Fundamentals Human Neuropsychology
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Paris

At the Limits of Consciousness

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University of Liège
BELGIUM

LIÈGE université
GIGA
CRC Human Imaging

Consciousness

awareness

perception

cognition

imagination

thought

mind

experience

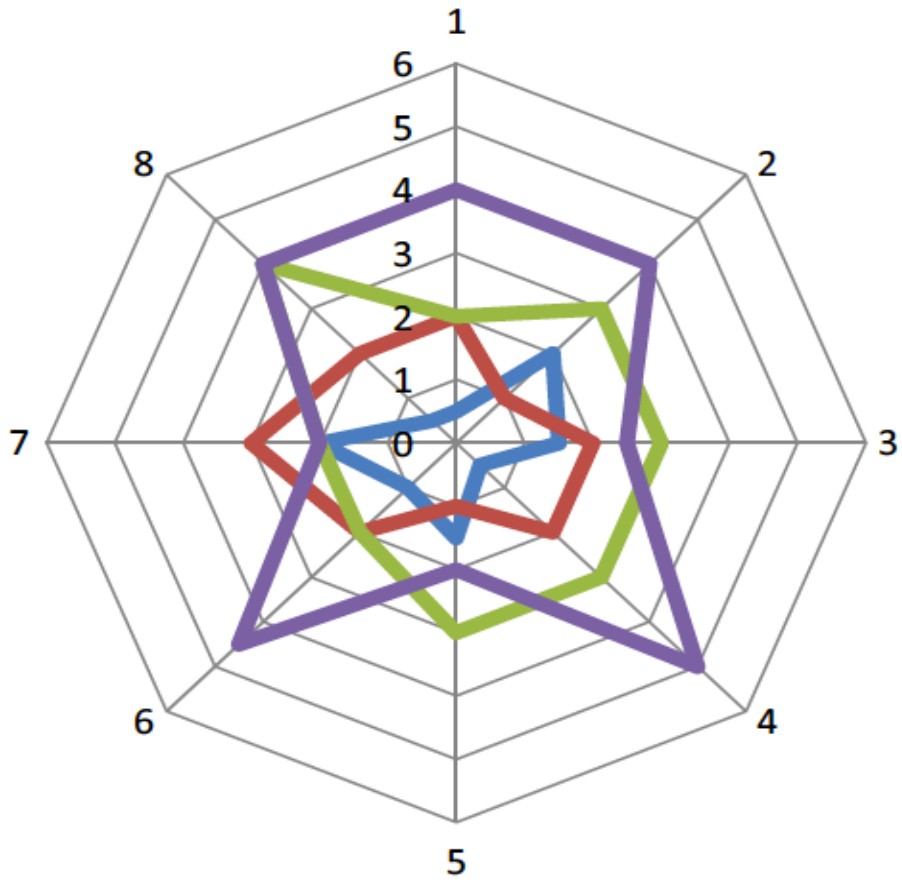
self-awareness

NeuroEthics

Animals

Psychotherapy

Consciousness is multidimensional



Bayne, Hohwy, Owen. *Trends Cogn Sci* 2016

Which are these dimensions?

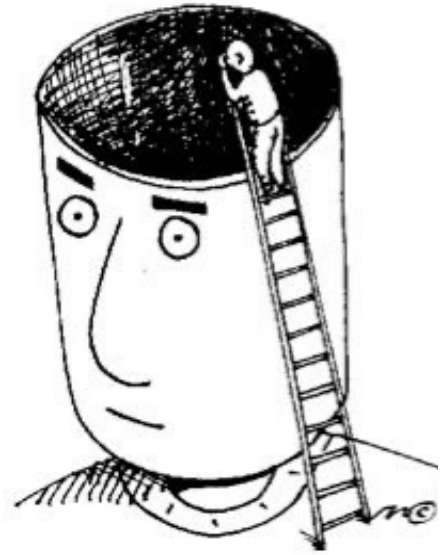
How can I measure them?

Why does it matter?

Approaches to Consciousness

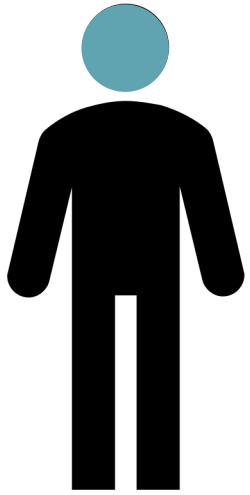
Clinical

Disorders of Consciousness



Wakefulness

Mind Blanking



Embodiment

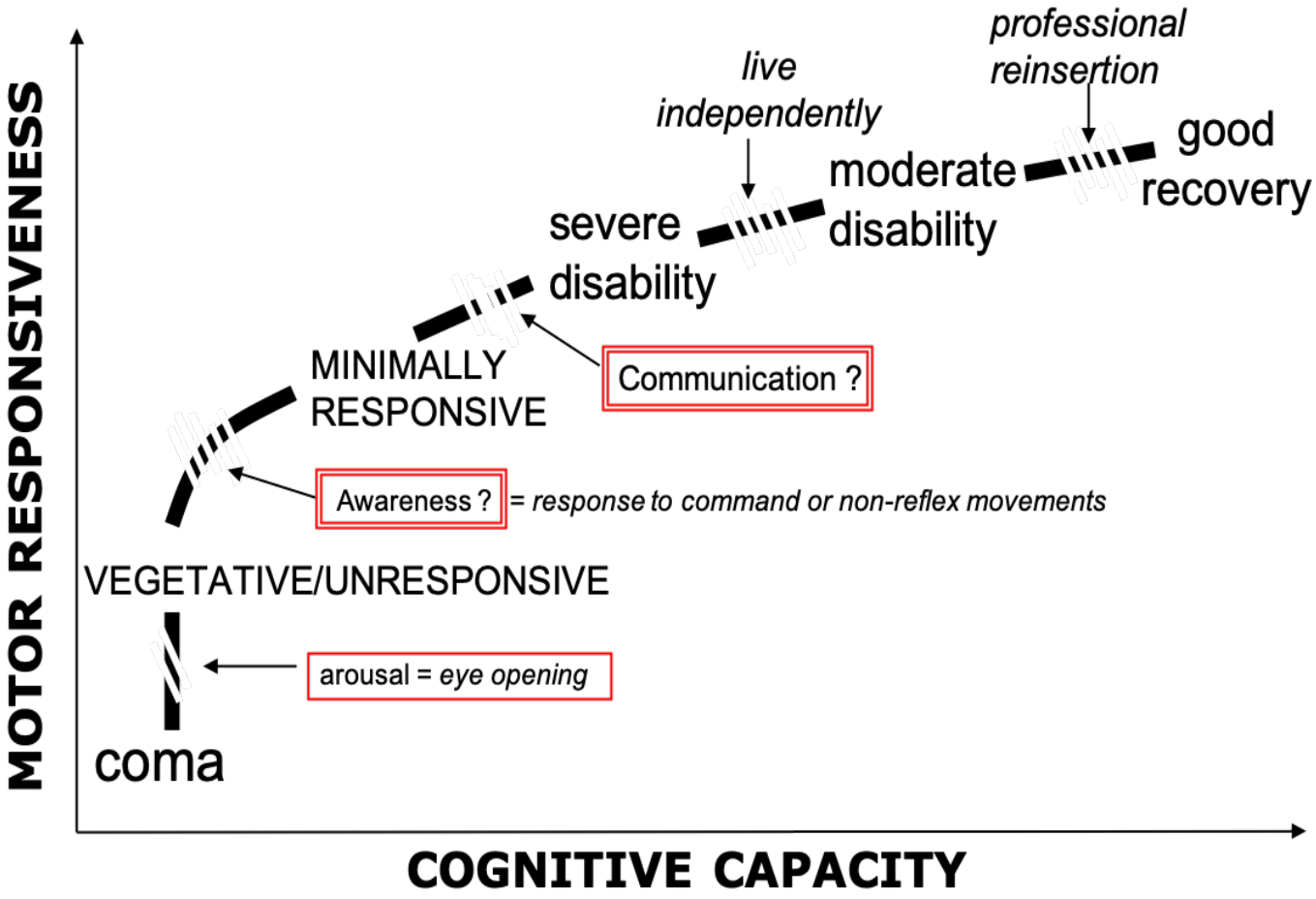
Brain-Body Interactions

PART 1

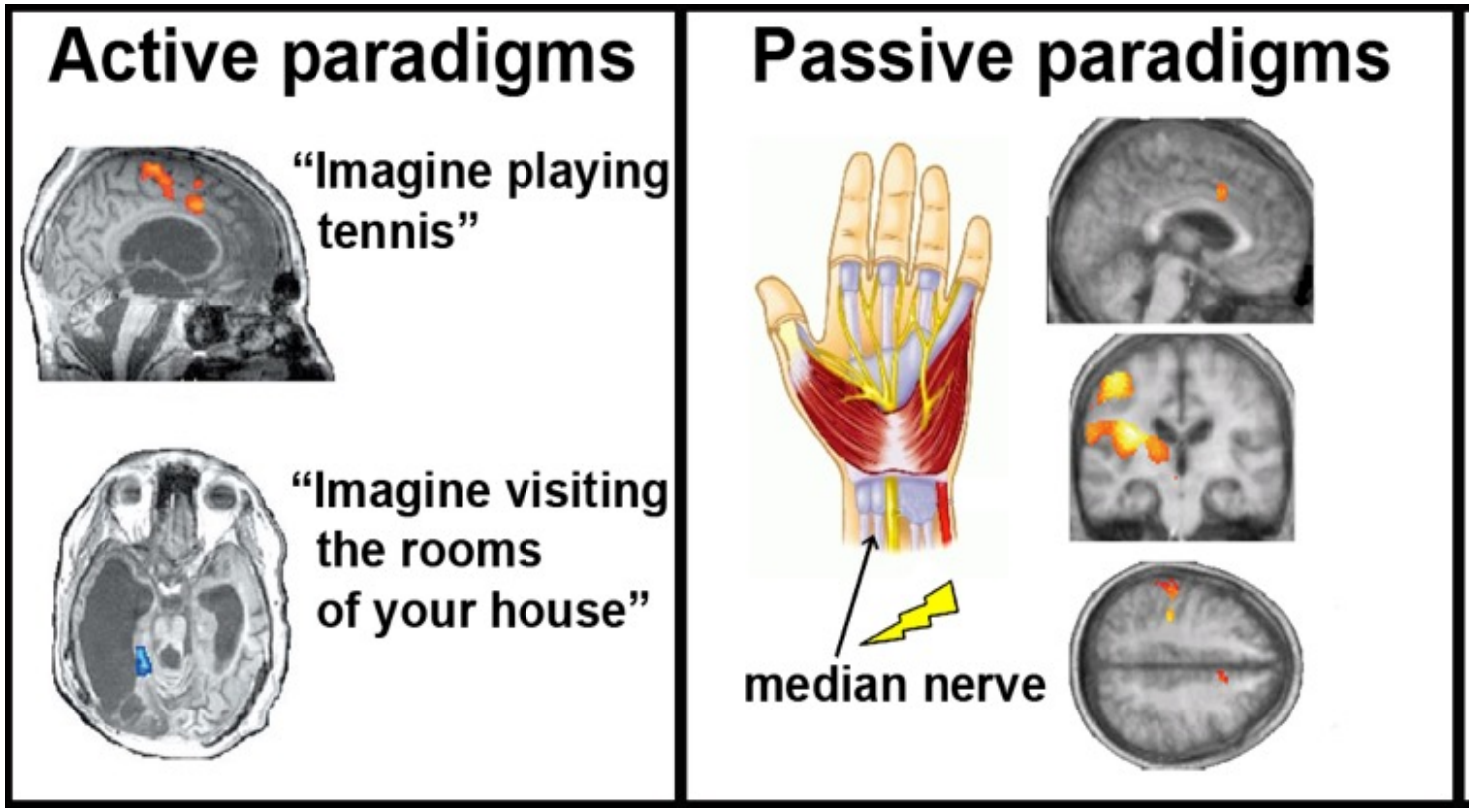
The Clinical Paradigm

Terri Schiavo °1963
Cardiac arrest-vegetative 1990
† 2005 USA

Inferring Consciousness from Behavior



Inferring Consciousness from Neuroimaging



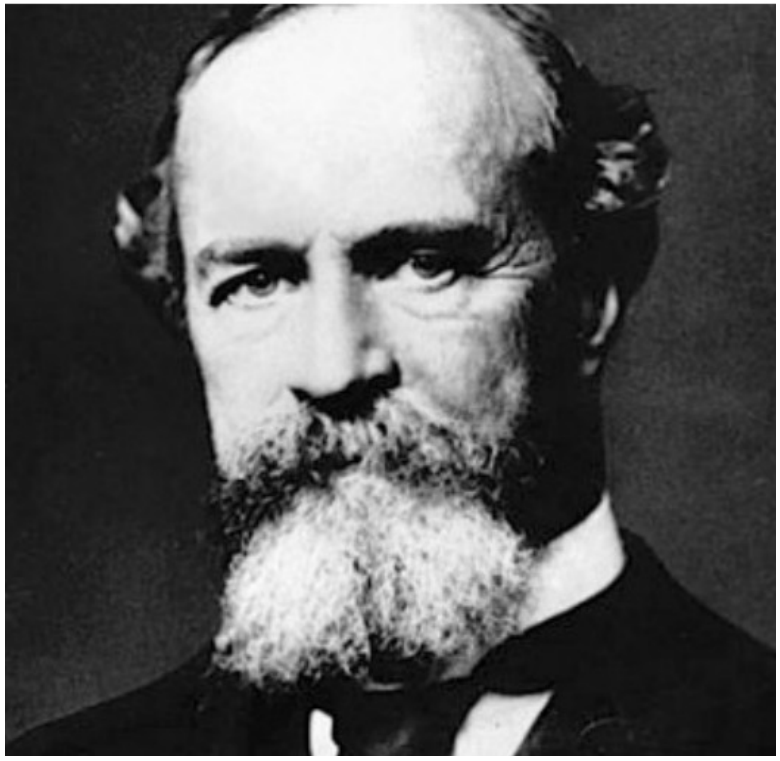
Owen et al, *Science* 2006
Monti & Vanhaudenhuyse et al, *NEJM* 2010

Boly et al, *Lancet Neurol* 2008

The Spontaneous mind

The stream of thought (Chapter IX)

The principles of psychology 1890



William James (1842-1910)

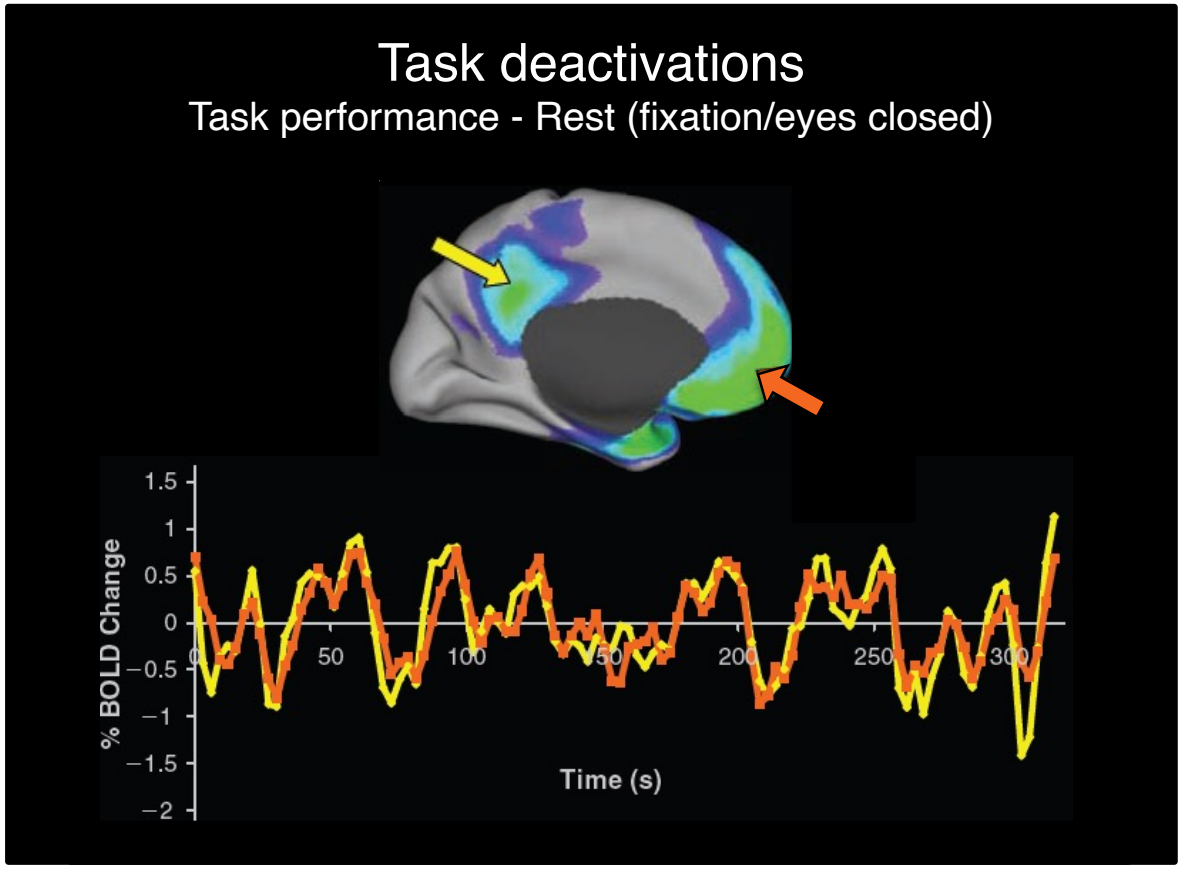
Resting …costs

- The human brain ~2% body's weight
- 80% of its energy for neuronal signaling
- Evoked changes <5%

While conscious awareness is […] energetically inexpensive, it is dependent upon a very complex, dynamically organize state of the brain that is achieved at great expense

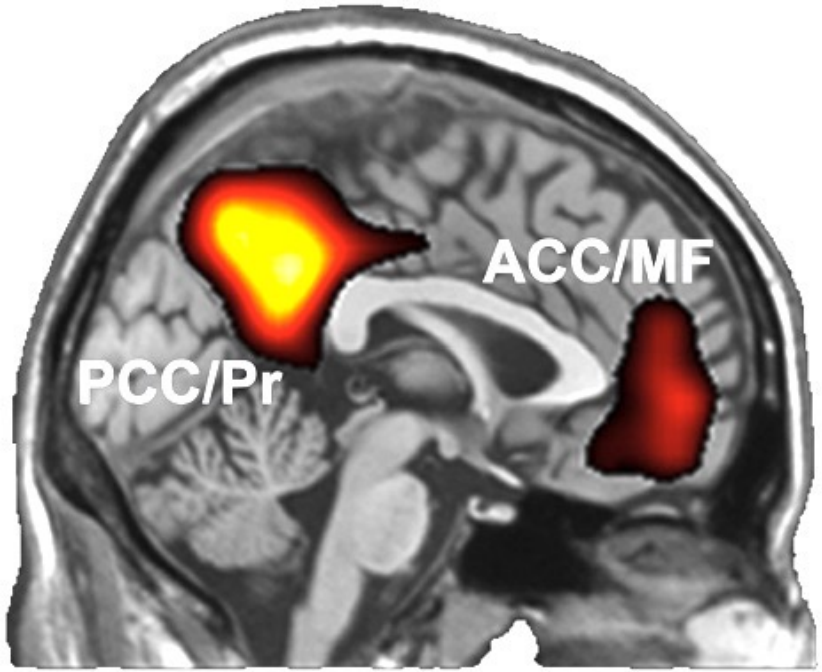
Raichle & Snyder, 2009 In: Laureys S, Tononi G *The Neurology of Consciousness*. Oxford: Elsevier Academic Press

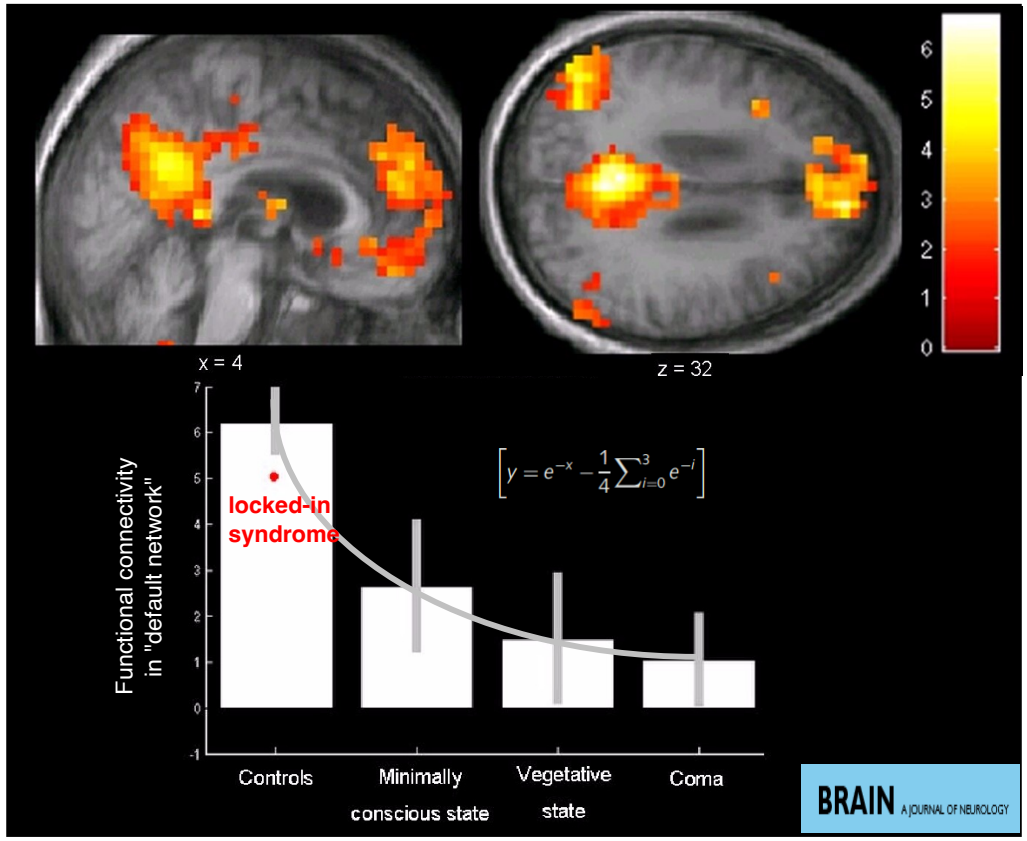
Default mode of function



Demertzi & Whitfield-Gabrieli, in: Neurology of Consciousness 2nd ed. 2015
Demertzi, Soddu, Laureys, *Curr Opin Neurobiology* 2013
Demertzi et al, *Front Hum Neurosci* 2013
Raichle et al, *PNAS* 2001

The Default Mode Network

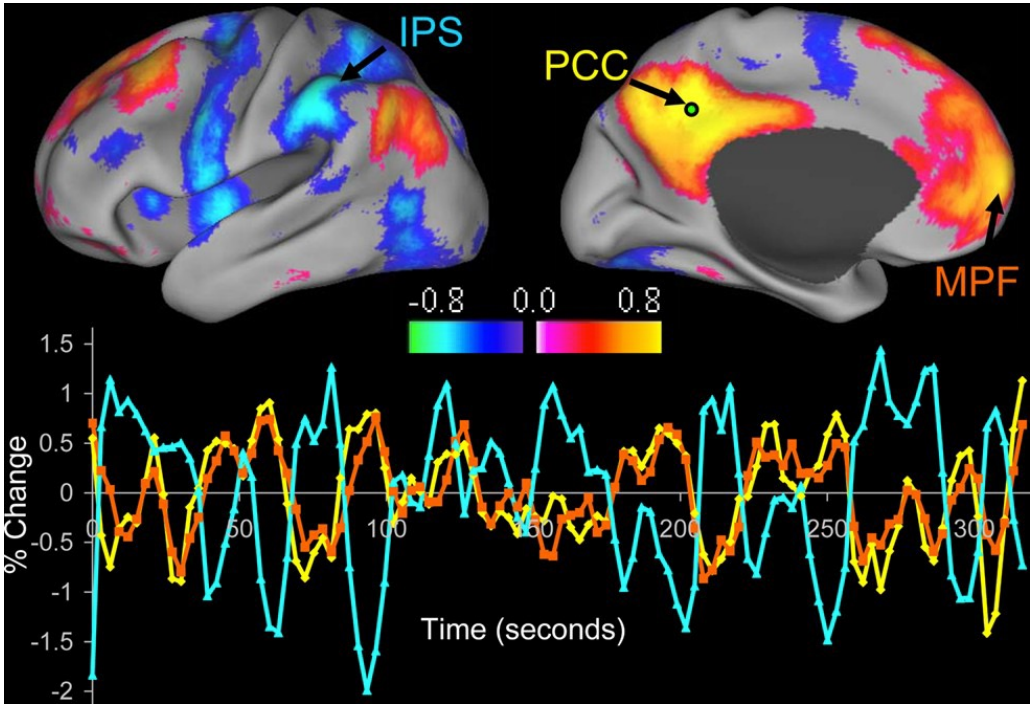




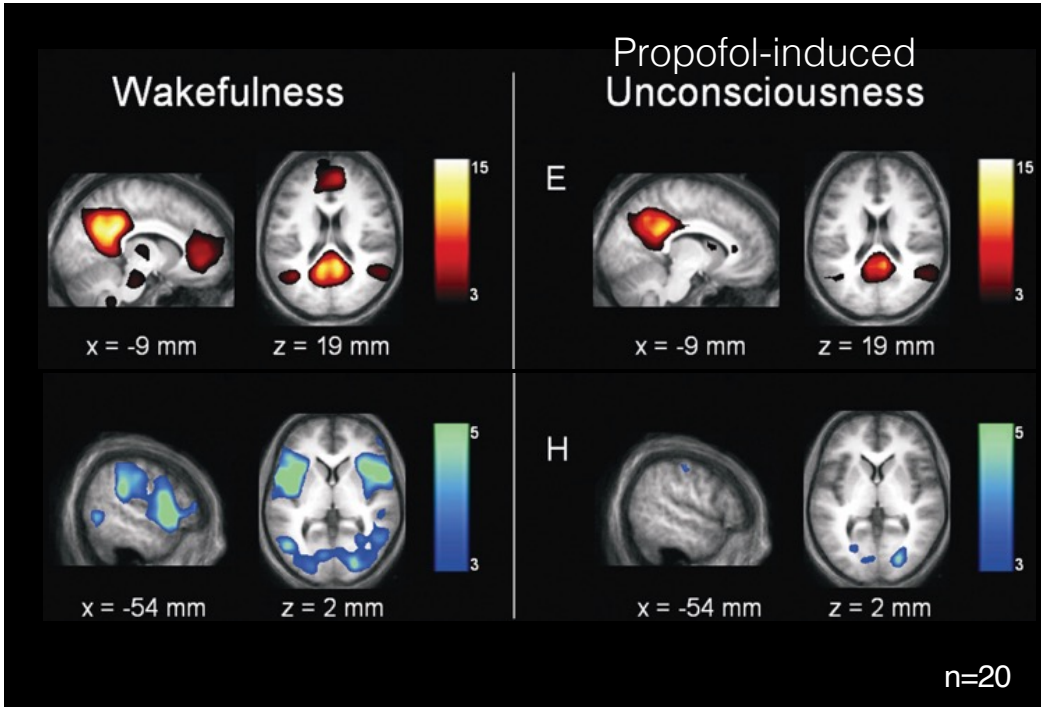
Demertzi & Whitfield-Gabrieli, in: Neurology of Consciousness 2nd ed. 2015
Demertzi, Soddu, Laureys, *Curr Opin Neurobiology* 2013
Demertzi et al, *Front Hum Neurosci* 2013
Raichle et al, *PNAS* 2001

Vanhaudenhuyse & Noirhomme et al, *Brain* 2010

Functional Anticorrelations



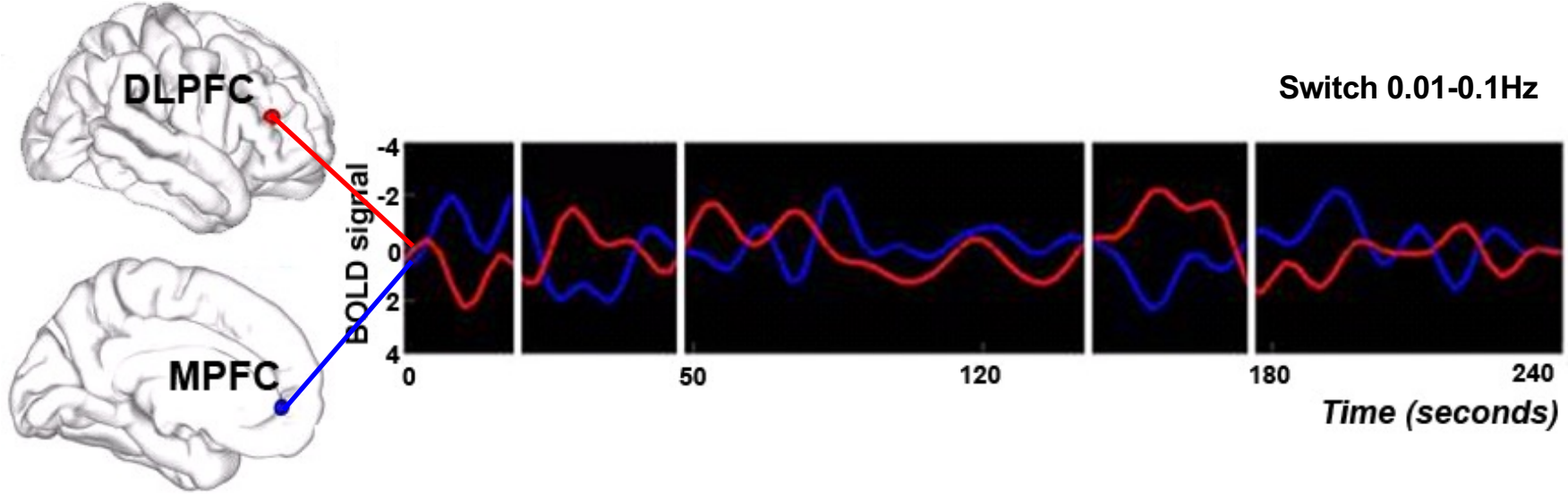
Fox et al, *PNAS* 2005



Boveroux et al, *Anesthesiology* 2010

Anticorrelations reflect cognition

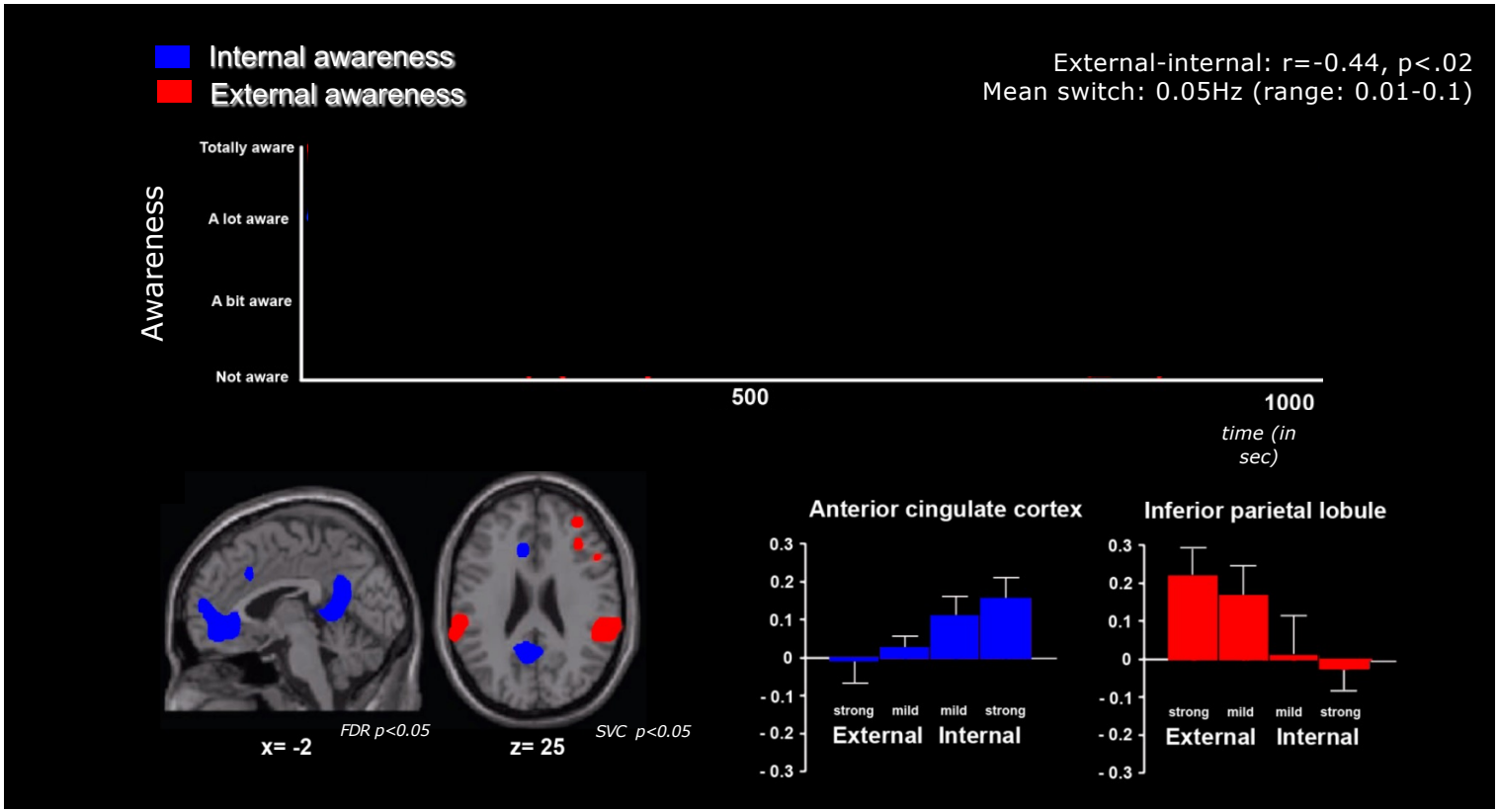
External awareness
***or* anticorrelated network**



Internal awareness
***or* Default mode network**

Demertzi & Whitfield-Gabrieli, in: *Neurology of Consciousness* 2nd ed. *2015*
Demertzi, Soddu, Laureys, *Curr Opin Neurobiology* 2013
Demertzi et al, *Front Hum Neurosci* 2013

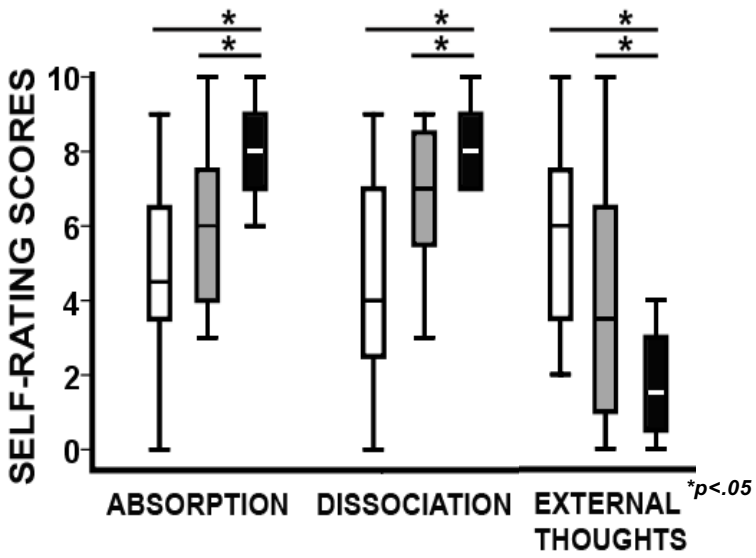
Anticorrelations reflect cognition

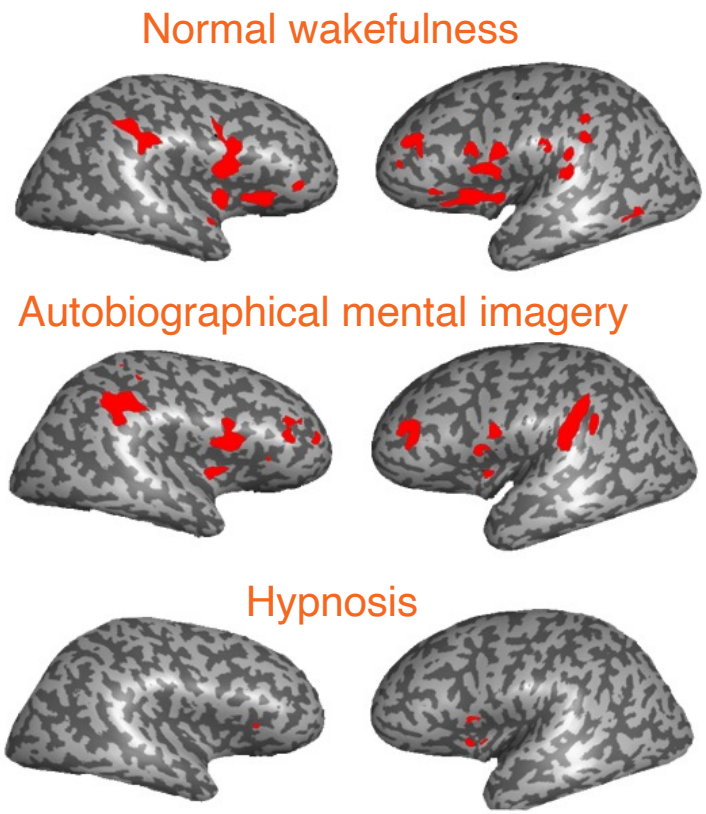


Vanhaudenhuyse*, Demertzi* et al, *J Cogn Neurosci* 2011

Anticorrelations are reduced in hypnosis

- ☐ Normal wakefulness
- ☐ Autobiographical mental imagery
- ■ Hypnosis



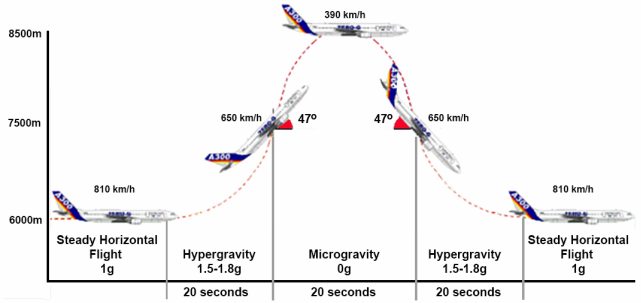


p<0.05 corrected for multiple comparisons

Demertzi, Soddu, Faymonville et al, *Prog Brain Res* 2011
Demertzi, Vanhaudenhuyse, Noirhomme, Faymonville, Laureys, *J Physiol Paris* 2015

Anticorrelations reduced after exposure to extreme environments

Parabolic flight

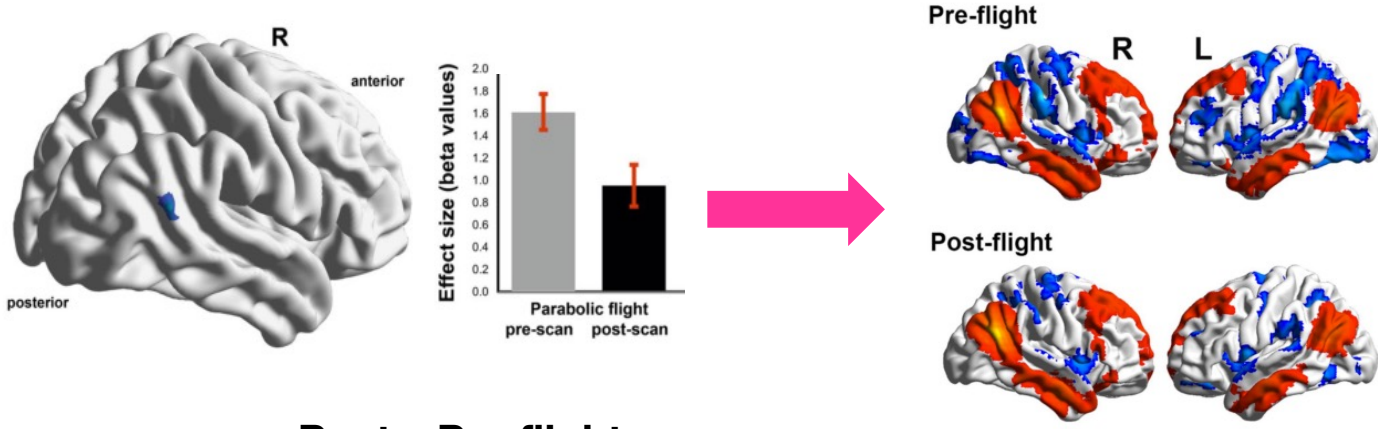


Flight trajectory

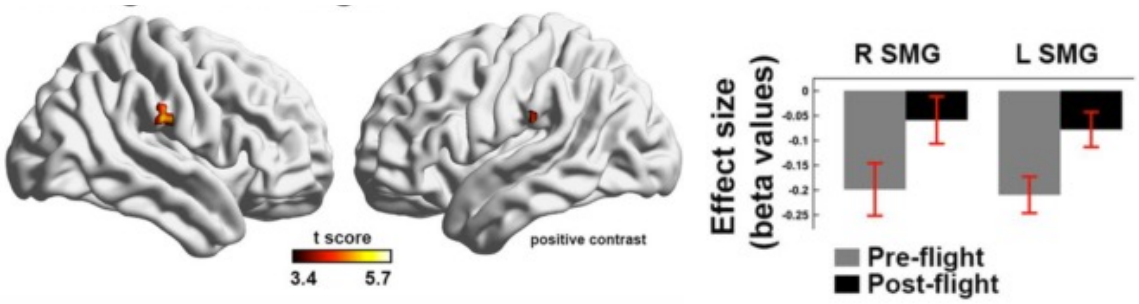
Angelique Van Ombergen[1], Floris L. Wuyts[1], Ben Jeurissen[2], Jan Sijbers[2], Floris Vanhevel[3], Steven Jillings[1], Paul M. Parizel[3], Stefan Sunaert[4], Paul H. Van de Heyning[1], Vincent Dousset[5], Steven Laureys[6] & Athena Demertzi[6,7]

SCIENTIFIC REPORTS

Anticorrelations reduced after exposure to extreme environments

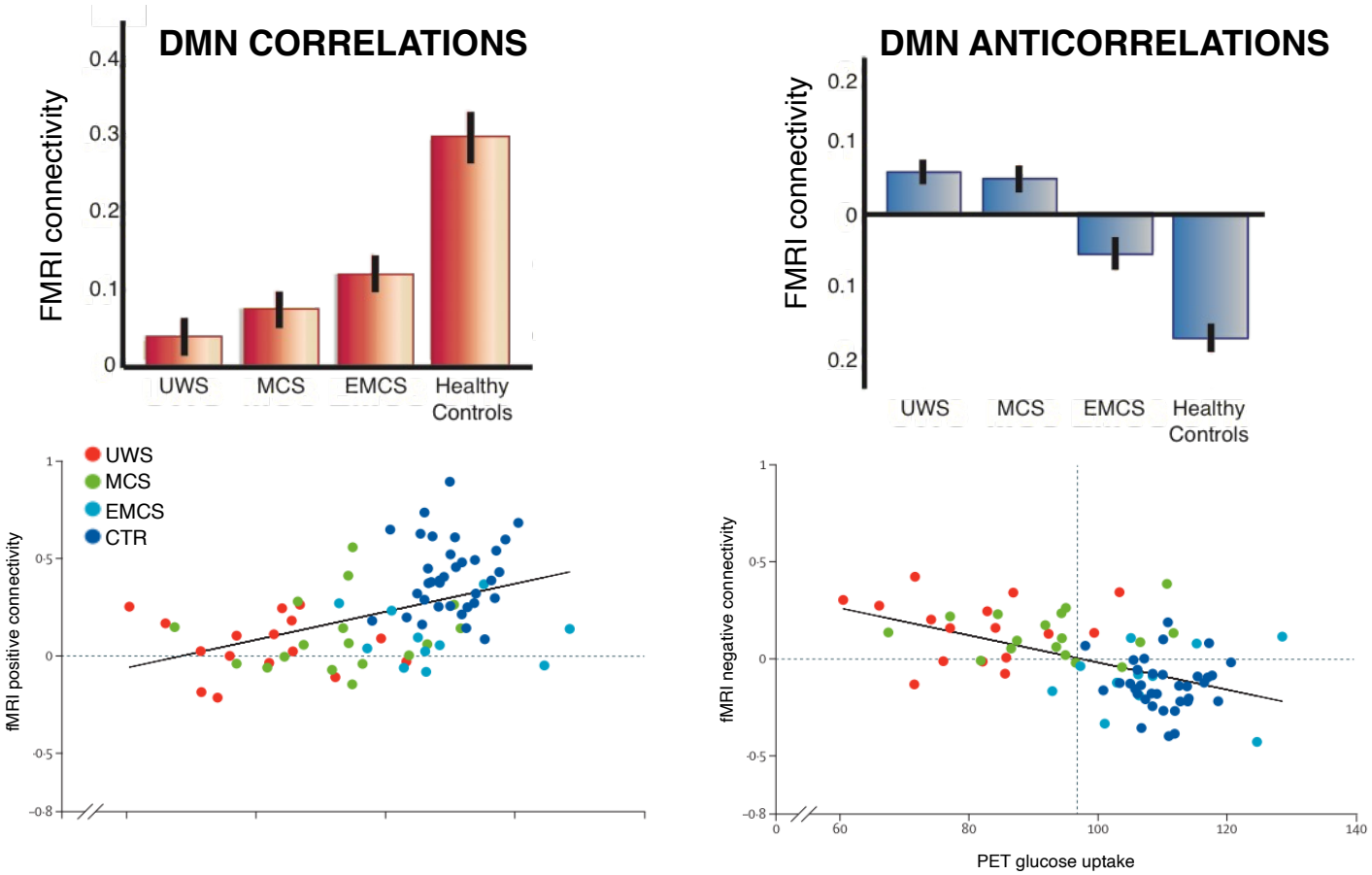


Post – Pre flight



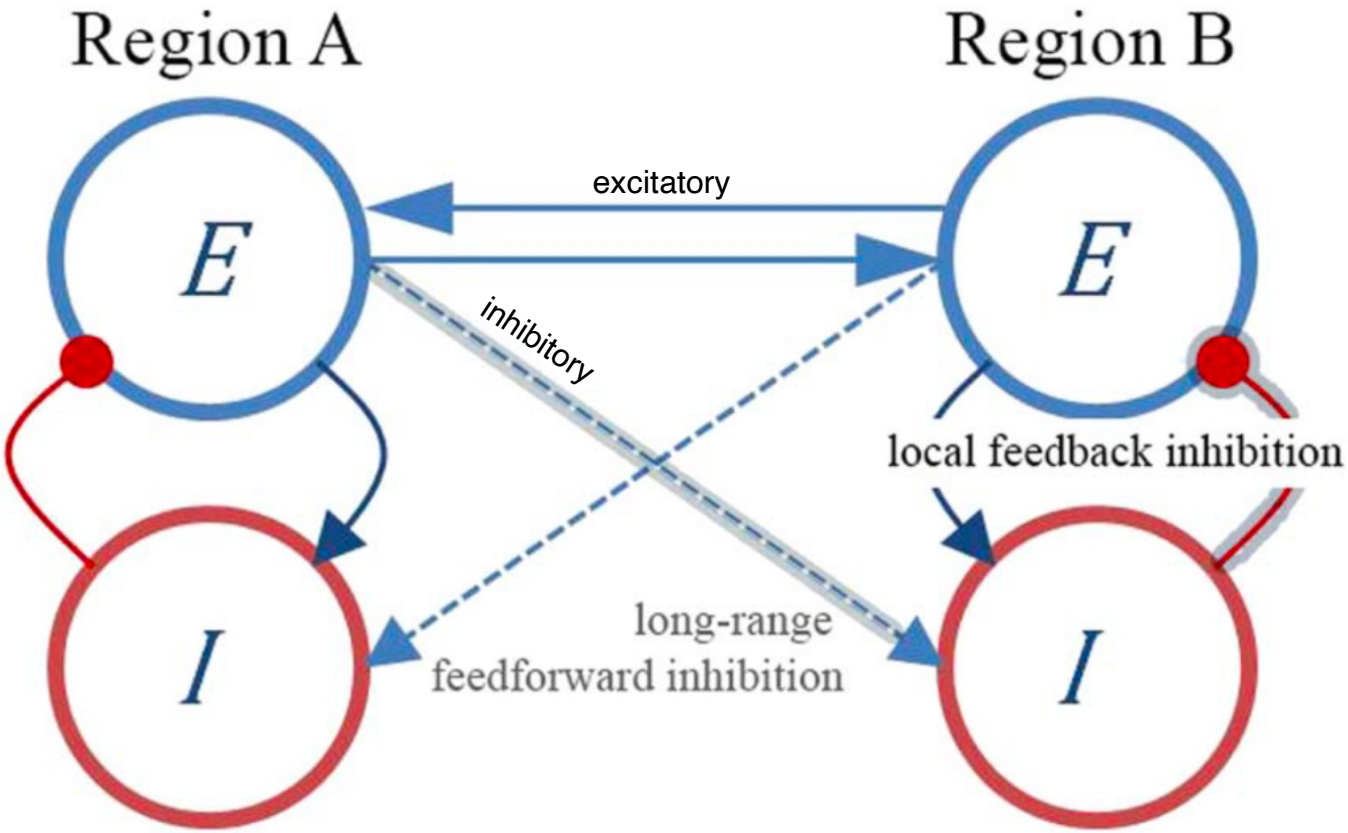
Van Ombergen … and Demertzi, *Sci Reports* 2017
Demertzi et al, *Brain Str Funct* 2015

No Anticorrelations in DoC Patients



Di Perri, …, Demertzi*, Laureys*, Soddu*, *Lancet Neurol* 2016

Anticorrelations are a prerequisite for Consciousness

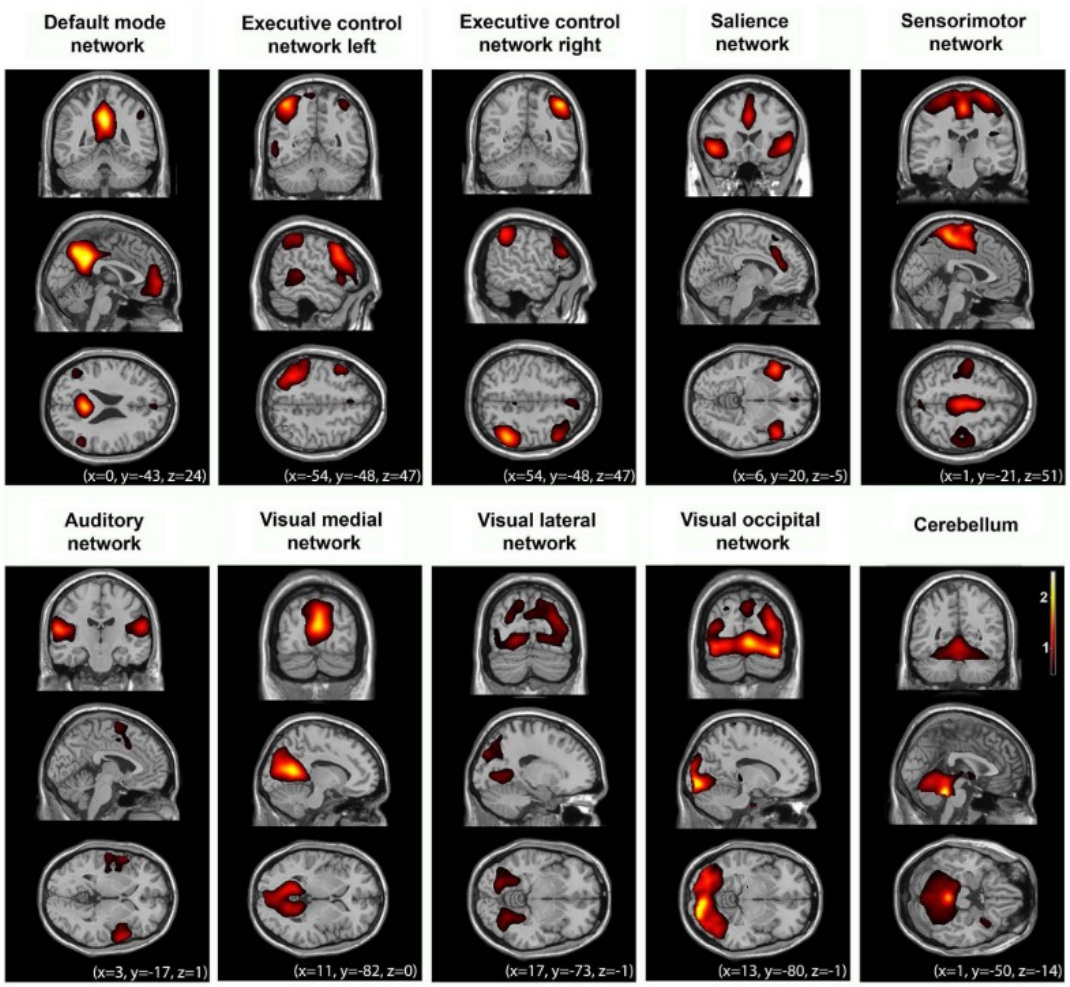


Ignition

Deco et al., *Sci Adv* 2021
Joglekar et al, *Neuron* 2018

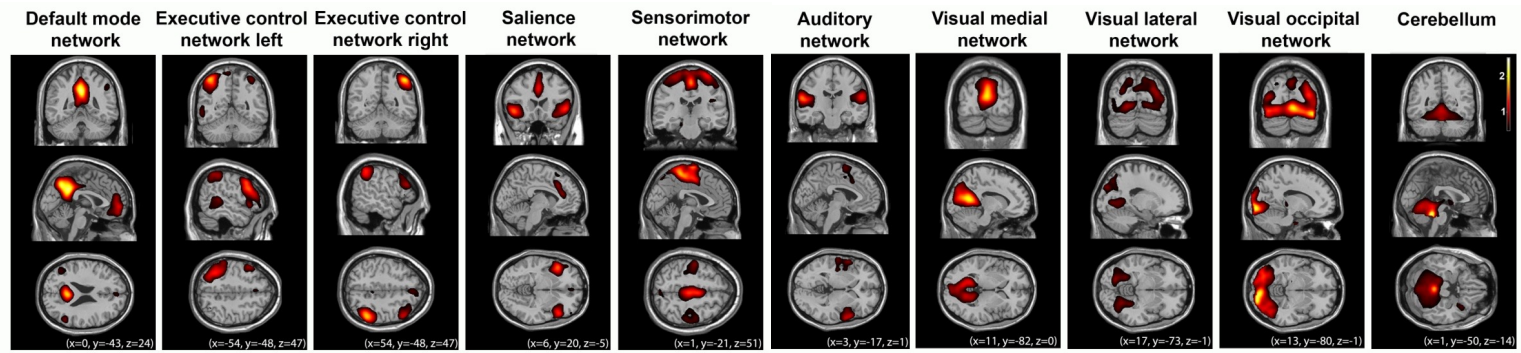
Demertzi, Kucyi, Ponce-Alvarez, Keliris, Whitfield-Gabrieli, Deco. ***Network Neurosci*** 2022

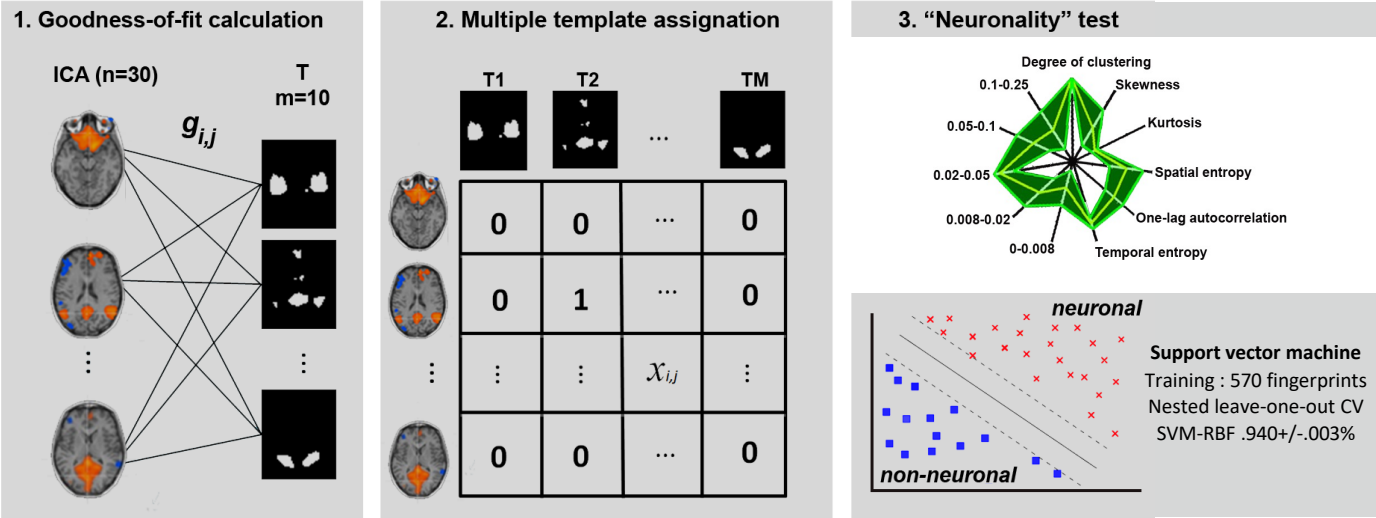
Resting State has Multiple Networks



Biswal et al., *Magn Reson. Med* 1995
Smith et al, *PNAS* 2009
Heine et al, *Front Psych 2012*

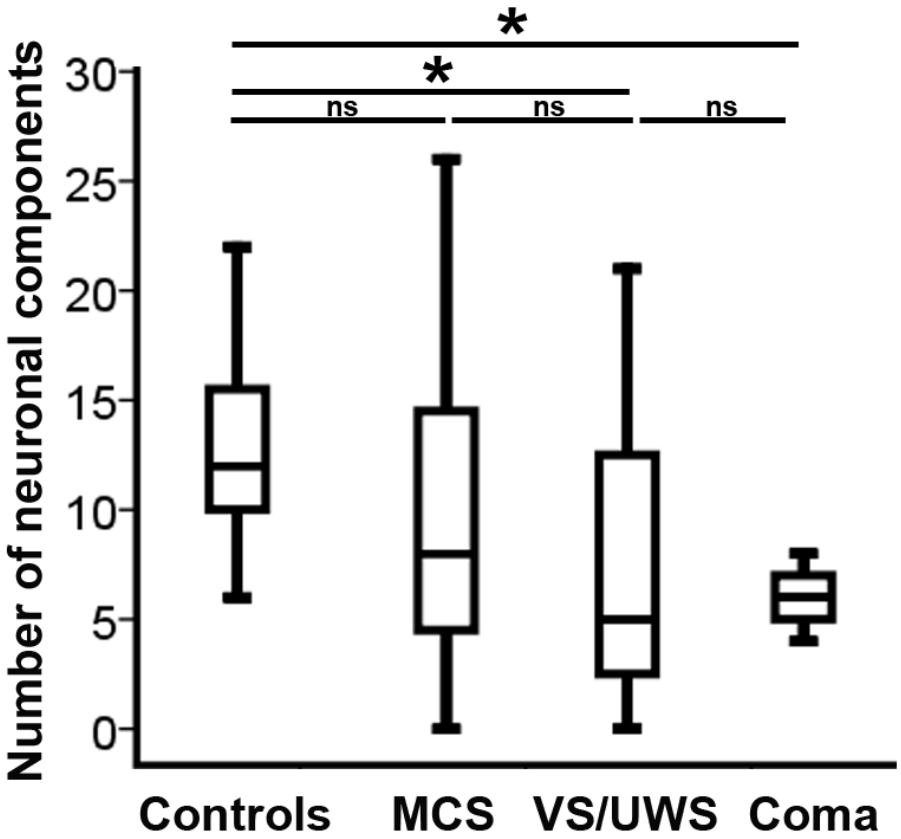
Which Network Differentiates Patients Best?





Demertzi & Gómez et al, Cortex 2014

Network Neuronality Differentiates Patients from Healthy



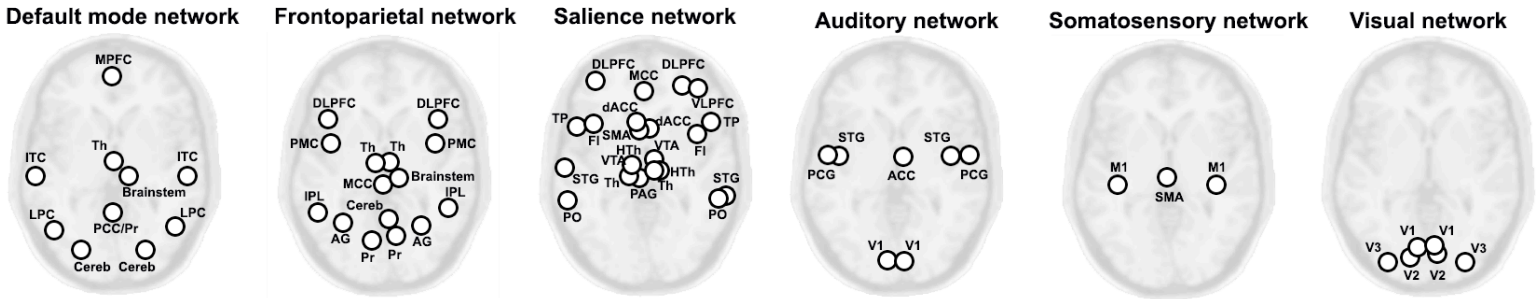
Single-subject classification

Performance measures	Accuracy	TPR healthy	TPR patients
	Healthy vs. all patients		
Neuronality	85.3	.82	.87
Neuronality & GOF	82.6	.70	.89
GOF	80	.78	.81

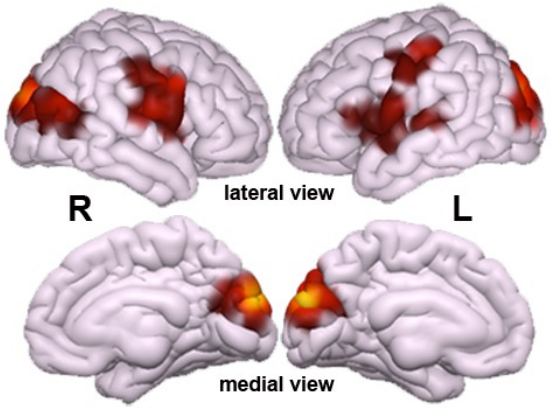
□ Controls (n=27)
▒ MCS (n=24)
■ VS/UWS (n=24)

Demertzi & Gómez et al, Cortex 2014

Which Network Differentiates Patients Best?



- 26 MCS, 19 VS/UWS
- 14 trauma, 28 non-trauma, 3 mixed
- 34 patients assessed >1m post-insult

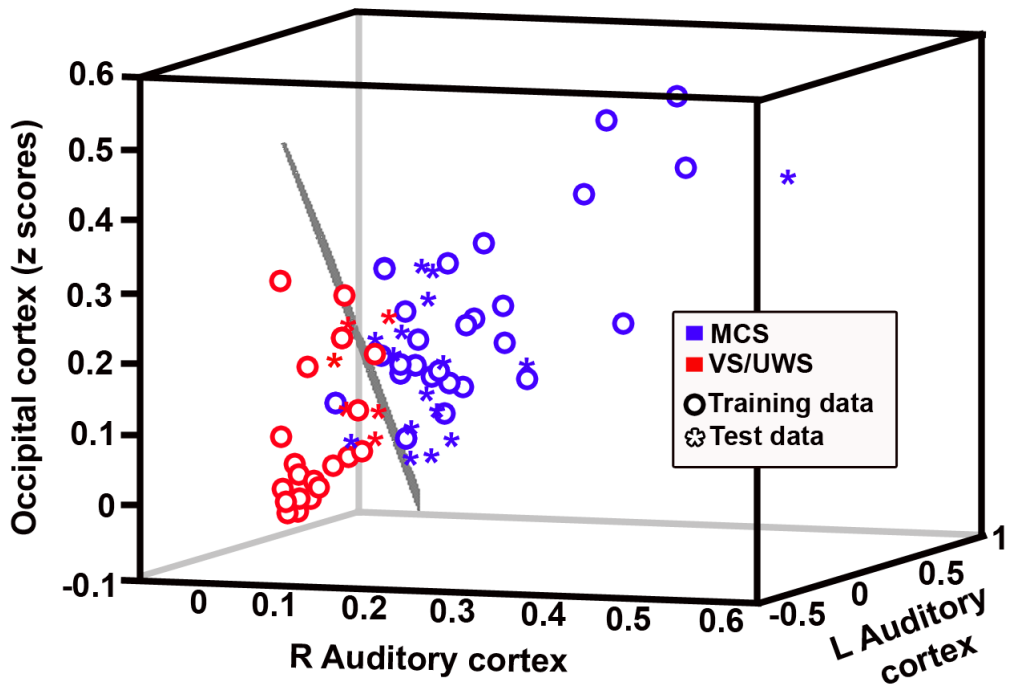


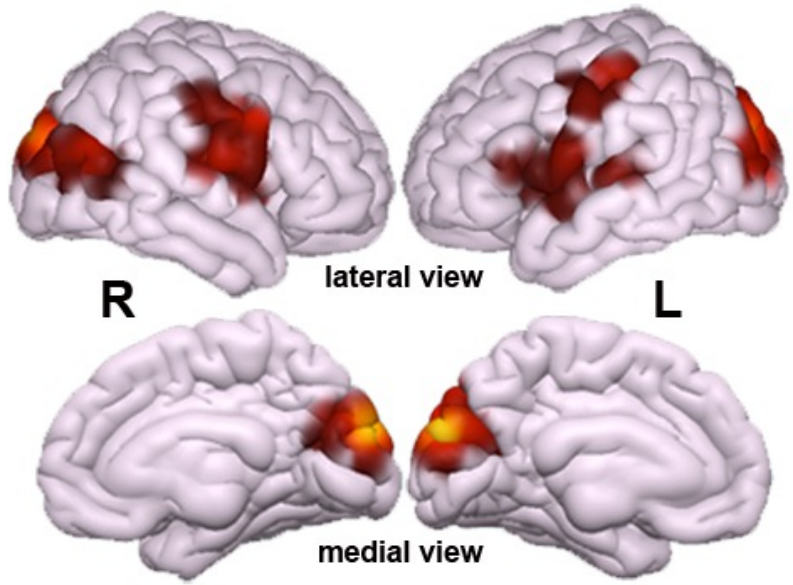
	Feature selection criterion (t-test)			Single-feature classification		
Network	**t value**	**Rank**	**p value**	**TP MCS**	**TN VS/UWS**	**Accuracy**
Auditory	8.32	1	<.001	25	18	43/45
Visual	7.79	2	<.001	23	15	38/45
Default mode	6.95	3	<.001	23	15	38/45
Frontoparietal	6.82	4	<.001	23	15	38/45
Salience	6.21	5	<.001	24	15	39/45
Sensorimotor	5.87	6	<.001	24	13	37/45

Demertzi & Antonopoulos et al, ***Brain*** 2015

Patient separation based on cross-modal interactions

- Training set: 45 DOC (26 MCS, 19 VS/UWS)
  - 14 trauma, 28 non-trauma, 3 mixed
  - 34 patients assessed >1m post-insult
- Test set:
  - **16 MCS**, **6 VS/UWS** (15 non-trauma; all chronic)
  - 2 different centers

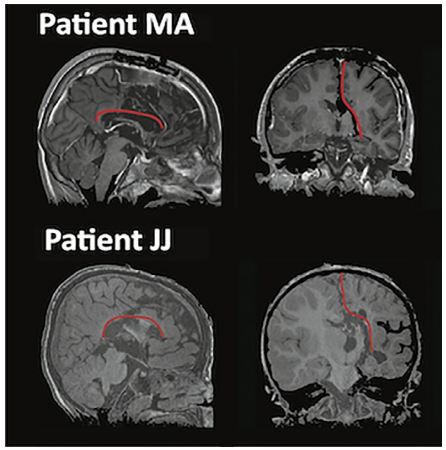




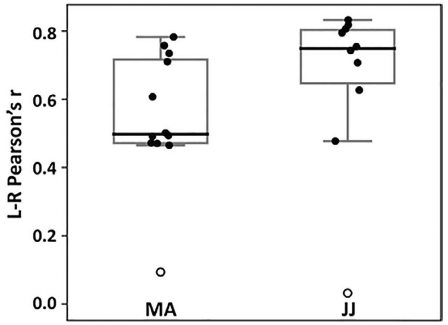
Demertzi & Antonopoulos et al, ***Brain*** 2015

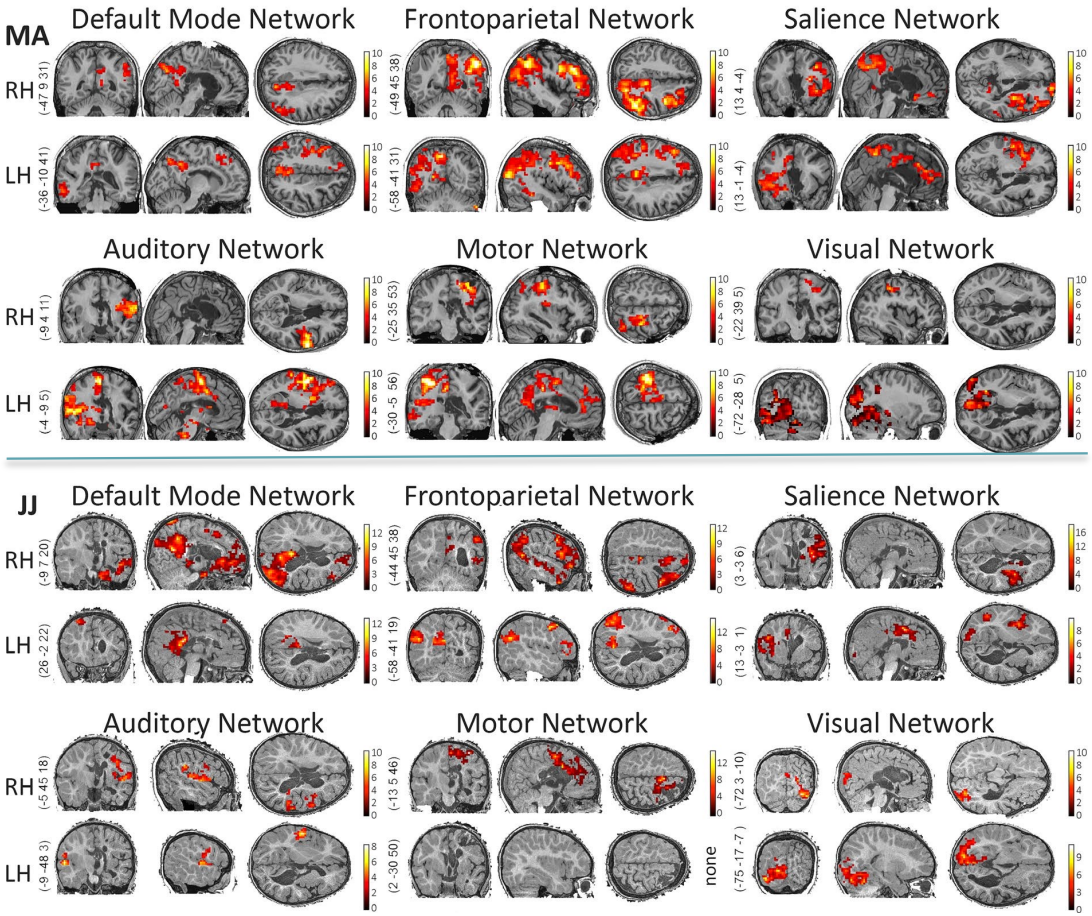
Complete hemispheretomy

Complete hemispherotomy



Inter-hemispheric connectivity





Blauwblomme* & Demertzi*, Tacchela, Fillon, Bourgeois, Losito, Eisermann, Marinazzo, Raimondo, Alcauter, Van De Steen, Colenbier, Laureys, Dangouloff Ros, Naccache, Boddaert, Nabbout et al, ***Epilepsia Open*** 2020

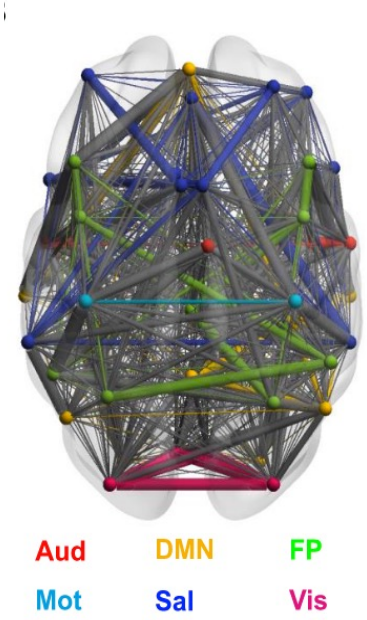
ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

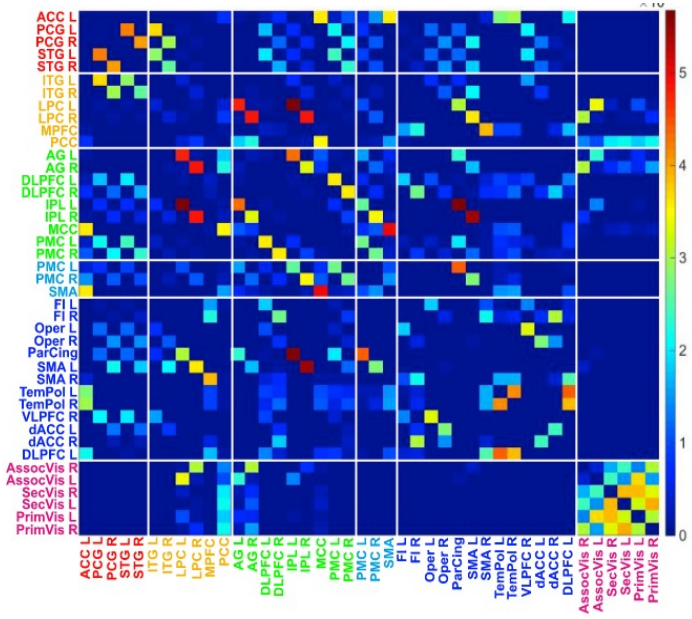
Necker ENFANTS MALADES HÔPITAL UNIVERSITAIRE

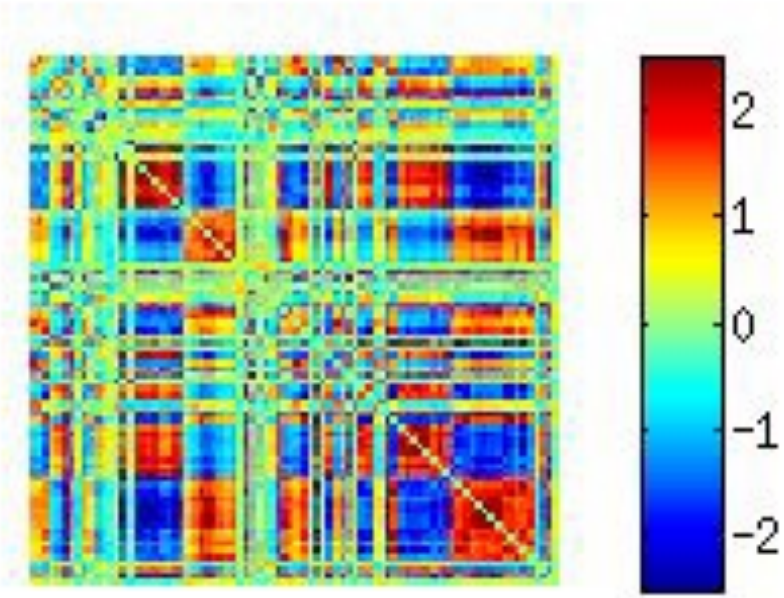
The brain as a network

100 billion neurons, ~100 trillion synaptic connections

The Connectome

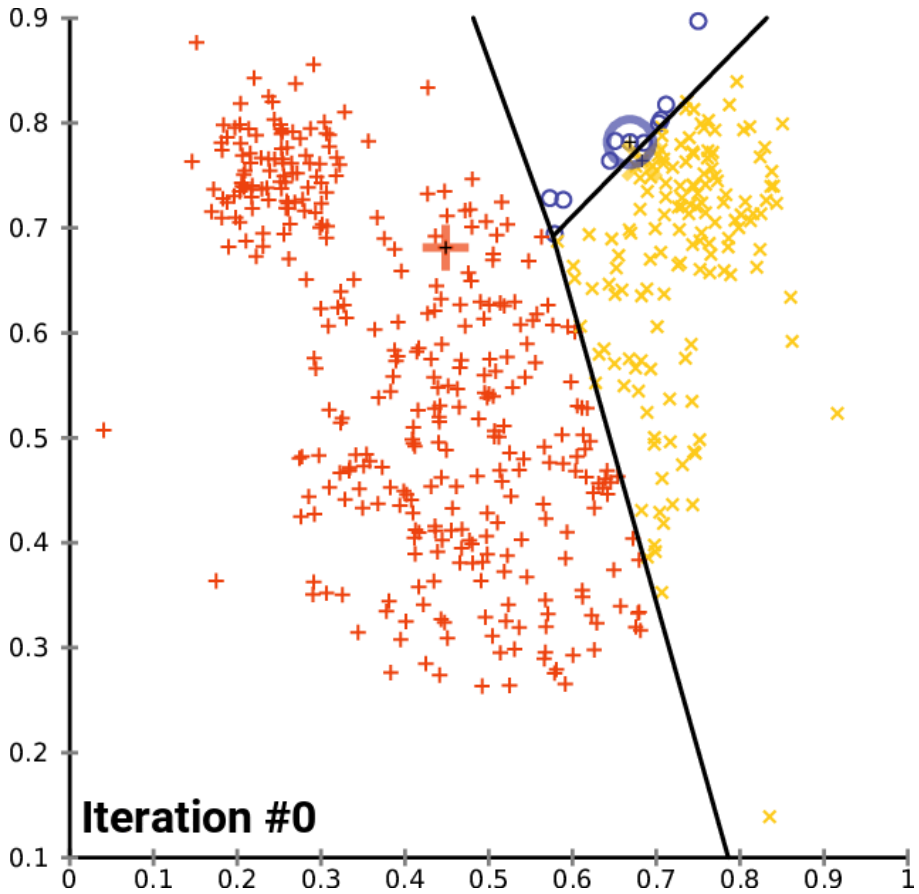




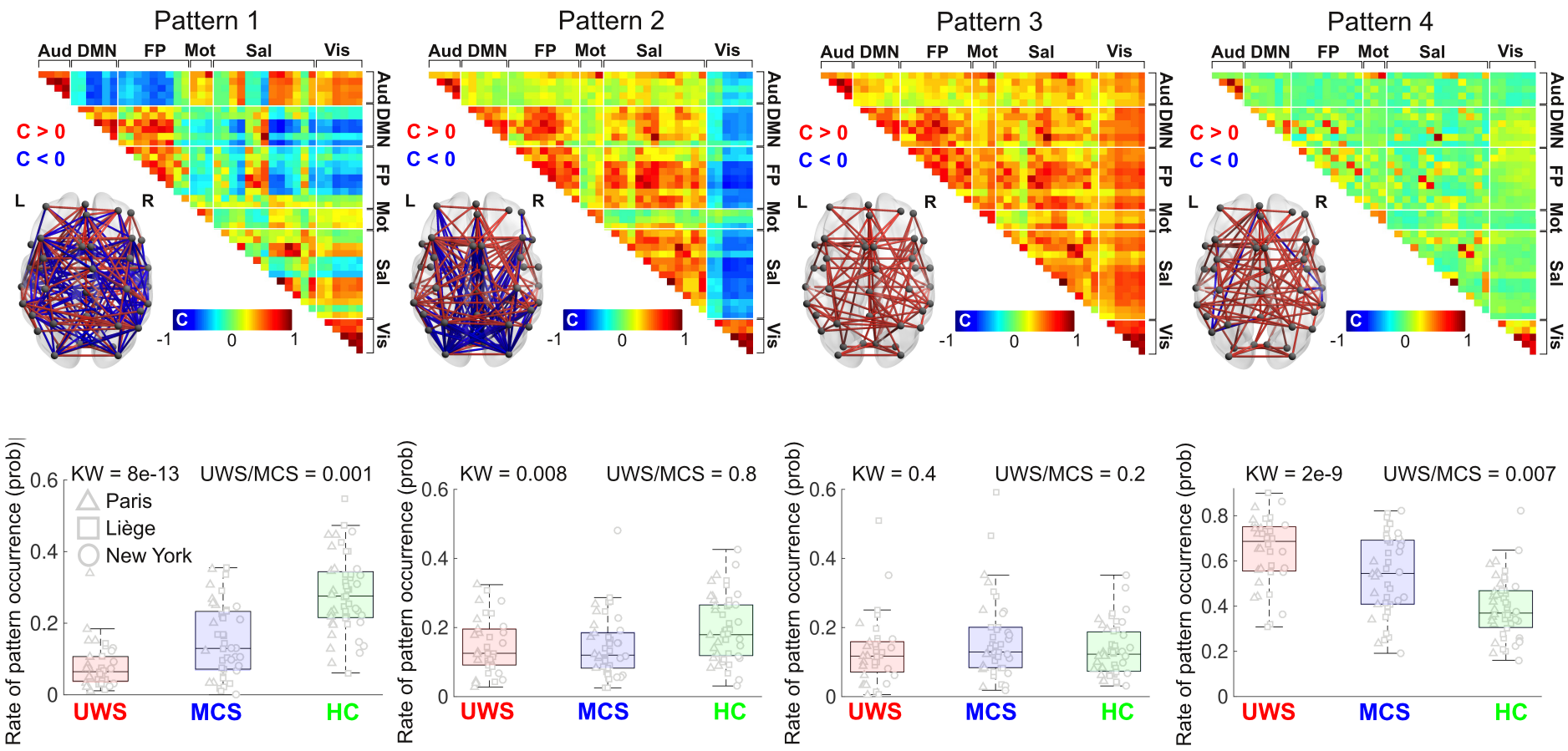


Fornito, Zalesky, Bullmore. Ch 1: An Introduction to Brain Networks. *Fundamentals of Brain Network Analysis, Academic Press* 2016
Sporns, Tononi, & Koetter. ***PLoS Comput Biol*** 2005

Unsupervised Clustering

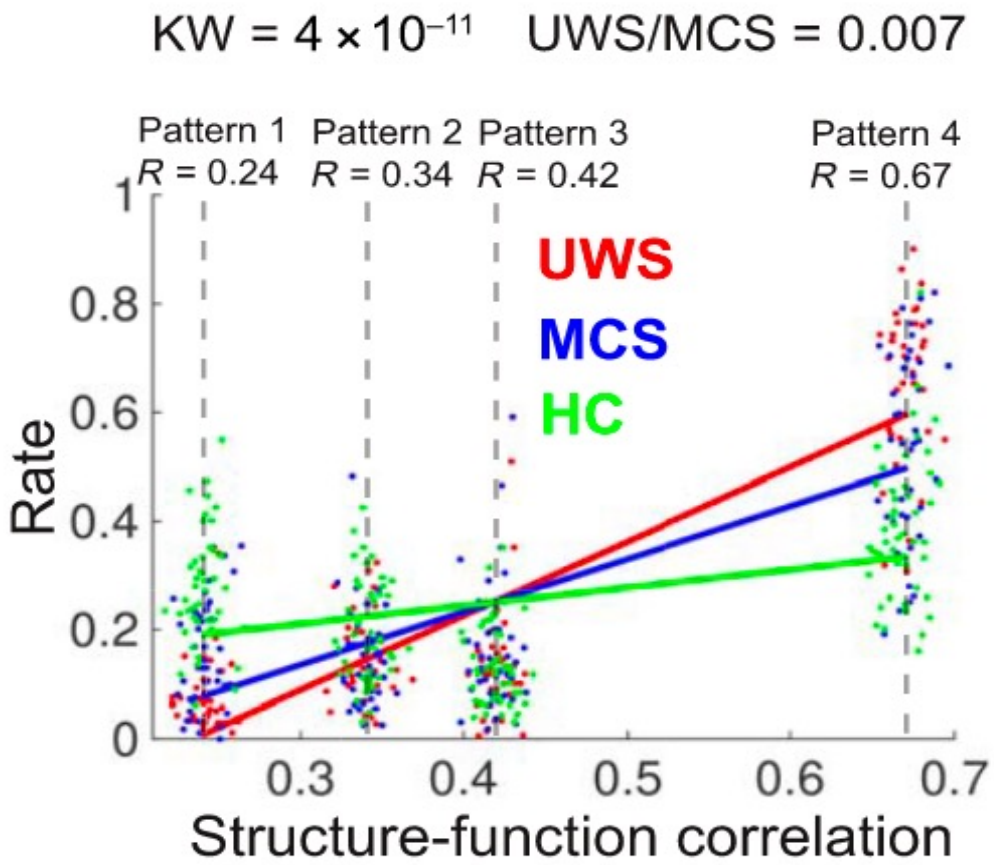


“Rich” connectivity in communicating states



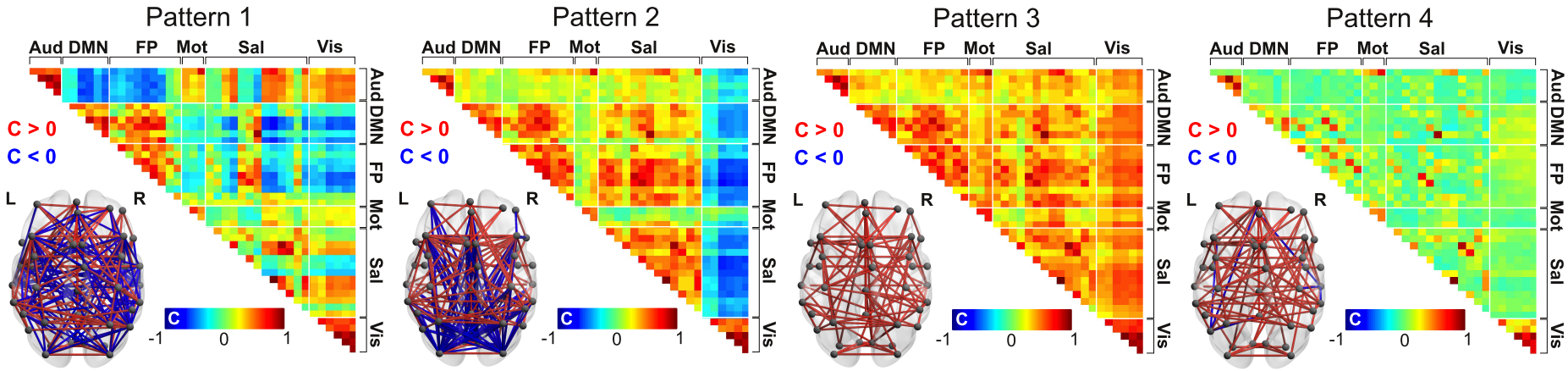
Demertzi* & Tagliazucchi*, Dehaene, Deco, Barttfeld, Raimondo, Martial, Fernández-Espejo, Rohaut, Voss, Schiff, Owen, Laureys, Naccache, Sitt.
Science Advances 2019

“Poor” connectivity reflects anatomy

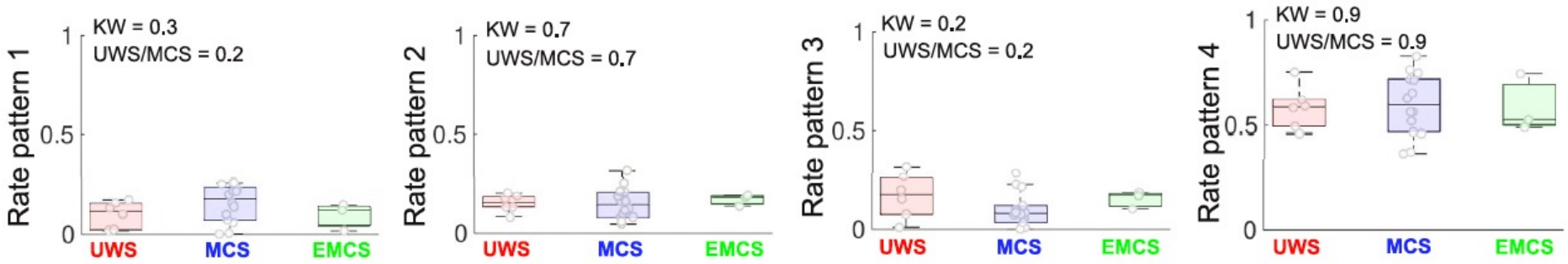


Demertzi* & Tagliazucchi*, Dehaene, Deco, Barttfeld, Raimondo, Martial, Fernández-Espejo, Rohaut, Voss, Schiff, Owen, Laureys, Naccache, Sitt. ***Science Advances*** 2019

“Poor” connectivity in Unconsciousness

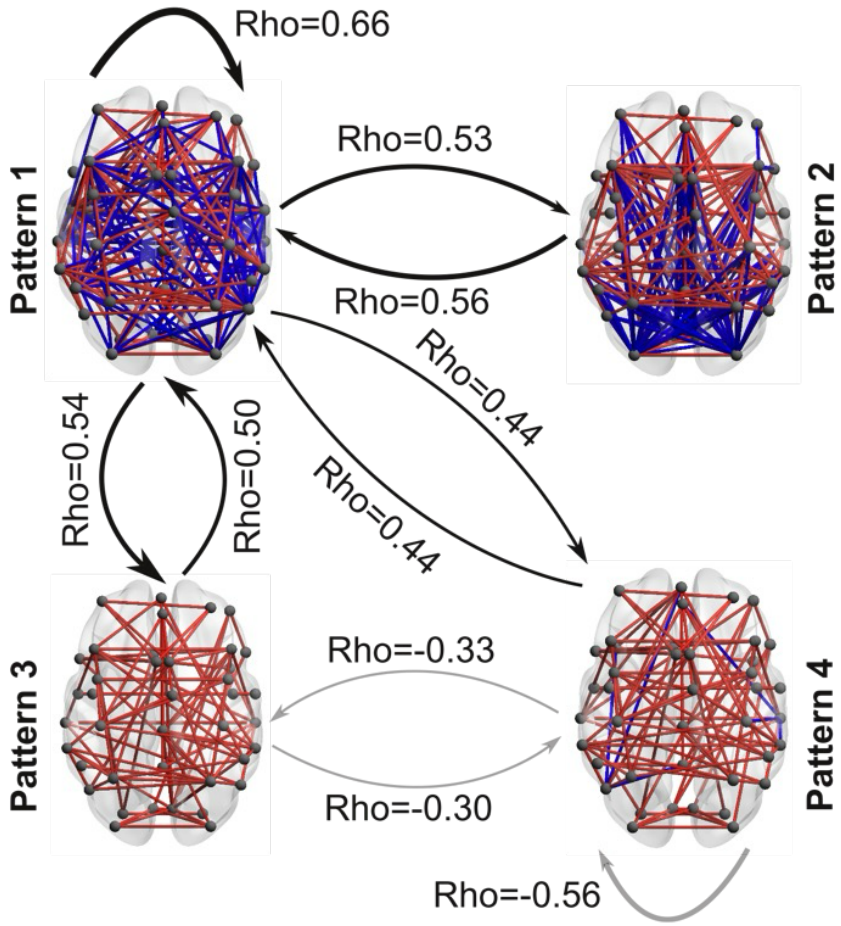


Propofol anesthesia



Demertzi* & Tagliazucchi*, Dehaene, Deco, Barttfeld, Raimondo, Martial, Fernández-Espejo, Rohaut, Voss, Schiff, Owen, Laureys, Naccache, Sitt. ***Science Advances*** 2019

Higher dynamism in conscious states

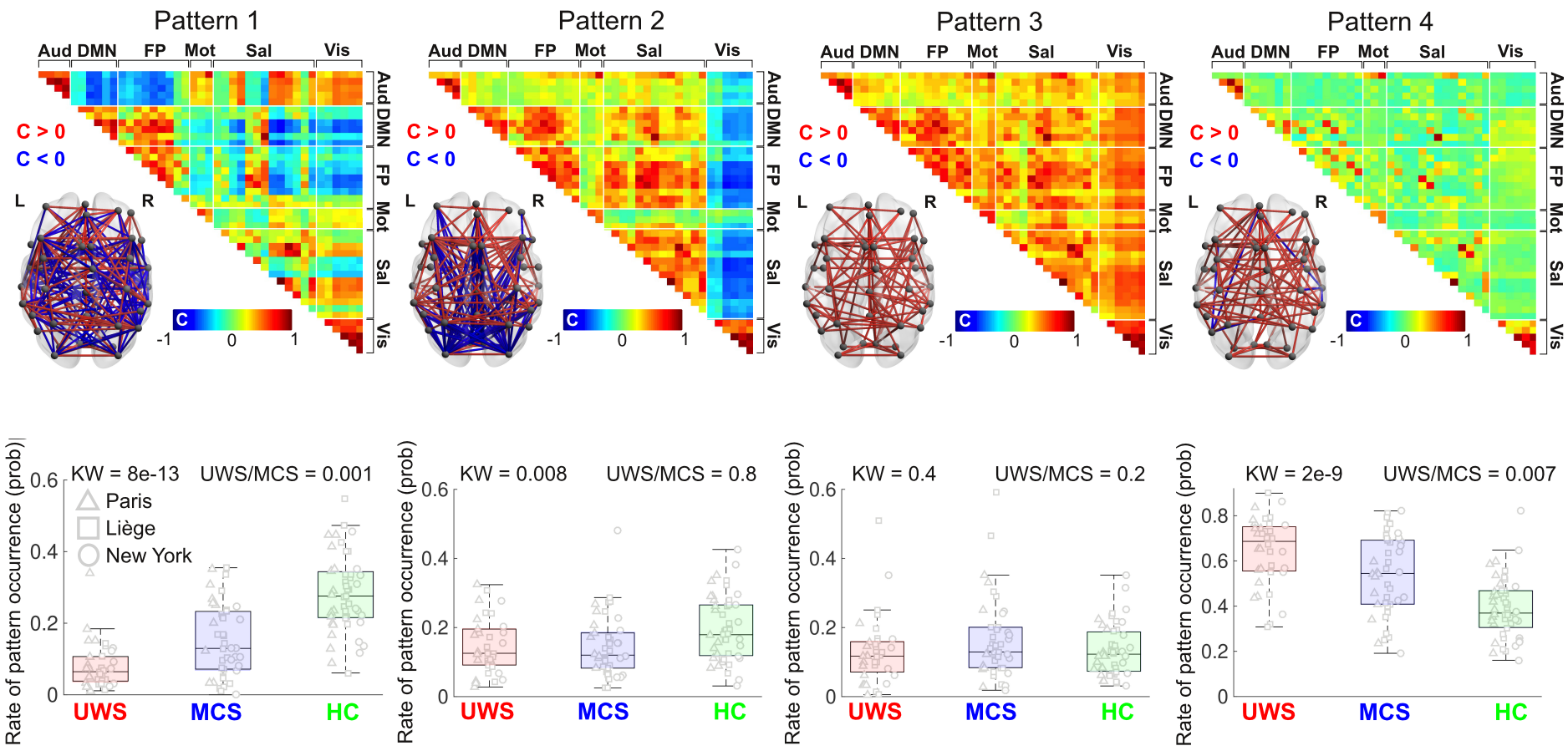


Healthy > MCS > UWS

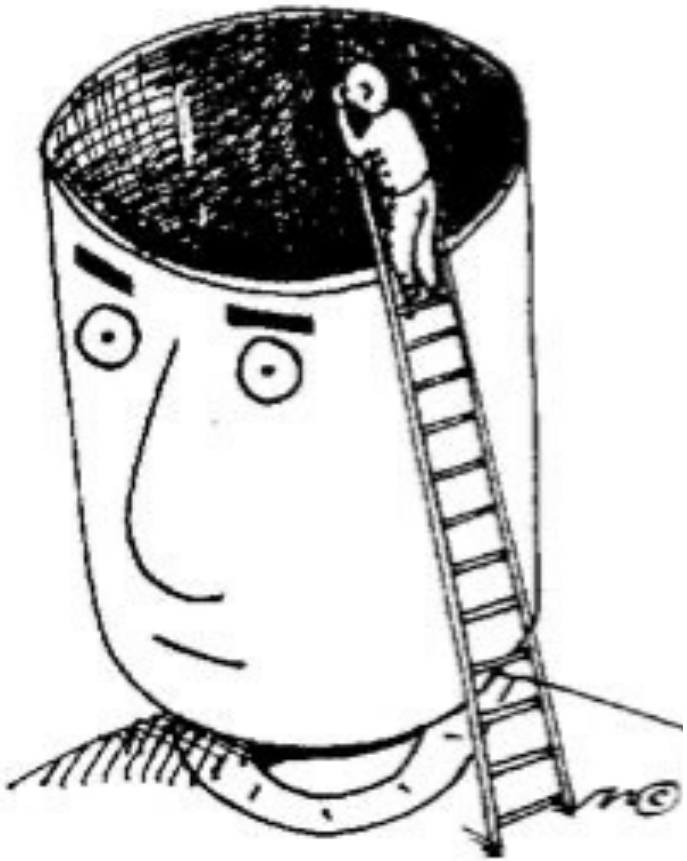
UWS > MCS > Healthy

Demertzi* & Tagliazucchi*, Dehaene, Deco, Barttfeld, Raimondo, Martial, Fernández-Espejo, Rohaut, Voss, Schiff, Owen, Laureys, Naccache, Sitt.
Science Advances 2019

What do these patterns mean?

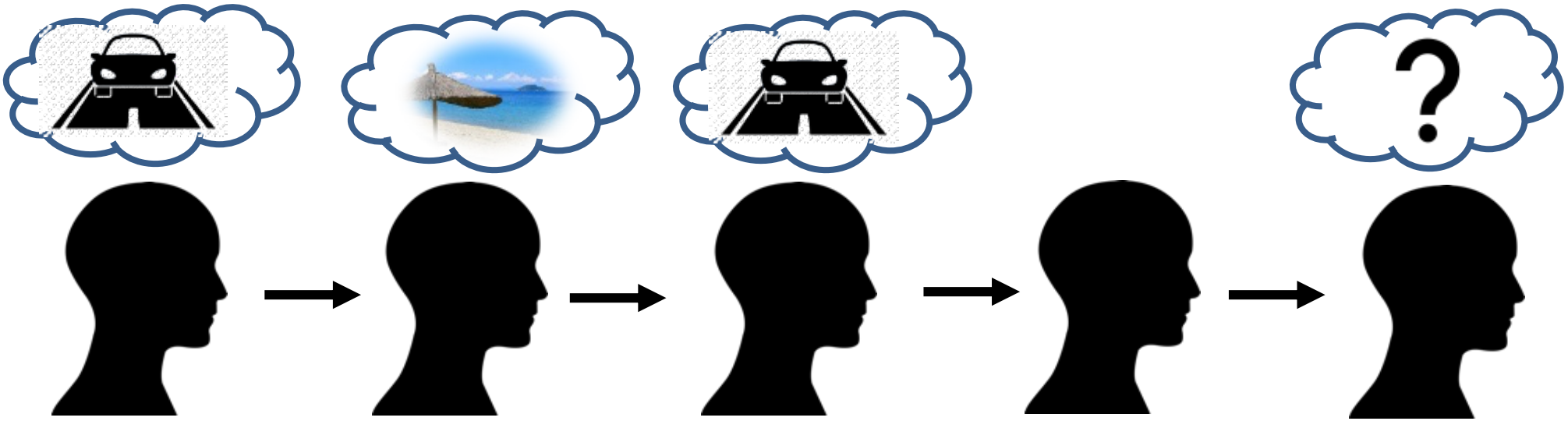


Demertzi* & Tagliazucchi*, Dehaene, Deco, Barttfeld, Raimondo, Martial, Fernández-Espejo, Rohaut, Voss, Schiff, Owen, Laureys, Naccache, Sitt.
Science Advances 2019



PART 2
Mind Blaking

Mental states

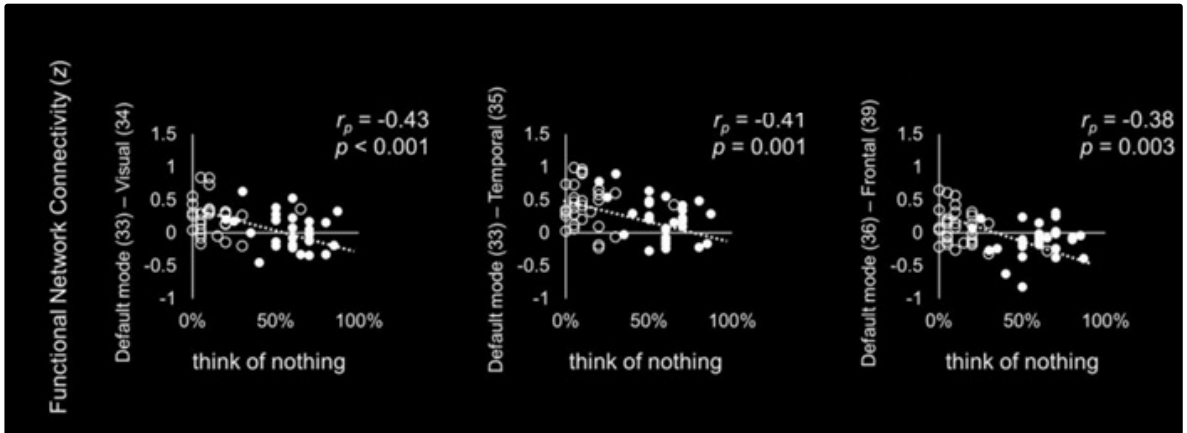


Slide courtesy: Boulakis Paris, Physiology of Cognition Lab

Christoff et al, *Nat Rev Neurosci* 2016

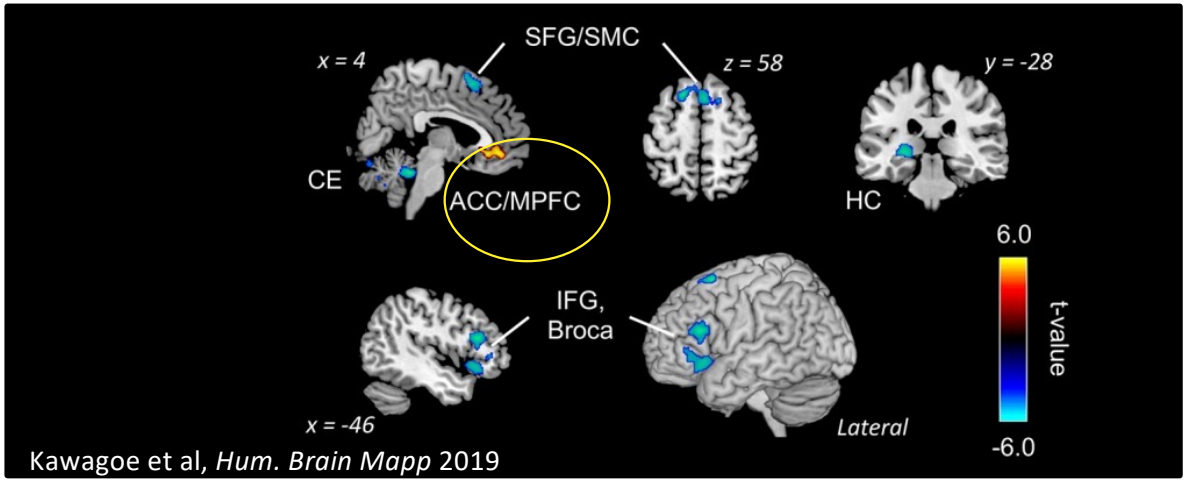
Voluntary Mind Blanking?

”Keep awake, fixate on the cross, and think of nothing as best you can. When you realise that you are thinking about something, disengage your attention and again try to think of nothing”.



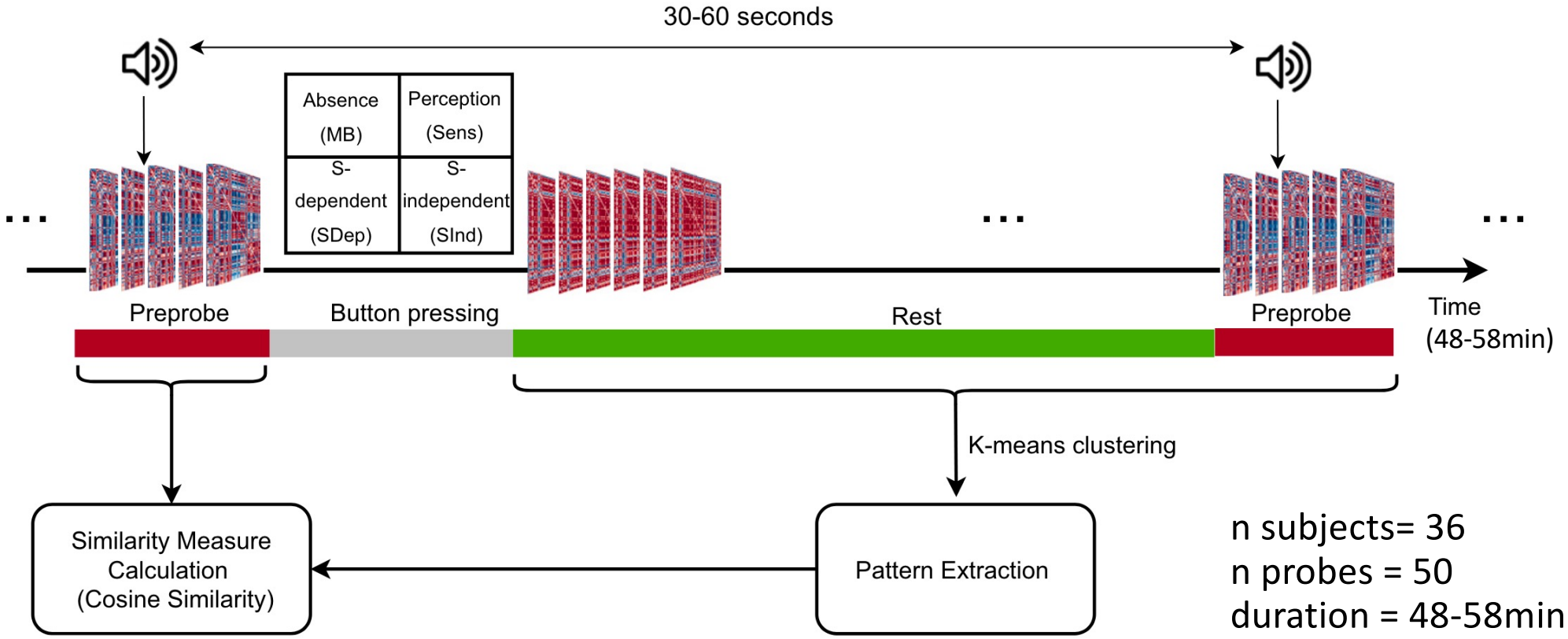
Kawagoe et al , *Eur J Neurosci* 2018

“When you realize that you are thinking about something, disengage your attention and again try to think of nothing during the scans”



Kawagoe et al, *Hum. Brain Mapp* 2019

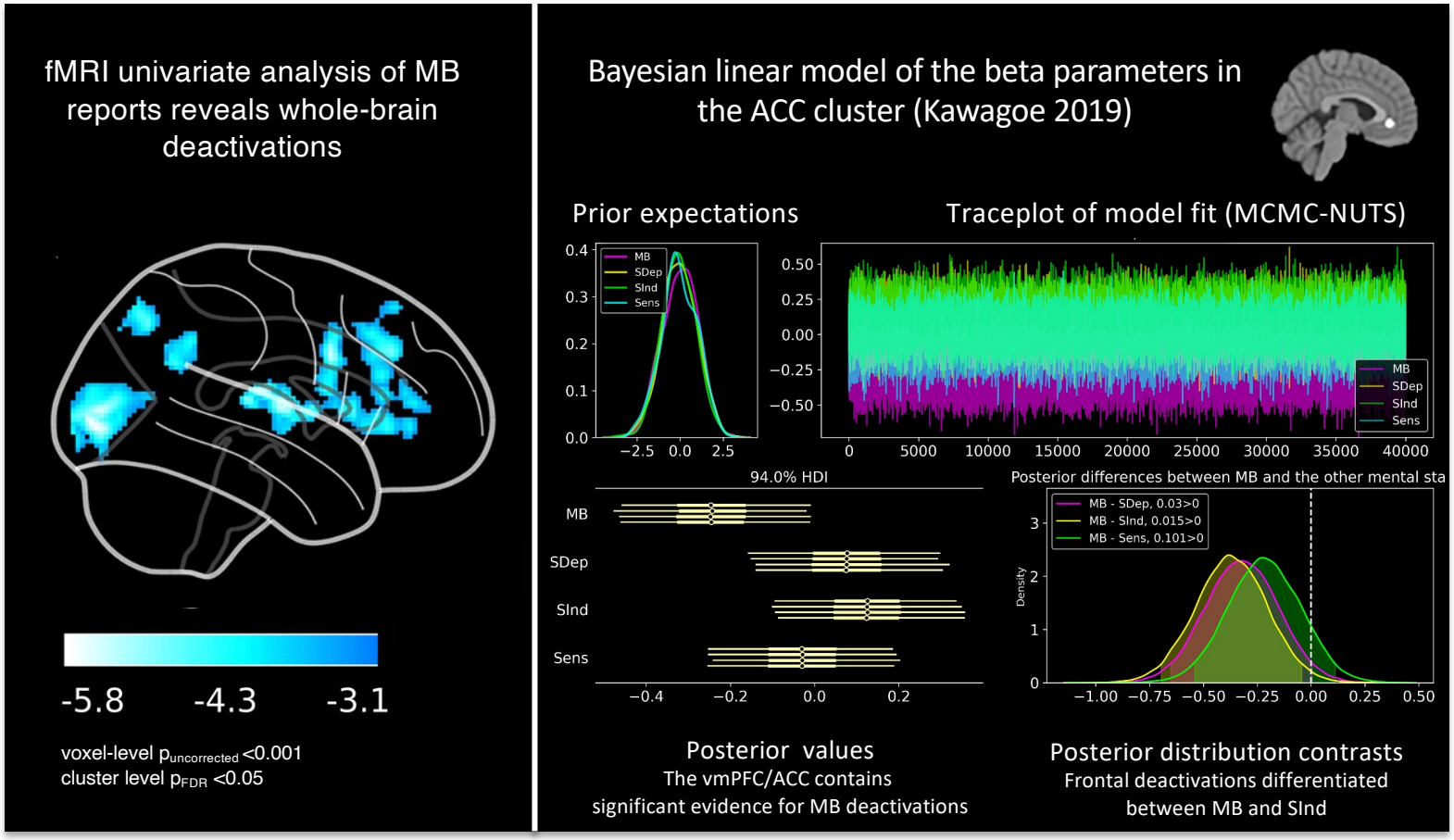
Probing MB reports



n subjects= 36
n probes = 50
duration = 48-58min

Mortaheb, Van Calster, Raimondo, Klados, Boulakis, Georgoulaa, Majerus, Van De Ville*, Demertzi*. *PNAS* 2022
Van Calster, D'Argembeau, Salmon, Peters, Majerus, *J Cogn Neurosci* 2017

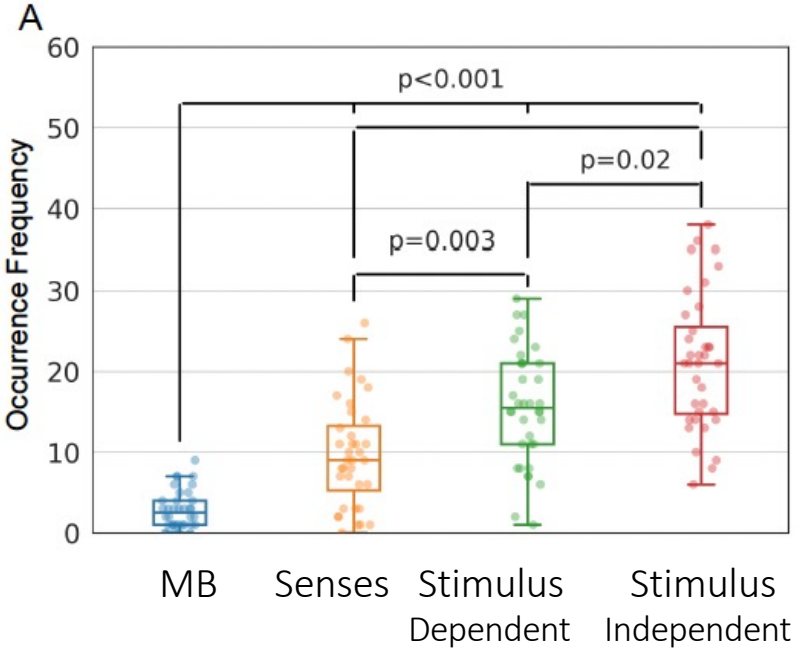
Probed Mind Blanking linked to widespread deactivations



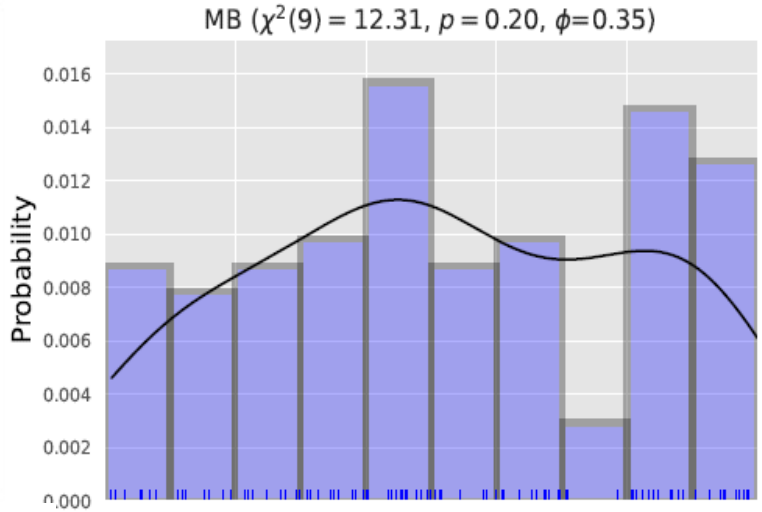
Boulakis, Mortaheb, Van Calster, Majerus, Demertzi. *JNeurosci* 2023

Mind Blanking is Sparse

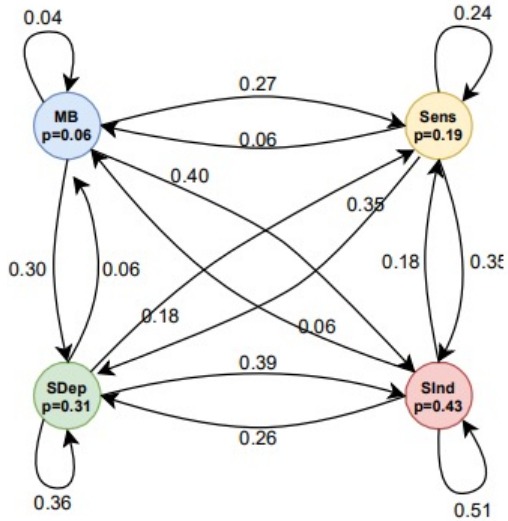
Less frequent



Equally probable across time



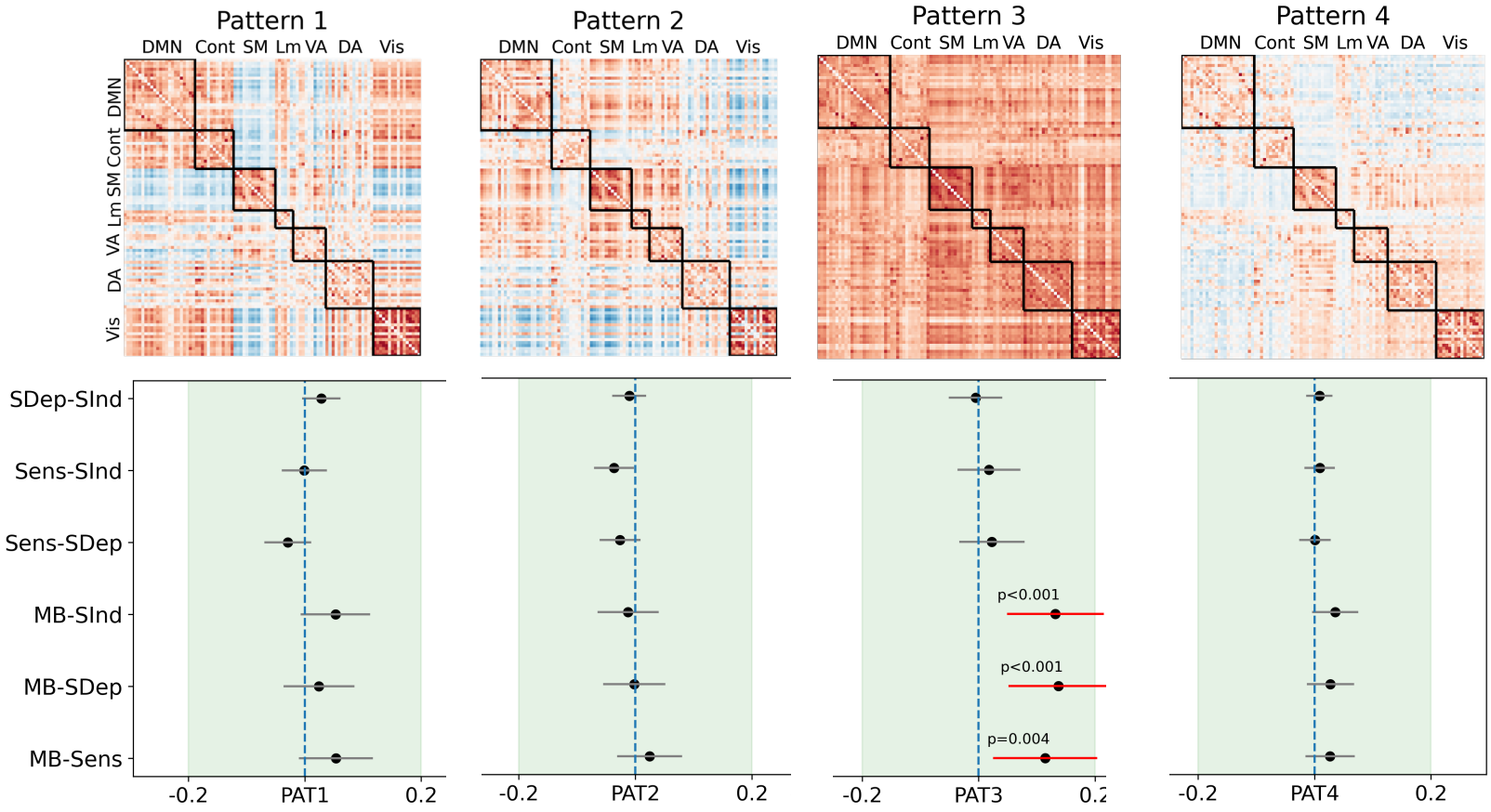
Transient relay



n subjects= 36
n probes = 50
duration = 48-58min

Mortaheb, Van Calster, Raimondo, Klados, Boulakis, Georgoulaa, Majerus, Van De Ville*, Demertzi*. ***PNAS*** 2022
Van Calster, D'Argembeau, Salmon, Peters, Majerus, ***J Cogn Neurosci*** 2017

MB is linked to a hyper-connected pattern

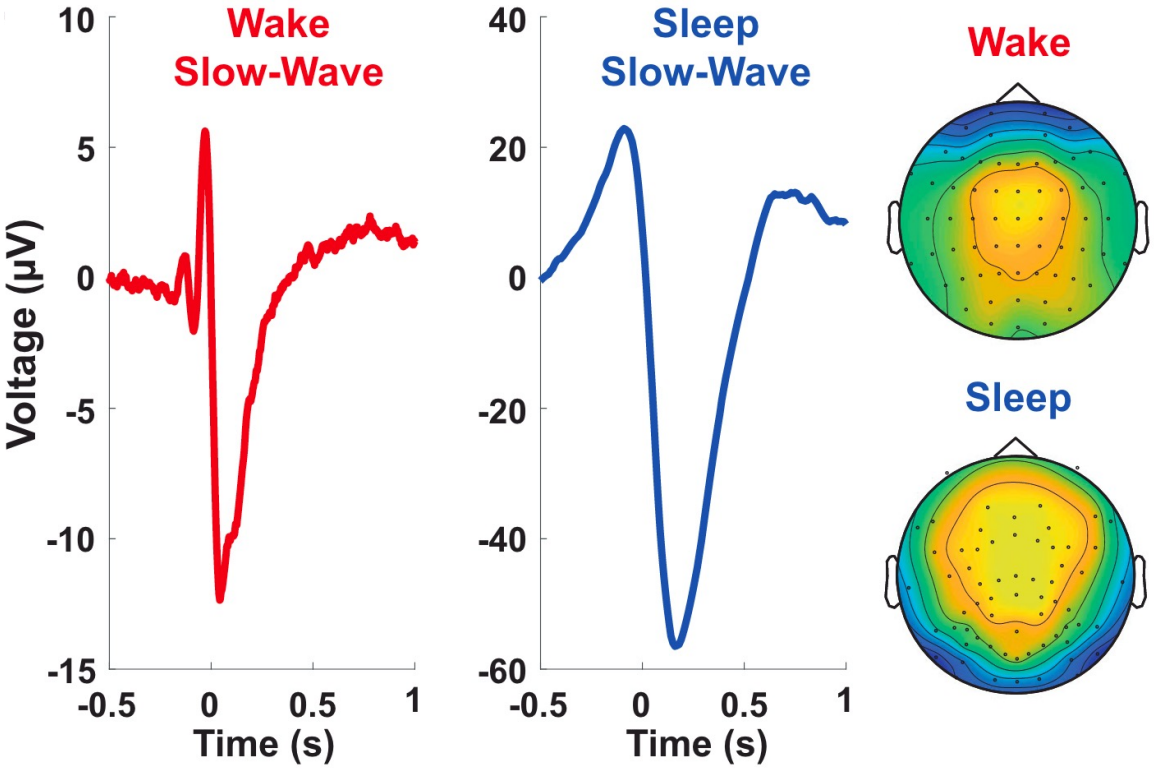


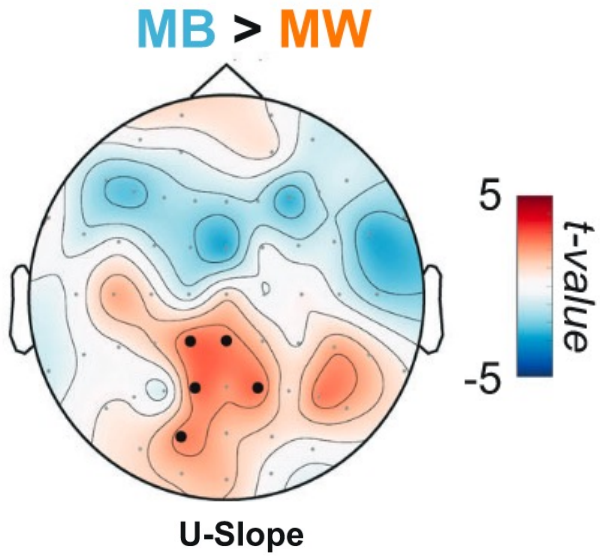
Mortaheb, Van Calster, Raimondo, Klados, Boulakis, Georgoulaa, Majerus, Van De Ville*, Demertzi*. ***PNAS*** 2022

Slow wave-like activity in wakefulness

Properties of slow waves

Predictive of mental states

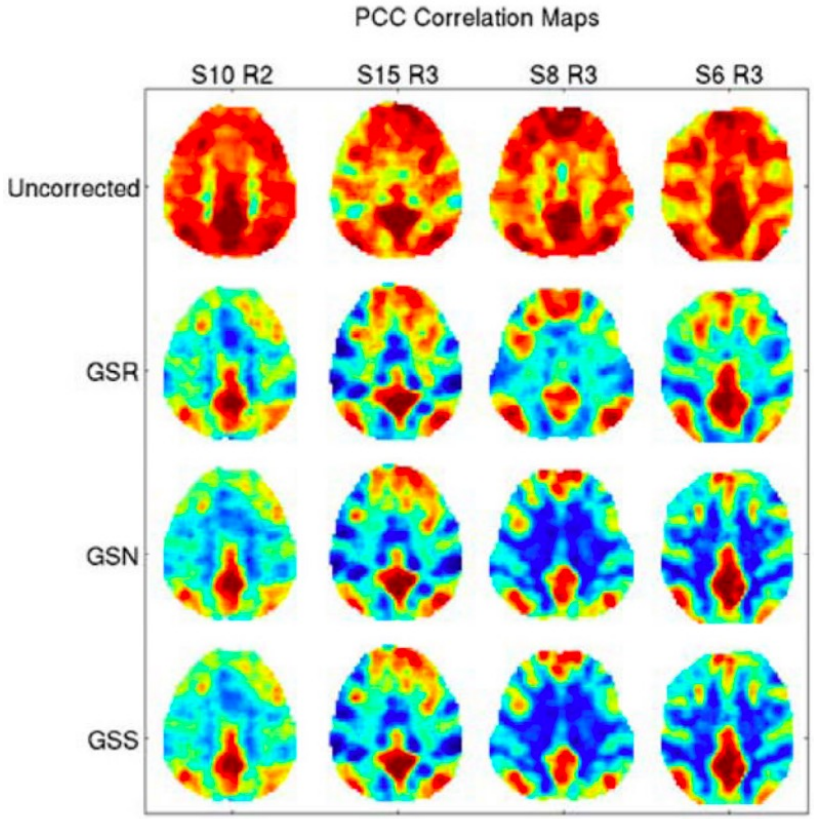




Andrillon et al, ***Nat Communications*** 2021

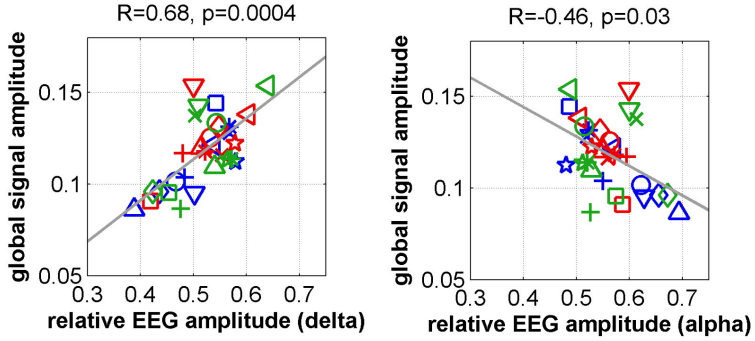
Higher Global Signal amplitude → Lower vigilance

The Global Signal

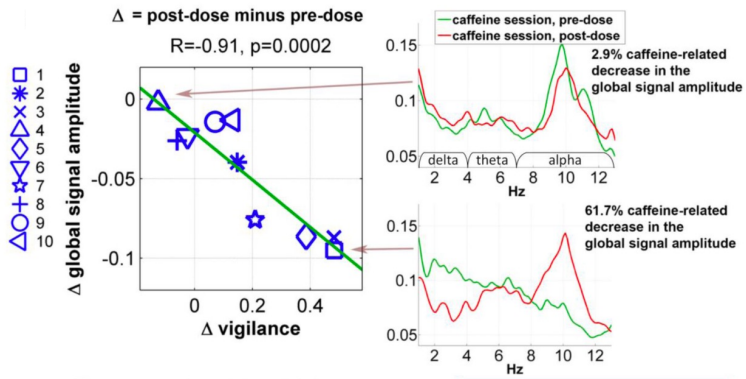


Liu et al, ***NeuroImage*** 2017

GS amplitude is linked to low arousal

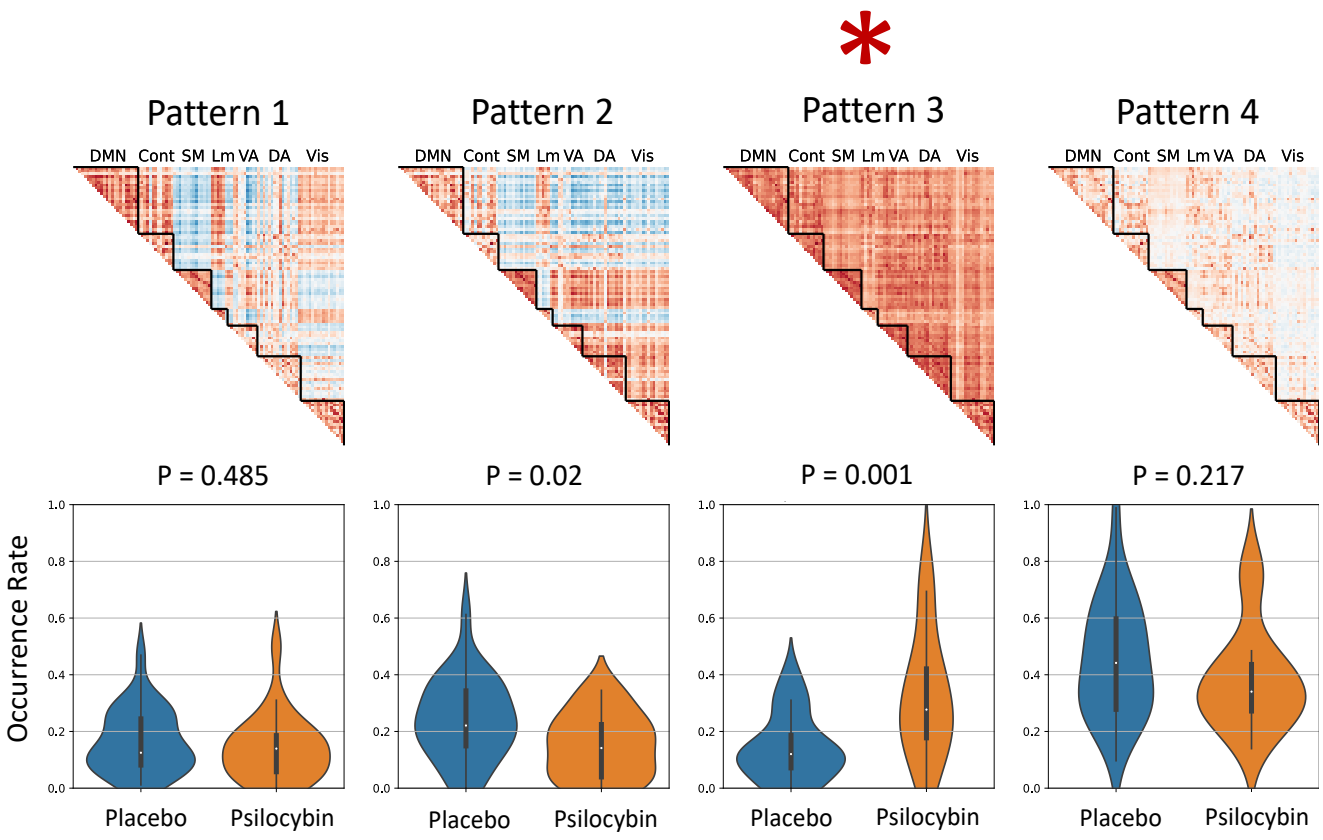


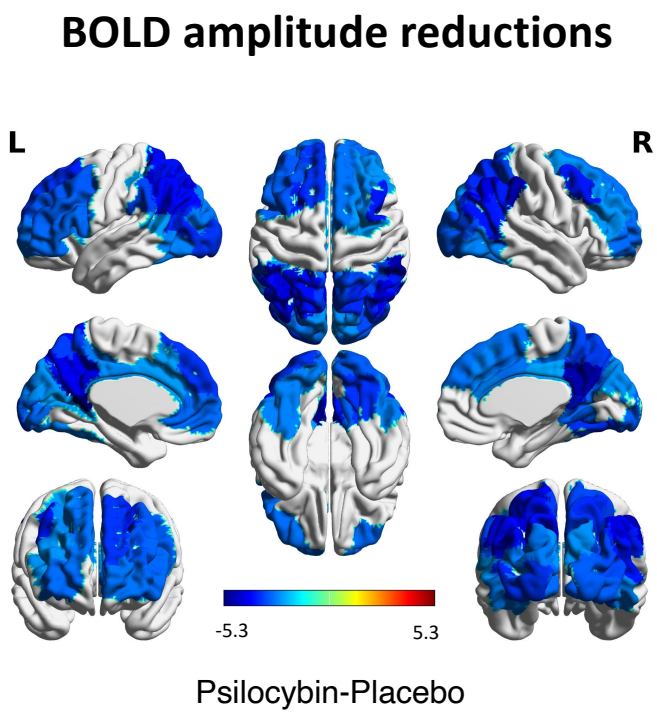
GS amplitude decreases with caffeine intake



Wong et al, ***Neuroimage*** 2013

Lower Global Signal amplitude → Higher vigilance



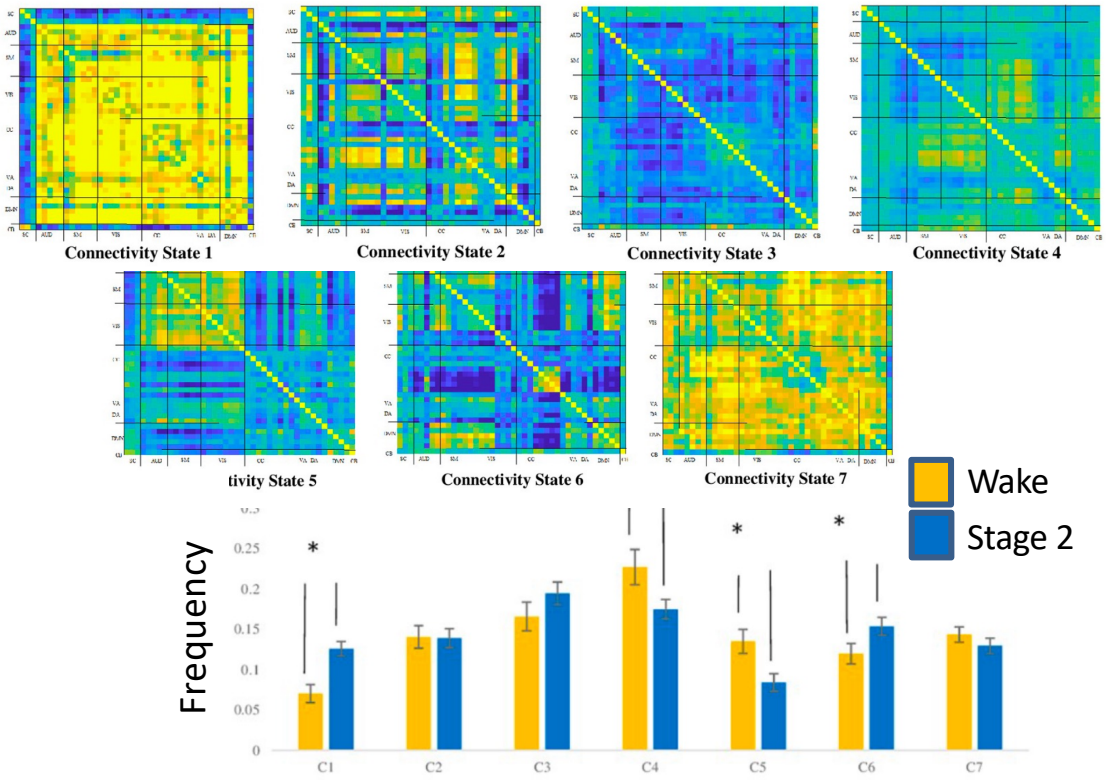


Mortaheb, Fort, Mason, Mallaroni, Ramaekers, Demertzi. ***Biol Psychiatry-CNNI*** 2024

Higher connectivity in unconscious states

NREM sleep

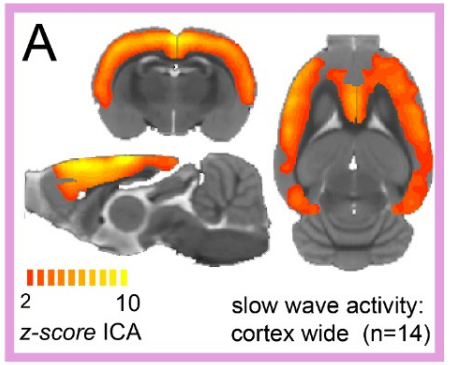
Humans

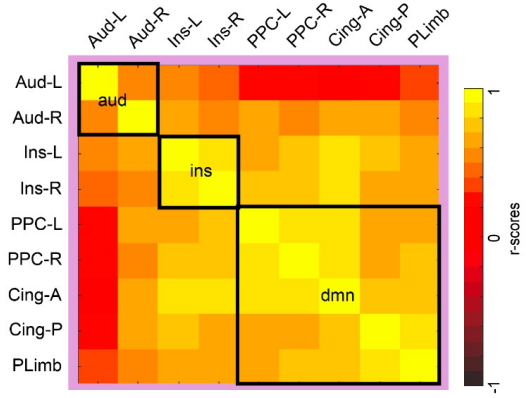


El-Baba et al, ***PLOS One*** 2019

Isoflurane anesthesia

Rats

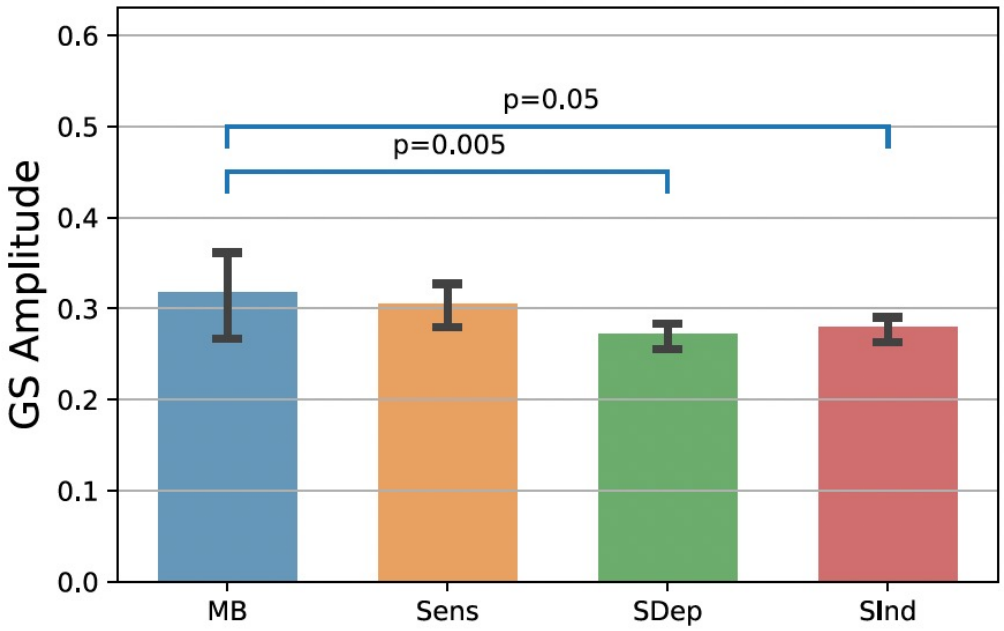




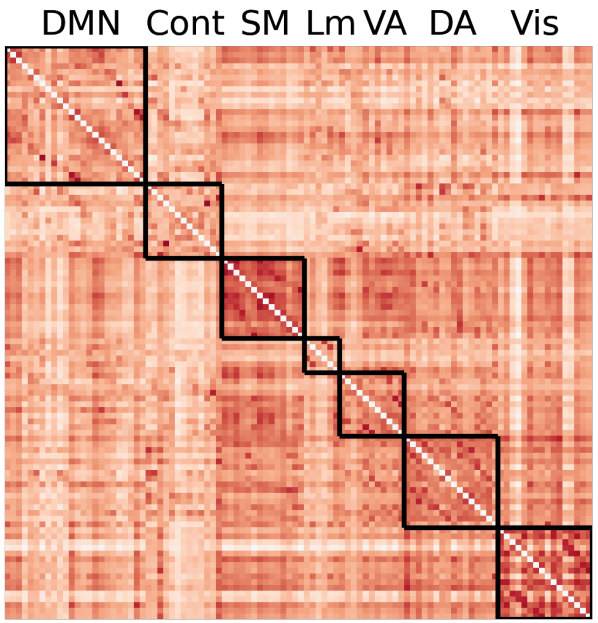
Aedo-Jury et al, ***eLife*** 2019

Hypothesis: MB is Mediated by Low Arousal Levels

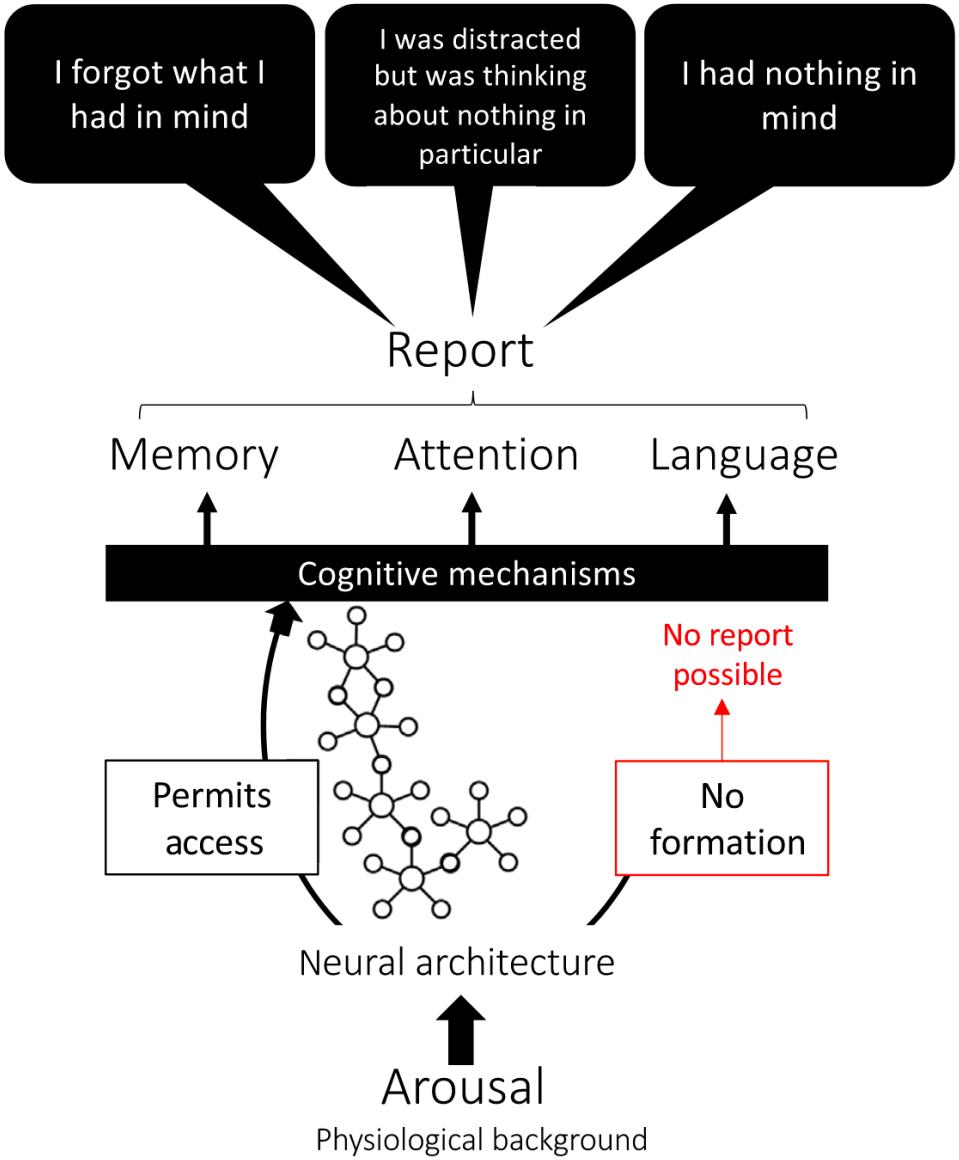
Higher Global Signal Amplitude



"Hyperconnectivity"



Mortaheb, Van Calster, Raimondo, Klados, Boulakis, Georgoulaa, Majerus, Van De Ville*, Demertzi*. ***PNAS*** 2022

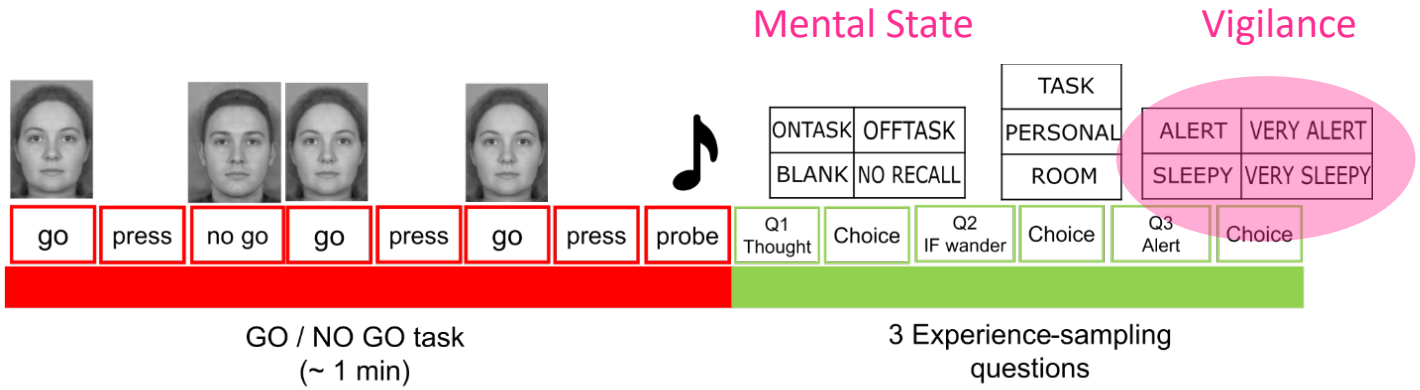


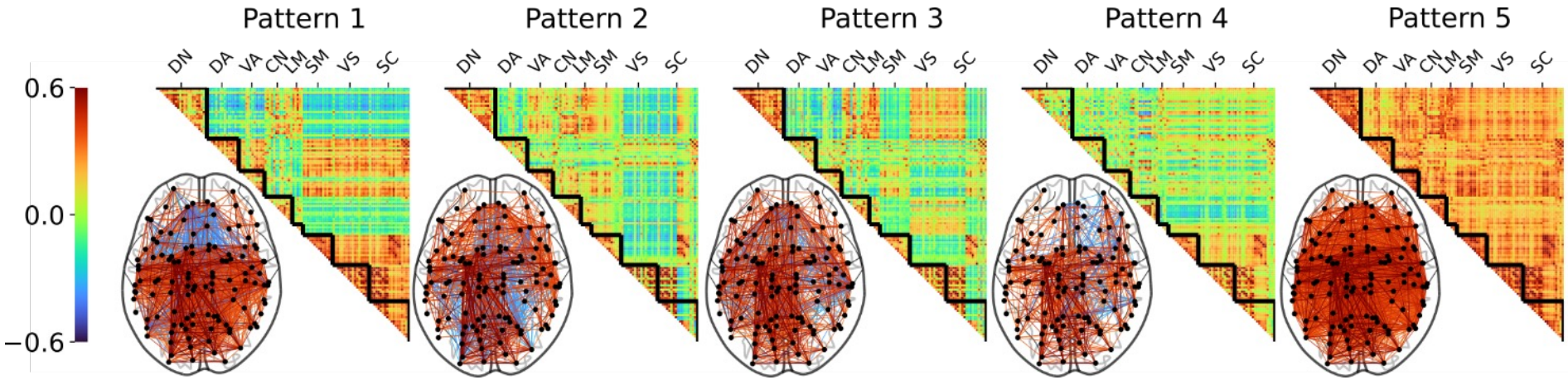
A physio-cognitive account of the phenomenology of MB

Andrillon, Lutz, Windt, Demertzi. ***Trends Cogn Sci*** 2025

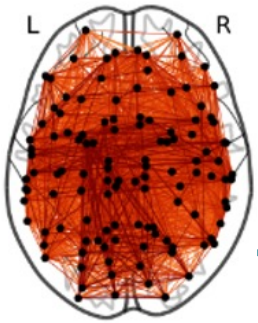
Bridging fMRI-EEG

Sustained Attention to Response Task (SART)



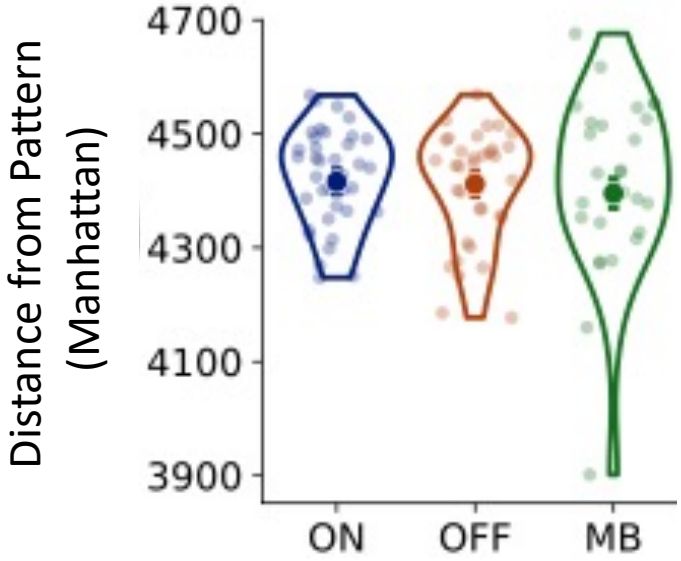


Boulakis, Kusztor, Tsuchiya, Andrillon, Demertzi. ***In prep***

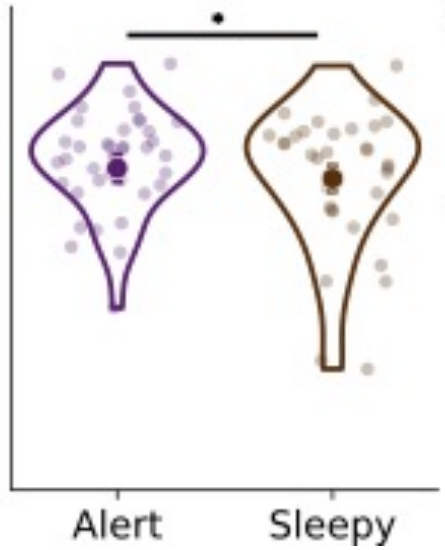


MB-Hyperconnectivity depends on vigilance

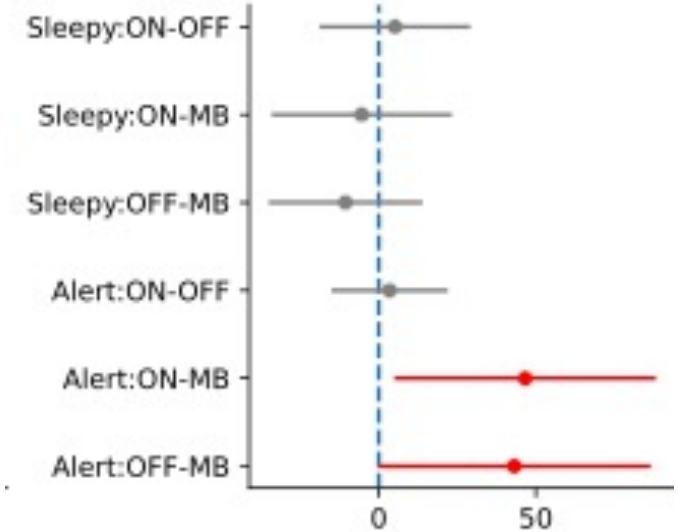
No evidence for Hyperconnectivity-MB link



Hyperconnectivity closer to Sleepy

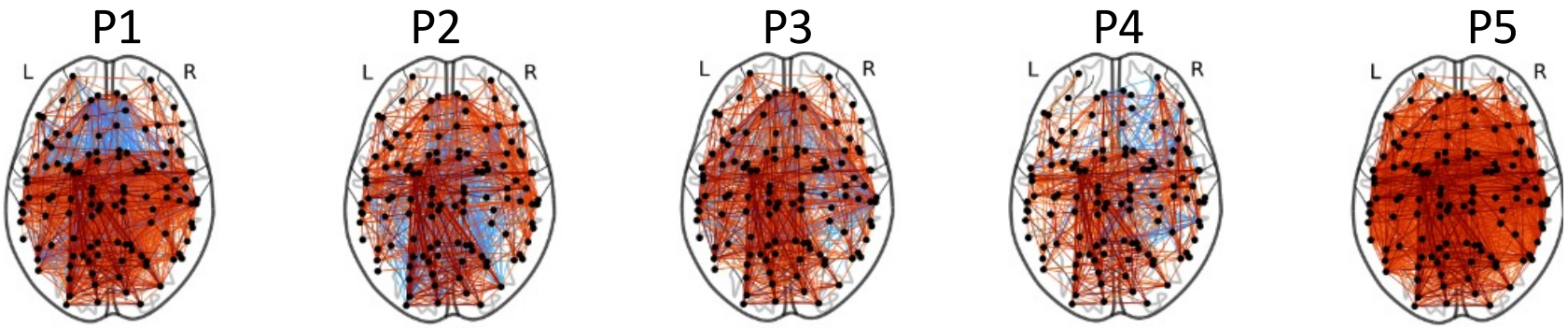


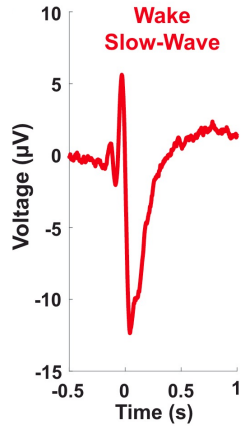
When ALERT, MB reports are closer to Hyperconnectivity

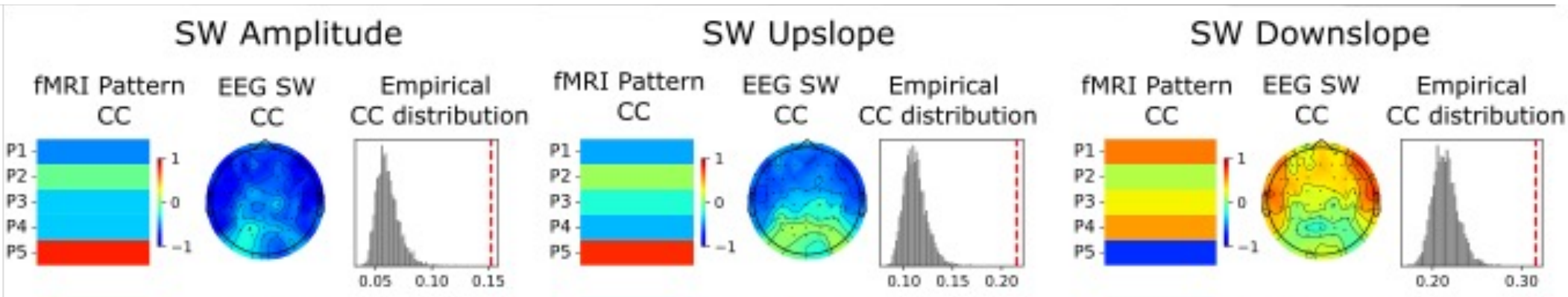


Boulakis, Kusztor, Tsuchiya, Andrillon, Demertzi. ***In prep***

Hyperconnectivity is linked to Slow-Wave-Like Activity

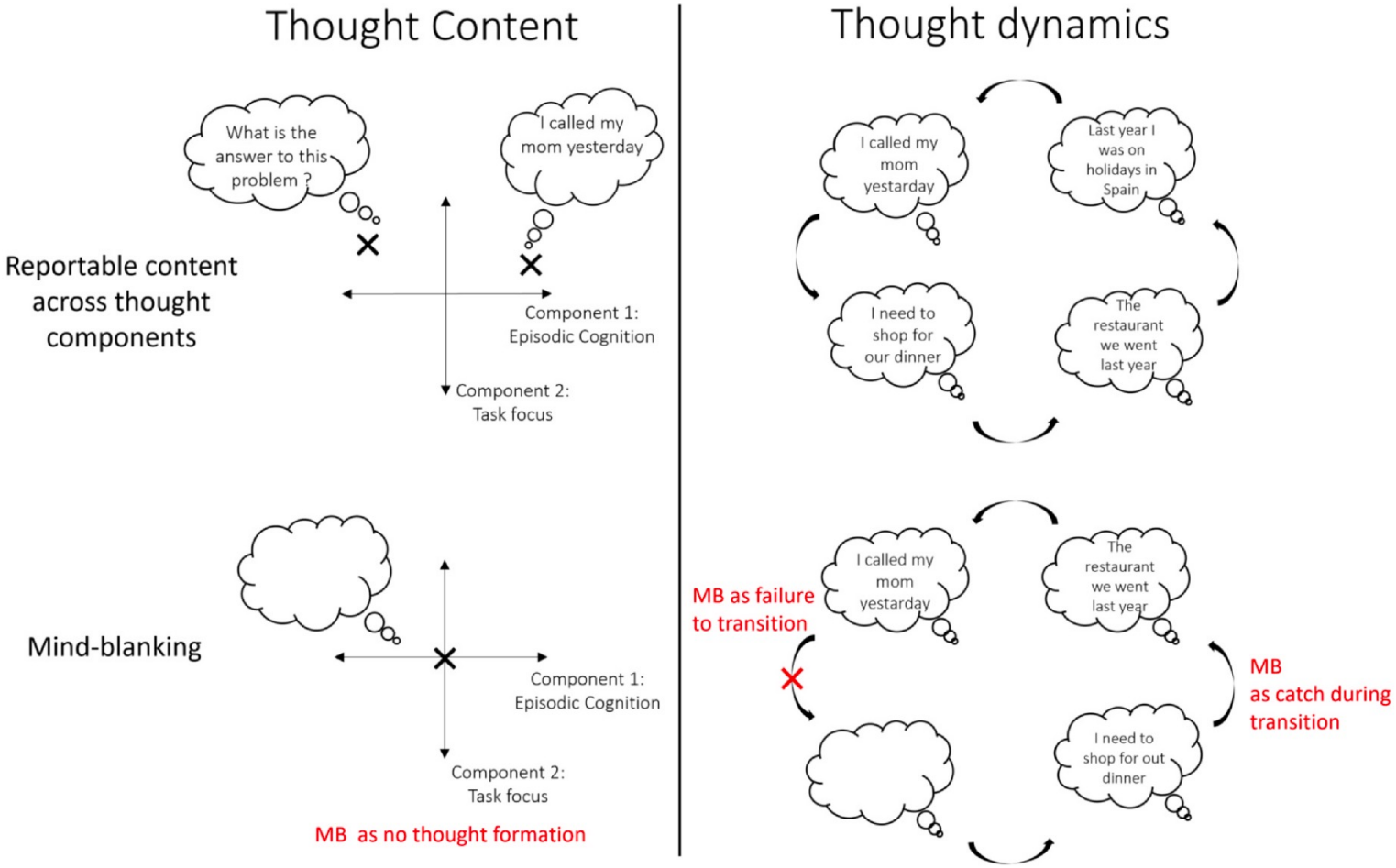




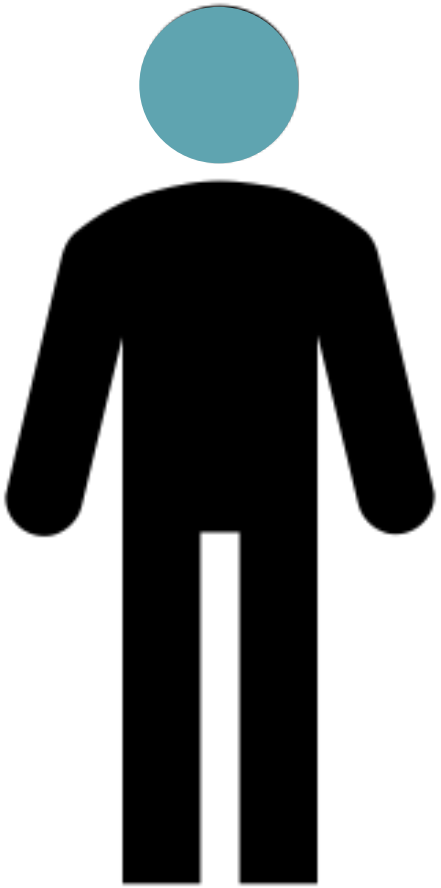


Boulakis, Kusztor, Tsuchiya, Andrillon, Demertzi. ***In prep***

Different mechanisms of MB



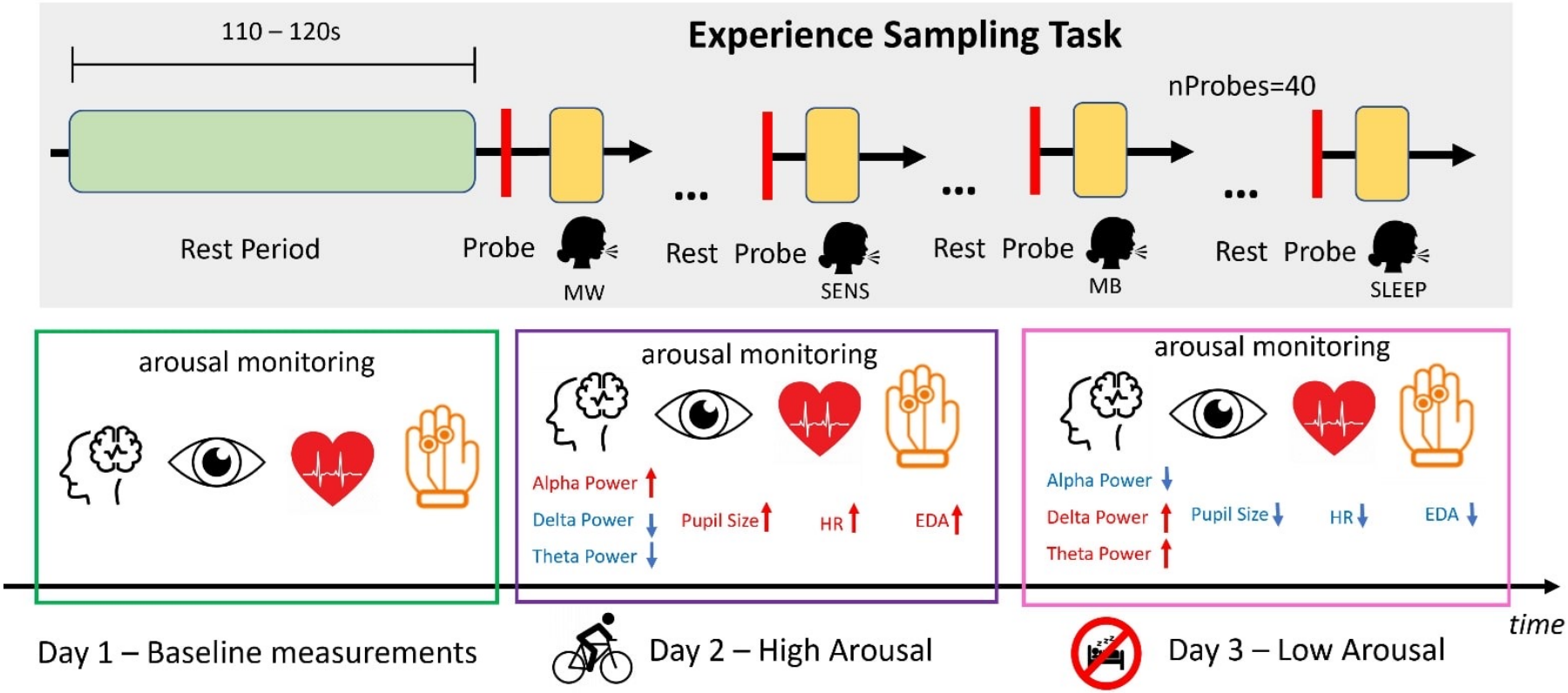
Boulakis & Demertzi. ***Curr Opinion Behav Sciences*** 2025



PART 3

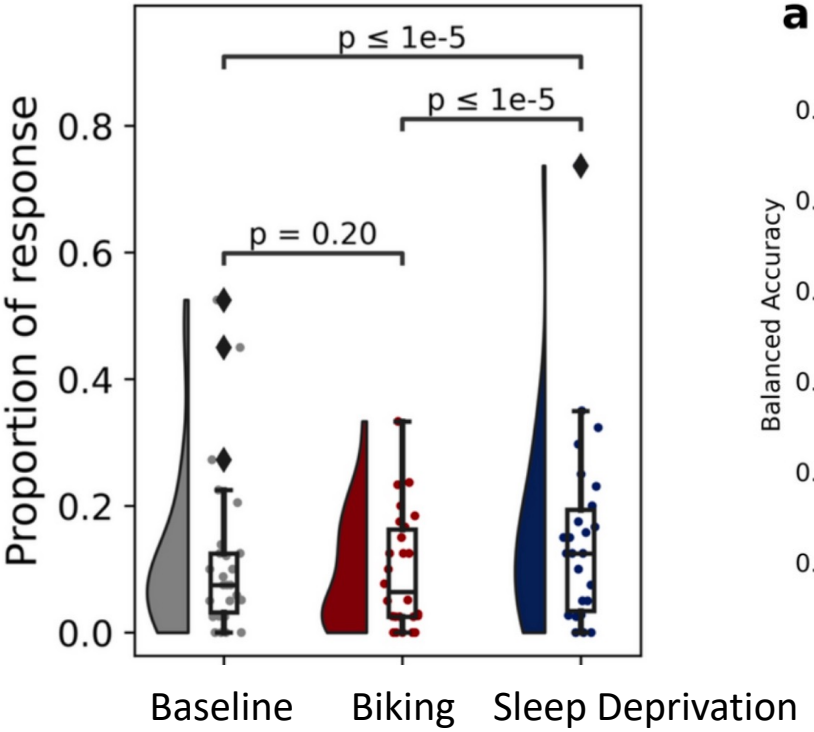
Brain – Body Interactions

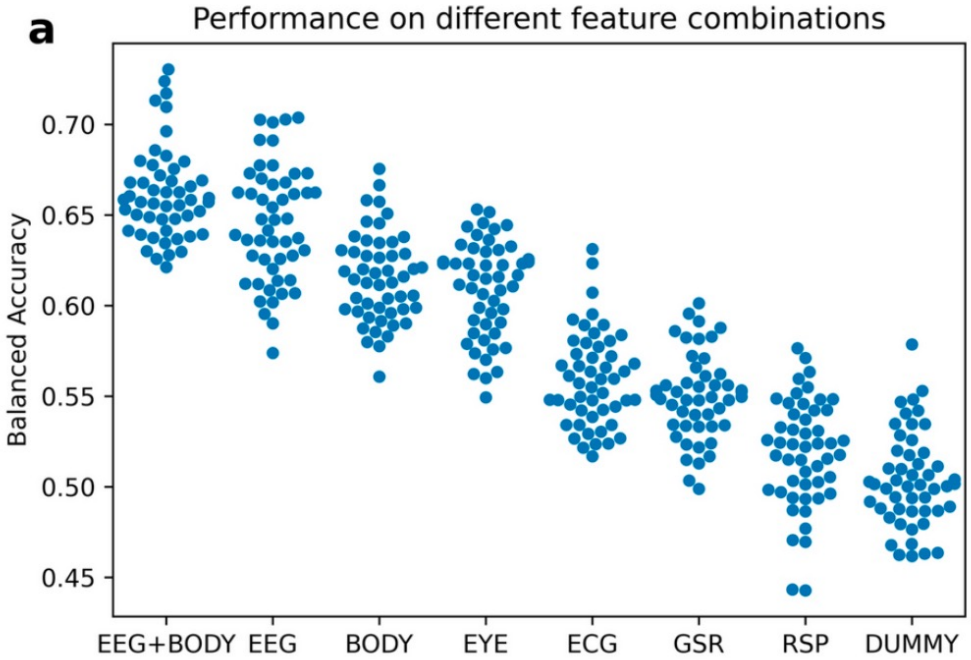
Does arousal mediate MB?



Boulakis, Simos, Zoi, Mortaheb, Schmidt, Raimondo, Demertzi. Registered Report Stage2 (results), *biorχiv* 2024

Altered arousal increases MB reports

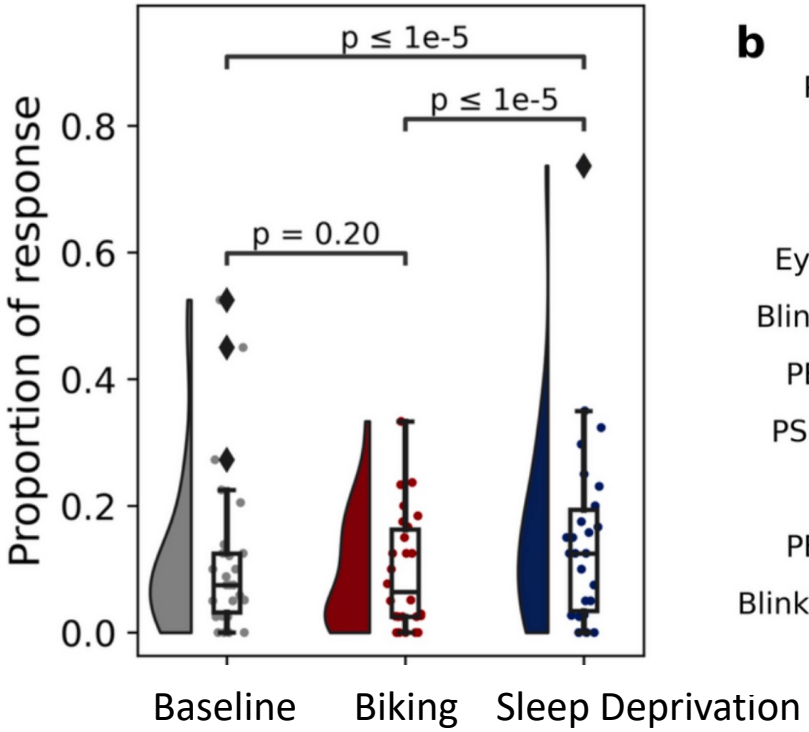


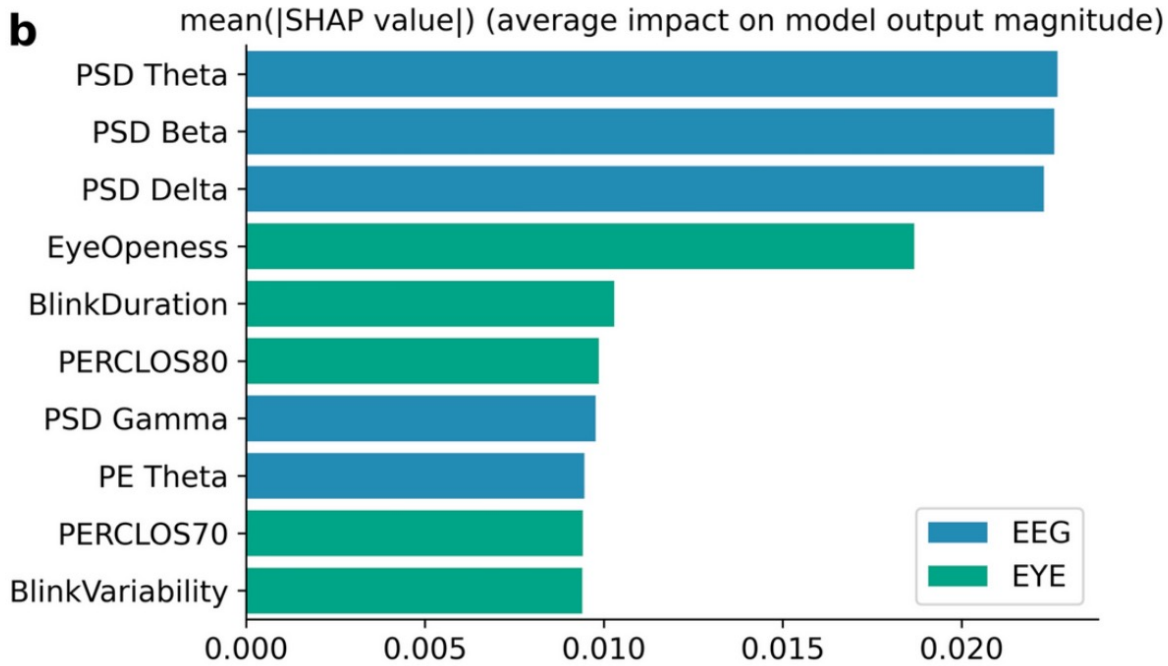


but MB was more frequent in
first half of post-exercise vs. second half

Boulakis, Simos, Zoi, Mortaheb, Schmidt, Raimondo, Demertzi. ***Sci Rep*** 2025

MB can be predicted by brain <u>and</u> body features





but MB was more frequent in
<u>first half</u> of post-exercise vs. second half

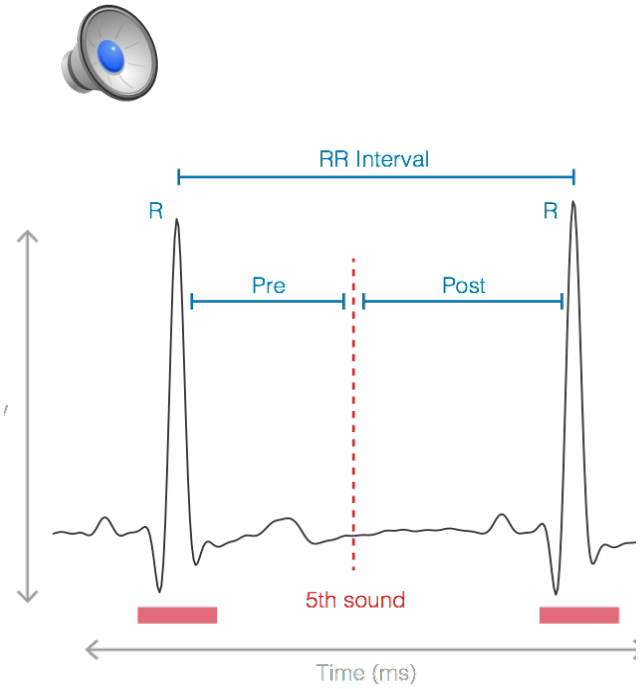
Boulakis, Simos, Zoi, Mortaheb, Schmidt, Raimondo, Demertzi. ***Sci Rep*** 2025

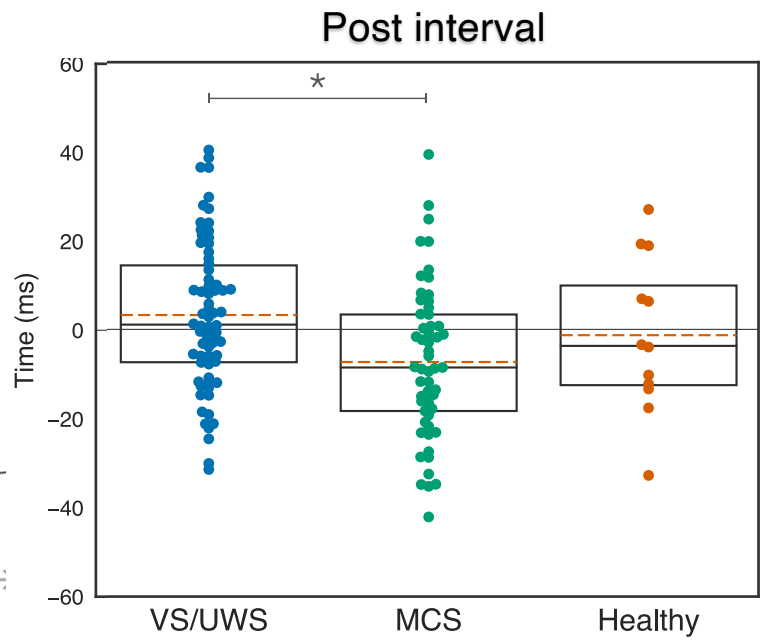
Cardiac reactions to oddballs in MCS

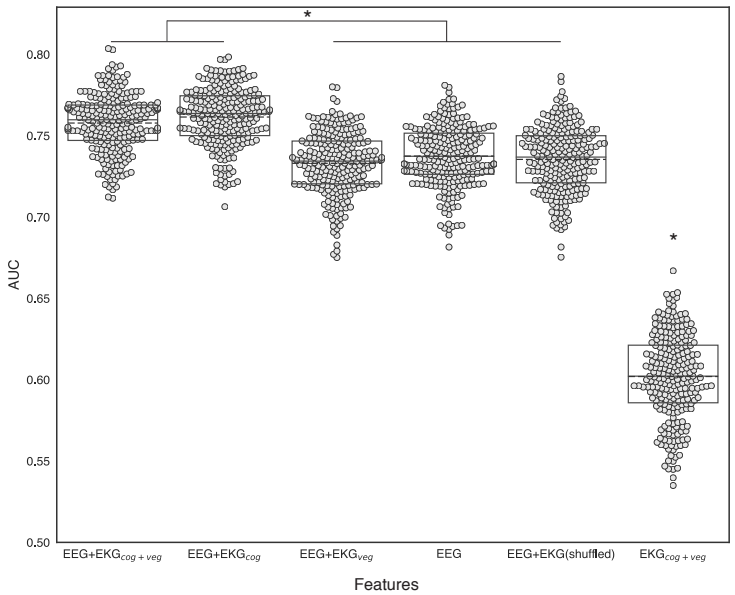
Auditory oddball paradigm
Bekinschtein et al., PNAS, 2009

Cardiac cycle-phase acceleration only in MCS

Electrocardiographic markers carry independent information from EEG





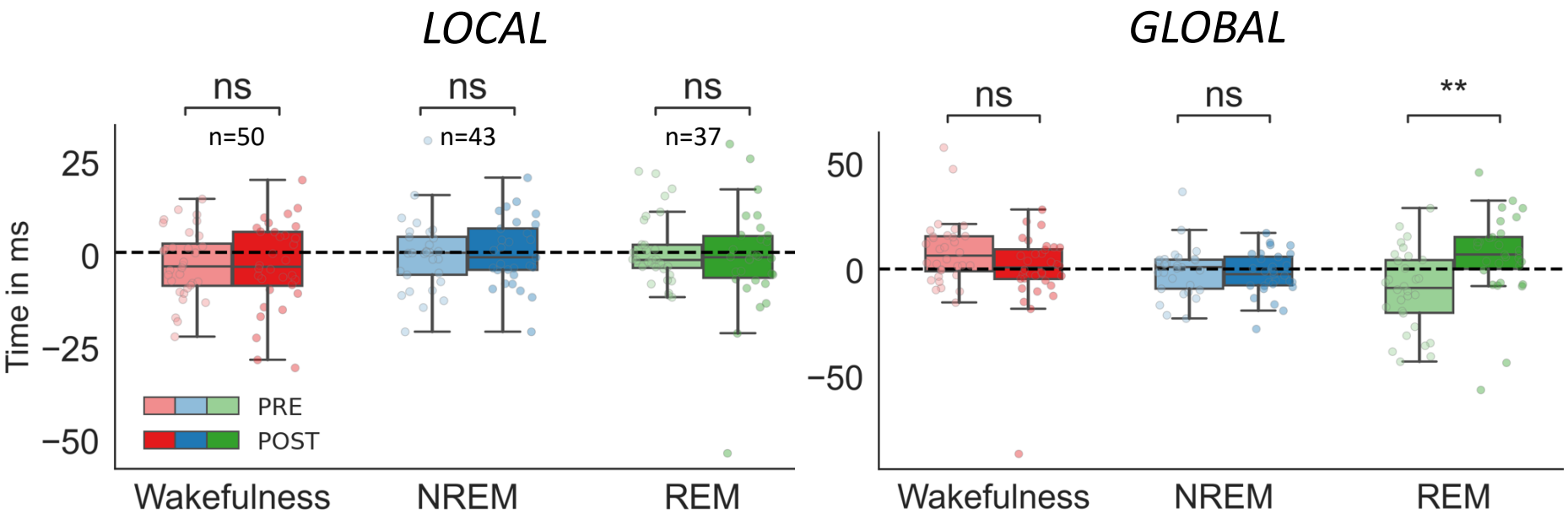


Raimondo, Rohaut, Demertzi, Valente, Engemann, Salti, Fernandez Slezak, Naccache, Sitt. *Annals of Neurology* 2017

Cardiac reactions to oddballs in <u>sleep</u>

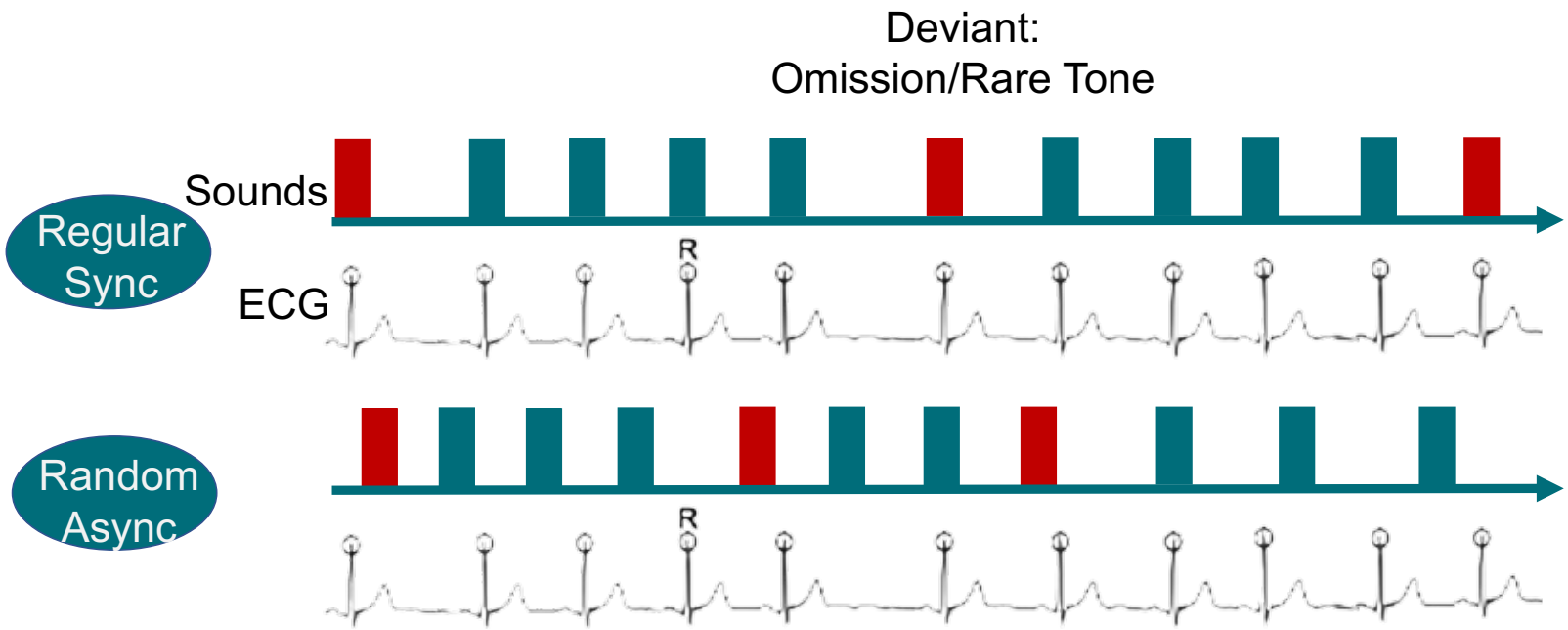
EEG: Strauss, Sitt, King, Elbaz, Azizi, Buiatti, Naccache, van Wassenhove, Dehaene, S, *PNAS* 2015
EEG: Blume, Niedernhuber, Spitschan, Slawik, Meyer, Bekinschtein, & Cajochen. *Sleep* 2022

Cardiac deceleration for global deviants only in REM



Koroma, Boulakis, Raimondo, Blume, Strauss, Demertzi. *In prep*

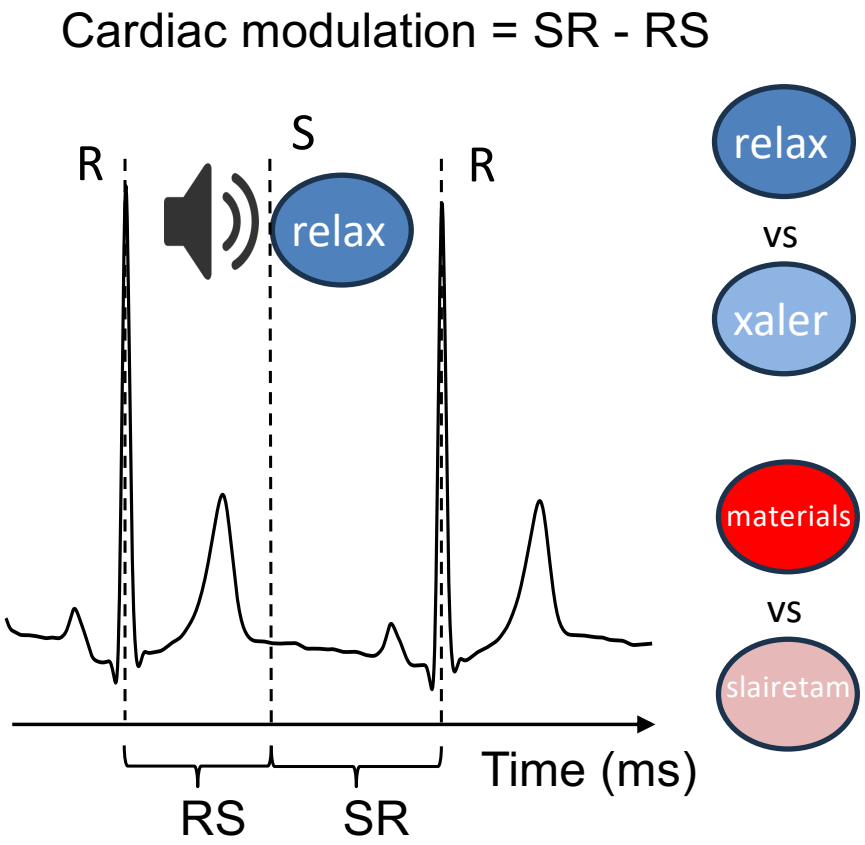
Cardiac responses to omitted sounds presented in synchrony to heartbeats

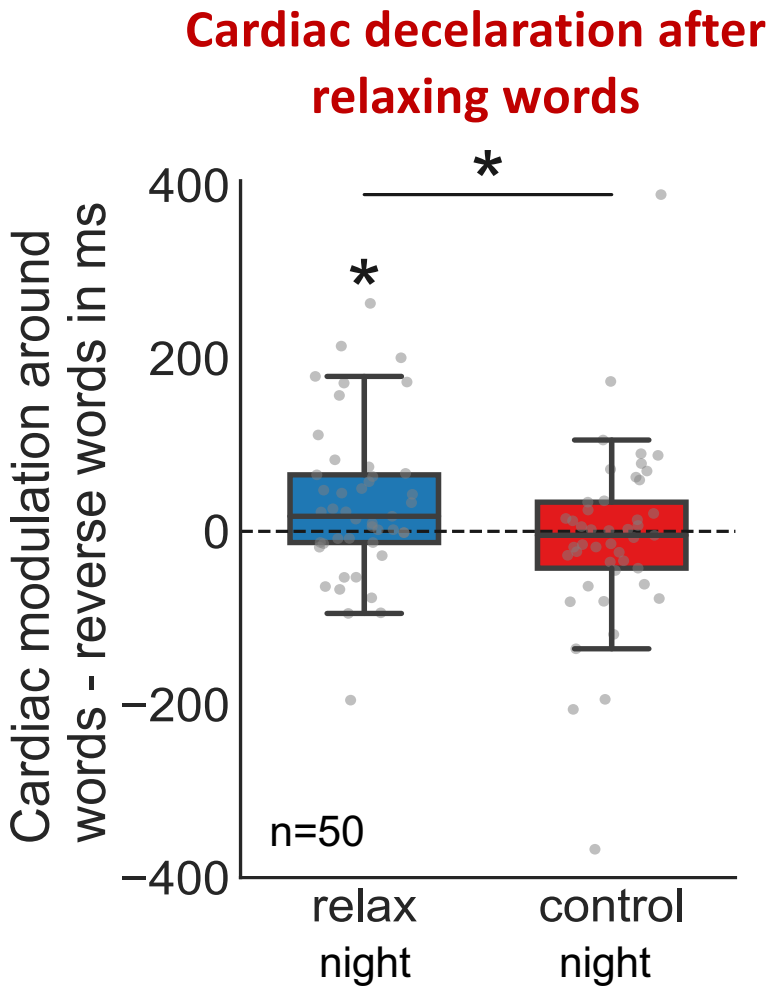


Cardiac deceleration for sound omissions and rare tones in synchronous condition only

Koroma, Nguy, Pelentritou, De Lucia, Demertzi. *In prep*
Pelentritou, Pfeiffer, Schwartz, De Lucia. *Comm Biology* 2024

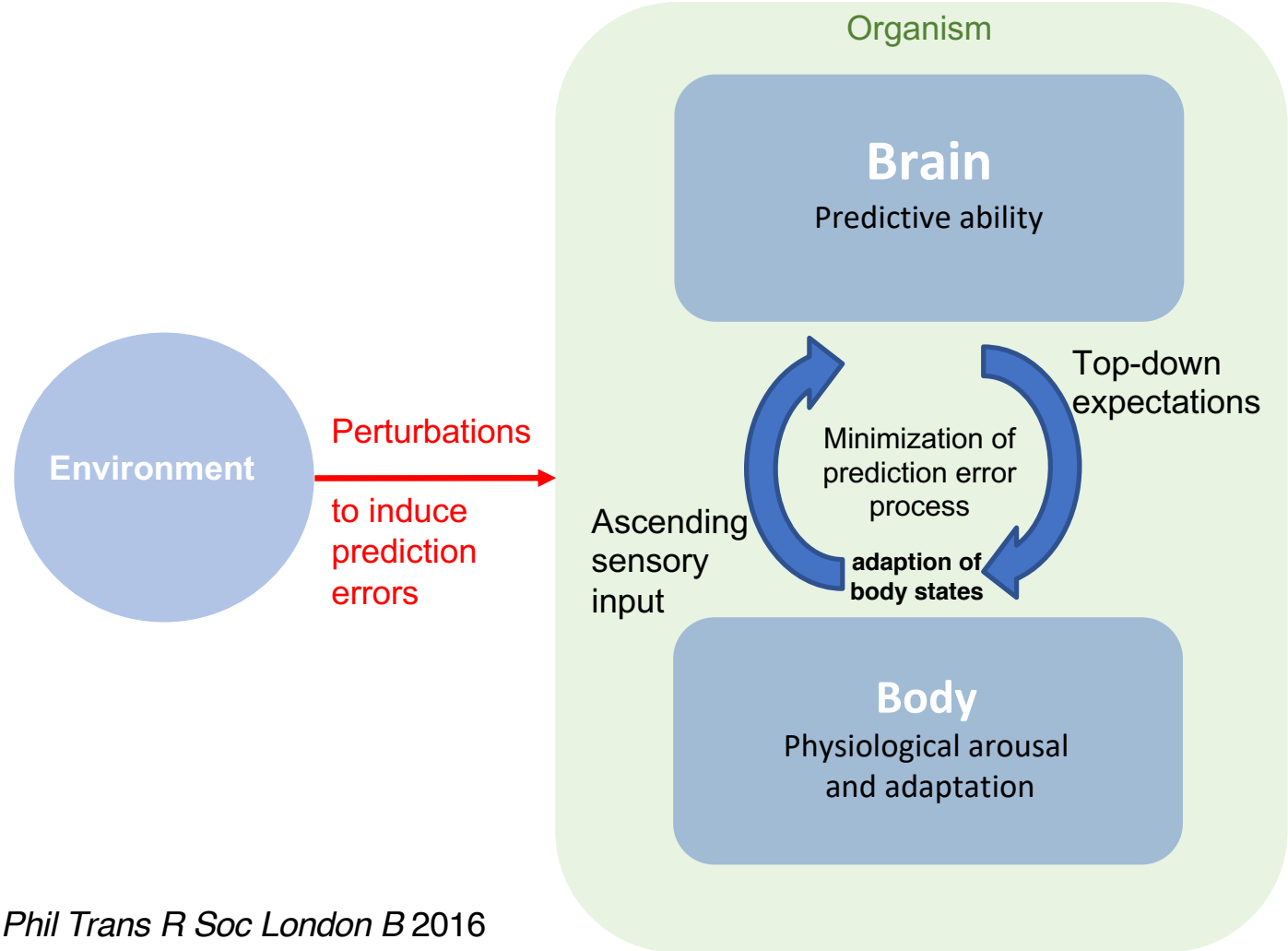
Cardiac responses to word-induced relaxation during sleep





Koroma, Beck, Schmidt, Rasch, Demertzi, A. *J Sleep Res* 2024

The embodied perspective

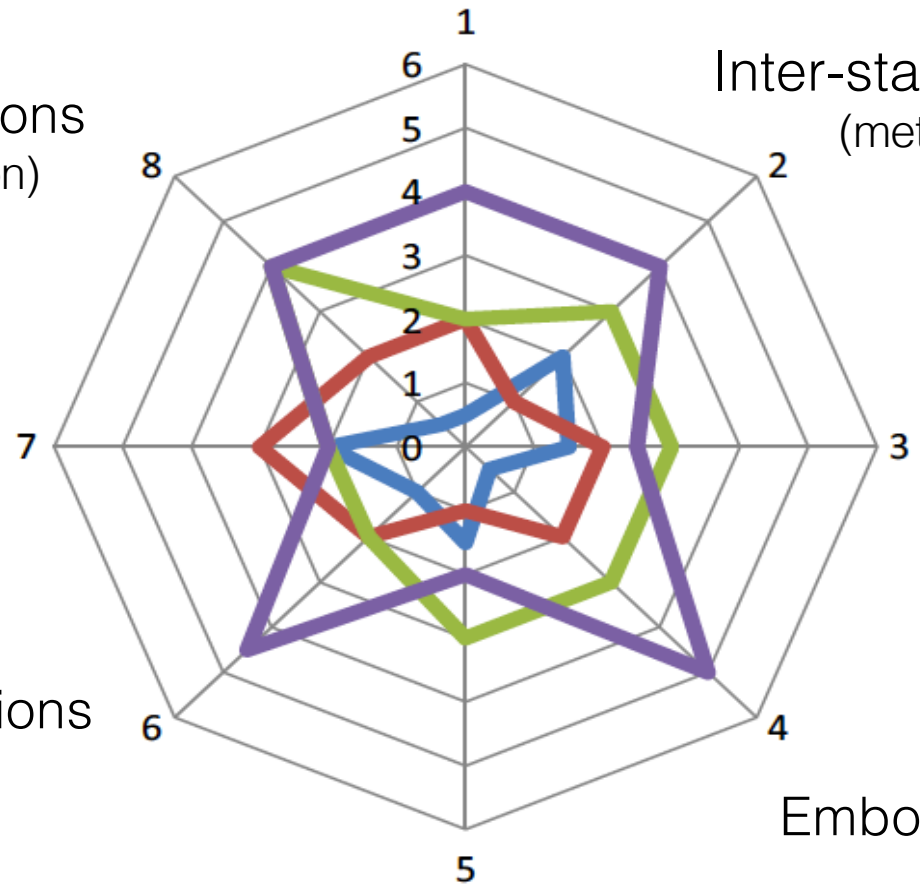


Seth & Friston. *Phil Trans R Soc London B* 2016

Consciousness is multidimensional

Cross-modal interactions
(multi-sensory integration)

Inter-state dynamism
(metastability)



"Rich" inter-regional communication
(arousal)

Functional Anticorrelations
(neural inhibition)

Embodied responsiveness
(active inference)

Bayne, Hohwy, Owen *Trends Cogn Sci* 2016

Attend!

Submit!

Physiology of Cognition Lab

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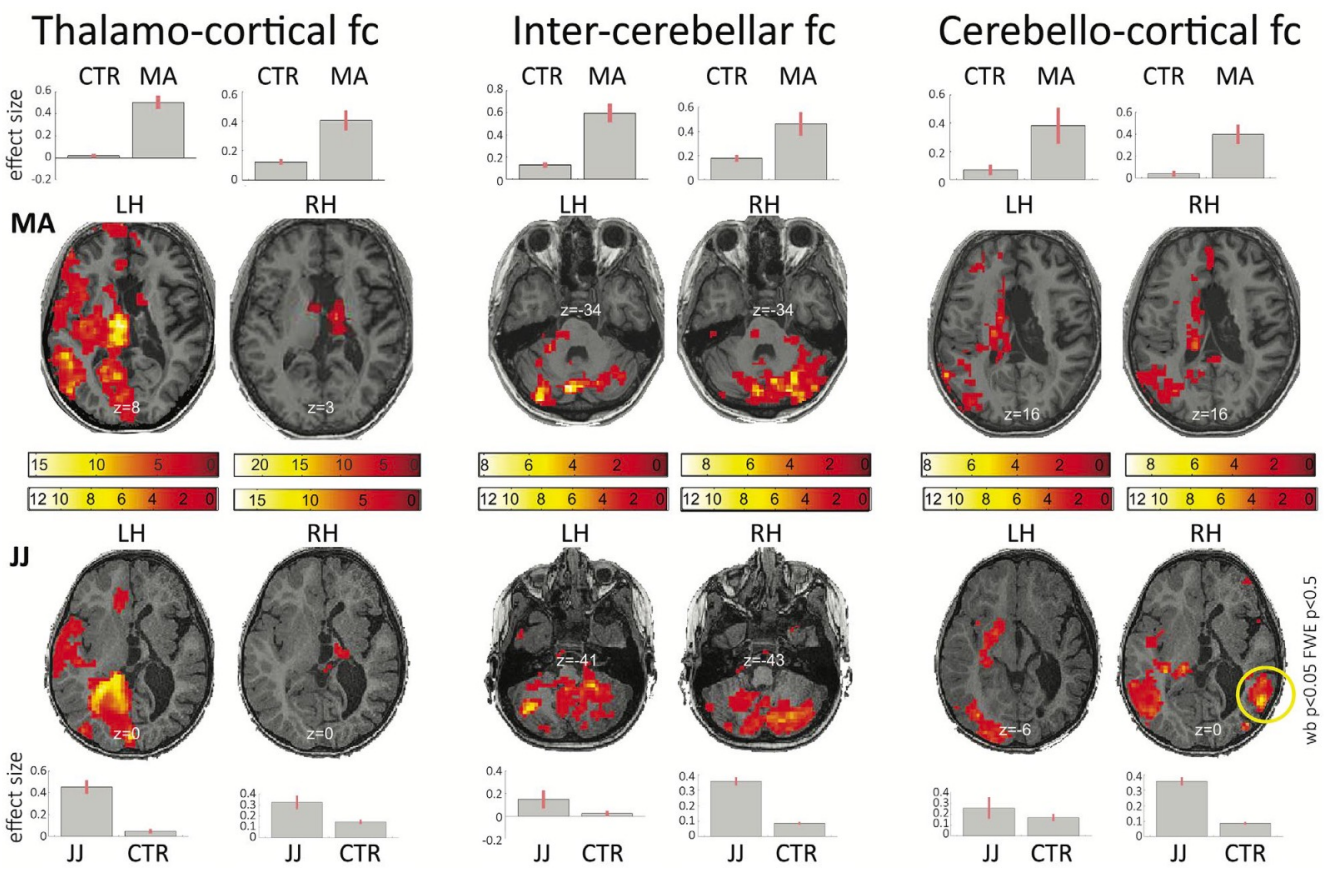
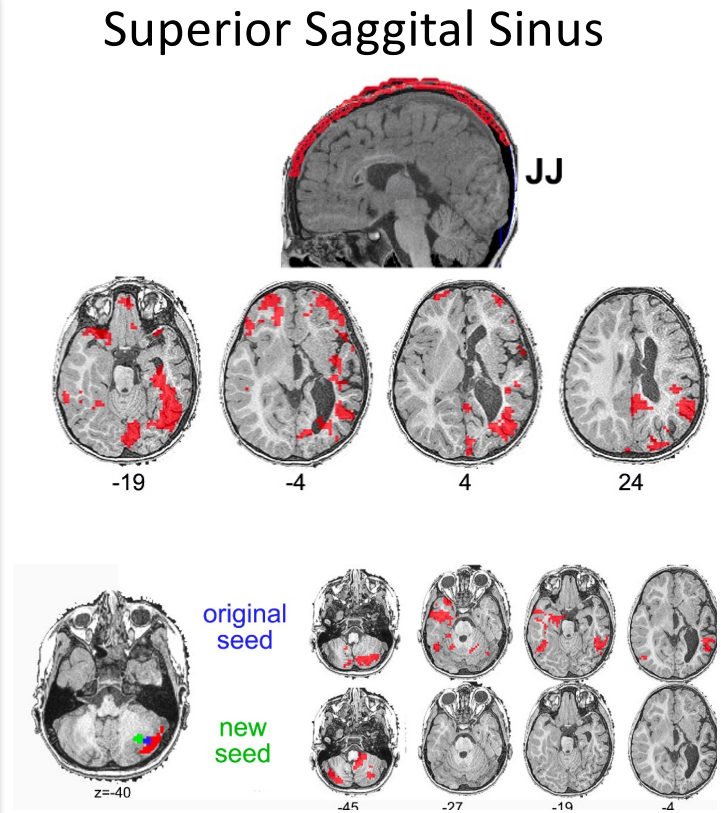
Marzia DE LUCIA
Andria PELENTRITOU
Christine BLUME
Jan REMAEKERS
Natasha MASON
Pablo MALLARONI

Mediation of subcortical regions in functional reorganization

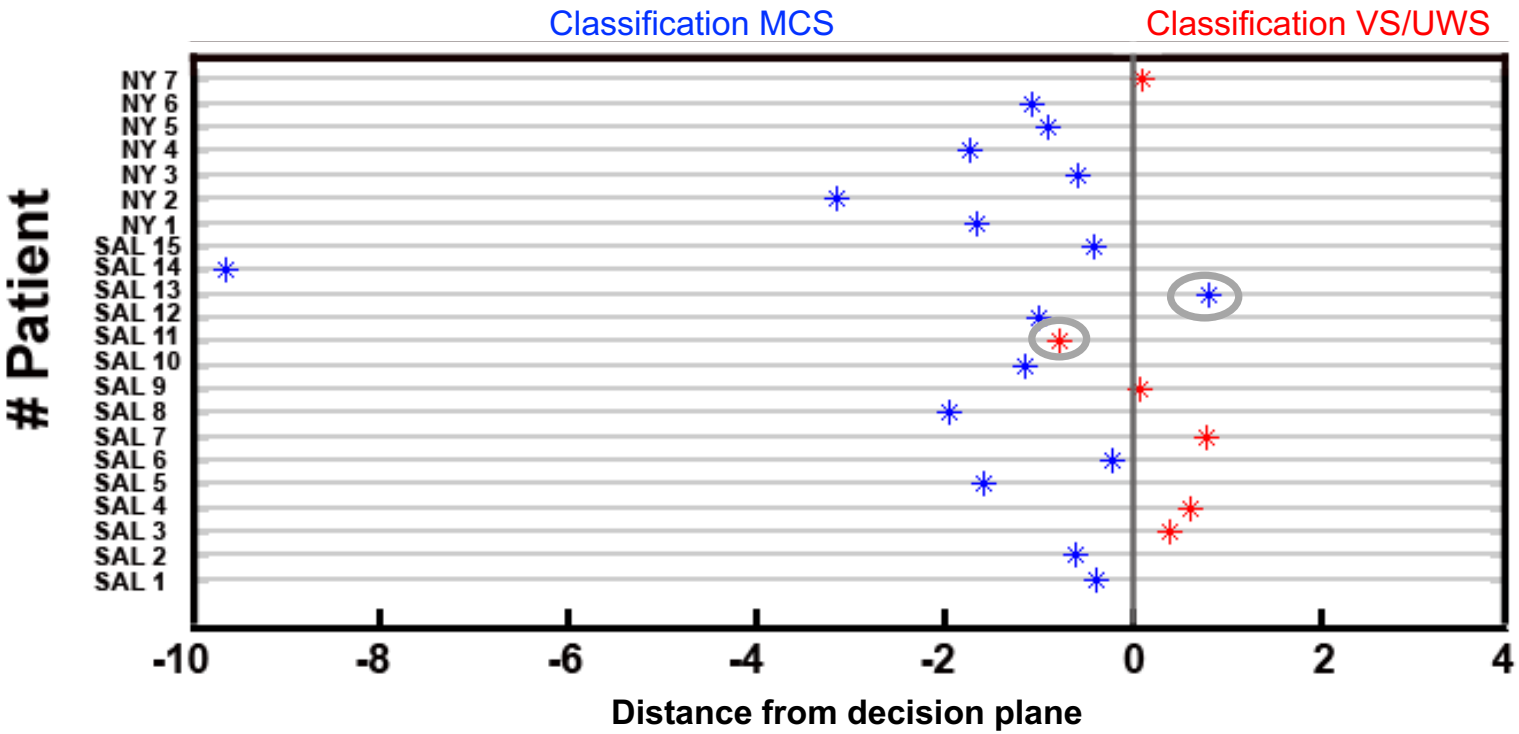


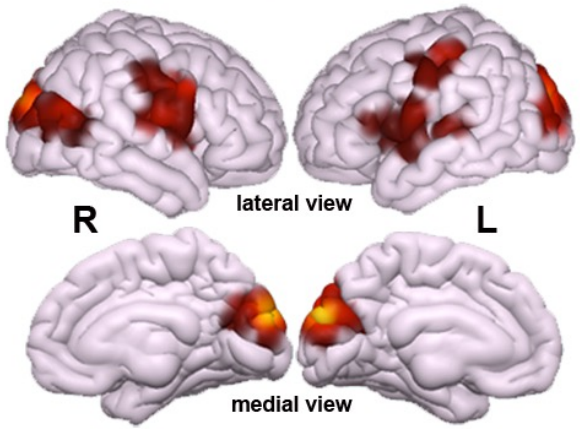


Blauwblomme* & Demertzi*, Tacchela, Fillon, Bourgeois, Losito, Eisermann, Marinazzo, Raimondo, Alcauter, Van De Steen, Colenbier, Laureys, Dangouloff Ros, Naccache, Boddaert, Nabbout et al, ***Epilepsia Open*** 2020

DOC separation based on cross-modal interactions

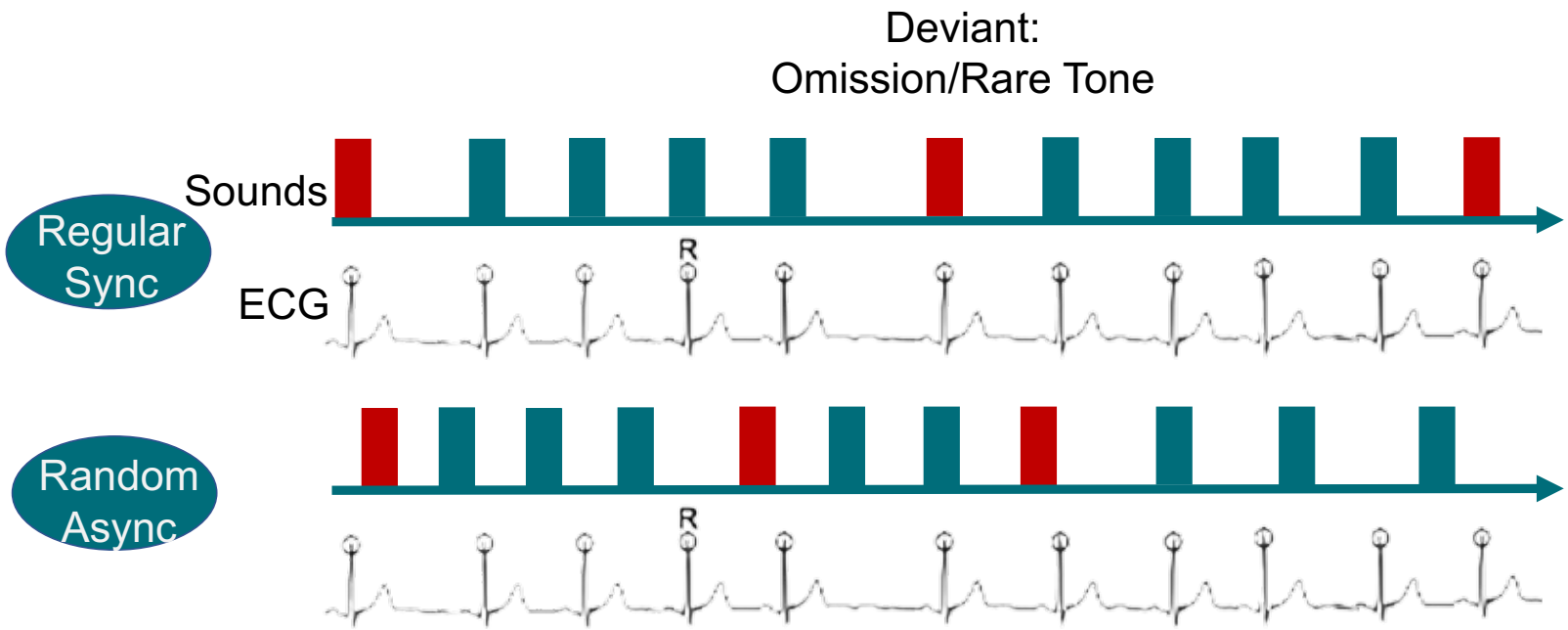
- Training set: 45 DOC (26 MCS, 19 VS/UWS)
  - 14 trauma, 28 non-trauma, 3 mixed
  - 34 patients assessed >1m post-insult
- Test set:
  - **16 MCS**, **6 VS/UWS** (15 non-trauma; all chronic)
  - 2 different centers





Demertzi & Antonopoulos et al, ***Brain*** 2015

Cardiac responses to omitted sounds presented in synchrony to heartbeats



Cardiac deceleration for sound omissions and rare tones in synchronous condition only

Koroma, Nguy, Pelentritou, De Lucia, Demertzi. *In prep*
Pelentritou, Pfeiffer, Schwartz, De Lucia. *Comm Biology* 2024