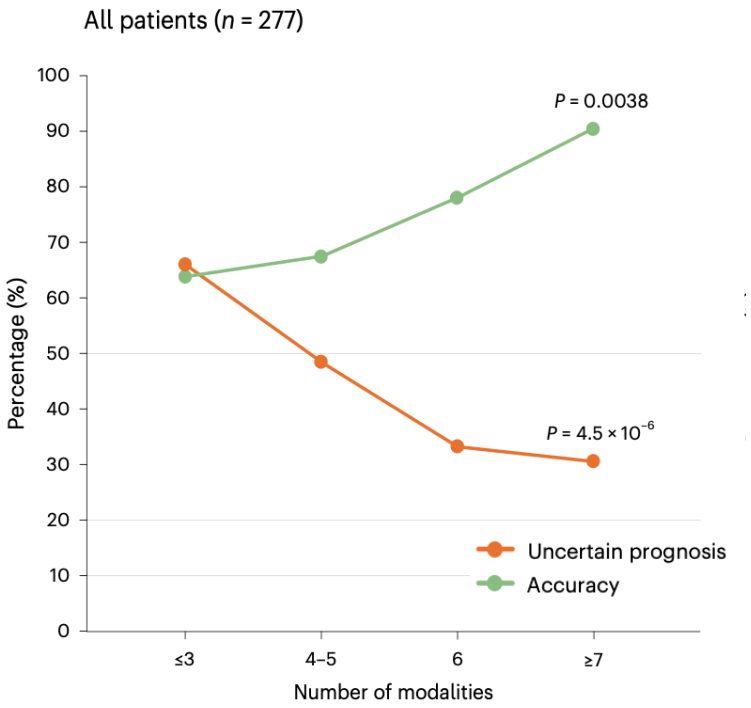


Classification of individual subjects



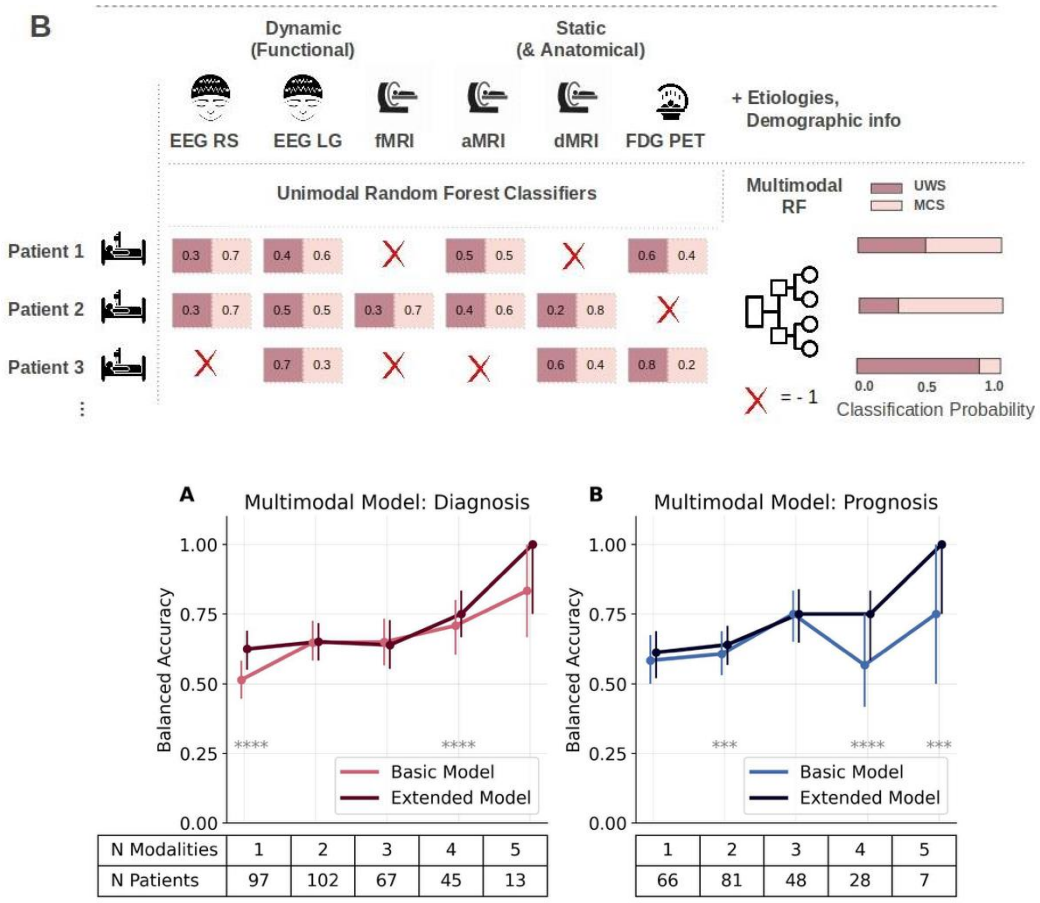
Sitt, King*,et al. Brain (2014); Engemann*, Raimondo*, et al. Brain (2018)*

Multimodal assessment improves neuroprognosis performance



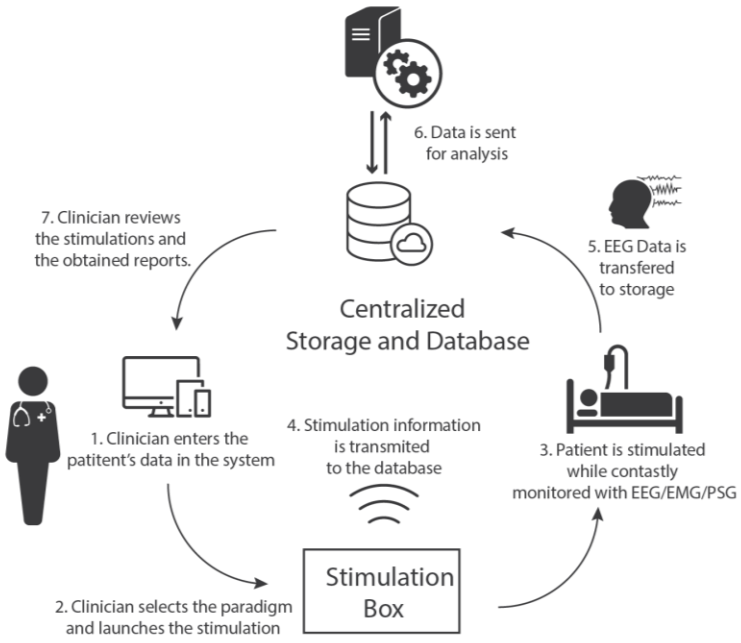
nature medicine

Rohaut, et al, Nature Medicine 2024



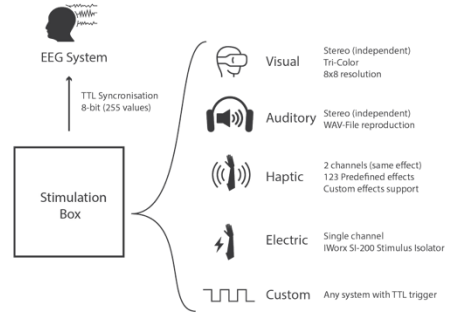
Manasova, et al, medRxiv 2024

NeuroMeters



A fully automatized neurophysiological evaluation environment for DOC patients

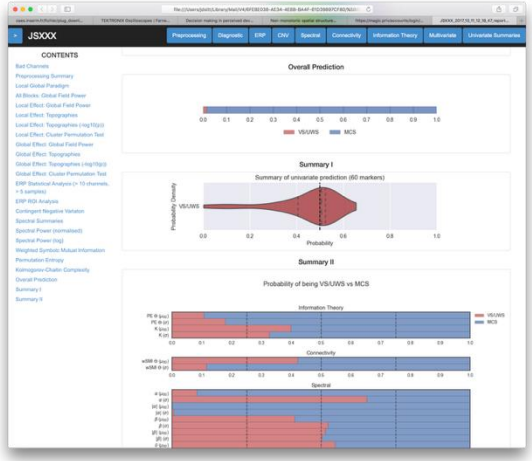
A stimulation box to standardize cognitive EEG evaluation in the clinics



Automated web-based server for EEG analysis

https://demo.doc-eeg.net

Provides predictions of a new patient's state



4 International patents / more than 2000 recordings analyzed

Boxes in 8 clinical sites, 1 R01 Clinical trial

CARNOT and NeuroCatalyst Grants

Research lines

Neurophysiological signatures of consciousness-state

Non-invasive stimulation

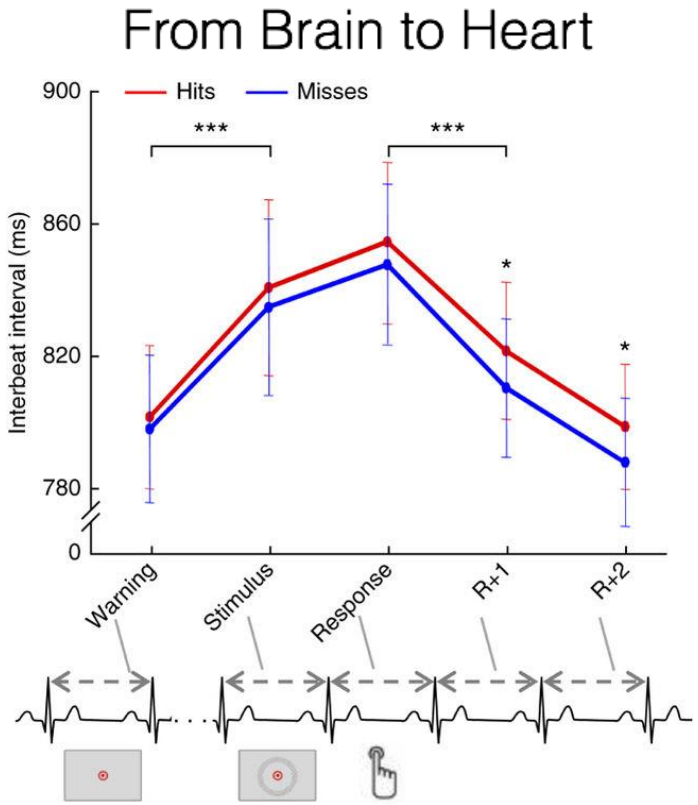
Brain-body interactions

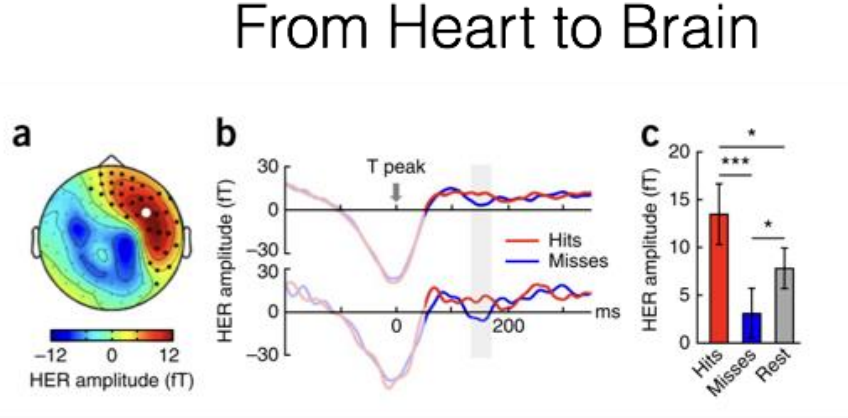
fMRI Dynamics

Computational Modeling

States biomarkers <-> content of consciousness dynamics

Brain-Heart Interaction

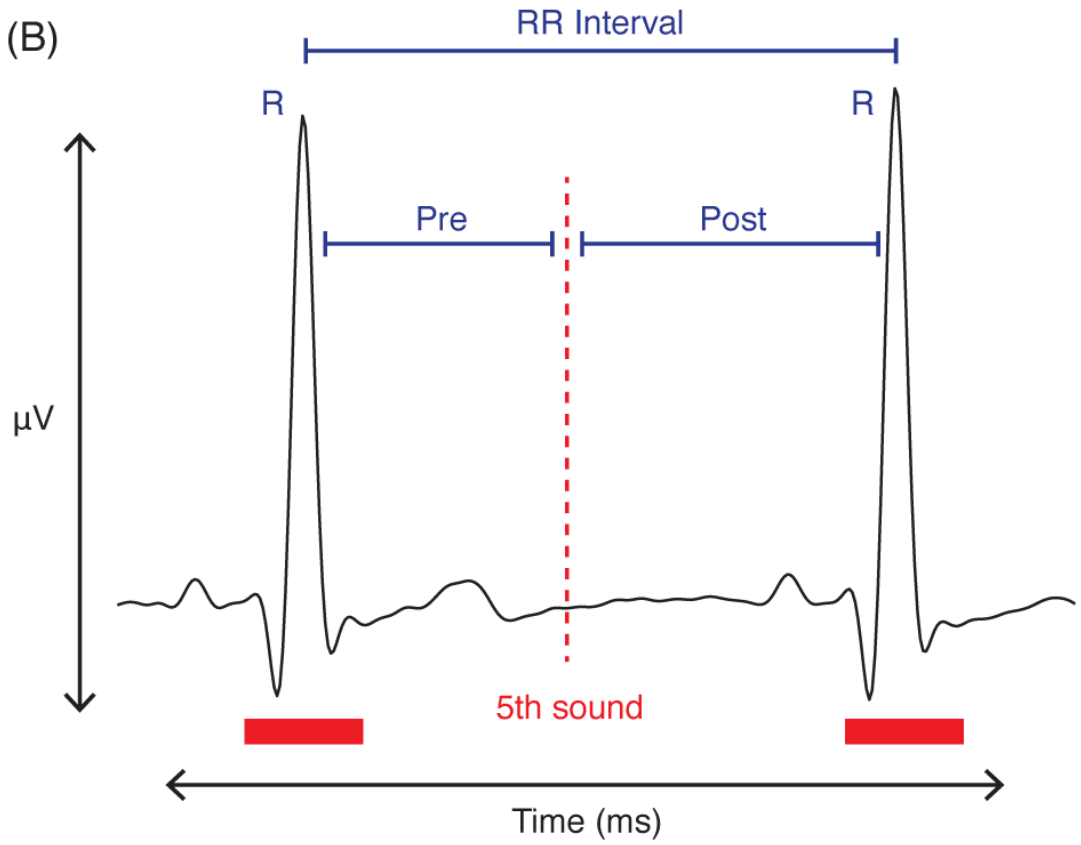




Park et Al, Nature Neuroscience, 2014

Can these ideas be translated to evaluate DOC patients ?

Cognitive processing -> heart cycle



Predictions

1) Post interval only

2) Impact: Global > Local

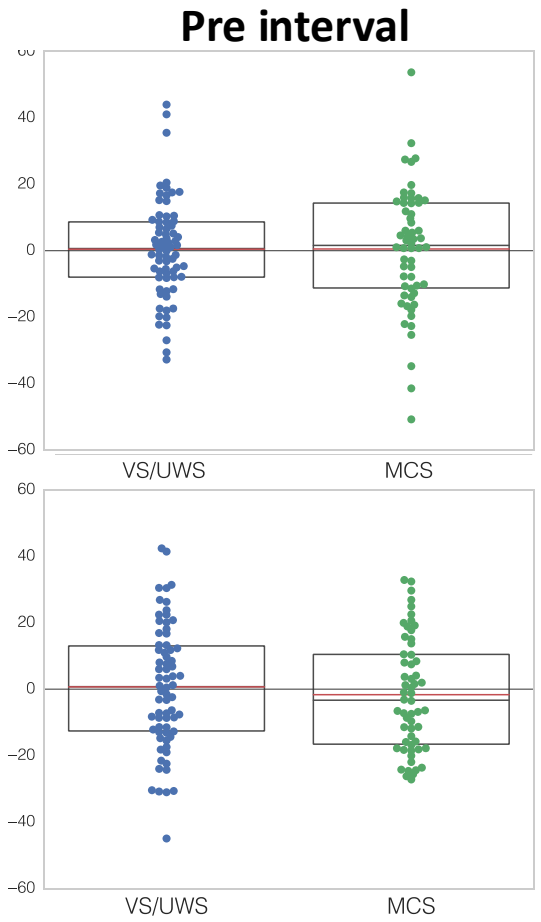
3) MCS > VS

Raimondo, et. al., Annals of Neurology (2017)

Modulation of the heart cycle

Local Deviant versus Local Standard

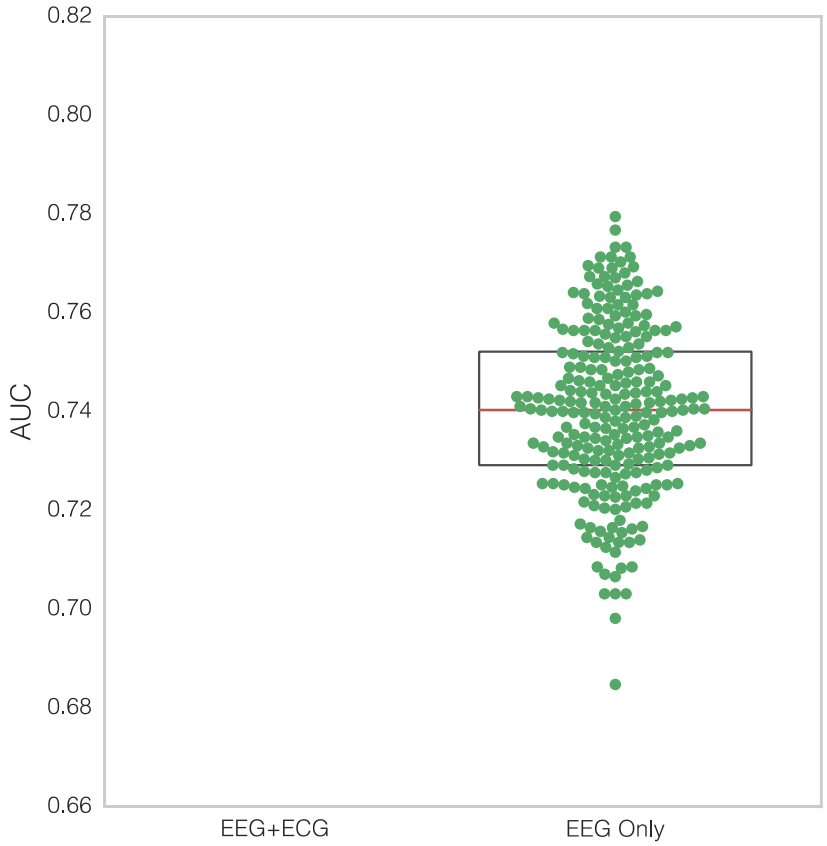
Global Deviant versus Global Standard



Is this useful for single subject characterization ? MVPA approach…

Raimondo, et. al., Annals of Neurology (2017)

Cardiac and EEG measures are synergic?

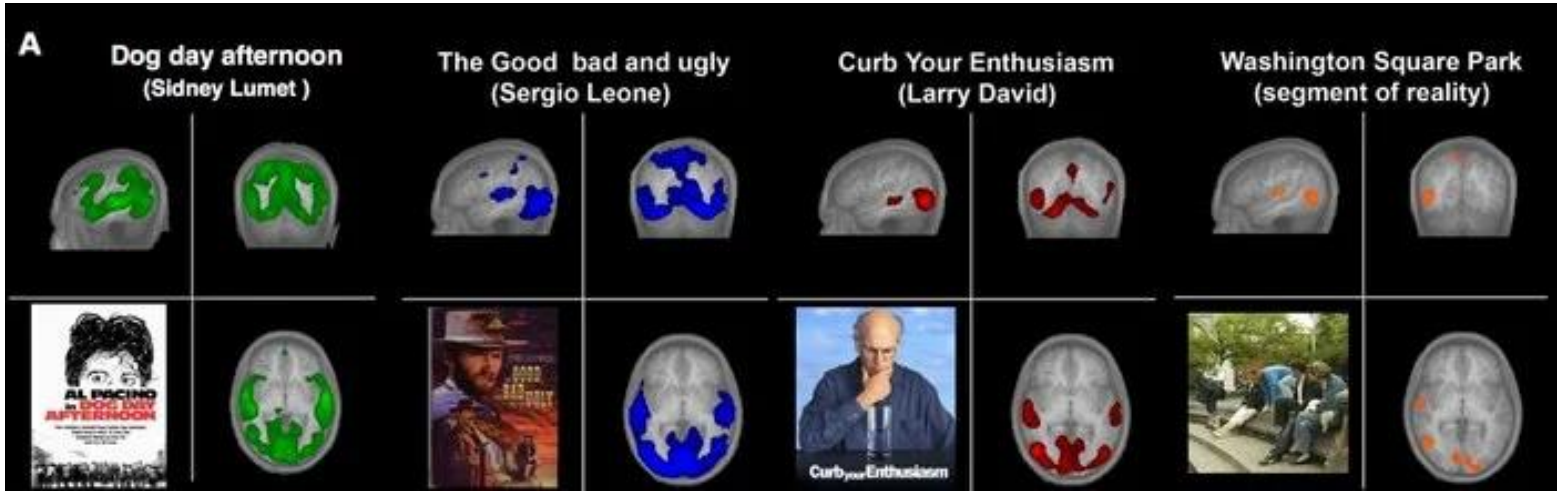


Raimondo, et. al., Annals of Neurology (2017)

Naturalistic stimuli

Inter-subject synchronization and cognition

Brain synchronization



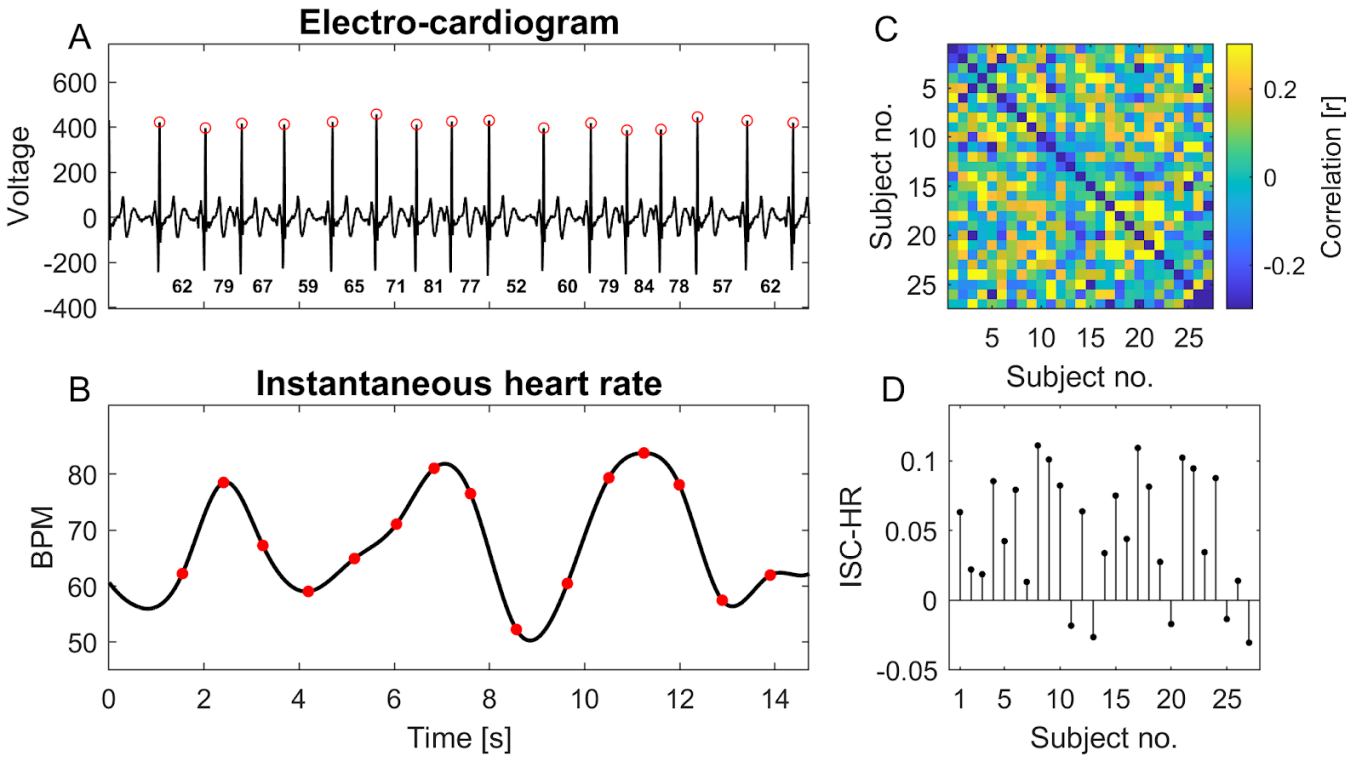
Ecological Stimulus
Brain synchronization between subject with stronger synchronization in thriller movies.

Hasson, Science, 2004

How about
physiological signals
and patients?

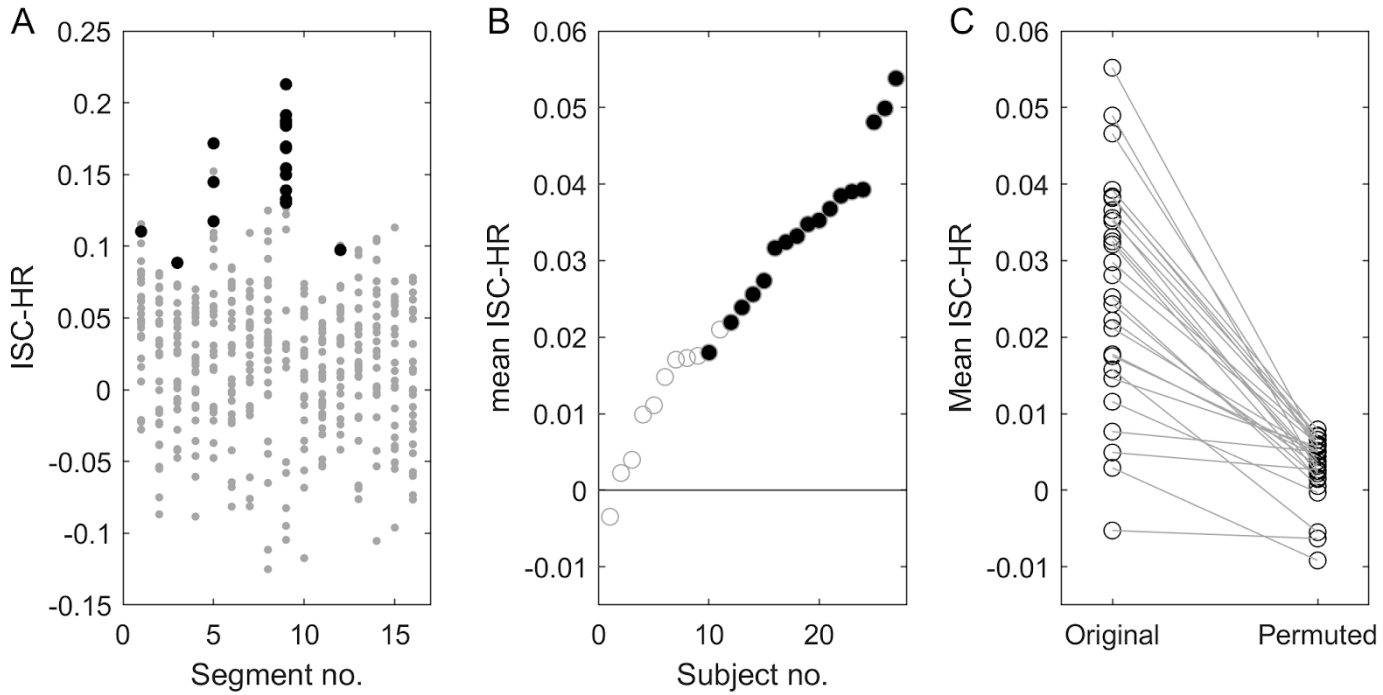
Our results…

How to measure HR synchronization



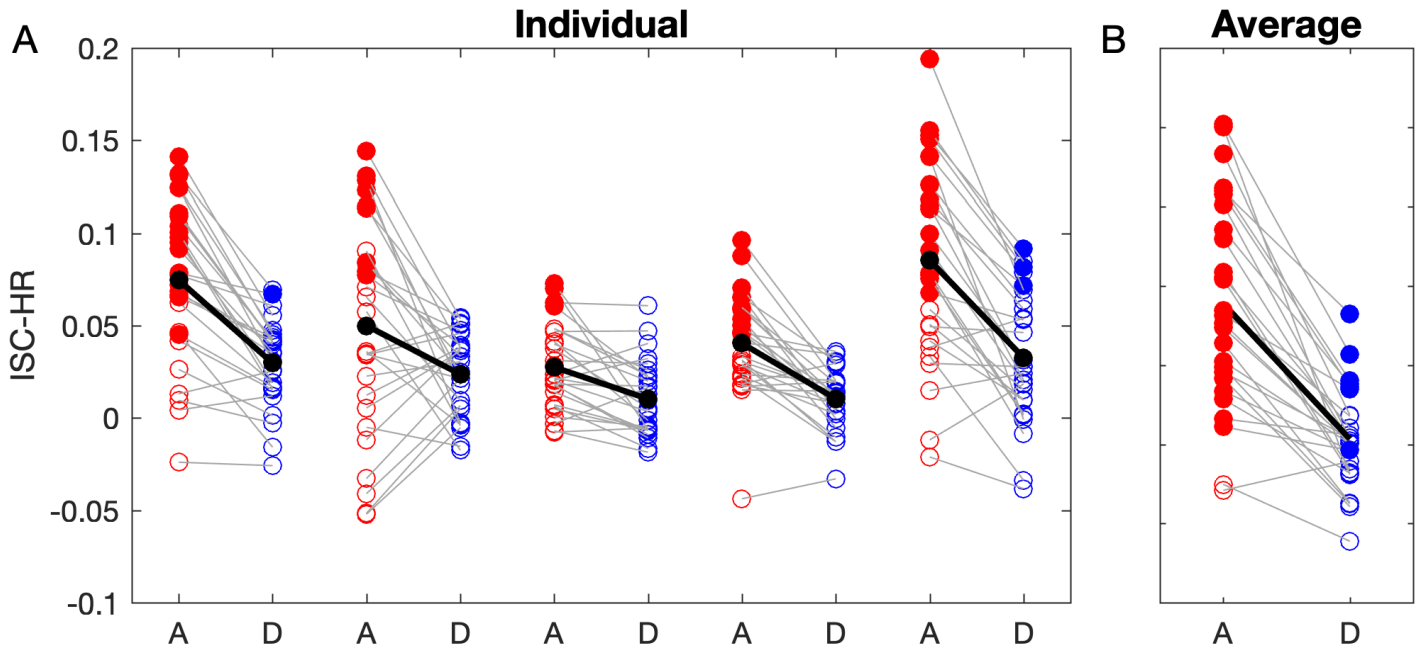
Perez*, Madsen*, et al, cell reports 2021

Exp 1: Synchronization with a story



Perez*, Madsen*, et al, cell reports 2021

Experiment 2: modulation of attention

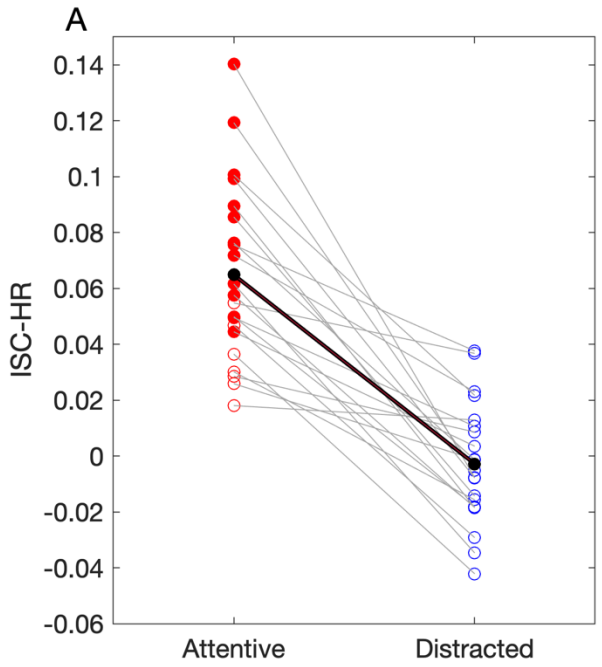


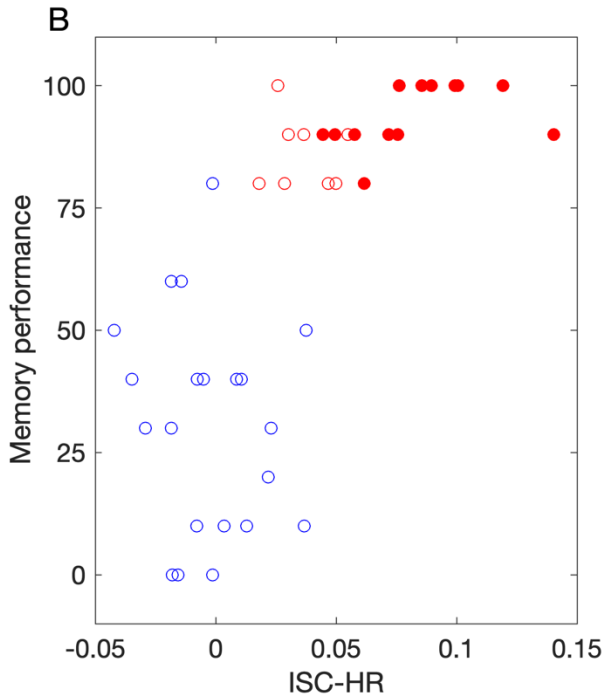
A= attentional condition

D= non attentional condition

Perez*, Madsen*, et al, cell reports 2021

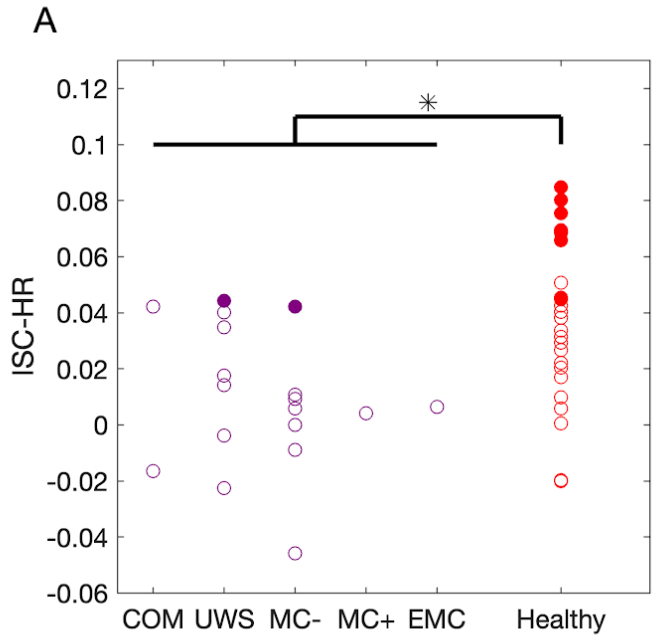
Experiment 3: ISC predicts memory

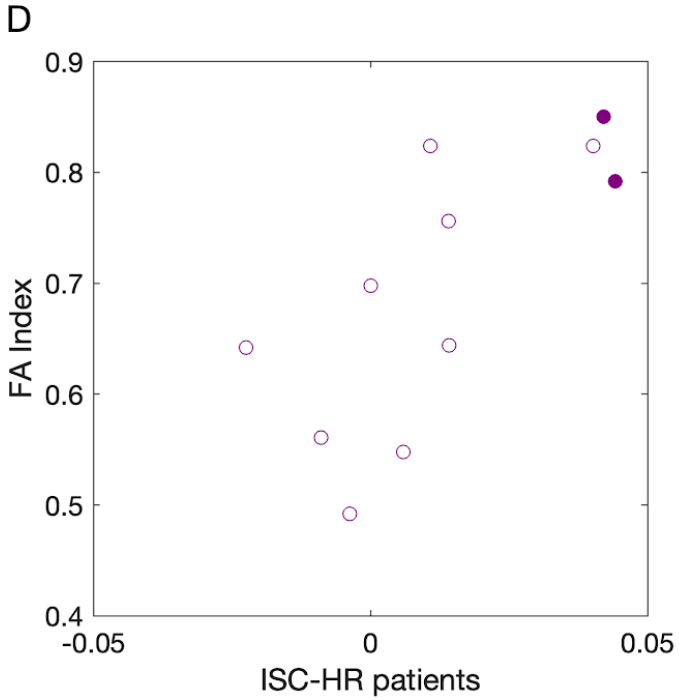




Perez*, Madsen*, et al, cell reports 2021

Experiment 4: ISC predicts recovery in DOC
a proof-of-concept





Perez*, Madsen*, et al, cell reports 2021

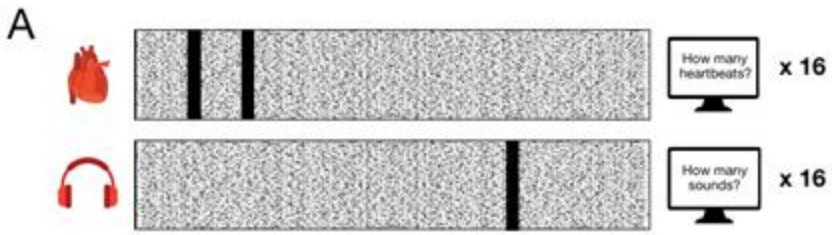
Command following

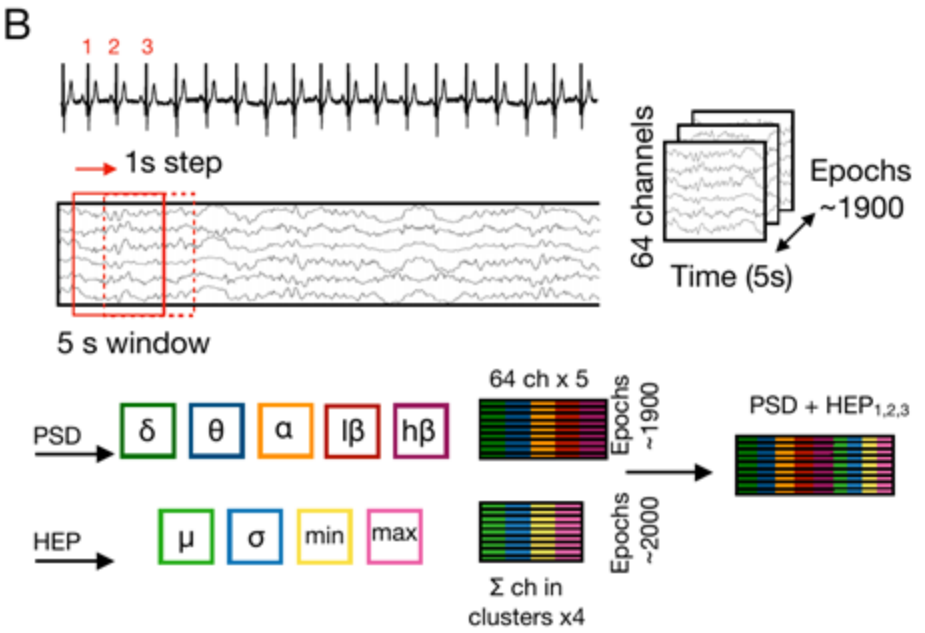
Detecting attention to interoceptive or exteroceptive processes

ECOS Sud

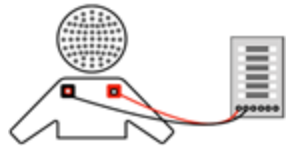
Emilia Flo

Experimental design and subject-level analysis

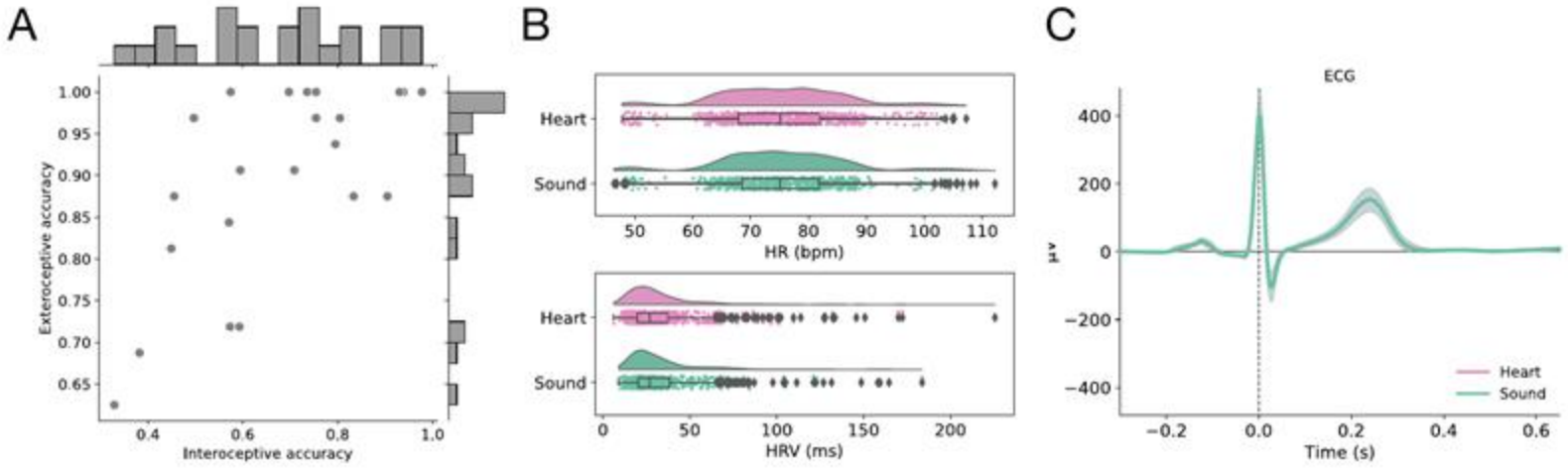




22 healthy participants
EEG 64 channels
ECG



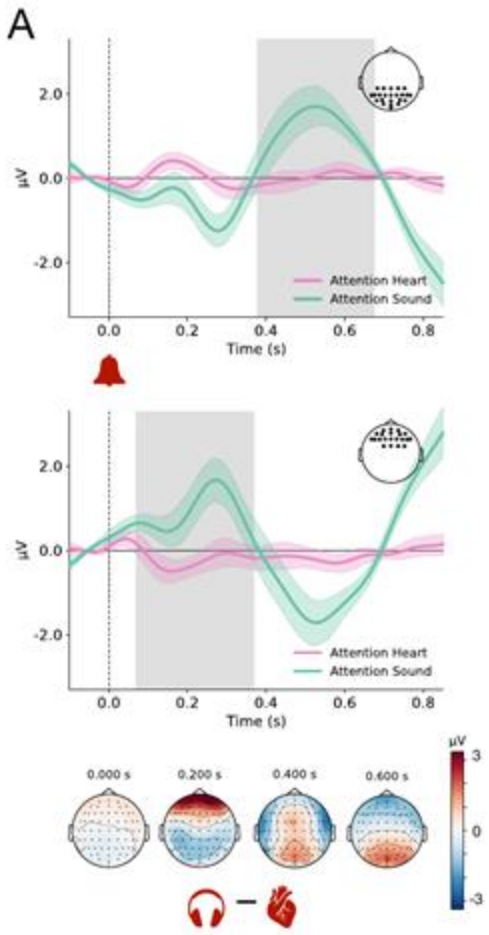
Task performance across subjects and heart activity

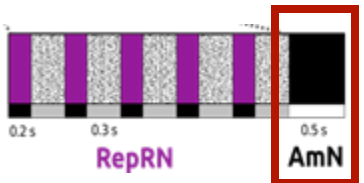


- Participants show high perfomance for exteroceptive trials
- Overall engagement in task
- No differences in heart activity between conditions

HEP and AmN evoked are oppositely modulated by interoceptive and exteroceptive attention

Brain response to AmN



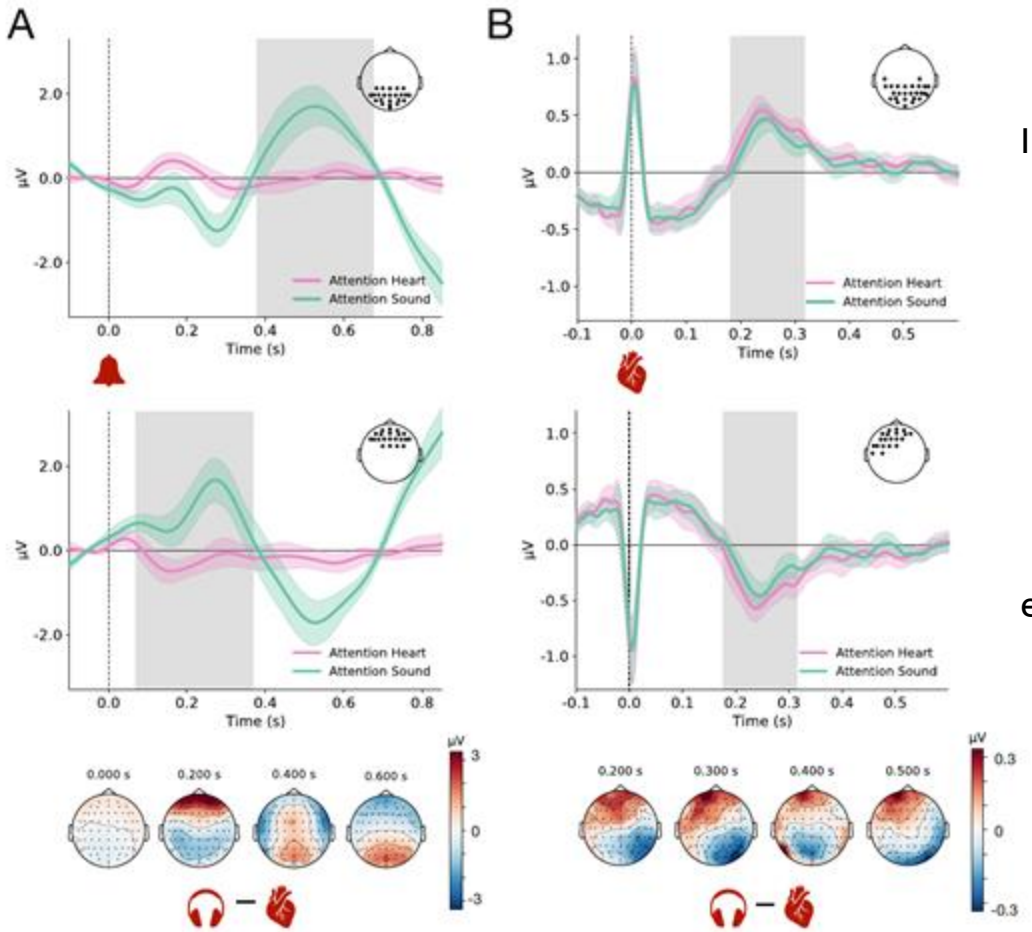


Increased P300 brain response during sound attention

HEP and AmN evoked are oppositely modulated by interoceptive and exteroceptive attention

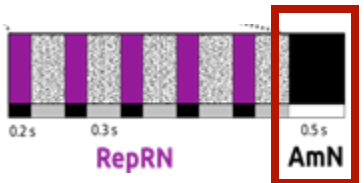
Brain response to AmN

Brain response to Heartbeats

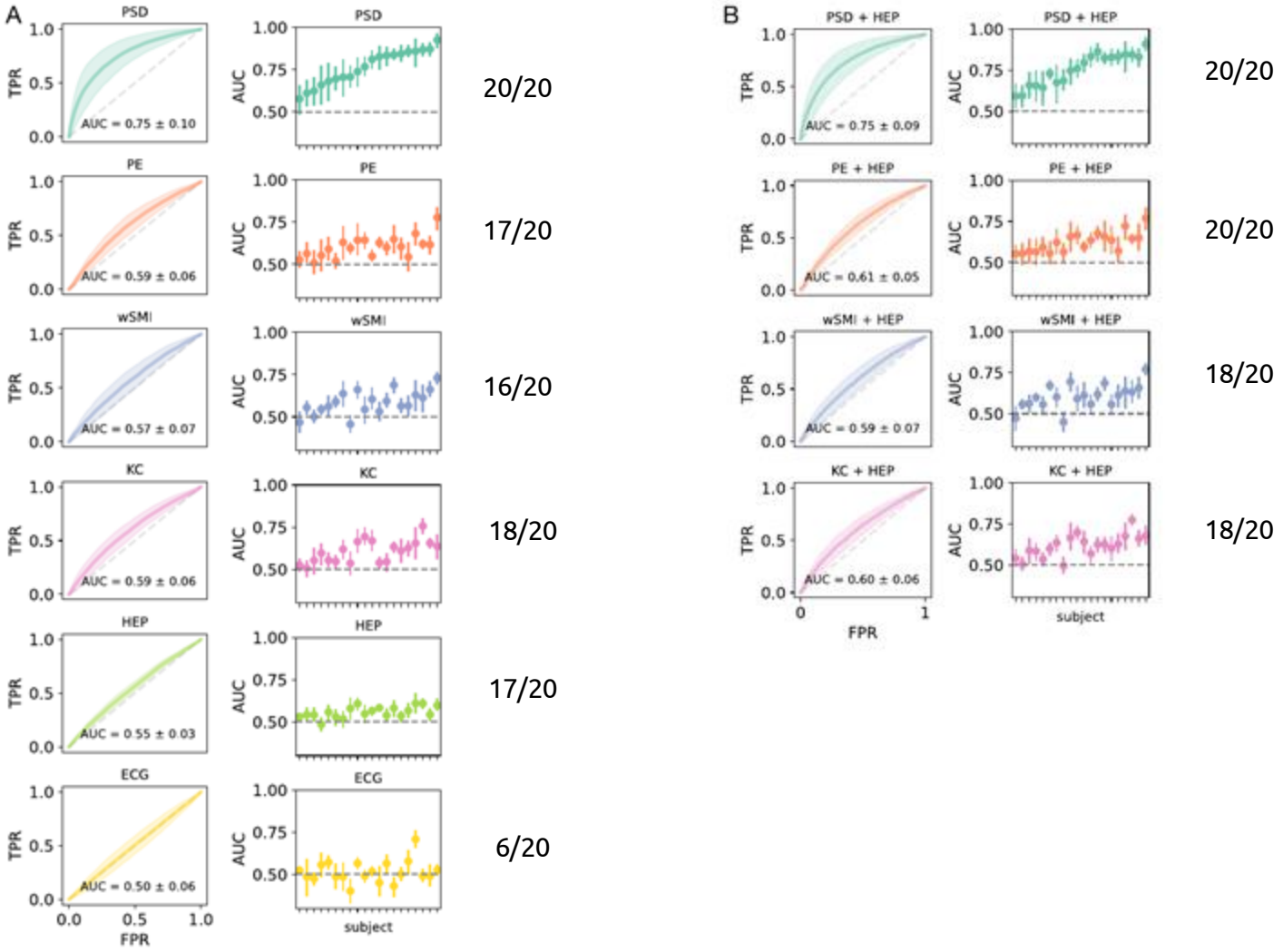


Increased P300 brain response during sound attention

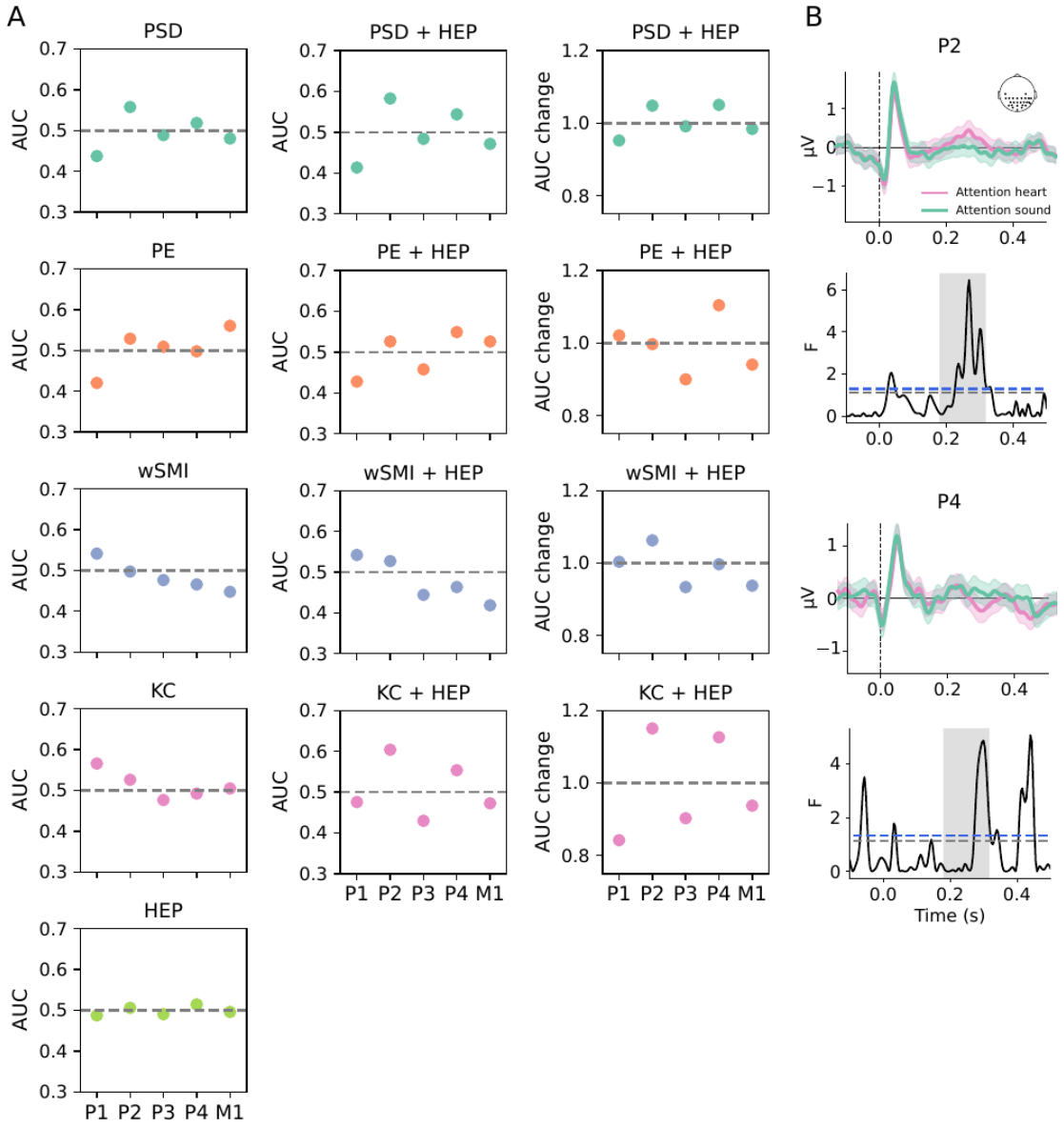
HEP amplitude is modulated by interoceptive-exteroceptive attention



Brain dynamics and brain response to the heart are informative of attention orientation at the individual level.



Brain dynamics and brain response to heartbeats to detect command following in non-communicative patients.



Research lines

Neurophysiological signatures of consciousness-state

Non-invasive stimulation

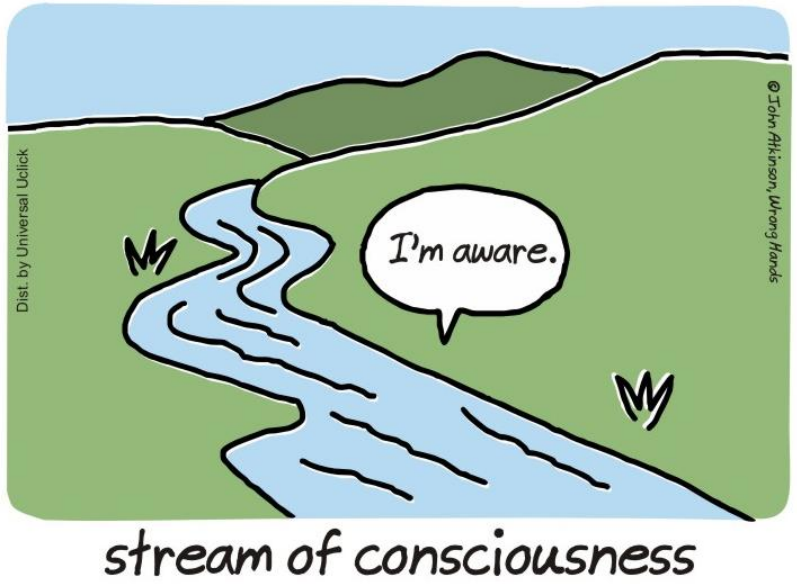
Brain-body interactions

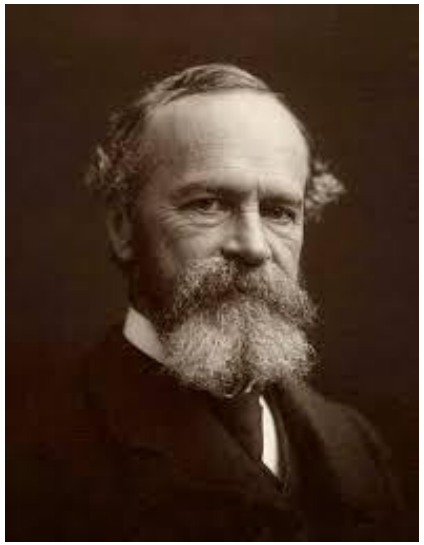
fMRI Dynamics

Computational Modeling

States biomarkers <-> content of consciousness dynamics

Dynamics predictions….

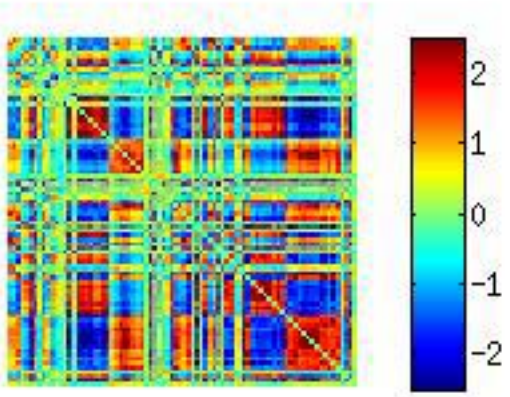


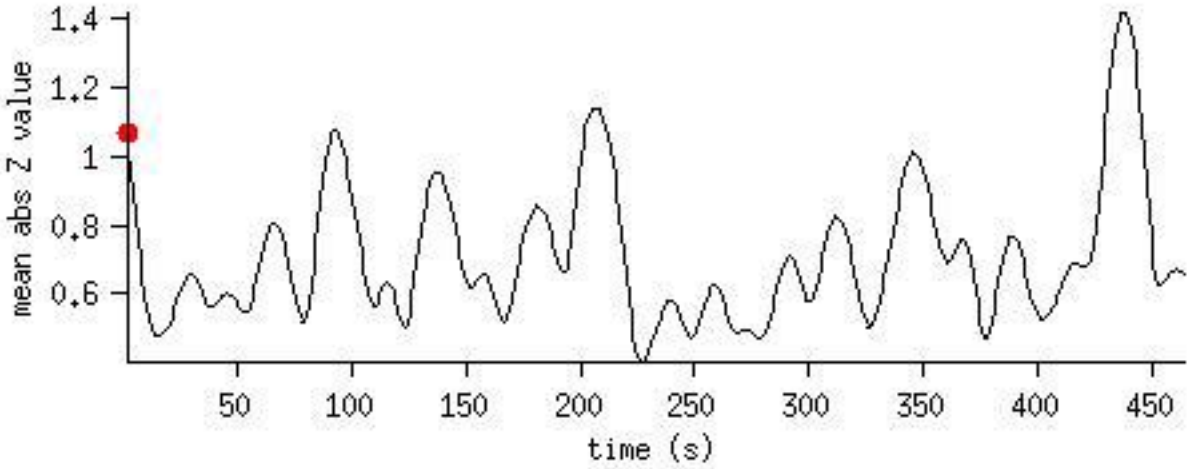


Research program using an experimental model of unconsciousness (anesthesia), non-human primates and neuroimaging

Collaboration with Bechir Jarraya @ Neurospin

fMRI sliding window dynamical patterns



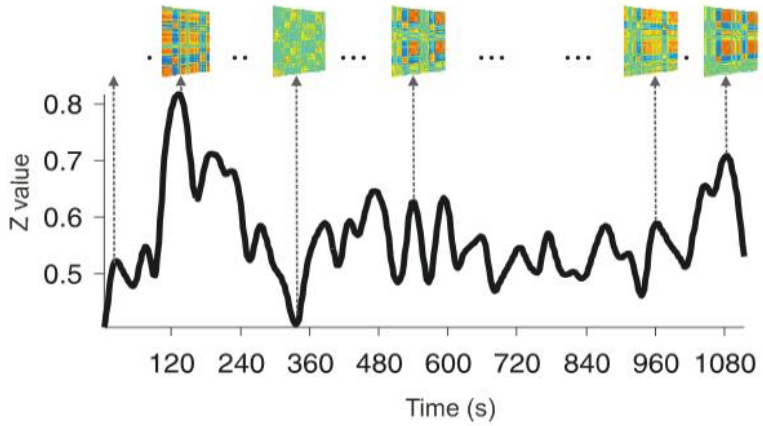


Different patterns emerge and disappear

Conscious state fingerprint?

Signatures of consciousness in the dynamics of fMRI resting-state activity

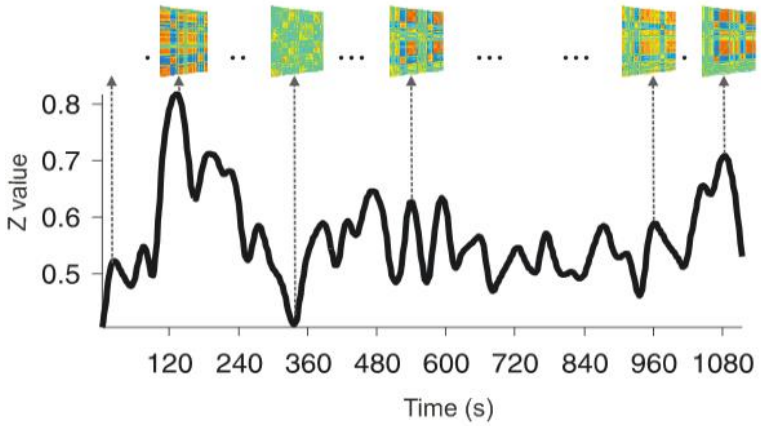
(1) Awake/anesthesia monkey rs-fMRI sessions



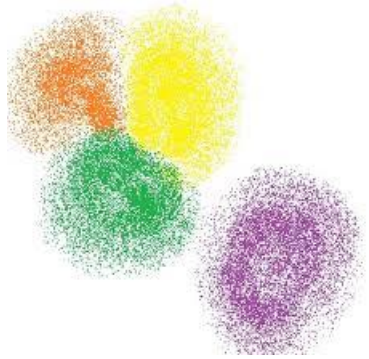
Barttfeld, Uhrig*, Sitt*, et al. (2015) PNAS; Uhrig*, Sitt*, et al. (2018) Anesthesiology*

Signatures of consciousness in the dynamics of fMRI resting-state activity

(1) Awake/anesthesia monkey rs-fMRI sessions



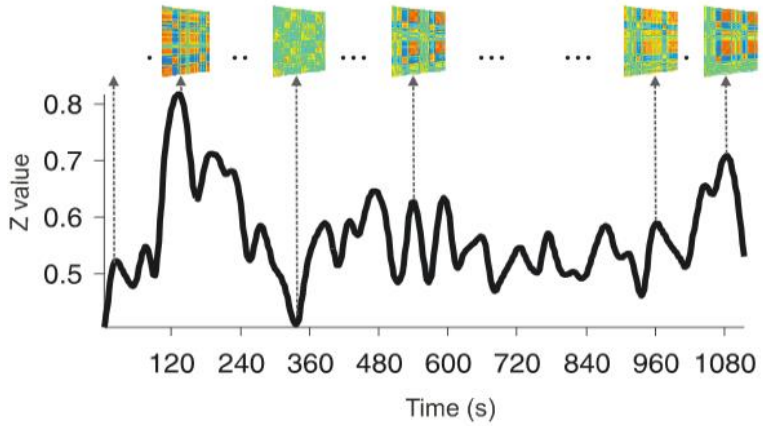
(2) Unsupervised 'brain-pattern' classification



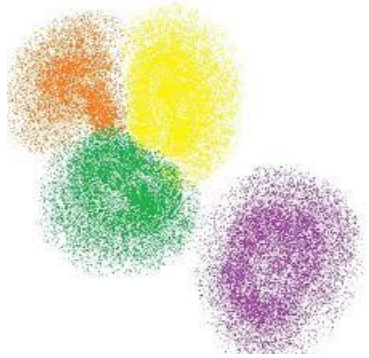
Barttfeld, Uhrig*, Sitt*, et al. (2015) PNAS; Uhrig*, Sitt*, et al. (2018) Anesthesiology*

Signatures of consciousness in the dynamics of fMRI resting-state activity

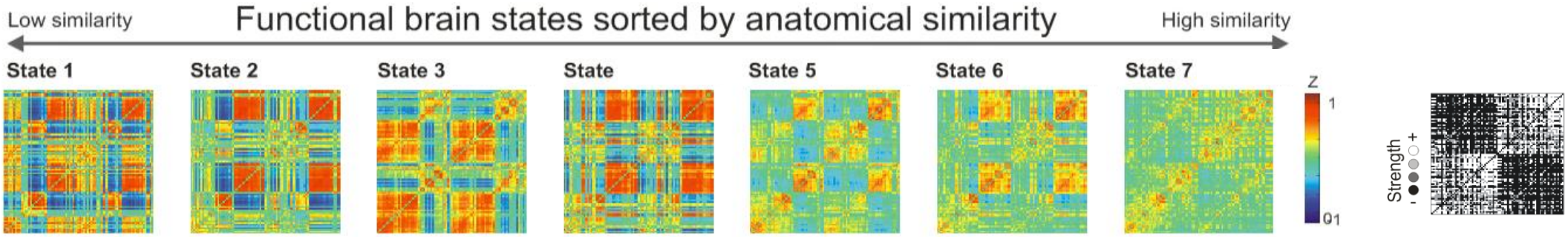
(1) Awake/anesthesia monkey rs-fMRI sessions



(2) Unsupervised 'brain-patterns' classification

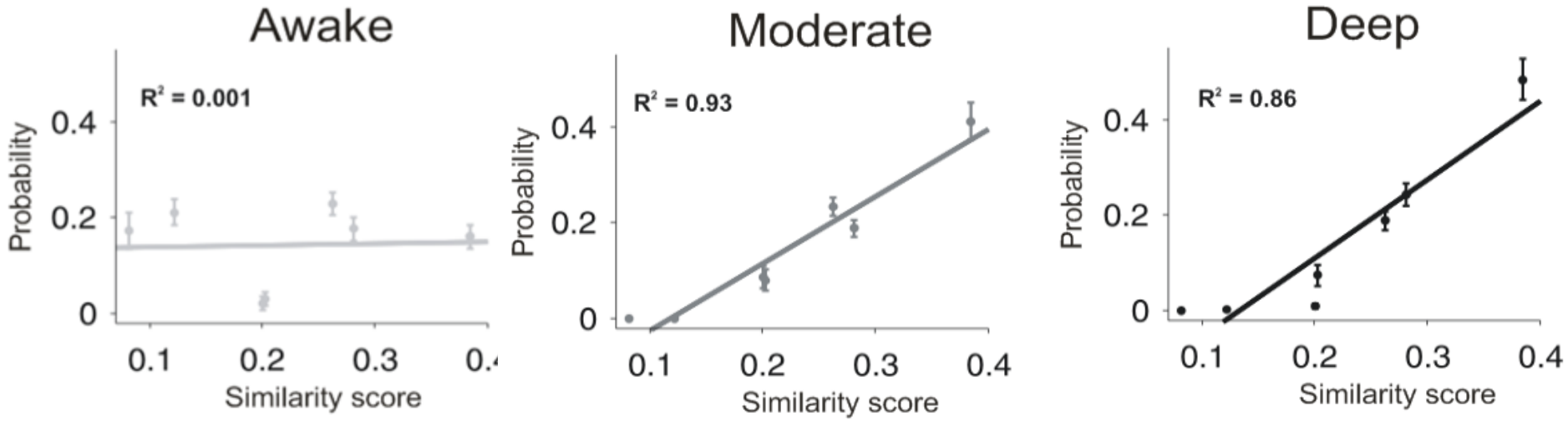


(3) 'brain-patterns' characterization by similarity to structural connectivity



Barttfeld, Uhrig*, Sitt*, et al. (2015) PNAS; Uhrig*, Sitt*, et al. (2018) Anesthesiology*

Probability of 'brain-patterns' is a direct function of anesthesia level



•On awake condition, the brain freely explores all states. No relation exists between probability and structural connectivity.

• Under anesthesia, the exploration is restricted and **dominated by the states that resemble the anatomical connectivity.**

Barttfeld, Uhrig*, Sitt*, et al. (2015) PNAS; Uhrig*, Sitt*, et al. (2018) Anesthesiology*

DOC fMRI dynamics a multi-centric study

159 fMRI recordings

4 clinical sites (Paris, Liege, NY, London-ont-)

47 healthy controls

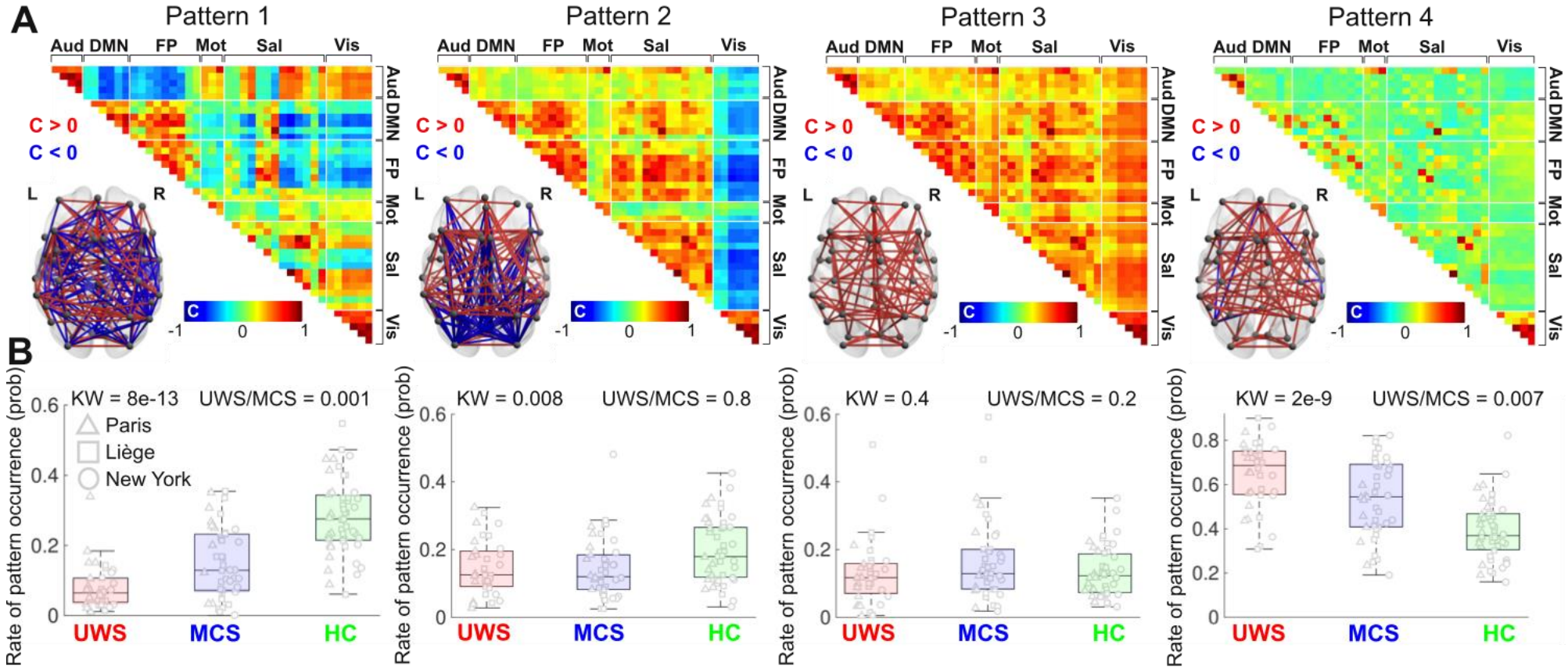
89 awake patients (42 MCS, 47 VS)

23 anesthetized patients (3 EMCS, 14 MCS,6 VS)

Athina Dermetzi
Enzo Tagliazuchi

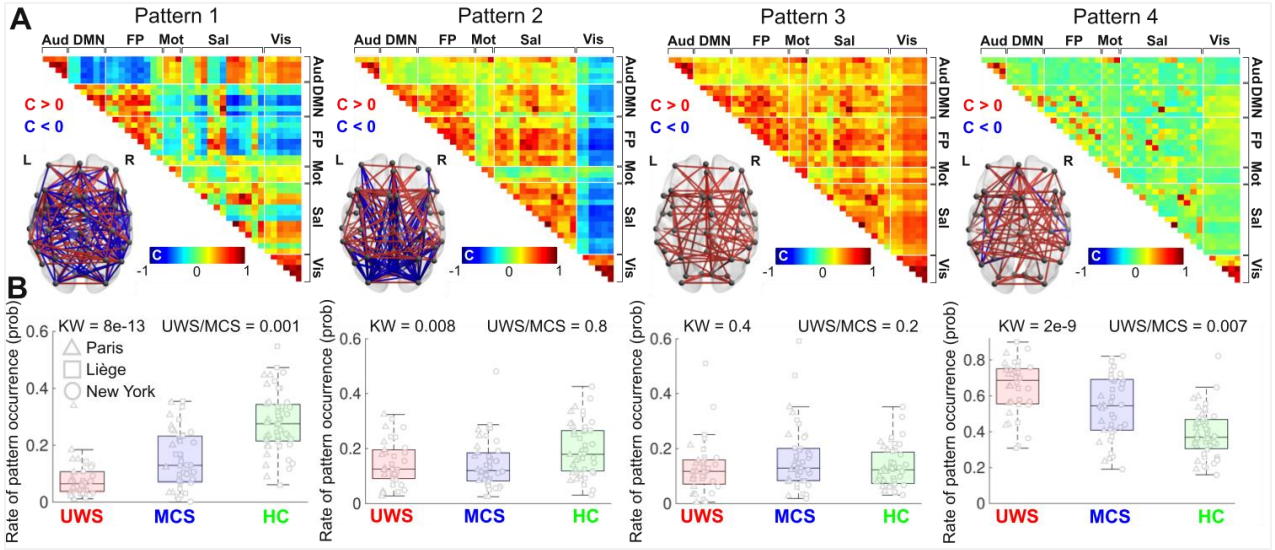
Science Advances
AAAS

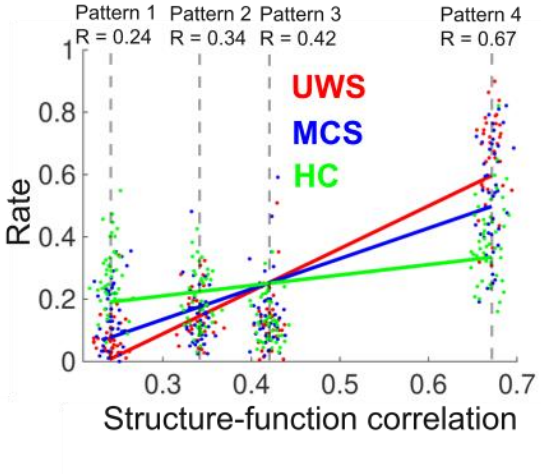
DOC fMRI dynamics a multi-centric study

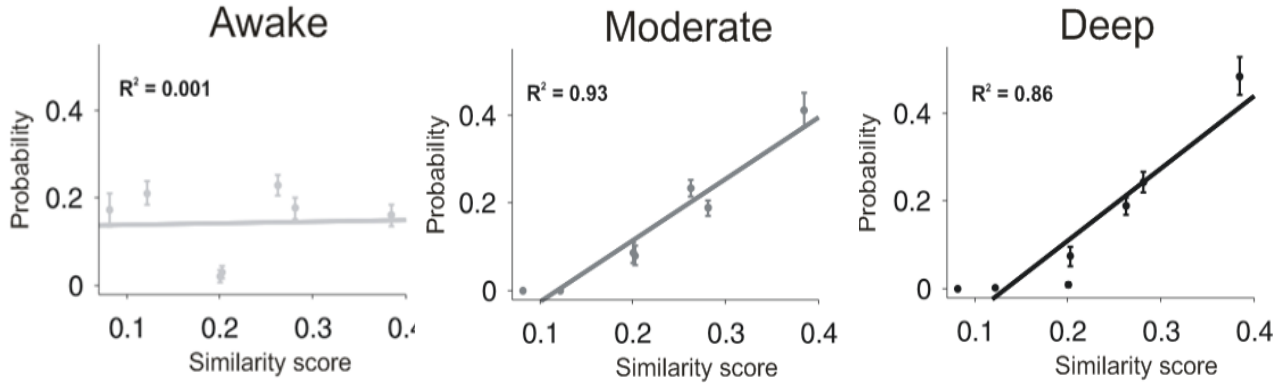


Demertzi, Tagliazucchi*, …, Sitt. Science Advances (2019)*

fMRI DOC multi-centric study

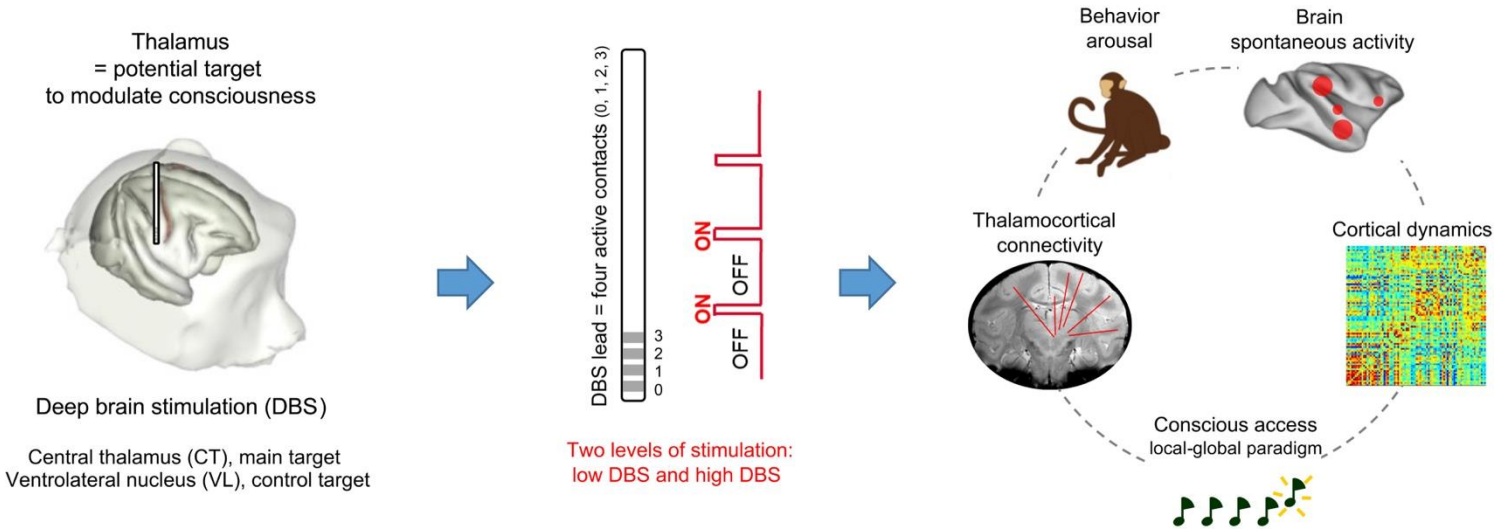


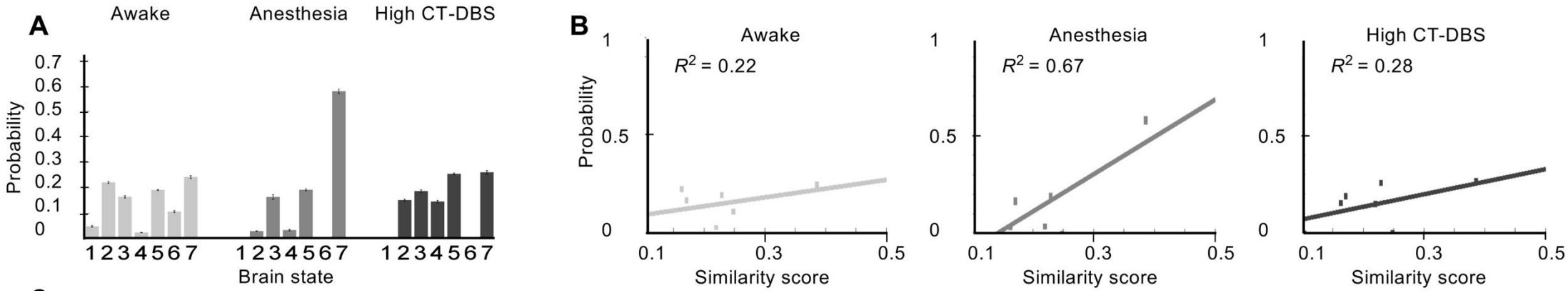




Demertzi, Tagliazucchi*, …, Sitt. Science Advances (2019)*

Thalamic DBS to restore consciousness





*Tasserie et al (2022) Science adv / **tDCS** Hoffner et al eLife (2024)*

Science Advances

AAAS

Research lines

Neurophysiological signatures of consciousness-state

Non-invasive stimulation

Brain-body interactions

fMRI Dynamics

Computational Modeling

States biomarkers <-> content of consciousness dynamics

Conscious content?

Brain pattern dynamics during movie watching

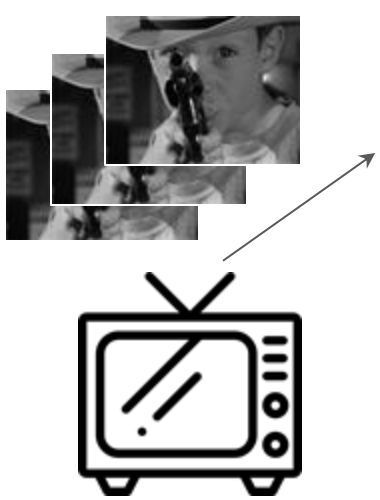
Basak Turker

Lorina Naci
Adrian Owen

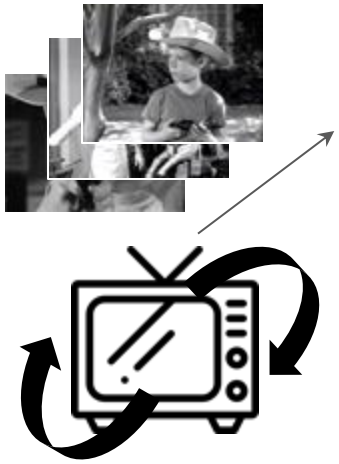
Conscious content

Attention to movies synchronizes brain states

Turker, … , **SITT Scientific Reports** 2023



Regular Movie



Scrambled Movie

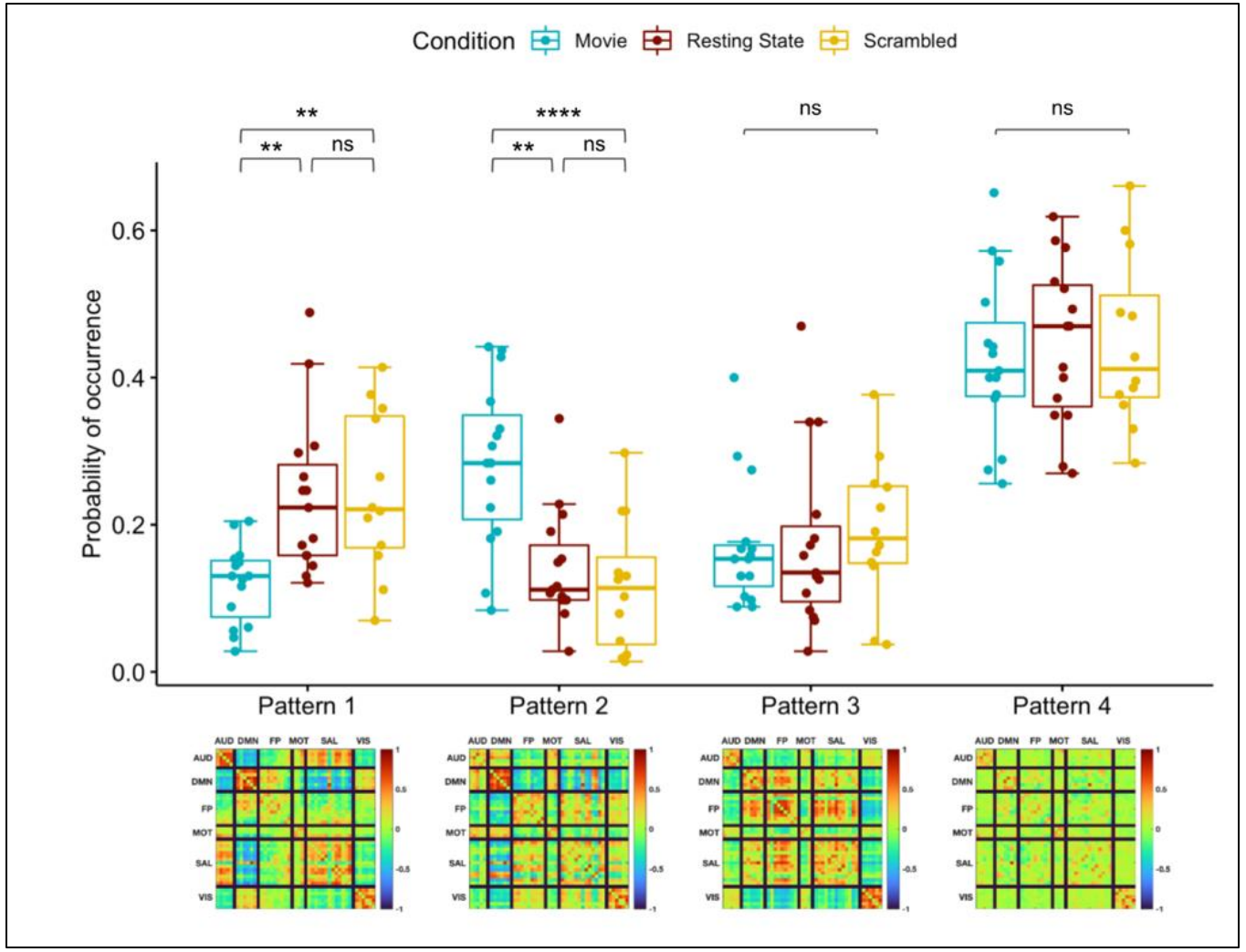
Resting State

Conscious content

Attention to movies synchronizes brain states

Turker, … , **SITT**
Scientific Reports 2023

Emergence of "specific" patterns associated to the task

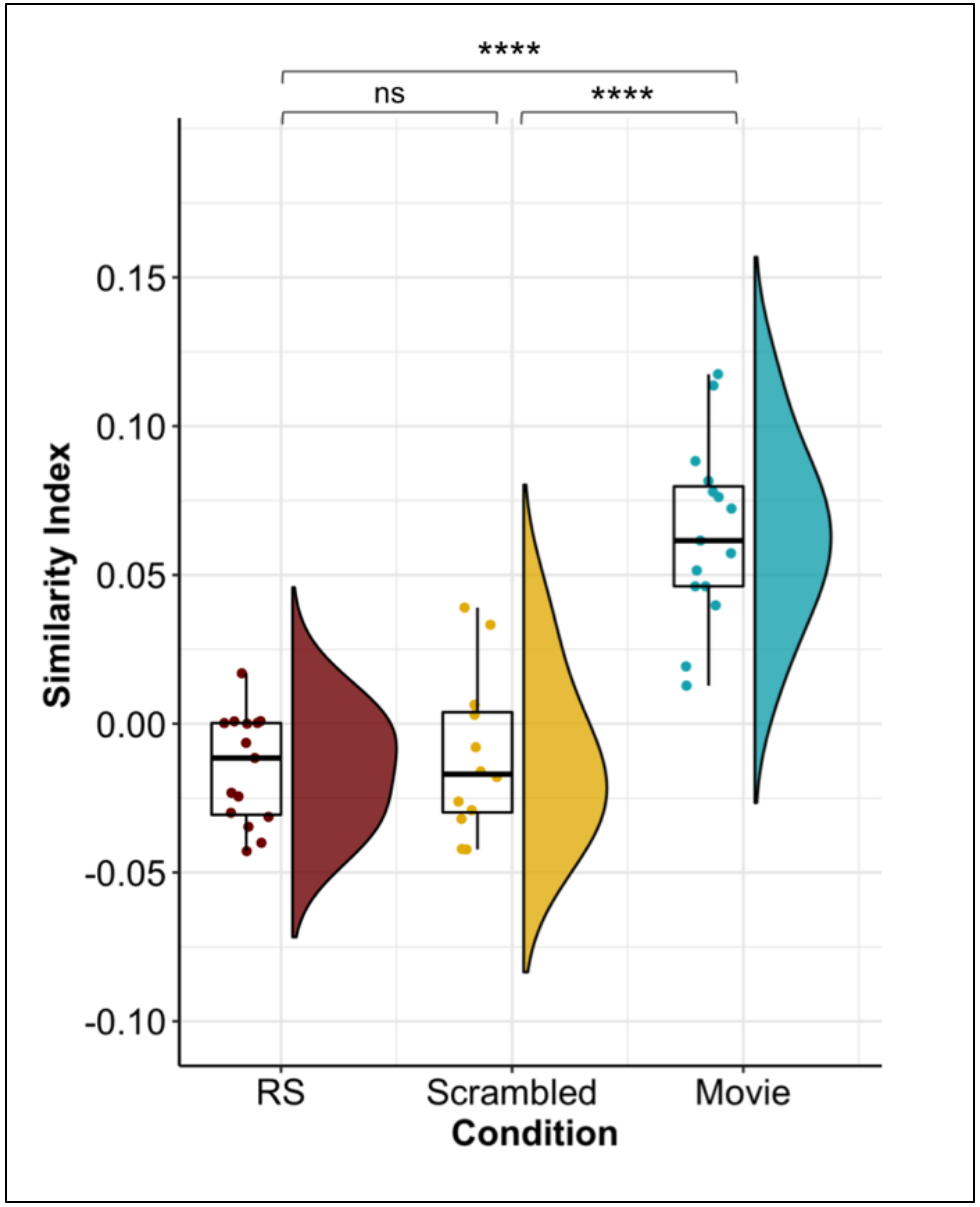


Conscious content

Attention to movies synchronizes brain states

Turker, … , **SITT**
Scientific Reports 2023

Synchronization across individuals of brain patterns only in the movie condition

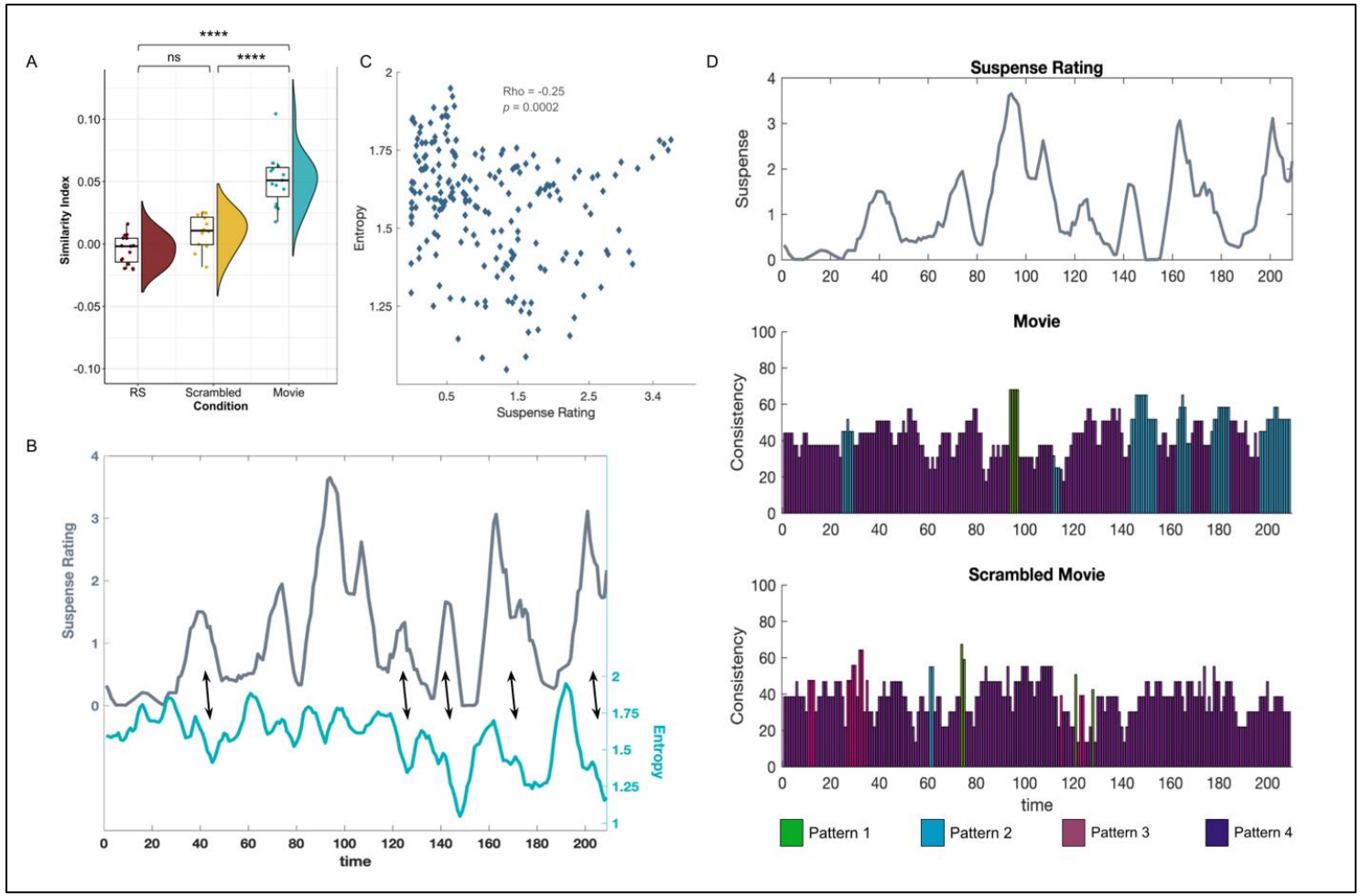


Conscious content

Attention to movies synchronizes brain states

Turker, … , **SITT**
Scientific Reports 2023

Synchronization across individuals increases with level of suspense in the movie



Conscious content

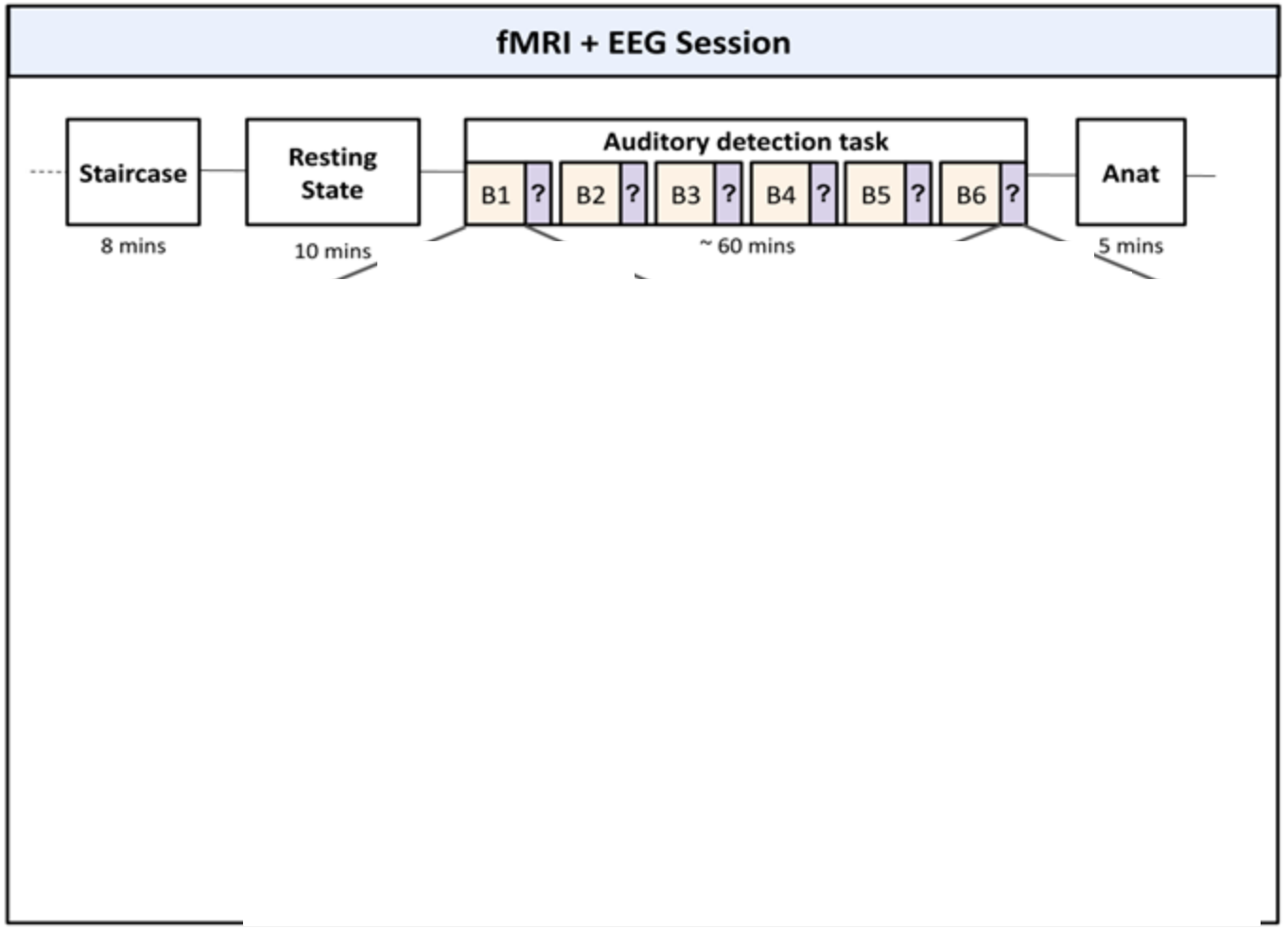
Brain pattern dynamics predicts conscious access

Basak Turker

Claire Sergent

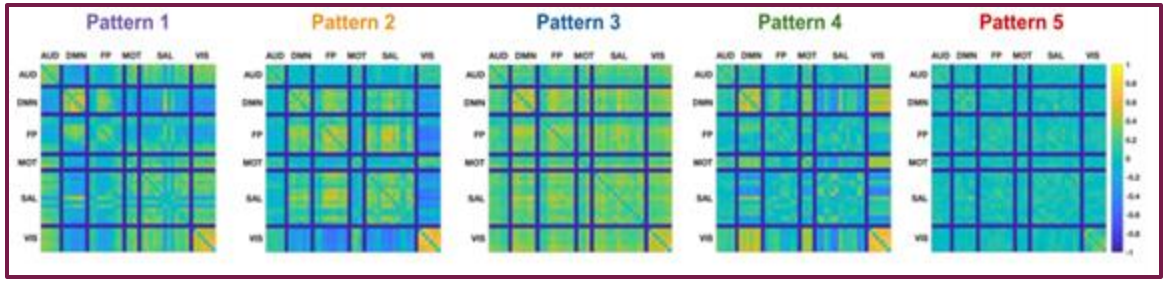
Design

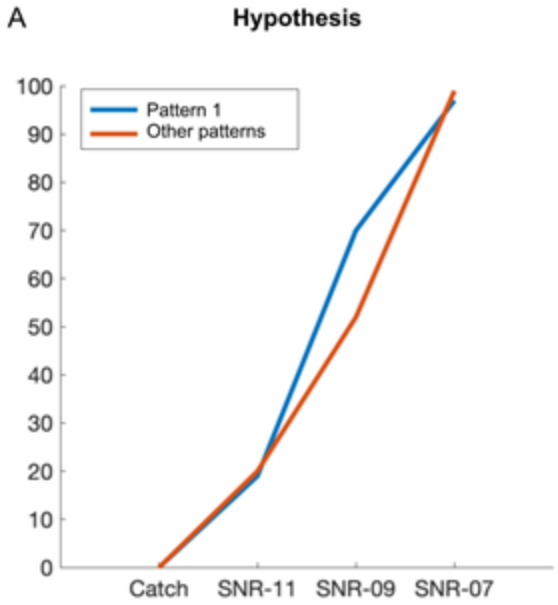
- Simultaneous EEG and fMRI acquisitions
- 25 participants (13 women, mean age: 24.6 ± 4.2)
- Native French speakers



Sergent al. *Nature Communications* (2021)

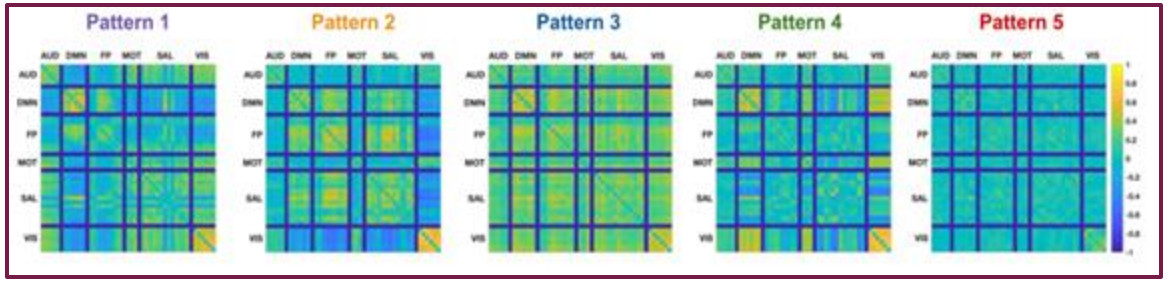
Hypothesis and results

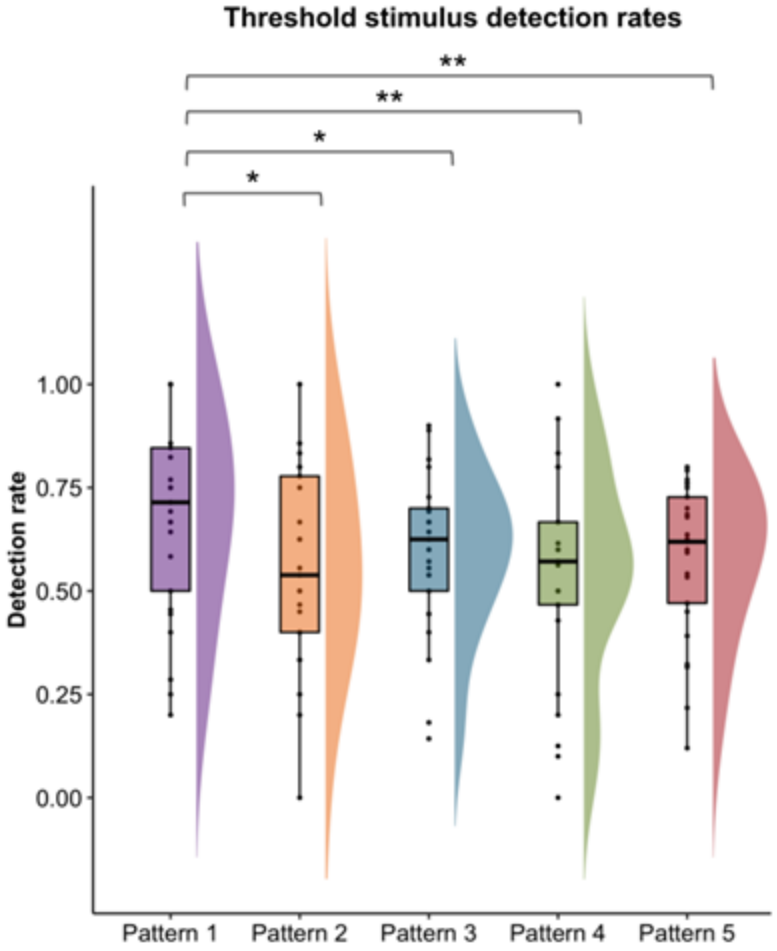


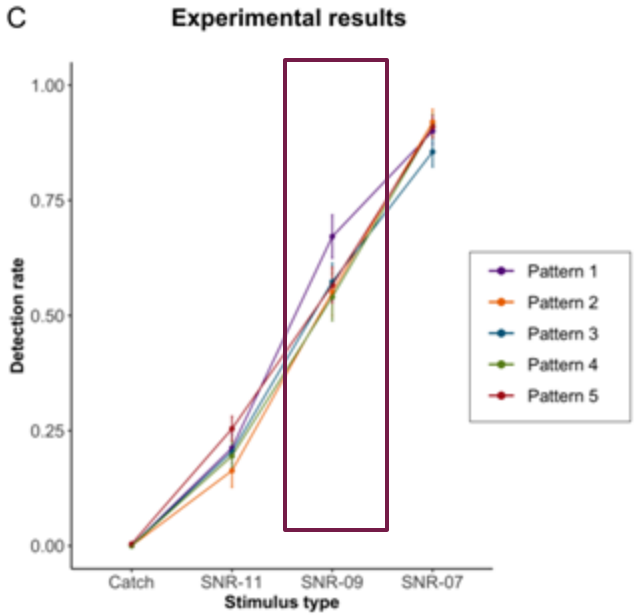


Turker, B., … , & Sitt, JD. *Communication Biology (2024)*

Results

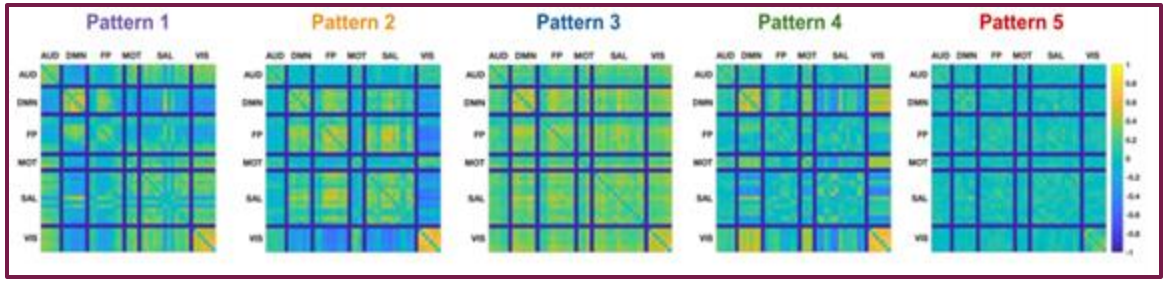


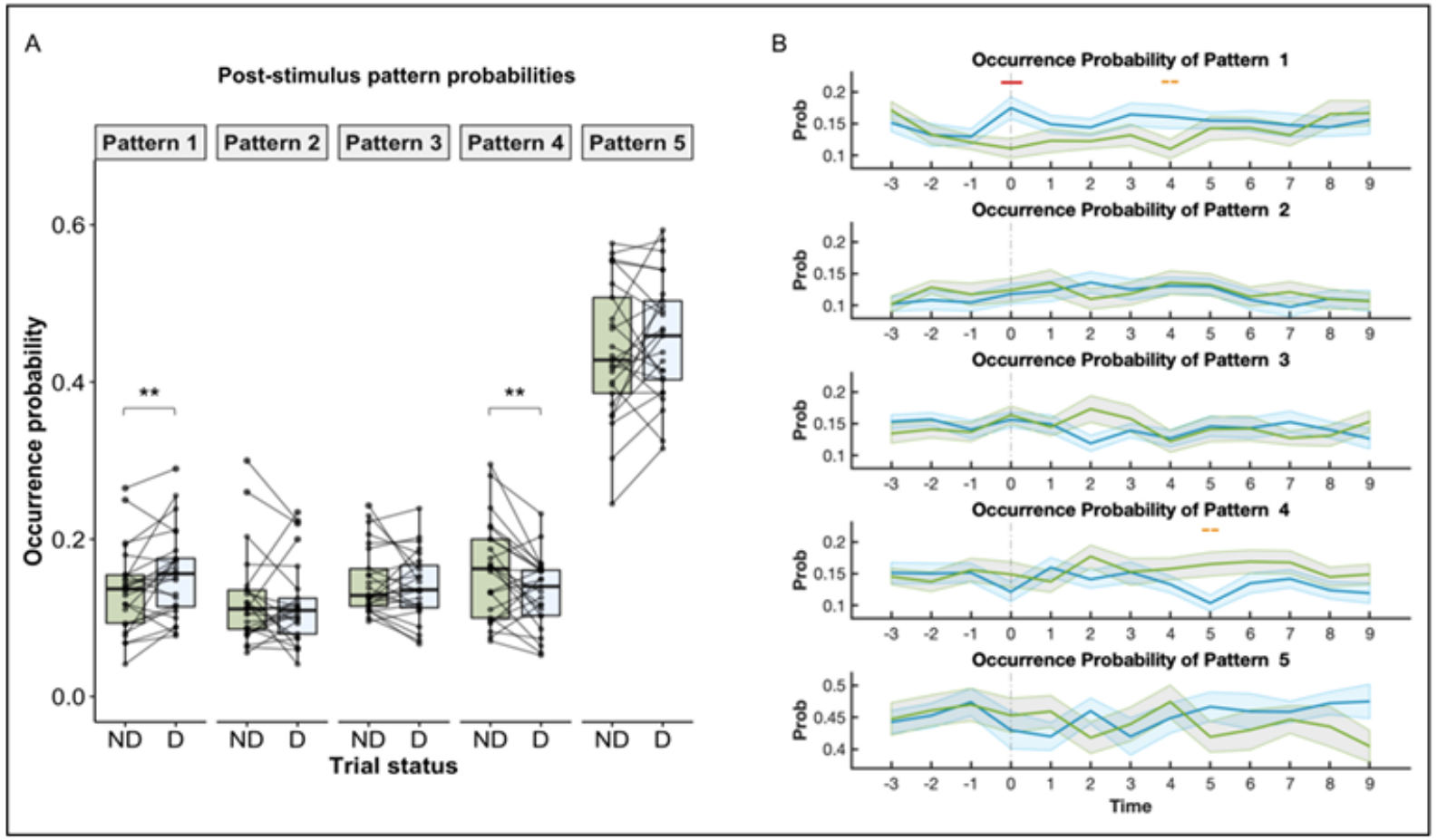




Turker, B., … , & Sitt, JD. *Communication Biology (2024)*

Results





Post conscious access also affects the brain pattern dynamics

Turker, B., … , & Sitt, JD. *Communication Biology (2024)*

Take home messages…

- Generalization and out-of-sample validation of our EEG consciousness markers. Automated web-based pipeline.
- New exciting brain-body biomarkers
- Clinical validation of dynamic fMRI global brain patterns as markers of conscious and content states

Thanks!

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Ivan Mindlin

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Athena Demertzi, CSG, Liege, Belgium

Federico Raimondo, Jūlich, Germany

PerBrain consortium (Munich, Milan, Rehovot)

ModelDX consortium (Liege, Cluj, Barcelona)

jacobo.sitt@icm-institute.org. Open PhD / PostDoc positions, come chat!

#ERAPerMed FLAG-ERA ICM Paris Brain Institute Inserm La science pour la santé From science to health