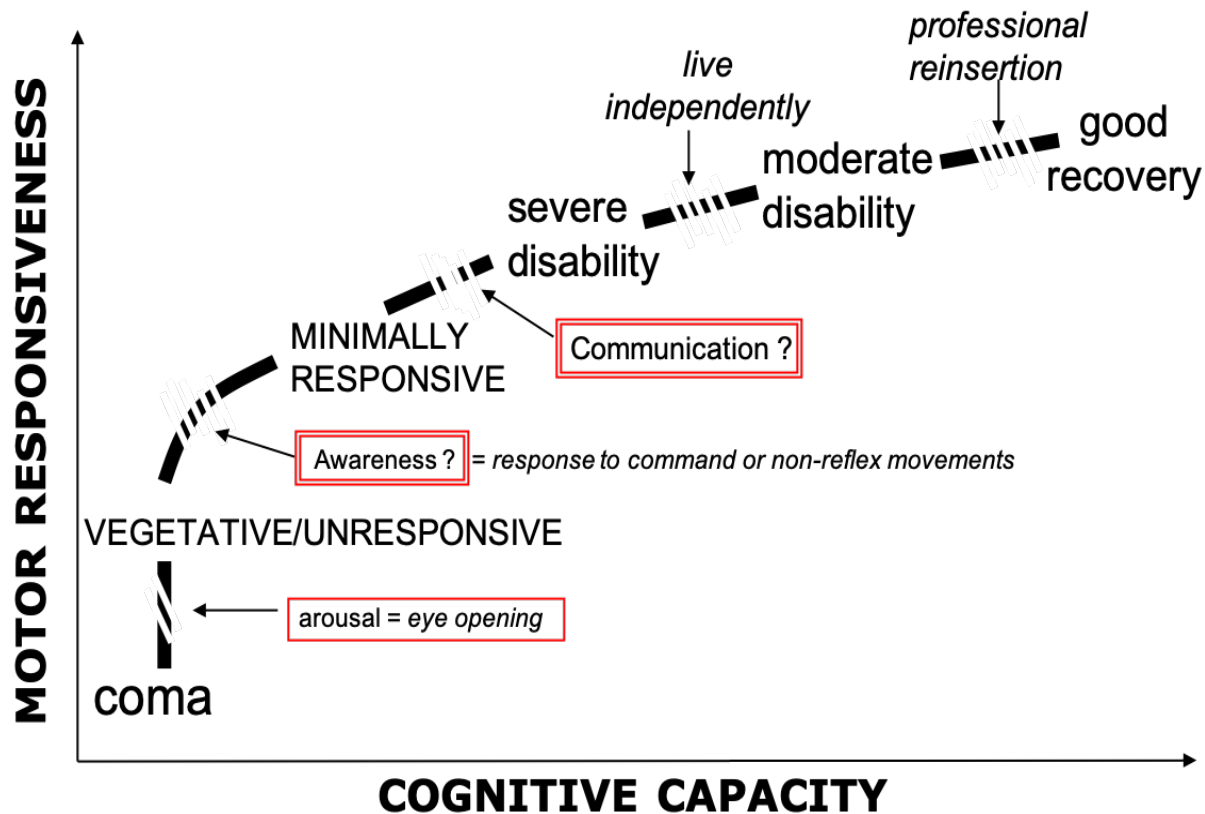


# At the boundaries of mental state reportability

Athena Demertzi, PhD  
FNRS Research Associate  
Director, Physiology of Cognition

Université de Liège

# Consciousness inferred from behavior



Source: Google pictures (Credit: CC-BY-SA; M Appelman)

# The ethical imperative of Consciousness

## We cannot always trust behavior

n=103 post-comatose patients

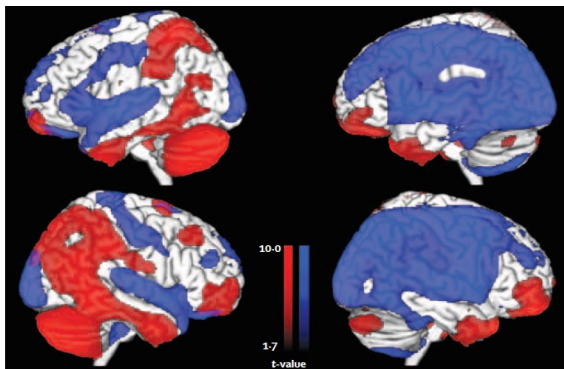
45 Clinical diagnosis of VS  
18 Coma Recovery Scale MCS



40% misdiagnosis

Schnakers et al, *Ann Neurol* 2006; *BMC Neurol* 2009

### Standardized assessment & Neuroimaging



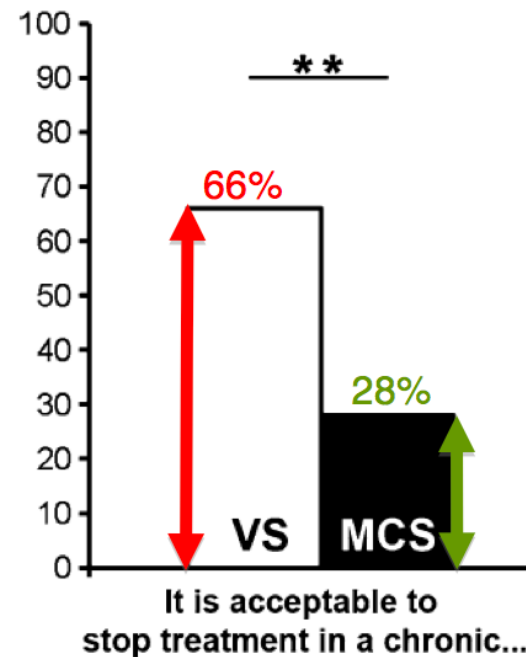
Coma Recovery Scale-Revised results			
	UWS	MCS	Total
Clinical consensus diagnosis			
18F-FDG PET			
VS/UWS	24 (21%)	5 (4%)	29 (26%)
MCS	12 (11%)	71 (63%)	83 (74%)
Total	36 (32%)	76 (68%)	112 (100%)

UWS=unresponsive wakefulness syndrome. MCS=minimally conscious state.

Table 2: Diagnostic results by modality

## End-of-life support for “unconscious” patients

2,475 medical professionals



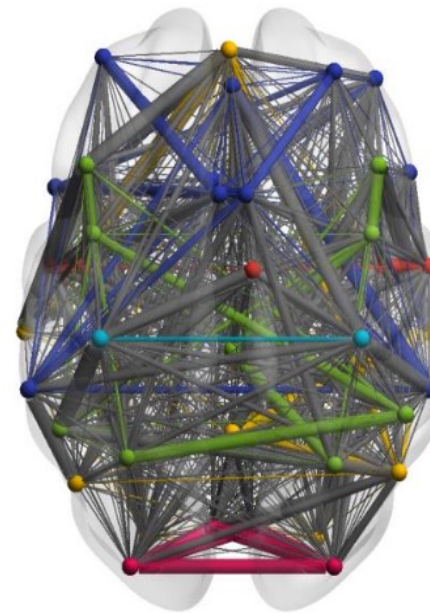
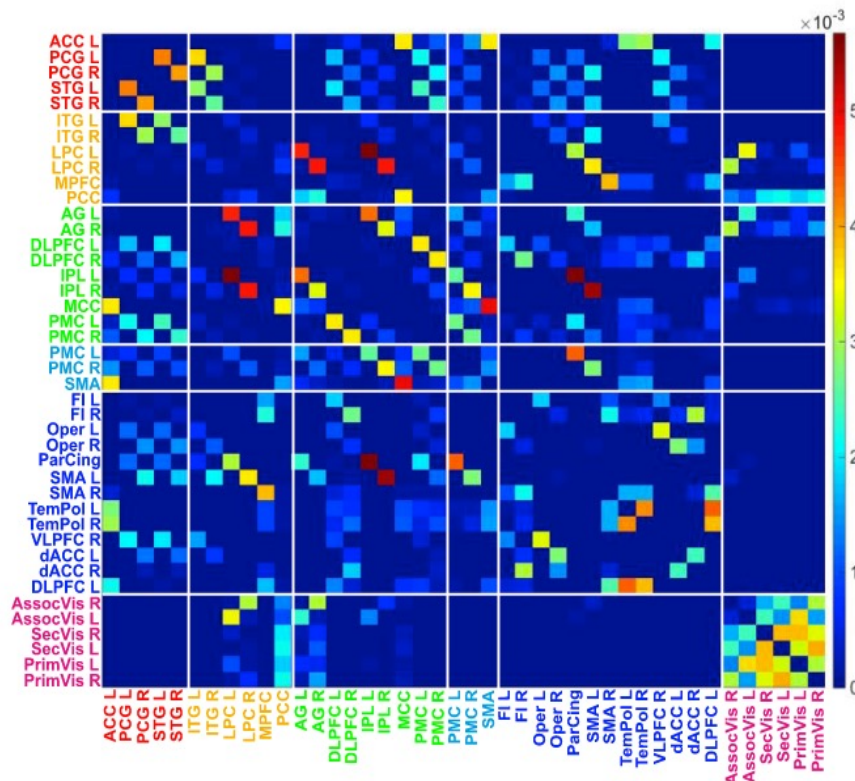
Demertzi et al, *Prog Brain Res* 2009  
Demertzi et al, *J Neurol* 2011  
Demertzi & Racine et al, *Neuroethics* 2012



# The brain as a network

100 billion neurons, ~100 trillion synaptic connections

## The Connectome

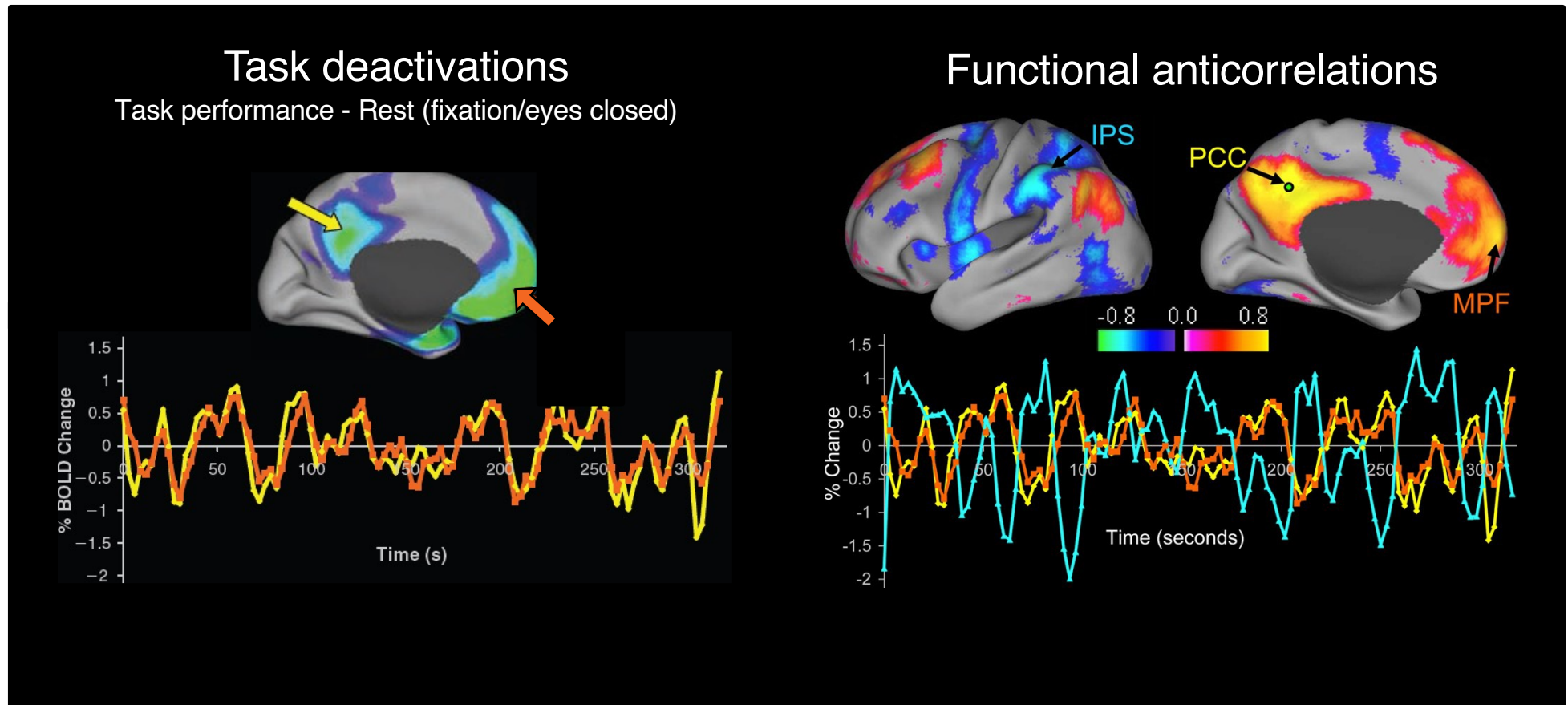


Aud      DMN      FP  
 Mot      Sal      Vis

A matrix representing  
 all possible  
 pairwise anatomical  
 connections  
 between neural  
 elements of the brain

Sporns, Tononi, & Koetter.  
*PLoS Comput. Biol.* 2005

# Default mode of brain function



Demertzi & Whitfield-Gabrieli, in: Neurology of Consciousness 2<sup>nd</sup> ed. 2015

Demertzi, Soddu, Laureys, *Curr Opin Neurobiology* 2013

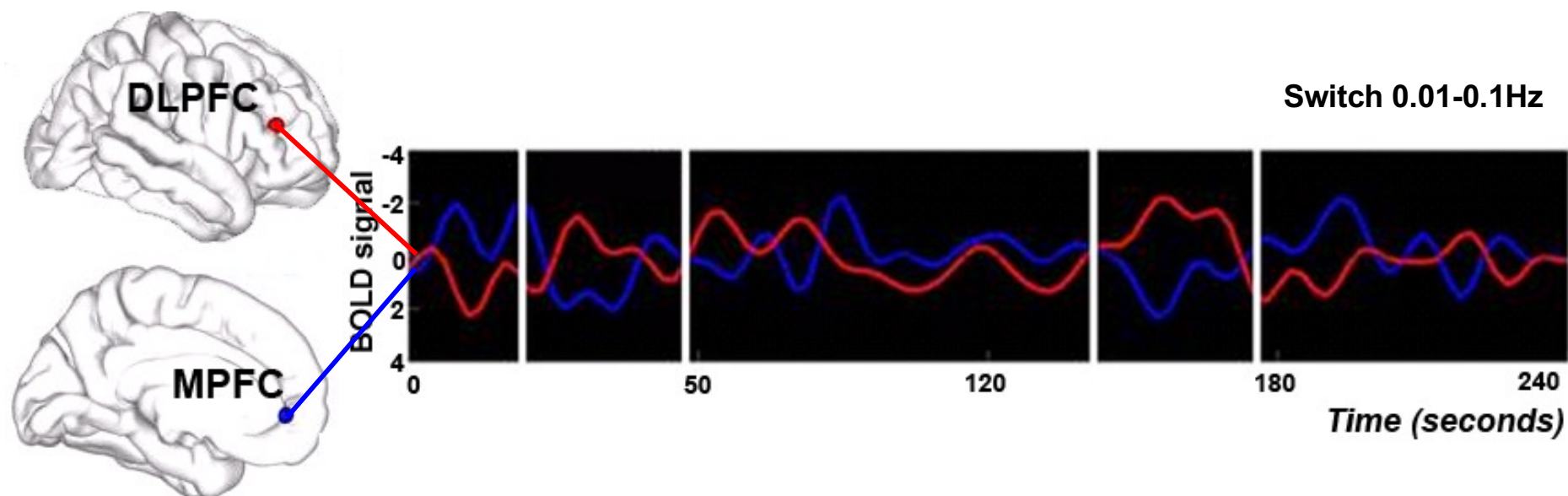
Demertzi et al, *Front Hum Neurosci* 2013

Raichle et al, *PNAS* 2001

Fox et al, *PNAS* 2005

# Anticorrelations inform cognitive function?

**External awareness  
or anticorrelated network**

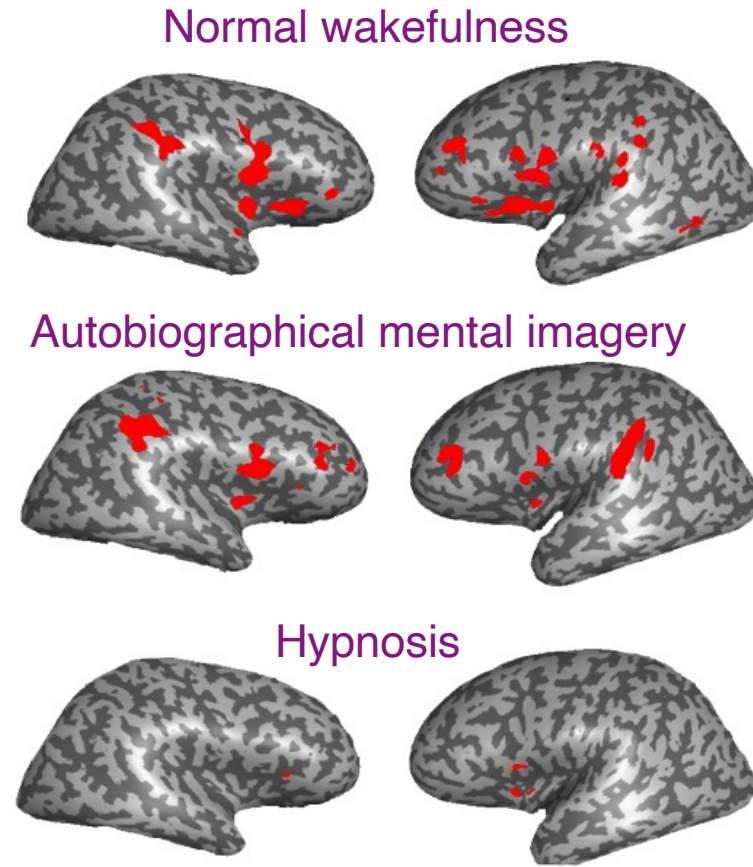
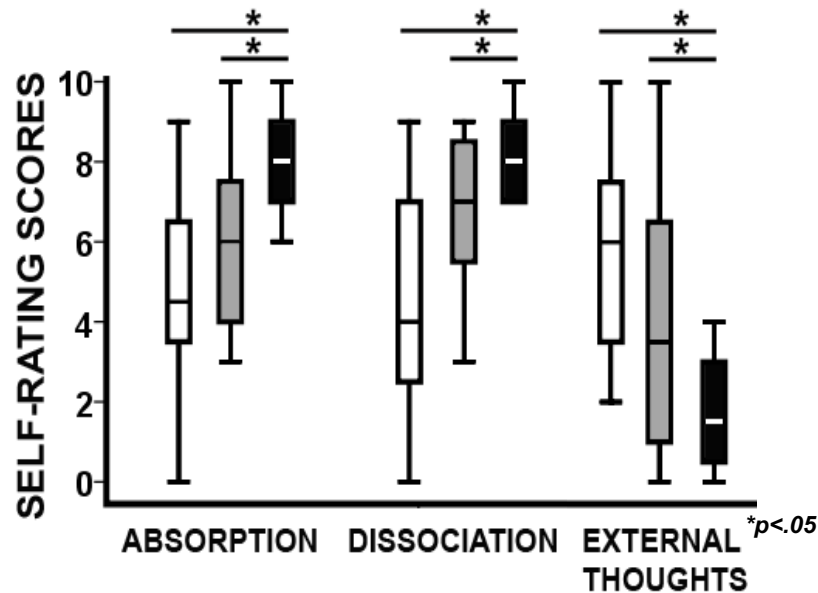


**Internal awareness  
or Default mode network**

- Vanhaudenhuyse\*, Demertzi\* et al, *J Cogn Neurosci* 2011
- Demertzi, Soddu, Laureys, *Curr Opin Neurobiology* 2013
- Demertzi & Whitfield-Gabrieli, in: *Neurology of Consciousness* 2<sup>nd</sup> ed. 2015
- Demertzi et al, *Front Hum Neurosci* 2013
- Demertzi, Kucyi, Ponces-Alvarez, Keliris, Whitfield-Gabrieli, Deco. *Netw Neurosci* in press

# Modified awareness reduces anticorrelations

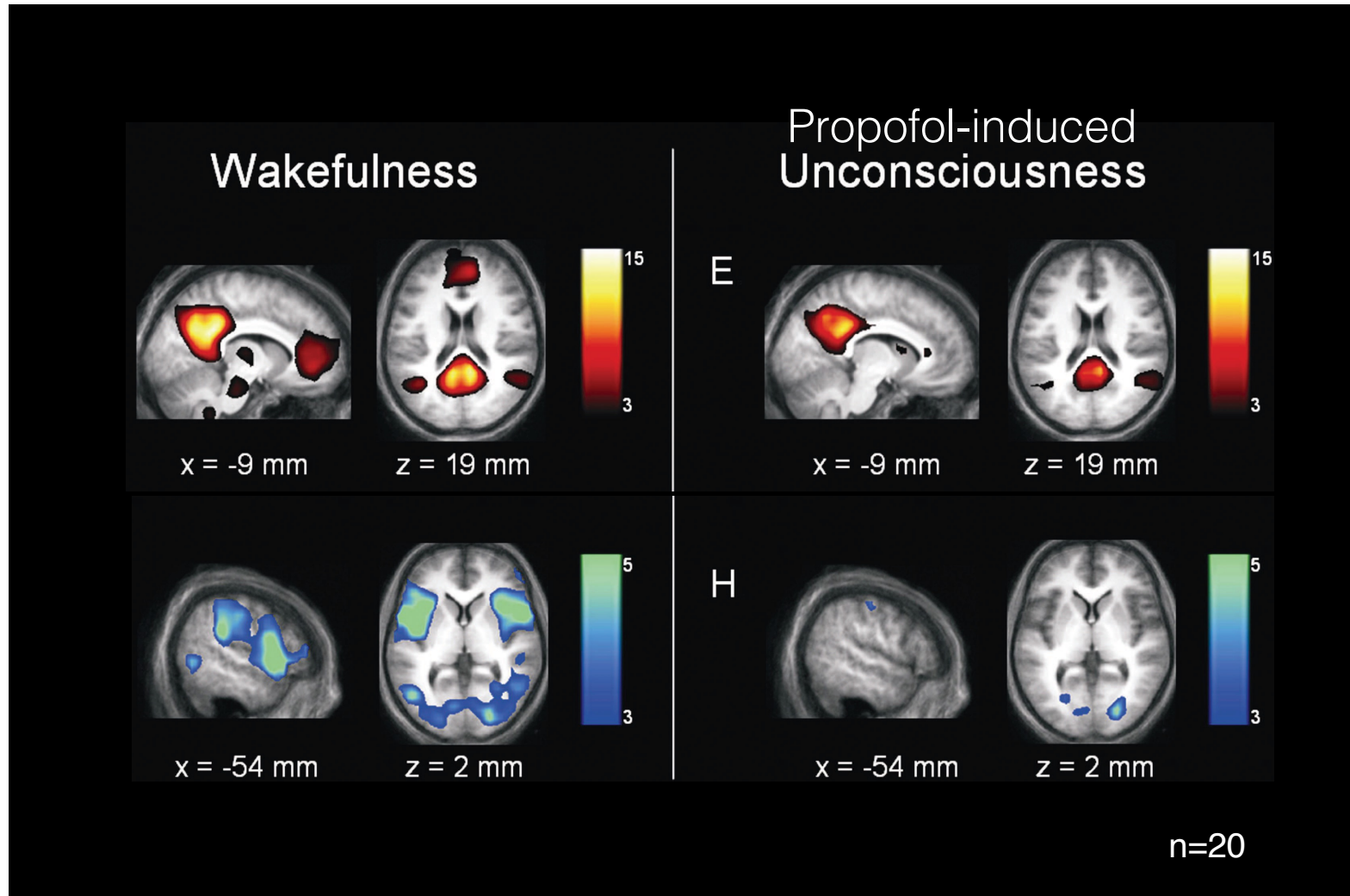
- Normal wakefulness
- ▒ Autobiographical mental imagery
- Hypnosis



*p < 0.05 corrected for multiple comparisons*



# Modified arousal reduces anticorrelations

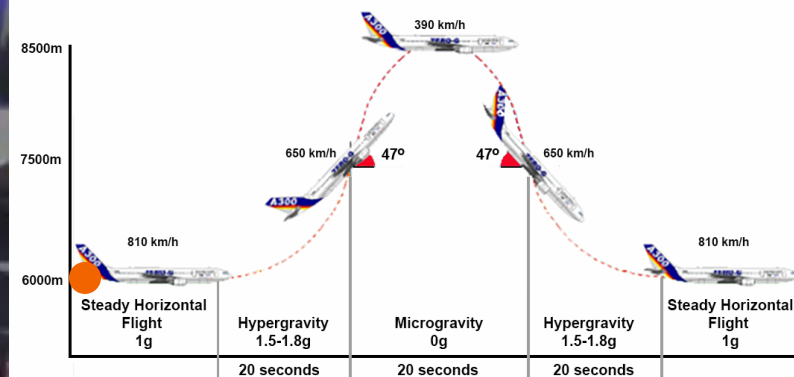


# Extreme environment reduces anticorrelations

## Parabolic flight



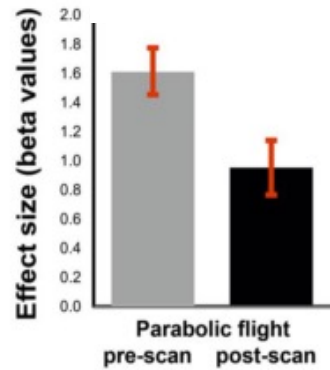
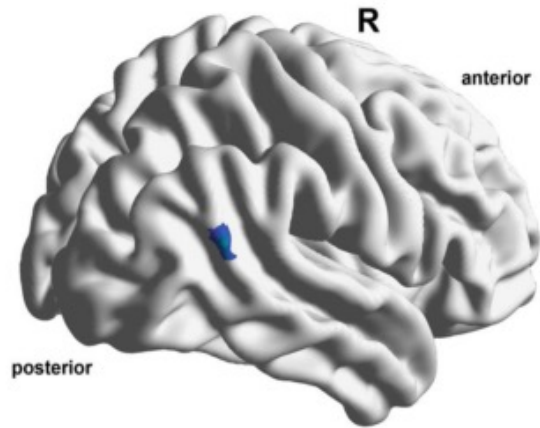
European Space Agency



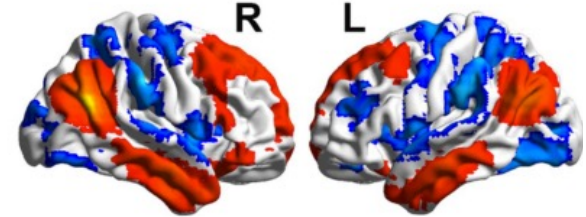
Flight trajectory

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

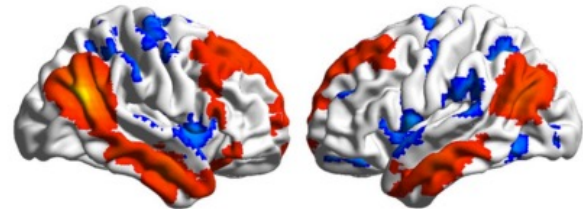
# Extreme environment reduces anticorrelations



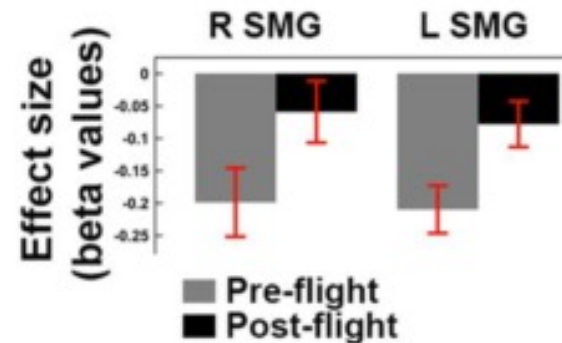
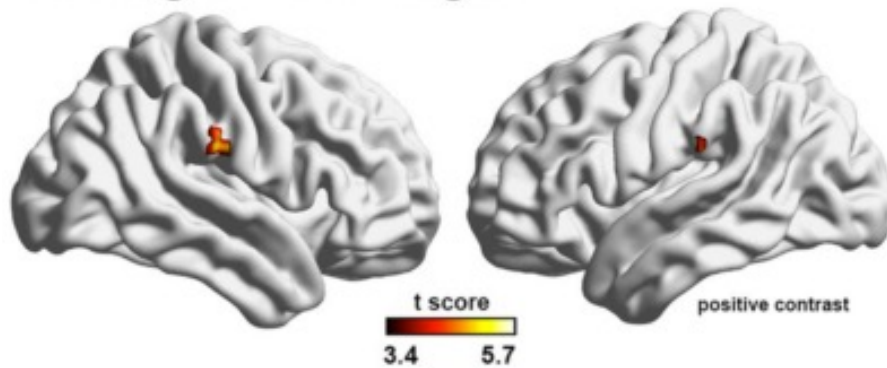
Pre-flight



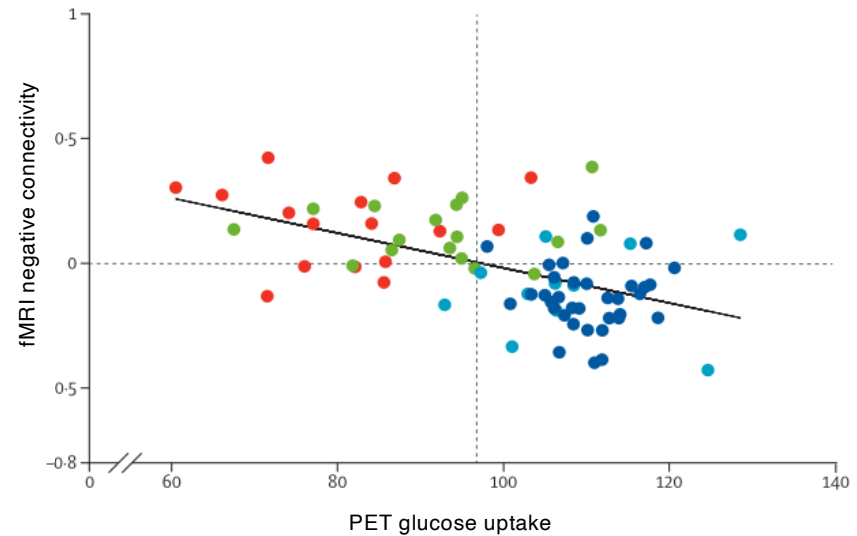
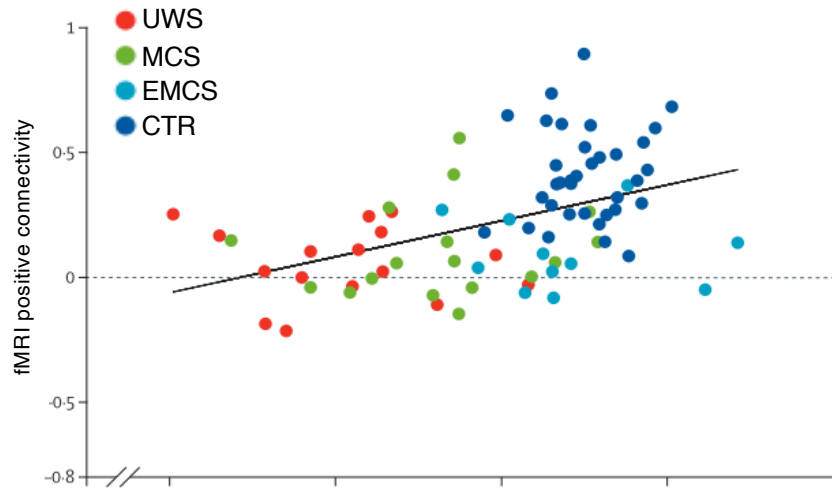
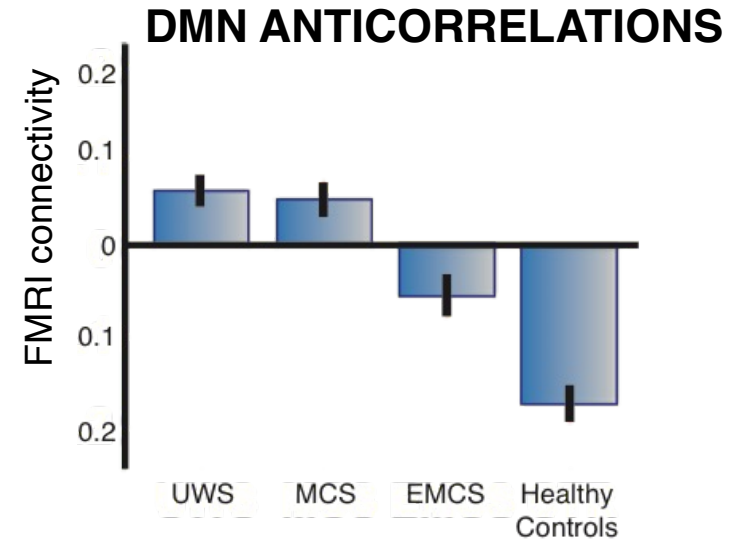
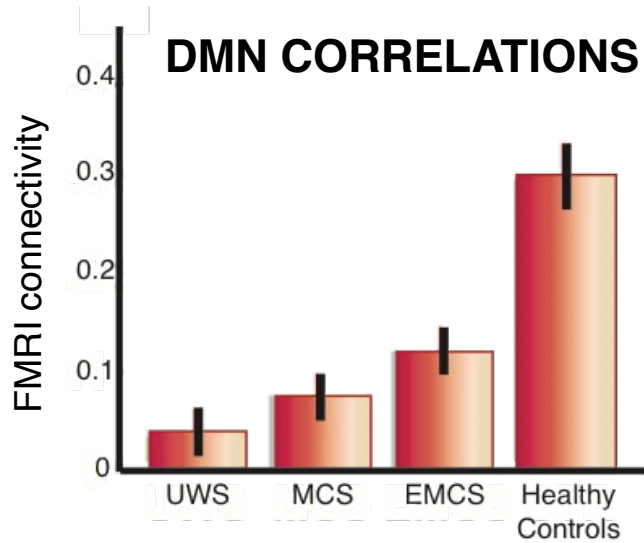
Post-flight



**Post – Pre flight**



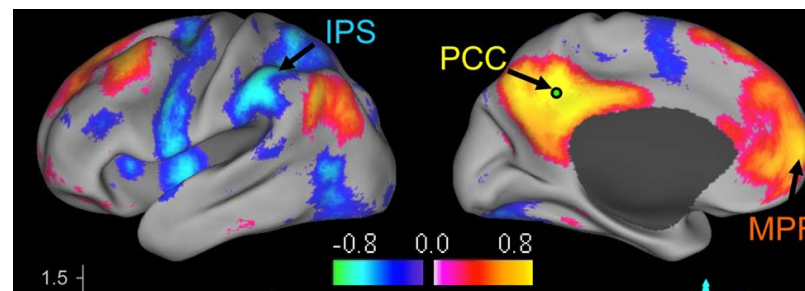
# No anticorrelations in DOC



# Anticorrelations and Consciousness

Anticorrelations **reduce** in intensity or are undetectable in :

- unresponsive brain-damaged patients (Di Perri et al., 2016; Threlkeld et al., 2018)
- hypnosis (Demertzi et al., 2011)
- in deep anesthesia (Boveroux et al., 2010)
- after sleep deprivation (De Havas et al., 2012; Yeo et al., 2015)
- slow wave sleep and REM (Chow et al., 2013)
- deep sedation (Luppi et al., 2019)



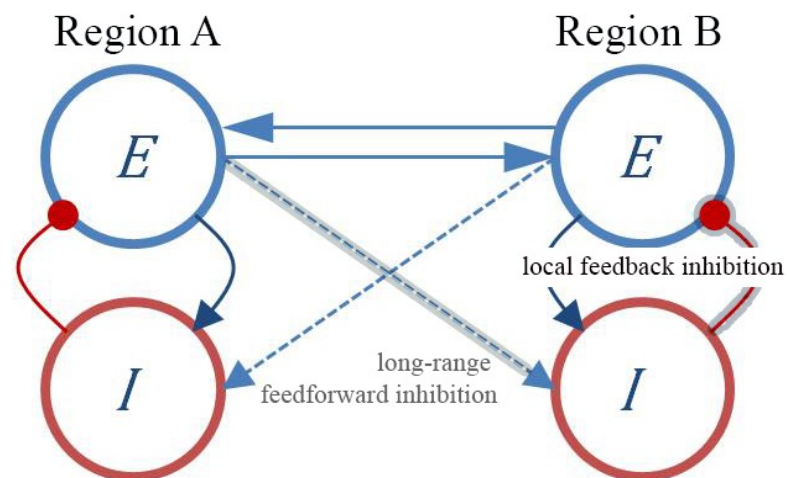
Anticorrelations **recover**:

- at post-anesthetic period (Nir et al., 2020)
- after emergence from a disorder of consciousness (Di Perri et al., 2016; Threlkeld et al., 2018).

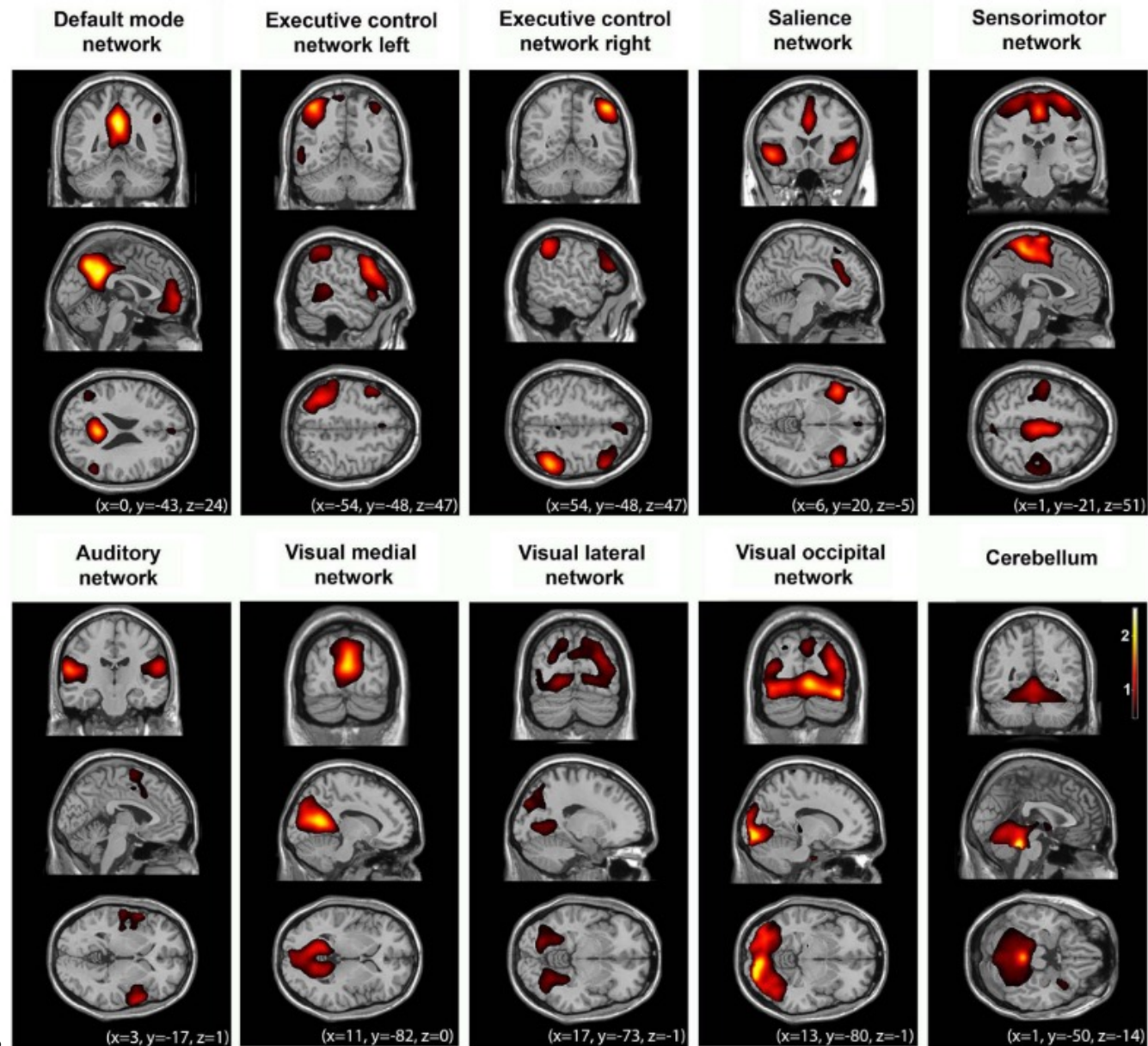
Anticorrelations **contribute** to:

- cognitive function (Keller et al., 2015; Vanhaudenhuyse et al., 2011),
- greater intensity lead to better within-subject performance (Kucyi et al., 2017)
- between-subject performance (Spreng et al., 2010).
- life span
  - start weak in children, strengthen during adolescence, end up fully anticorrelated in young adulthood (Chai et al., 2014)
  - get selectively decreased during healthy aging (Keller et al., 2015)

## neural inhibition



# More networks during rest

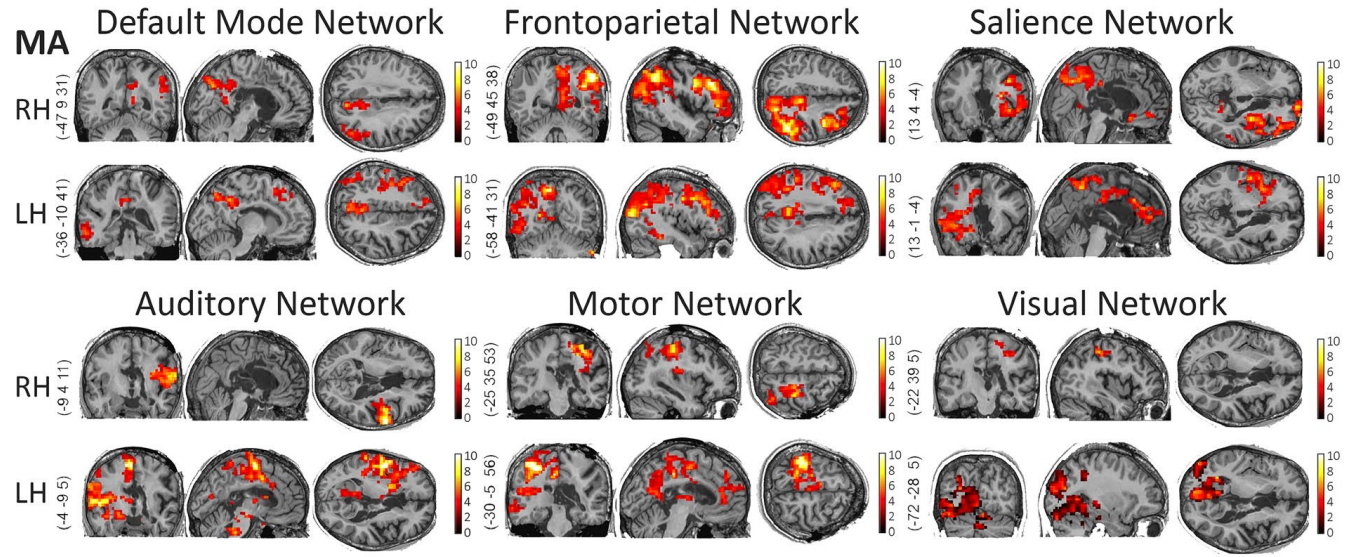
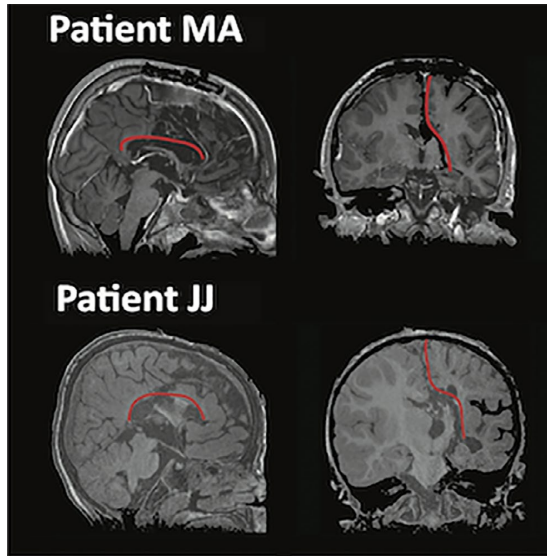


Biswal et al., *Magn Reson. Med* 1995  
Smith et al, *PNAS* 2009  
Heine et al, *Front Psych* 2012

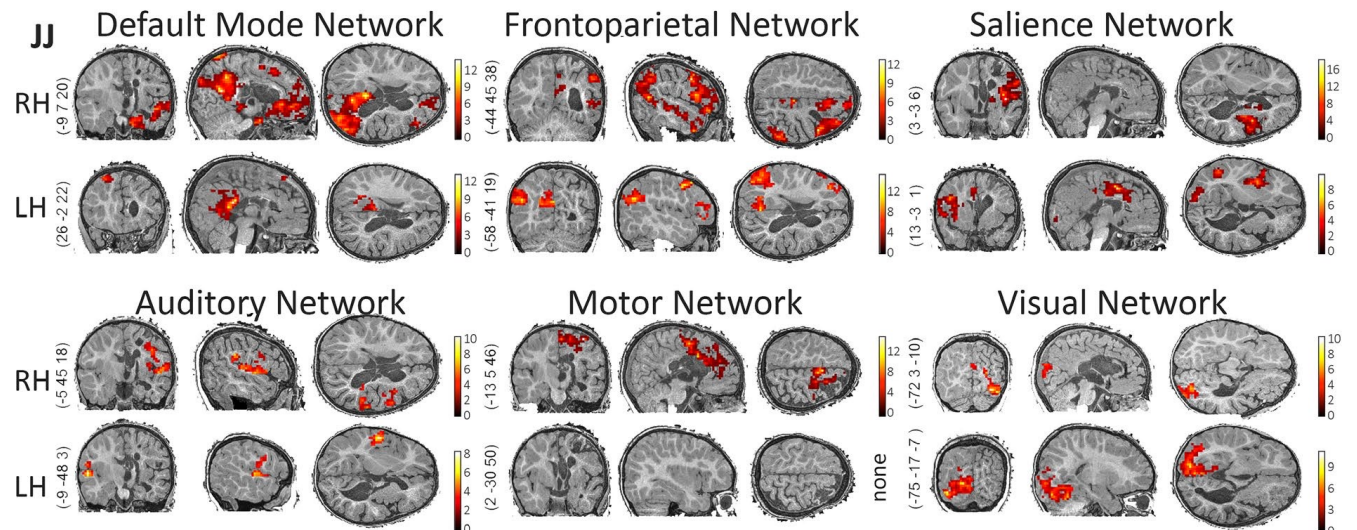
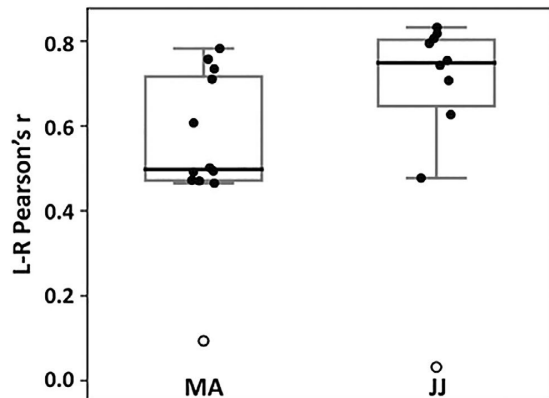


# Lower cross-modal interaction in the isolated brain

## Complete hemispherotomy

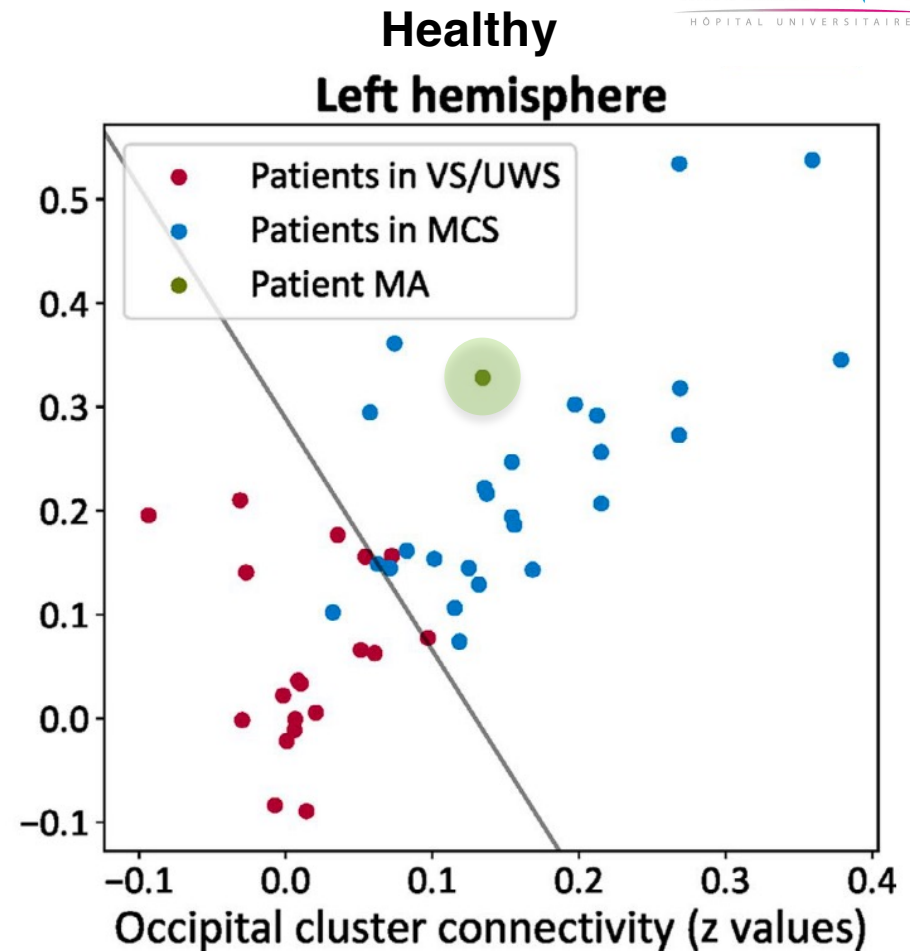
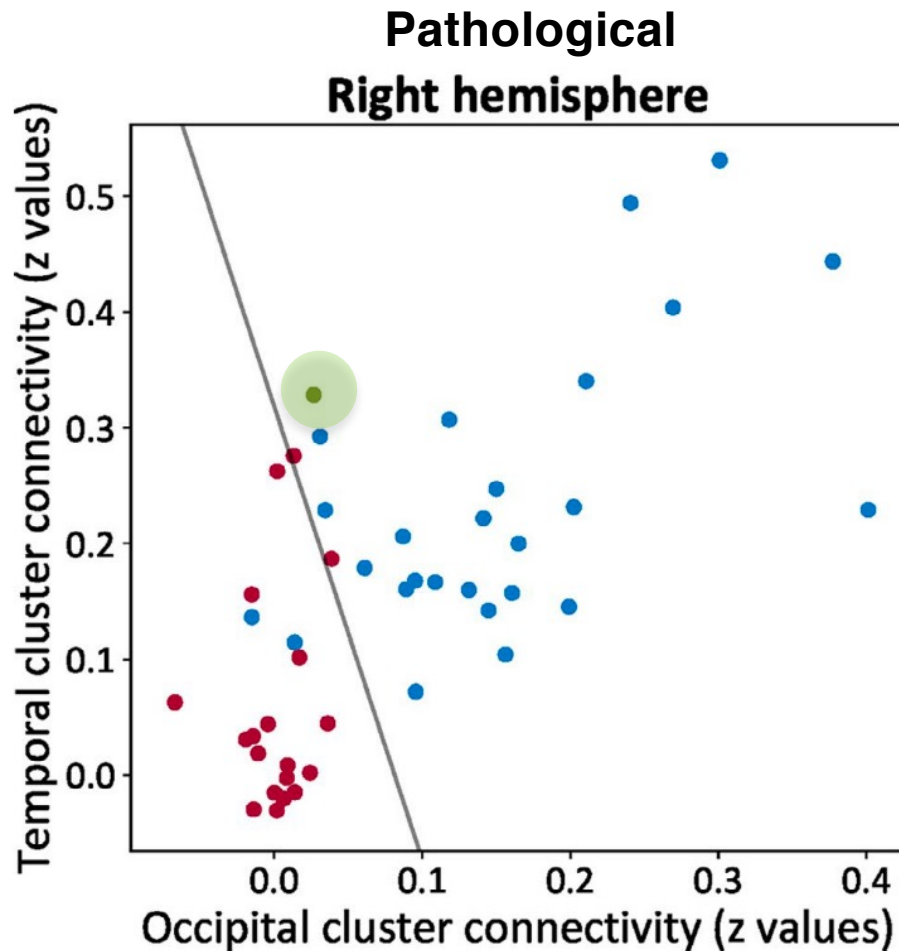


## Inter-hemispheric connectivity



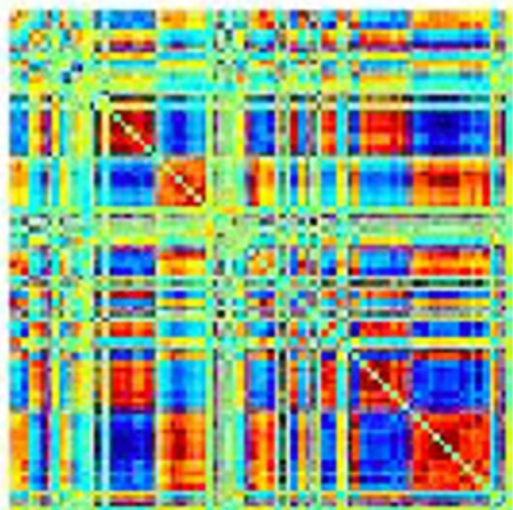


# Lower cross-modal interaction in the isolated brain

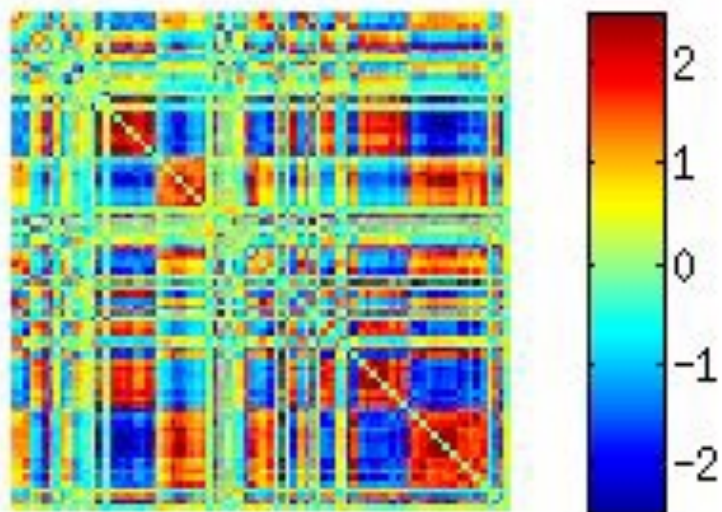


# Brain dynamics and cognition

## Averaged connectome



## Time-varying connectome



## Typical wakefulness

Performance, emotion and cognition

Alavash et al, *Neuroimage*, 2016; Shine et al *Neuron*, 2016; Friston *Neuroimage*, 1997; Thompson et al, *Hum Brain Mapp*, 2013

## Unconsciousness

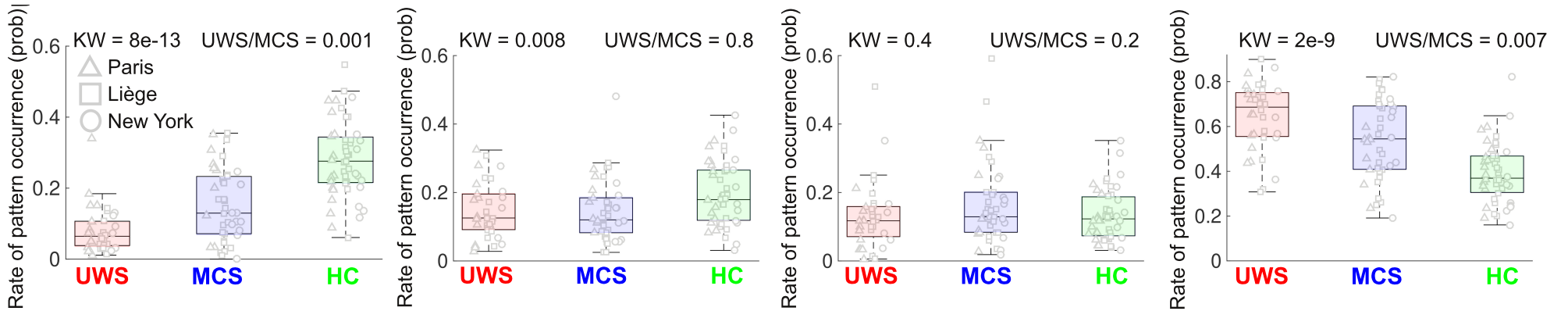
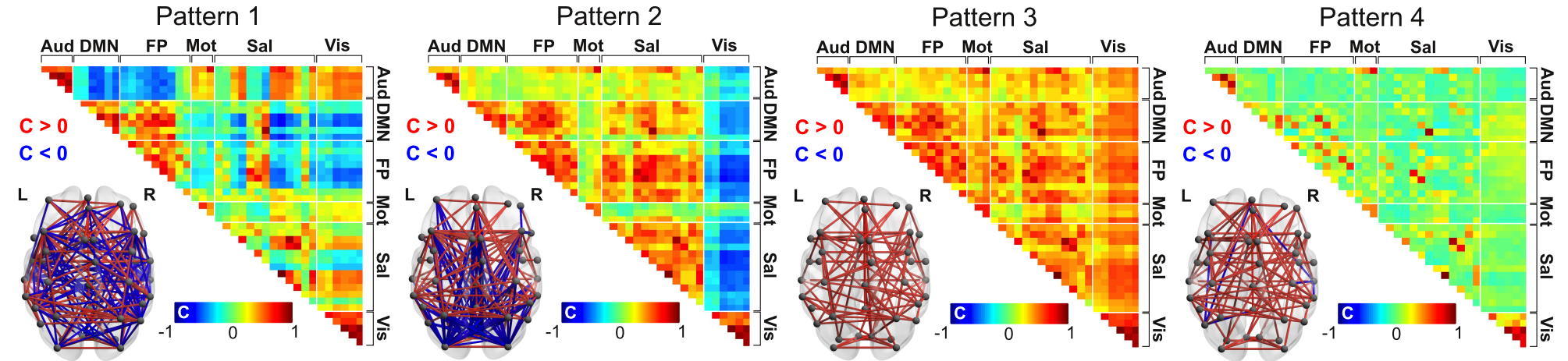
Rigid spatiotemporal organization, less metastable dynamics

- **sleep** (Tagliazucchi et al, *PNAS* 2013; Wang et al, *PNAS* 2016; Wilson et al., *Neuroimage* 2015; Chow et al, *PNAS* 2013)
- **anesthesia**
  - **humans** (Tagliazucchi et al, *J. R. Soc. Interface* 2016; Kafashan et al, *Front Neural Circuits*, 2016; Amico et al, *PLoS One* 2014)
  - **animals** (Barttfeld et al, *PNAS* 2014; Grandjean et al, *Neuroimage* 2017; Liang et al, *Neuroimage* 2015)

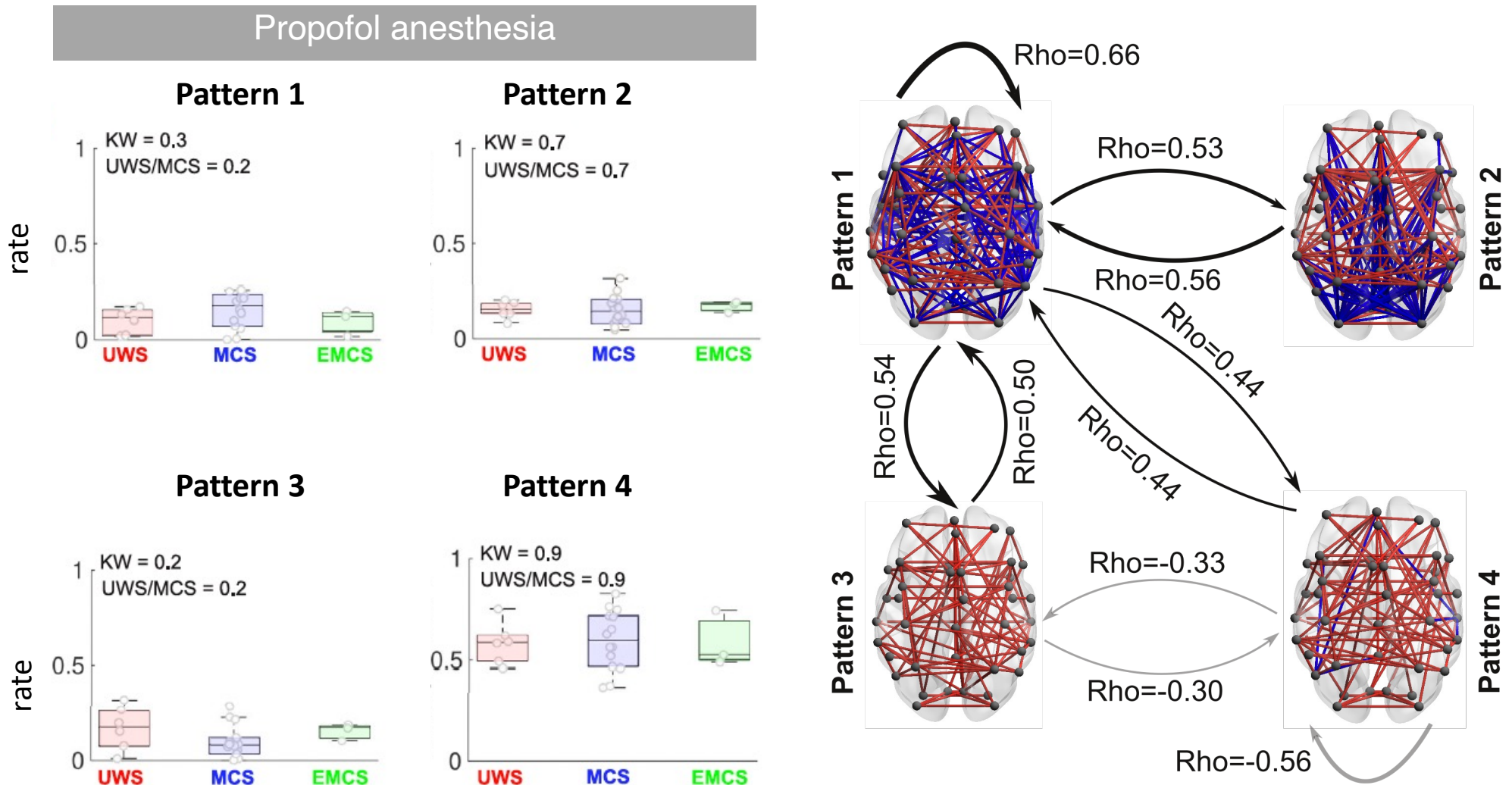


The brain cannot map the complexity of internal and external world  
(Dehaene et al, *Trends Cog Sci*, 2006; Tononi et al, *Nat Rev Neurosci*. 2016)

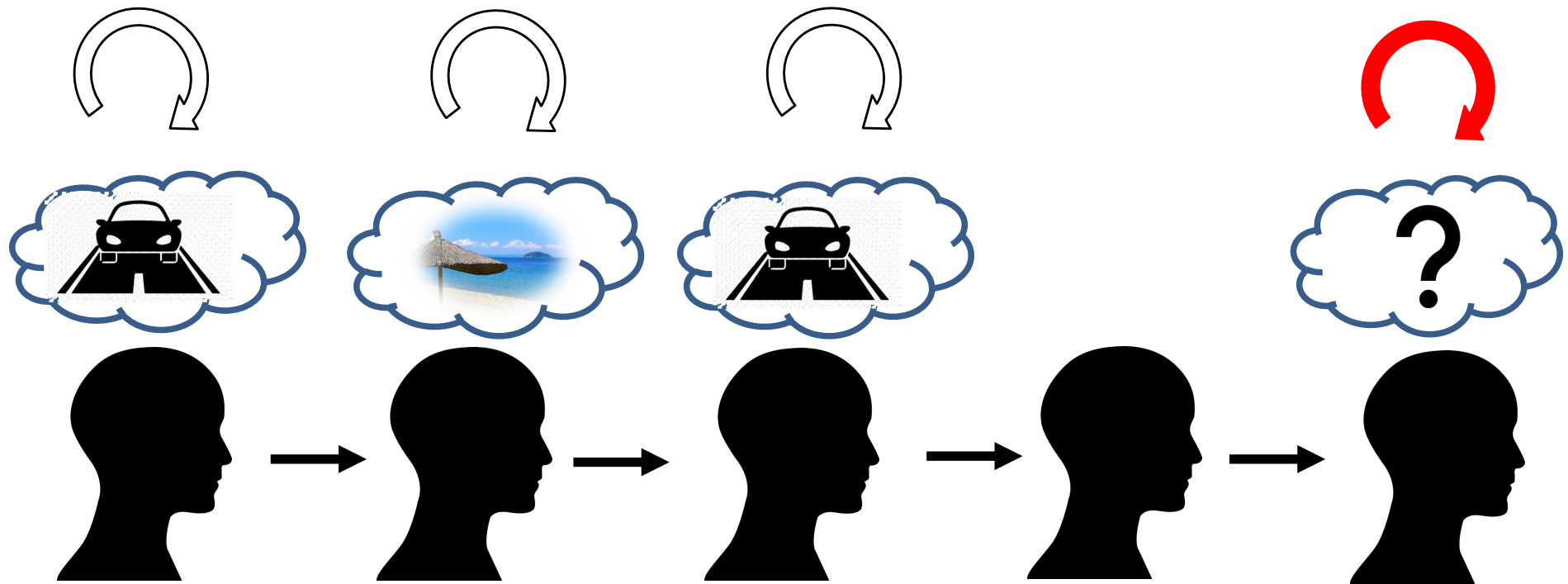
# Complex patterns in higher conscious states



# More chances to transition when conscious



# Mental states

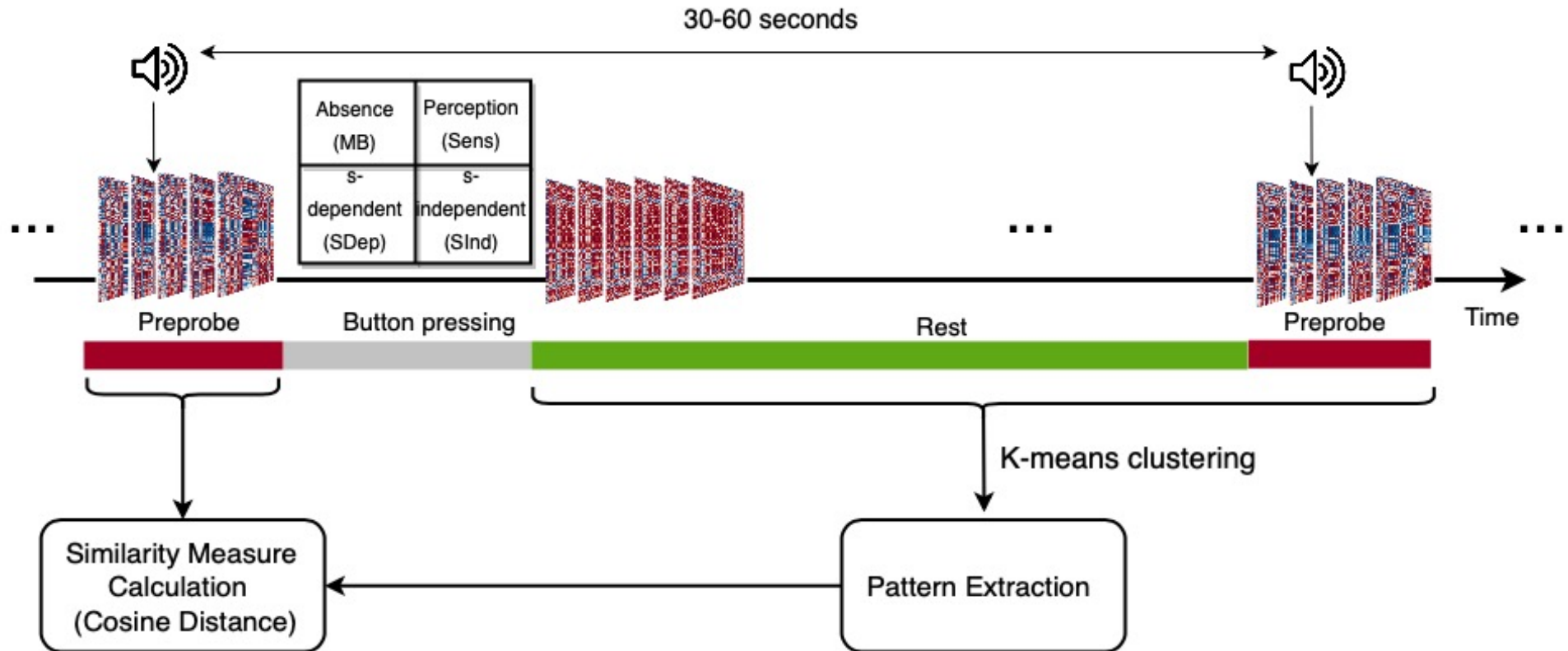


Slide courtesy: Boulakis Paris

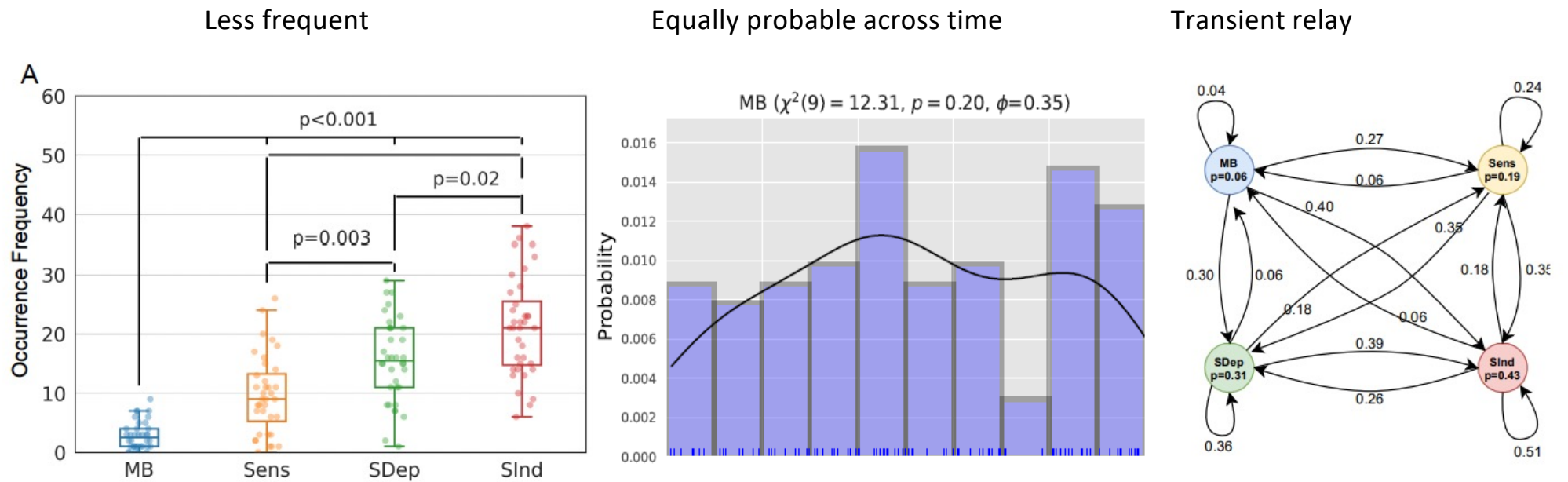


Mortaheb Sepehr

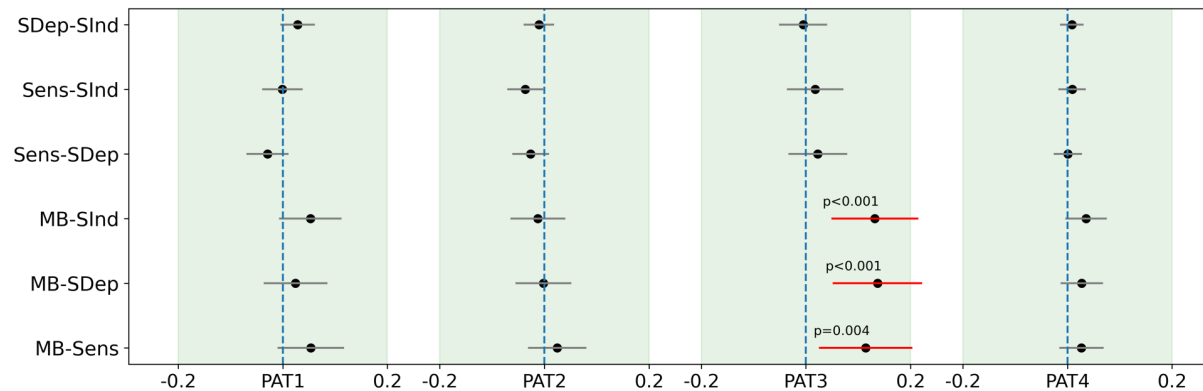
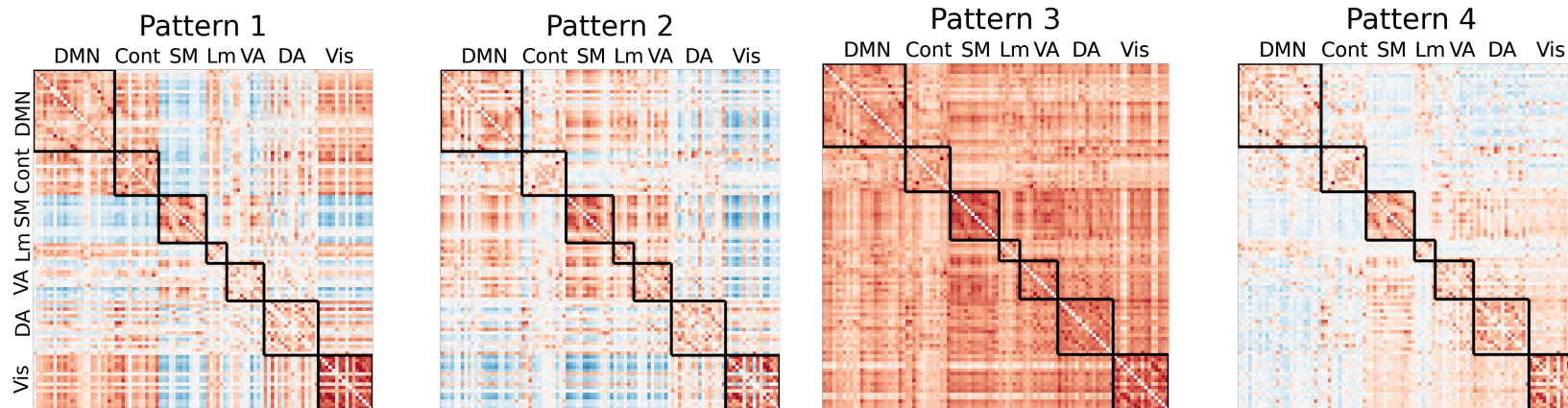
# Experience-sampling



# Mind Blanking has a distinct behavioral profile



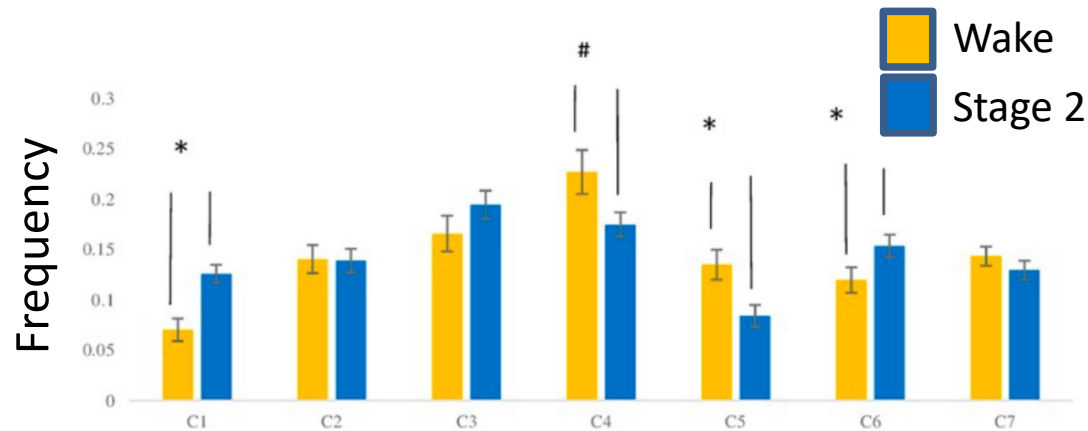
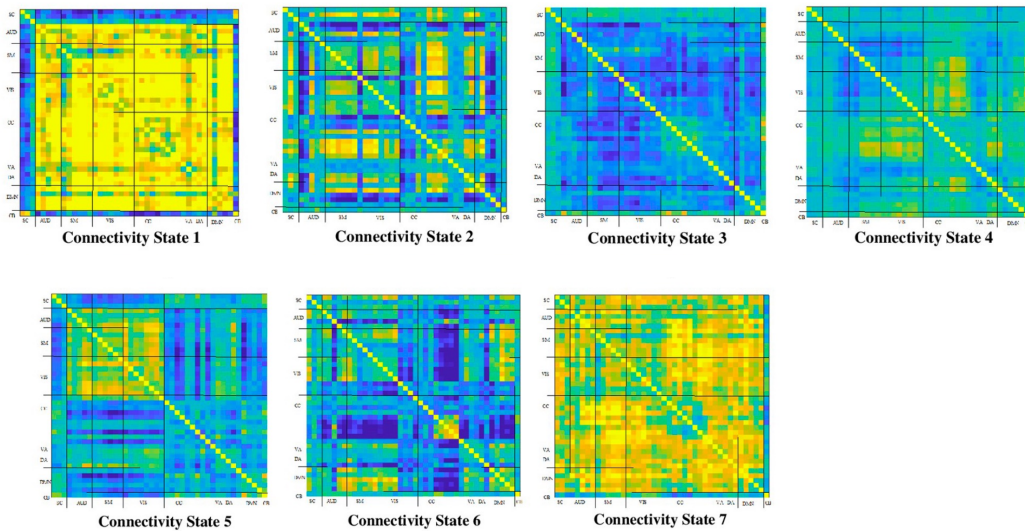
# MB is linked to a hyper-connected state





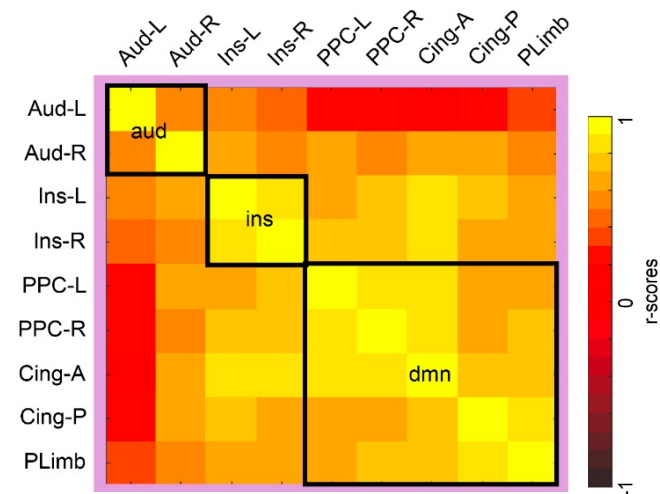
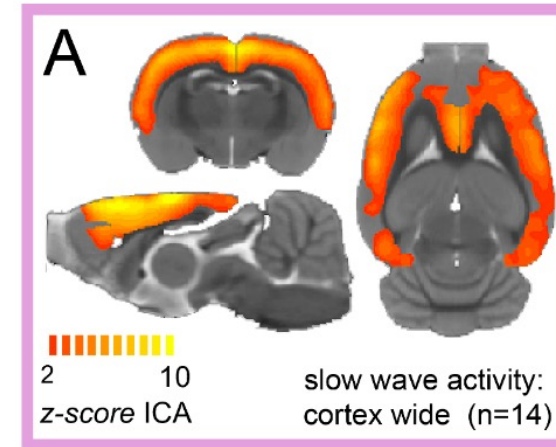
# Higher functional connectivity due to slow waves

## NREM sleep Humans



El-Baba et al, *PLOS One* 2019

## Isoflurane anesthesia Rats



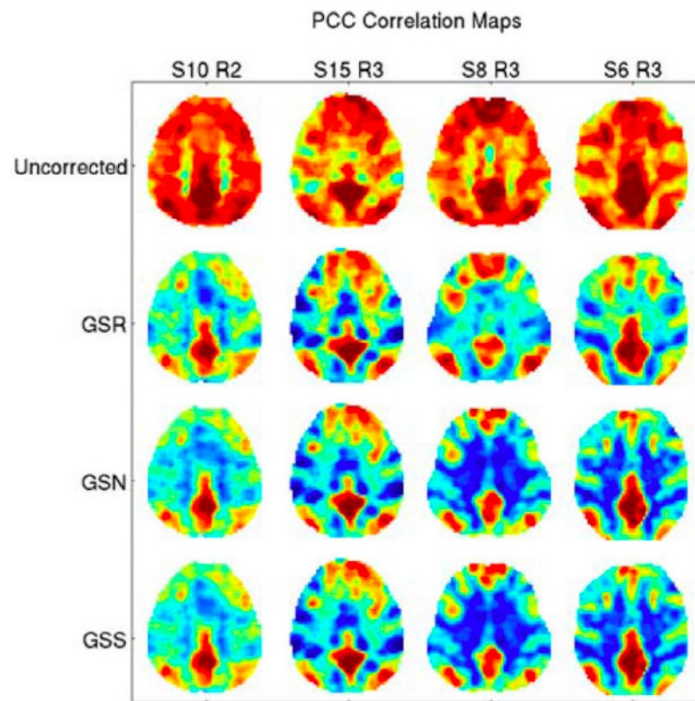
Aedo-Jury et al, *eLife* 2019

# Lower cortical arousal in MB?

## Global signal

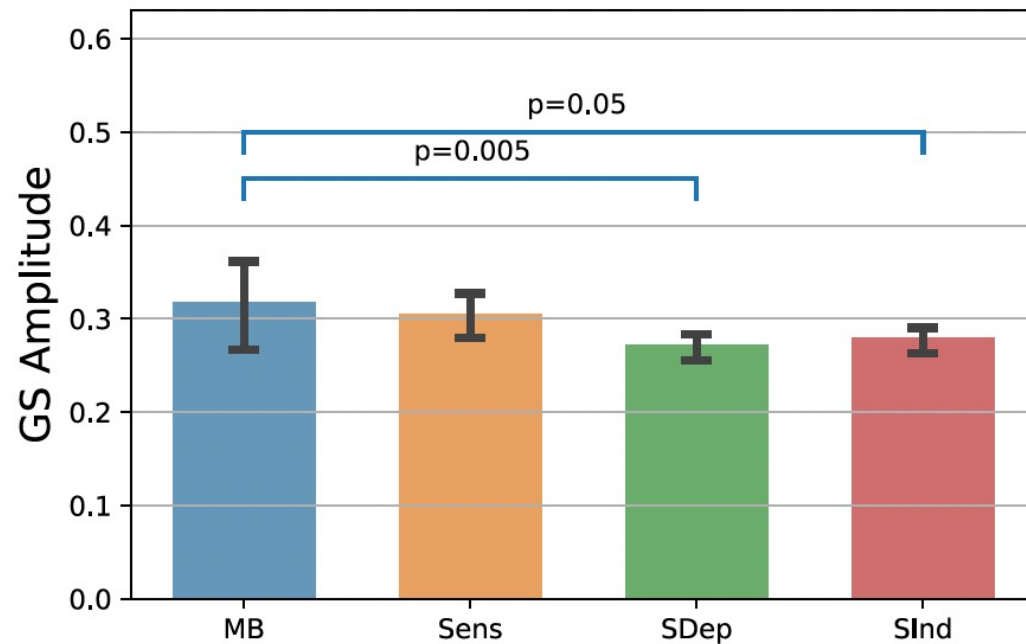
### Average voxel timeseries

Zarahn, Aguirre, D'Esposito, *NeuroImage* 1997  
 ("Global flow" in PET, Friston et al., 1990)



Liu et al, *NeuroImage* 2017

### Higher Global Signal Amplitude around MB reports

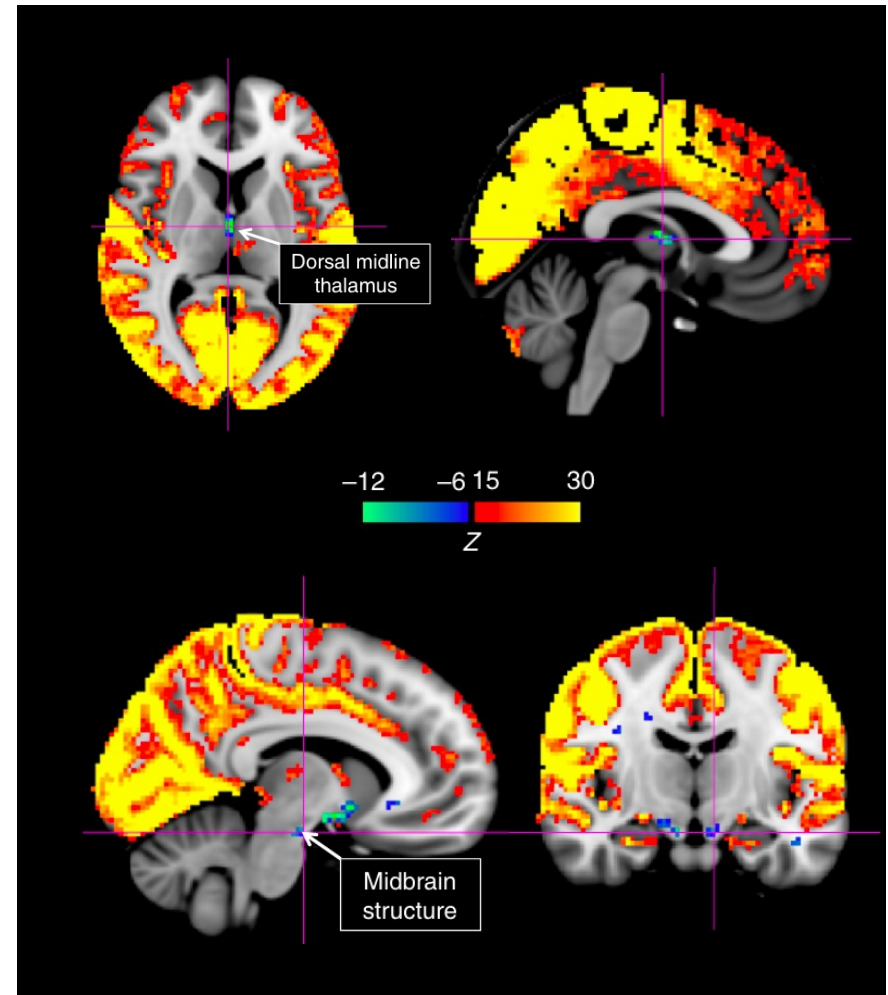
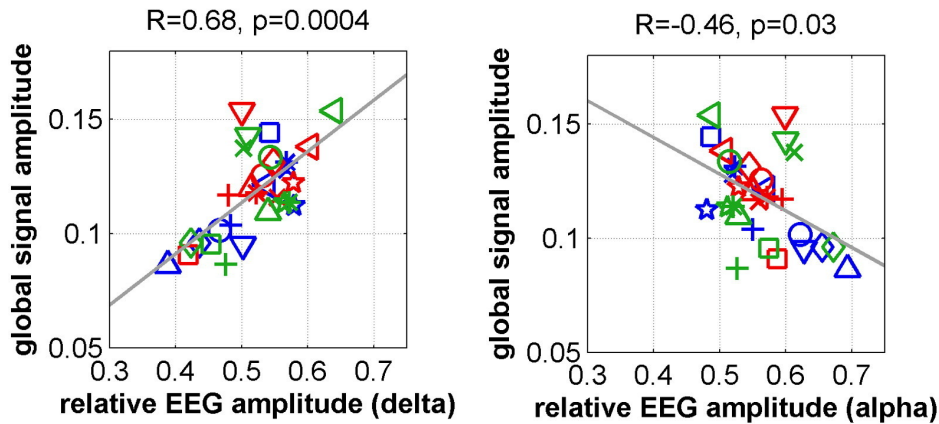


Mortaheb, et al, *PNAS accepted*

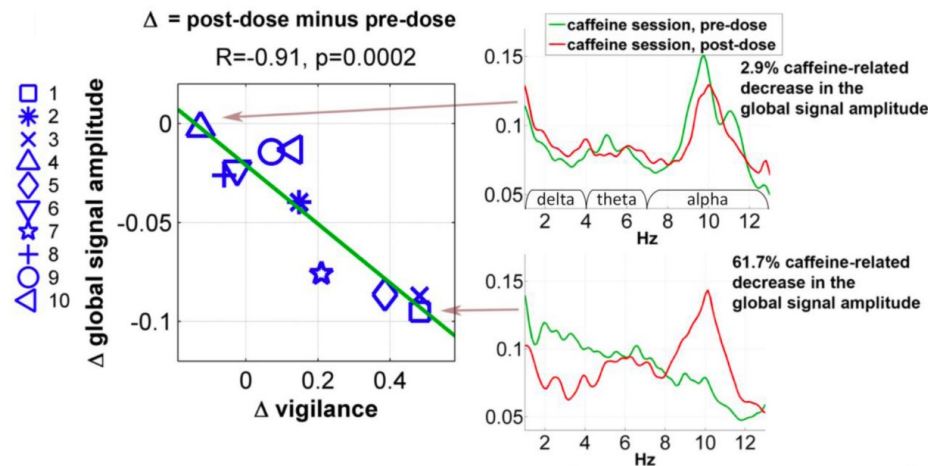
# GS amplitude and Arousal

GS amplitude is linked to low arousal

GS amplitude linked to signal decreases in subcortical structures of arousal



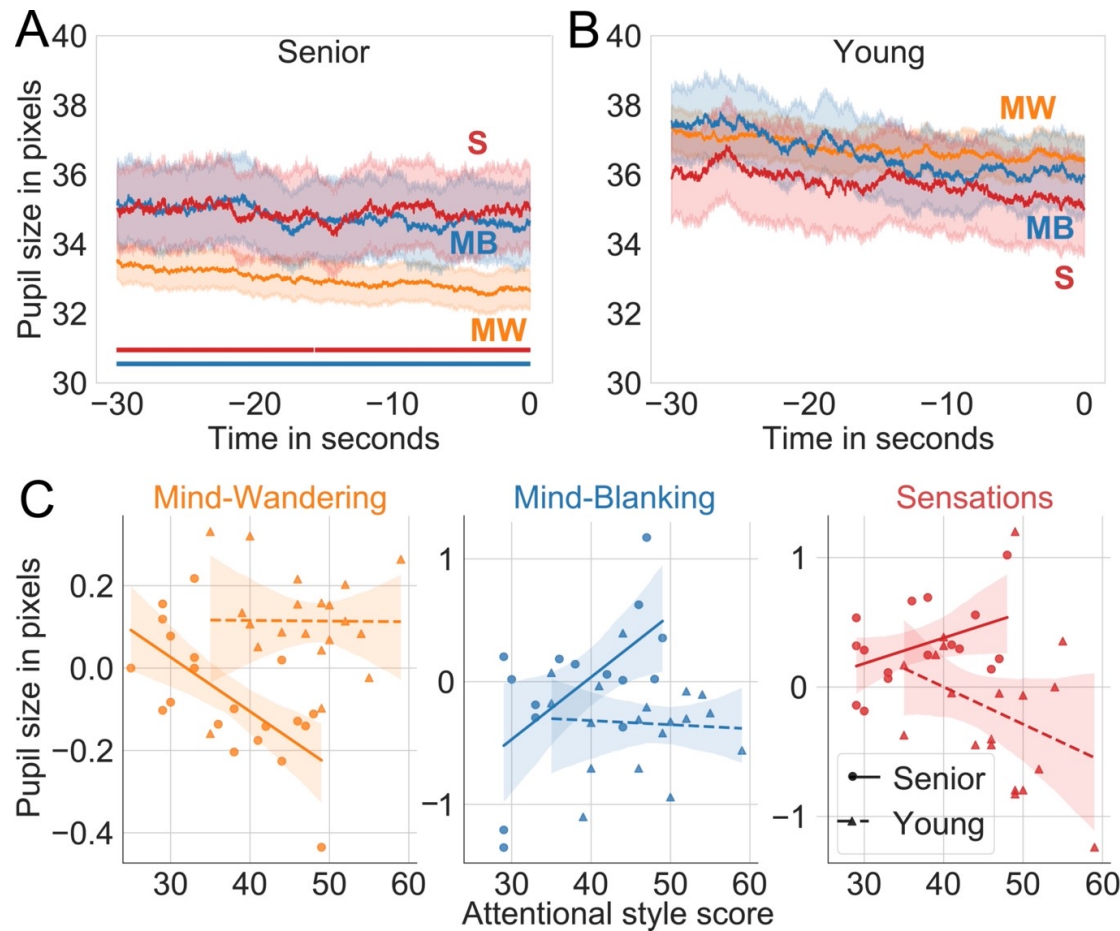
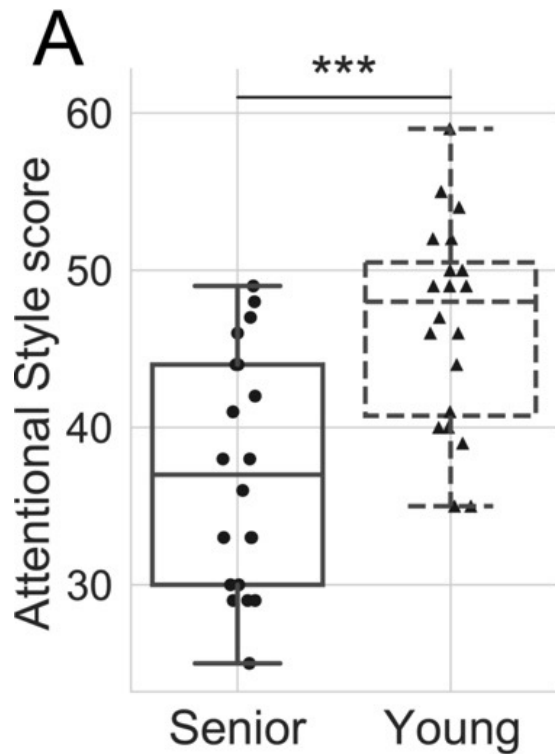
GS amplitude decreases with caffeine intake



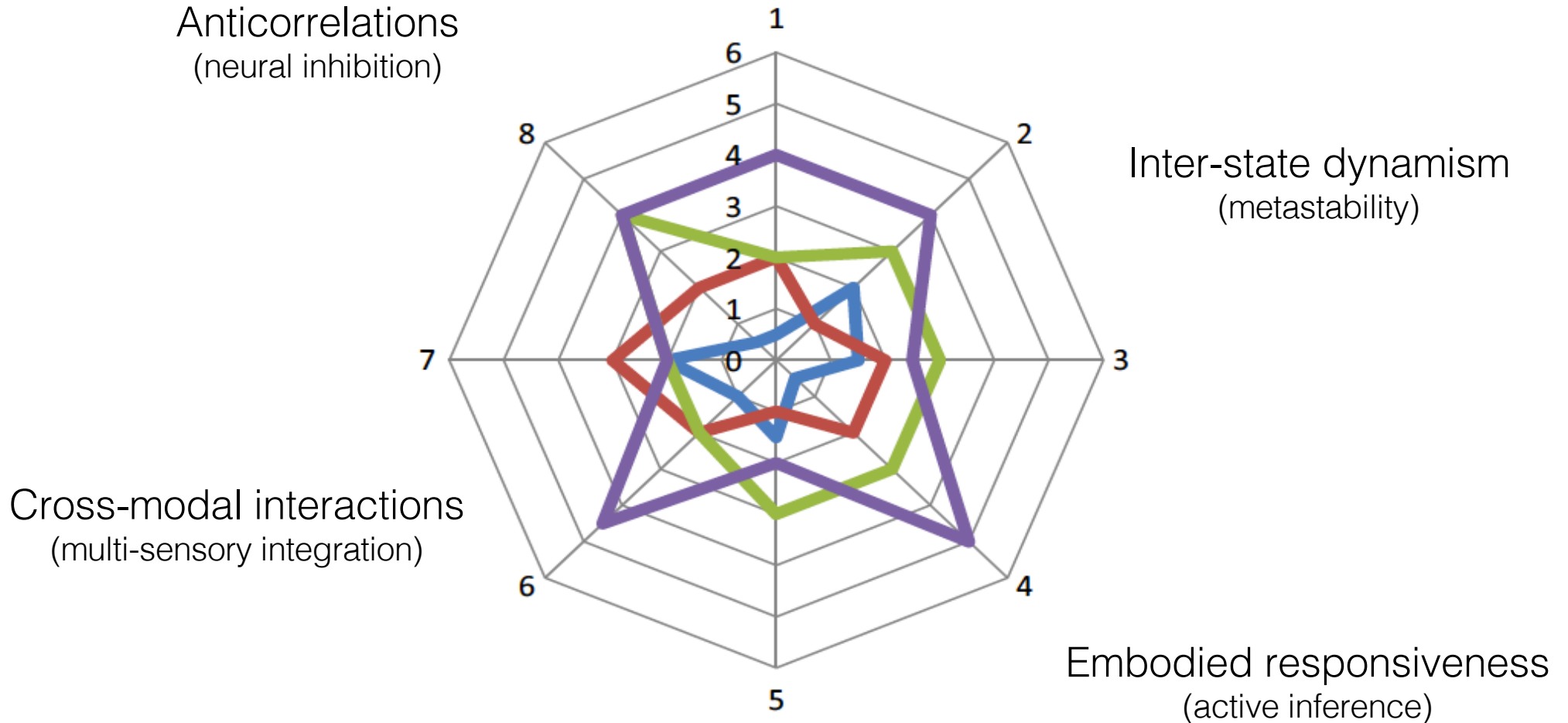


Koroma Matthieu

# Mental state reportability depends on attentional style & arousal

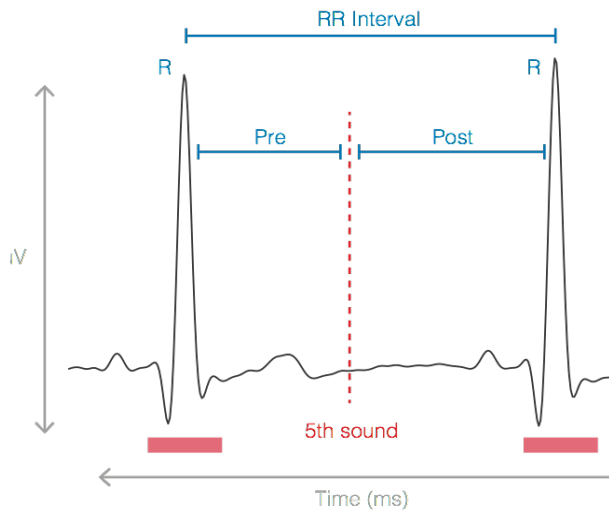


# Consciousness is multidimensional

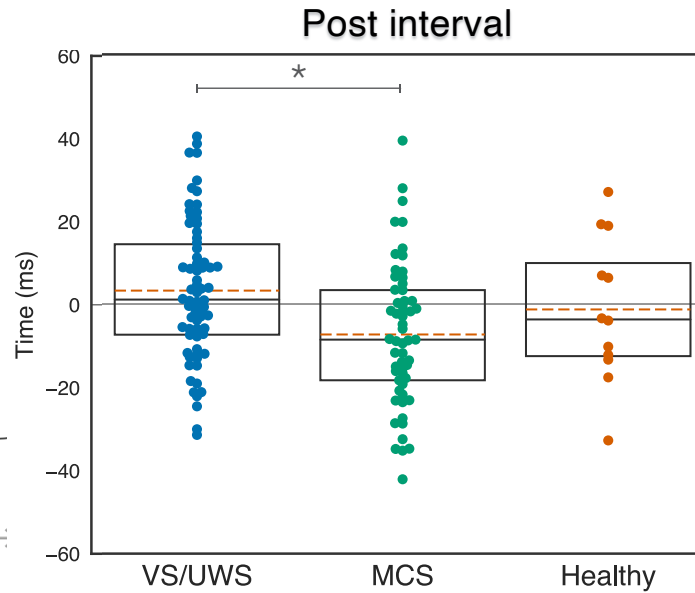


# Cardiac reactions to oddballs in MCS

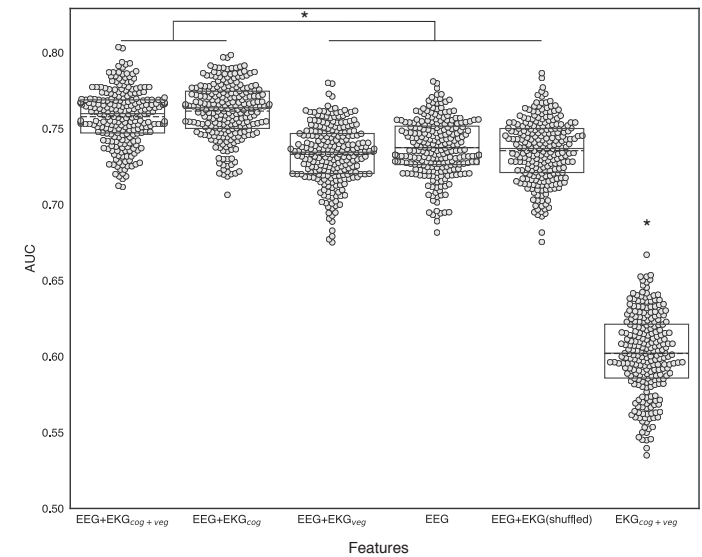
Auditory oddball paradigm

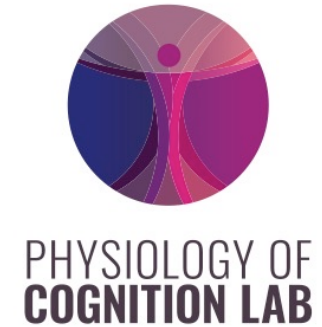


Cardiac cycle-phase acceleration only in MCS



Electrocardiographic markers carry independent information from EEG





Consciousness is a construct  
of collective consensus and concerns us all



@Ademertzi  
@PhysioCognGIGA



a.demertzi@uliege.be

**Physiology of Cognition**  
GIGA Institute  
Cyclotron Research Center  
Université de Liège

[www.gigaphysiologycognition.uliege.be](http://www.gigaphysiologycognition.uliege.be)