

Conscious and unconscious states after brain damage

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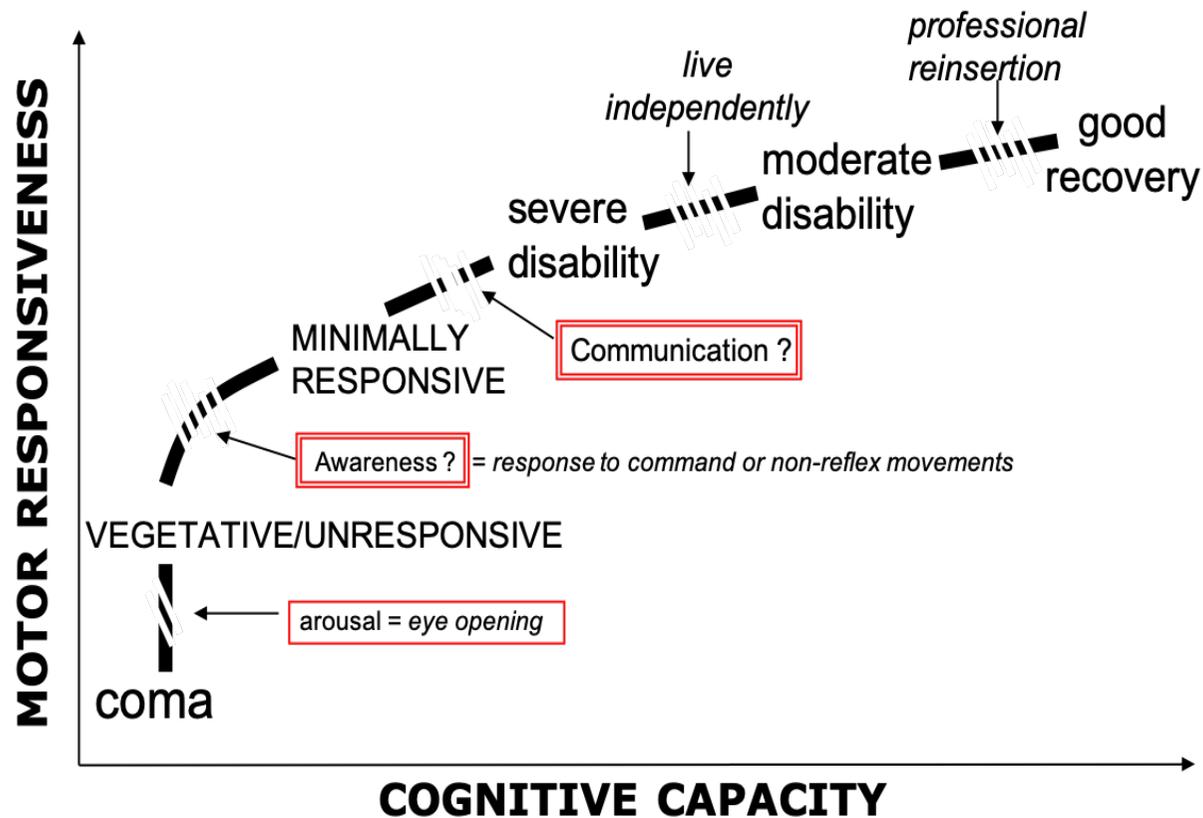
Symposium

An update on behavioural and neural signatures of attention and consciousness states after brain damage

8th Scientific Meeting of the
Federation of the European Societies of
Neuropsychology

Thessaloniki
29 September 2023

Mental life inferred from behavior



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

We cannot always trust behavior

JFK COMA RECOVERY SCALE - REVISED ©2004																	
Record Form																	
This form should only be used in association with the "CRS-R ADMINISTRATION AND SCORING GUIDELINES" which provide instructions for standardized administration of the scale.																	
Patient:		Diagnosis:					Etiology:										
Date of Onset:		Date of Admission:															
	Date																
	Week	ADM	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
AUDITORY FUNCTION SCALE																	
4 - Consistent Movement to Command *																	
3 - Reproducible Movement to Command *																	
2 - Localization to Sound																	
1 - Auditory Startle																	
0 - None																	
VISUAL FUNCTION SCALE																	
5 - Object Recognition *																	
4 - Object Localization: Reaching *																	
3 - Visual Pursuit *																	
2 - Fixation *																	
1 - Visual Startle																	
0 - None																	
MOTOR FUNCTION SCALE																	
6 - Functional Object Use †																	
5 - Automatic Motor Response *																	
4 - Object Manipulation *																	
3 - Localization to Noxious Stimulation *																	
2 - Flexion Withdrawal																	
1 - Abnormal Posturing																	
0 - None/Flaccid																	
OROMOTOR/VERBAL FUNCTION SCALE																	
3 - Intelligible Verbalization *																	
2 - Vocalization/Oral Movement																	
1 - Oral Reflexive Movement																	
0 - None																	
COMMUNICATION SCALE																	
2 - Functional: Accurate †																	
1 - Non-Functional: Intentional *																	
0 - None																	
AROUSAL SCALE																	
3 - Attention																	
2 - Eye Opening w/o Stimulation																	
1 - Eye Opening with Stimulation																	
0 - Unarousable																	
TOTAL SCORE																	

Denotes emergence from MCS[†]
Denotes MCS*

1

Giacino et al, *Neurology* 2002

Standardized assessment

n=103 post-comatose patients

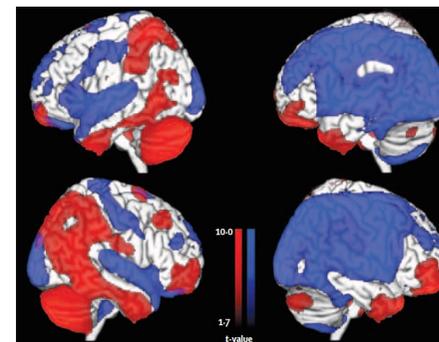
45 Clinical diagnosis of VS
18 Coma Recovery Scale MCS



40% misdiagnosis

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

Standardized assessment & Neuroimaging



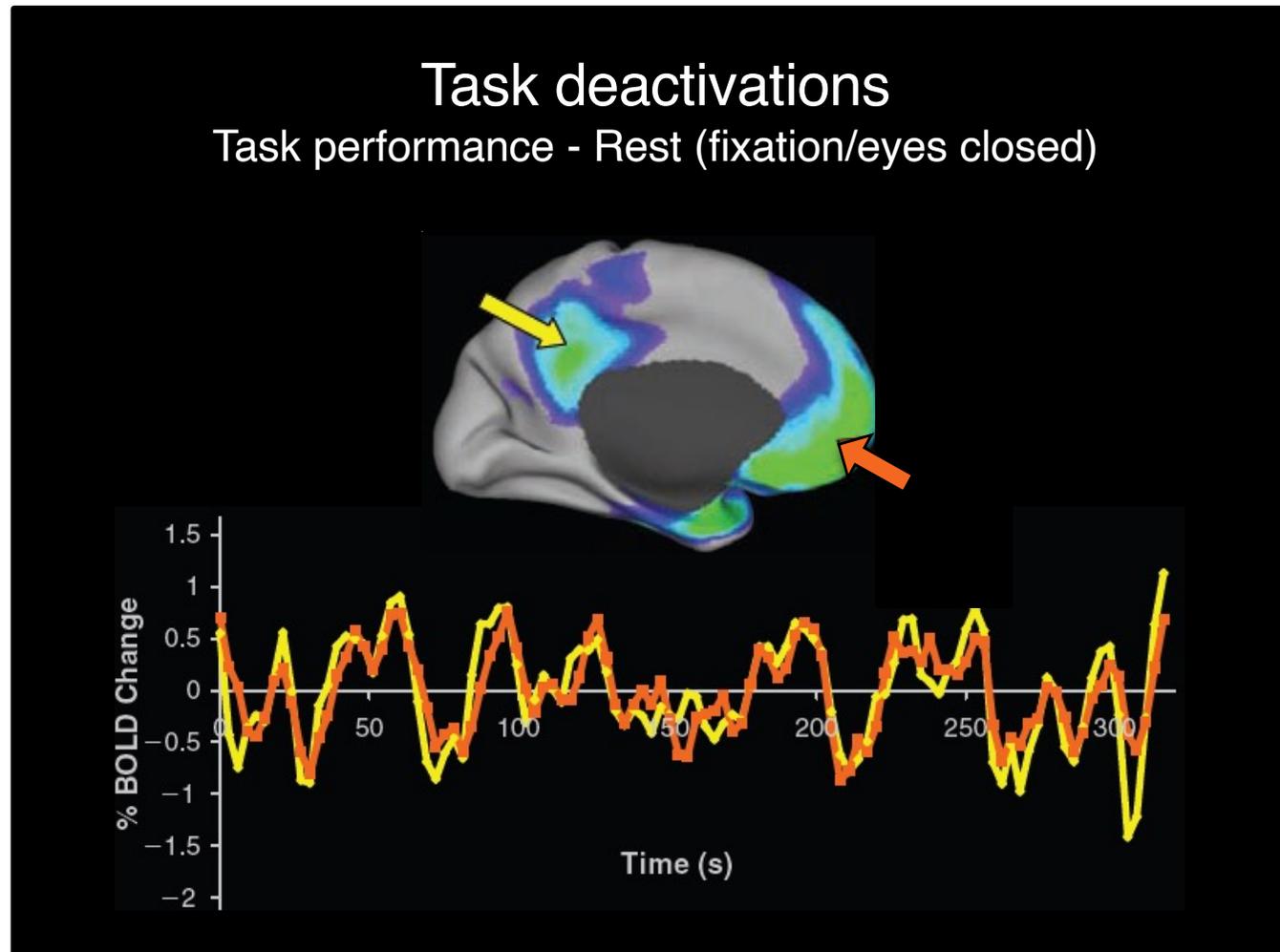
	Coma Recovery Scale-Revised results		
	UWS	MCS	Total
Clinical consensus diagnosis			
¹⁸F-FDG PET			
VS/UWS	24 (21%)	5 (4%)	29 (26%)
MCS	12 (11%)	71 (63%)	83 (74%)
Total	36 (32%)	76 (68%)	112 (100%)

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

Table 2: Diagnostic results by modality

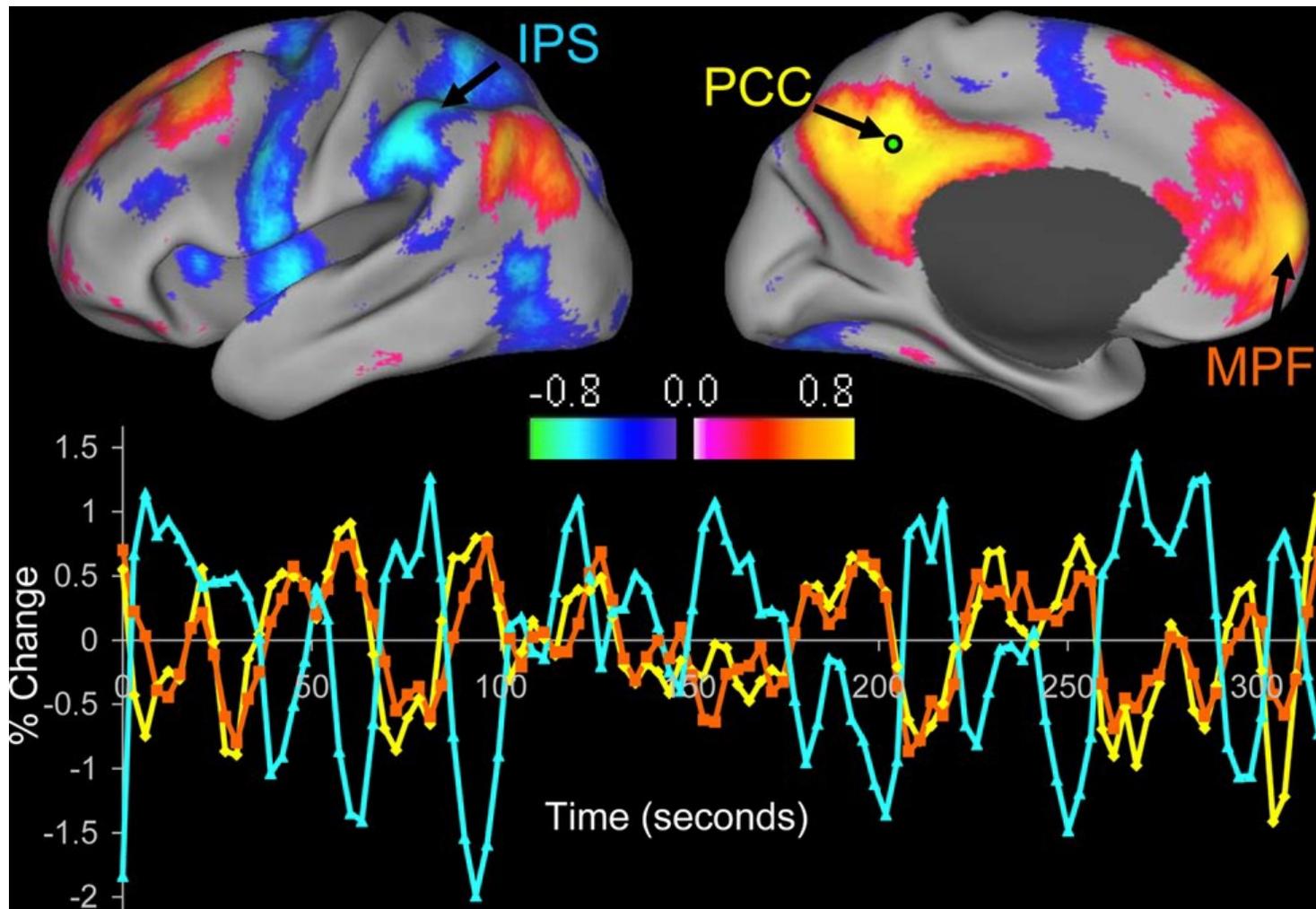
Stender & Gosseries et al, *Lancet* 2014

Default mode of brain function

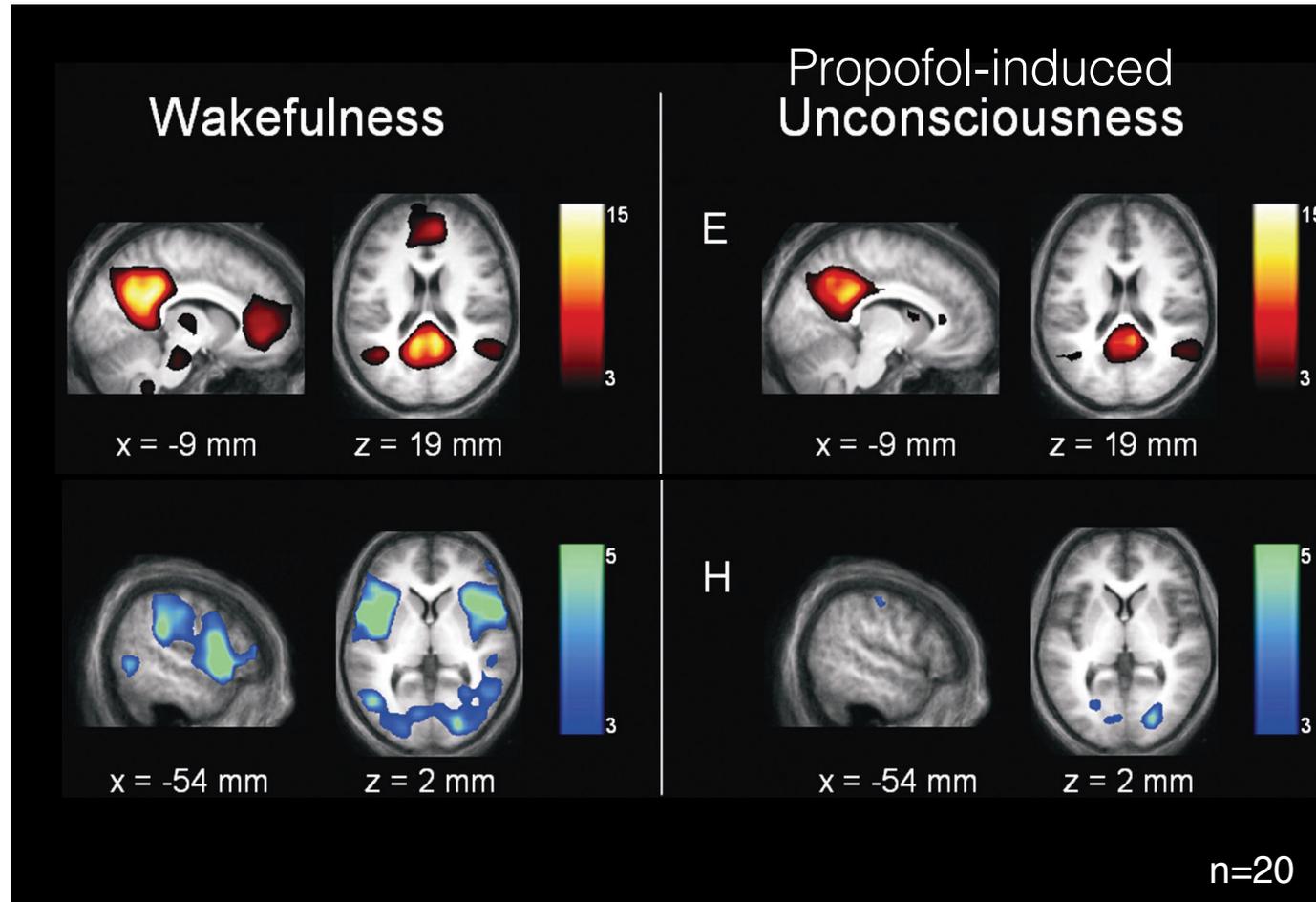


Demertzi & Whitfield-Gabrieli, in: *Neurology of Consciousness* 2nd ed. 2015
Demertzi, Soddu, Laureys, *Curr Opin Neurobiology* 2013
Demertzi et al, *Front Hum Neurosci* 2013
Raichle et al, *PNAS* 2001

Functional correlations & anticorrelations



Modified arousal reduces anticorrelations



Boveroux et al, *Anesthesiology* 2010

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

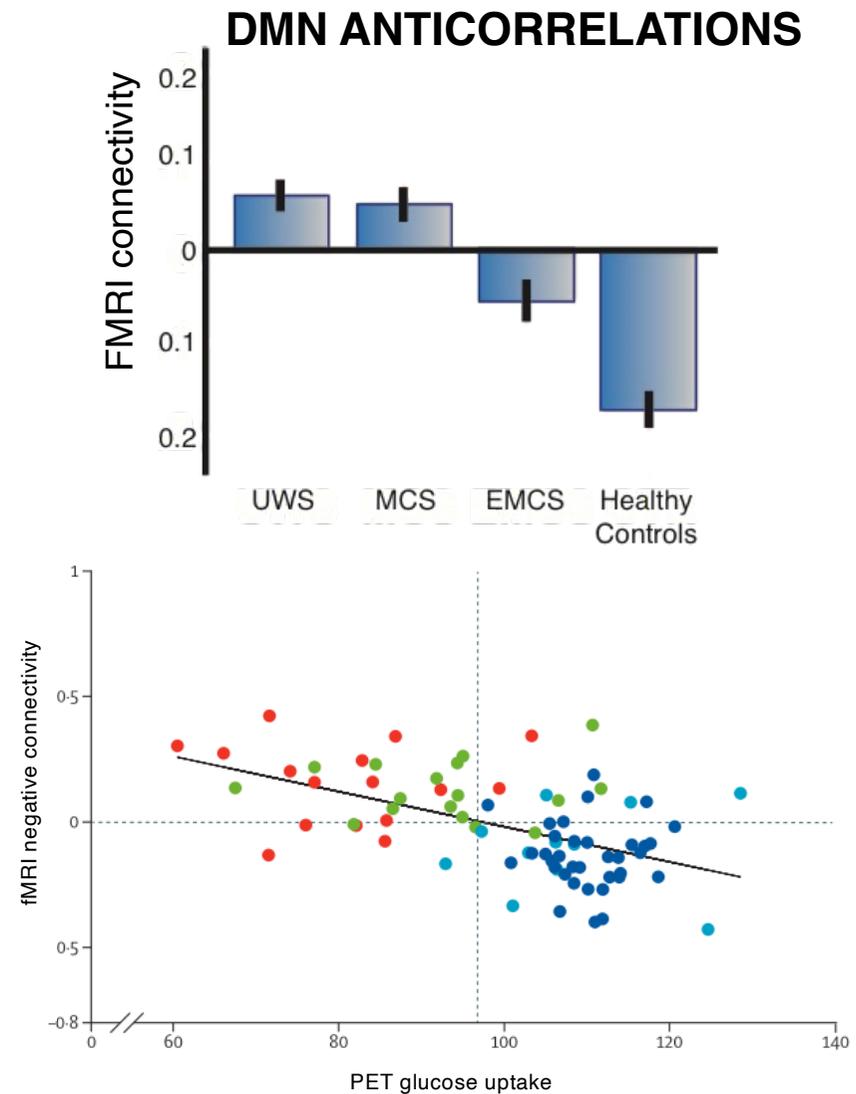
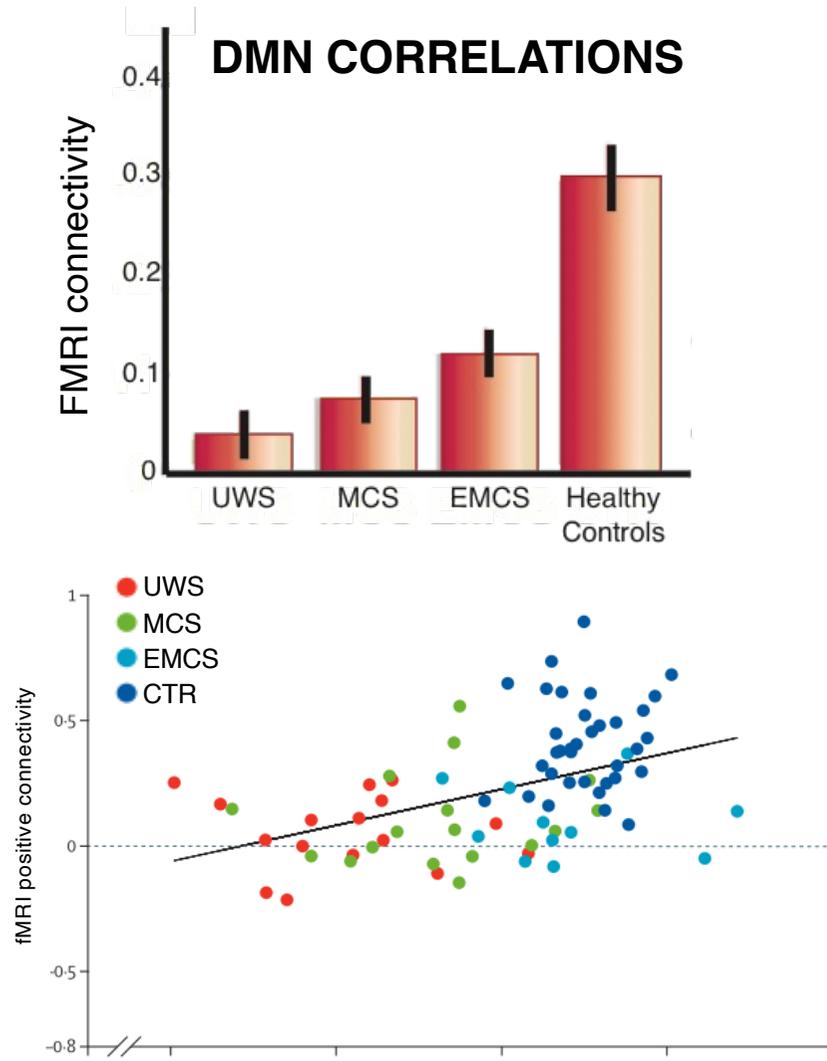
Demertzi, Soddu, Laureys, *Curr Opin Neurobiology* 2013

Demertzi & Whitfield-Gabrieli, in: *Neurology of Consciousness* 2nd ed. 2015

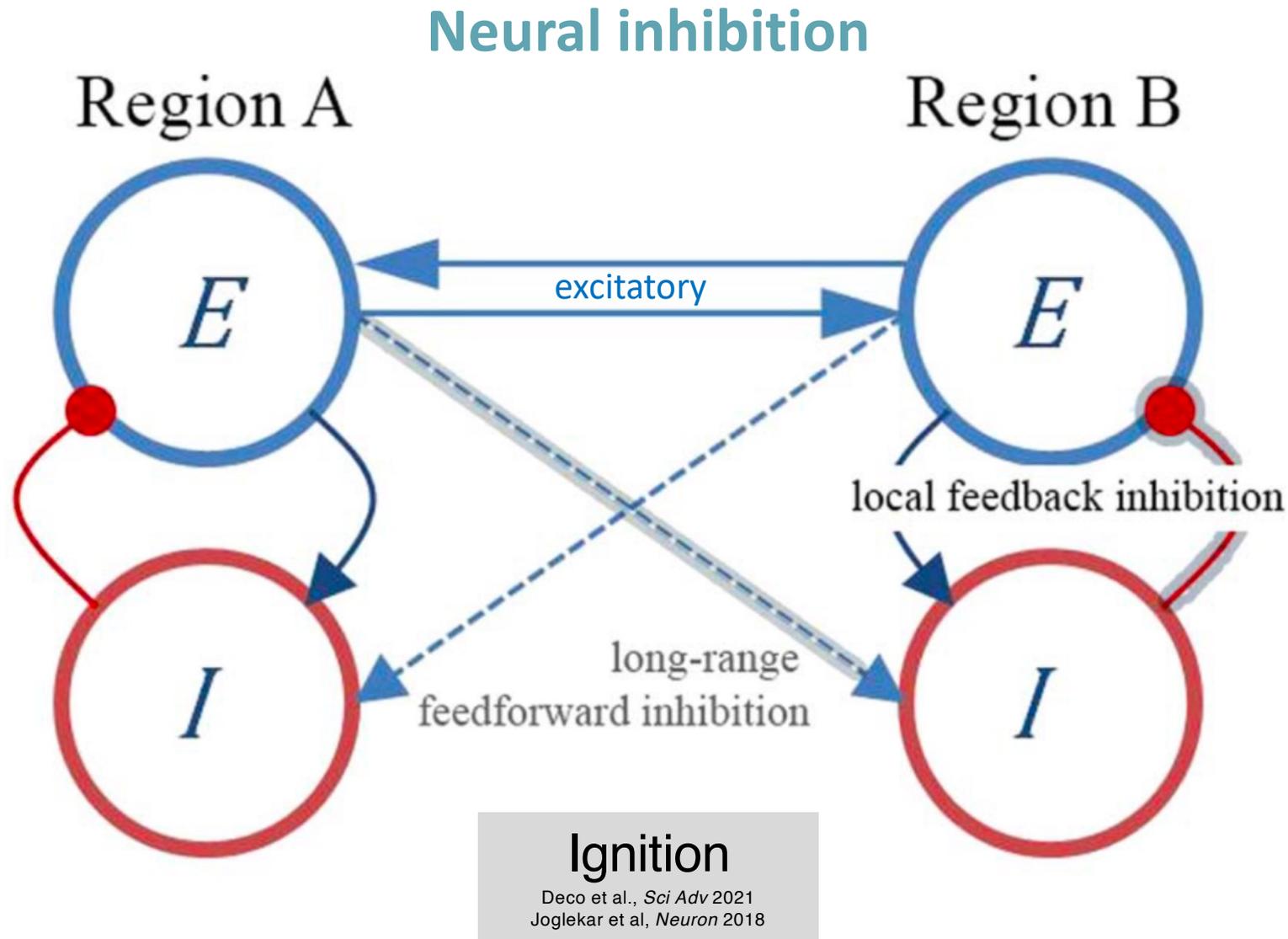
Demertzi et al, *Front Hum Neurosci* 2013

Demertzi, Kucyi, Ponces-Alvarez, Keliris, Whitfield-Gabrieli, Deco. *Netw Neurosci* in press

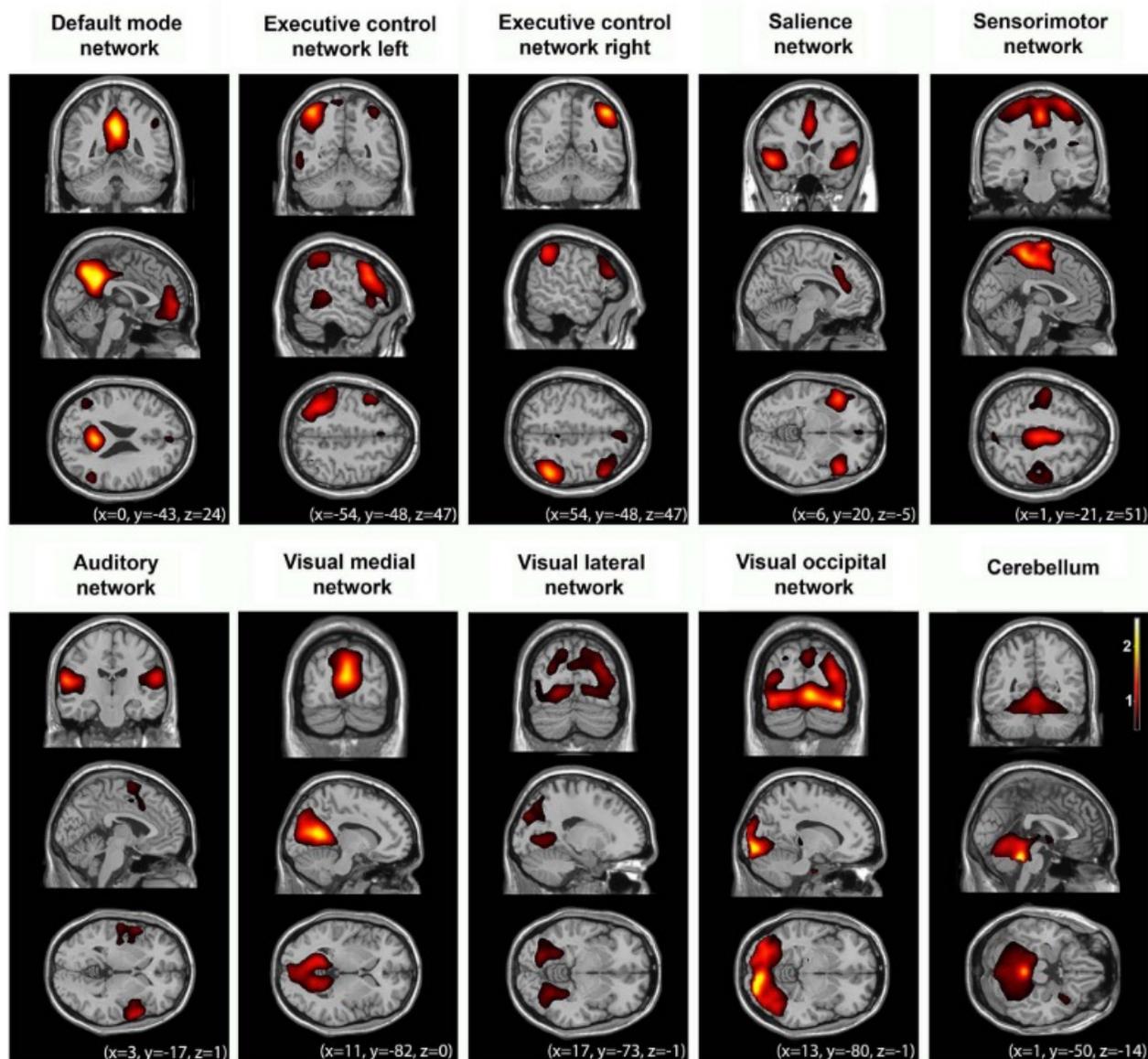
No anticorrelations in DOC



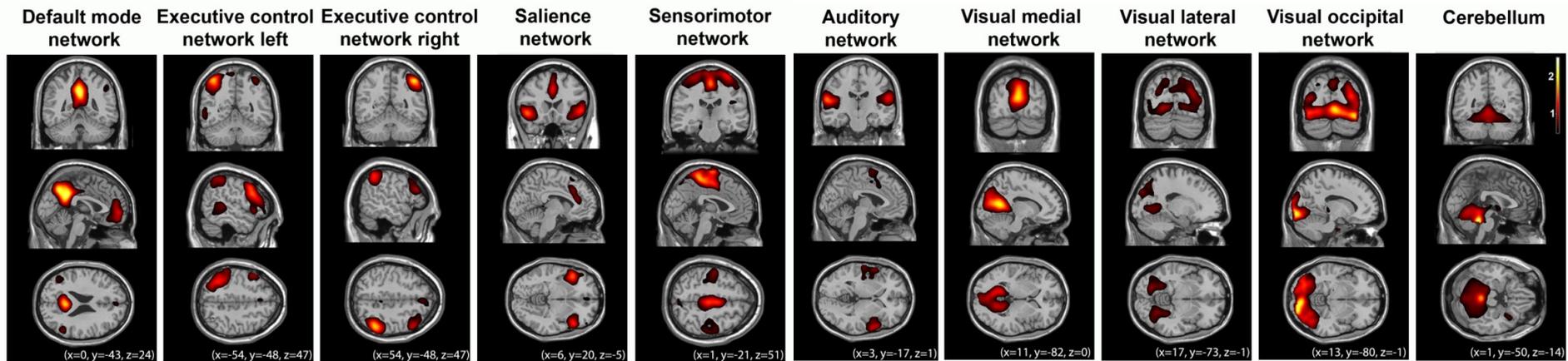
Anticorrelations \approx Consciousness



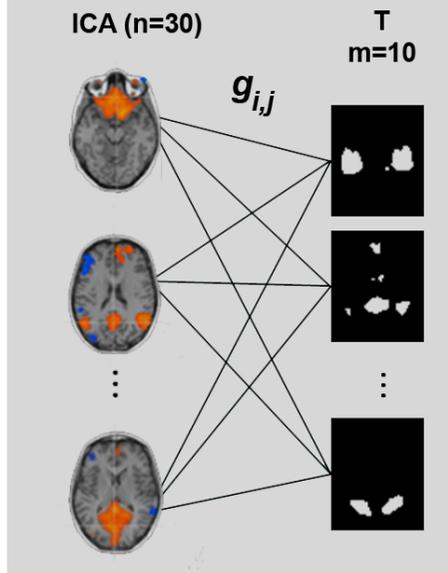
More networks at rest



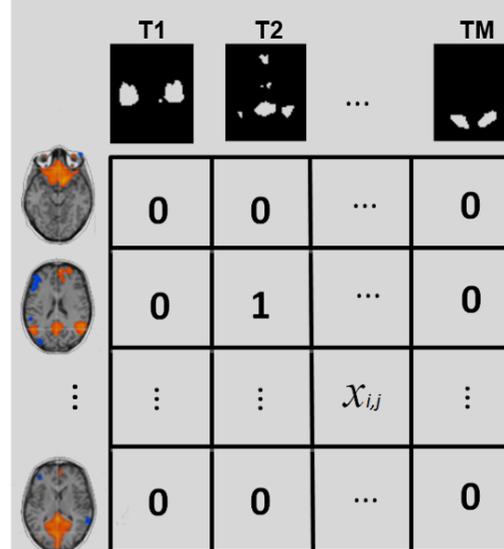
Data-driven approach



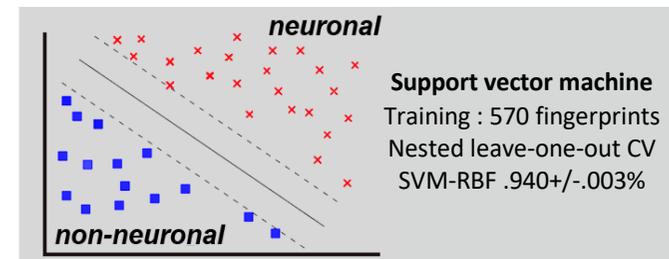
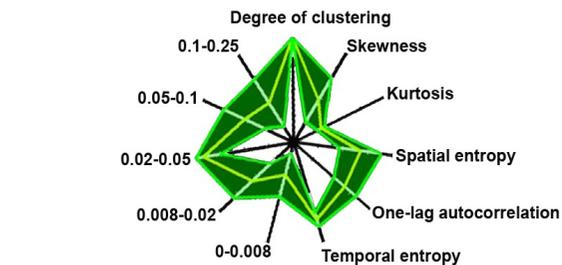
1. Goodness-of-fit calculation



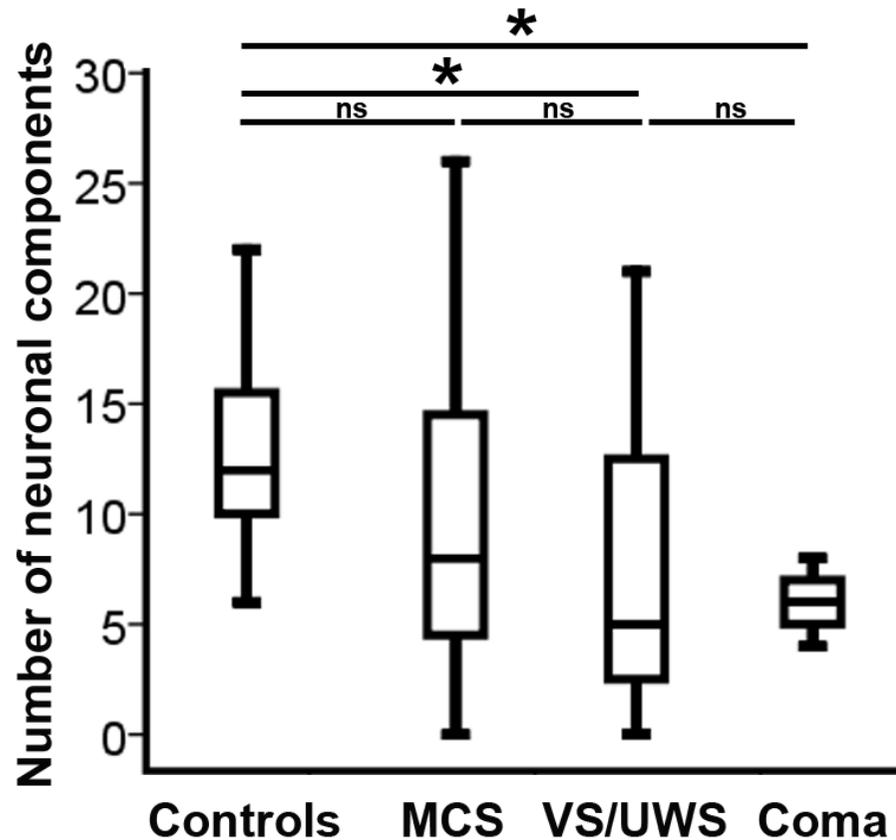
2. Multiple template assignment



3. "Neurality" test



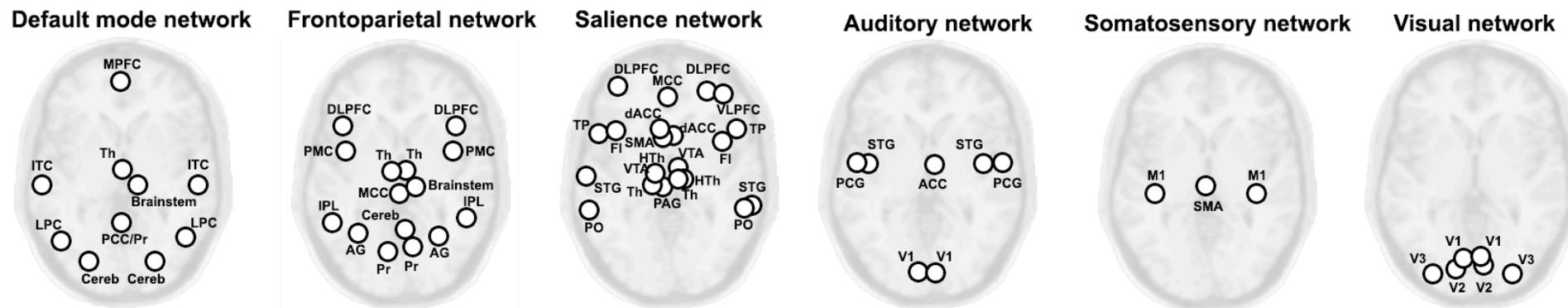
“Neuronality” separates single-patients



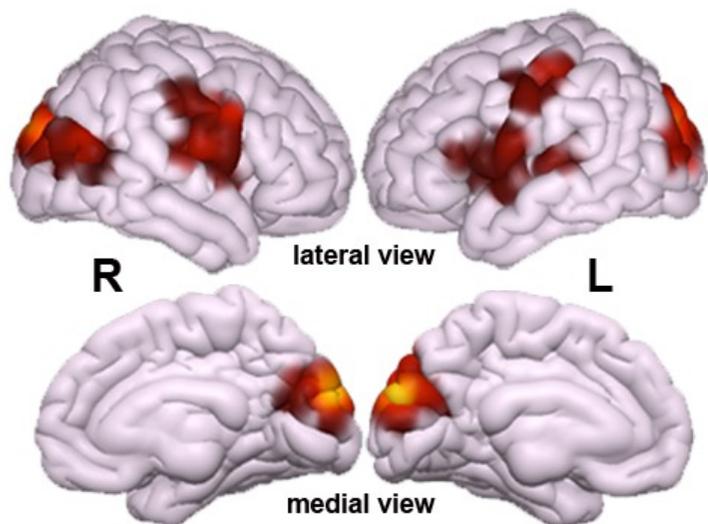
Single-subject classification (SVM)

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

Hypothesis-driven approach



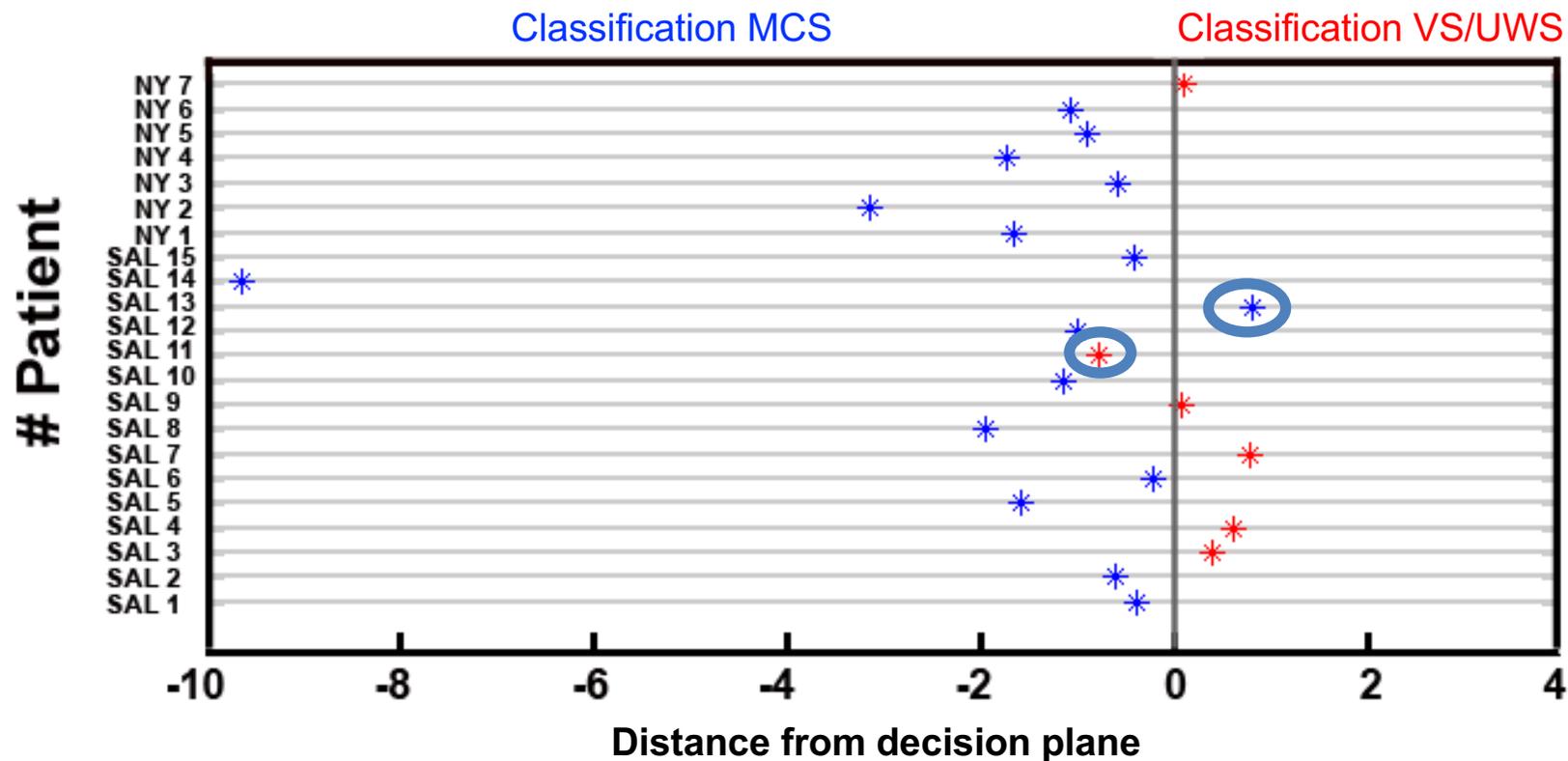
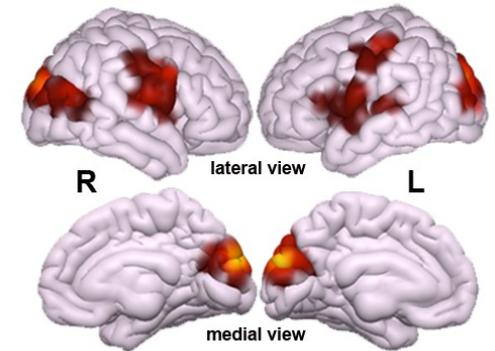
- 26 MCS, 19 VS/UWS
- 14 trauma, 28 non-trauma, 3 mixed
- 34 patients assessed >1m post-insult



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

Lower cross-modal interaction in UWS

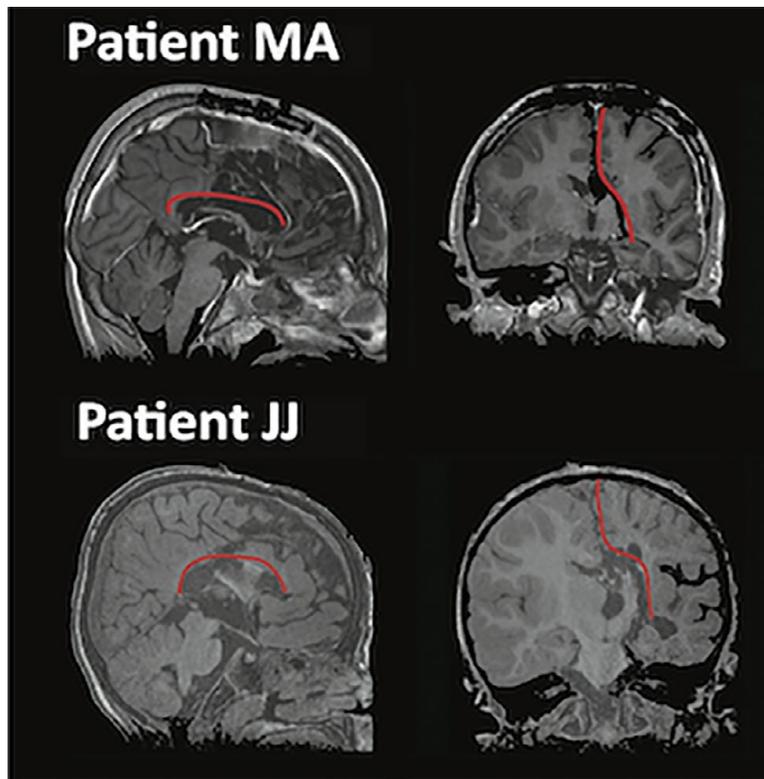
- Training set: 45 DOC (26 MCS, 19 VS/UWS)
 - 14 trauma, 28 non-trauma, 3 mixed
 - 34 patients assessed >1m post-insult
- Test set:
 - **16 MCS**, **6 VS/UWS** (15 non-trauma; all chronic)
 - 2 different centers



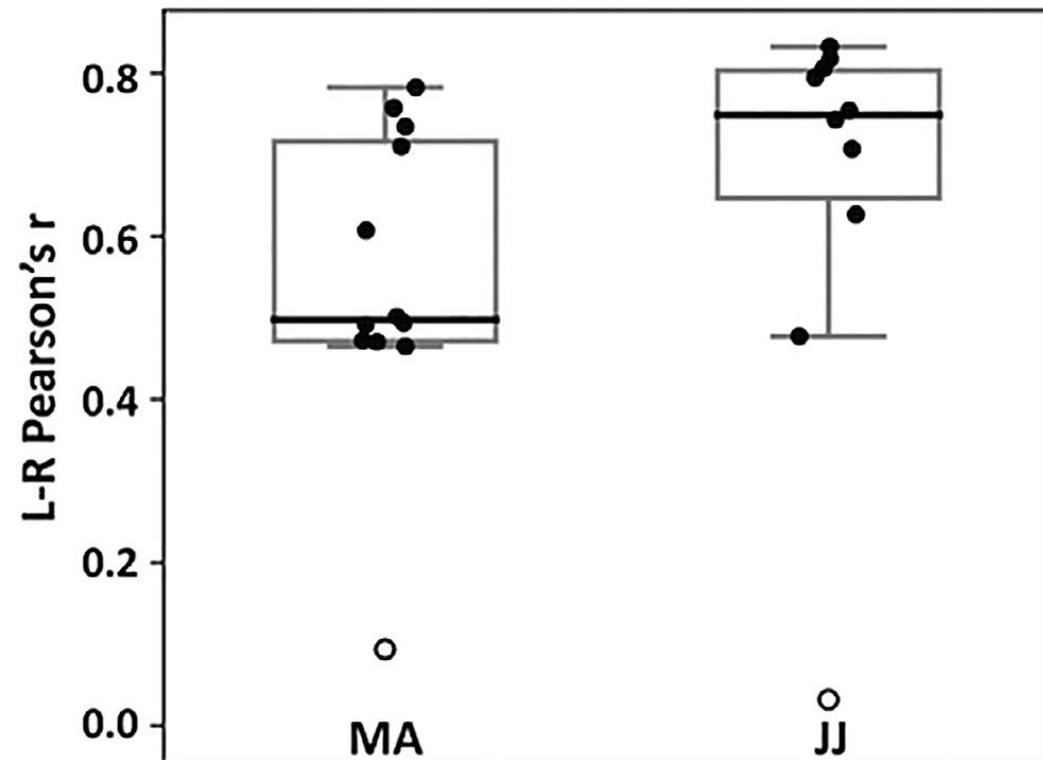
Complete hemispherectomy



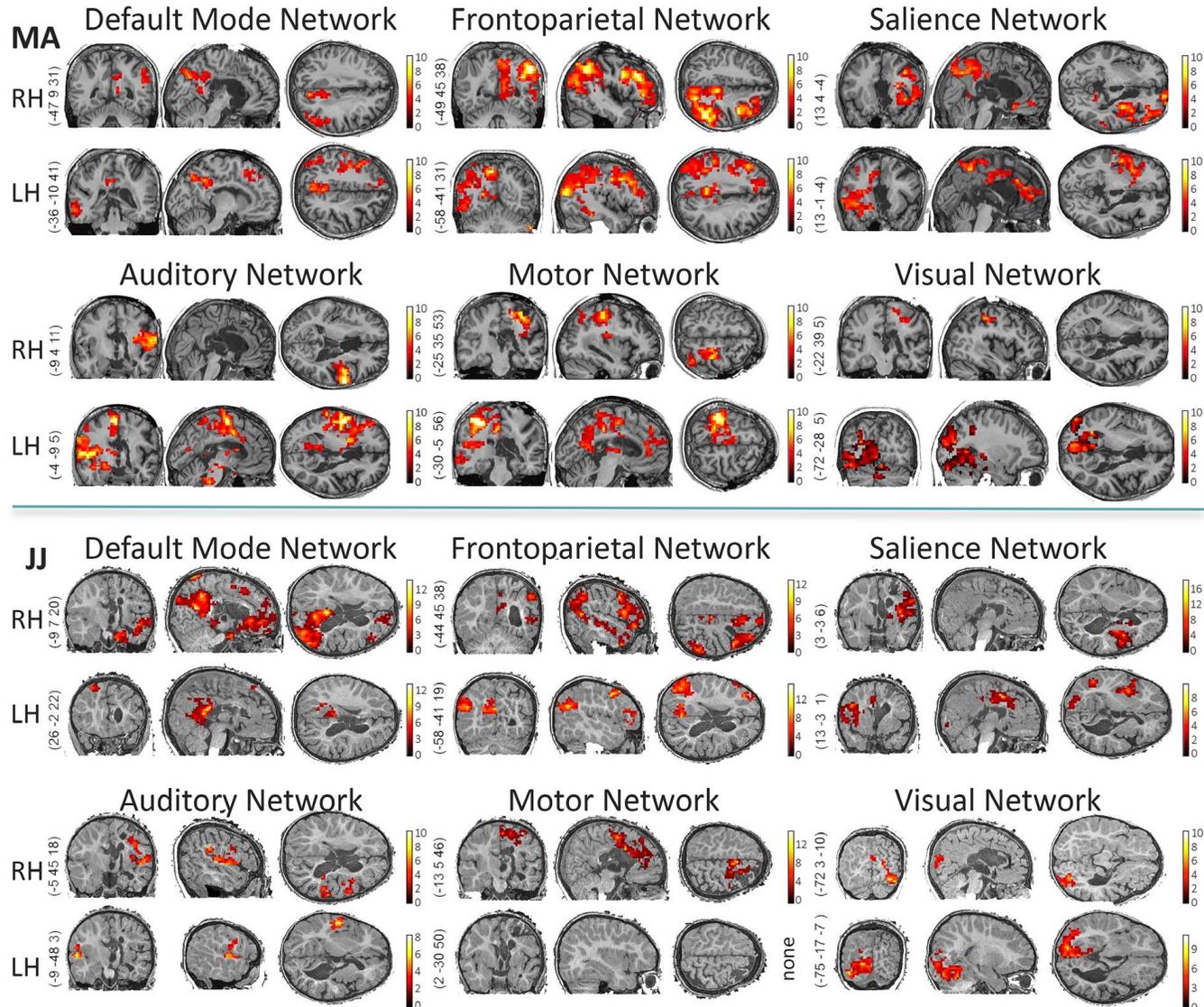
Operation



Inter-hemispheric connectivity

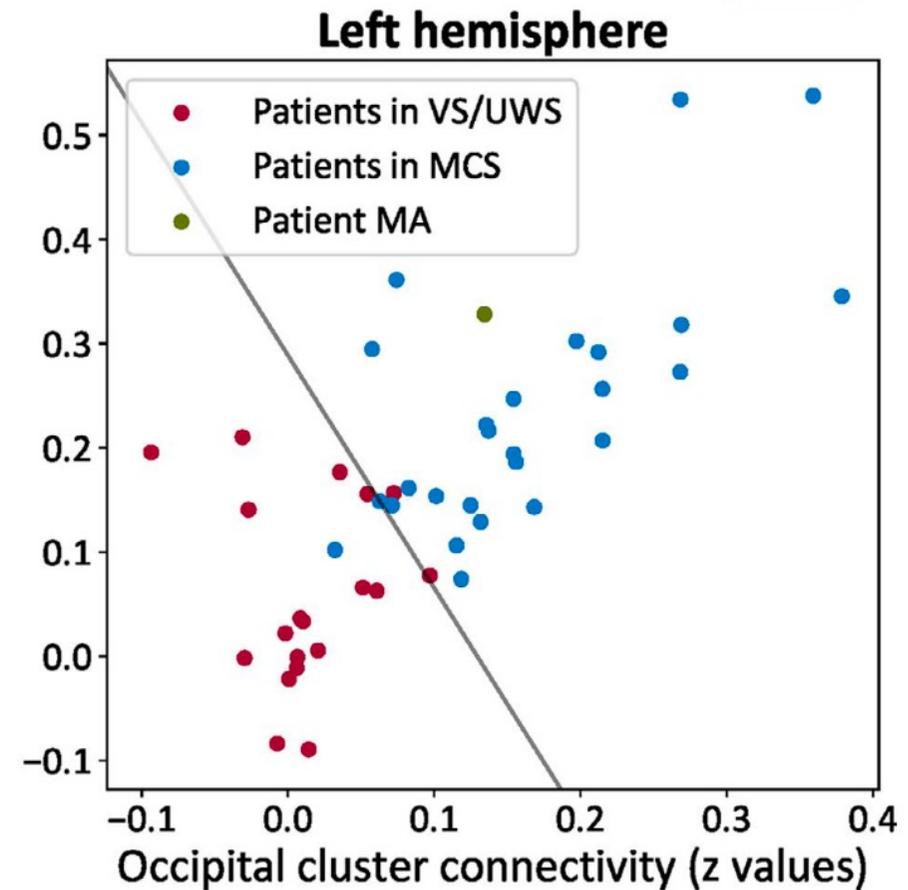
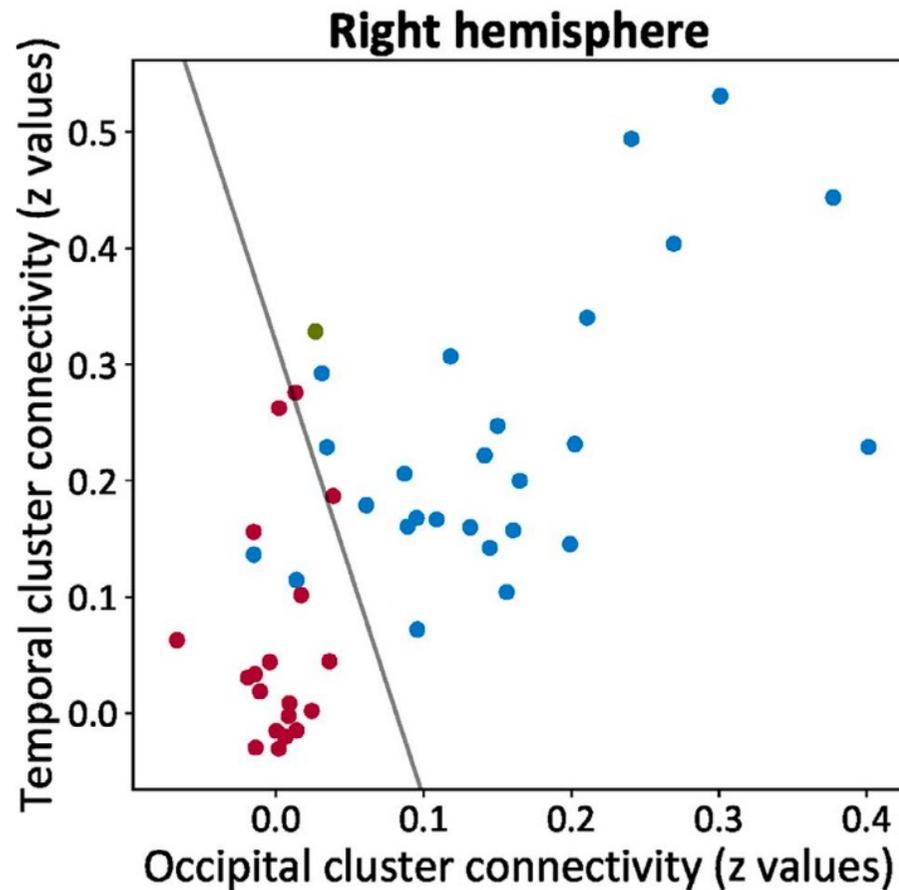


Networks get lateralized after complete hemispherotomy



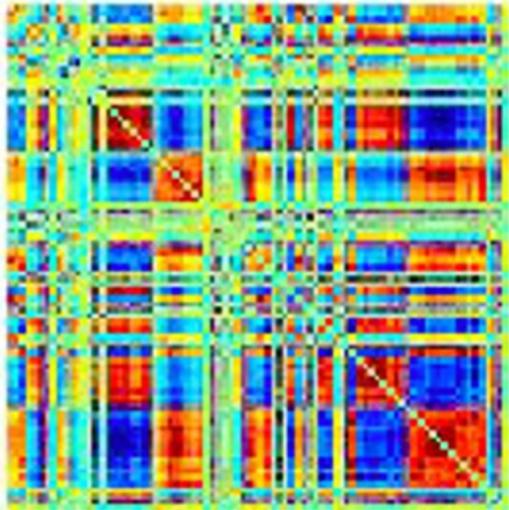


Lower Consciousness in the isolated tissue?

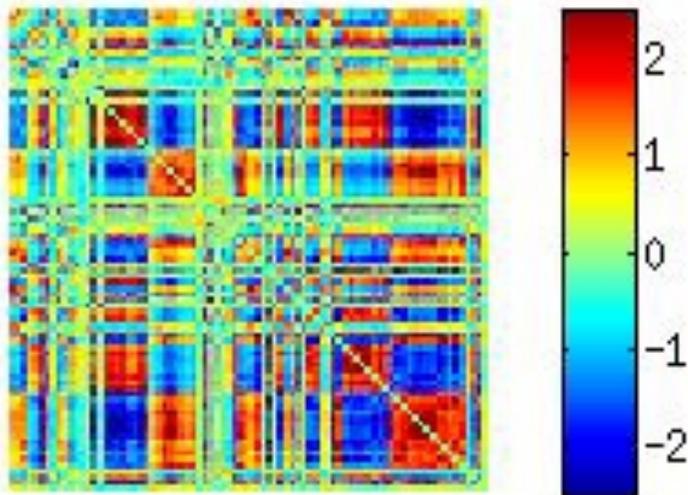


Brain dynamics and cognition

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

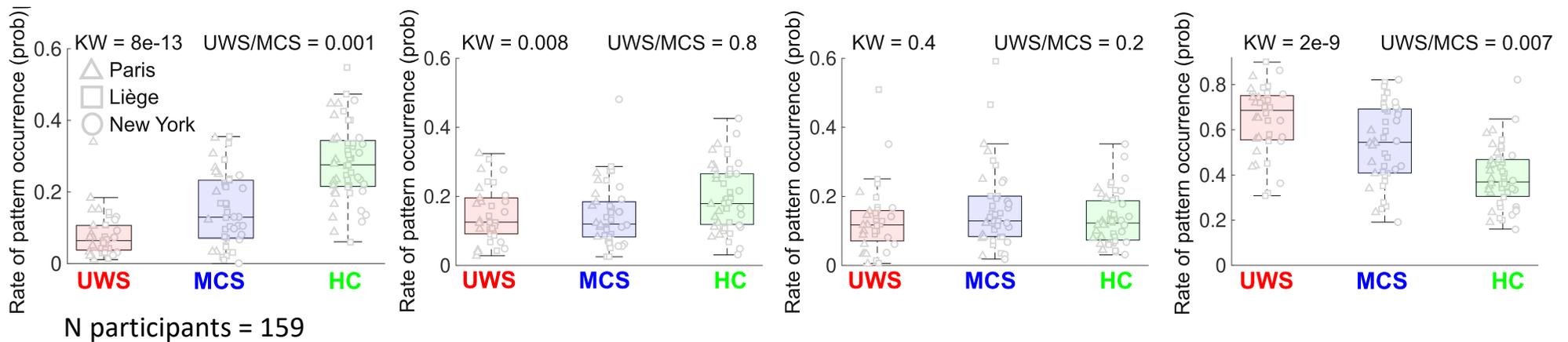
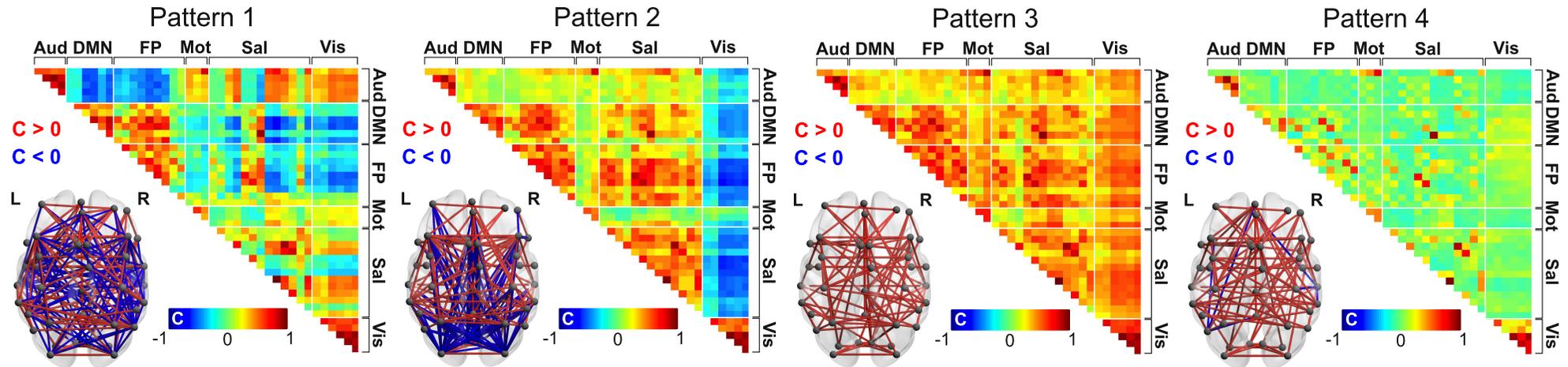
Rigid spatiotemporal organization, less metastable dynamics

- **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)

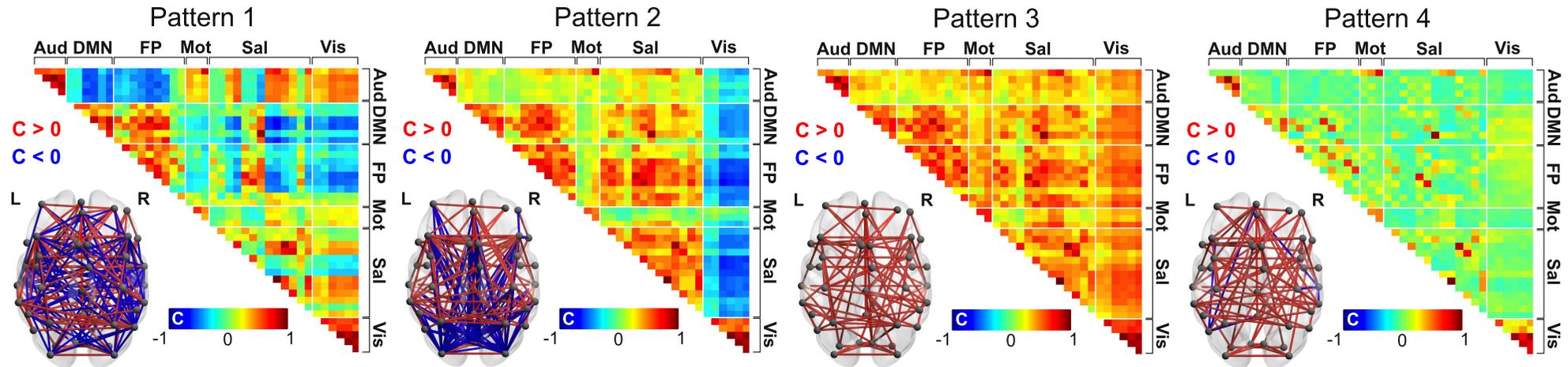


The brain cannot map the complexity of internal and external world
(Dehaene et al, *Trends Cog Sci*, 2006; Tononi et al, *Nat Rev Neurosci*. 2016)

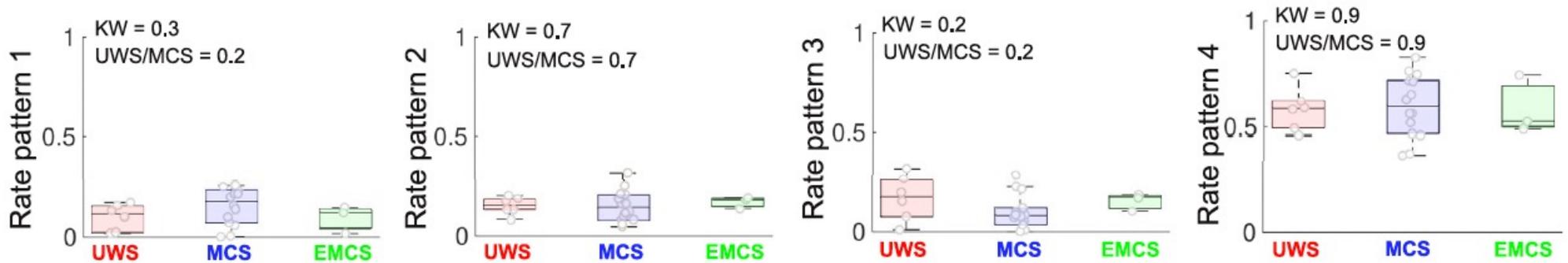
Complex patterns in communicating states



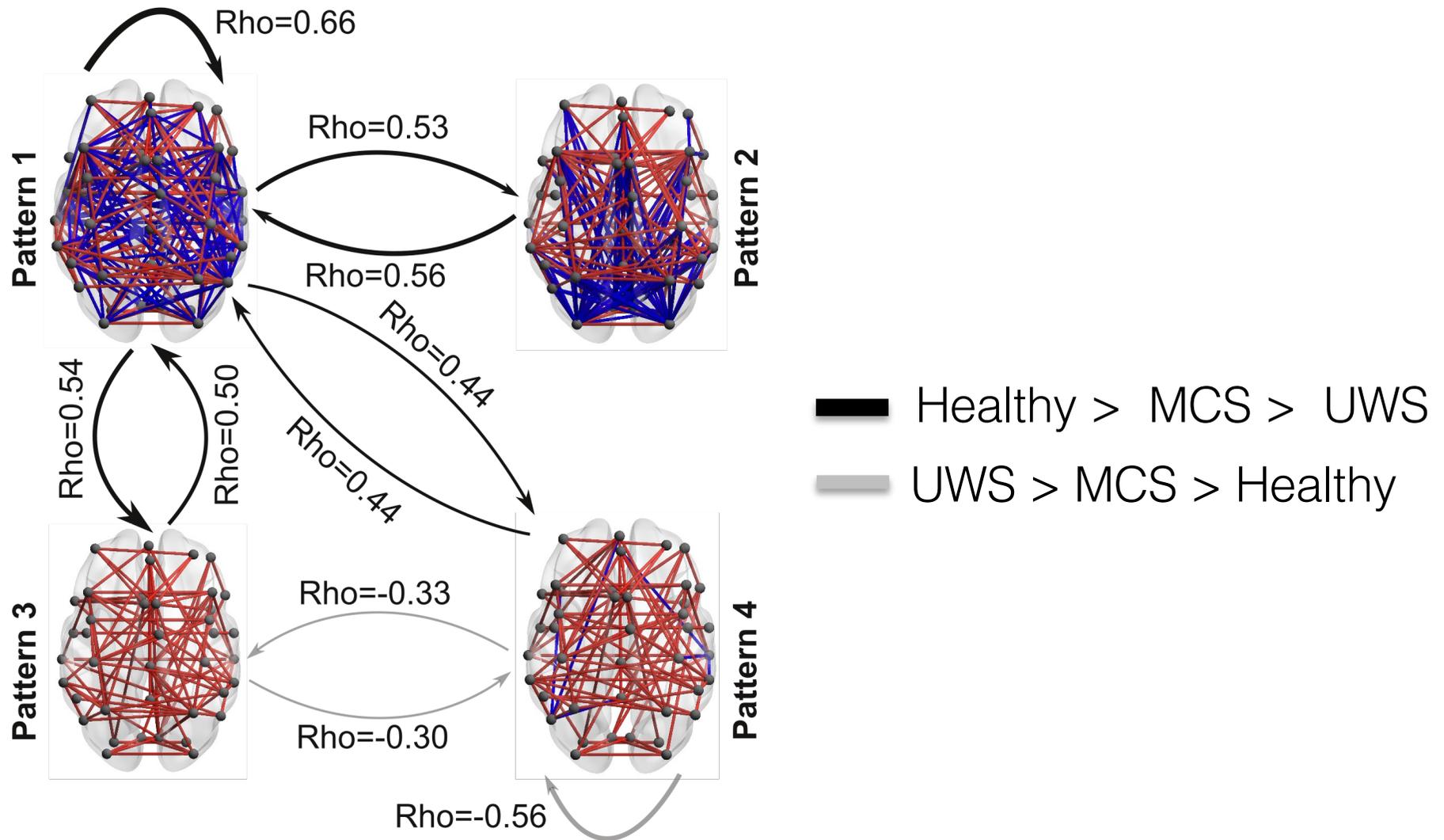
Simple patterns in unconsciousness



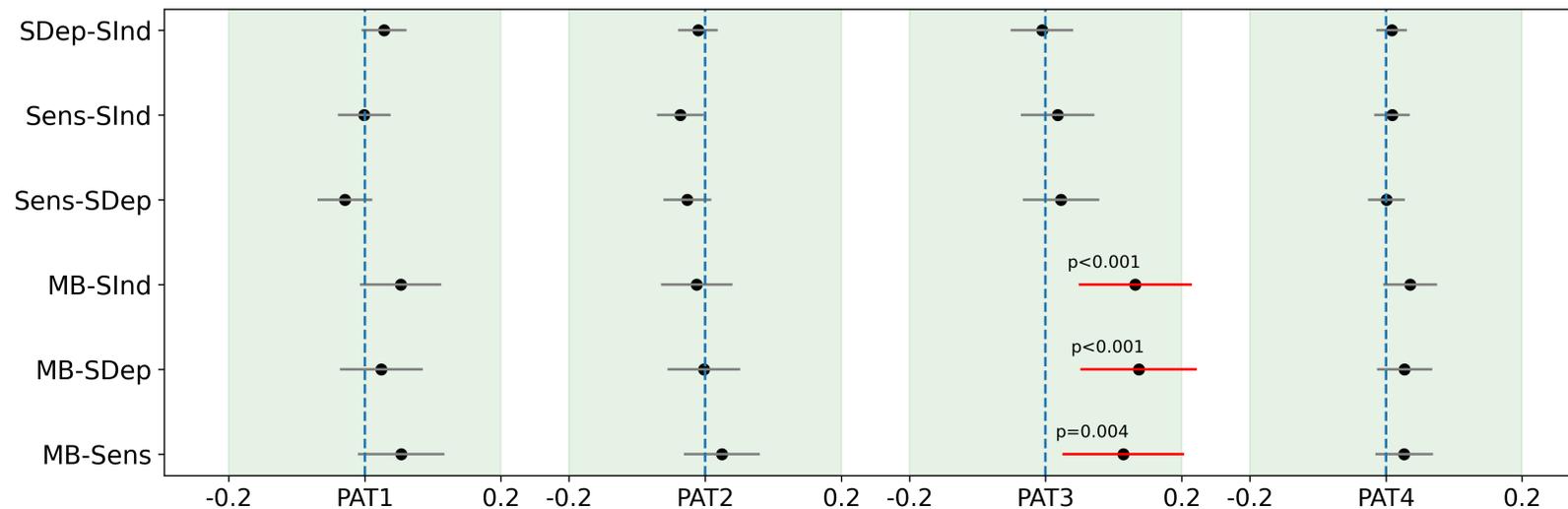
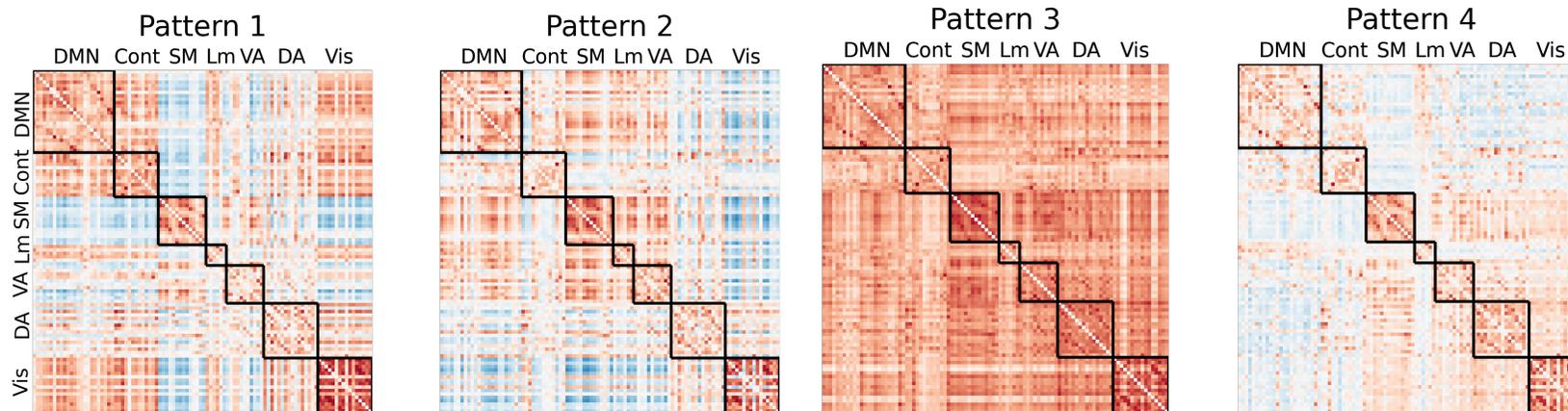
Propofol anesthesia



More chances to transition when conscious

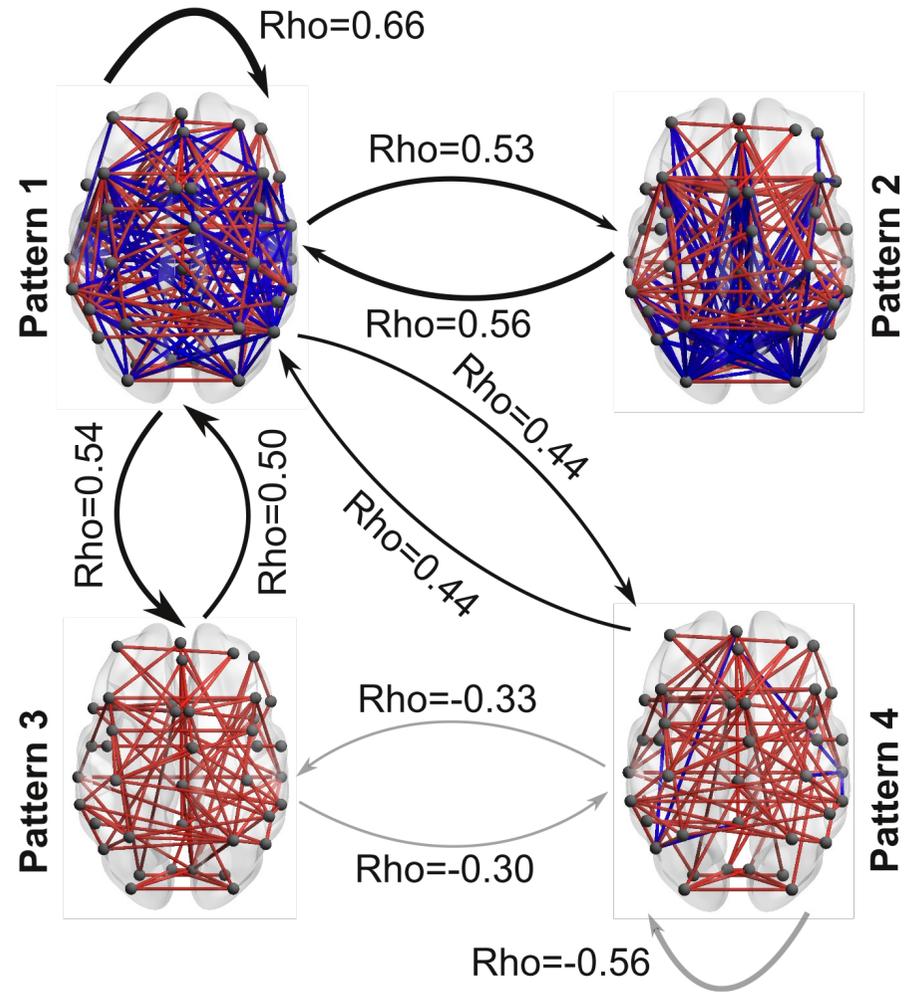
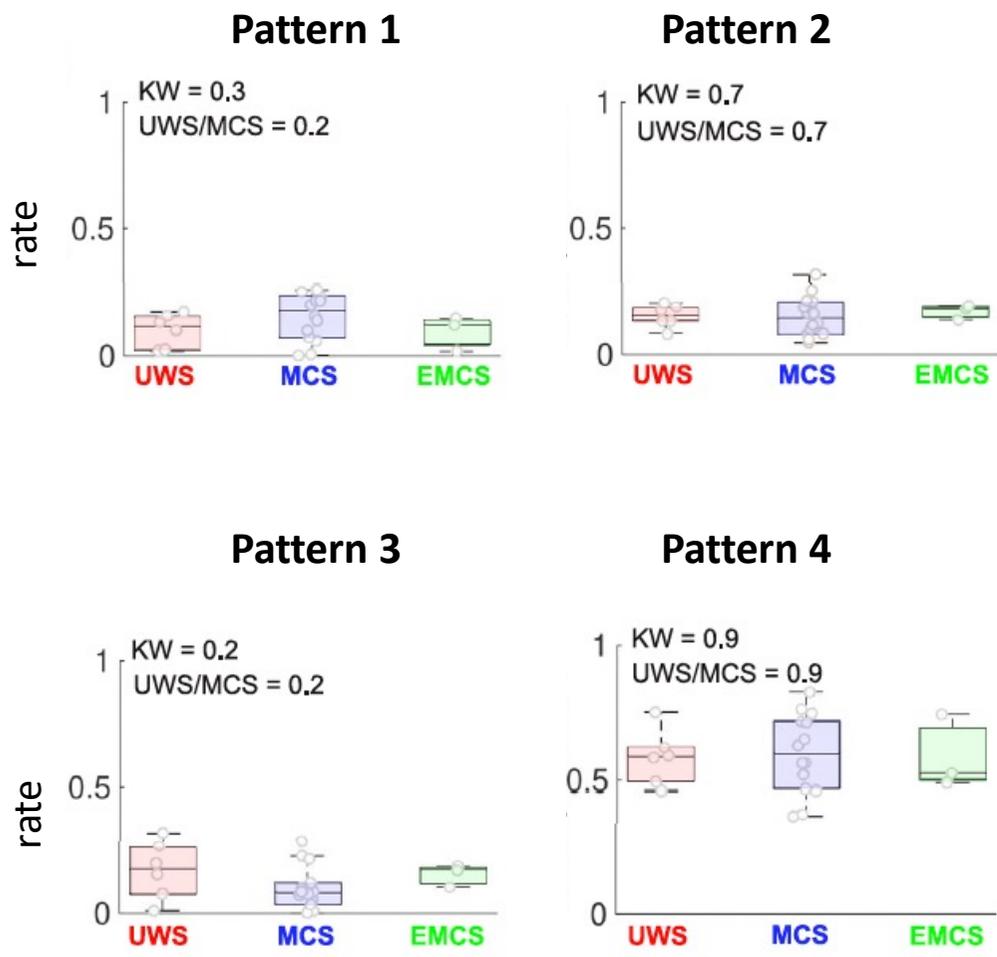


A hyper-connected pattern is linked to Mind Blanking reports



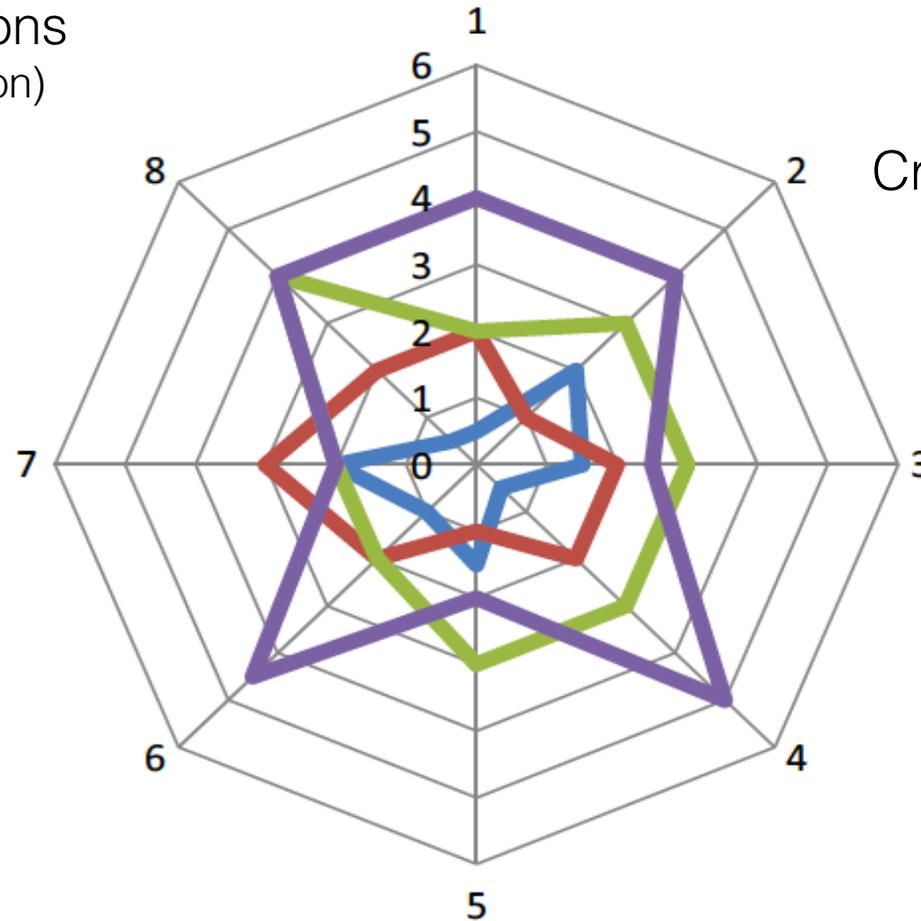
More chances to transition when conscious

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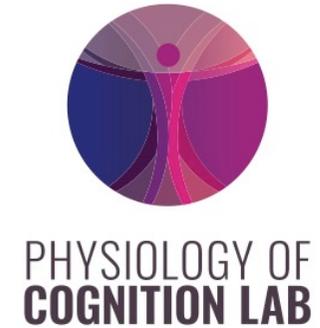
Consciousness is multidimensional

Anticorrelations
(neural inhibition)



Cross-modal interactions
(multi-sensory integration)

Inter-state dynamism
(metastability)



Consciousness is
a construct of collective consensus
and concerns us all

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