



Brain activity in coma & related states



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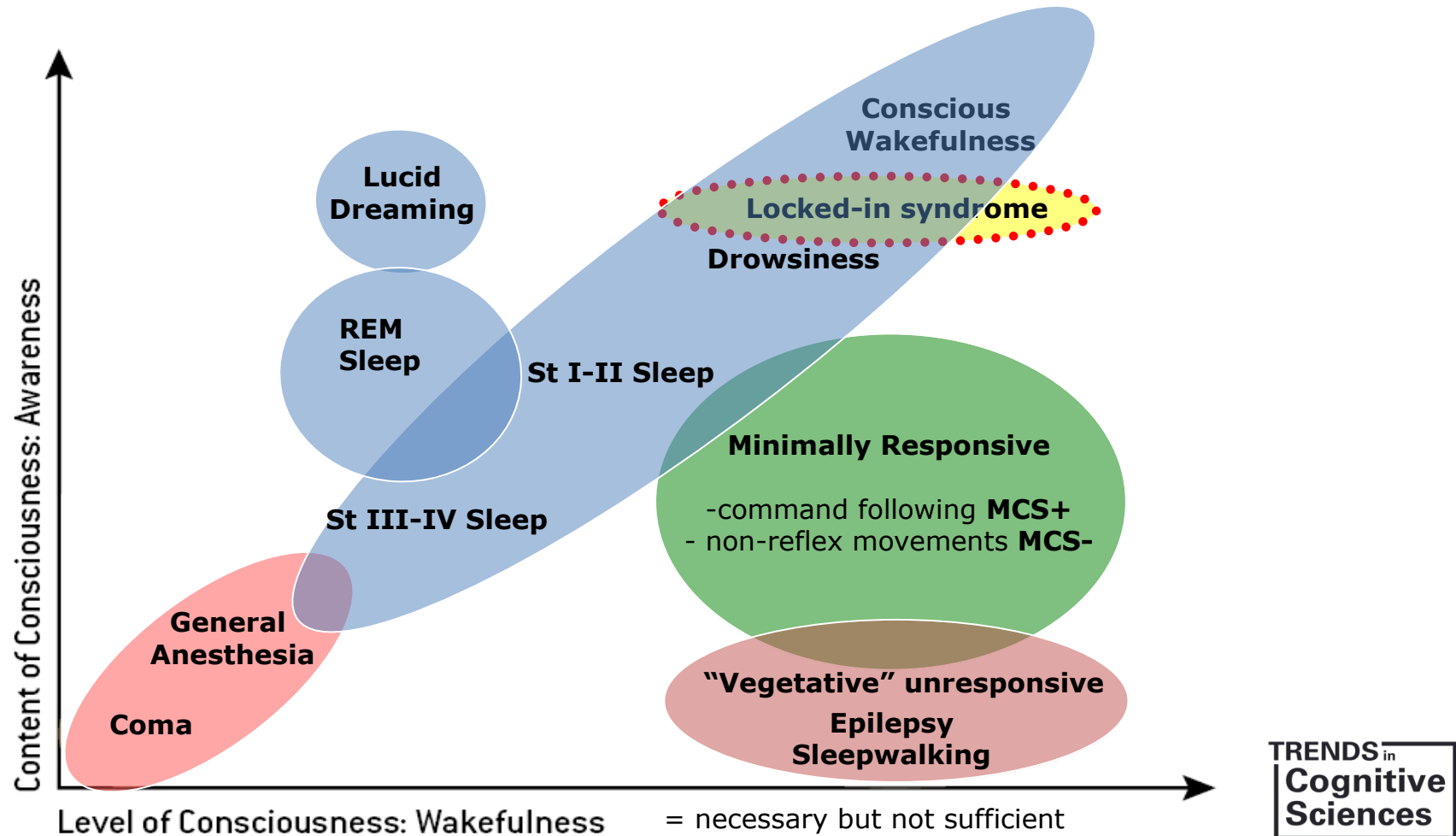


coma@ulg.ac.be
www.comascience.org

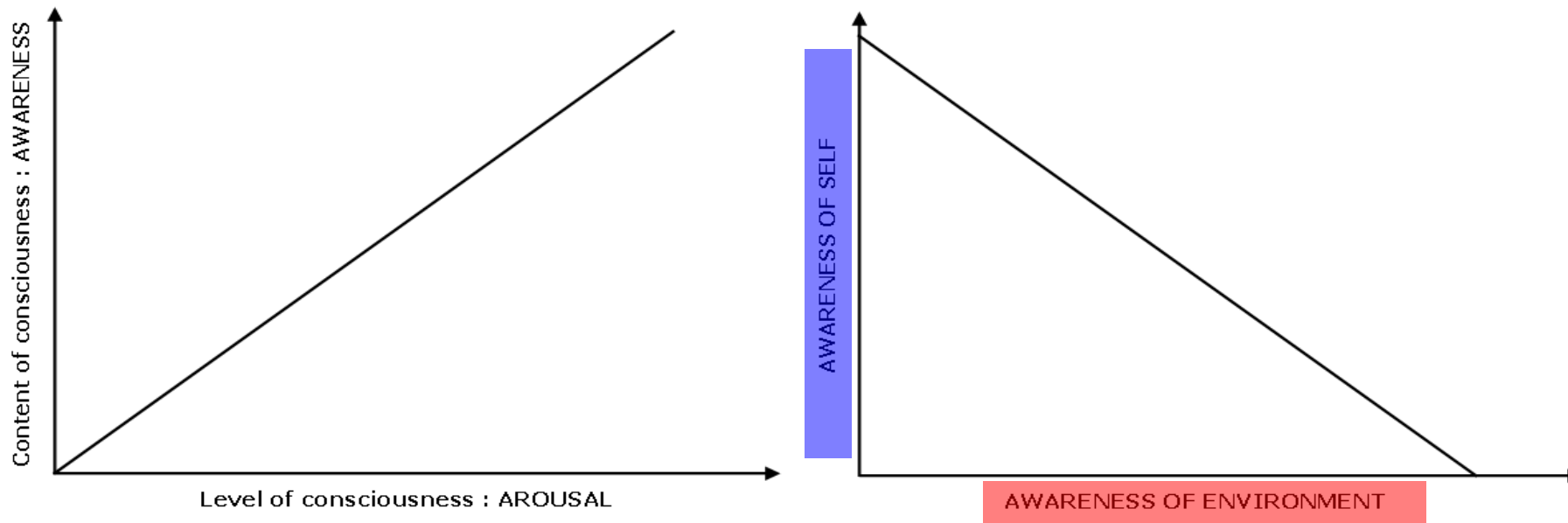




Arousal & awareness



Measuring awareness



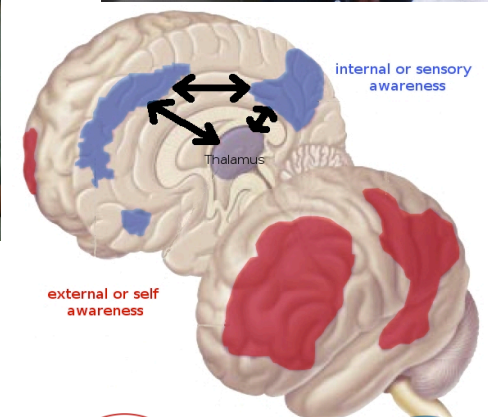
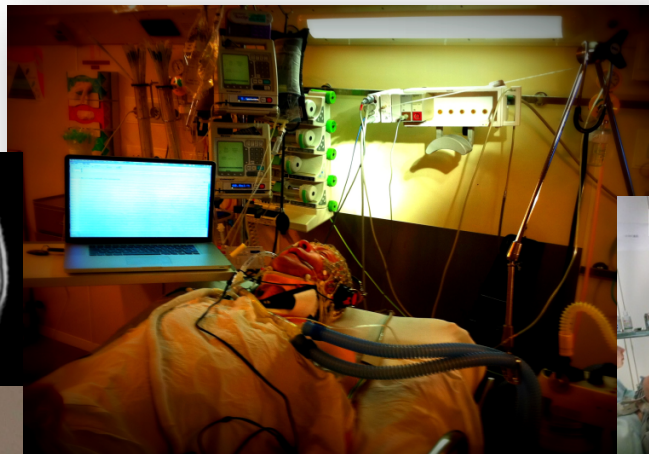
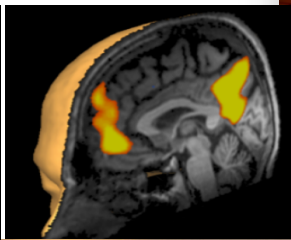
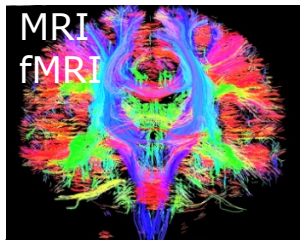
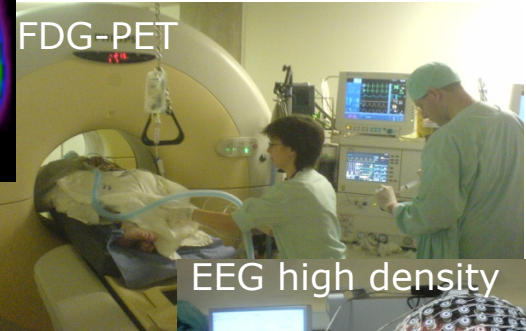
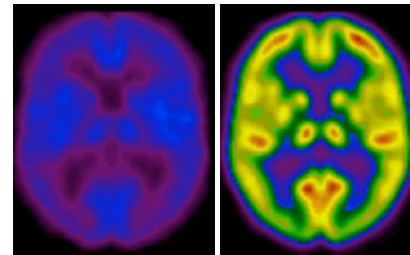
Demertzi, Soddu, Laureys, *Curr Opin Neurobiol* 2013
Boly et al, *Ann NY Acad Sci*, 2009

Measuring brain activity

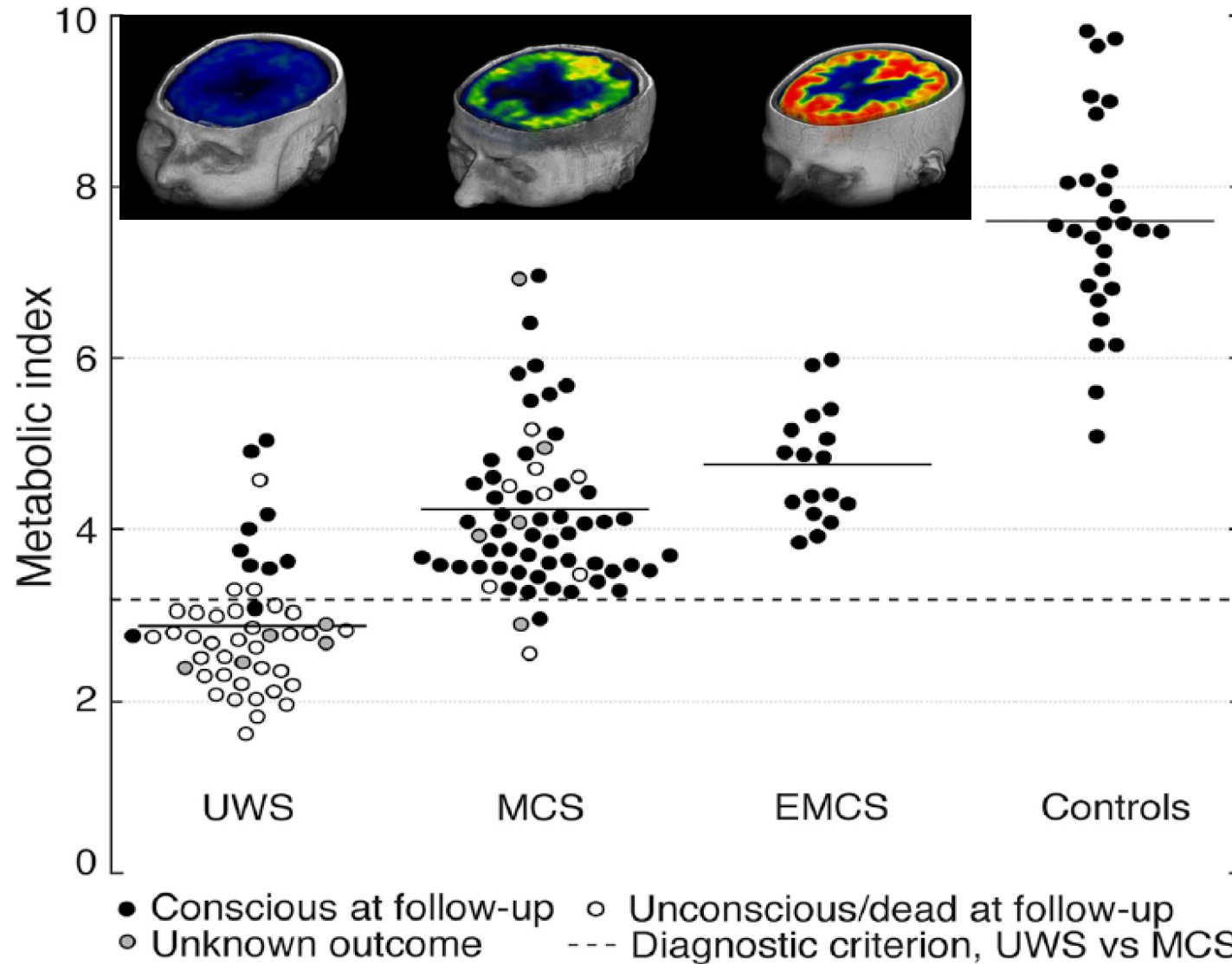


Altered states of consciousness

- Pathological : coma
- Pharmacological: anesthesia
- Physiological: hypnosis

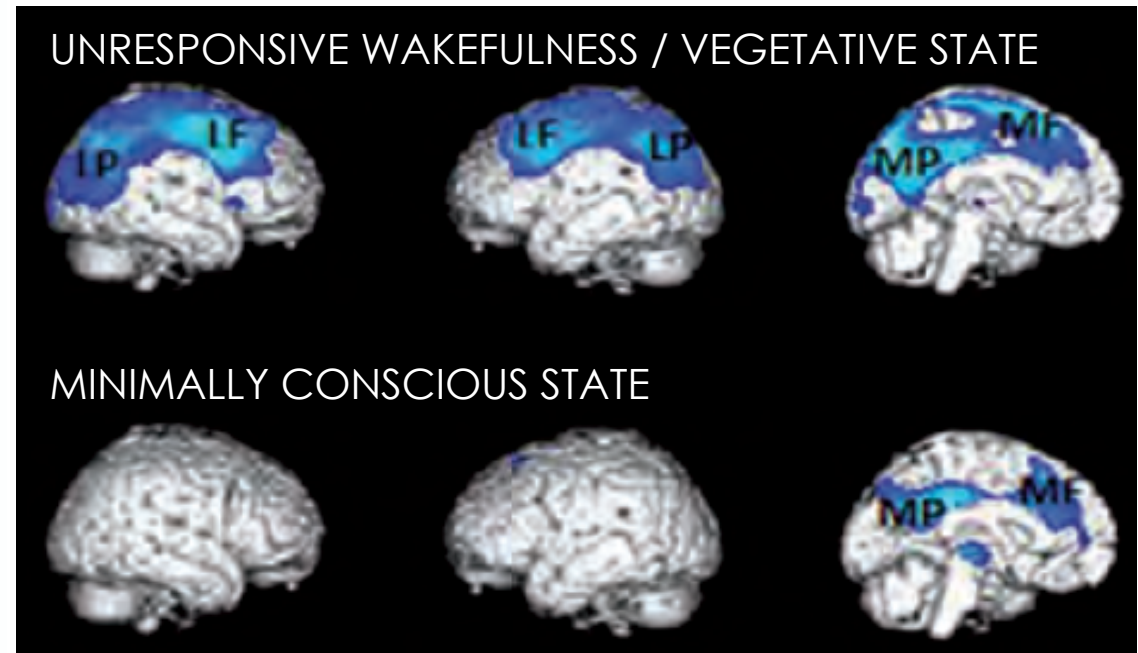
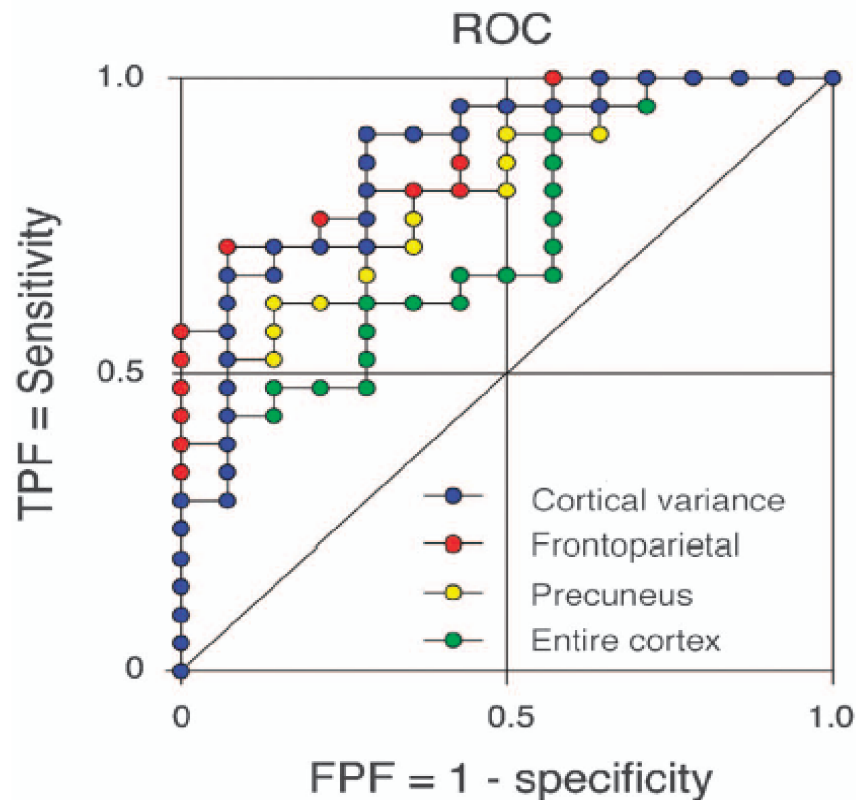


Consciousness and global brain function



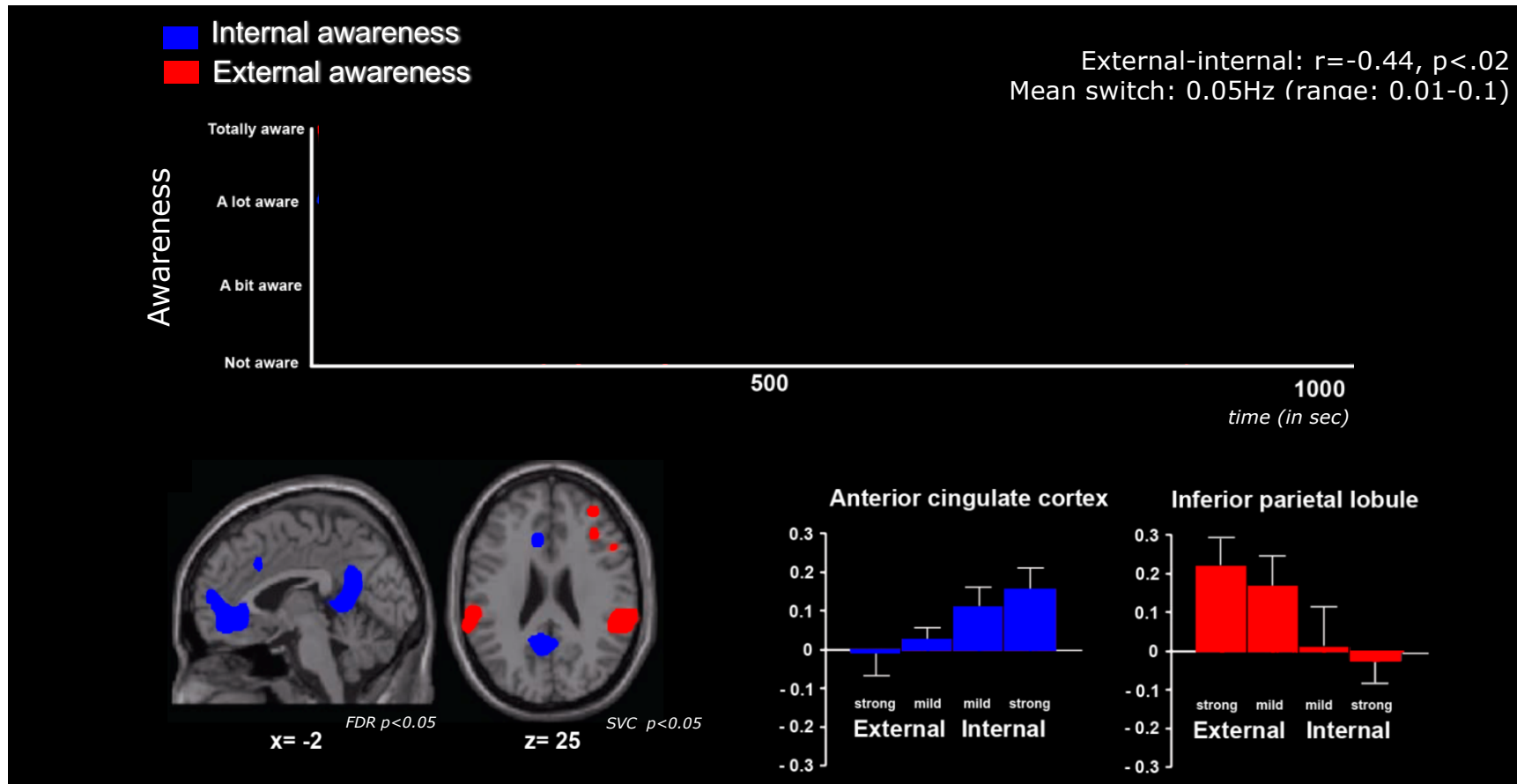
Stender et al, *Current Biology*, 2016

“Global workspace” of consciousness



Stender et al, *J Cereb Blood Flow & Metab*, 2015
Thibaut et al, *J Rehabil Med*, 2012

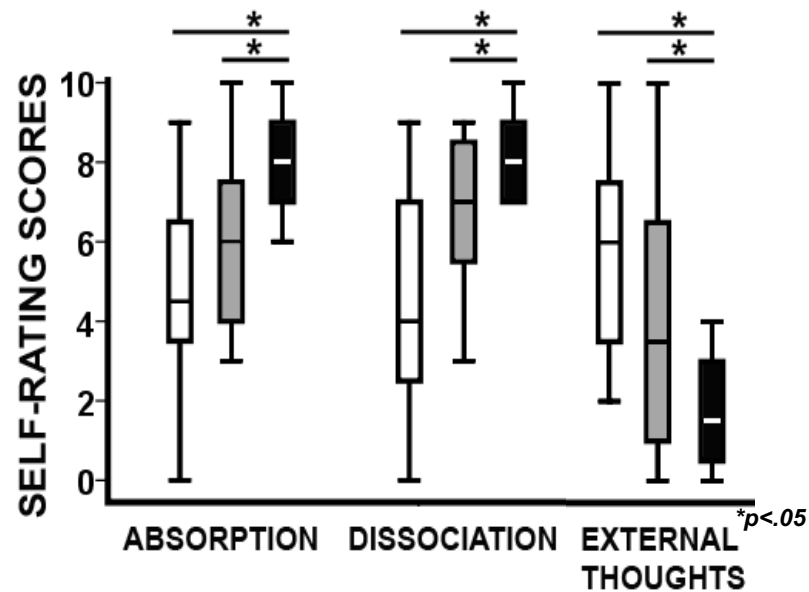
External & internal awareness (1)- typical



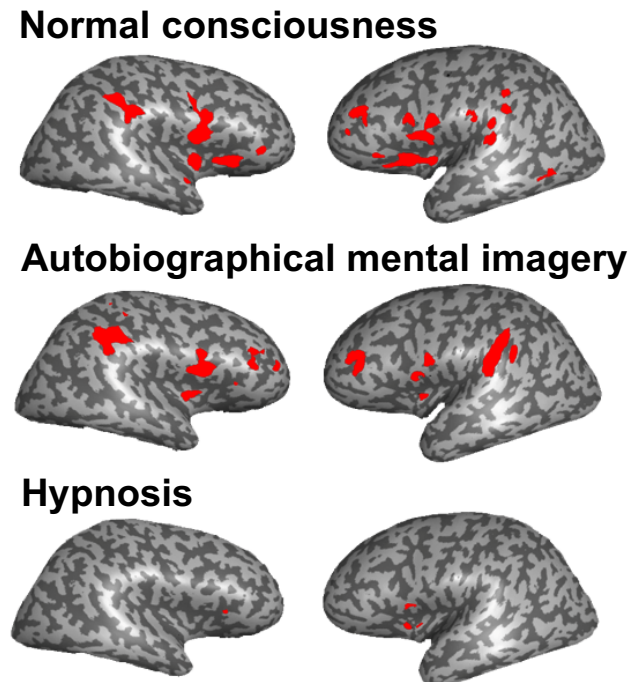
External & internal awareness (2)-hypnosis



- Normal consciousness
- ▒ Autobiographical mental imagery
- Hypnosis



EXTRINSIC SYSTEM



p < 0.05 corrected for multiple comparisons

Demertzi, Soddu, Faymonville et al, Progress in Brain Research 2011

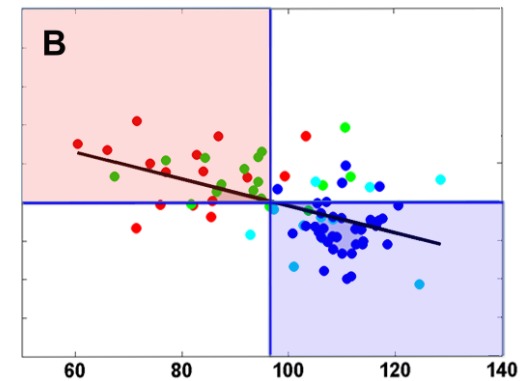
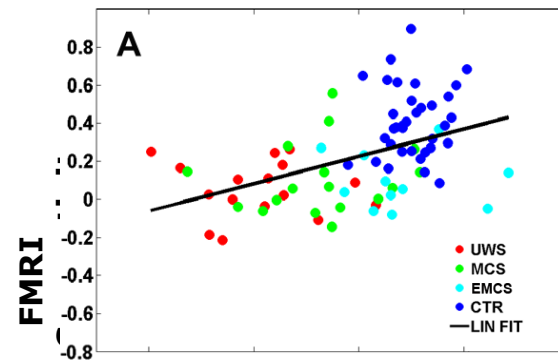
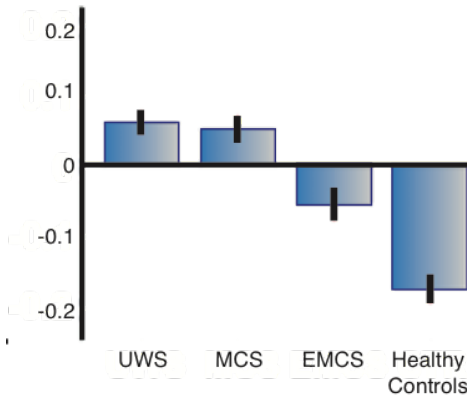
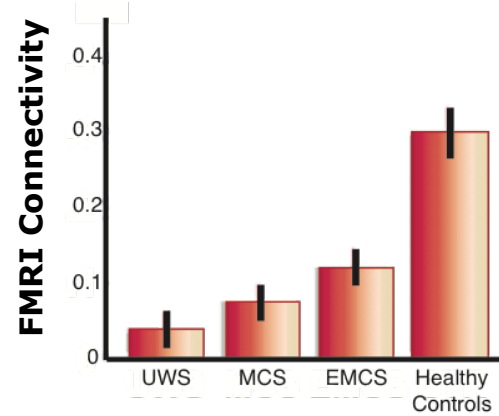
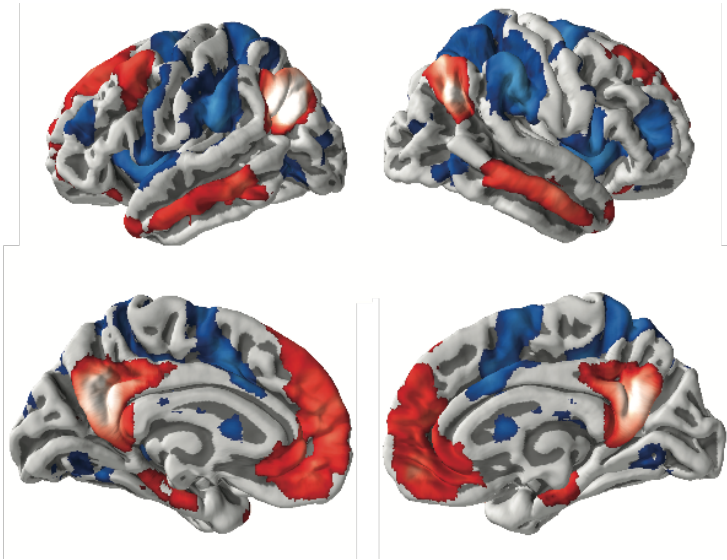
Demertzi, Vanhaudenhuyse, Noirhomme, Faymonville, Laureys, J Physiol Paris 2015

External & internal awareness (3)- DOC

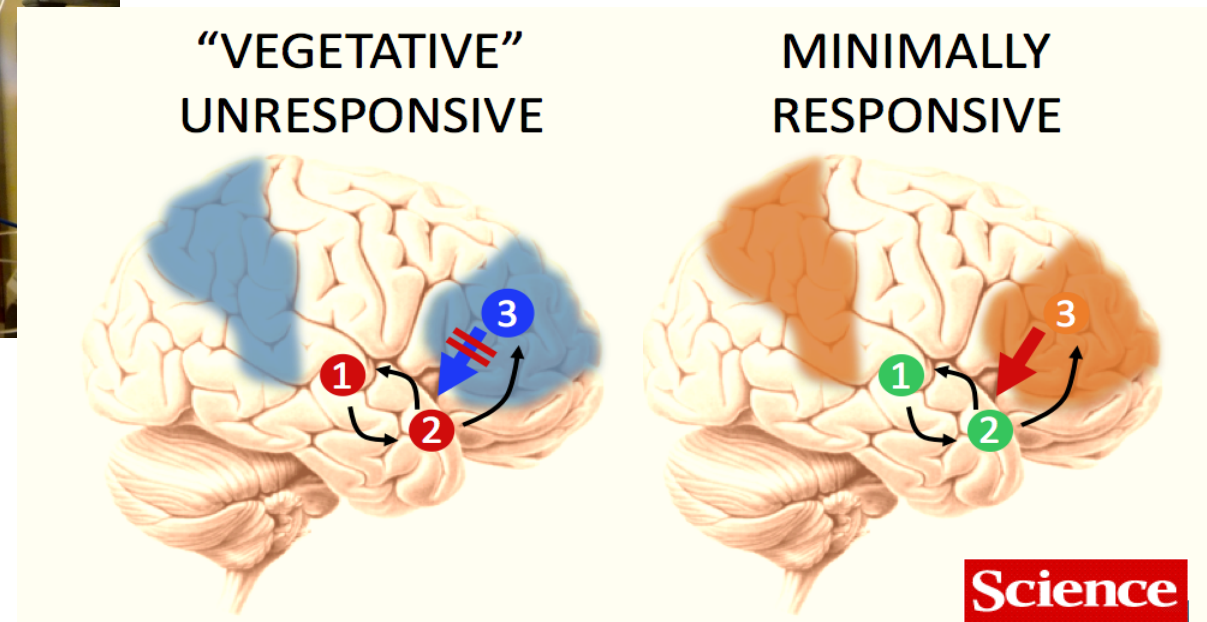


DMN CORRELATIONS

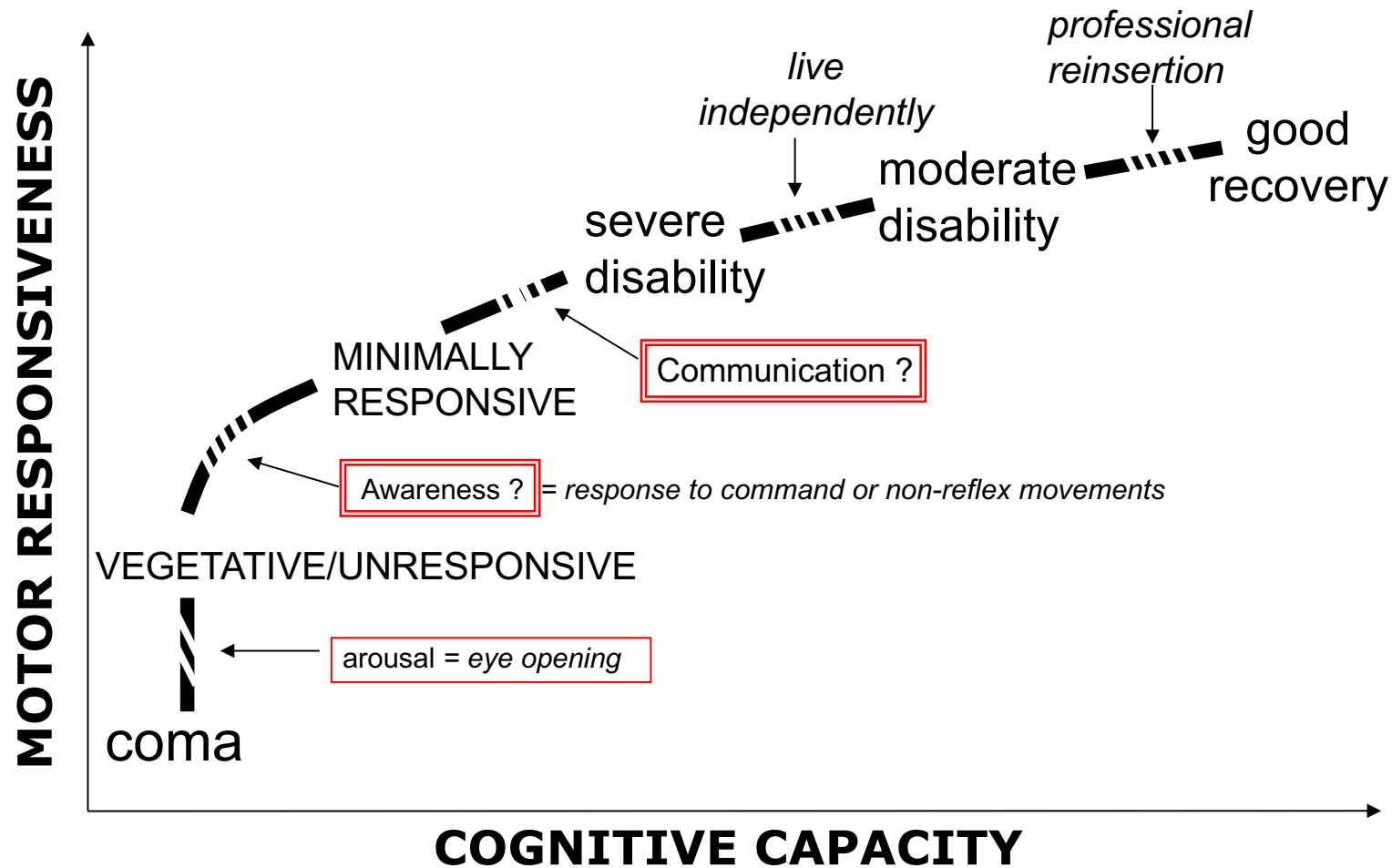
DMN ANTICORRELATIONS



Consciousness \approx top-down



Behavioral evaluation



Diagnostic error after coma



n=103 post-comatose patients

- 45 clinical consensus diagnosis 'vegetative state'
- 18 signs of awareness (Coma Recovery Scale)

↘ 30-40% potential misdiagnosis

JFK COMA RECOVERY SCALE - REVISED ©2004		Record Form	
Patient:	Date:		
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			

* **SELF-STUDY DVD OFFER** *

**COMA RECOVERY SCALE - REVISED:
GUIDELINES FOR ADMINISTRATION AND
SCORING**



coma@ulg.ac.be



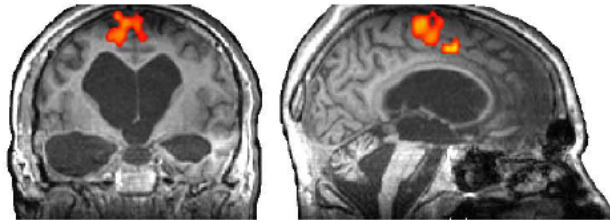
Schnakers et al, *BMC Neurology*, 2009
Stender et al, *Lancet*, 2014

fMRI-based

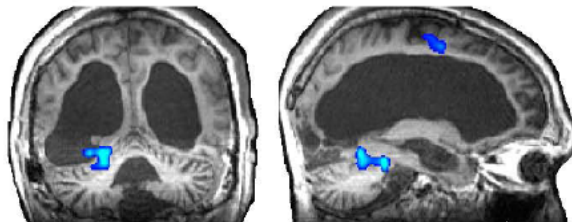


Imagine **Tennis** to answer 'YES'
Imagine **Navigating** to answer 'NO'

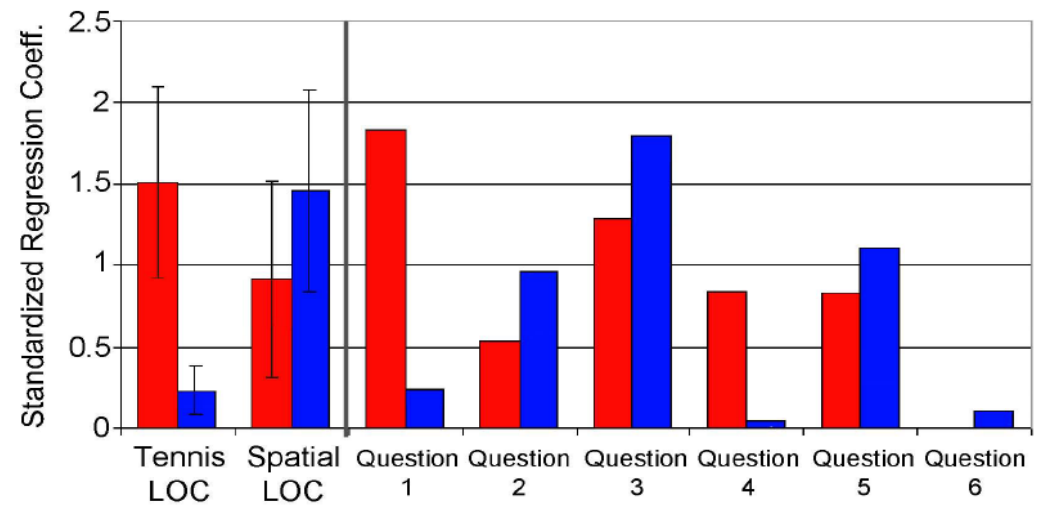
Is your father's name Alexander ?



Is your father's name Thomas ?



The NEW ENGLAND
JOURNAL of MEDICINE



EEG-based



“MOVE YOUR FOOT”

“MOVE YOUR HAND”



HEALTHY
CONTROL
SUBJECT



“VEGETATIVE”
UNRESPONSIVE
PATIENT



Noirhomme et al *NeuroImage* 2015

Lesenfants, Habbal et al *J Neural Engineering* 2014

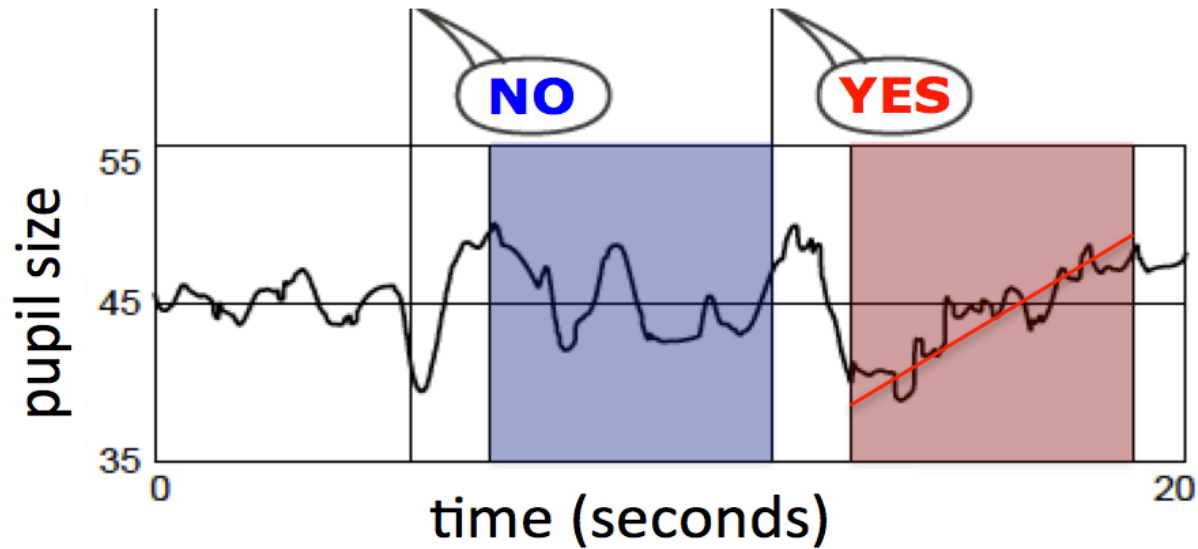
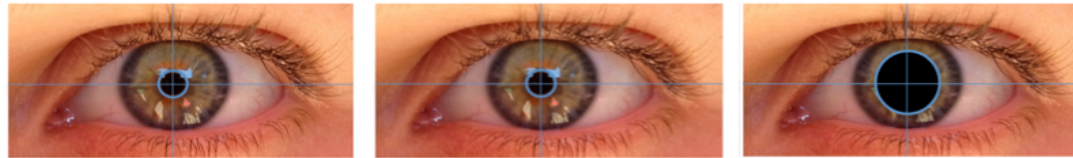
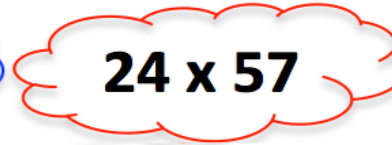
Cruse et al *Lancet*, 2011, also see Goldfine et al, *Lancet*, 2013



Pupil-based



IS YOUR
NAME CLARA?



Current
Biology

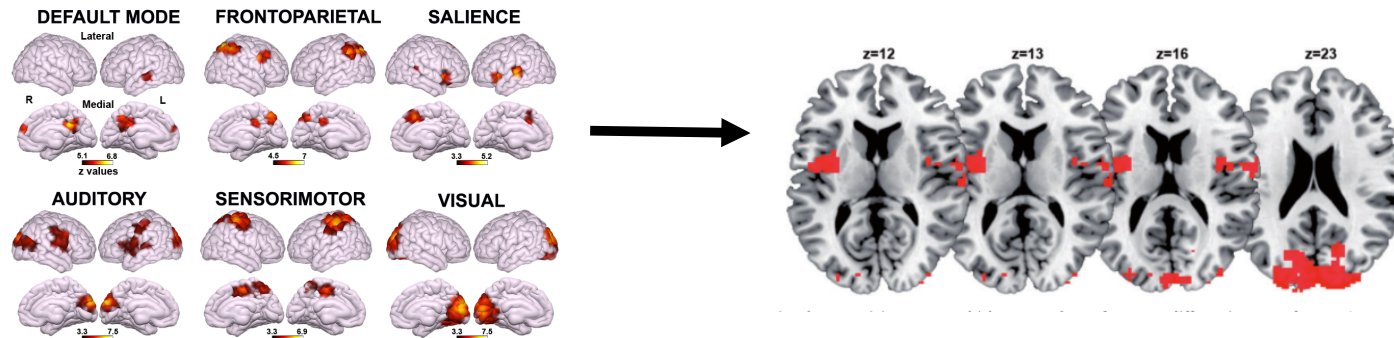
Philipps



Universität
Marburg

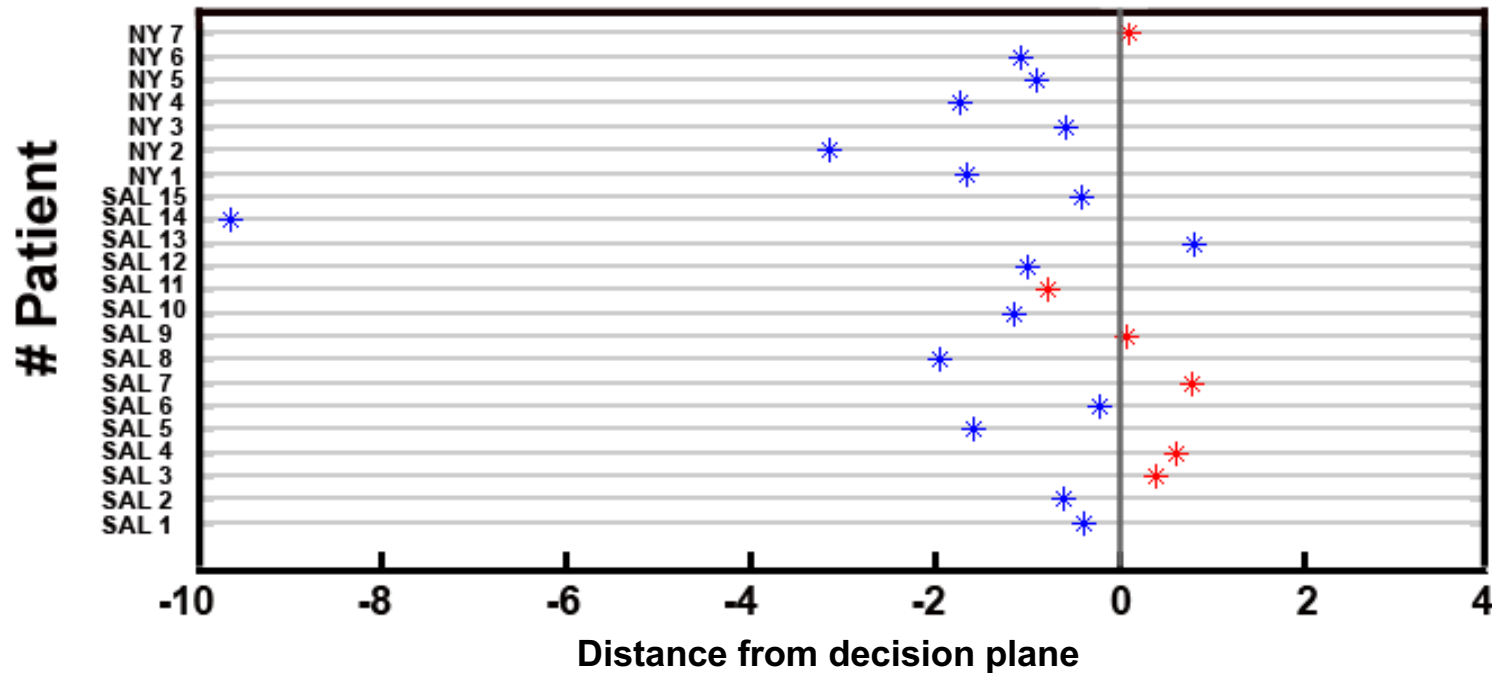


Individualized automated assessment



Classification MCS

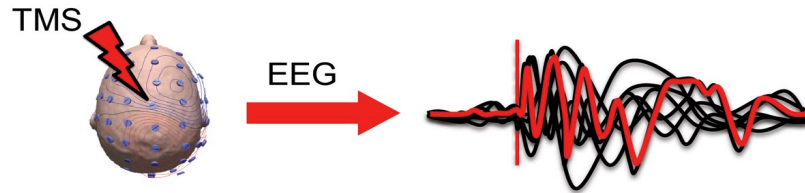
Classification VS/UWS



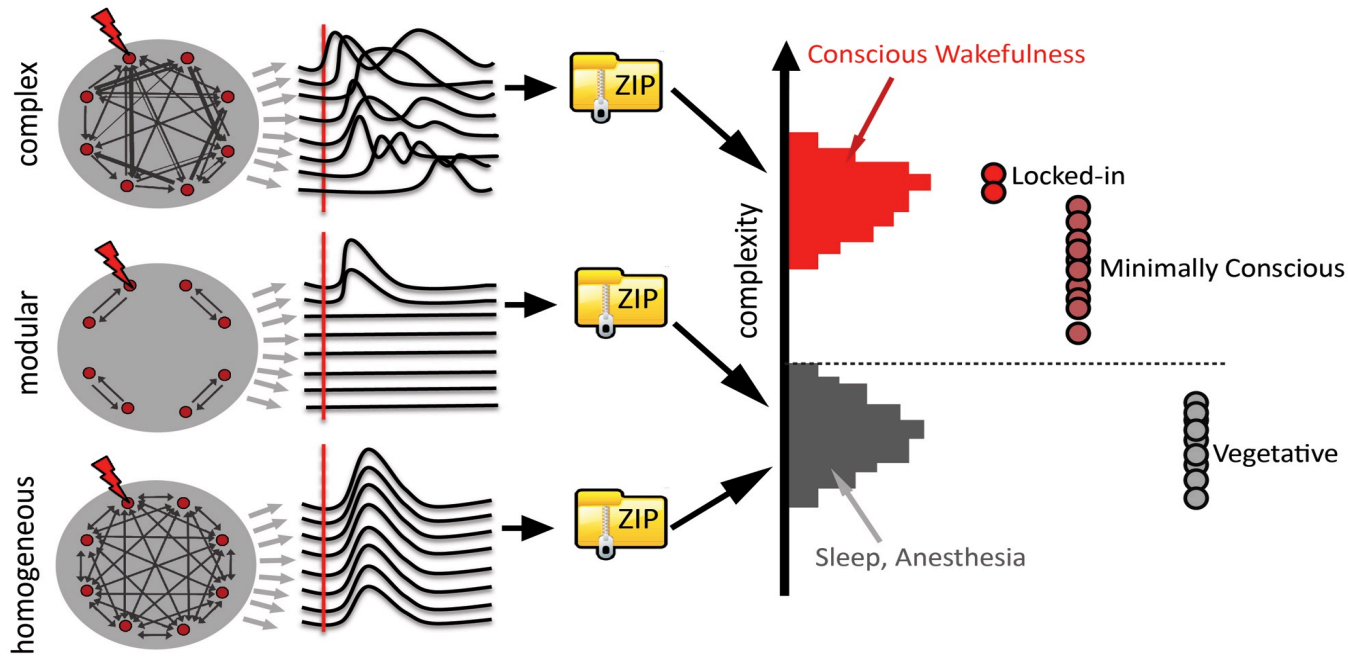
Individual thresholds (1)



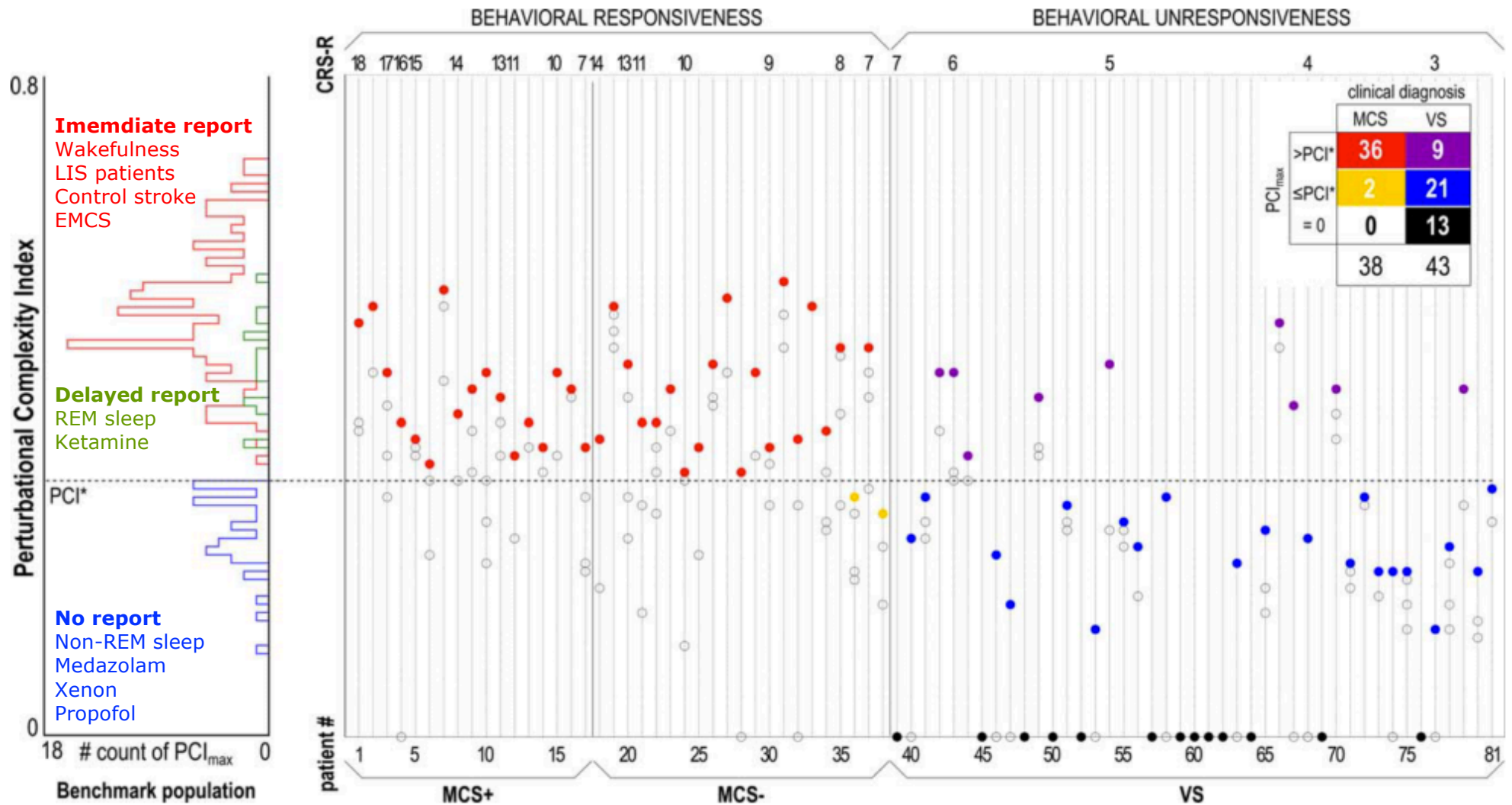
Perturbational Complexity Index



perturbation → recording → compression → reference scale → patients



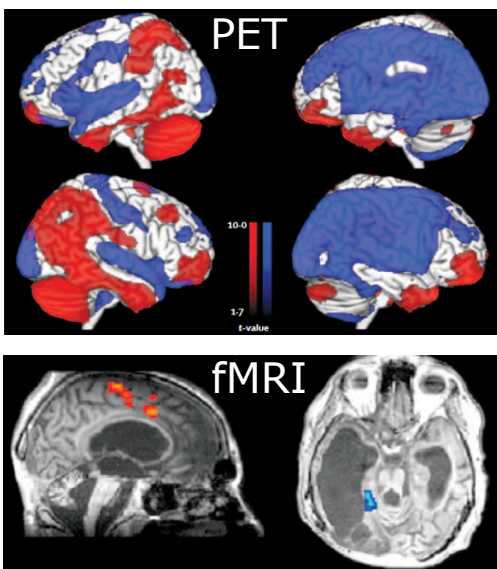
Individual thresholds (2)



Multi-modal imaging



130 patients (29/y)
 4 excluded (3%)
 81 MCS
 41 VS/UWS
 4 LIS
 110 chronic (87%)
 78 non-trauma (62%)



Coma Recovery Scale-Revised results			
	UWS	MCS	Total
Clinical consensus diagnosis			
VS/UWS	33 (37%)	18 (20%)	51 (57%)
MCS	2 (2%)	36 (40%)	38 (43%)
Total	35 (39%)	54 (61%)	89 (100%)
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%)
Mental imagery fMRI			
VS/UWS	25 (36%)	23 (33%)	48 (69%)
MCS	3 (4%)	19 (27%)	22 (31%)
Total	28 (40%)	42 (60%)	70 (100%)

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

Table 2: Diagnostic results by modality

35% clinical misdiagnosis

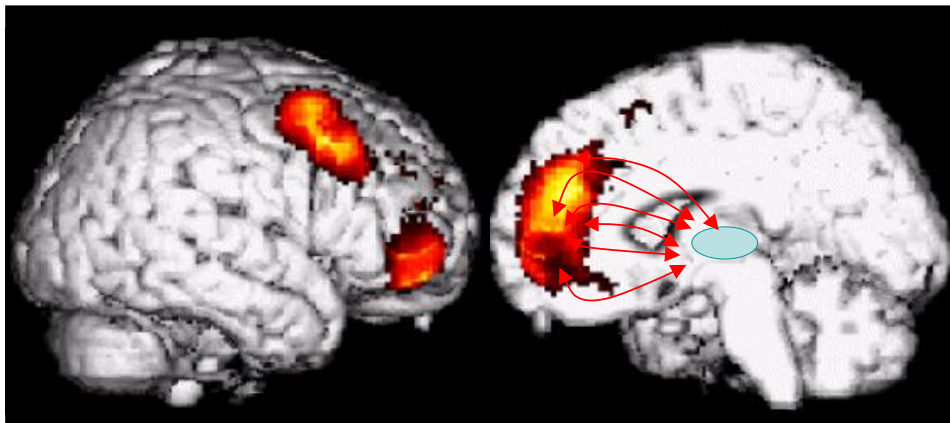
32% CRS-R misdiagnosis

THE LANCET

Consciousness \approx thalamo-cortical

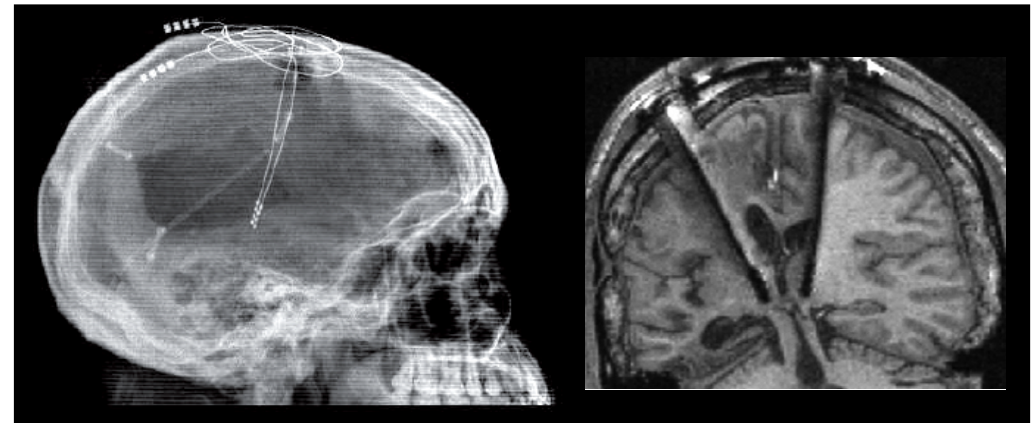


Intralaminar nuclei “reconnections”
in spontaneous recovery from
“vegetative” unresponsive state



Laureys et al, *Lancet* 2000

Intralaminar nuclei stimulation
induces “recovery” from
minimally responsive state

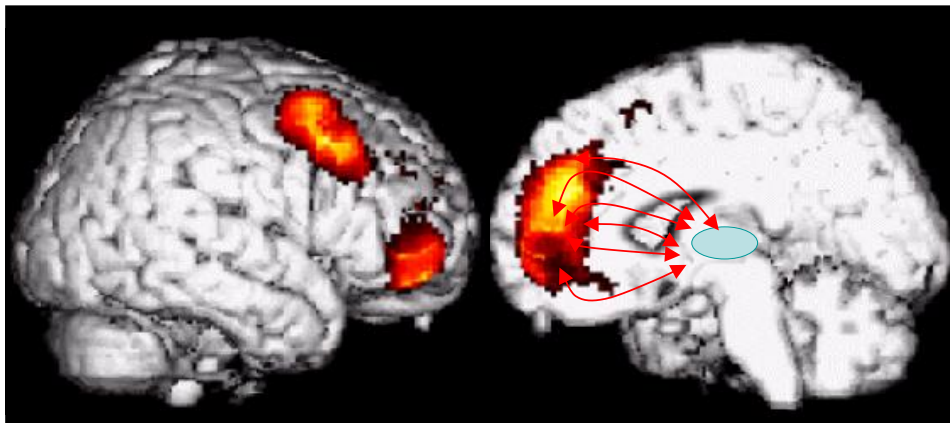


Schiff et al, *Nature* 2007

Consciousness \approx thalamo-cortical

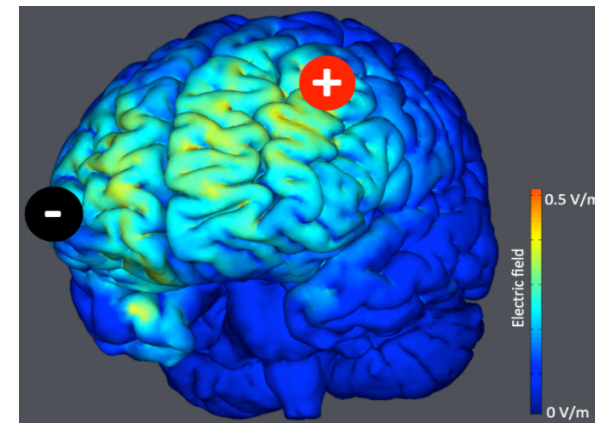


Intralaminar nuclei “reconnections”
in spontaneous recovery from
“vegetative” unresponsive state



Laureys et al, *Lancet* 2000

Transcranial direct current stimulation
(tDCS)



Thibaut et al, *Neurology* 2014

Ethical framework



The American Journal of Bioethics, 8(9): 3–12, 2008

Target Article

Neuroimaging and Disorders of Consciousness: Envisioning an Ethical Research Agenda

Joseph J. Fins, Weill Medical College of Cornell University*

Judy Illes, University of British Columbia*

James L. Bernat, Dartmouth Medical School**

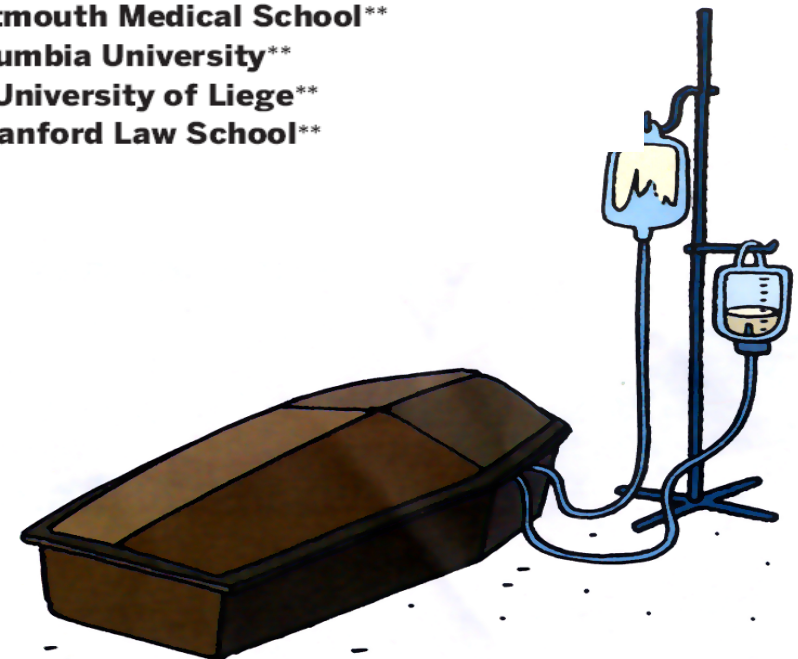
Joy Hirsch, Columbia University**

Steven Laureys, University of Liege**

Emily Murphy, Stanford Law School**

*Co-lead authors.

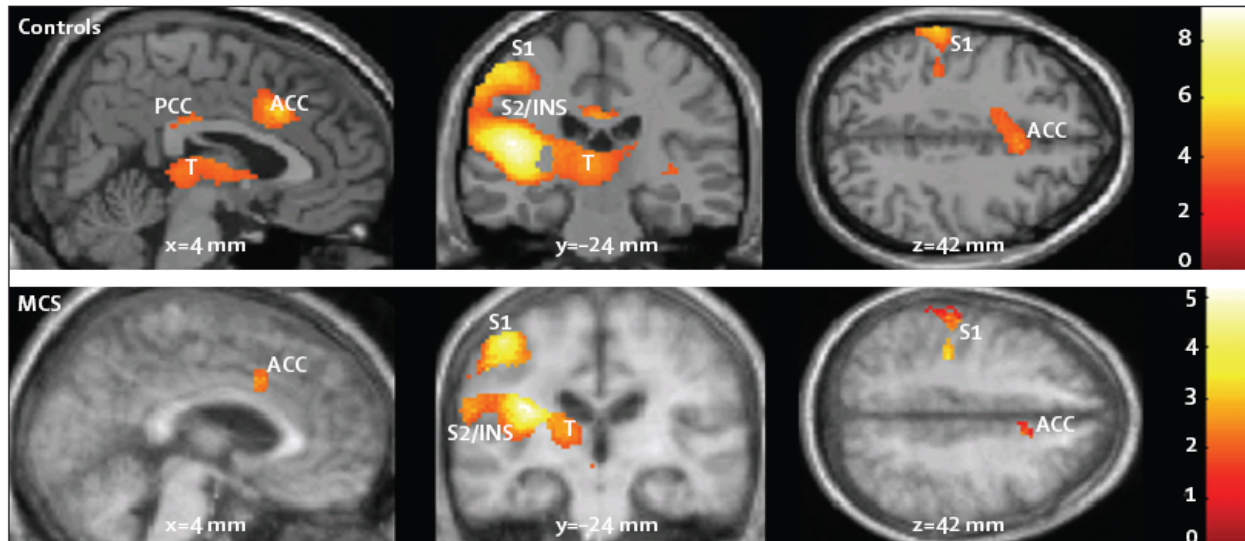
**Equal authors in alphabetical order.



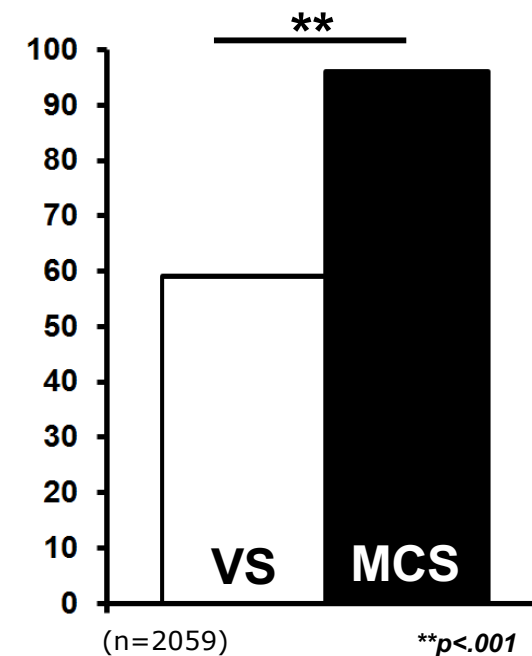
Pain in minimally conscious state



<http://neurology.thelancet.com>



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



Boly et al, *Lancet Neurol*, 2008

Demertzi et al, *Progr Brain Res* 2009
Demertzi & Racine et al, *Neuroethics* 2012

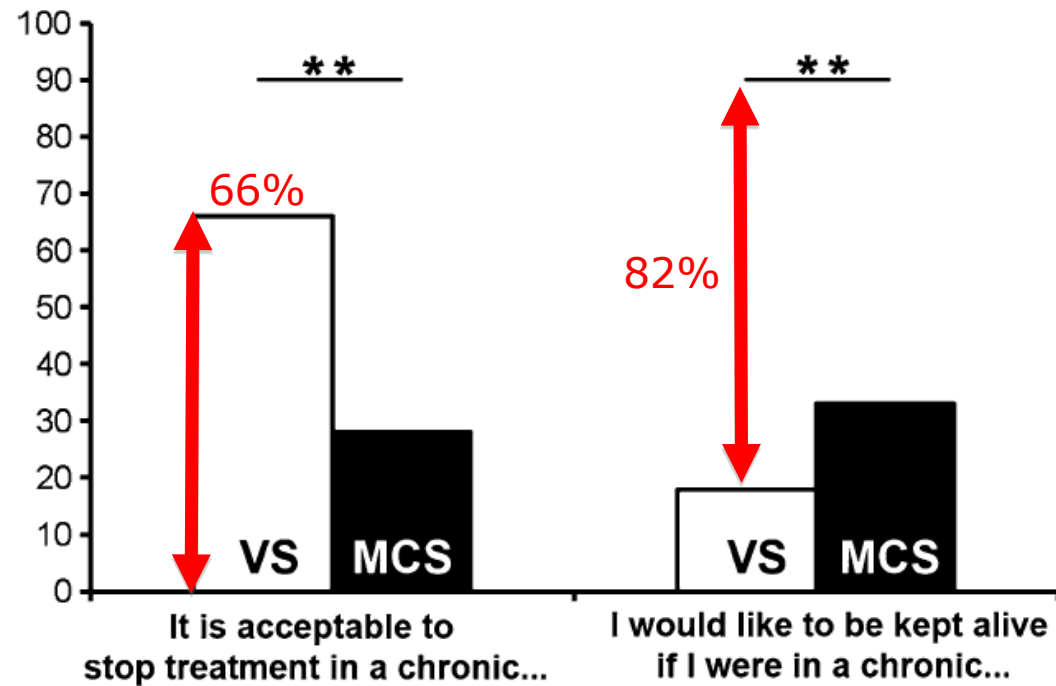
End of life options



- 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



Quality of life



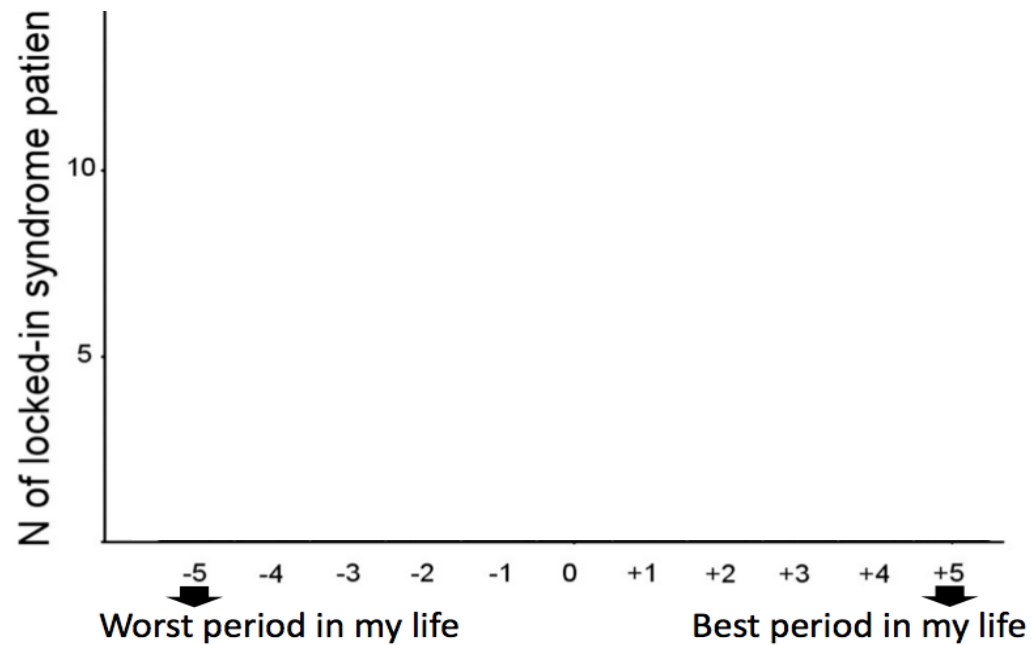
Open Access

Research



A survey on self-assessed well-being in a cohort of chronic locked-in syndrome patients: happy majority, miserable minority

Marie-Aur lie Bruno,¹ Jan L Bernheim,² Didier Ledoux,¹ Fr d ric Pellas,³ Athena Demertzi,¹ Steven Laureys¹



Conclusion

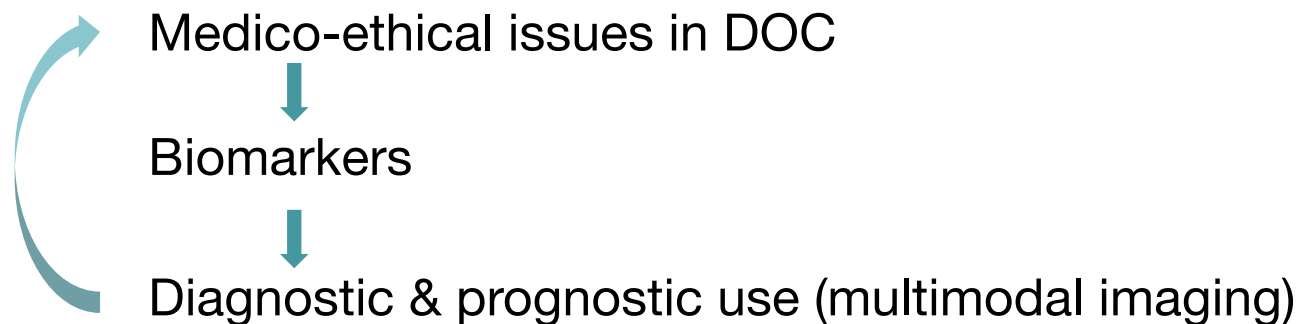
Confident diagnosis can be based on:

- probabilistic predictions
- multiple assessments with different technologies

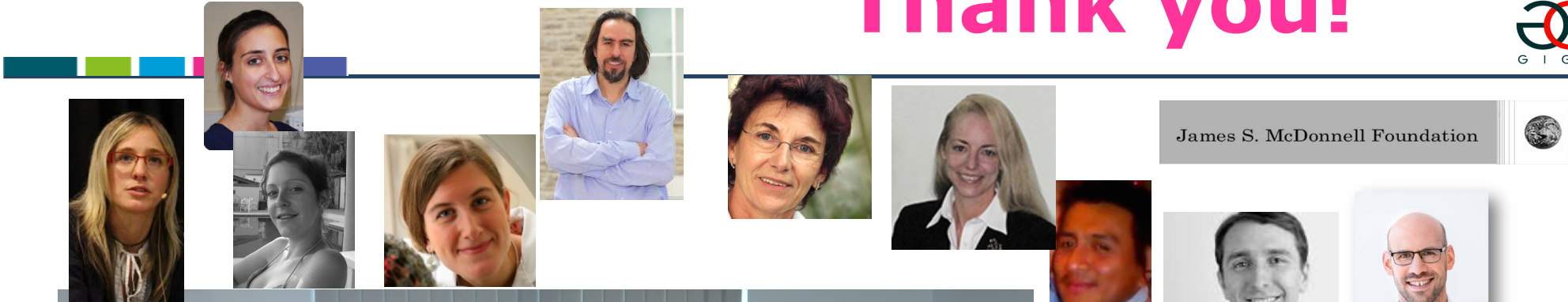
Need of a framework which will regulate the application order of techniques by balancing their:

- availability
- sensitivity
- specificity

based on underlying clinical assumptions about patients' conscious state



Thank you!



James S. McDonnell Foundation



Université de Liège



Coma Science Group

The departments of Neurology and Radiology
...and mostly patients and their families!

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a.demertzi@uliege.be



Human Brain Project

