

Ain't no rest for the brain

Neuroimaging and neuroethics in dialogue for non-communicating brain-injured patients

NUEVOS DESAFÍOS EN NEUROCIENCIAS COGNITIVAS
New Challenges in the field of Cognitive Neuroscience

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James S. McDonnell Foundation

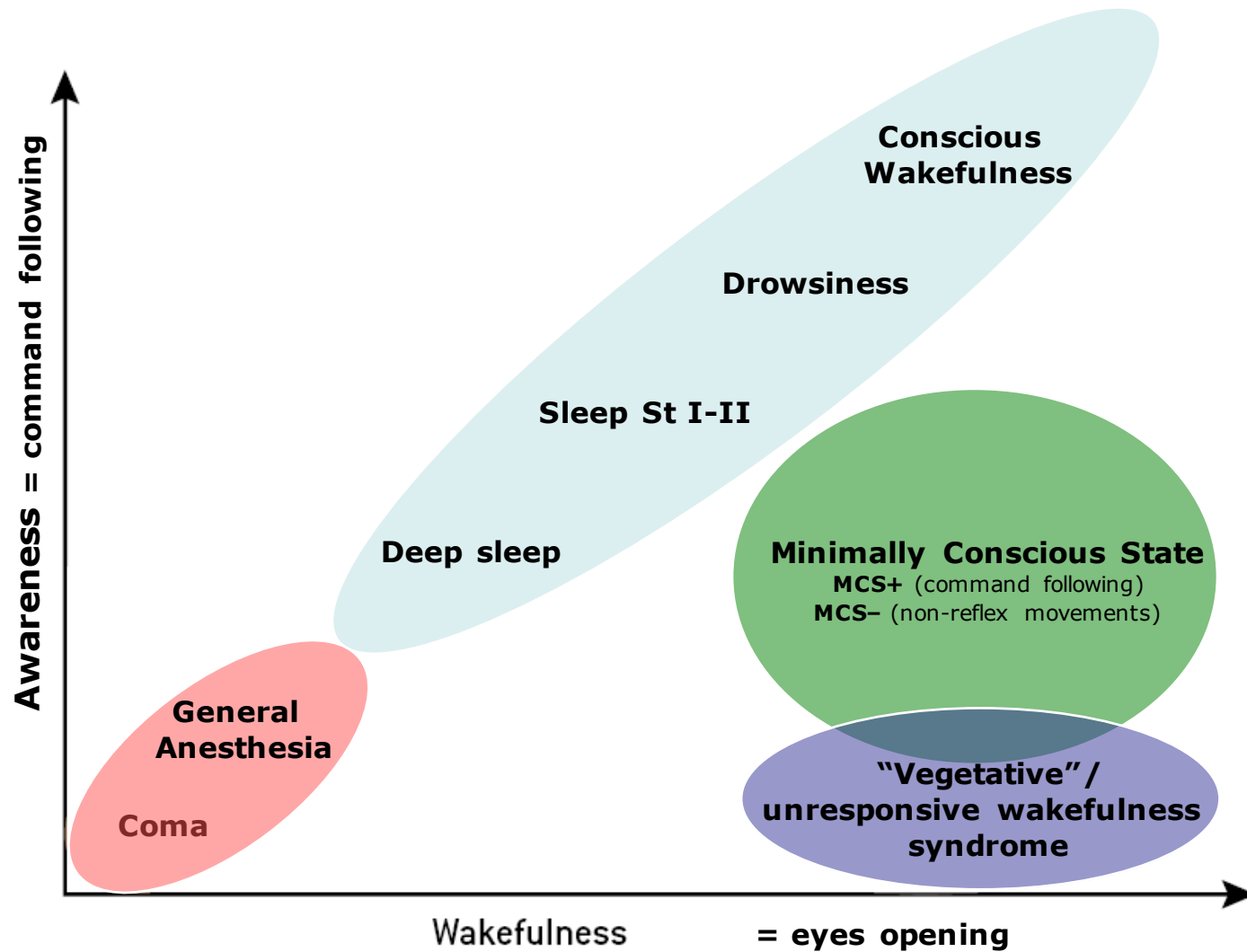


fnrs
LA LIBERTÉ DE CHERCHER

CHERCHER, TROUVER, GUÉRIR, POUR VOUS & AVEC VOUS.

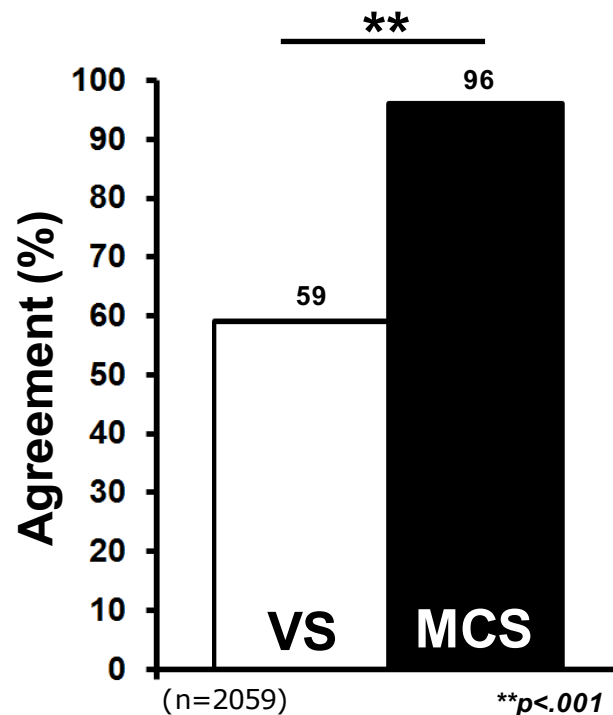


A clinical definition of consciousness



Attitudes towards pain

Do you think patients in a ...
can feel pain?



Question Predictors	Odds Ratio	95% Confidence Interval	p value
Do you think VS patients feel pain?			
Age	1.01	1.00 1.02	.050
Women	1.25	.99 1.58	.060
Northern Europe	1.00		
Central Europe	.81	.58 1.14	.240
Southern Europe	1.10	.76 1.60	.600
Paramedical professionals	1.56	1.20 2.00	<.001
Religious respondents	1.37	1.10 1.70	.004
Do you think MCS patients feel pain?			
Women	2.38	1.33 4.26	.003
Religious respondents	1.83	1.05 3.18	.031

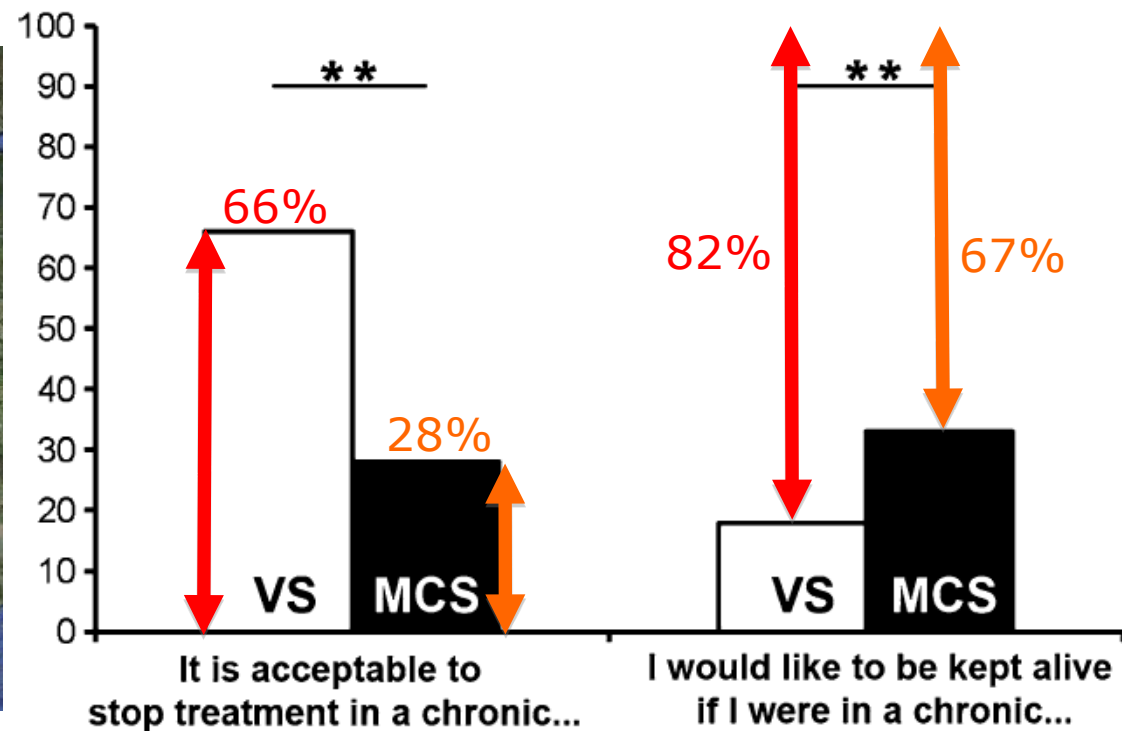
Predicted response: "agreement"

Attitudes towards end-of-life

- VS worse than death for the patient: 55%
- VS worse than death for their families: 80%
- MCS worse than VS for the patient: 54%
- MCS worse than VS for their families: 42%

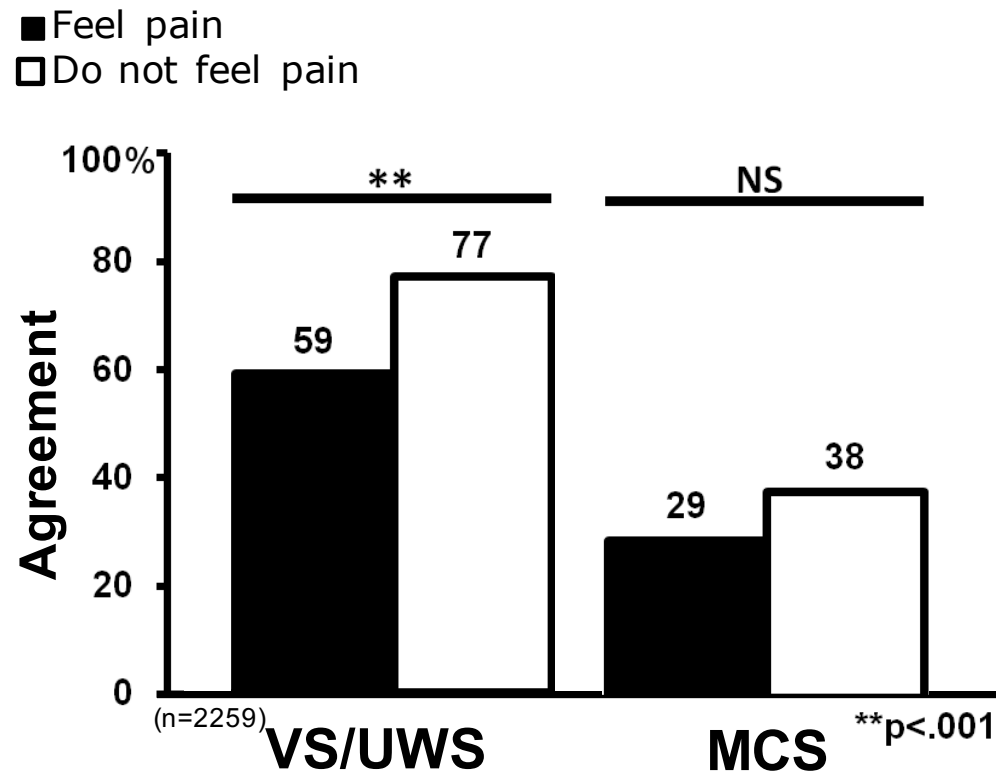


2,475 medical professionals

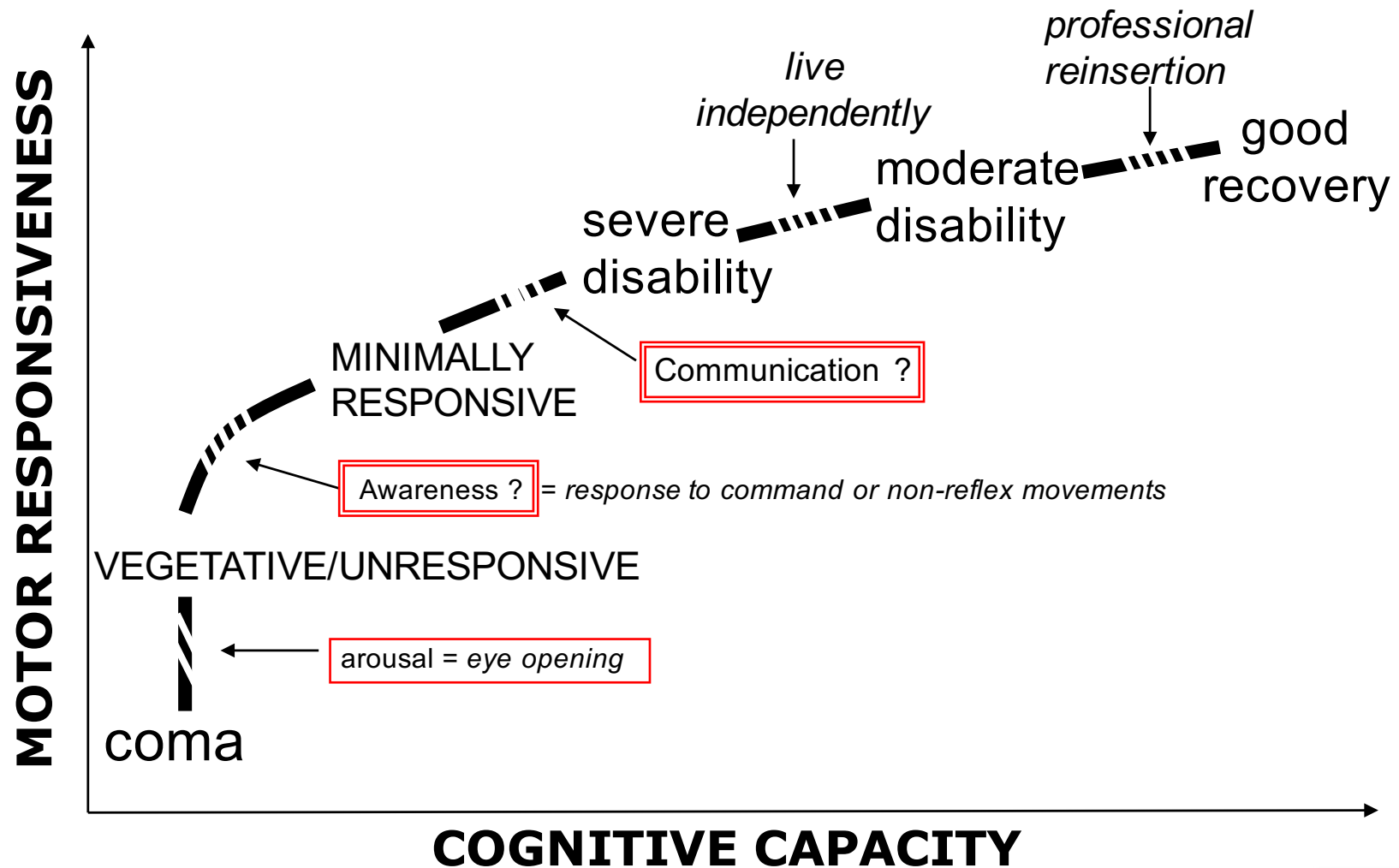


Attitudes towards pain and end-of-life

Treatment can be stopped in chronic...



Behavioral evaluation of patients



Behavioral diagnosis: gold standard?

Standardized assessment

n=103 post-comatose patients

45 Clinical diagnosis of VS

27 Coma Recovery Scale VS

 40% misdiagnosed

Schnakers et al, Ann Neurol 2006; BMC Neurol 2009

PET 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%)

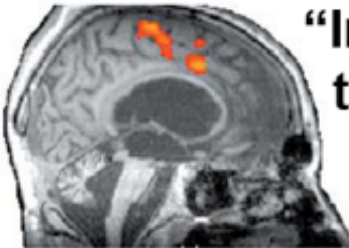

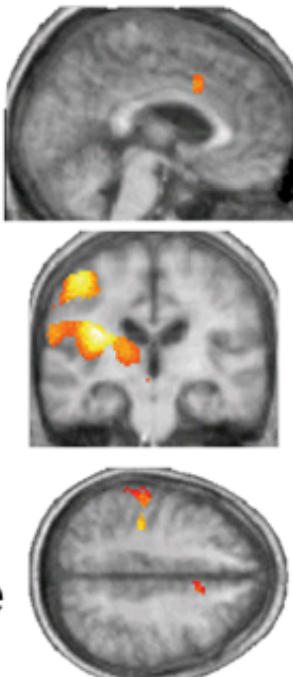

UWS=unresponsive wakefulness syndrome. MCS=minimally conscious state.

Table 2: Diagnostic results by modality

Stender et al, Lancet 2014

Detecting awareness with fMRI

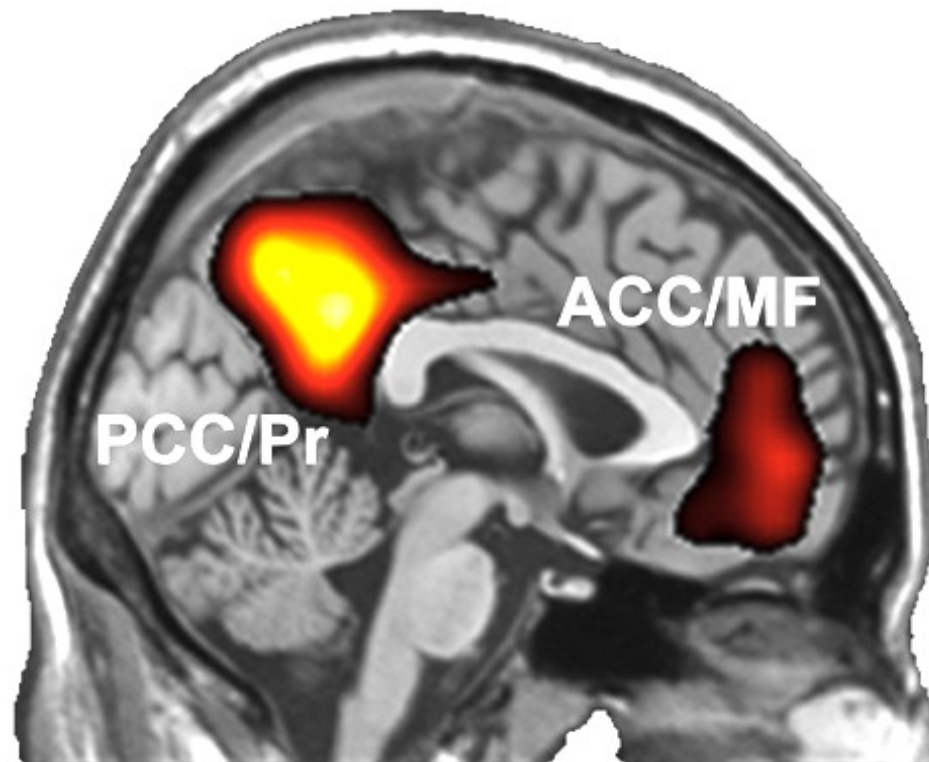


Active paradigms	Passive paradigms
 <p data-bbox="593 550 1008 662">“Imagine playing tennis”</p>	 <p data-bbox="1097 1093 1422 1141">median nerve</p> 
 <p data-bbox="593 885 1008 1061">“Imagine visiting the rooms of your house”</p> <p data-bbox="548 1173 1008 1228">Owen et al, Science 2006 Monti & Vanhaudenhuyse et al, NEJM 2010</p>	<p data-bbox="1568 1204 1870 1228">Boly et al, Lancet Neurol 200</p>

Heine, Di Perri, Soddu, Laureys, Demertzi
In: *Clinical Neurophysiology in Disorders of Consciousness*, Springer-Verlag 2015

Demertzi & Laureys, In: *I know what you are thinking: brain imaging and mental privacy*, Oxford University Press 2012

The brain's default mode of function

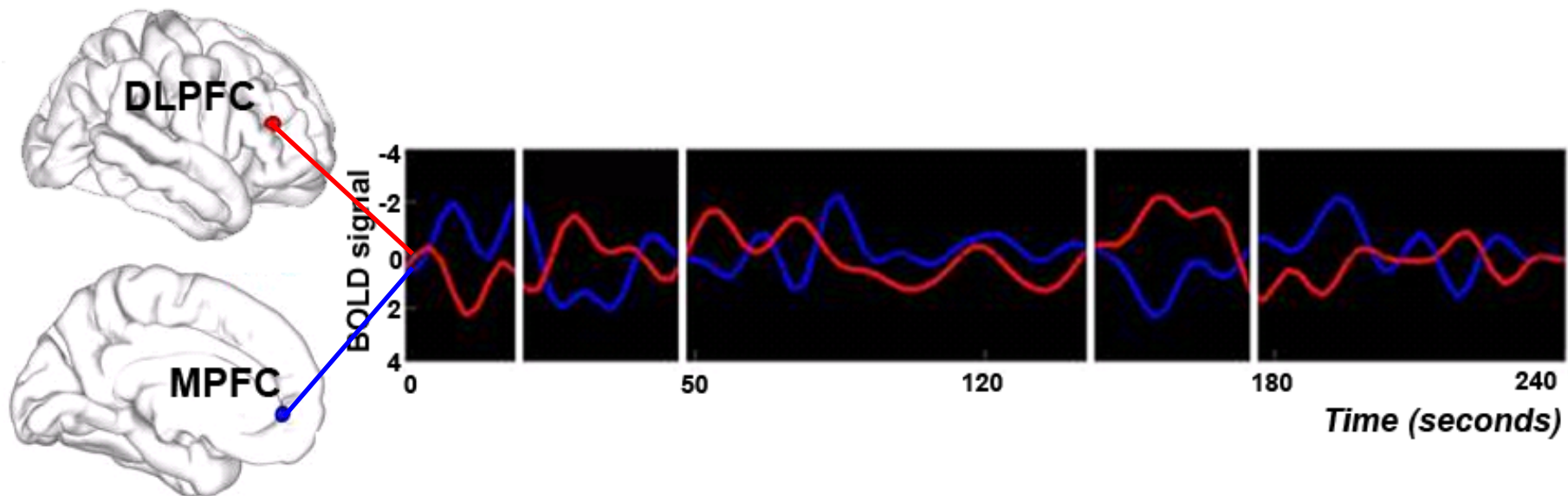


Demertzi & Whitfield-Gabrieli, in: Neurology of Consciousness 2nd ed. 2015
Demertzi, Soddu, Laureys, Curr Opin Neurobiology 2013
Demertzi et al, Front Hum Neurosci 2013
Raichle et al, PNAS 2001

The brain's default mode of function

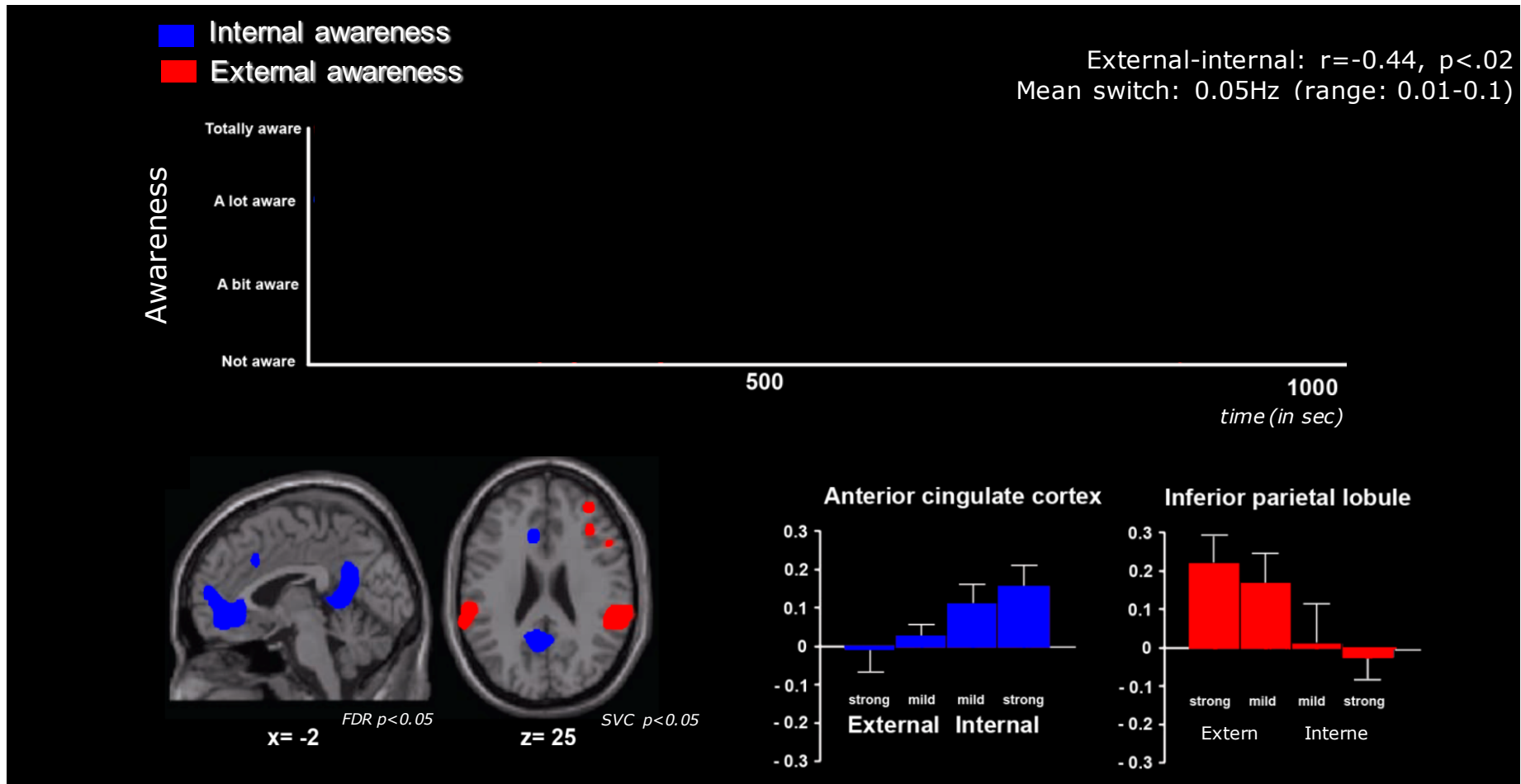


External awareness
or anticorrelated network



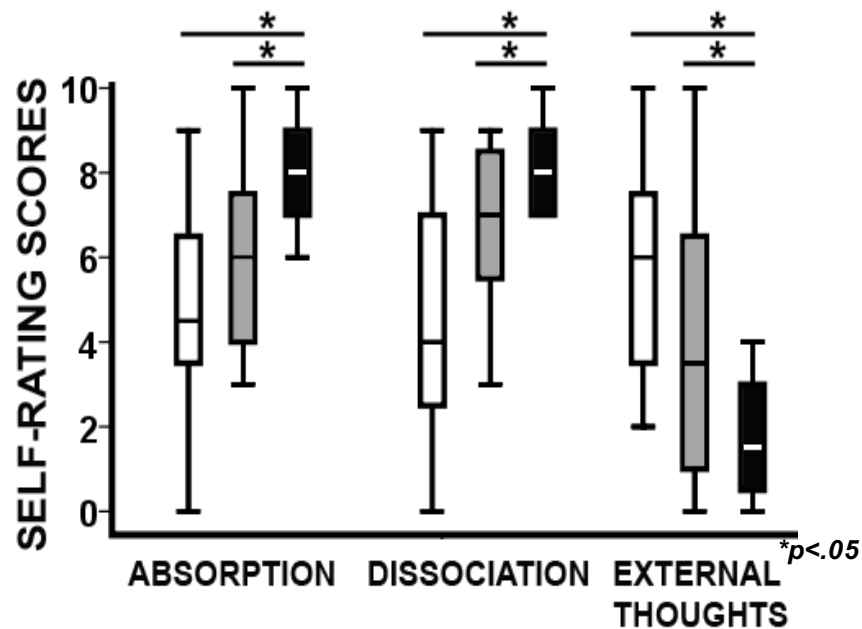
Internal awareness
or Default mode network

The cognitive counterpart of resting state



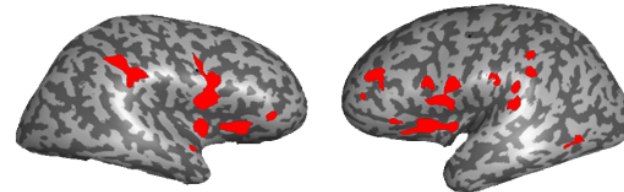
Anticorrelated activity is modified in hypnosis

- Normal consciousness
- Autobiographical mental imagery
- Hypnosis

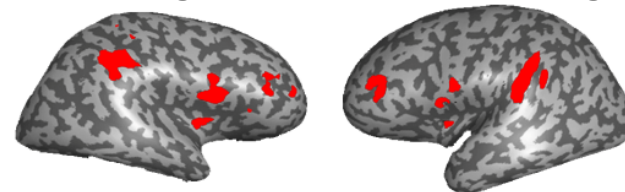


EXTRINSIC SYSTEM

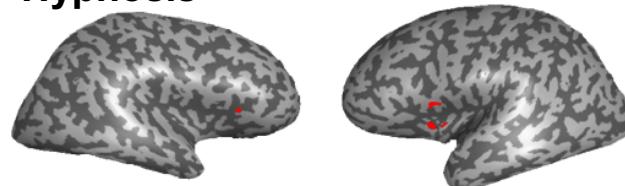
Normal consciousness



Autobiographical mental imagery

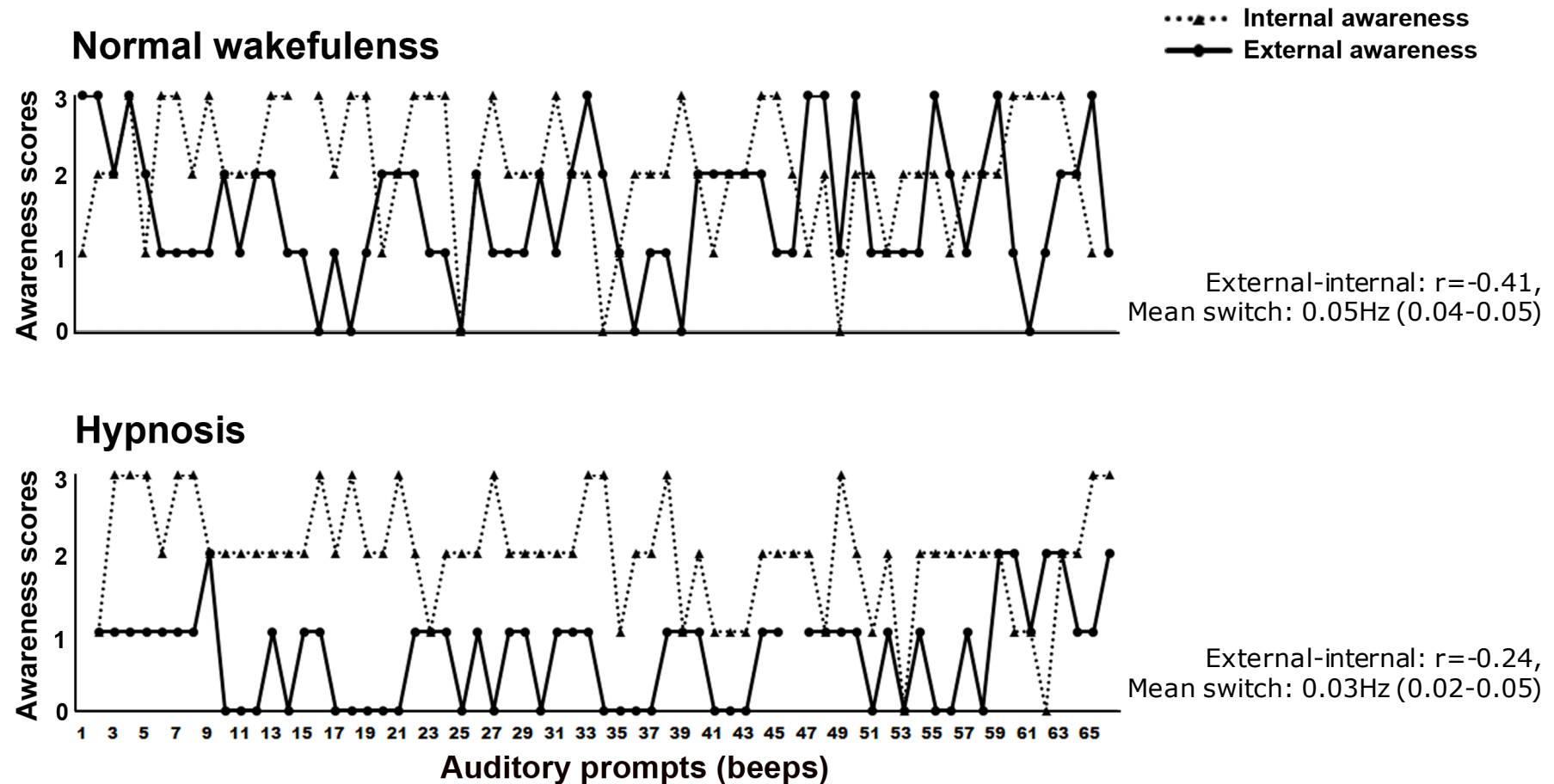


Hypnosis

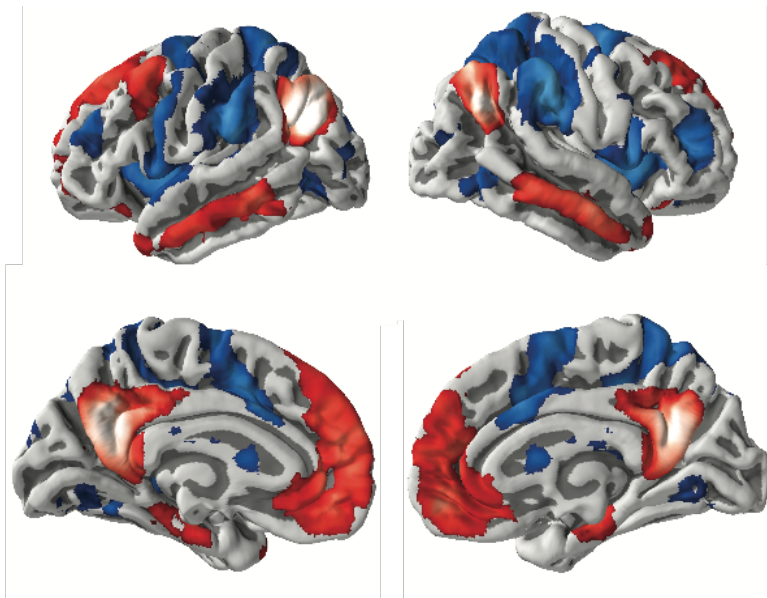


p < 0.05 corrected for multiple comparisons

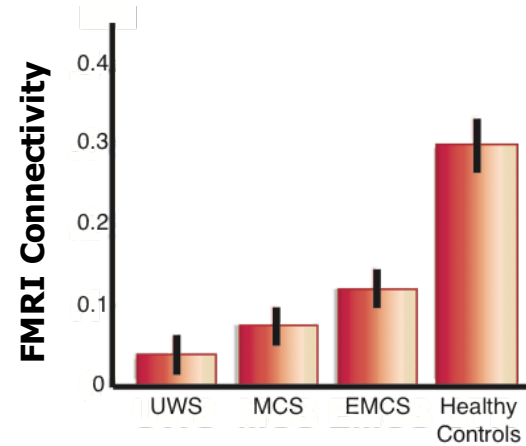
Awareness is modified in hypnosis



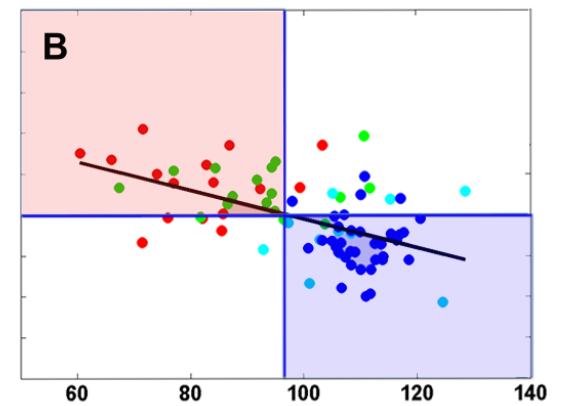
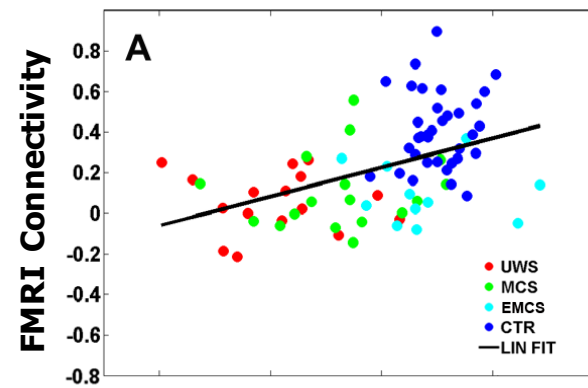
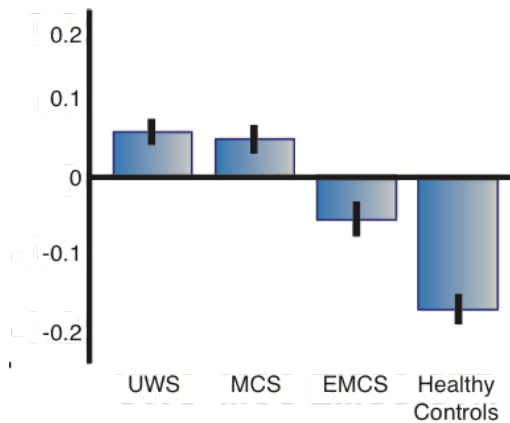
Anticorrelated activity is absent in DOC



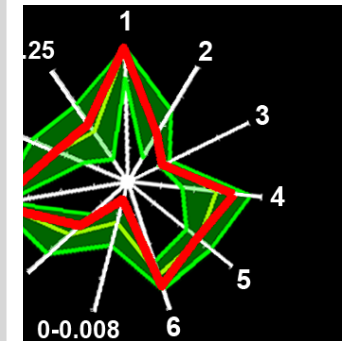
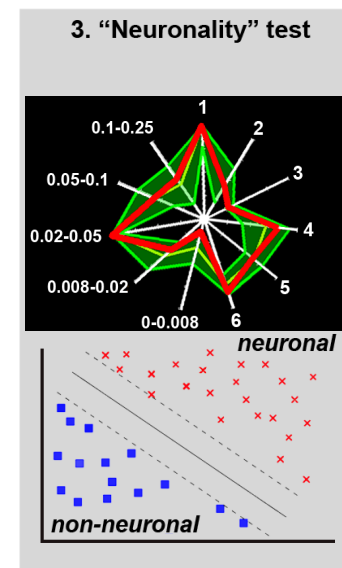
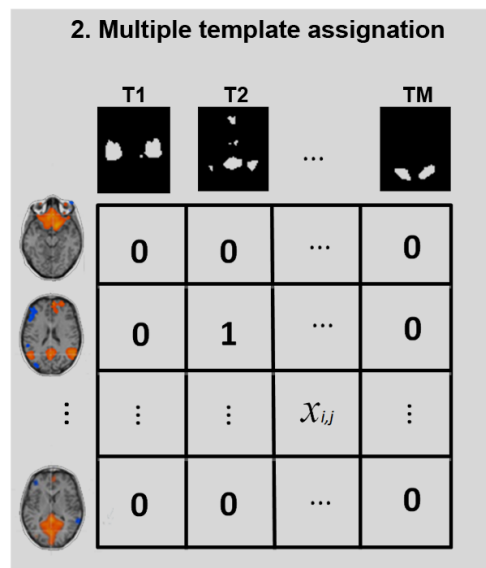
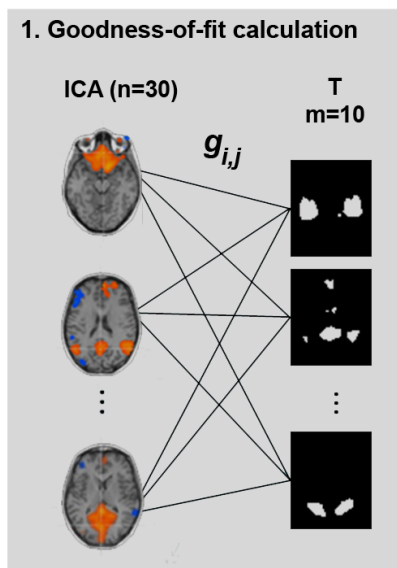
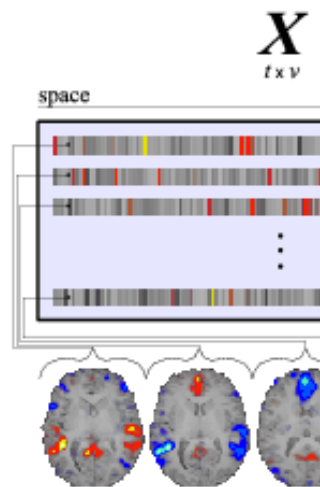
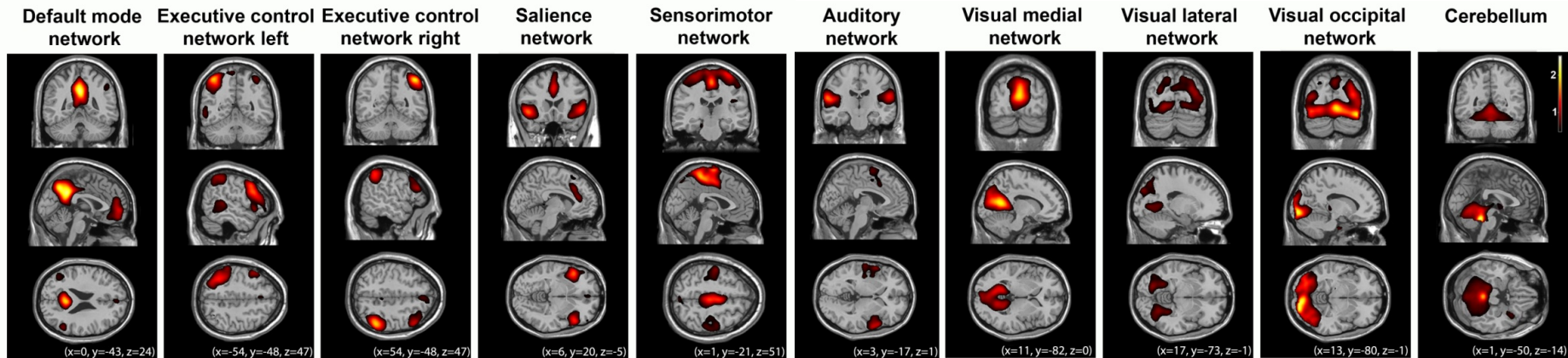
DMN CORRELATIONS



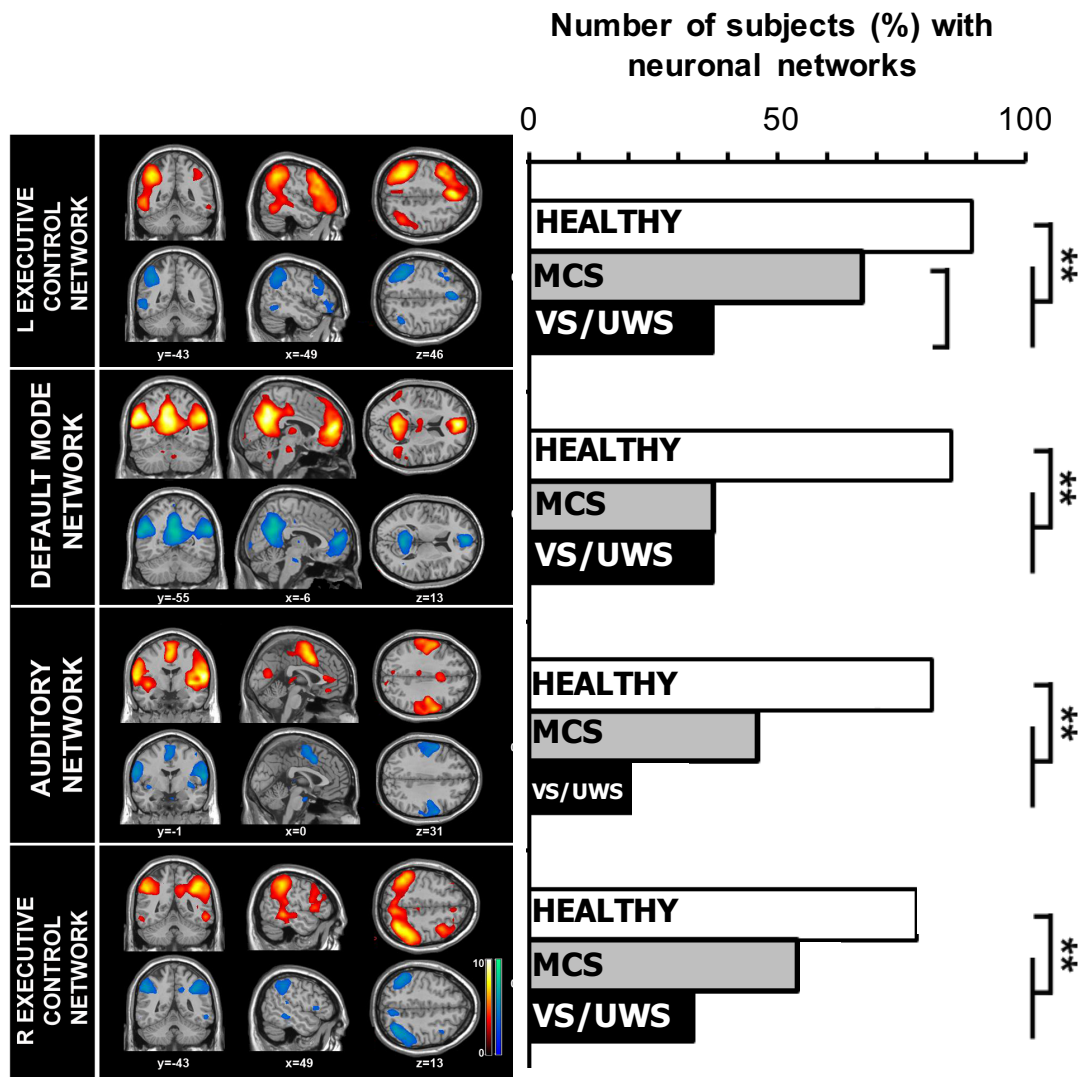
DMN ANTICORRELATIONS



Systems-level intrinsic connectivity



Fewer "neuronal" networks in DOC



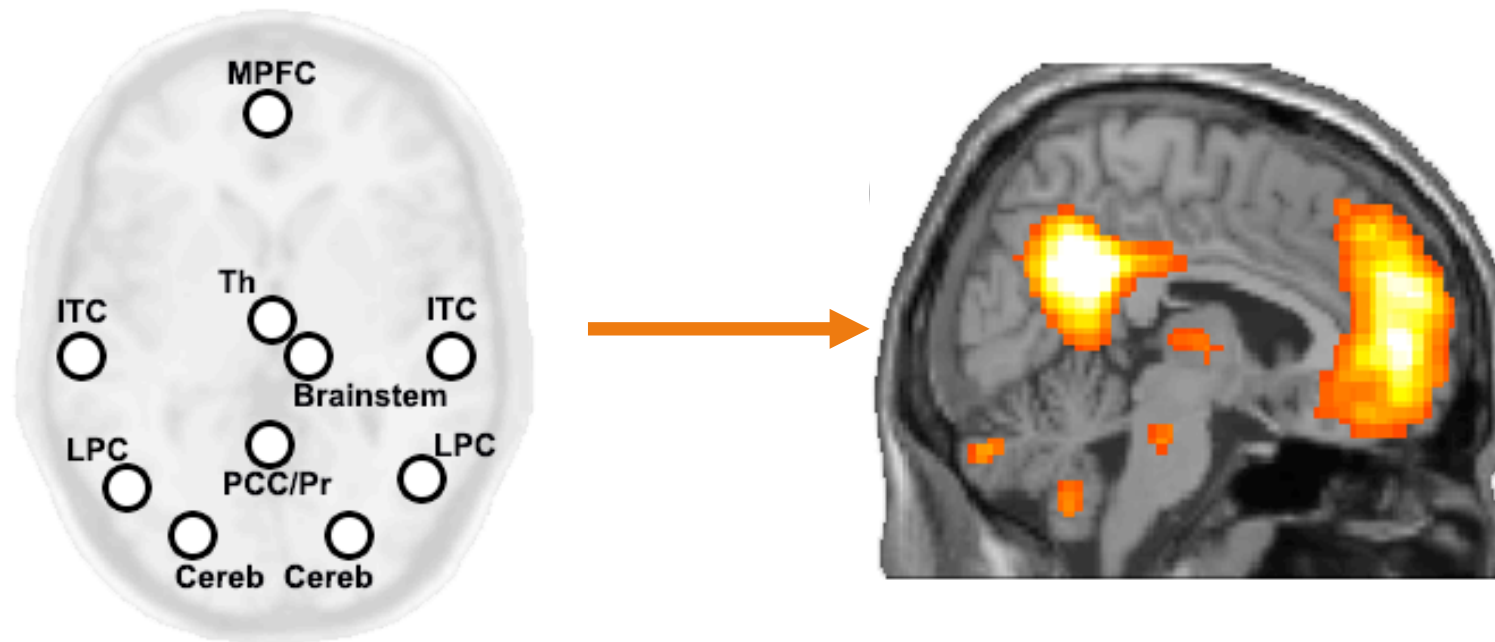
Single-patient classification

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

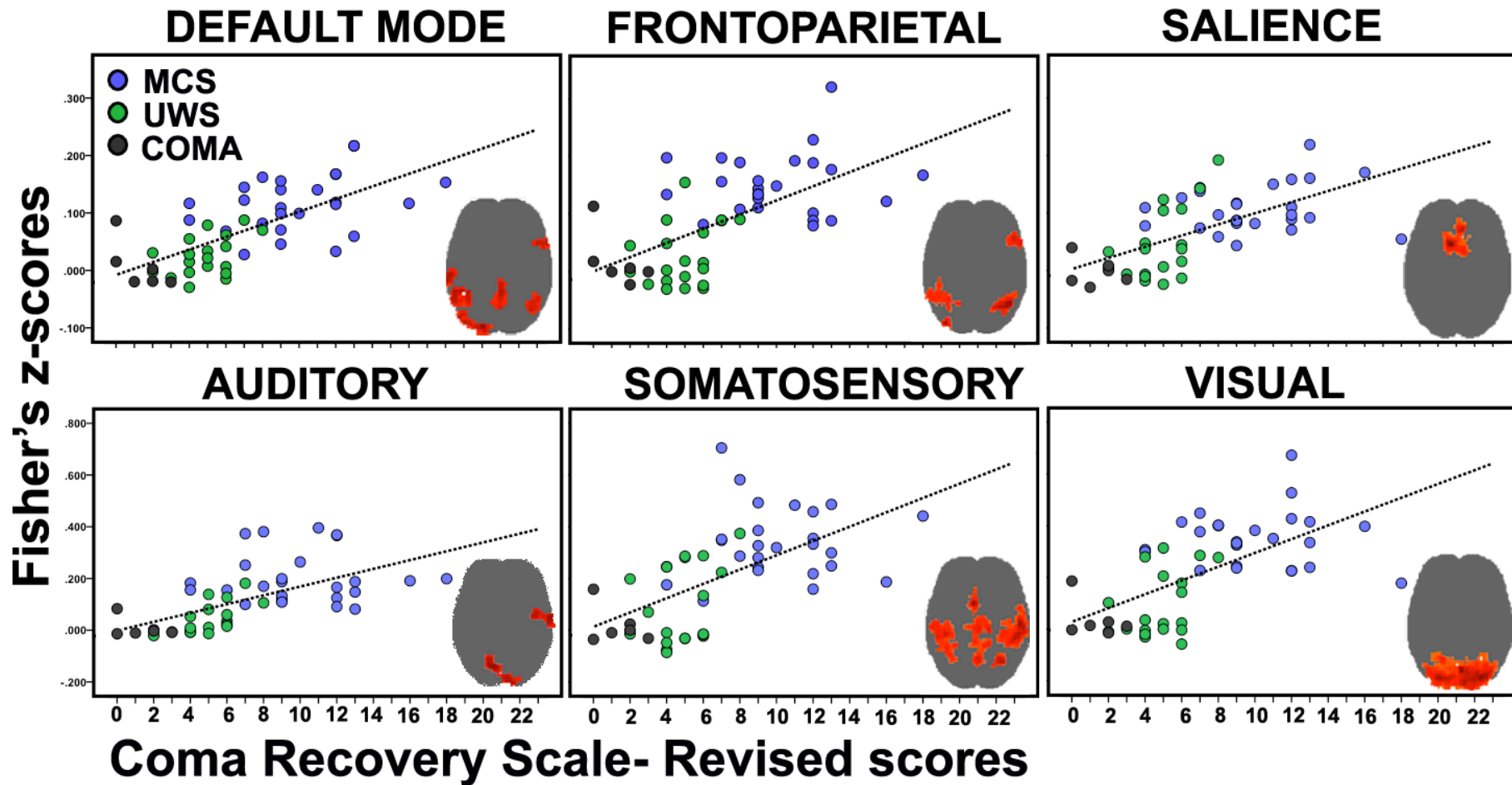
Intrinsic connectivity networks



Default mode network



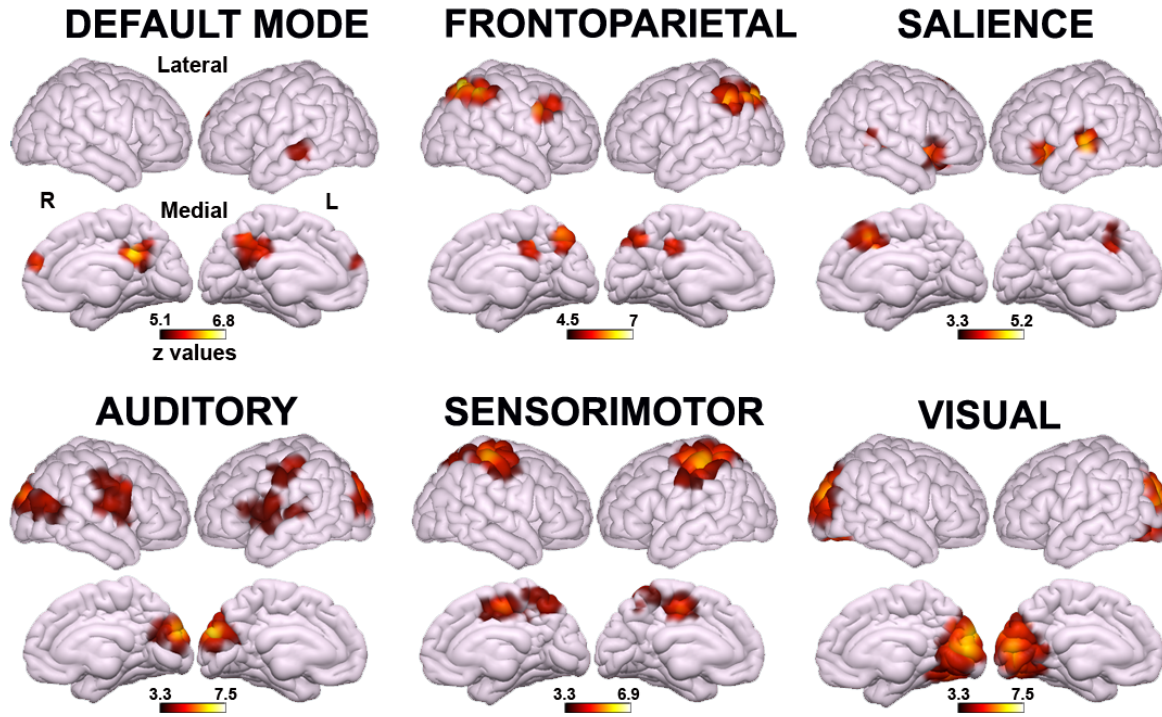
Intrinsic connectivity reflects the level of C



Which network discriminates best?



MCS > VS/UWS



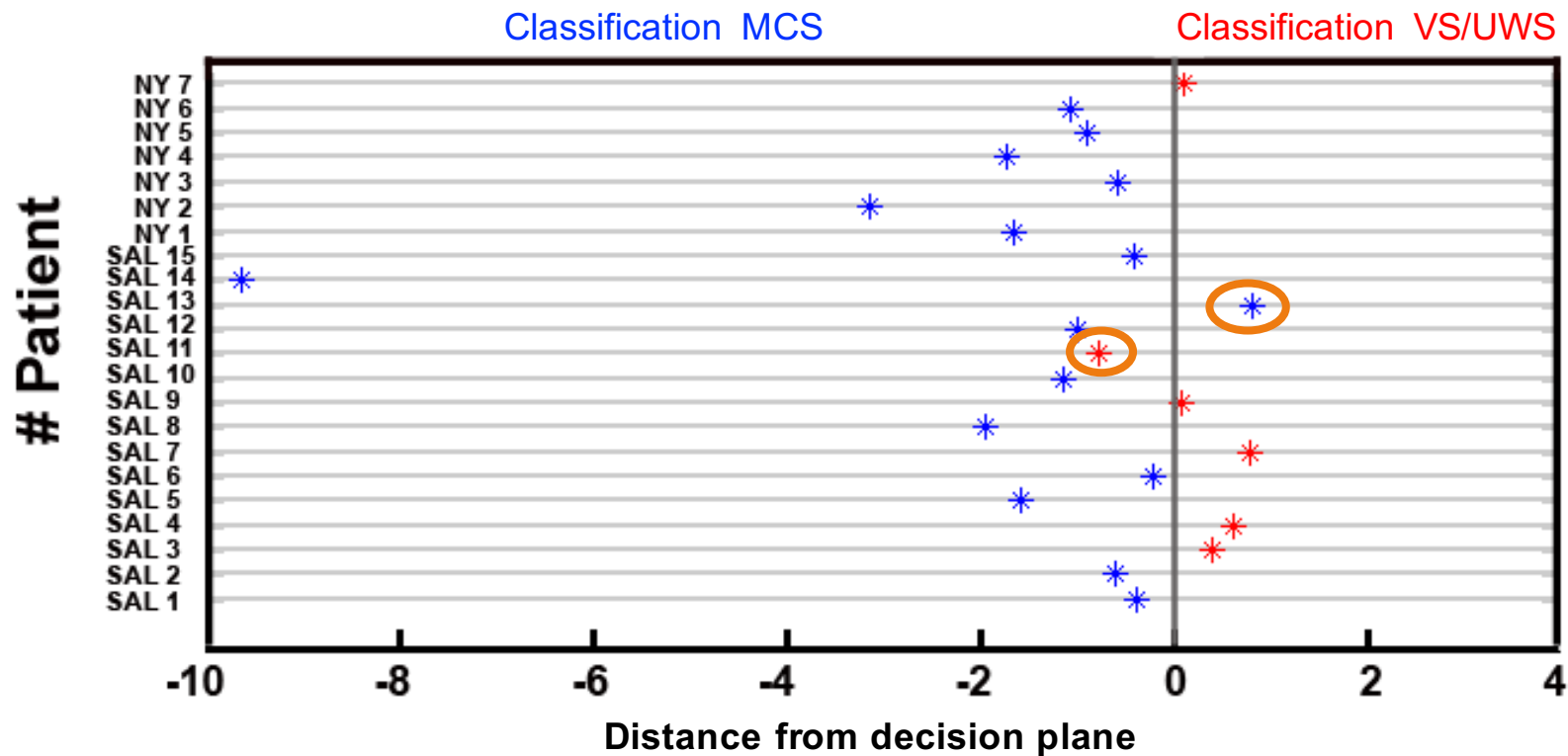
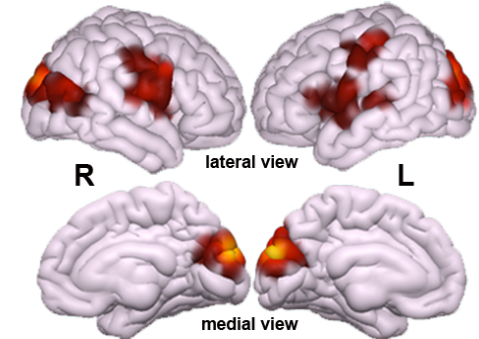
FWE $p < 0.05$ (cluster-level)

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

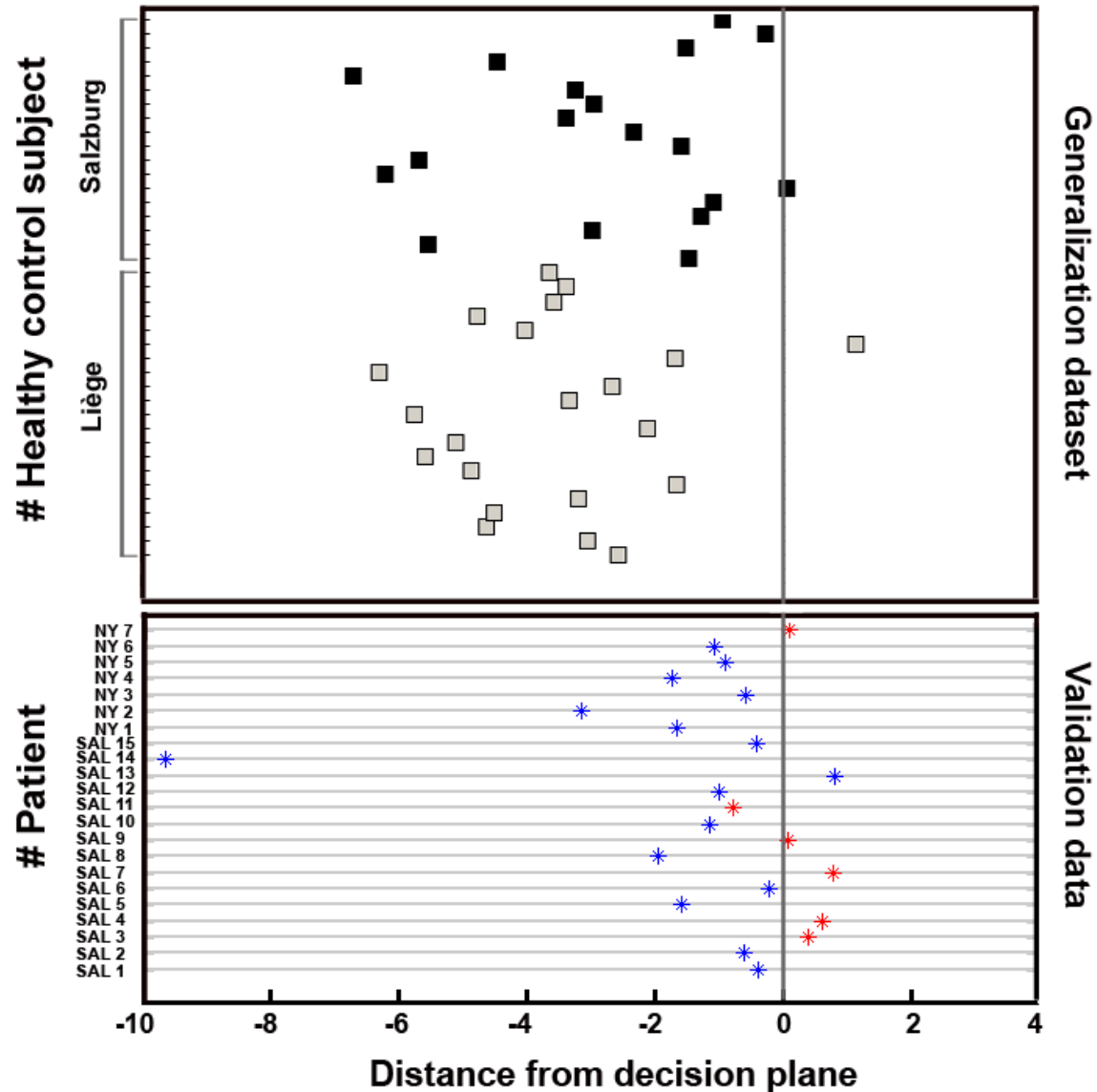
Crossmodal connectivity classifies independently assessed patients



- 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



Classifier generalizes to healthy

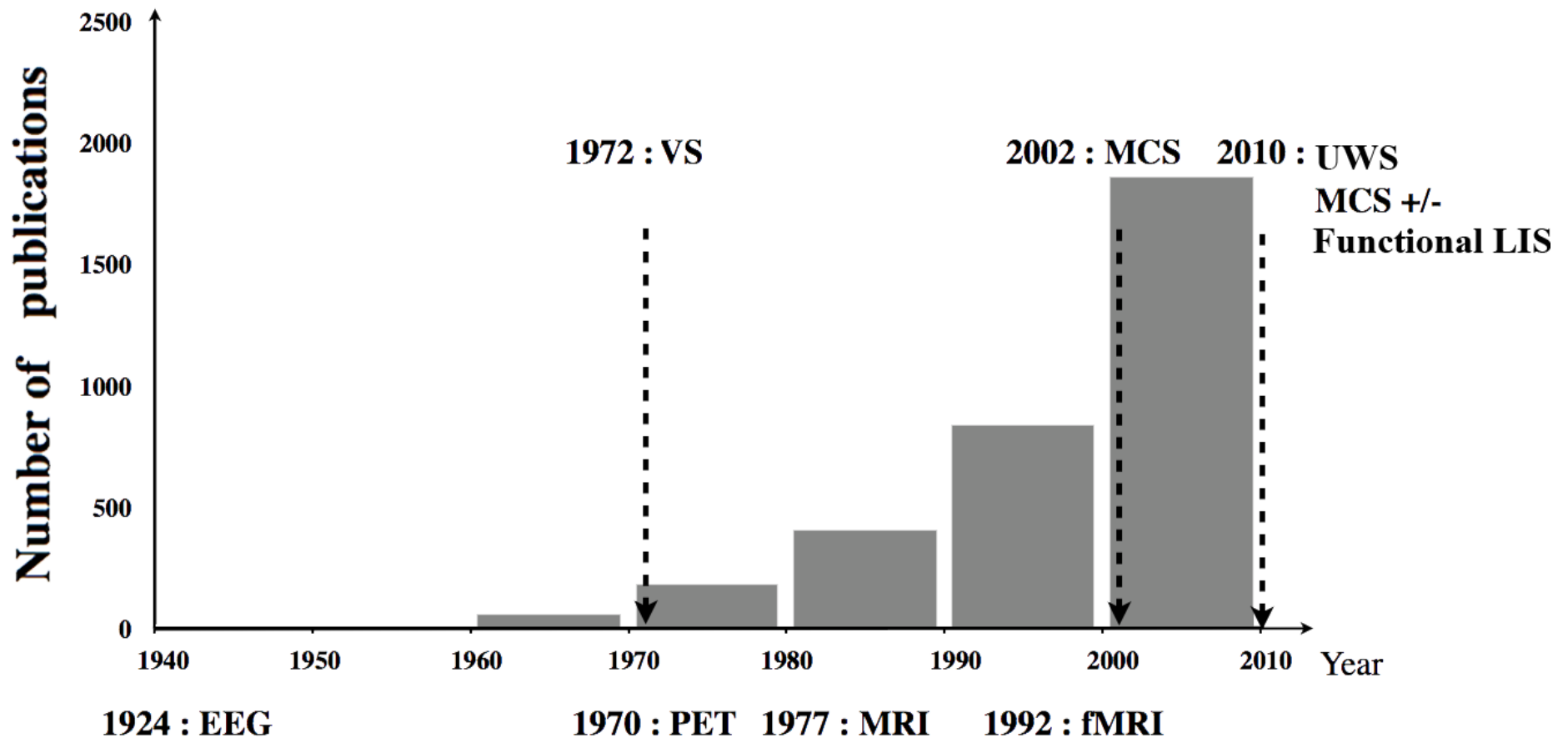


The ethical relevance of technology-based assessment



Results of Tests	Beneficial Effects	Harmful Effects
- brain activity than neurological examination	Relatives: decisions to limit life-sustaining treatment	Relatives: may lose hope, purpose, and meaning in life
+ brain activity than neurological examination	Clinical management: may be intensified by the chance of further recovery	Relatives: false hopes
Same as neurological examination	Clinicians & relatives: may be affirmed in their decision about the level of treatment	Clinicians & relatives: may be disappointed & treatment cost/effectiveness may be poor

New knowledge, new nosology

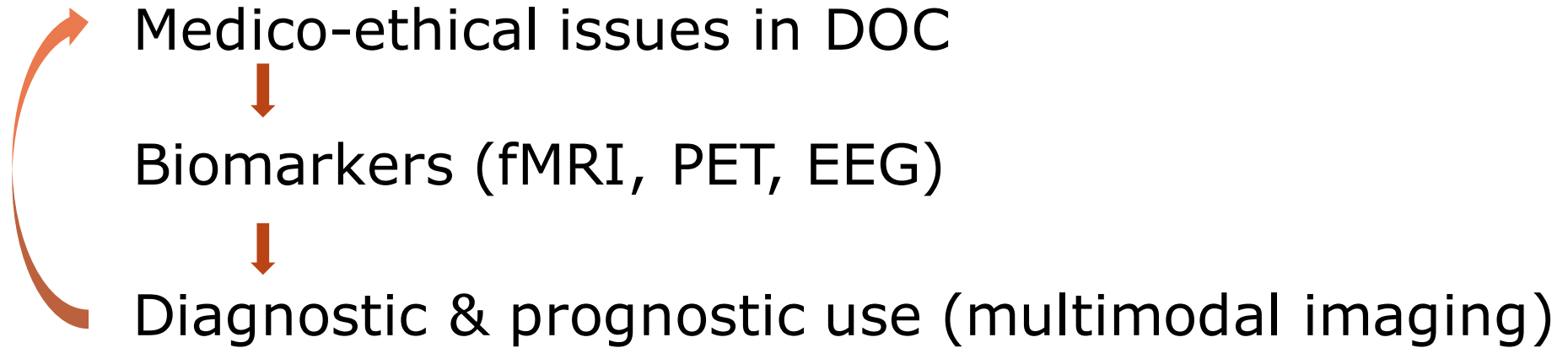


Neuro-ethical issues to consider



- The moral significance of Consciousness
 - ontological understanding: consciousness = personhood = moral agency
 - relational or contextual understanding: patients have value for others
- Legal challenges: responses to critical questions with NI
- Cognitive neuroscience is about brain/mind reading
 - to what degree do we neuroscientists have the right to interfere with a patient's intimacy, such as cognitive contents, in the absence of their consent?
 - in essence, where do we draw the limits of deciphering another person's cognitive content, like dreams, ongoing mentation etc? What is the additive value of it to a societal level?

Conclusions



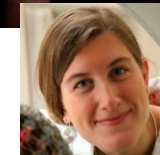
Thank you!



Coma Science Group & PICNIC Lab

The departments of Neurology and Radiology in Liège and Paris

...and mostly patients and their families!



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CHERCHER, TROUVER, GUÉRIR, POUR VOUS & AVEC VOUS.

