

# Quantifying states of consciousness by means of intrinsic brain connectivity

**Institute of Neuroscience and Medicine,  
Brain & Behaviour (INM-7)  
Research Centre**

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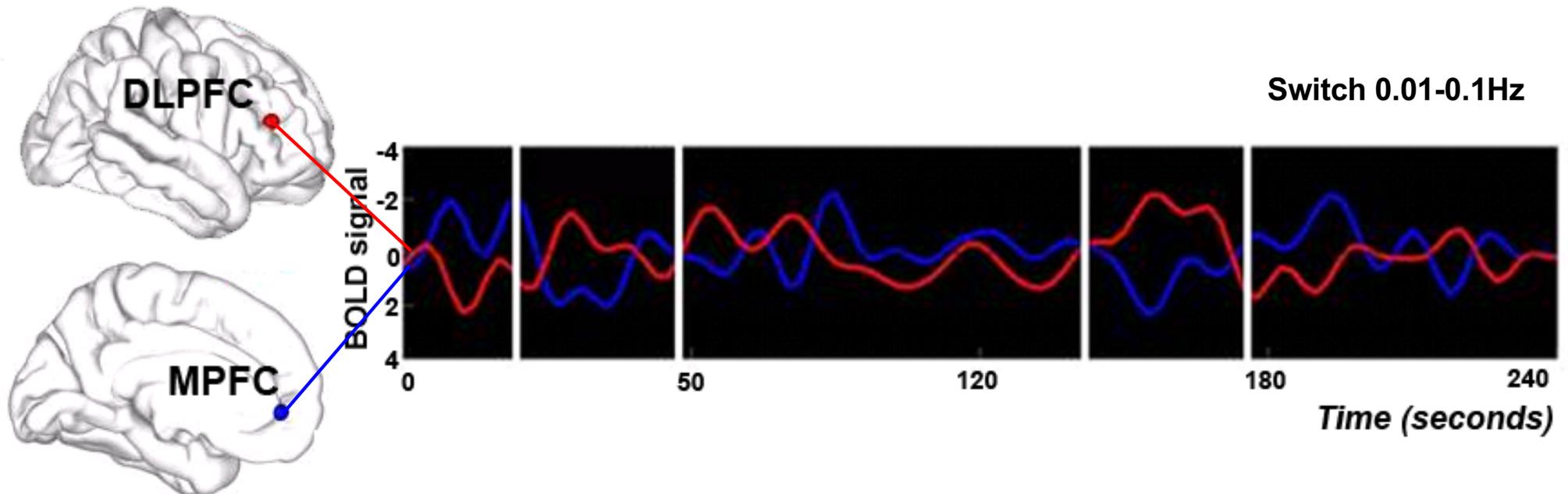
# What is Consciousness?





# A mode of awareness?

**External awareness  
or anticorrelated network**



**Internal awareness  
or Default mode network**

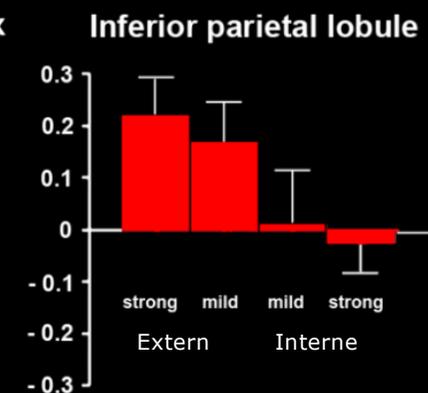
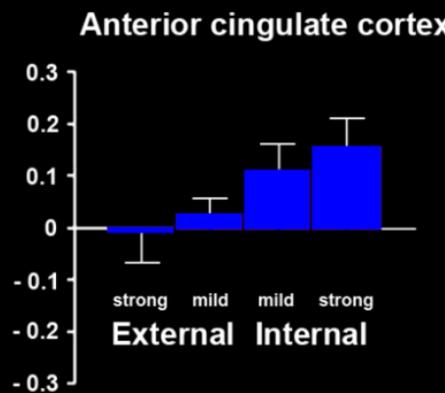
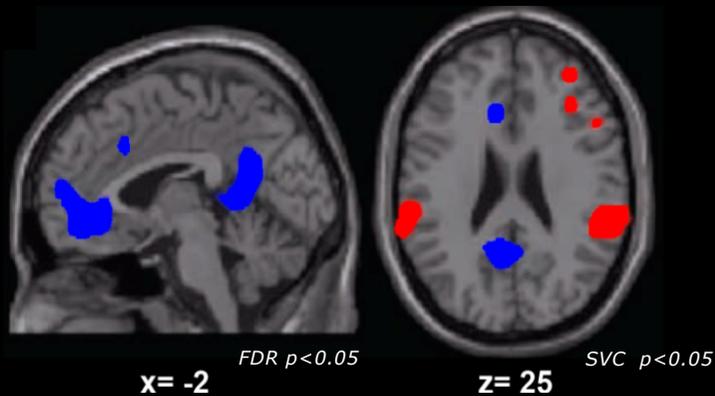
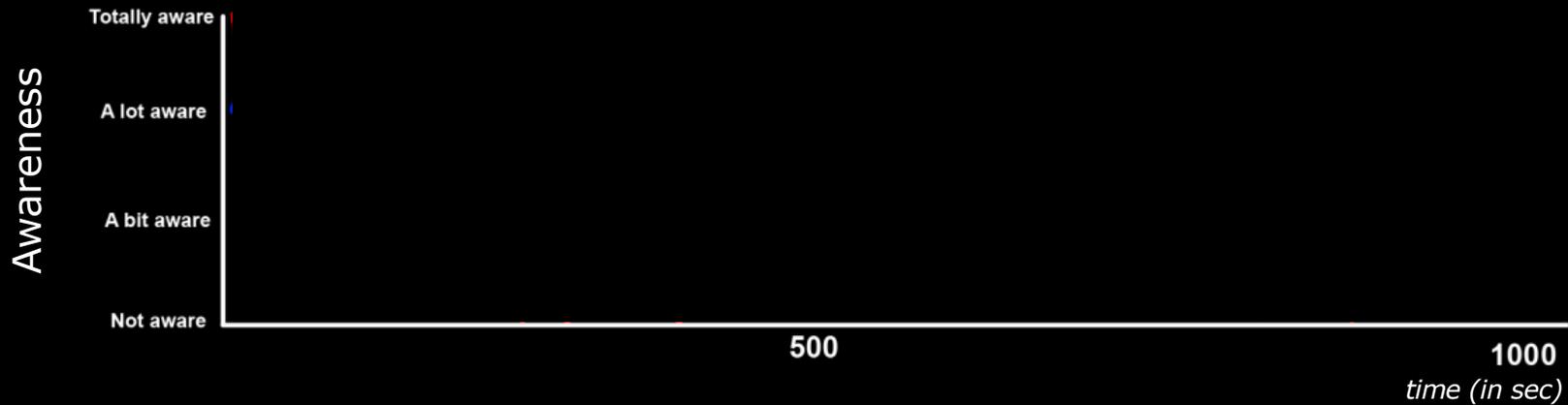
Demertzi, Soddu, Laureys, *Curr Opin Neurobiology* 2013  
Demertzi & Whitfield-Gabrieli, in: *Neurology of Consciousness* 2<sup>nd</sup> ed. 2015  
Demertzi et al, *Front Hum Neurosci* 2013  
Laureys, *Scientific American* 2007  
Fox et al, *PNAS* 2005

# Neurobehavioral relevance of the anticorrelations



■ Internal awareness  
■ External awareness

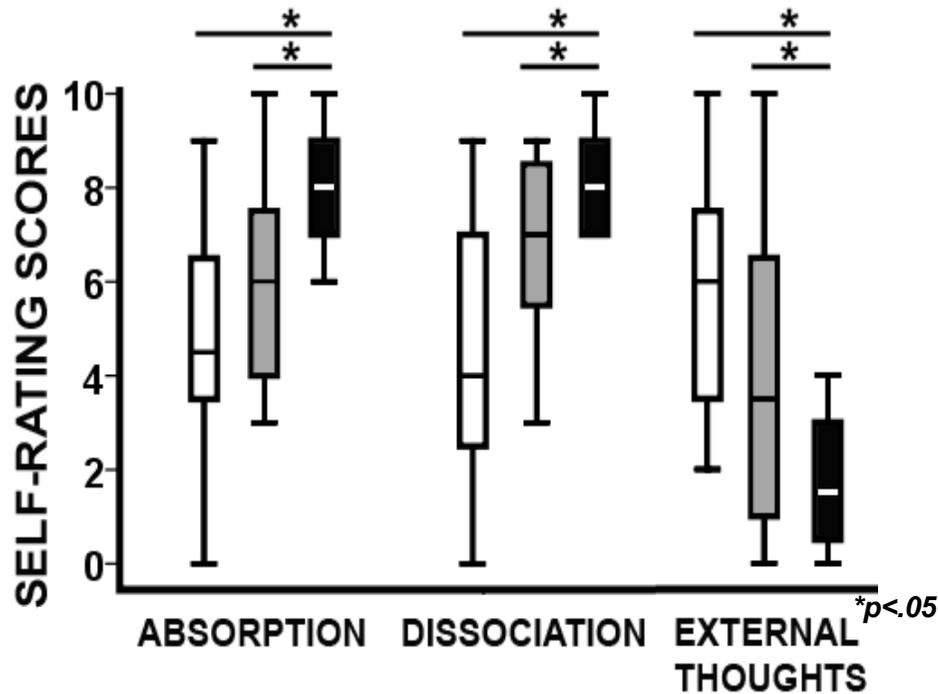
External-internal:  $r = -0.44$ ,  $p < .02$   
 Mean switch: 0.05Hz (range: 0.01-0.1)



# Anticorrelated connectivity is modified in hypnosis-Brain

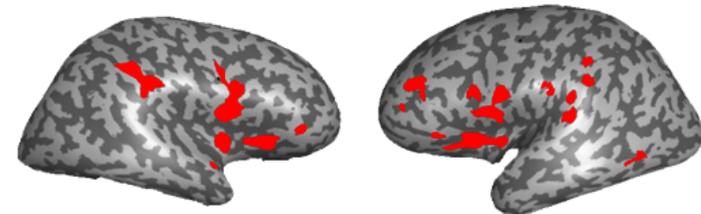


- Normal consciousness
- ▒ Autobiographical mental imagery
- Hypnosis

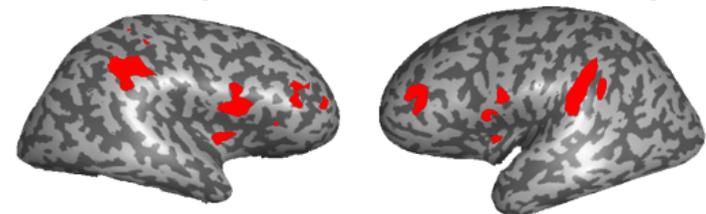


## EXTRINSIC SYSTEM

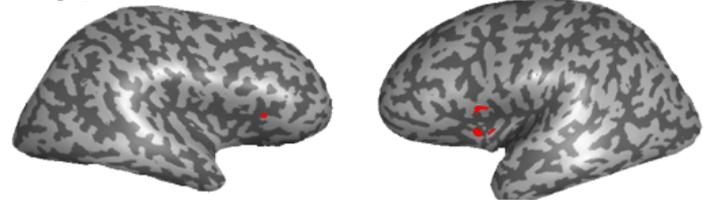
Normal consciousness



Autobiographical mental imagery

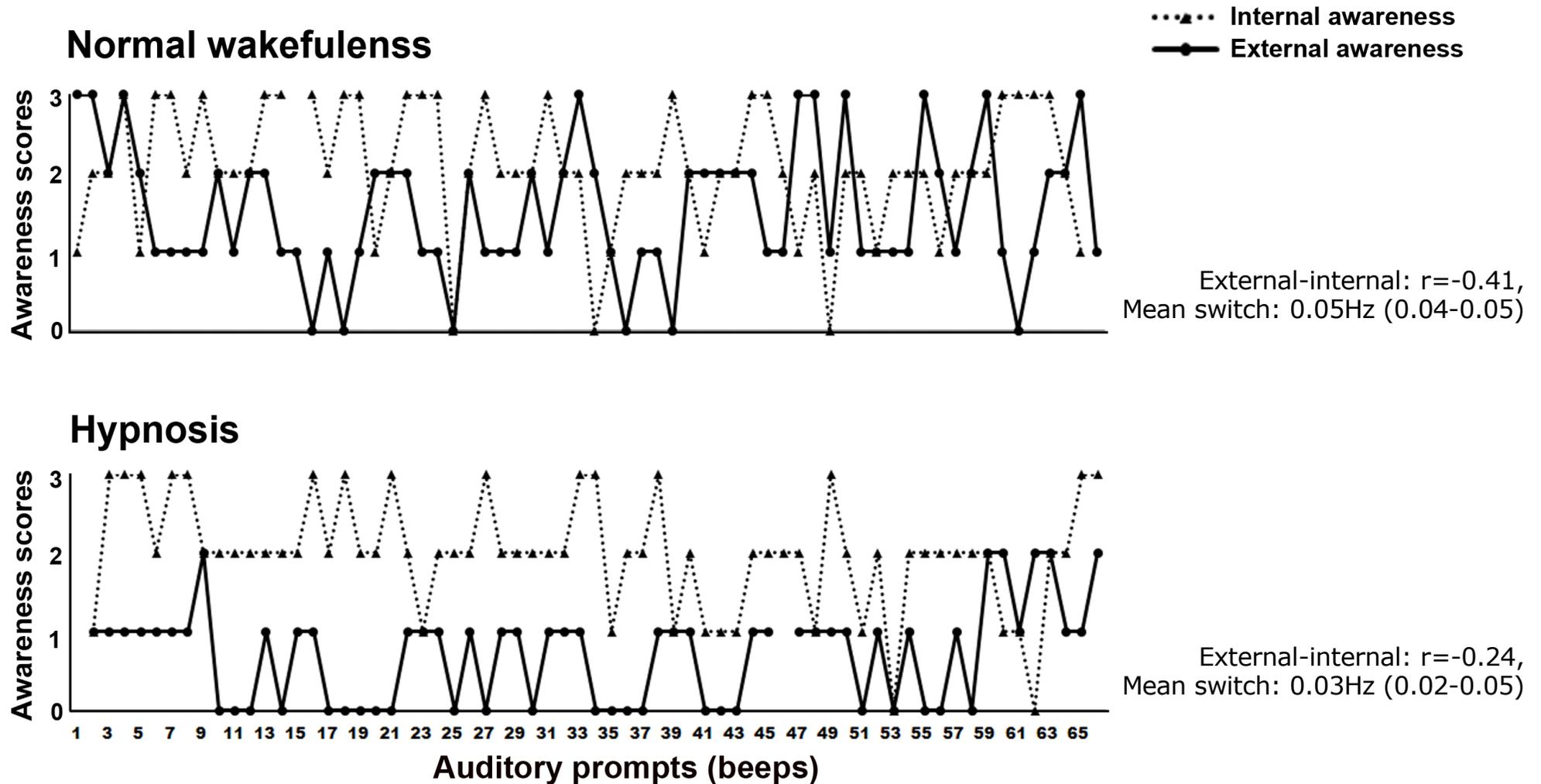


Hypnosis

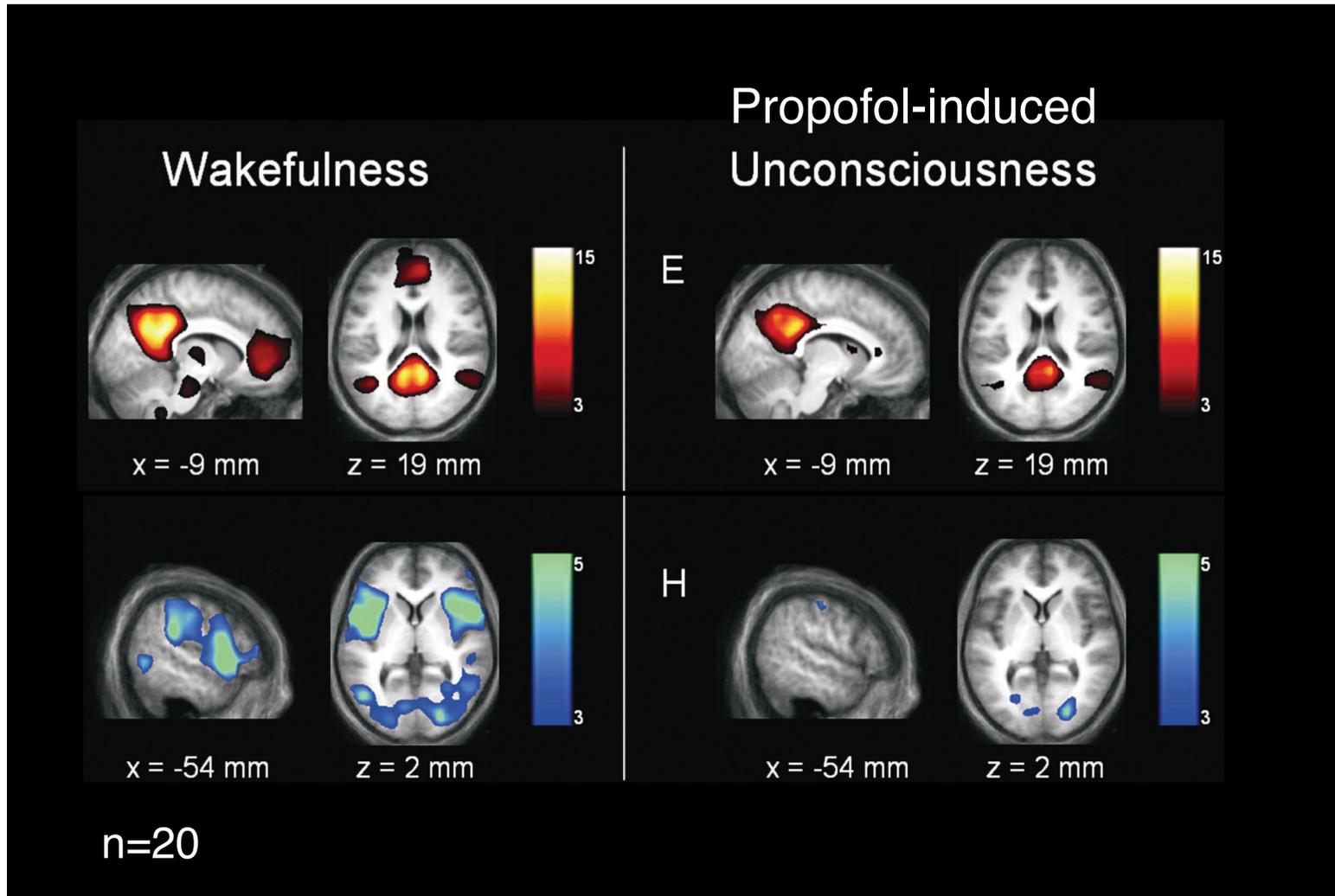


*p<0.05 corrected for multiple comparisons*

# Anticorrelated connectivity is modified in hypnosis-Behavior



# Anticorrelations reduce in anesthesia





# Effect of environment

SCIENTIFIC REPORTS

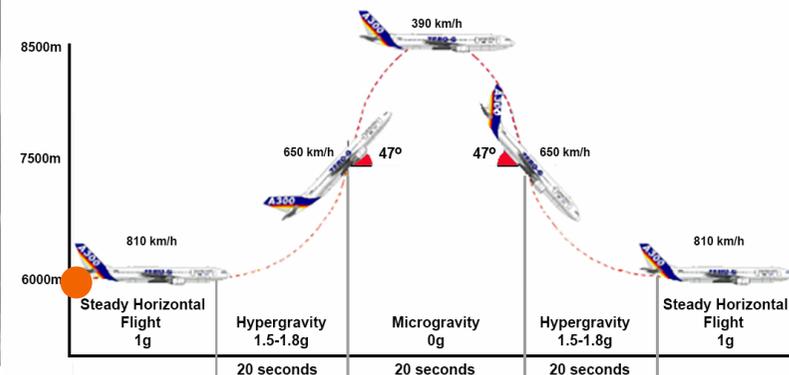
[www.nature.com/scientificreports/](http://www.nature.com/scientificreports/)



## Parabolic flight



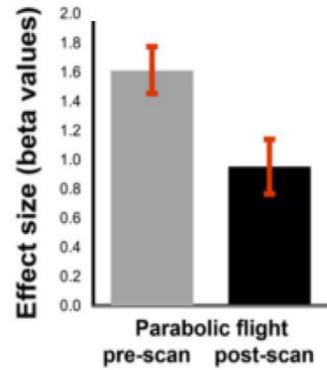
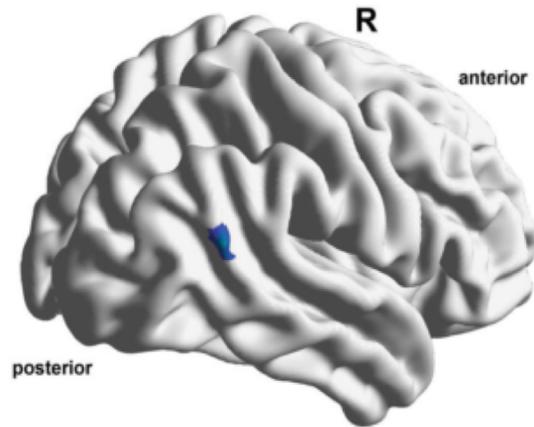
European Space Agency



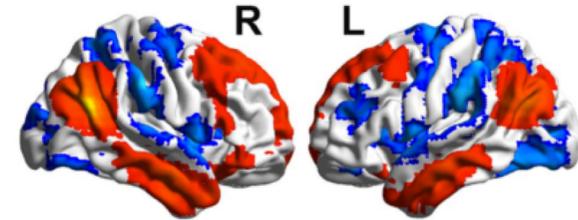
Parabolic flight trajectory

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>

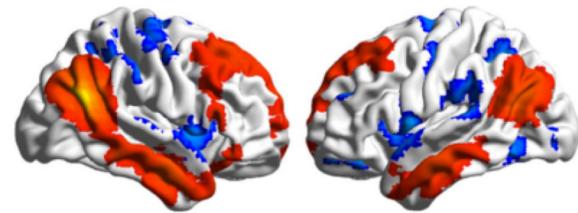
# Anticorrelations reduce in extreme environments



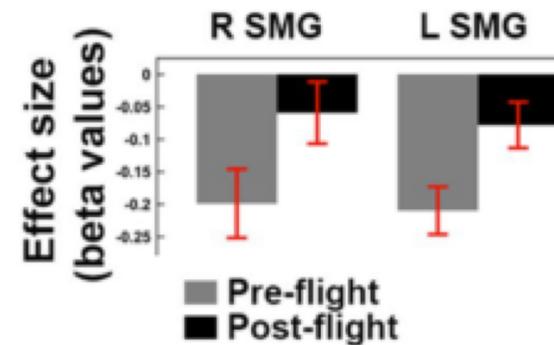
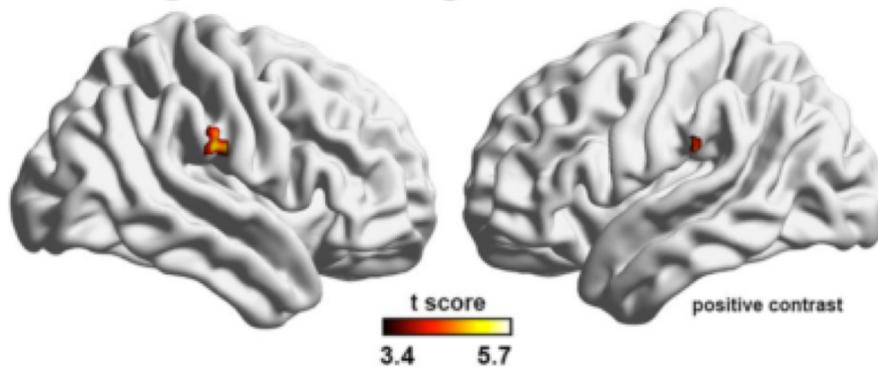
Pre-flight



Post-flight

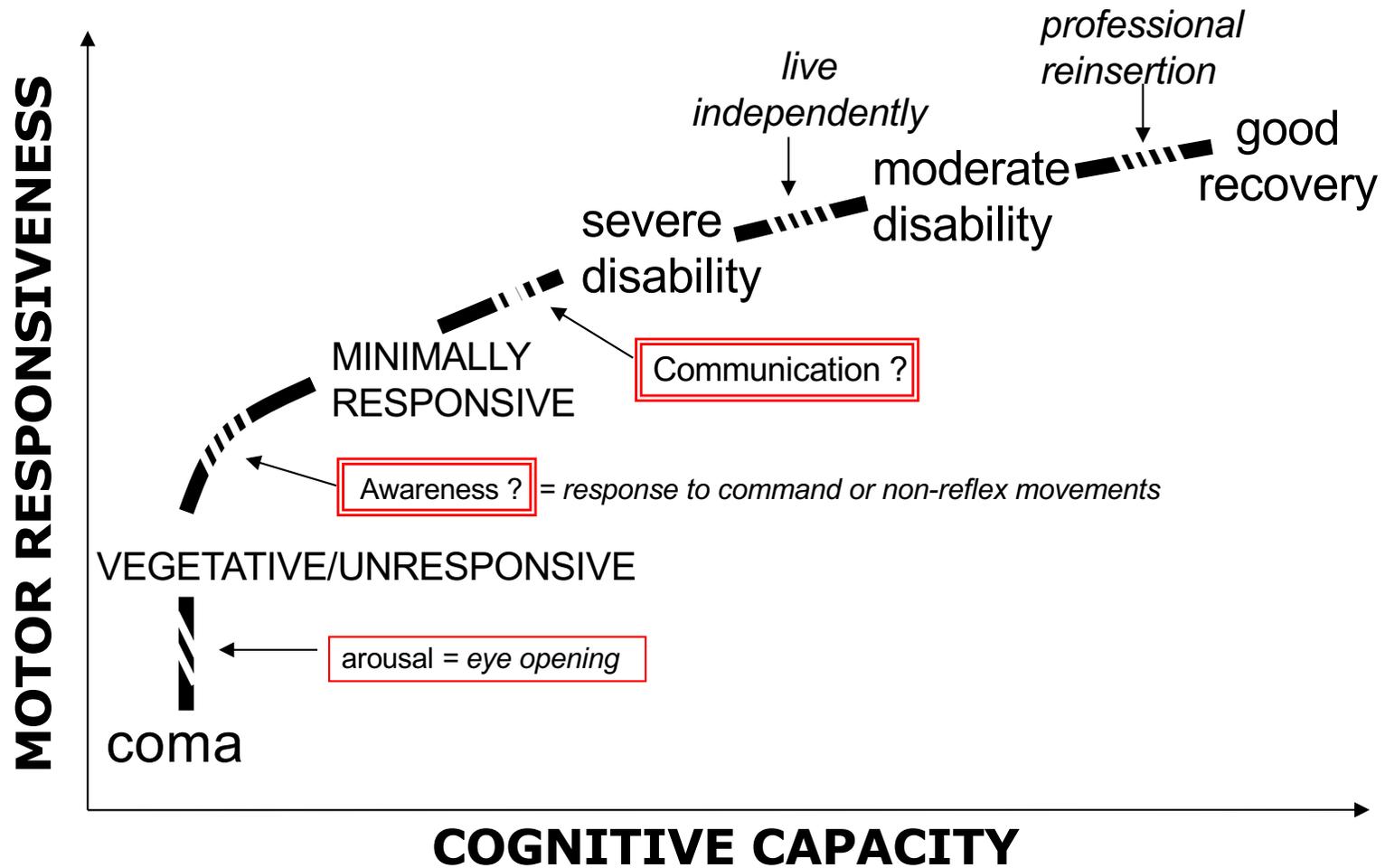


## Post – Pre flight



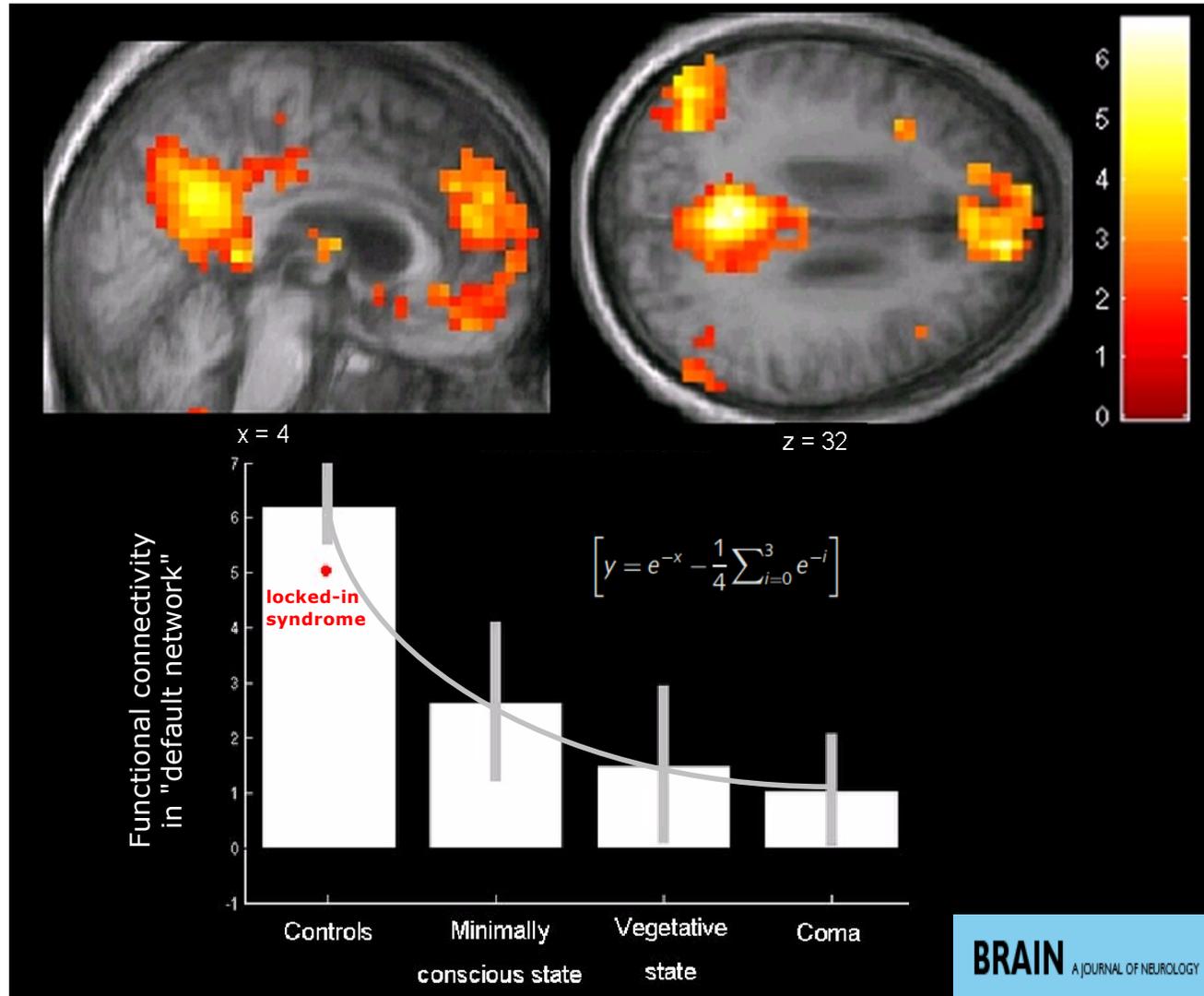


# Disorders of Consciousness



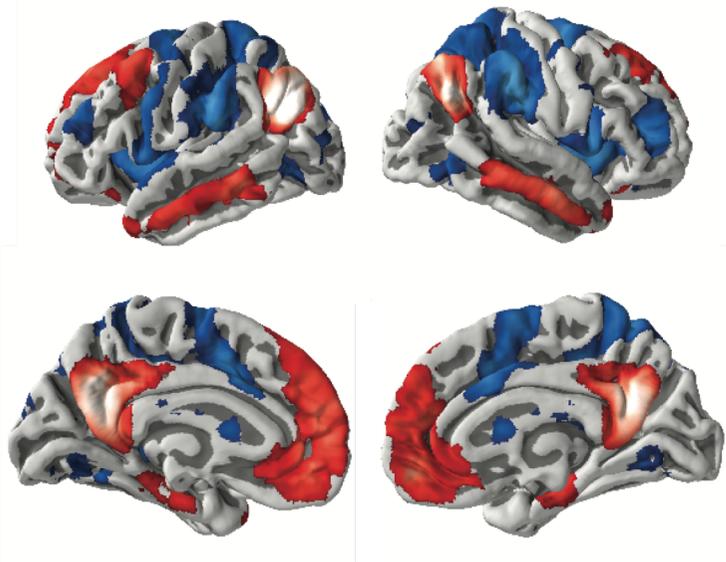


# Default mode network in DOC

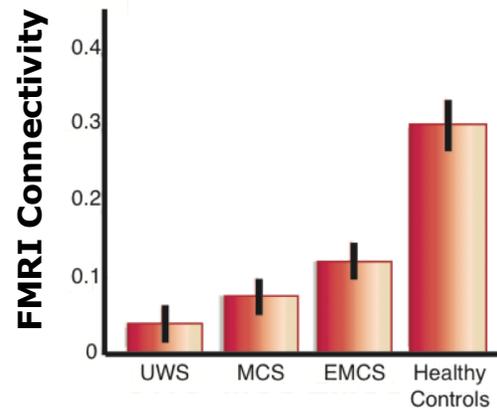




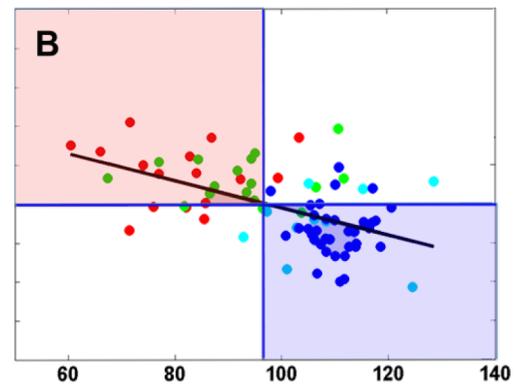
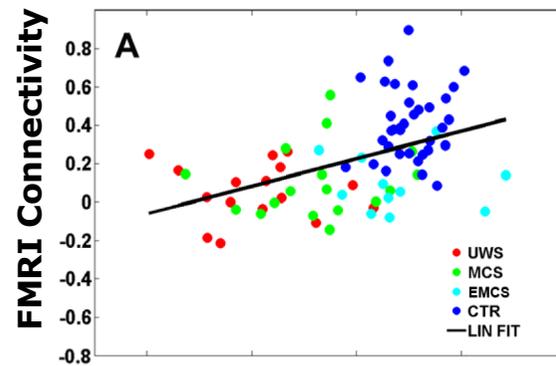
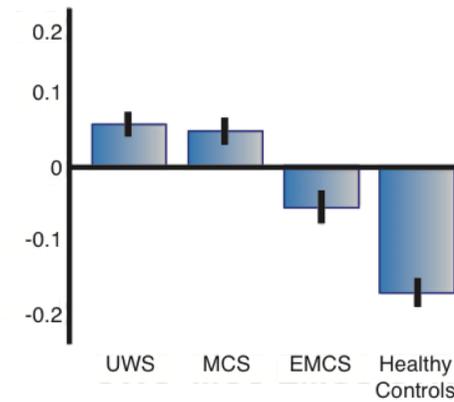
# Effect of pathology



**DMN CORRELATIONS**



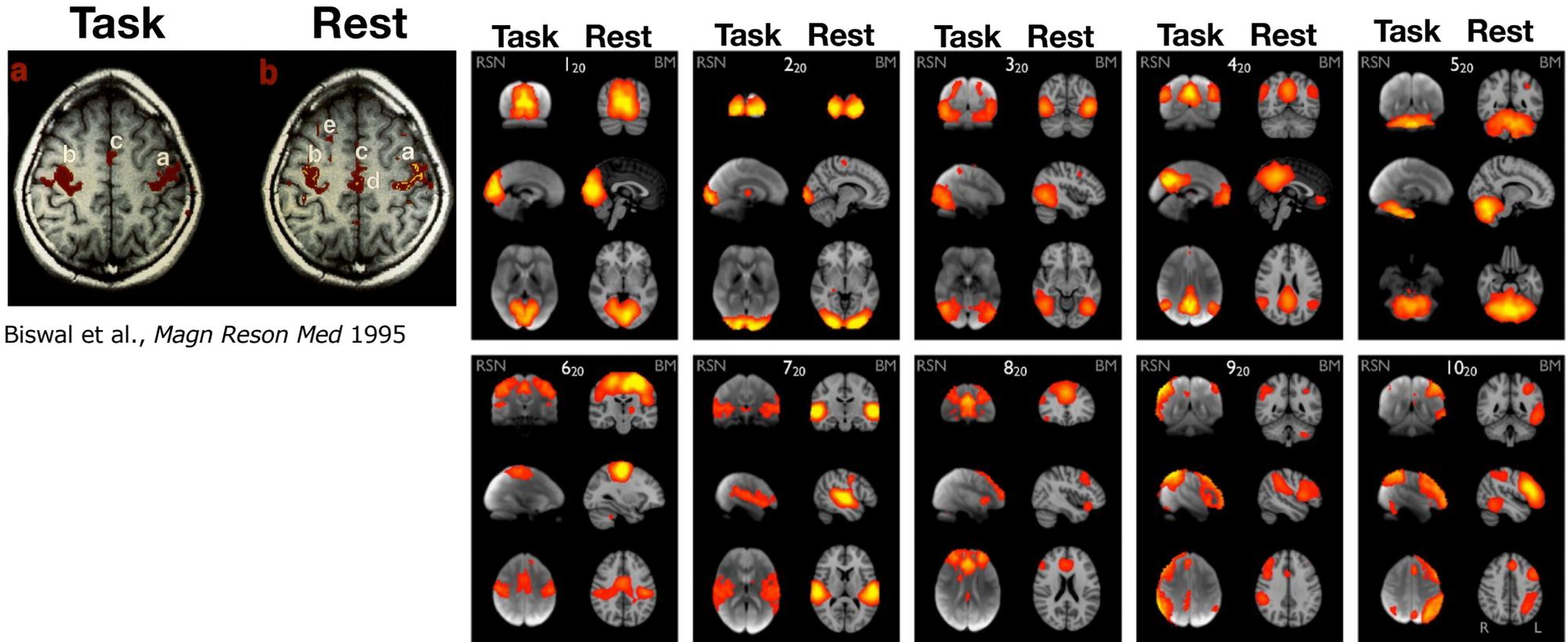
**DMN ANTICORRELATIONS**



**Brain metabolism**



# Intrinsic Connectivity Networks

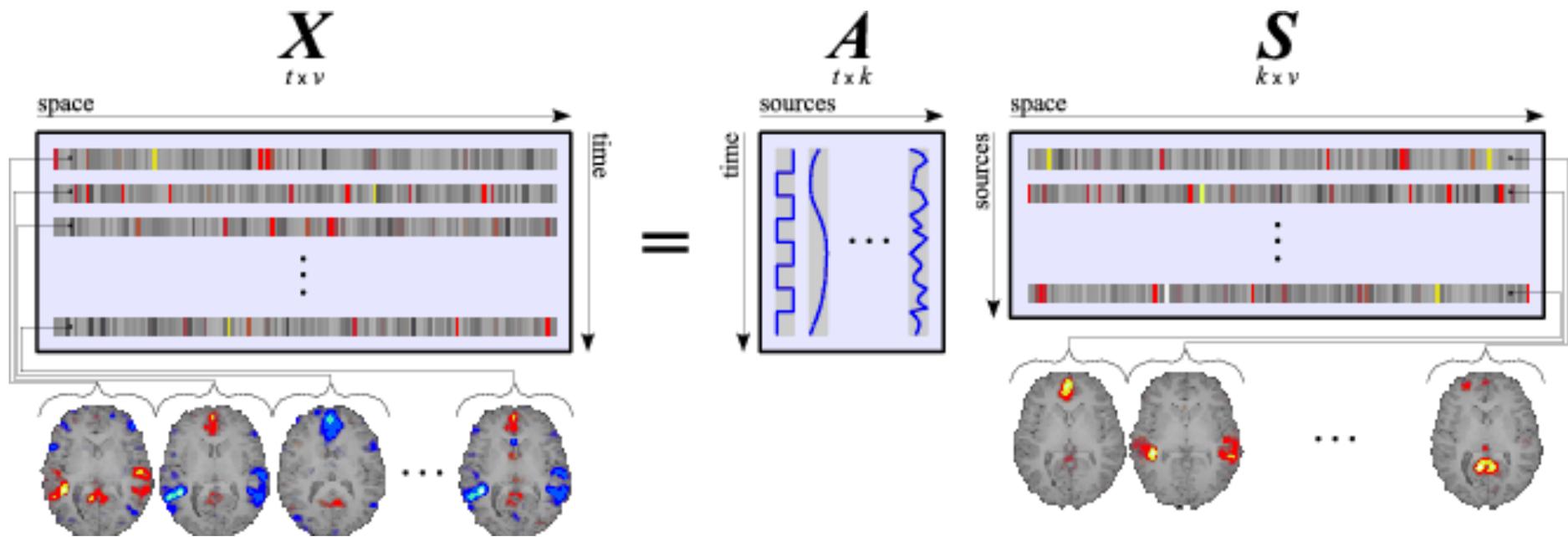


Biswal et al., *Magn Reson Med* 1995

Smith et al, *PNAS* 2009

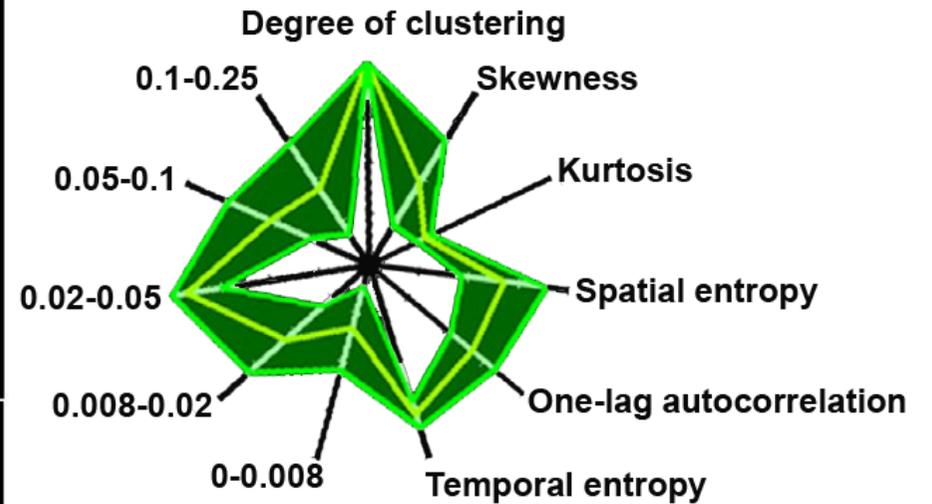
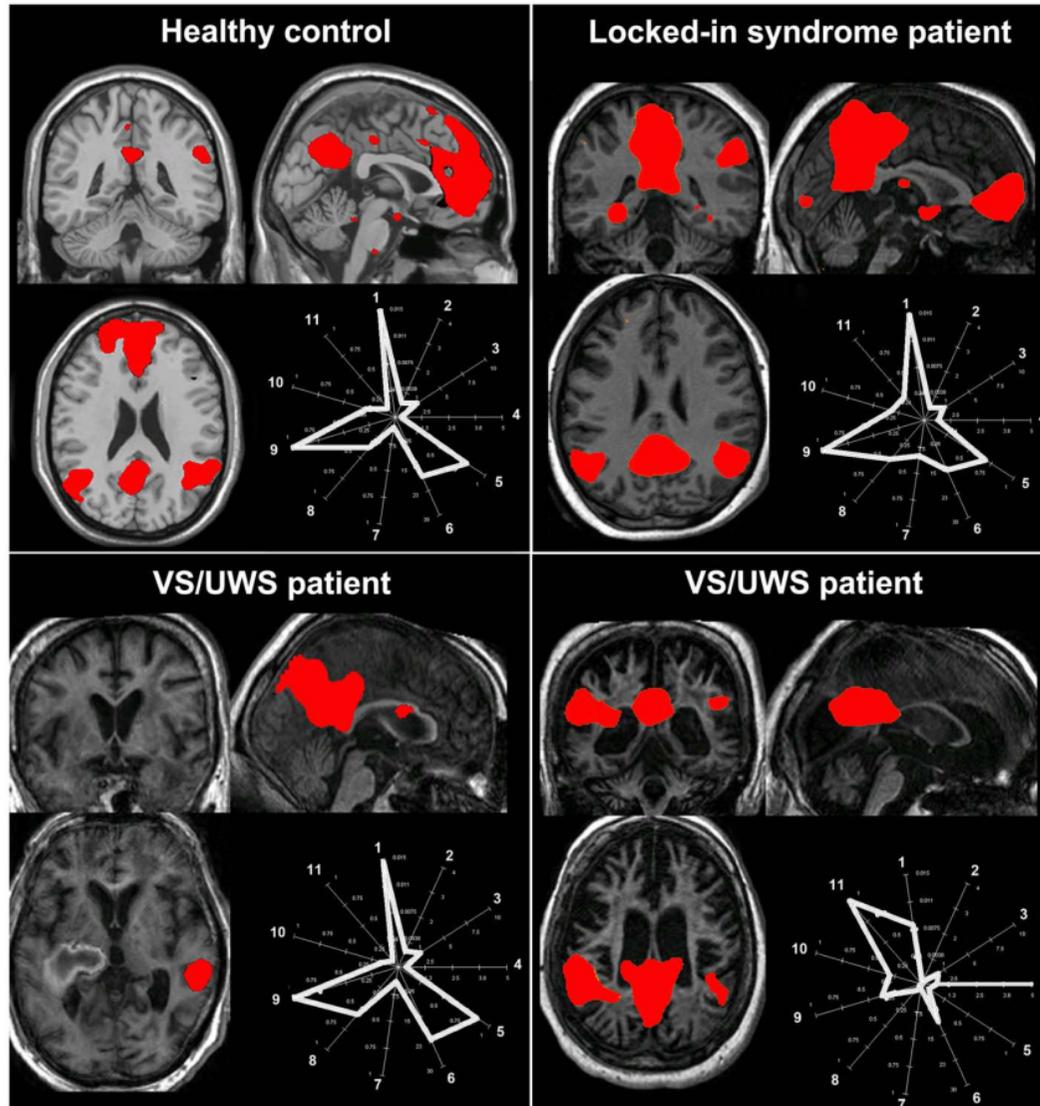


# Independent component analysis (ICA)



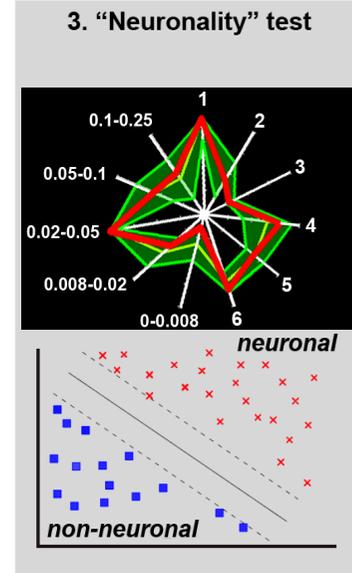
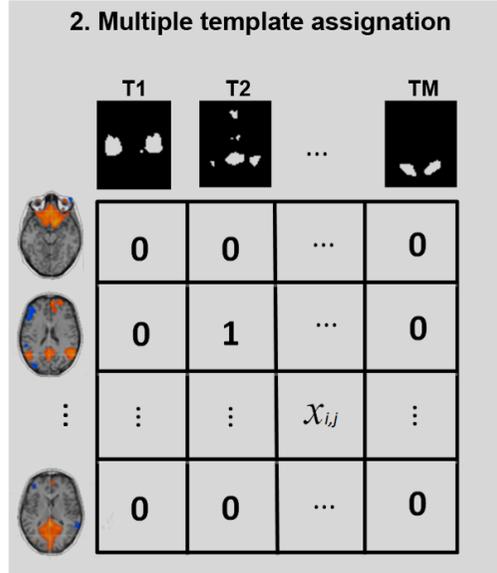
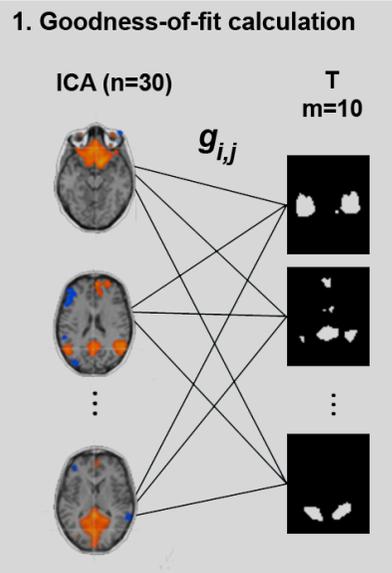
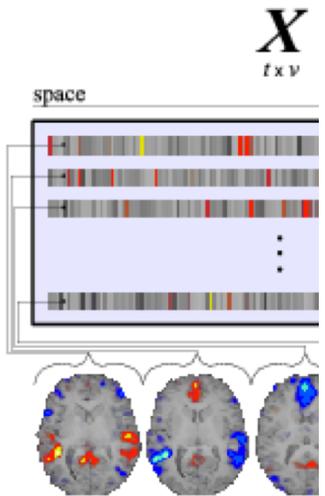
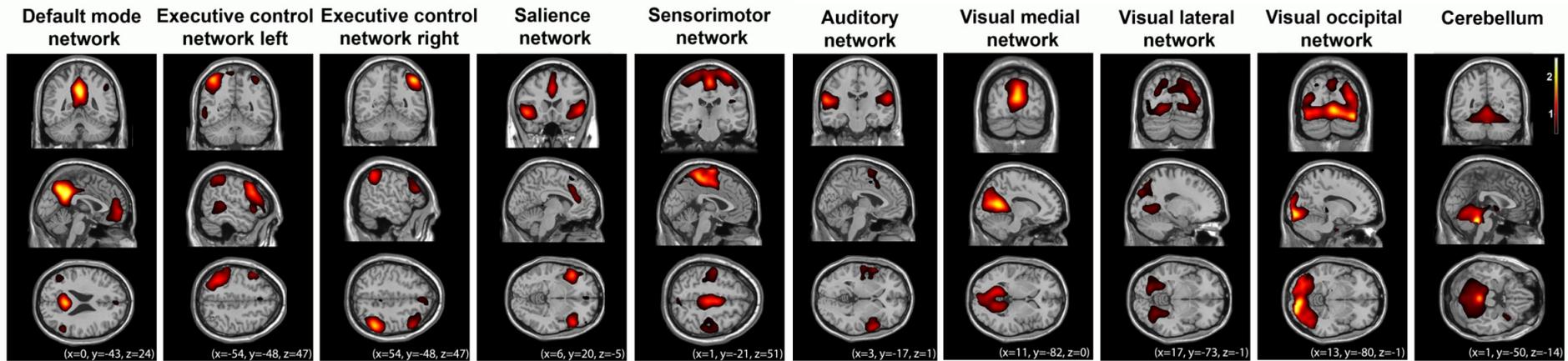


# A challenge...



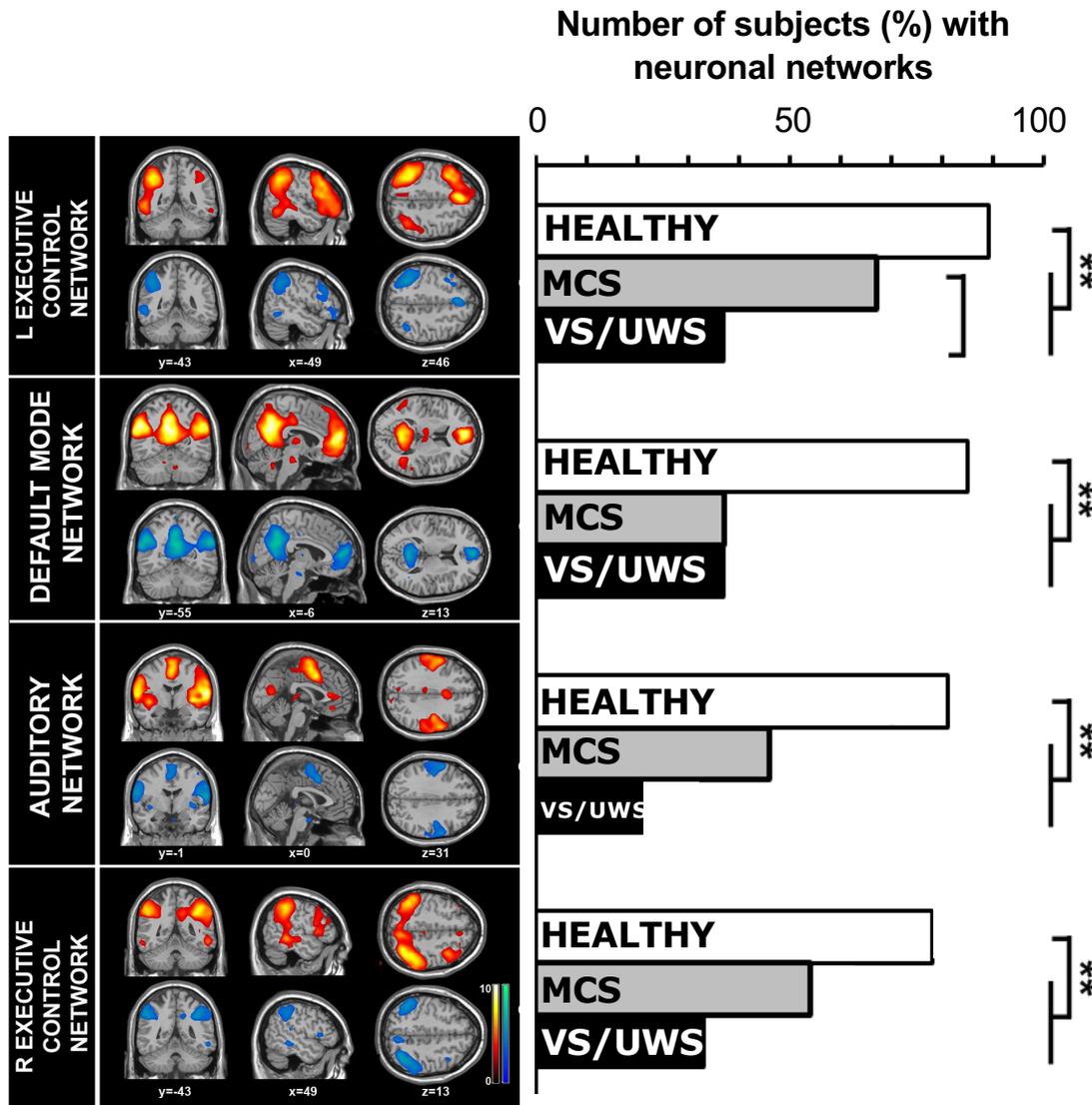


# Systems-level intrinsic connectivity





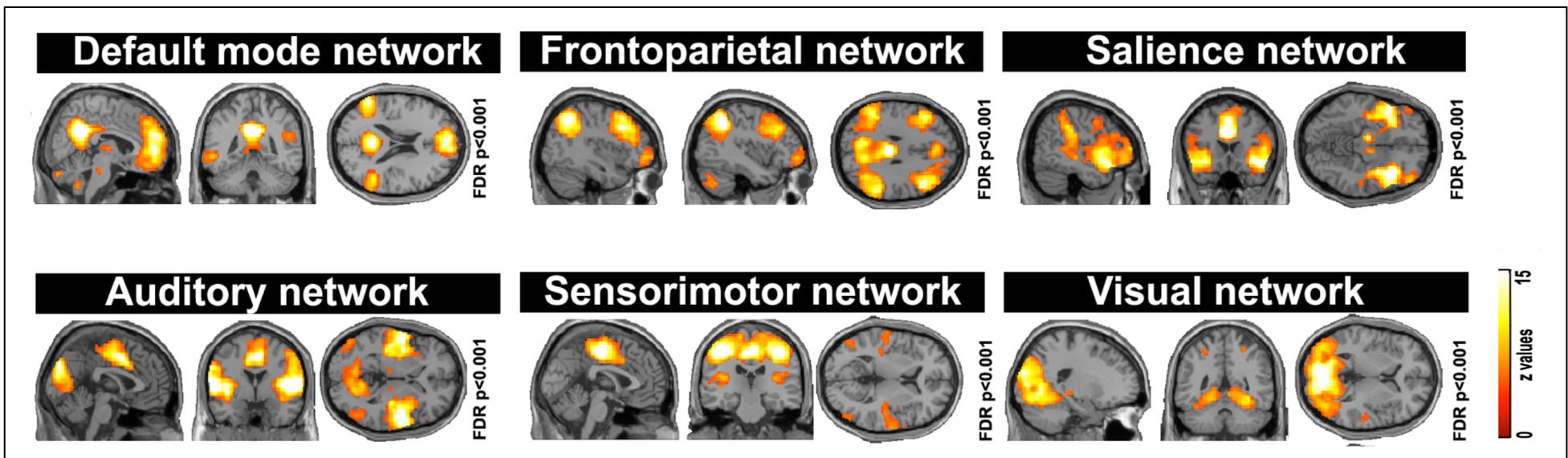
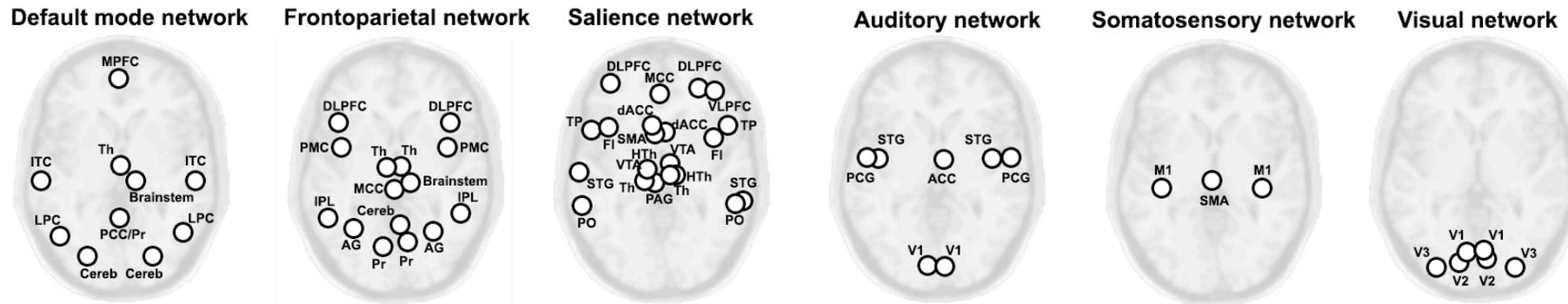
# Fewer “neuronal” networks in DOC



## Single-patient classification

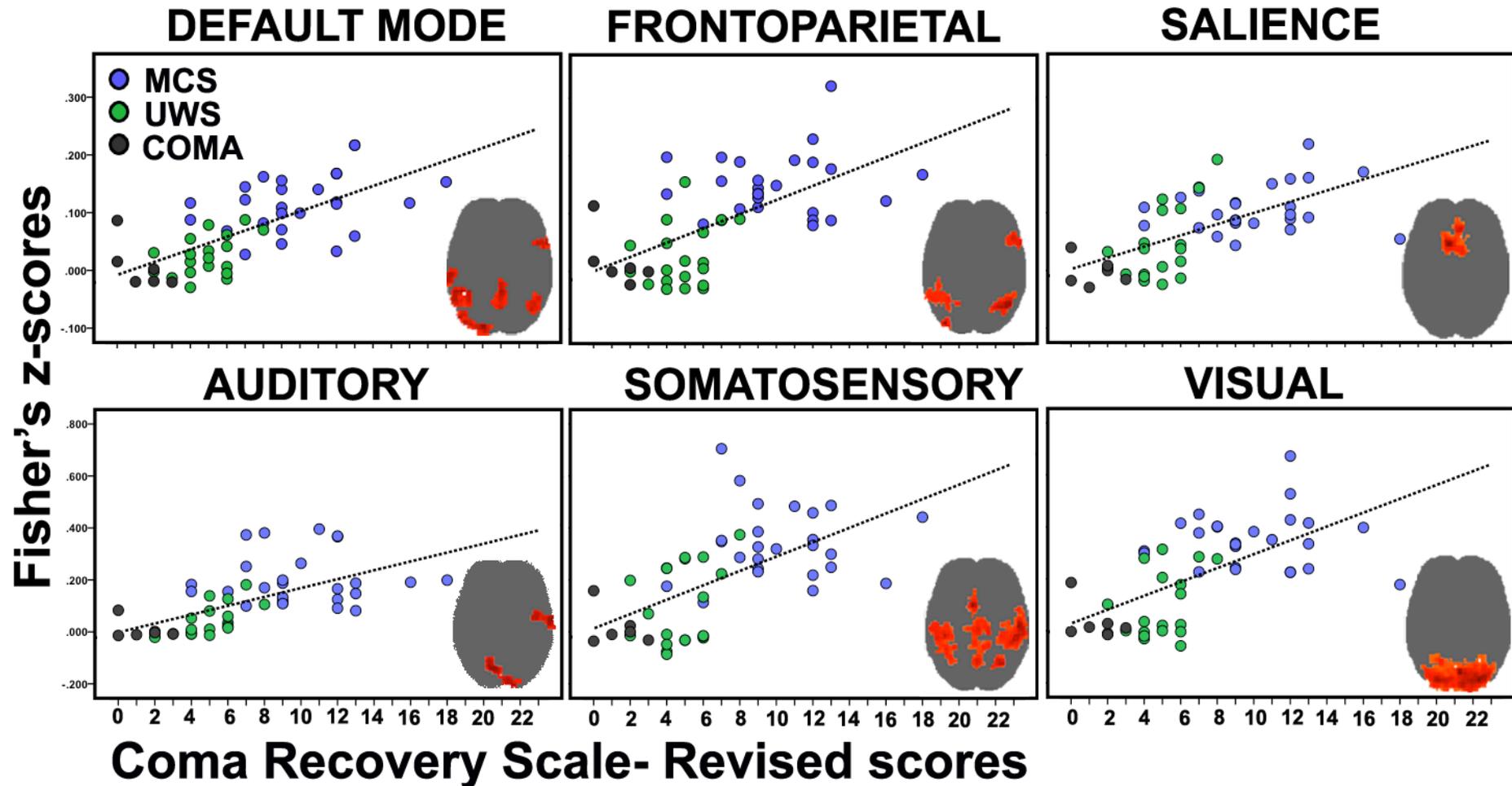
Performance measures	Accuracy	TPR healthy	TPR patients	Selected RSNs
	Healthy vs. all patients			
Neuronal	85.3	.82	.87	Auditory, DMN

# Seed-based functional connectivity





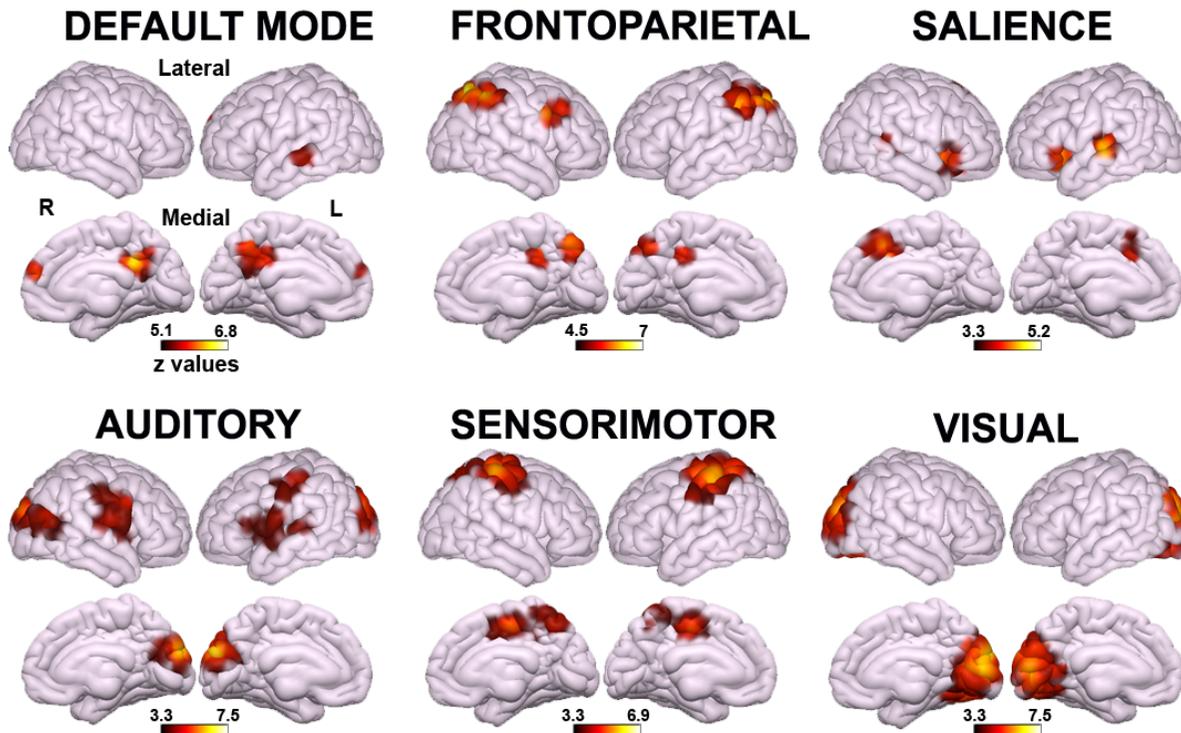
# Connectivity reflects C state





# Which network discriminates best?

## MCS > VS/UWS



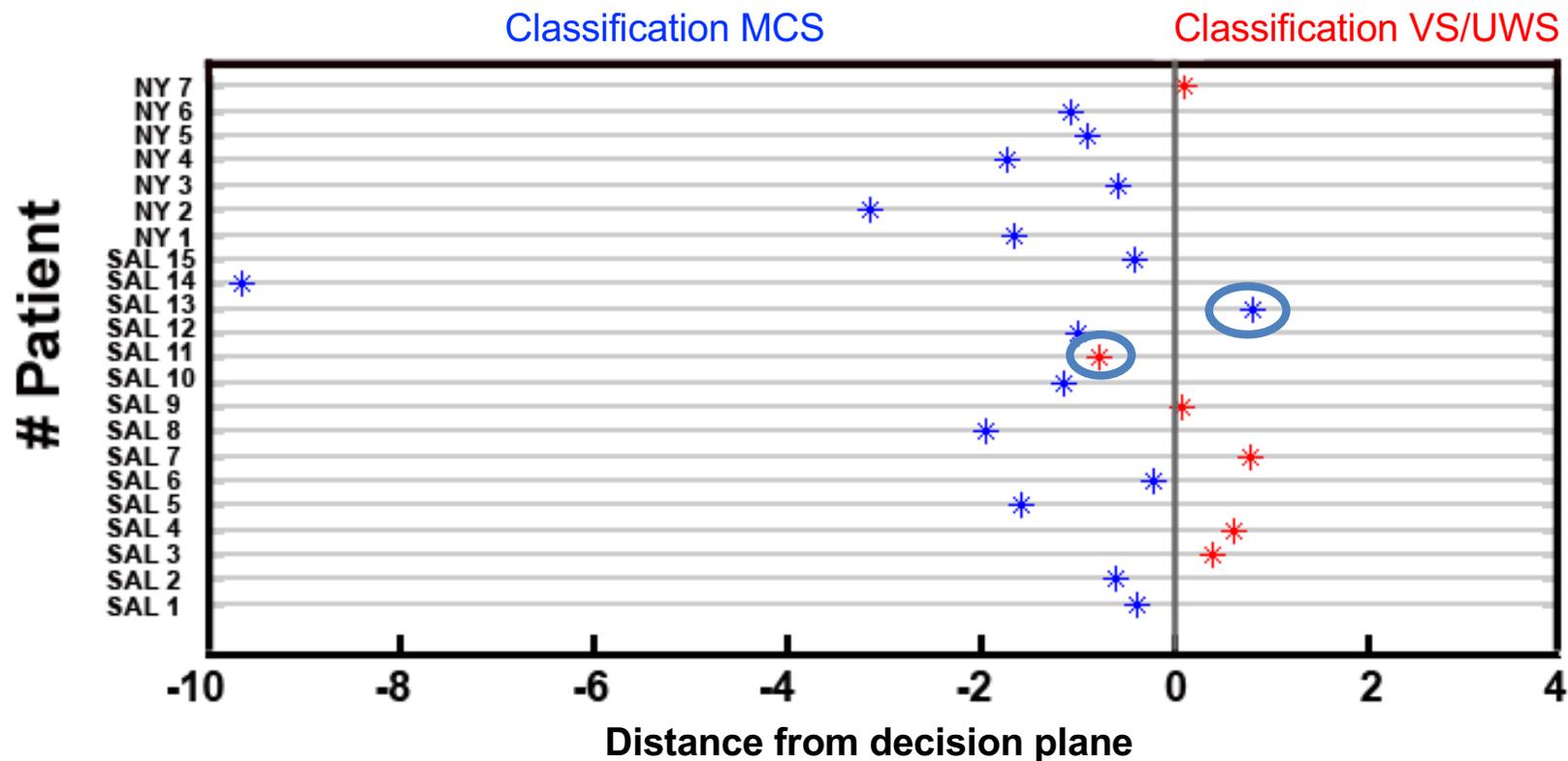
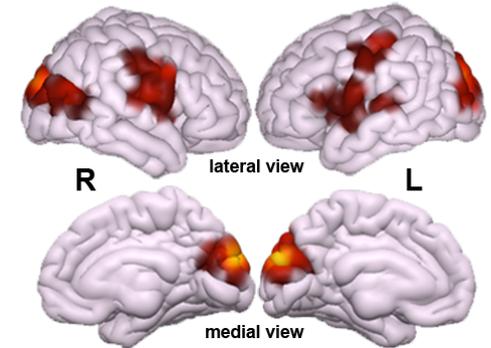
Network	Feature selection criterion (t-test)			Single-feature classification		
	t value	Rank	p value	TP MCS	TN VS/UWS	Accuracy
Auditory	8.32	1	<.001	25	18	43/45
Visual	7.79	2	<.001	23	15	38/45
Default mode	6.95	3	<.001	23	15	38/45
Frontoparietal	6.82	4	<.001	23	15	38/45
Salience	6.21	5	<.001	24	15	39/45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

FWE  $p < 0.05$  (cluster-level)



# Crossmodal connectivity classifies DOC

- 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** ( $M_{age}$ : 43y, 15 non-trauma; all chronic), from 2 different centers





# Interim conclusions

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RS functional connectivity :

- is linked to behavior and task performance *(Laird et al., 2011)*
- reflects physiological & pathological unconsciousness *(Heine et al, 2012)*
- permits single-patient automatic diagnosis *(Demertzi & Antonopoulos et al, 2015)*

**But**

it remains unclear to what extent it provides a  
representative estimate of cognition

*(Peterson et al, NeuroImage Clin. 2015)*



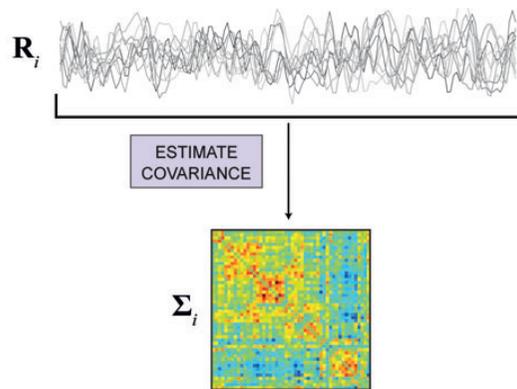
Ongoing interactions among distinct brain regions

*(Hutchison et al, NeuroImage 2013)*

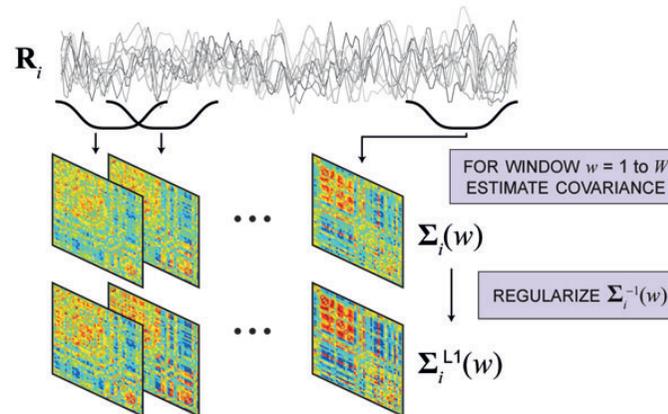


# From stationarity to dynamics

Stationary fc



Time-varying fc



Dynamic

$$x_t = A \cdot x_{t-1} + \epsilon_t$$



# Brain dynamics and cognition

**Typical wakefulness:** significance for performance, emotion and cognition

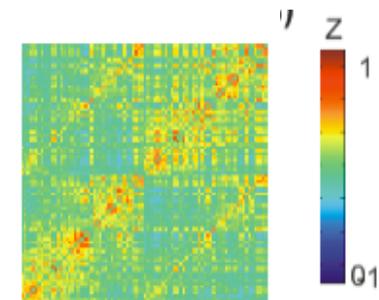
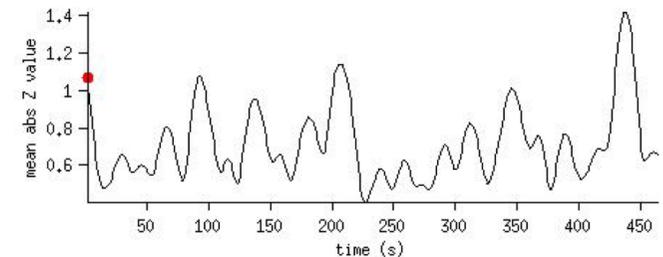
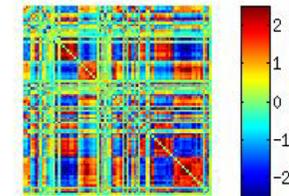
(Alavash, et al, *Neuroimage*, 2016; Shine et al., *Neuron*, 2016; Friston, *Neuroimage*, 1997; Thompson et al., *Hum. Brain Mapp*, 2013)

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



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



Barttfeld\*, Ulhig\*, Sitt\*, et al, *PNAS* 2015



# Study cohort (N=159)

James S. McDonnell Foundation



Grant Type: Collaborative Activity Award, Phase I & II (2008-2017)

## Main dataset

awake

	VS/UWS	MCS	CTR
LIEGE	17	23	21
PARIS	13	9	15
NY	6	10	11
Total	36	42	47

**n = 125**

## Validation datasets

sedated

CMD

LIEGE	
EMCS	3
MCS	14
UWS	6

**n = 23**

ONTARIO	
VS/UWS-	6
VS/UWS+	5

**n = 11**



# Methods



## EPI acquisition

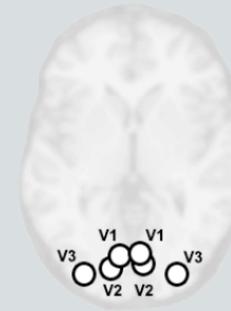


## Preprocessing

Slice-time correction  
Realignment  
Segmentation  
Normalization  
Smoothing  
Motion outliers (ART)  
aCompCor  
Regressing out realignment parameters and ART outliers  
Bandpass filtering [0.008-0.09Hz]

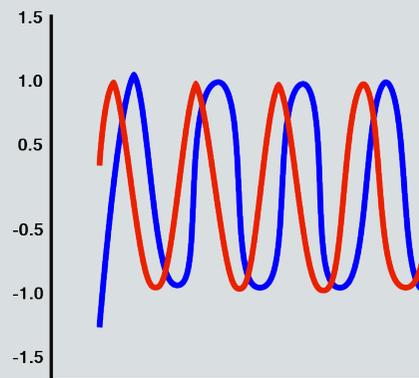
## Brain parcellation

(Sphere ROIs)

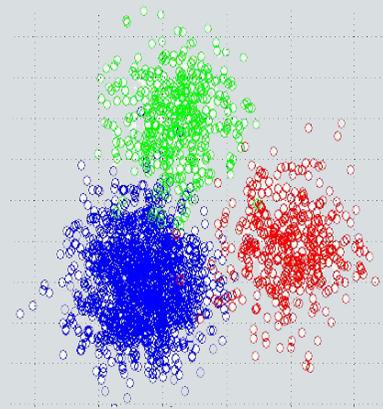


## ROI timeseries extraction

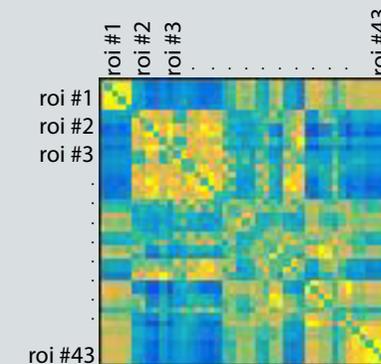
## Phase analysis (Hilbert transform)



## Unsupervised clustering (k-means)

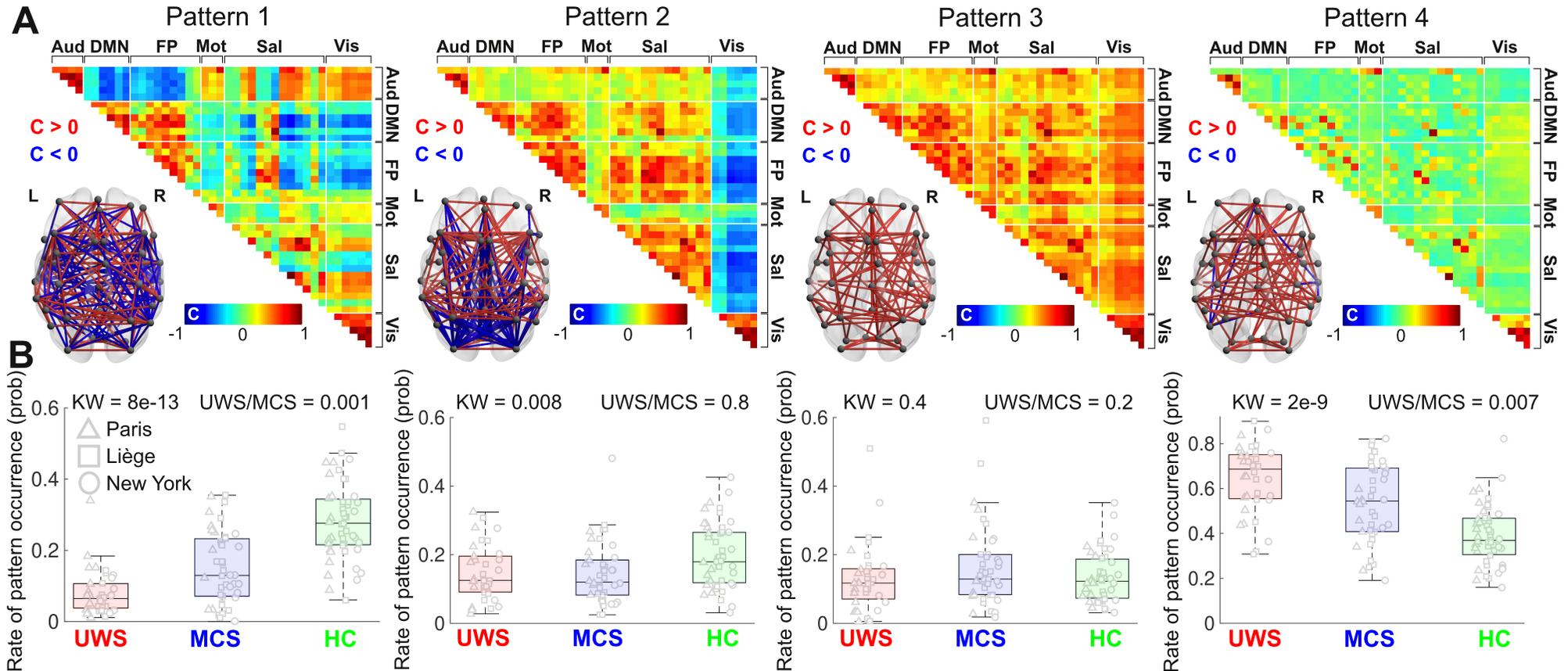


## State identification (cluster centroids)



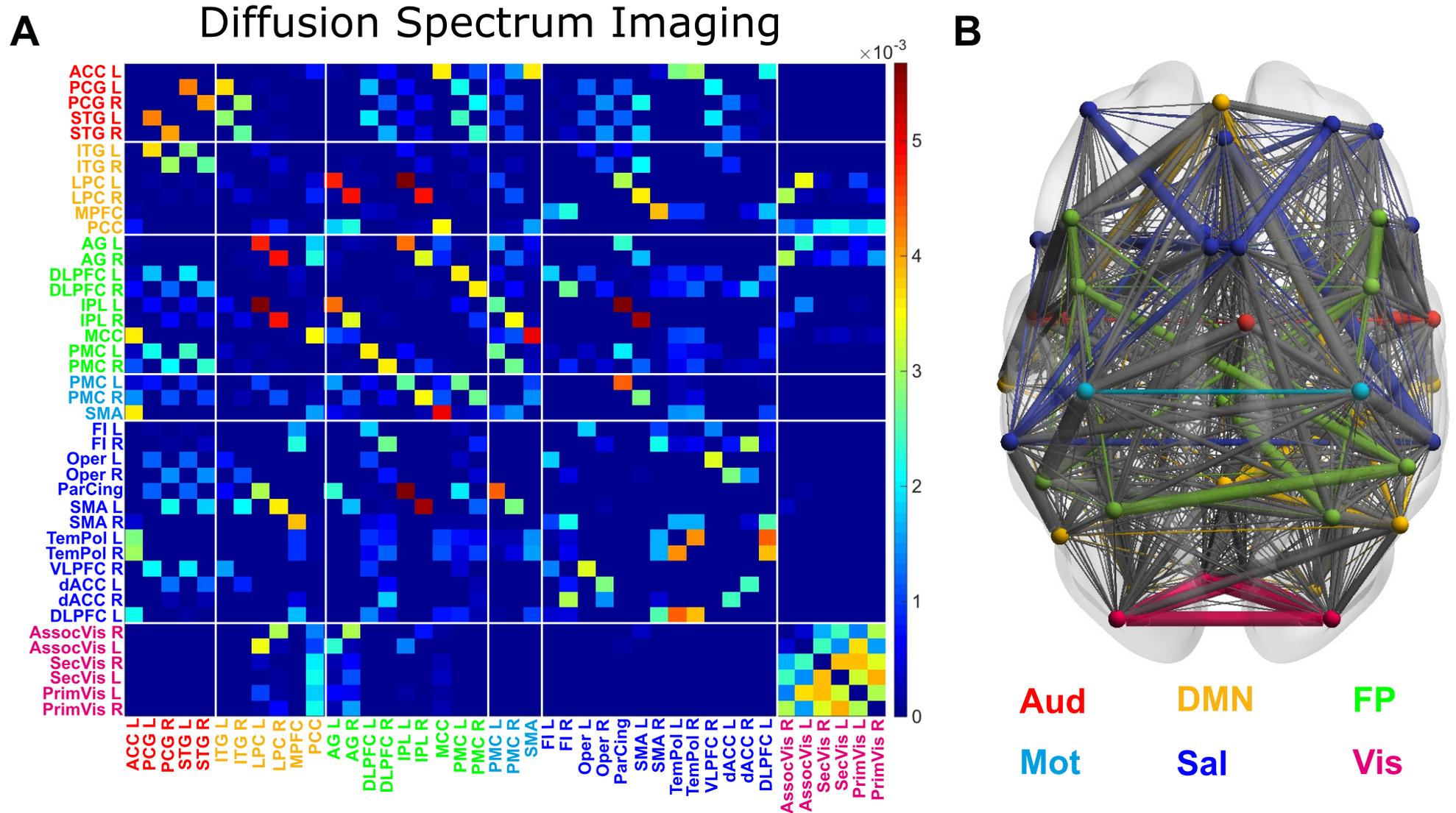


# Four brain patterns





# Structure-function correlation

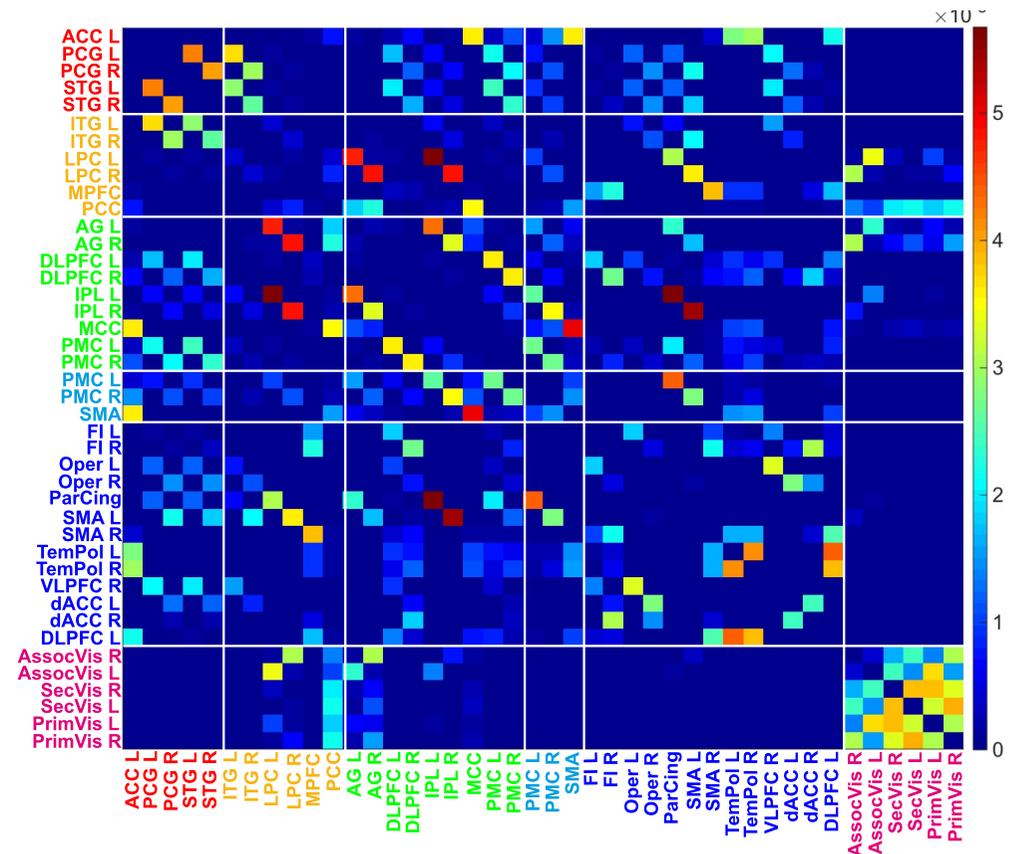
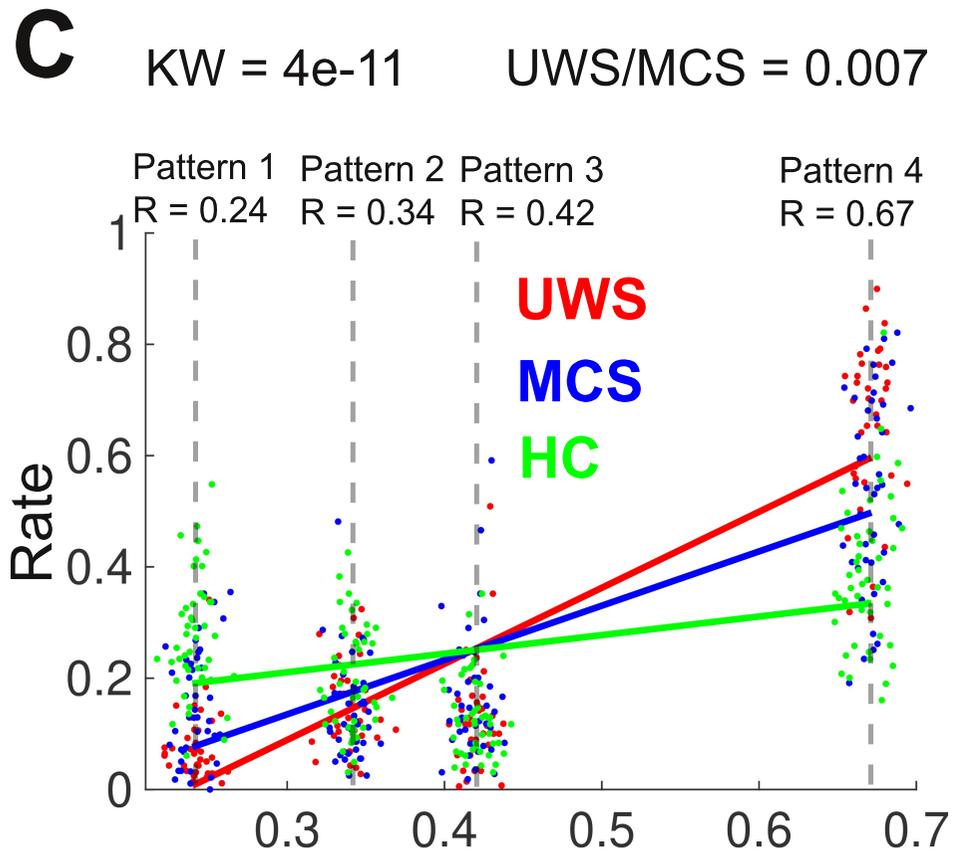


Hagmann, et al, *PLOS Biol.* 2008

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



# Structure-function correlation





# Dynamics: Markov Process

- *stochastic process that has no memory*
- *selection of next state depends only on current state, and not on prior states*
- *process is fully defined by a set of transition probabilities  $\pi_{ij}$*   
 $\pi_{ij}$  = probability of selecting state  $j$  next, given that presently in state  $i$ .  
Transition-probability matrix  $\Pi$  collects all  $\pi_{ij}$

## Transition-Probability Matrix

### ○ Example

- *system with three states*

$$\Pi \equiv \begin{pmatrix} \pi_{11} & \pi_{12} & \pi_{13} \\ \pi_{21} & \pi_{22} & \pi_{23} \\ \pi_{31} & \pi_{32} & \pi_{33} \end{pmatrix} = \begin{pmatrix} 0.1 & 0.5 & 0.4 \\ 0.9 & 0.1 & 0.0 \\ 0.3 & 0.3 & 0.4 \end{pmatrix}$$

*If in state 1, will stay in state 1 with probability 0.1*

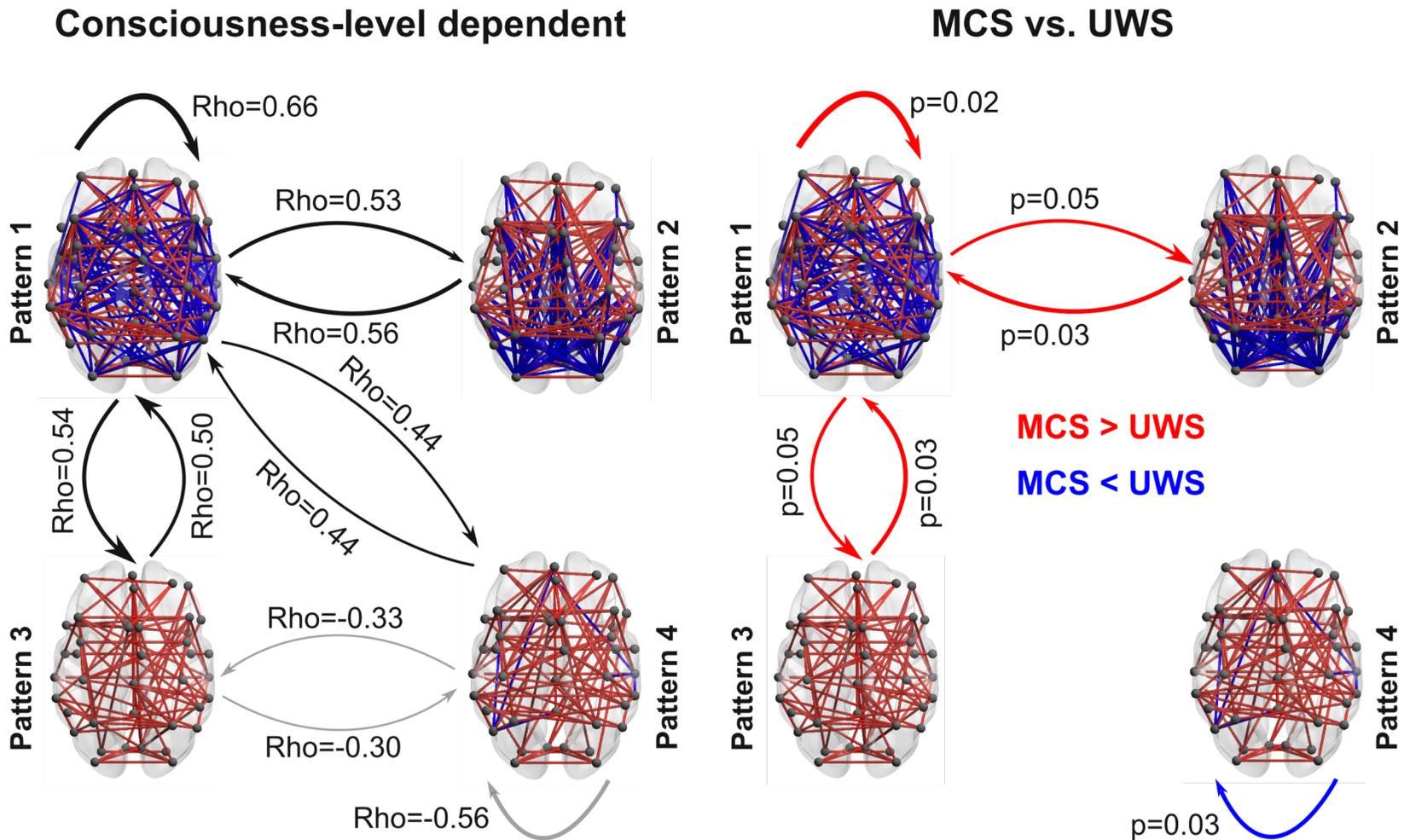
*If in state 1, will move to state 3 with probability 0.4*

*Never go to state 3 from state 2*

# Dynamics

More chances to transition if in higher conscious state

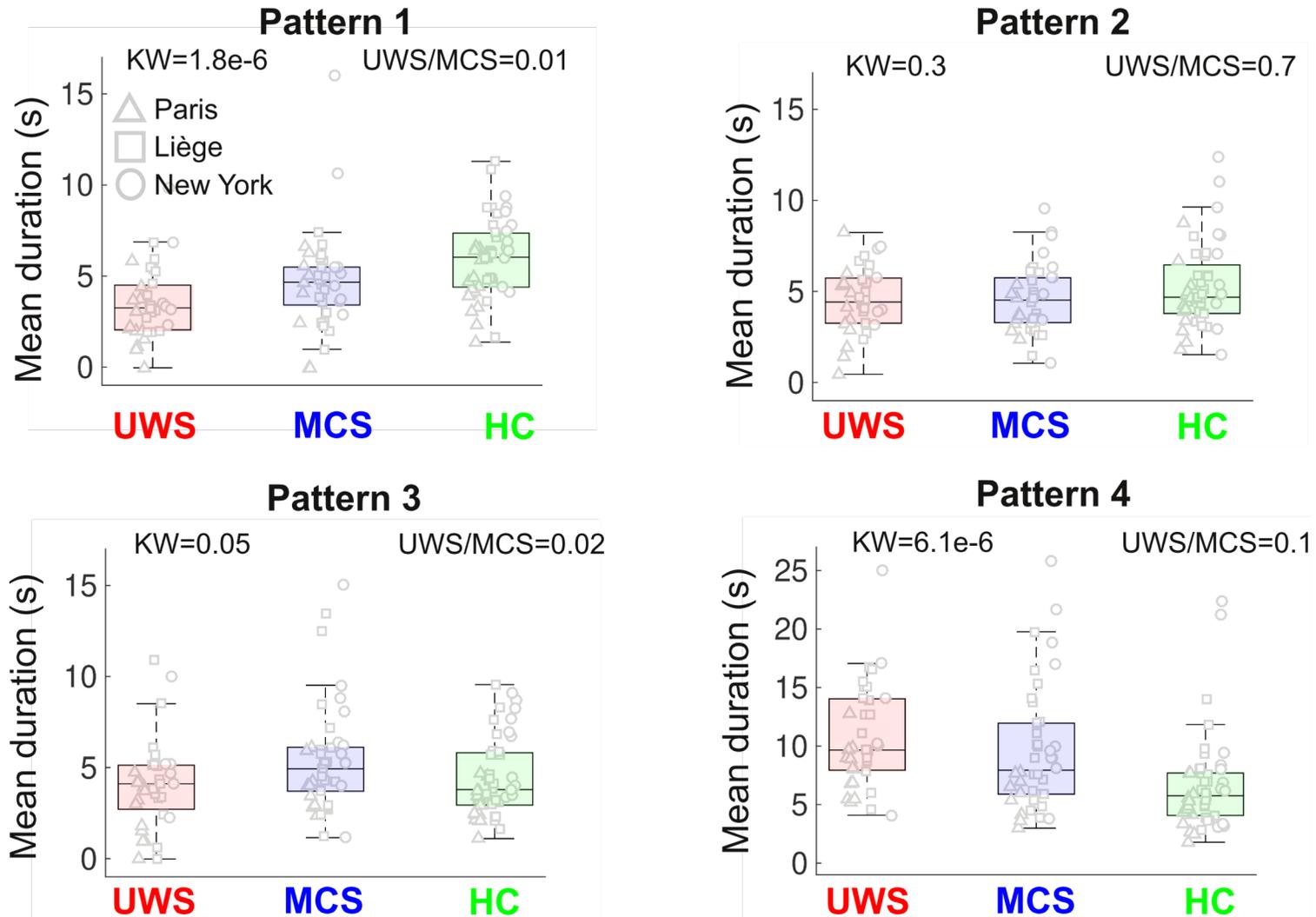
## A. Between-pattern transition probabilities



# Pattern exploration is longer for more complex patterns



## B. Duration of pattern occupation

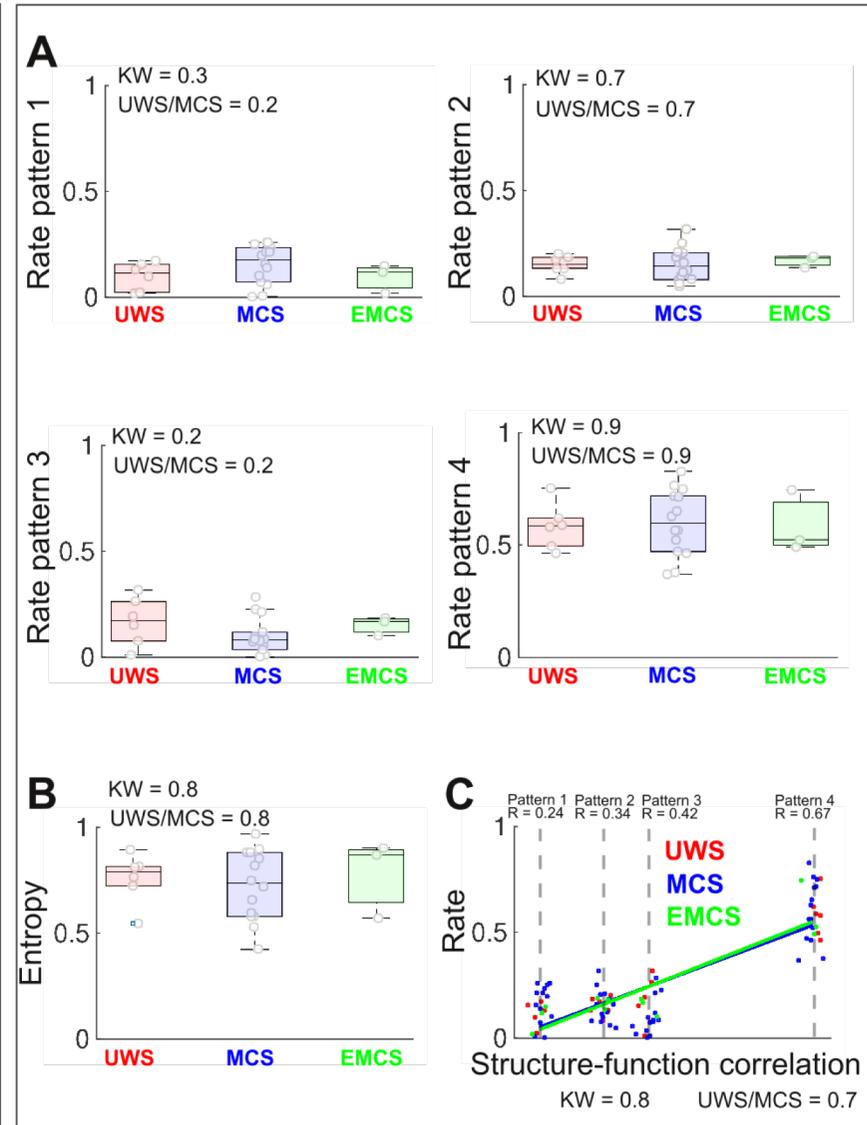
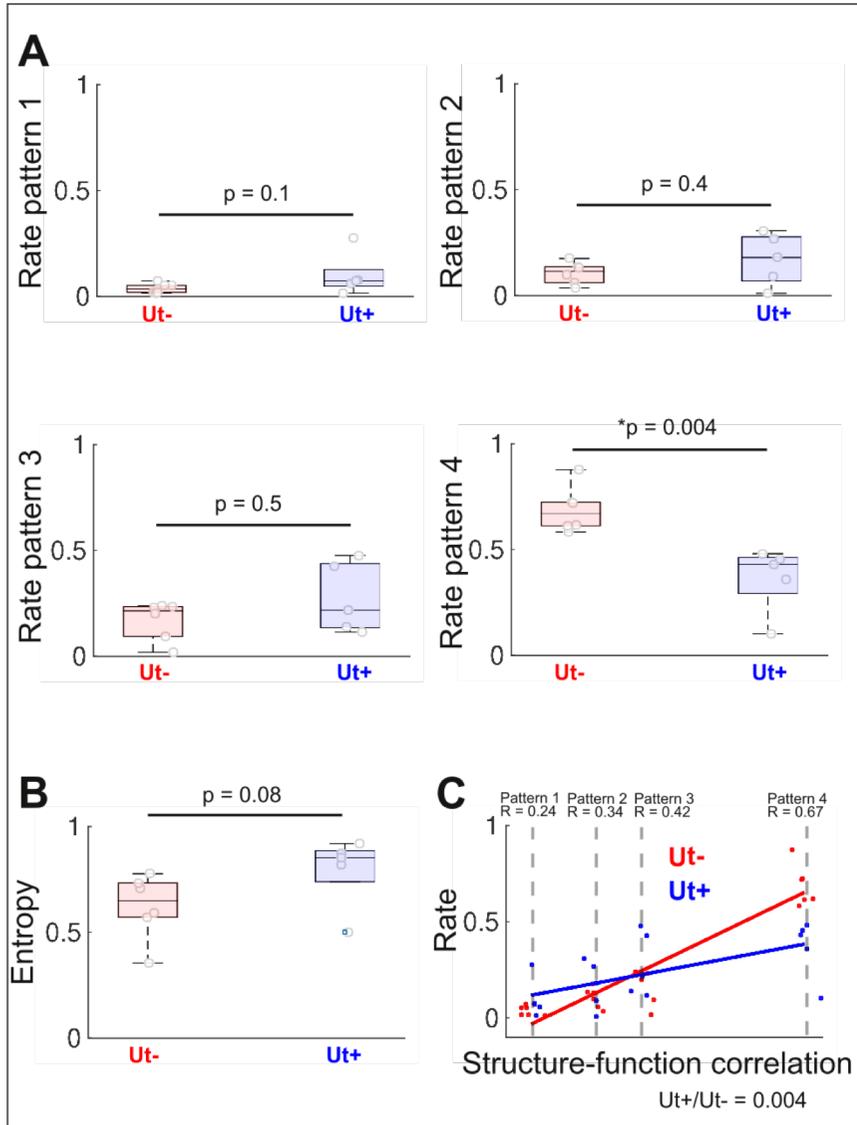




# Do we measure consciousness?

### Pattern prediction in cognitive-motor dissociation

### Pattern prediction in anesthesia



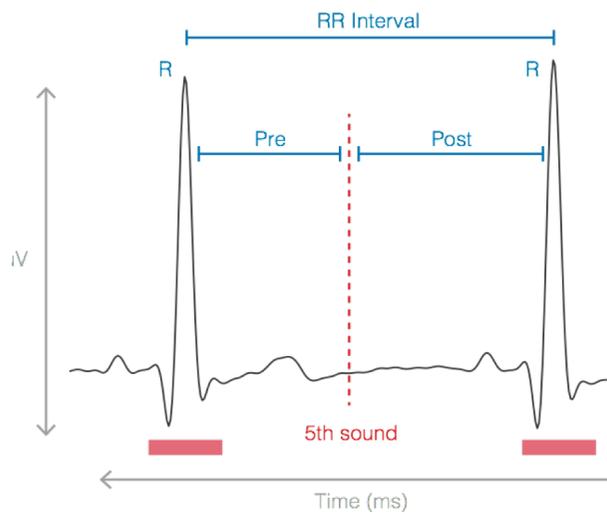


# FROM BRAIN TO BRAIN-BODY INTERACTIONS

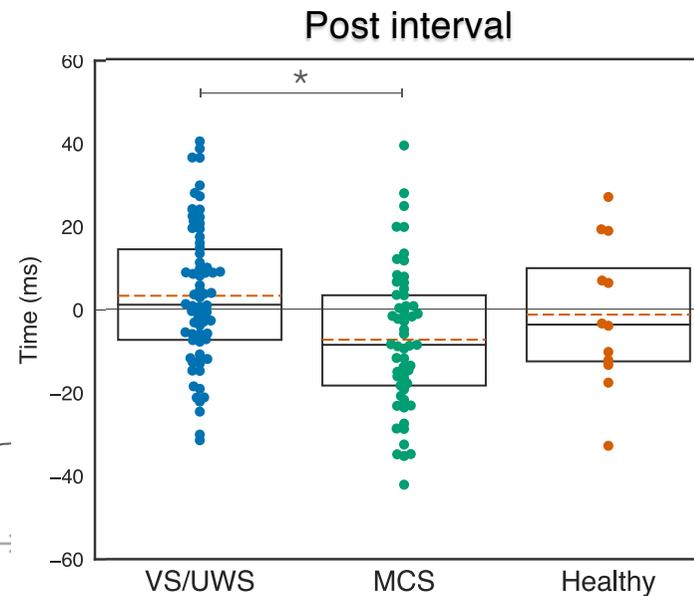
# Cognitive processing modulates autonomic somatic markers



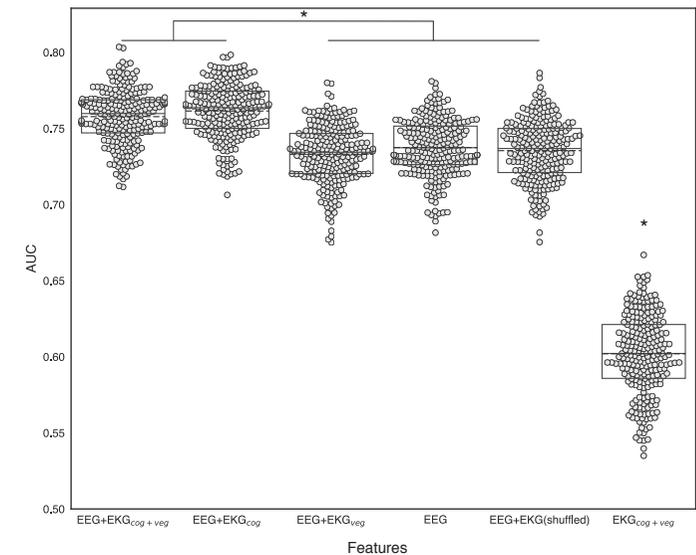
Auditory oddball paradigm



Cardiac cycle phase acceleration  
only in MCS

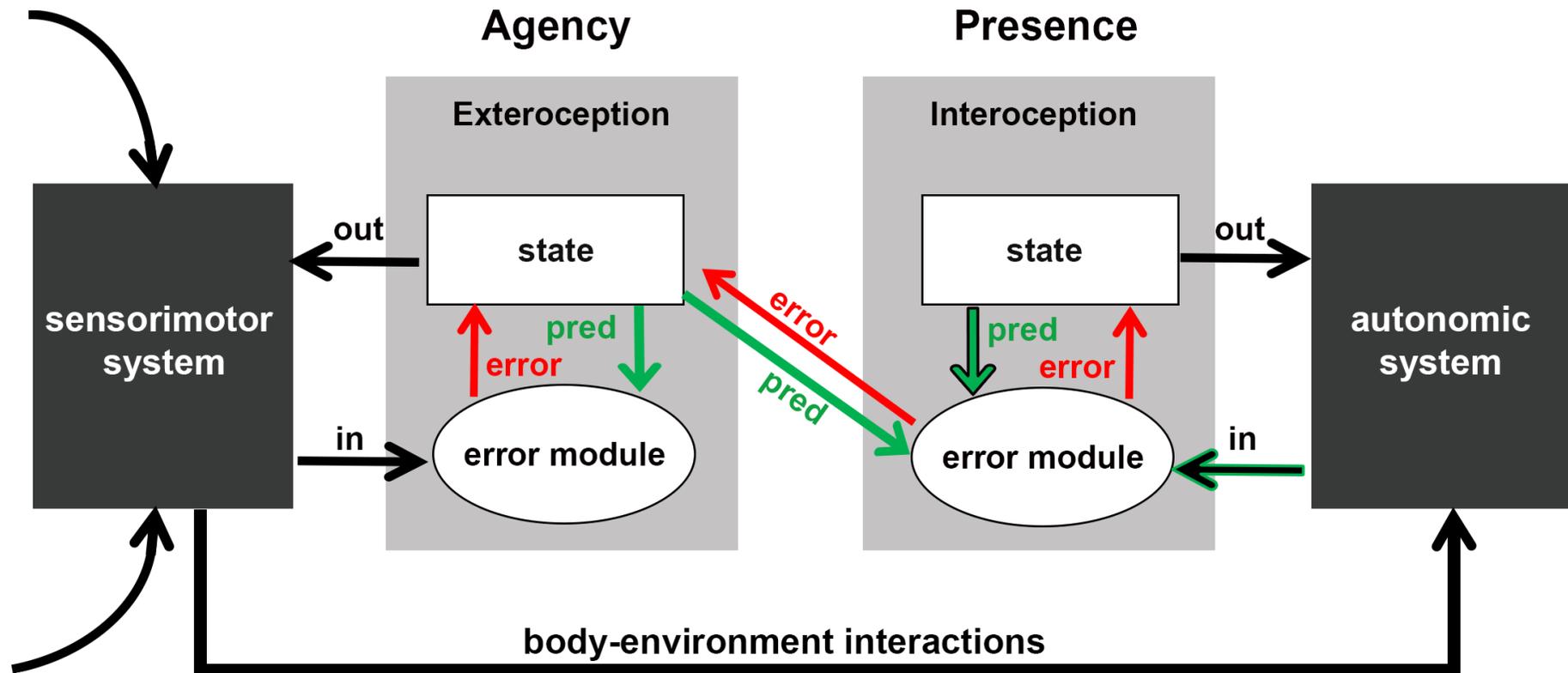


Electrocardiographic markers carry  
independent information from EEG





# Which model for Unconsciousness?



**!Apply to our lab!**



# Taken together...

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## **Consciousness needs a brain which:**

- is intrinsically organized
- shows complexity
- shows dynamic flexibility

## **Consciousness as brain-body interactions**

## **Consciousness as active inference**



Thank you

# Coma Science Group & PICNIC Lab

The departments of Neurology and Radiology in Liège & Paris

**...and mostly patients and their families!**

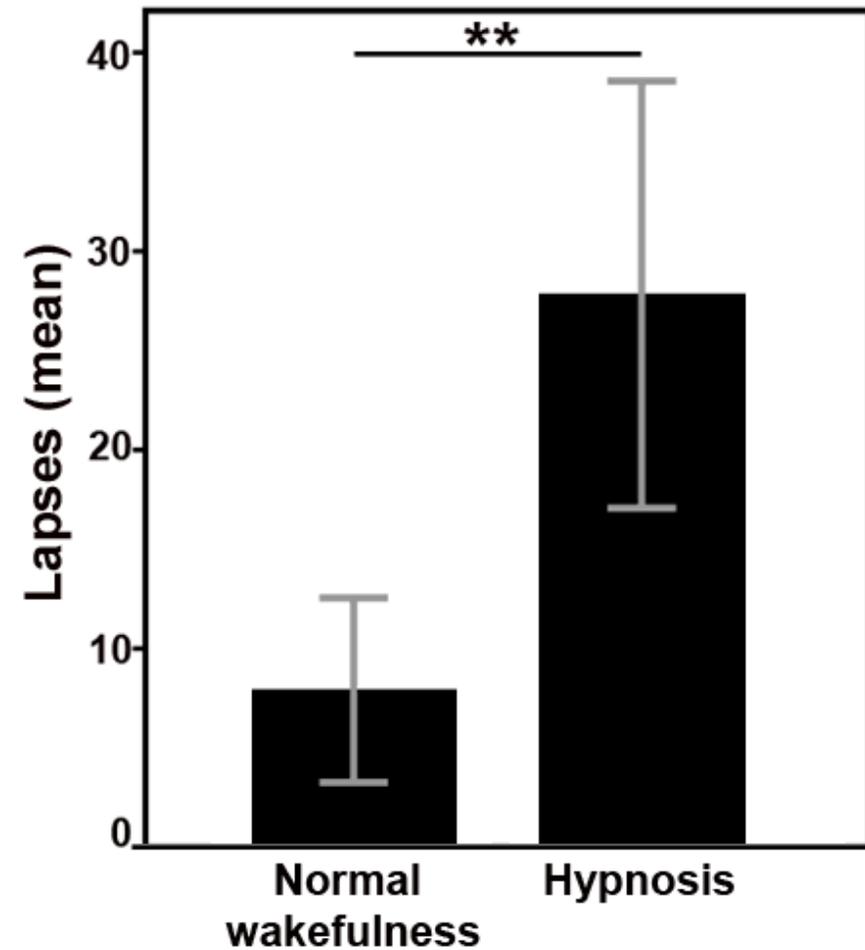
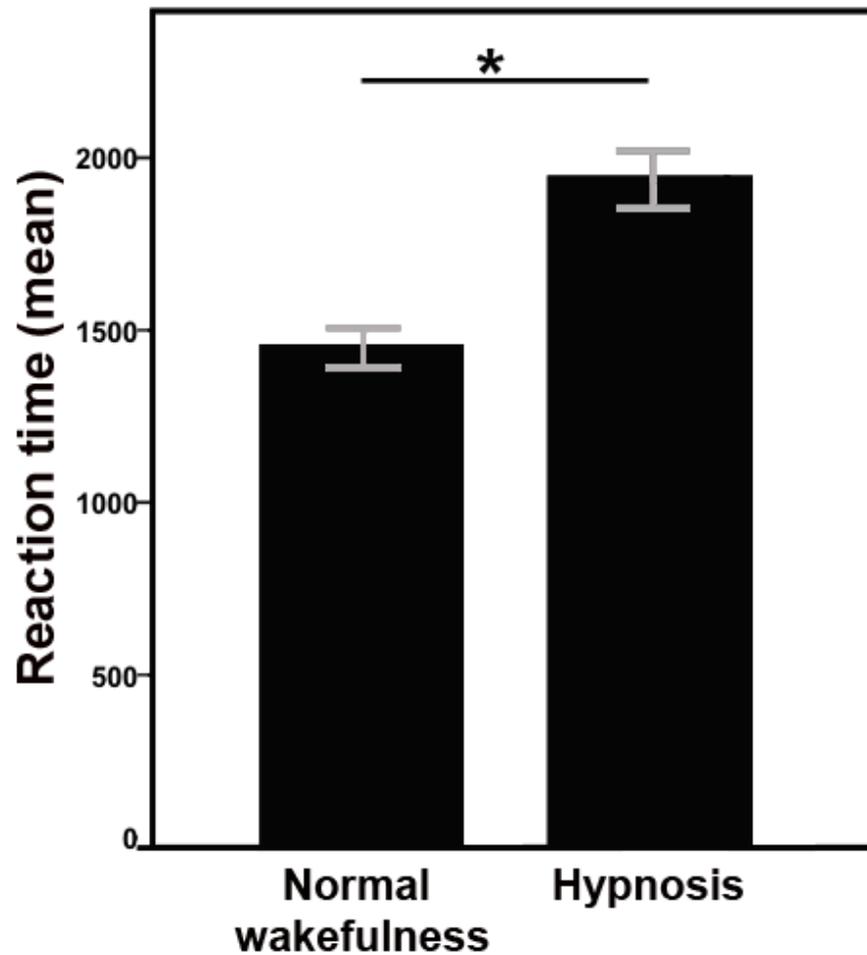


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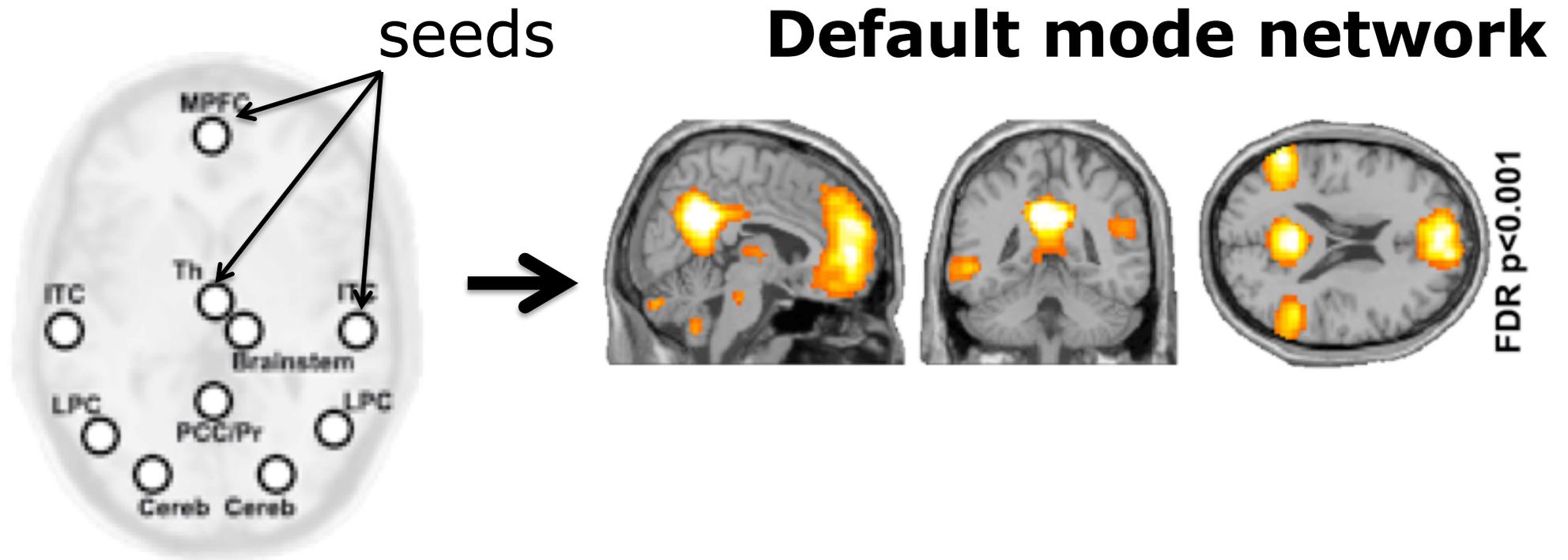


# Anticorrelated connectivity is modified in hypnosis-Behavior



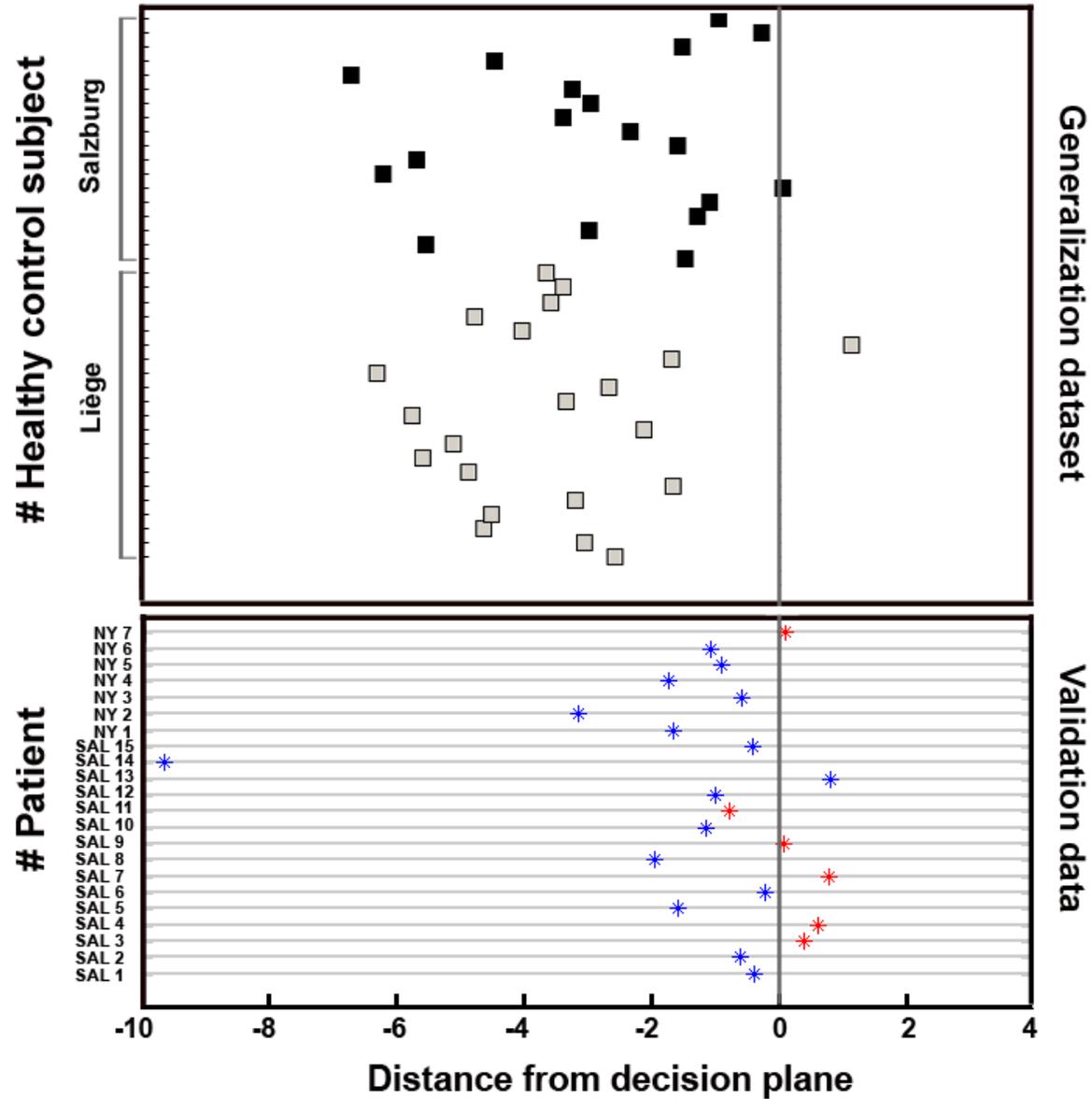


# Seed-based functional connectivity

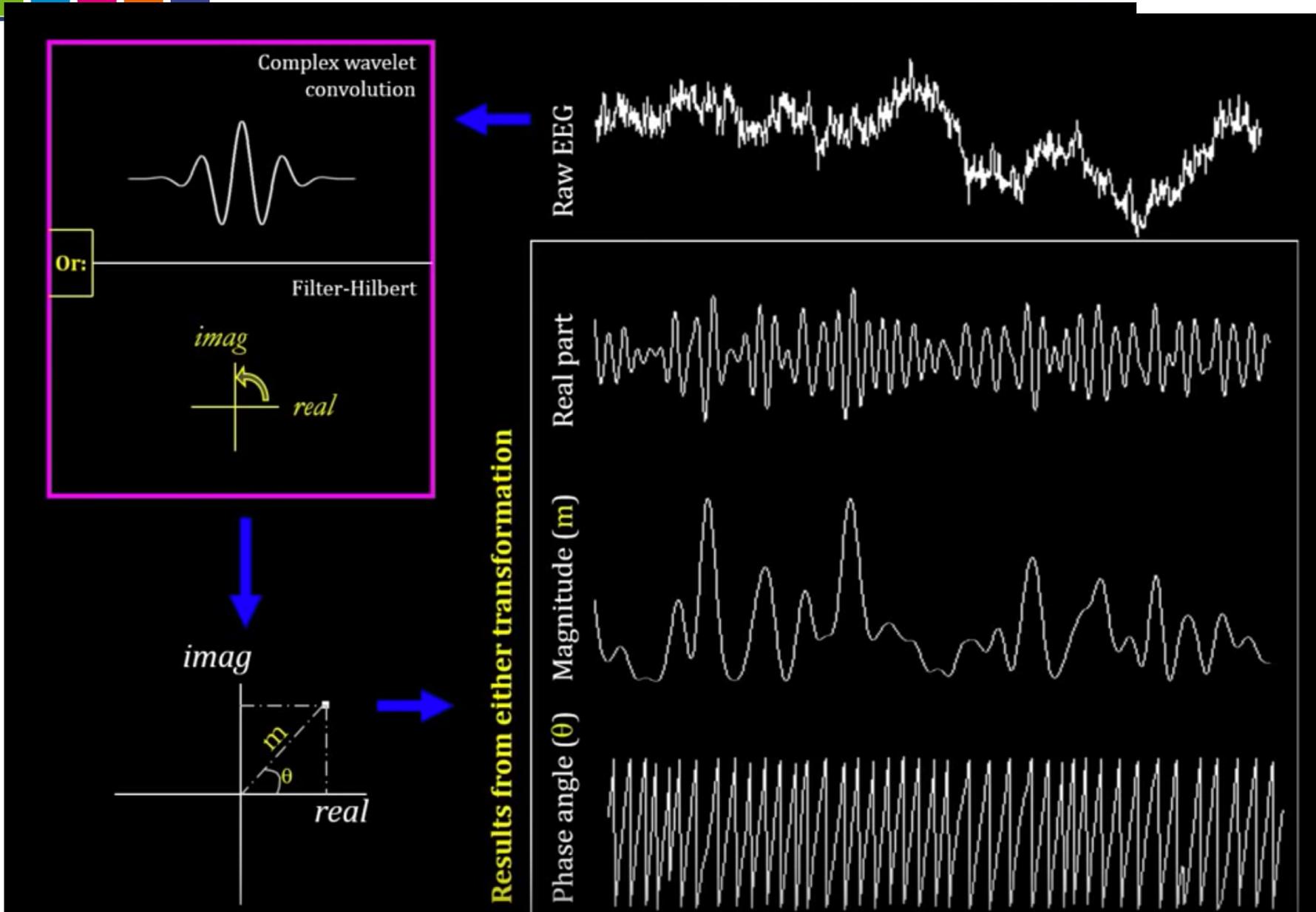




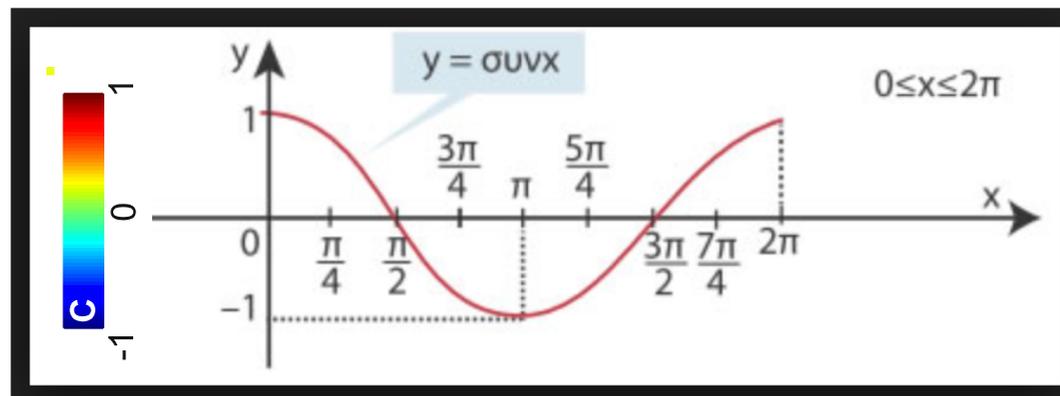
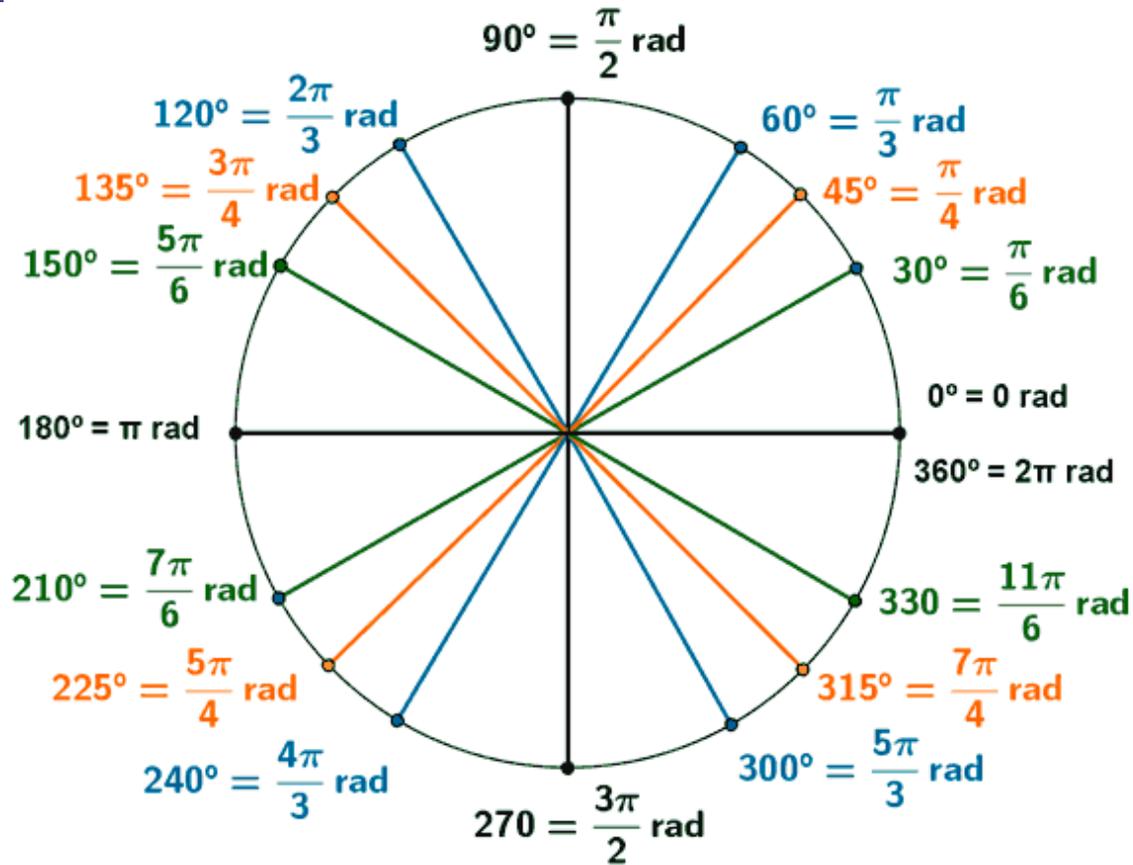
# Classifier generalizes to healthy



# The Hilbert transform

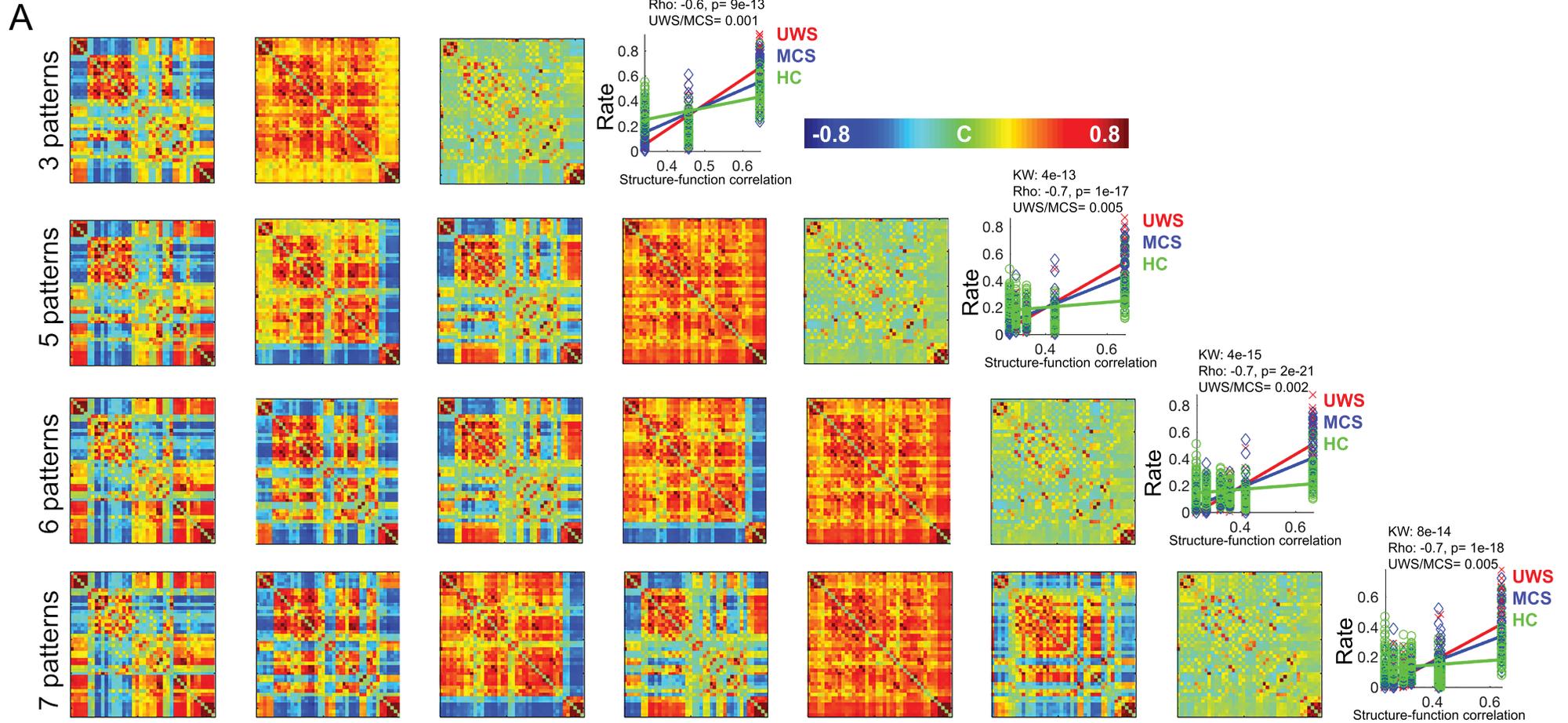


# Phase coherence



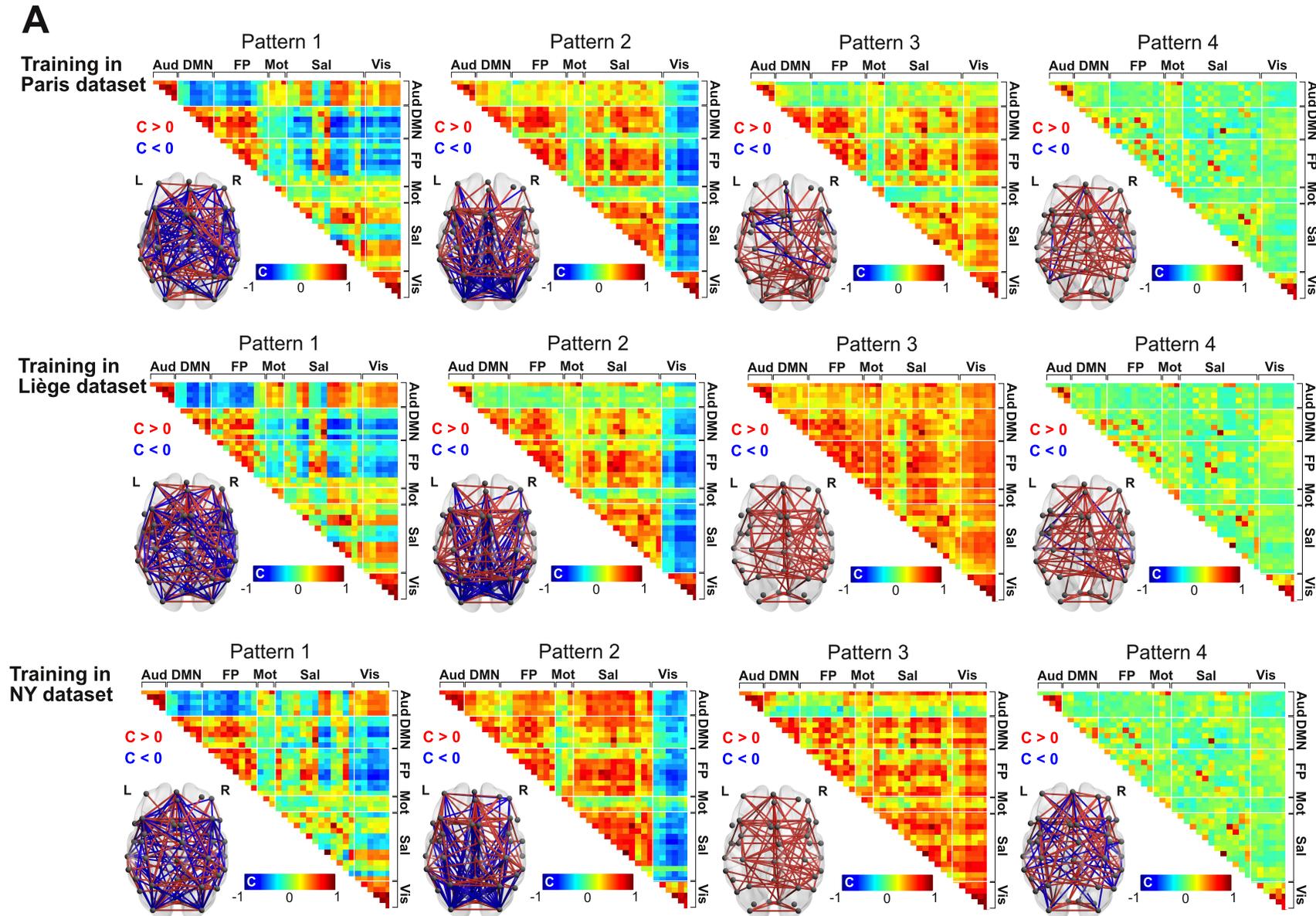


# Patterns (different k)



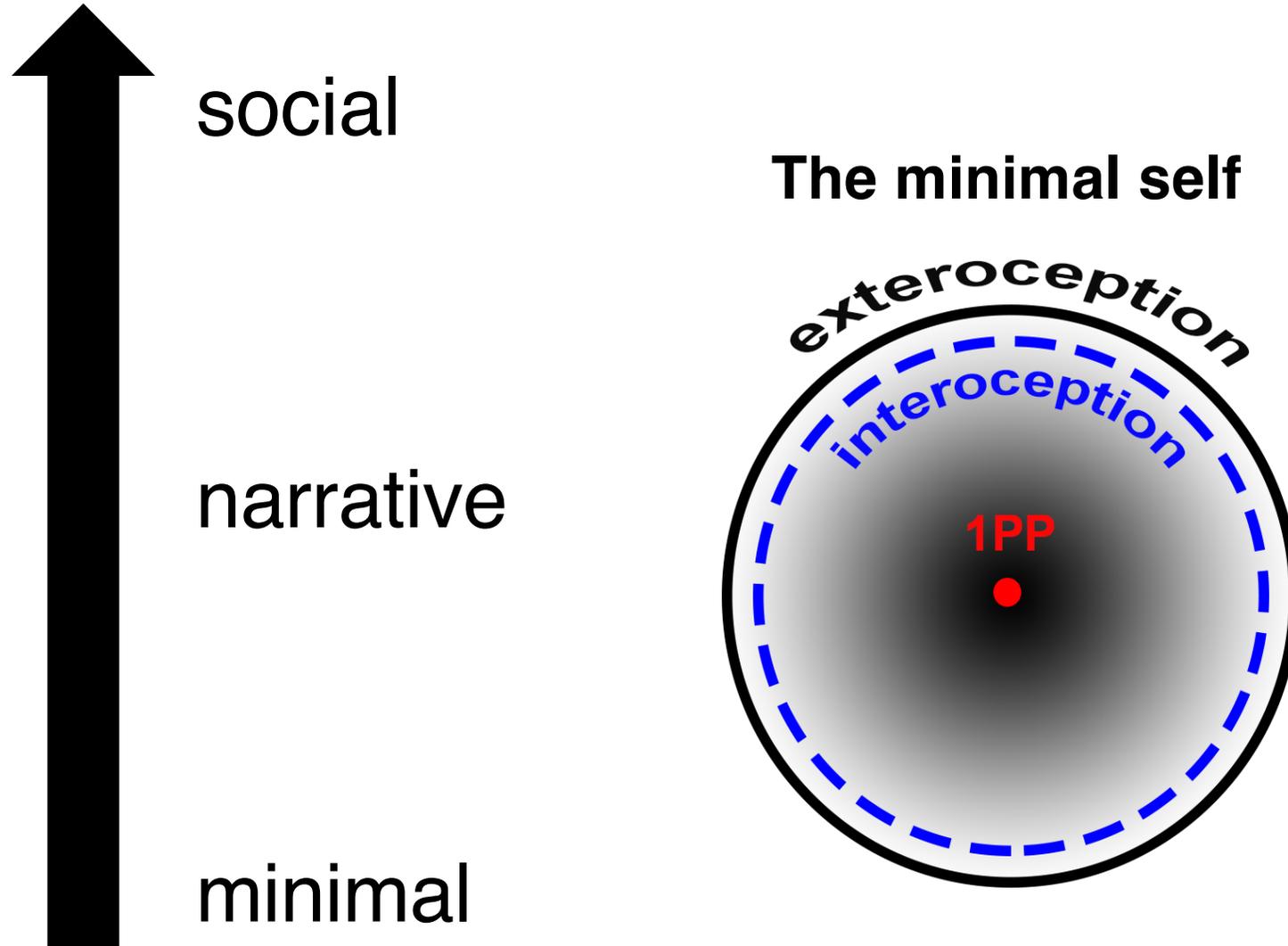


# Patterns (per site)





# Self = Consciousness?





# Anticorrelated brain systems

