

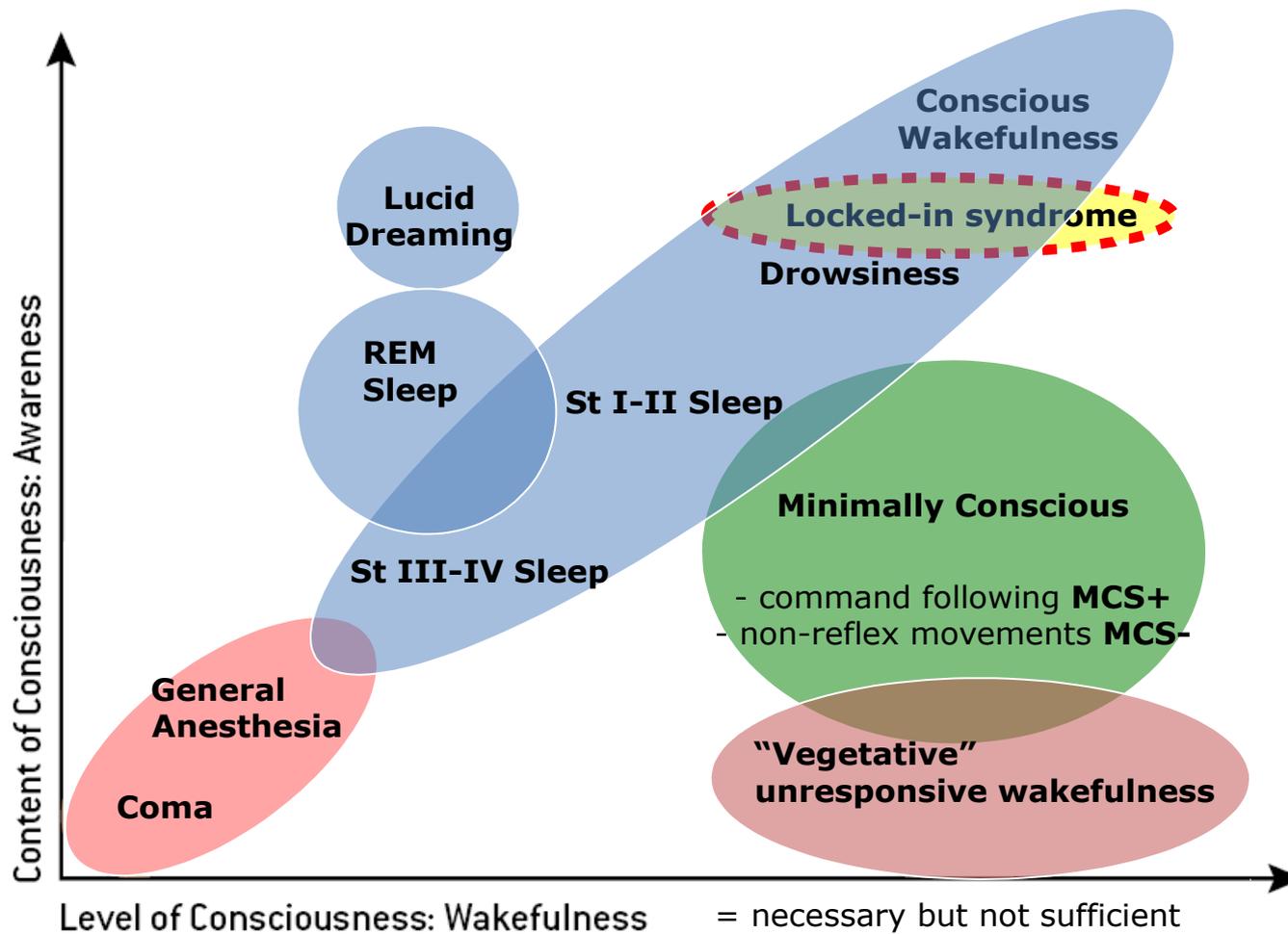
Neuroimaging & Consciousness

Georgios ANTONOPOULOS

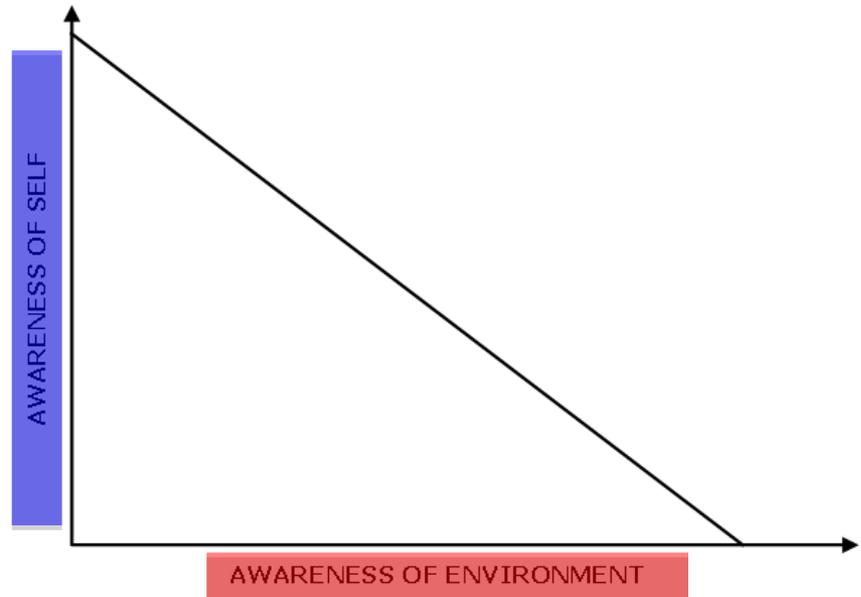
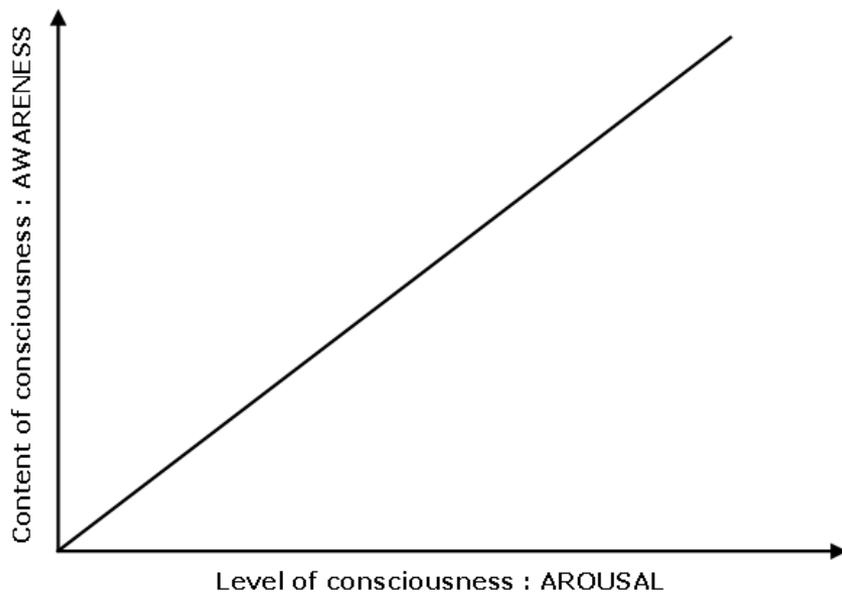
PhD student
Coma Science Group
GIGA Consciousness
University & University Hospital
Liège, Belgium



Arousal & awareness



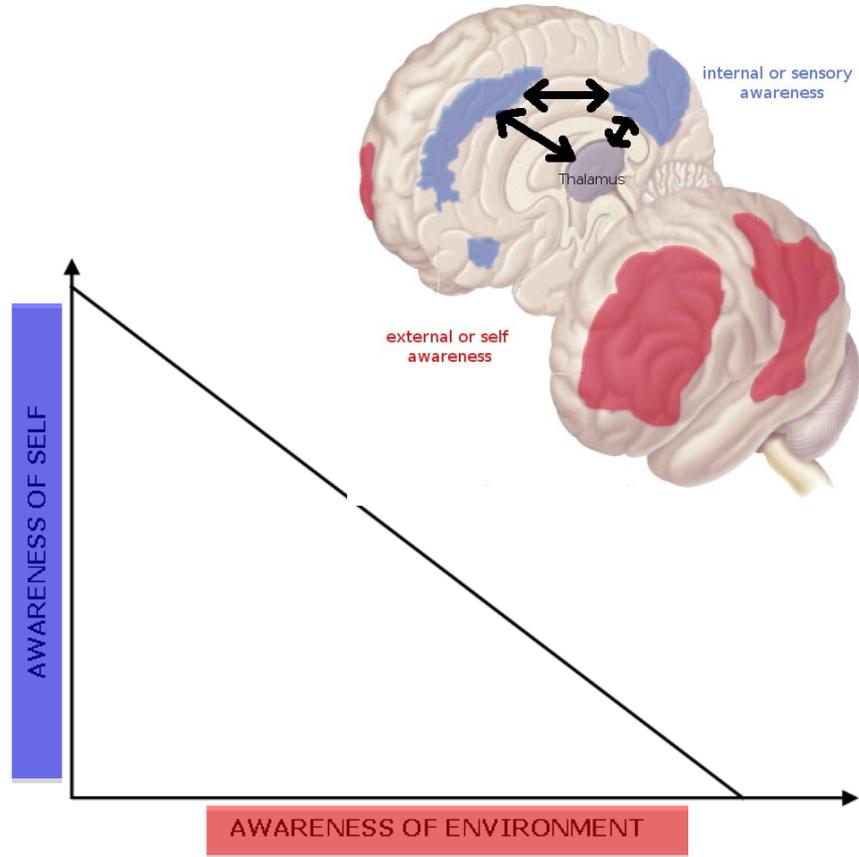
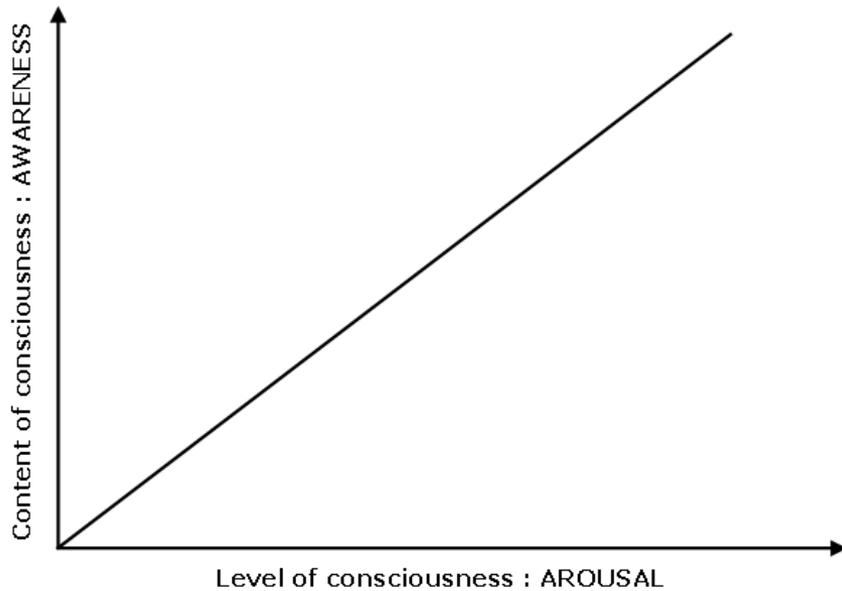
Measuring awareness



Boly et al, *Ann NY Acad Sci*, 2009

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

Measuring awareness



Boly et al, *Ann NY Acad Sci*, 2009

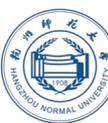
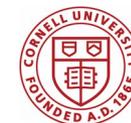
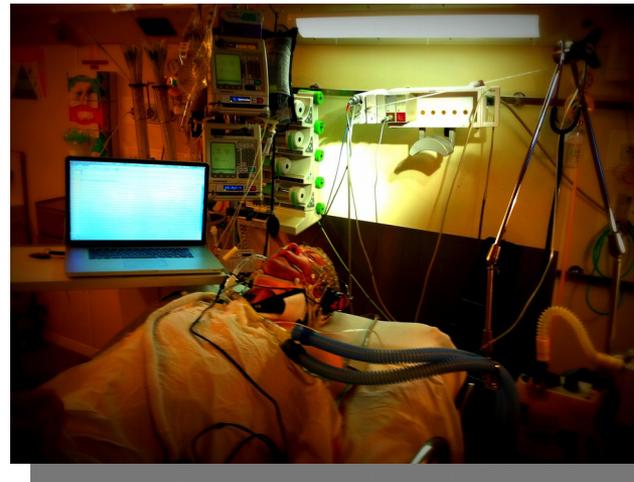
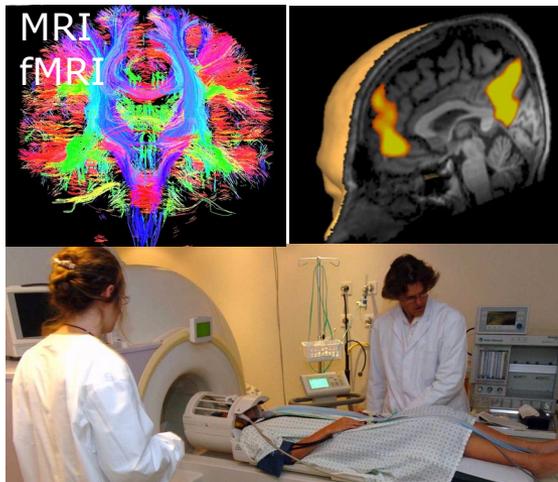
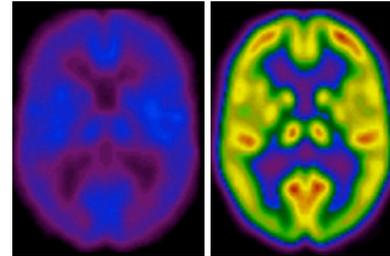
Vanhaudenhuyse & Demertzi et al, *J Cogn Neurosci*, 2011

Measuring brain activity

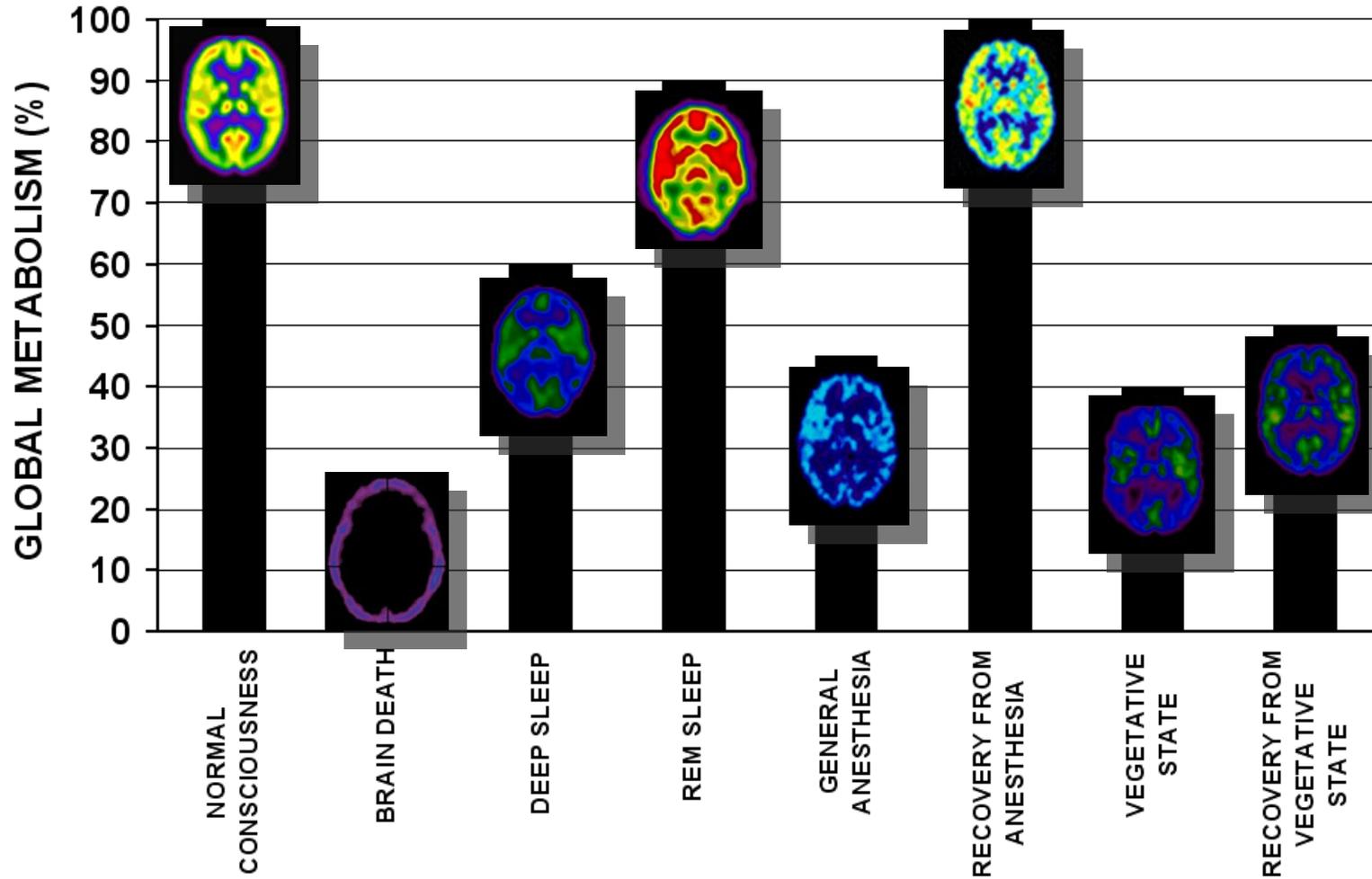


Altered states of consciousness

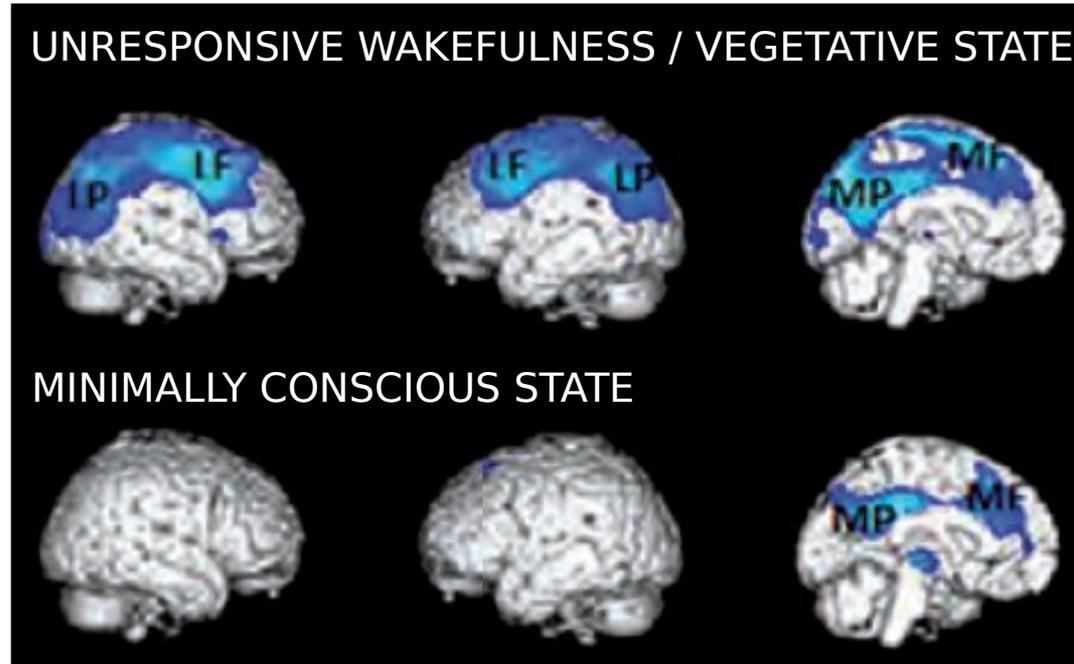
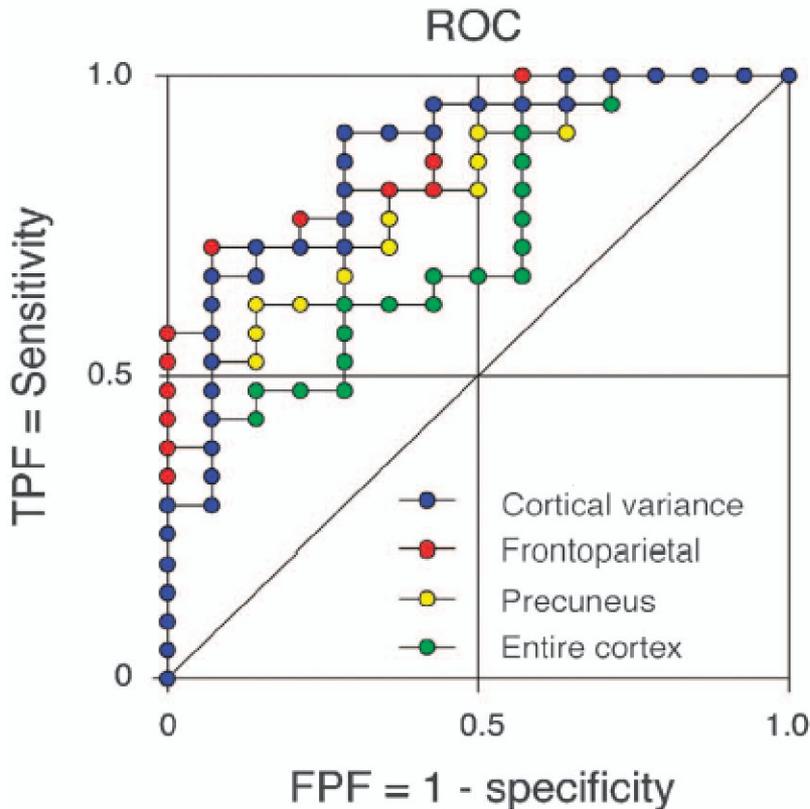
- Pathological: DoC
- Pharmacological: anaesthesia
- Physiological: hypnosis



Consciousness and global brain function

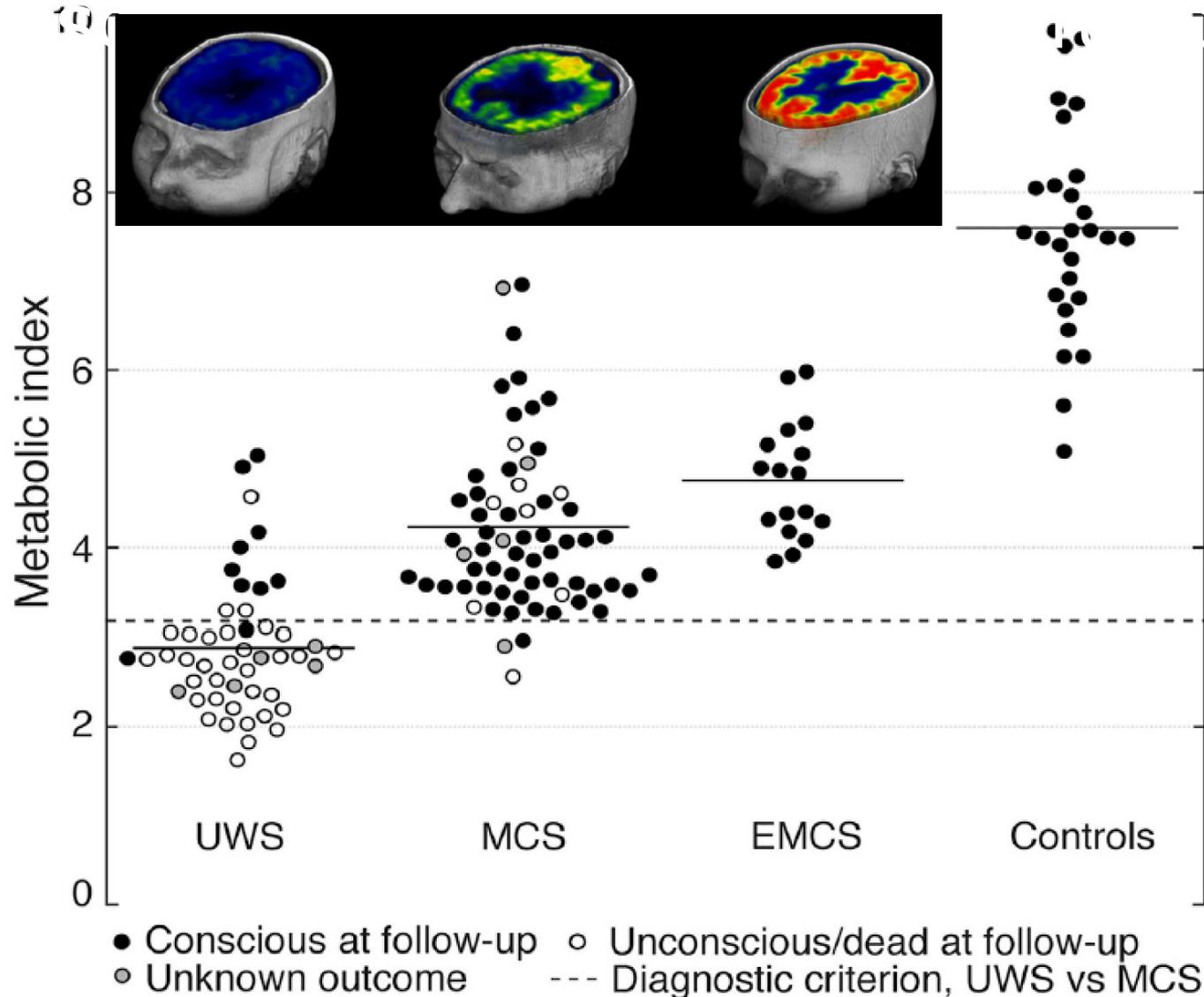


“Global workspace” of consciousness

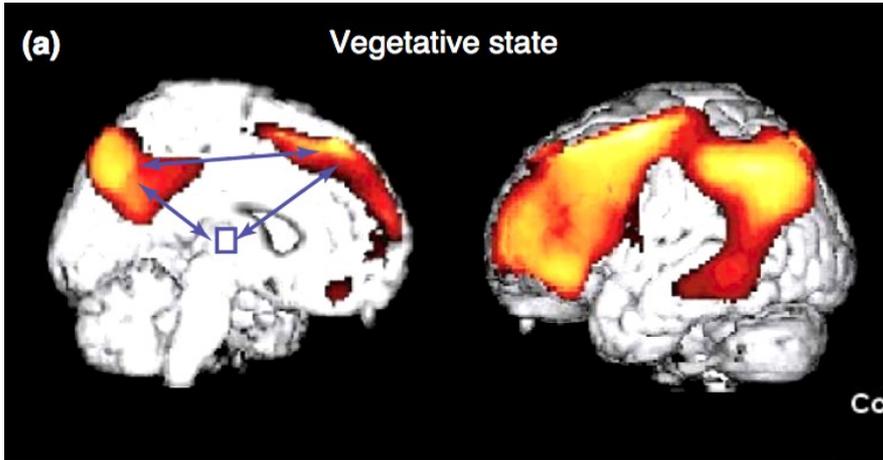


Stender et al, *J Cereb Blood Flow & Metab*, 2015
Thibaut et al, *J Rehabil Med*, 2012

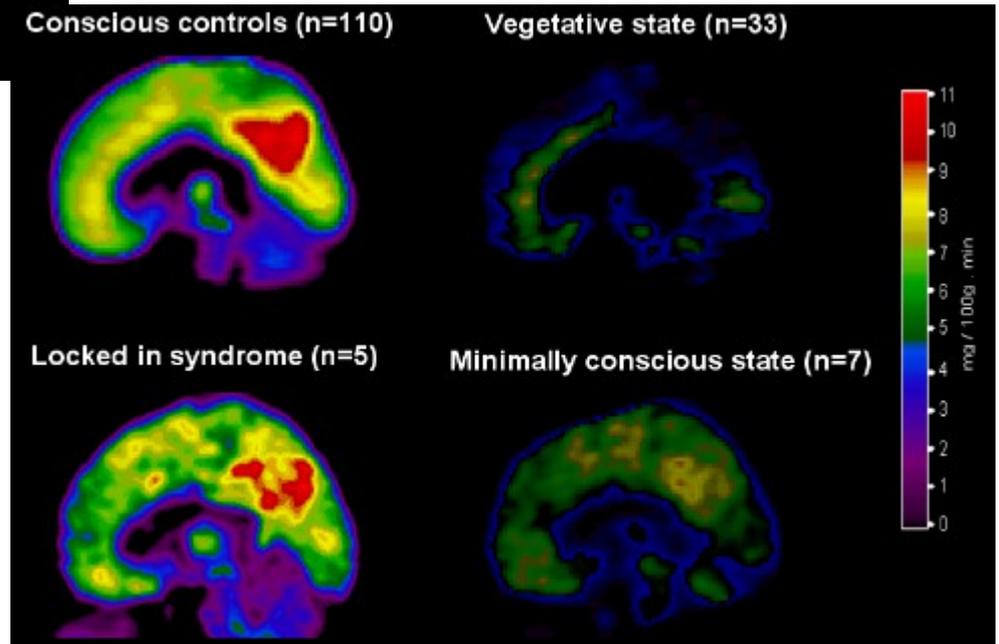
Consciousness and global brain function



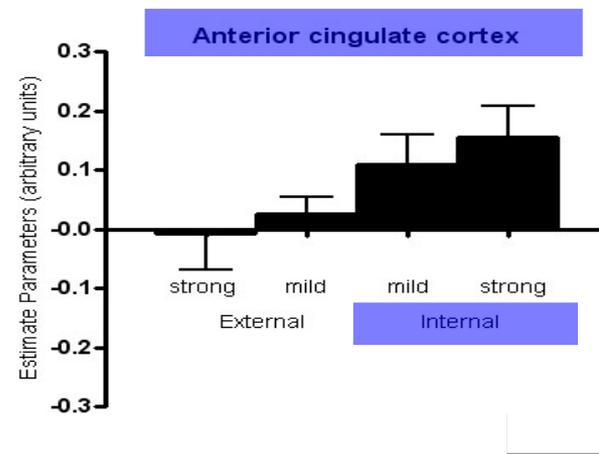
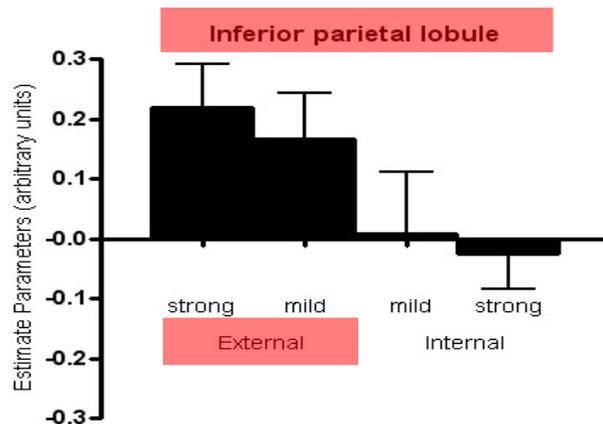
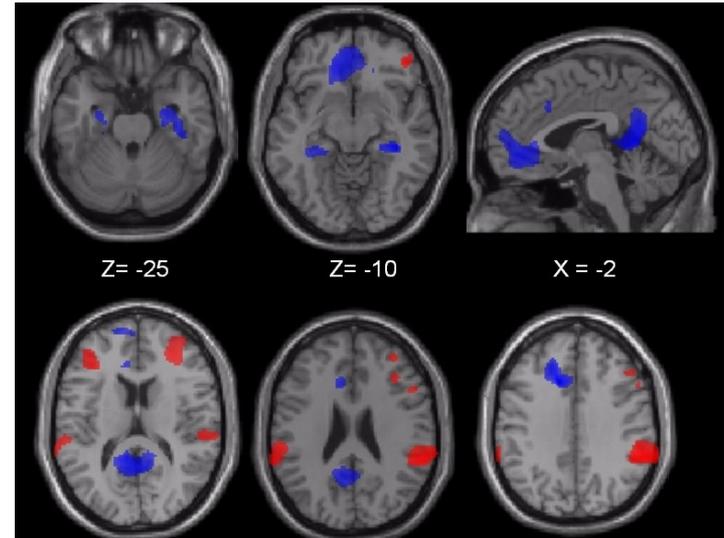
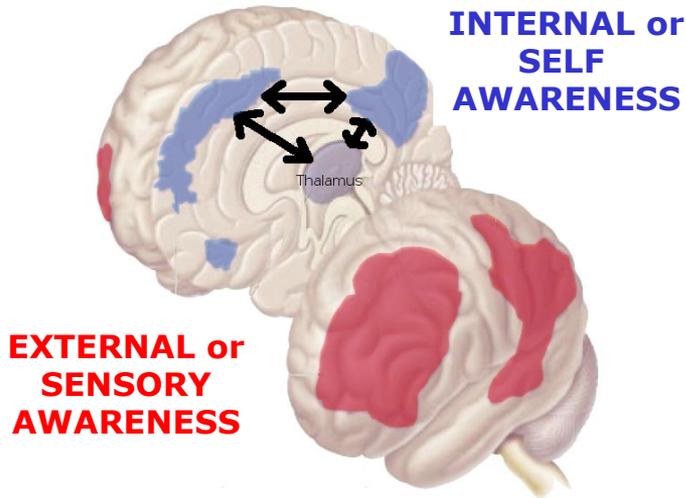
“Global workspace” of consciousness



Precuneus seems a critical hub

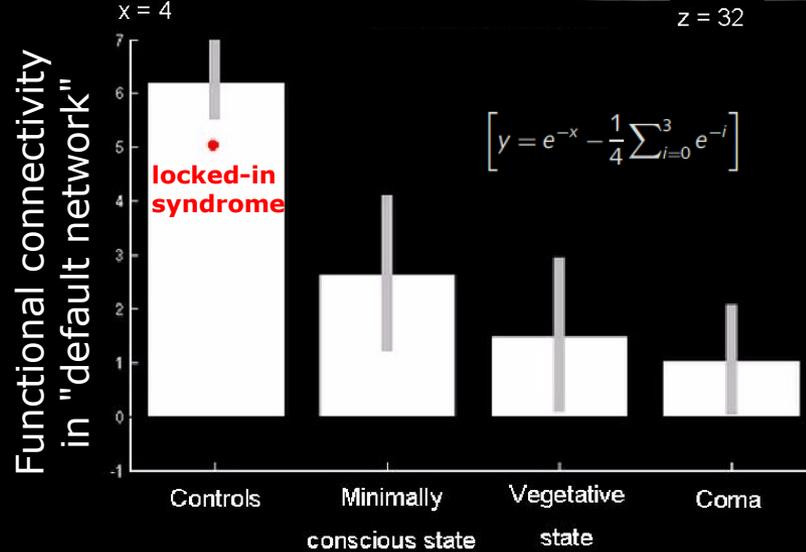
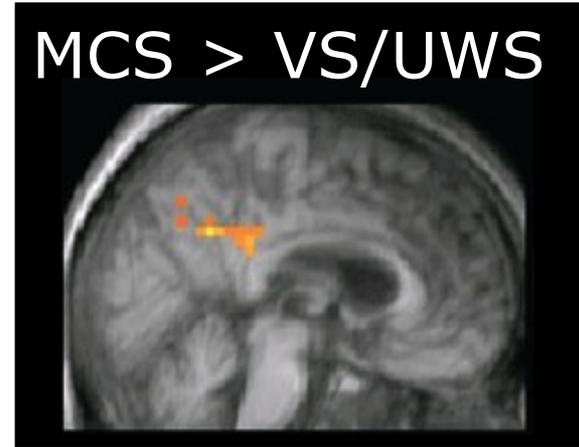
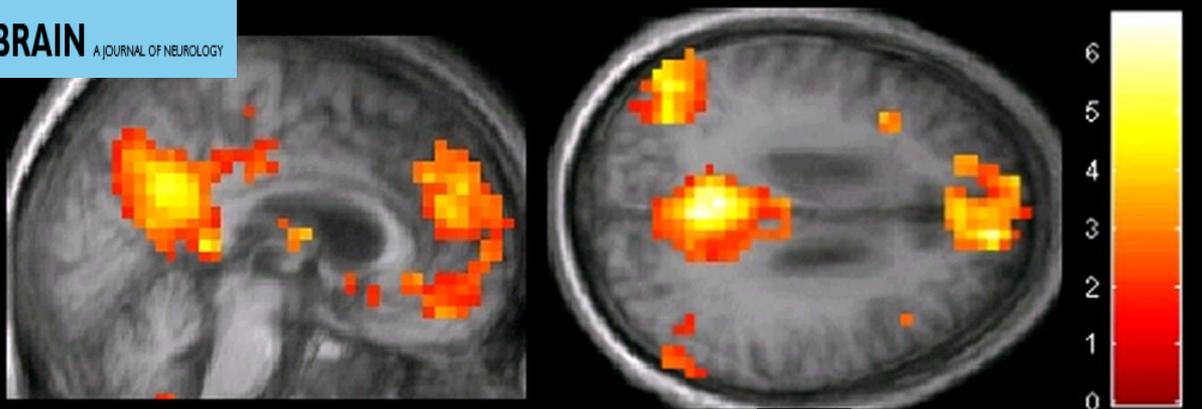


External & internal awareness



“Resting” fMRI after coma

BRAIN
A JOURNAL OF NEUROLOGY



Vanhaudenhuyse et al, *Brain*, 2010
Demertzi et al, *Brain*, 2015

Multi-modal imaging



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

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

40% potential misdiagnosis

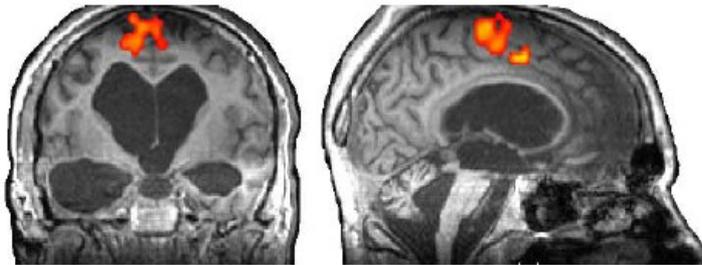
Solution: Coma Recovery Scale Revised (CRS-R)

fMRI-based communication

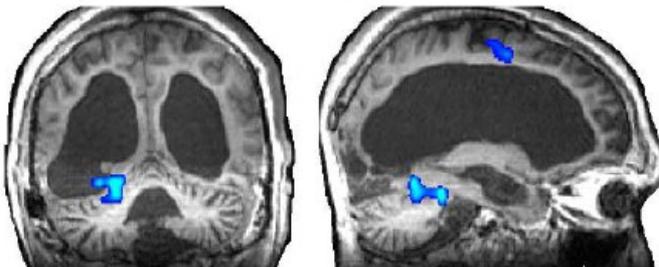


Imagine **Tennis** to answer 'YES'
Imagine **Navigating** to answer 'NO'

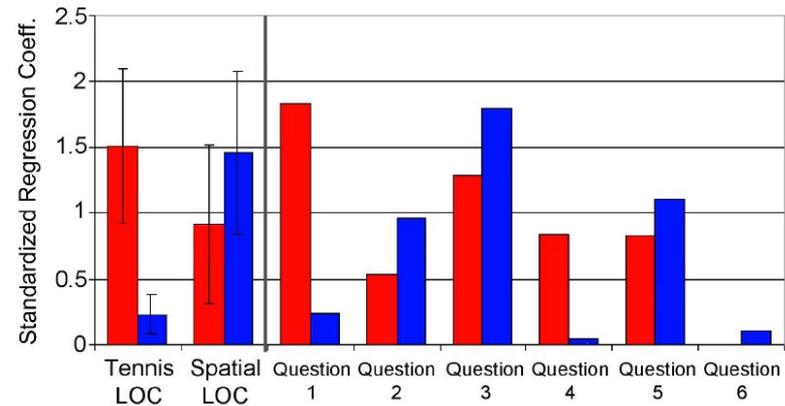
Is your father's name Alexander ?



Is your father's name Thomas ?



The NEW ENGLAND
JOURNAL of MEDICINE



Brain Computer Interfaces

“MOVE YOUR FOOT”



“MOVE YOUR HAND”



CONTROL
SUBJECT

“VEGETATIVE”
UNRESPONSIVE
PATIENT

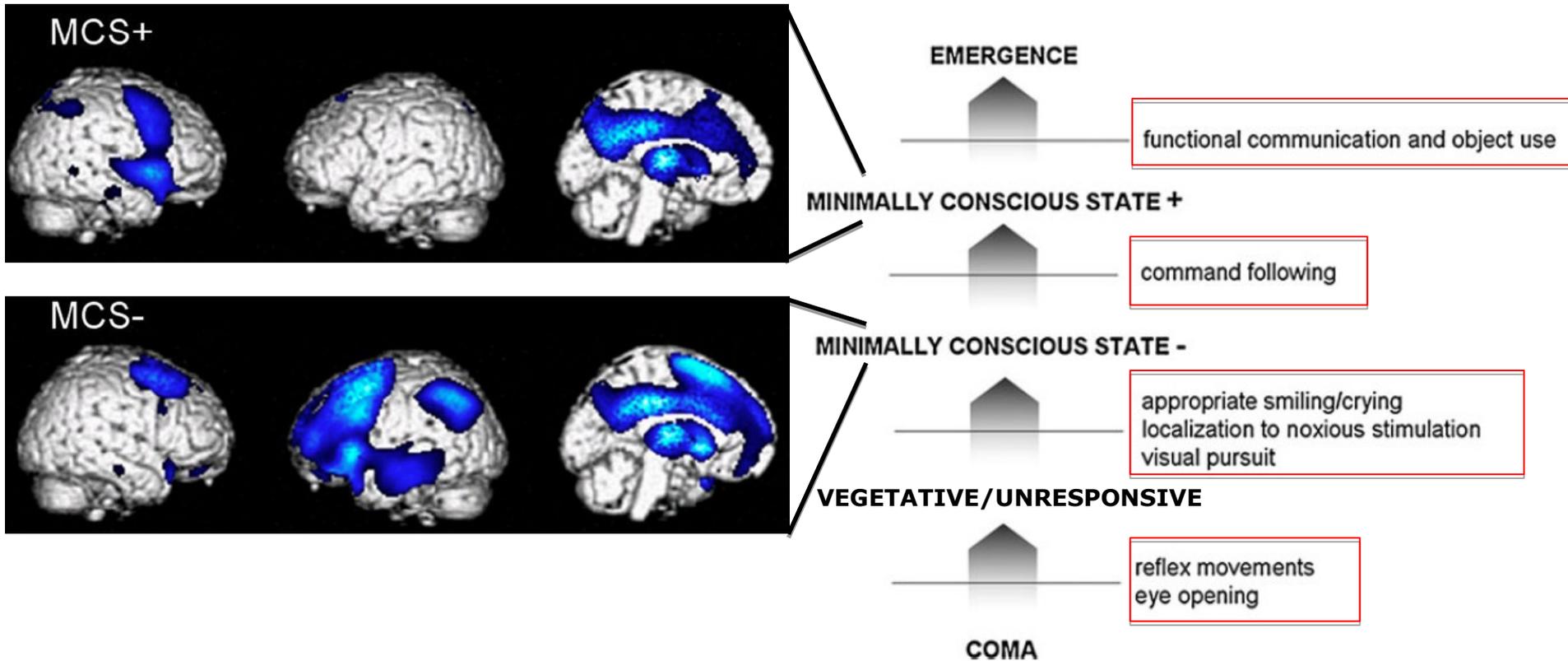


Noirhomme et al *NeuroImage* 2015

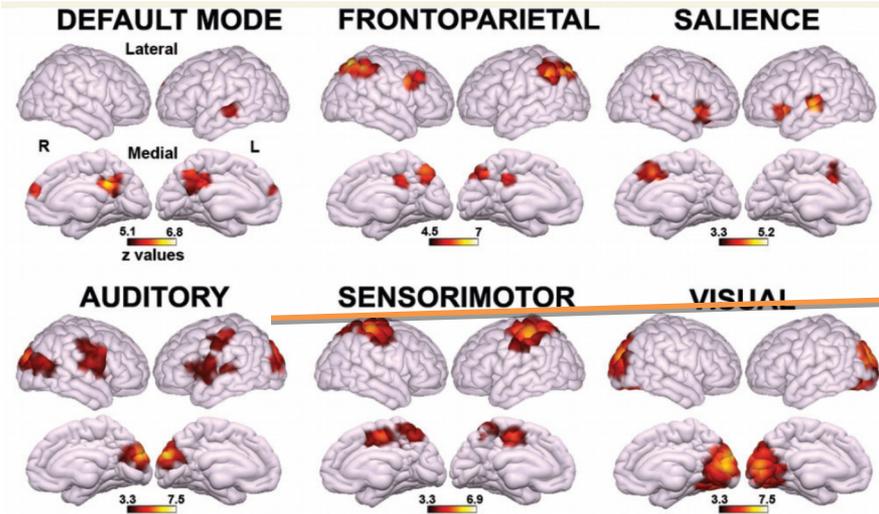
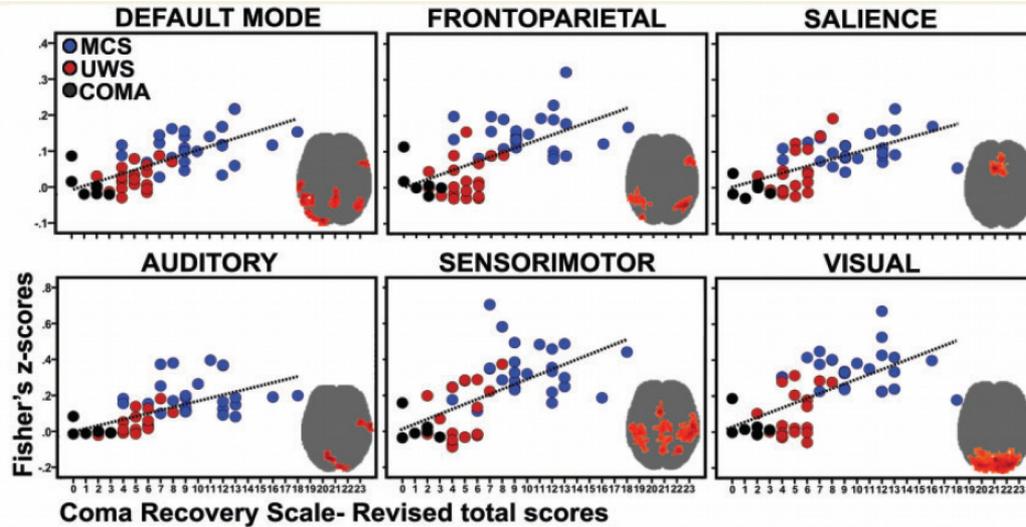
Lesenfants, Habbal et al *J Neural Engineering* 2014

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

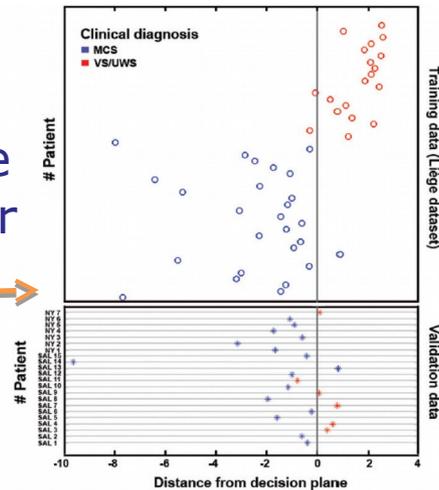
Aphasia and consciousness



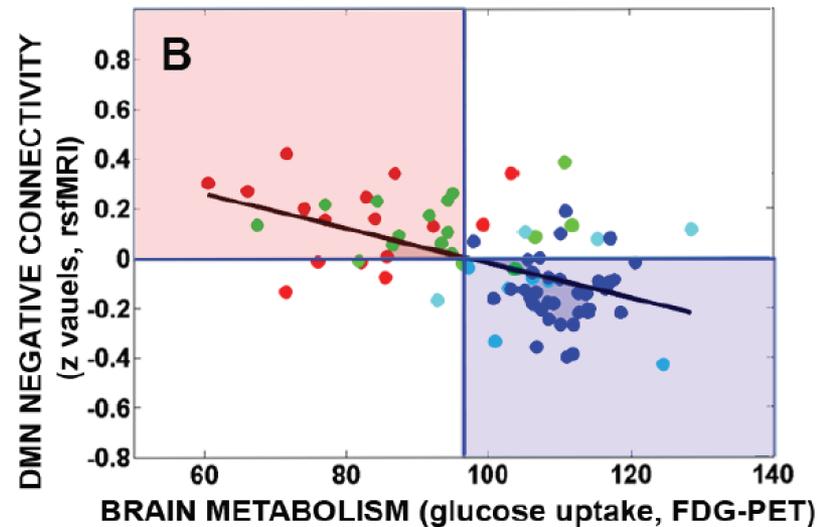
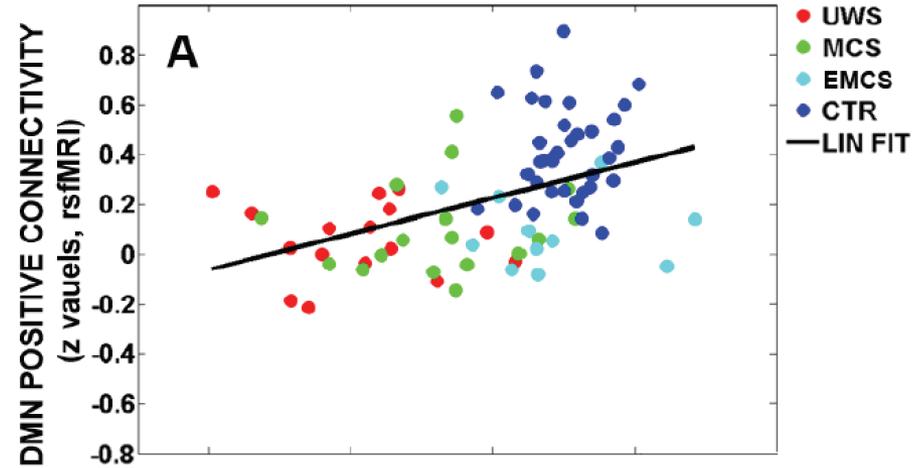
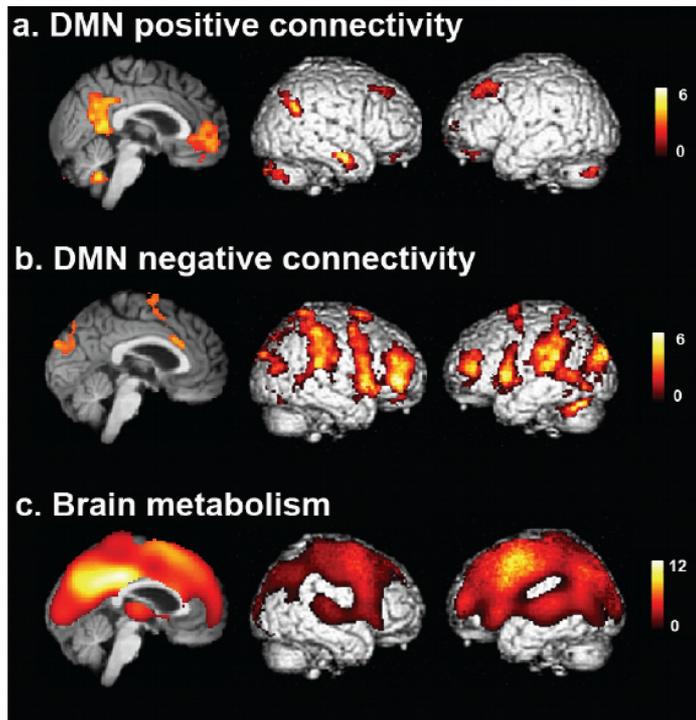
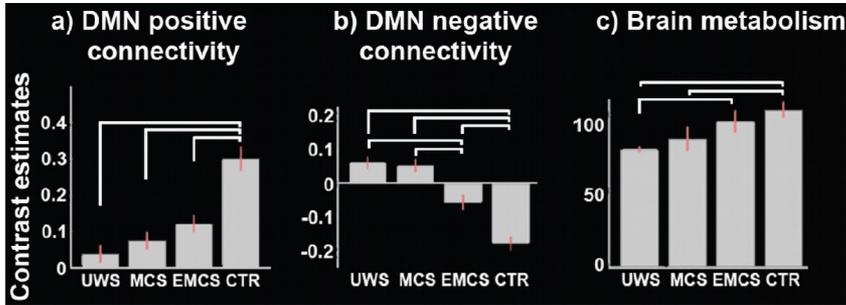
Classifying “resting” fMRI



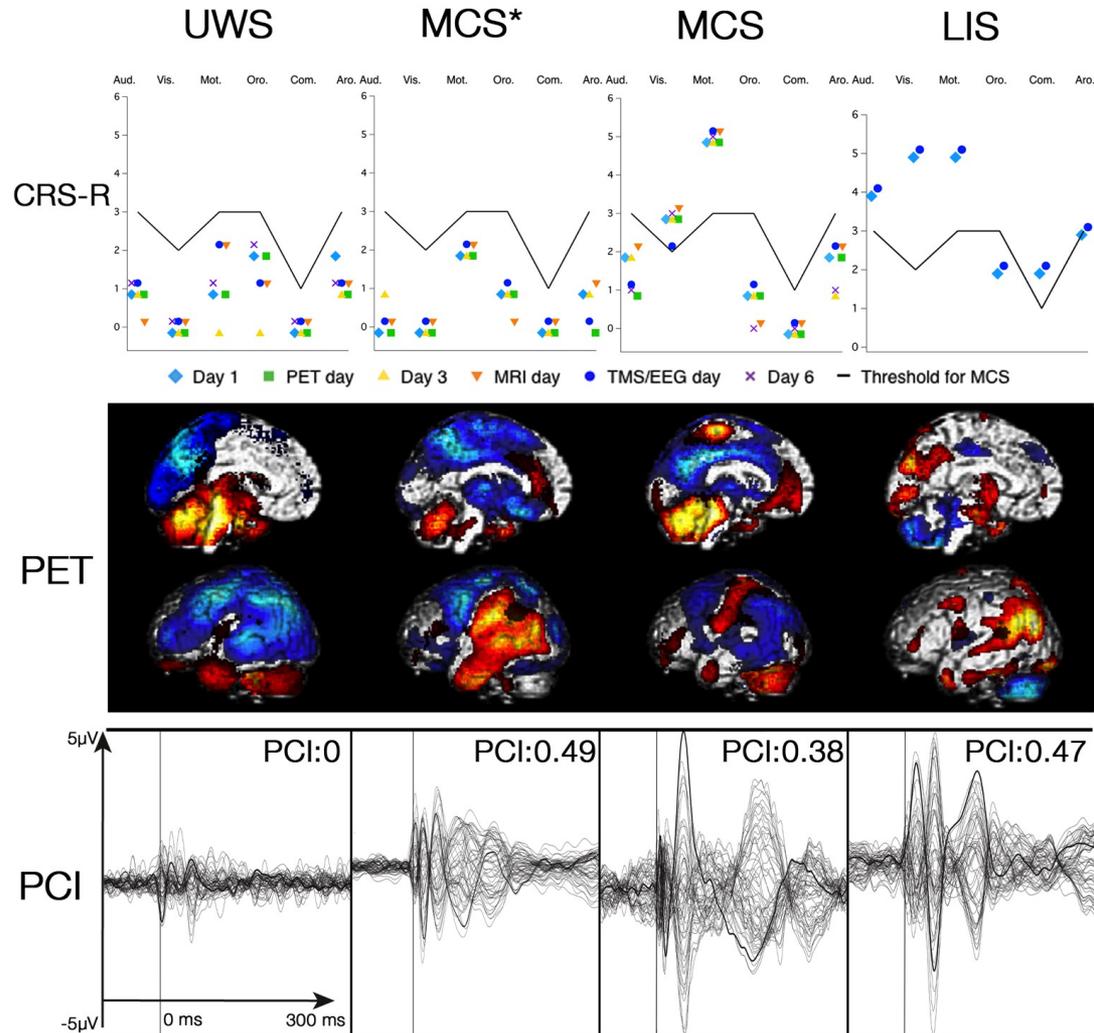
support
vector
machine
classifier



Pathological hyper-connectivity



Congruent PET & PCI results

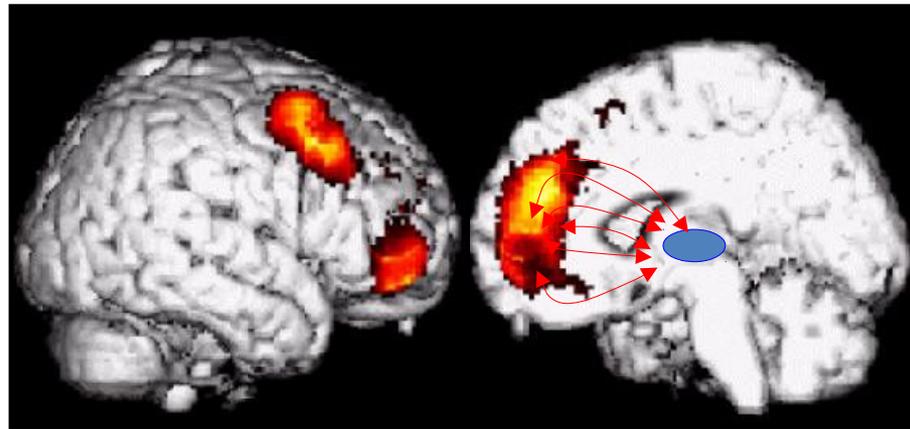


Consciousness \approx thalamo-cortical

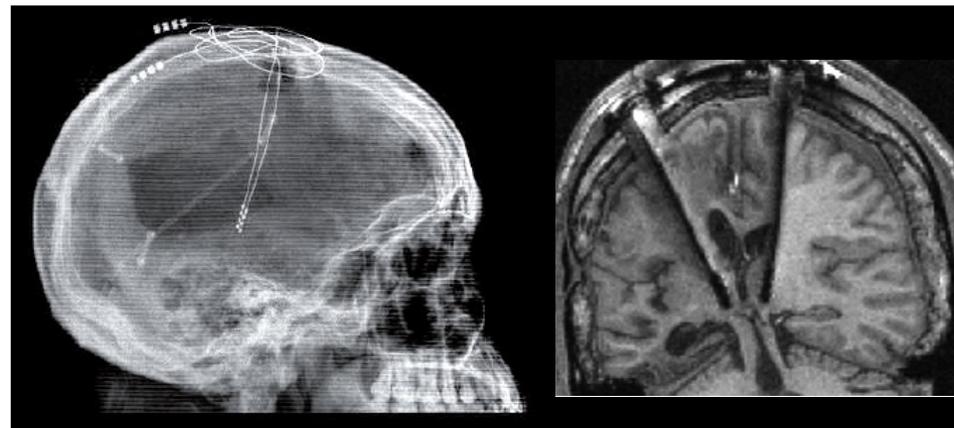


thalamo-cortical "reconnections"
in spontaneous recovery from
vegetative / unresponsive wakefulness

thalamo-cortical stimulation
induces "recovery" from
minimally responsive state



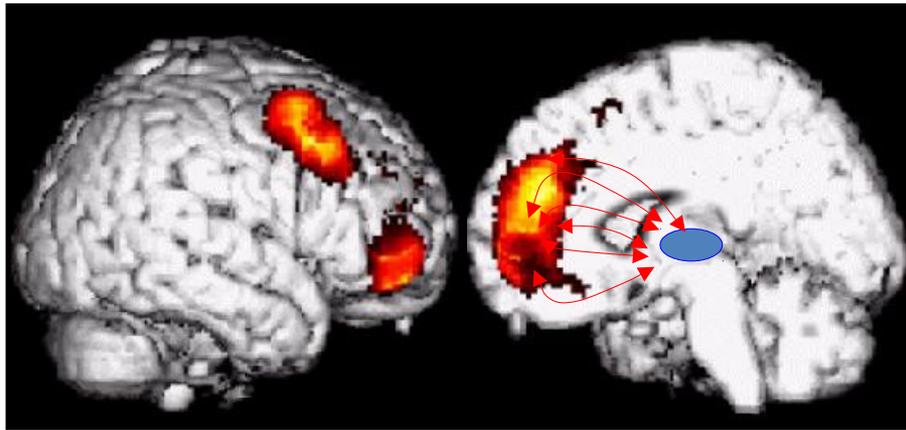
Laureys et al, *Lancet* 2000



Schiff et al, *Nature* 2007

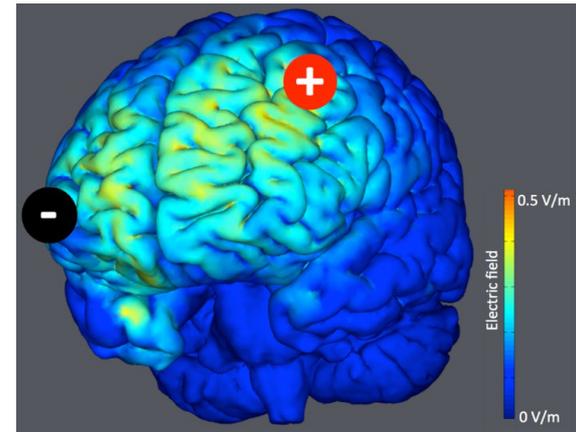
Consciousness \approx thalamo-cortical

thalamo-cortical “reconnections”
in spontaneous recovery from
vegetative / unresponsive wakefulness



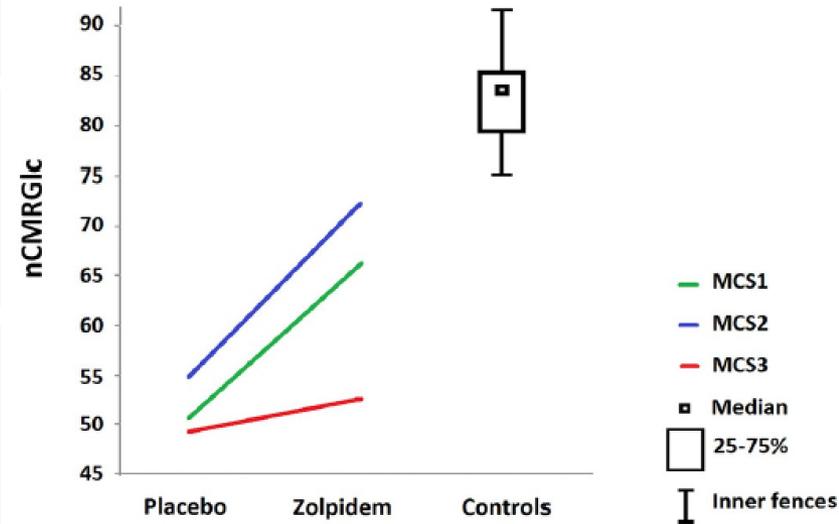
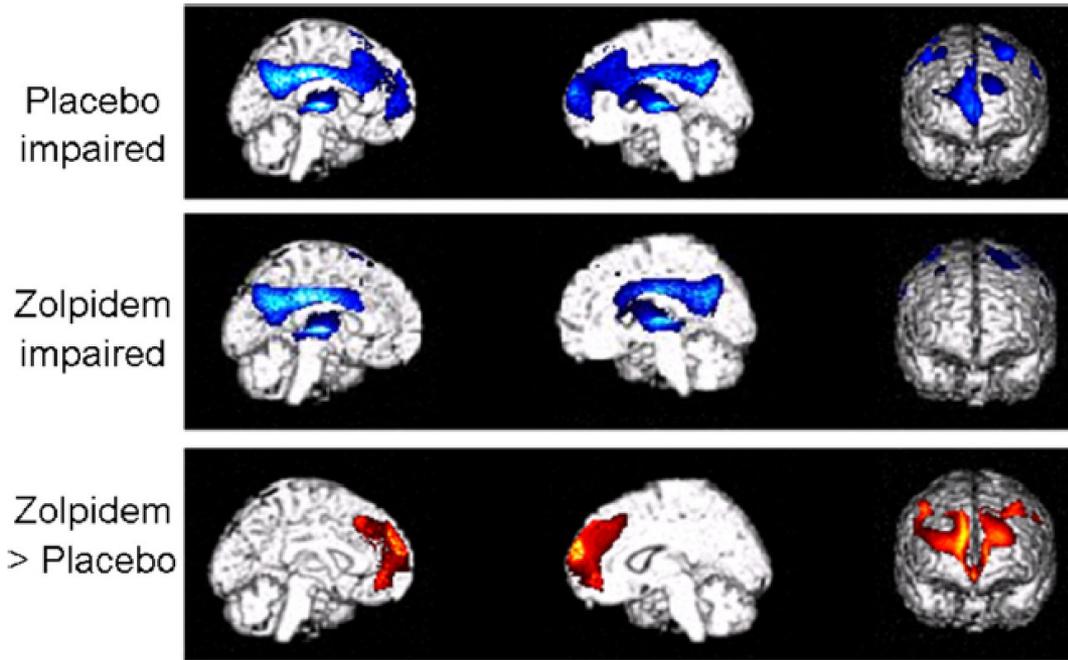
Laureys et al, *Lancet* 2000

Transcranial direct current stimulation
(tDCS)



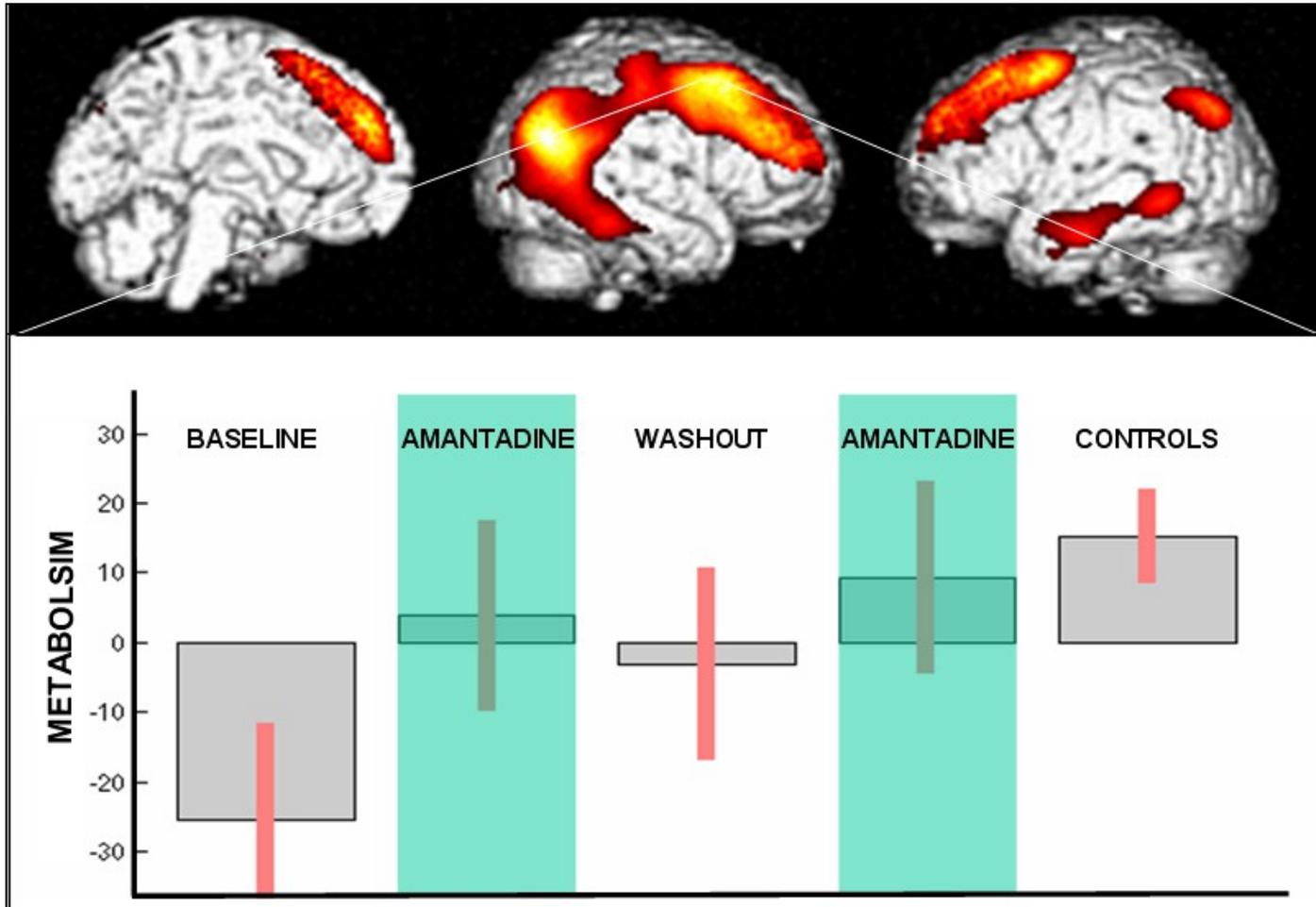
Thibaut et al, *Neurology* 2014 & *Brain Stim* 2015,
Thibaut et al, *Brain Injury* 2017
Cavaliere, *Front Cell Neurosci* 2016
Huang et al, *Brain Stim* 2017

Zolpidem treatment



Thonnard et al, *Funct Neurology*, 2013
 Chatelle et al, *Front Hum Neurosci*, 2014
 Williams... Schiff, *Elife*, 2013

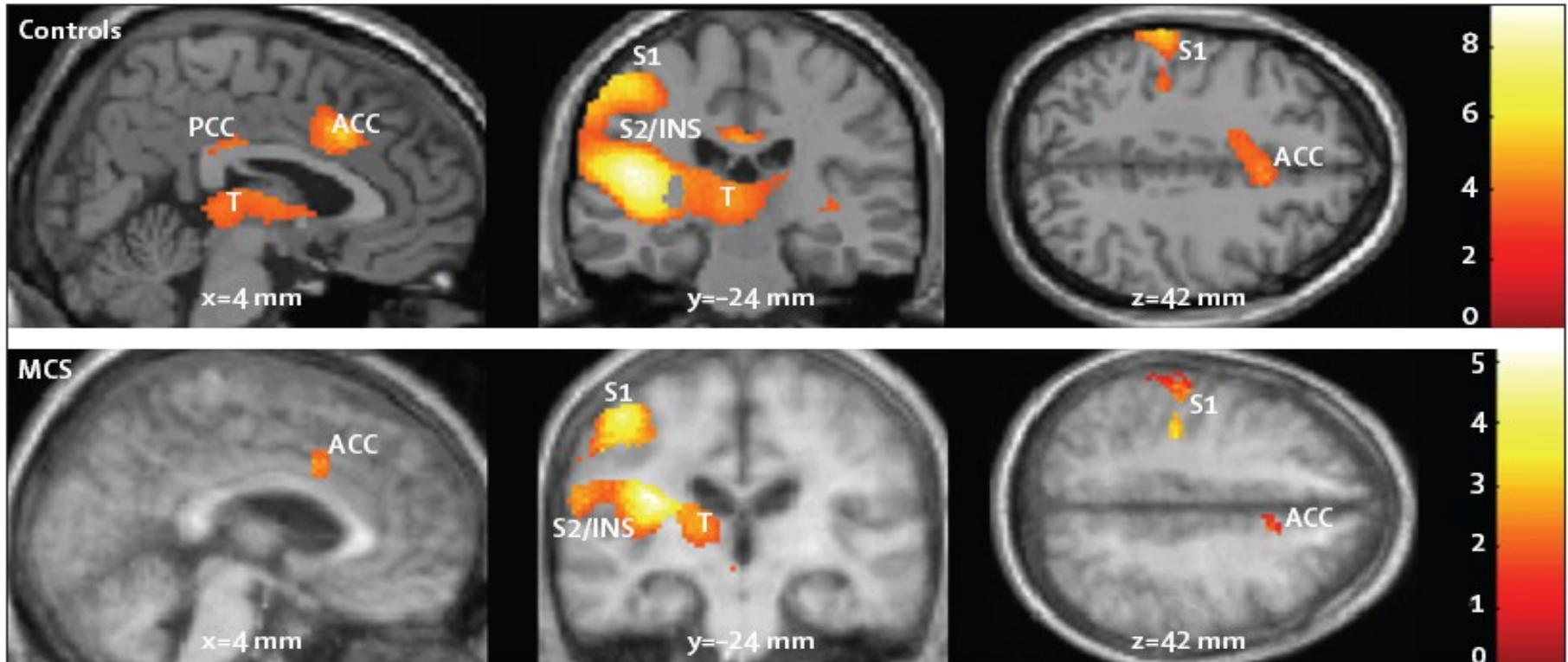
Amantadine treatment



Schnakers et al *J Neurol Neurosurg Psychiatry* 2008

Giacino et al *NEJM* 2012

Pain in minimally conscious state



Conclusion



Human conscious awareness

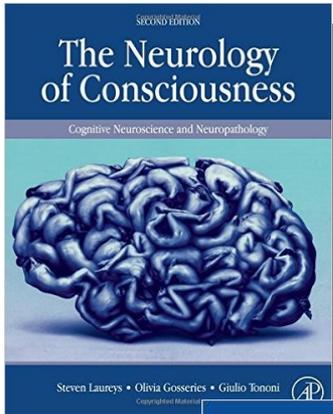
≈ emergent property of collective critical neural network dynamics, involving a frontoparietal global workspace
Awareness can be subdivided into internal and external awareness supported by different networks

Diagnostic use

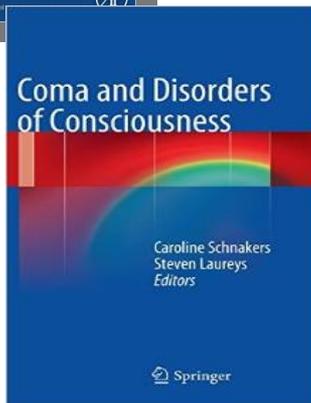
≈ 40% misdiagnosis
multimodal imaging

Therapeutic use

pain treatment / DBS thalamus / tDCS



Contact:
coma@ulg.ac.be



James S. McDonnell Foundation



Fondazione Europea Ricerca Biomedica

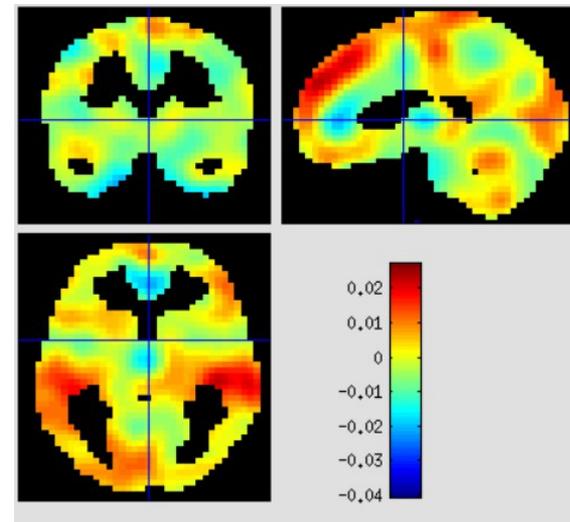
PET & Machine Learning

What a machine can “see”?

- Diagnosis
- Brain Activity Patterns

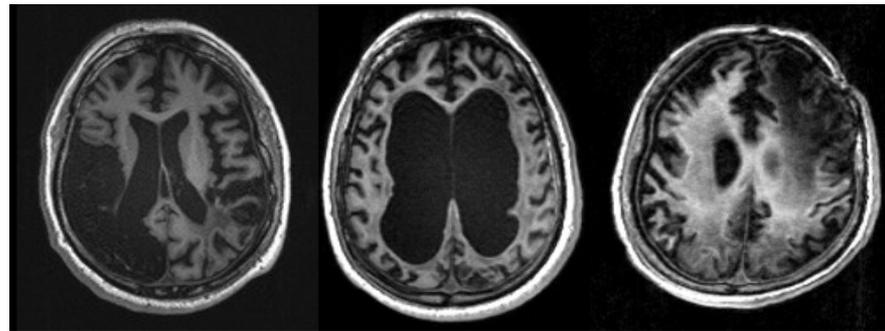
FDG-PET Automatic Classification

Pipeline → Preprocessing (spatial Normalization, **Intensity Scaling**)

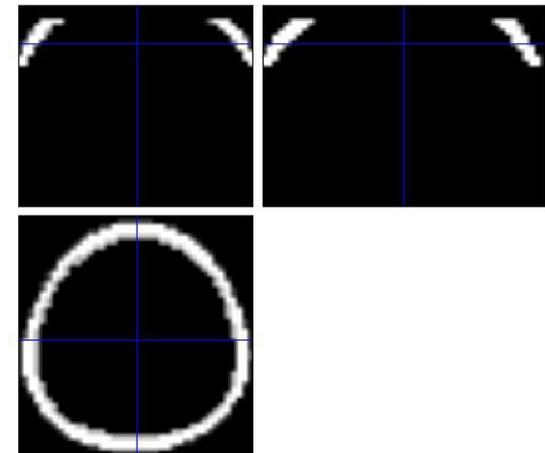


Processing Challenges

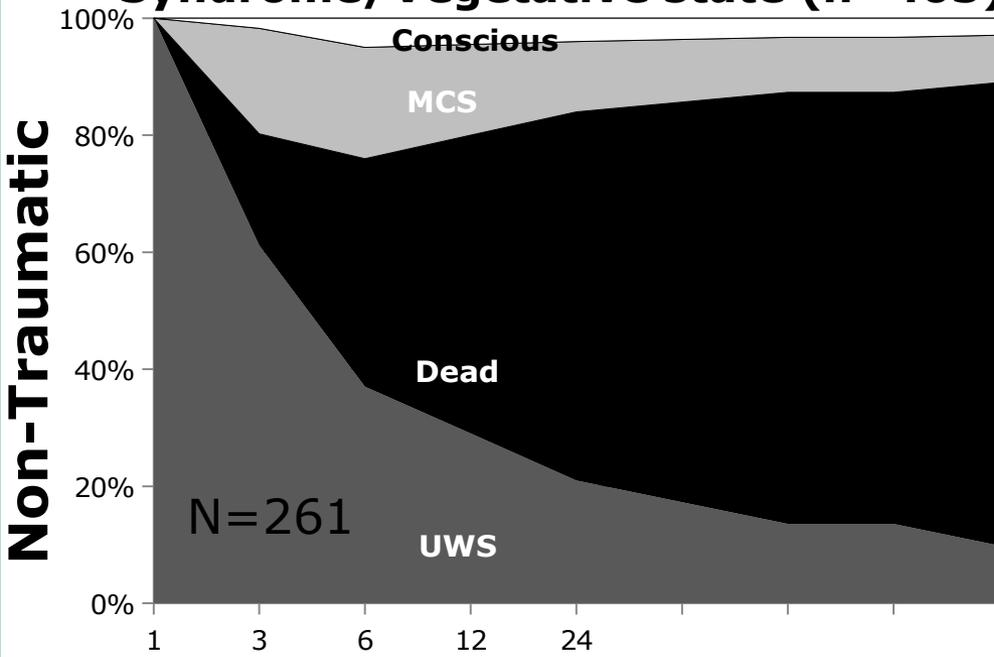
- Very big deformation
- No reference region can be selected



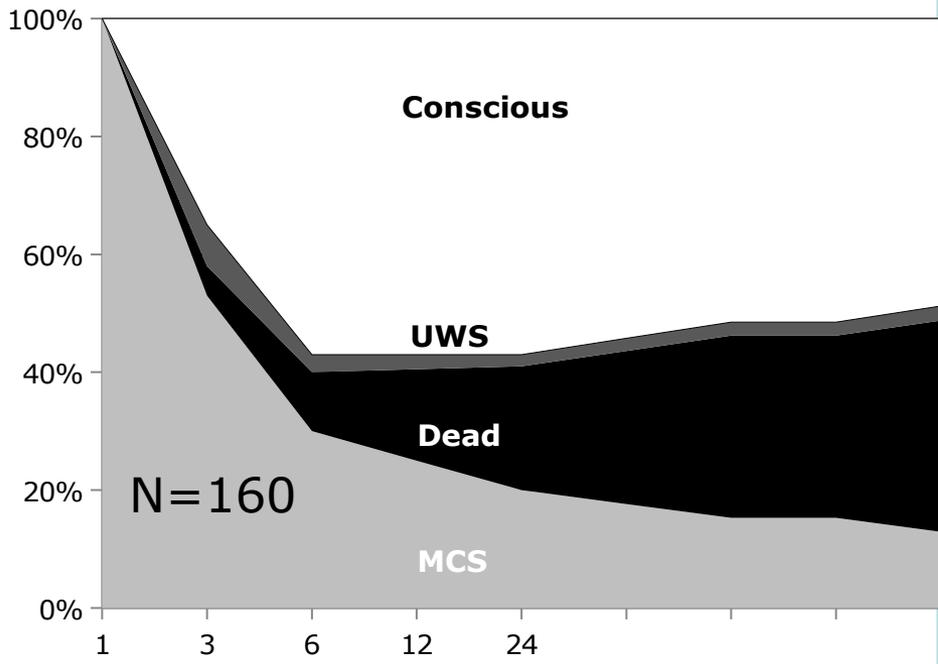
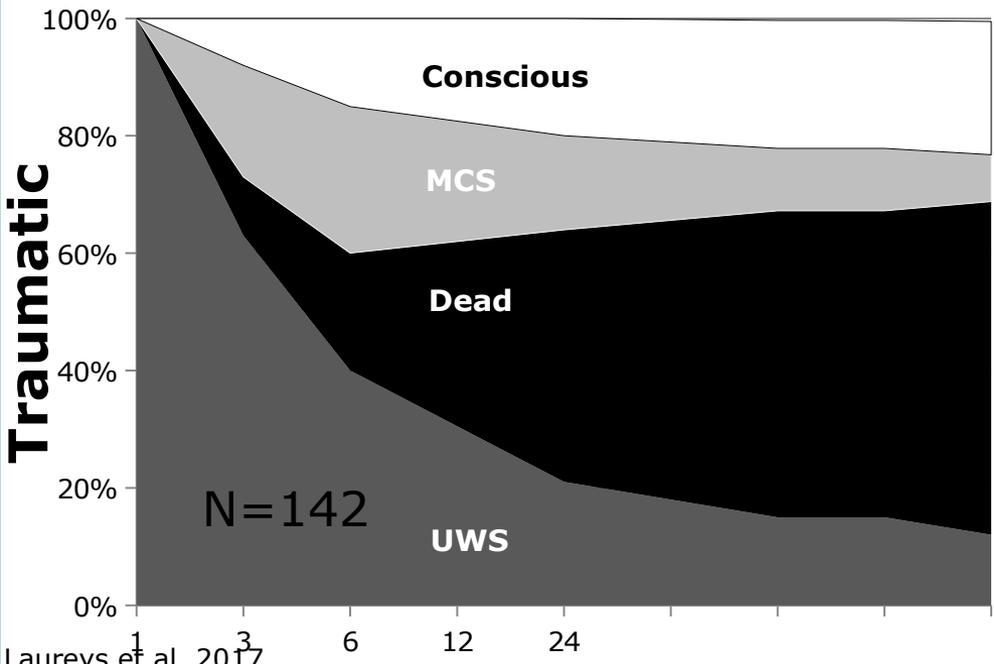
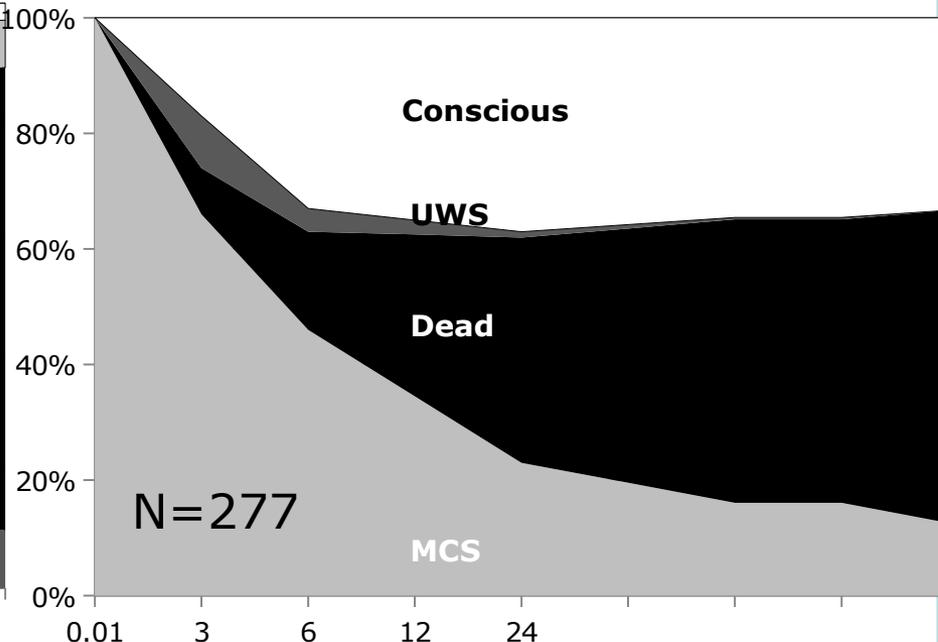
- In squirrel Monkeys:
- No suitable cerebral reference region is available, quantify brain receptors using muscle as reference region (Le Foll et al. 2007)



Unresponsive Wakefulness Syndrome/Vegetative state (n=403)

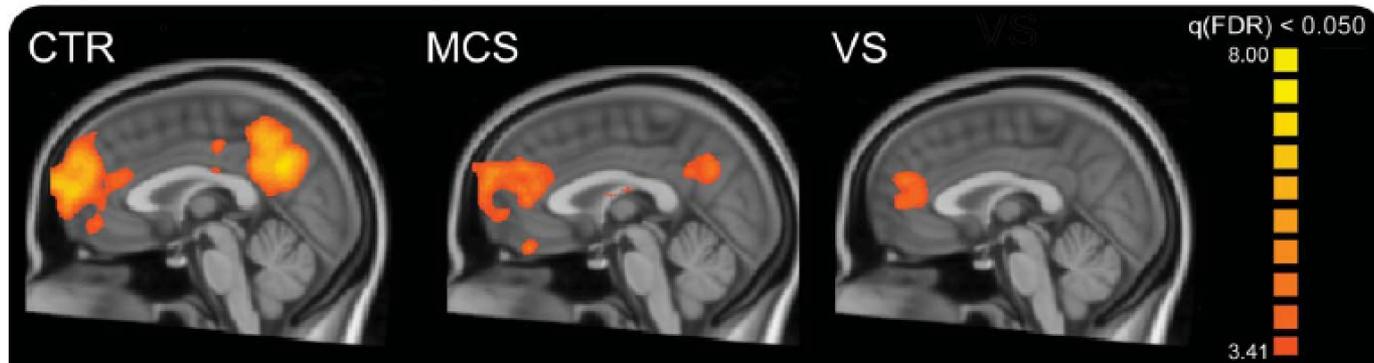


Minimally conscious state (n=437)



Pathological hyper-connectivity

Hypo-connectivity in DOC



Hyper-connectivity in DOC



Predicting therapeutic response

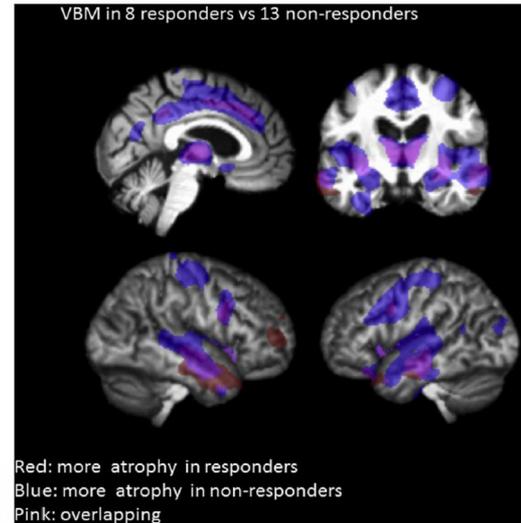


Brain Stimulation 8 (2015) 1116–1123

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: www.brainstimjrn1.com



Clinical Response to tDCS Depends on Residual Brain Metabolism and Grey Matter Integrity in Patients With Minimally Conscious State

Aurore Thibaut^{a,*,1}, Carol Di Perri^{a,1}, Camille Chatelle^{b,c}, Marie-Aurélié Bruno^a, Mohamed Ali Bahri^d, Sarah Wannez^a, Andrea Piarulli^{a,e}, Claire Bernard^f, Charlotte Martial^a, Lizette Heine^a, Roland Hustinx^f, Steven Laureys^a

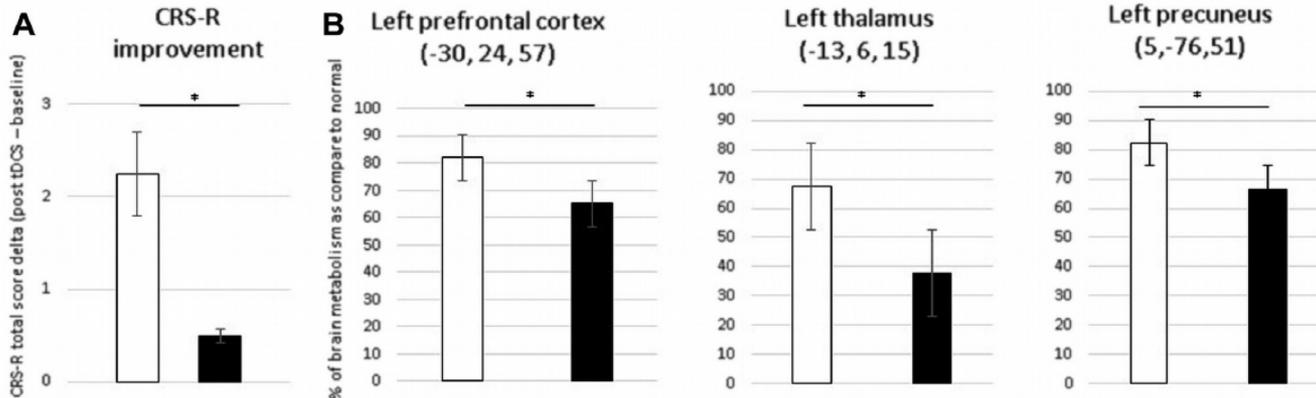


Figure 4. (A) Left: Mean and standard deviation of Coma Recovery Scale Revised (CRS-R) total score changes in tDCS responders and non-responders. (B) Right: Mean and standard deviation of normalized glucose metabolism (% of normal) in left dorsolateral prefrontal cortex (DLPFC), left thalamus and precuneus in tDCS responders and non-responders. * $P < 0.05$.

End-of-life issues



European
Neurological Society

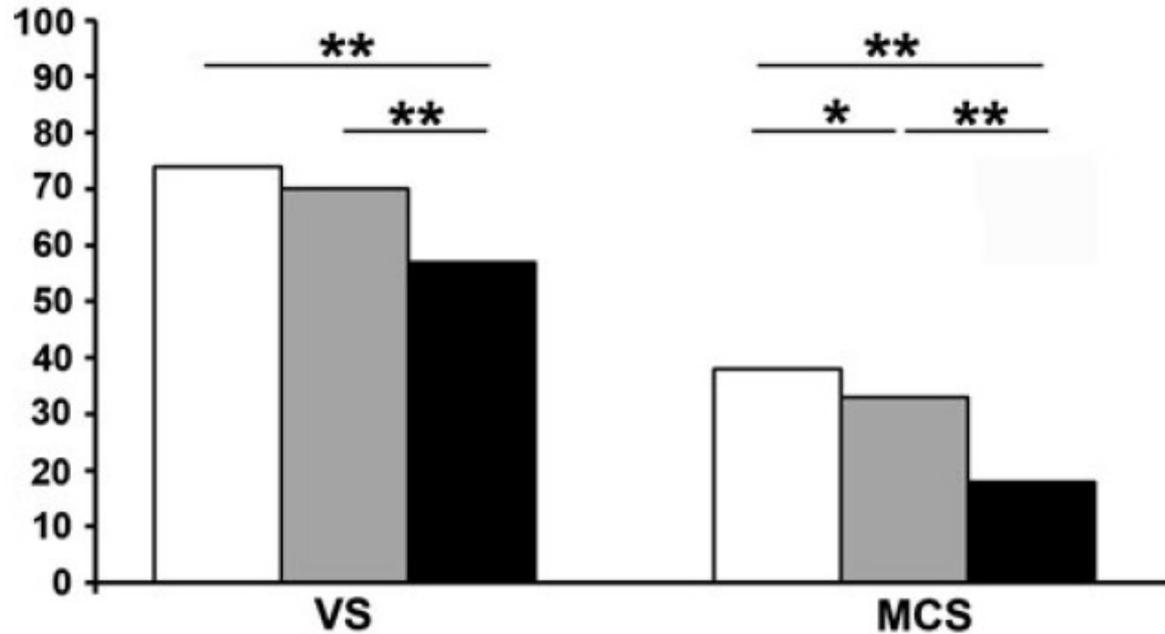


Attitudes towards end-of-life issues in disorders of consciousness: a European survey

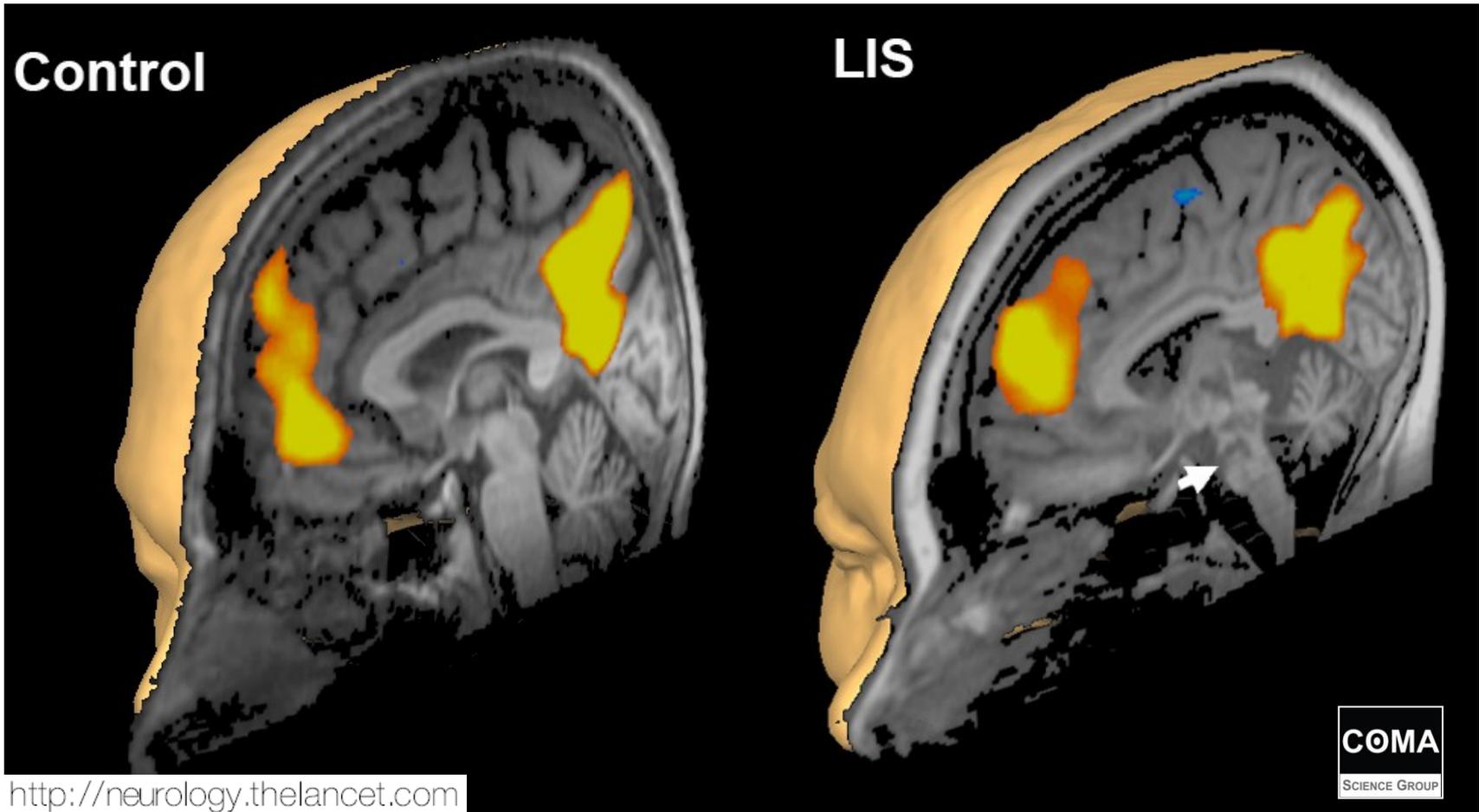
A. Demertzi · D. Ledoux · M.-A. Bruno ·
A. Vanhaudenhuyse · O. Gosseries · A. Soddu ·
C. Schnakers · G. Moonen · S. Laureys

2,475 medical professionals

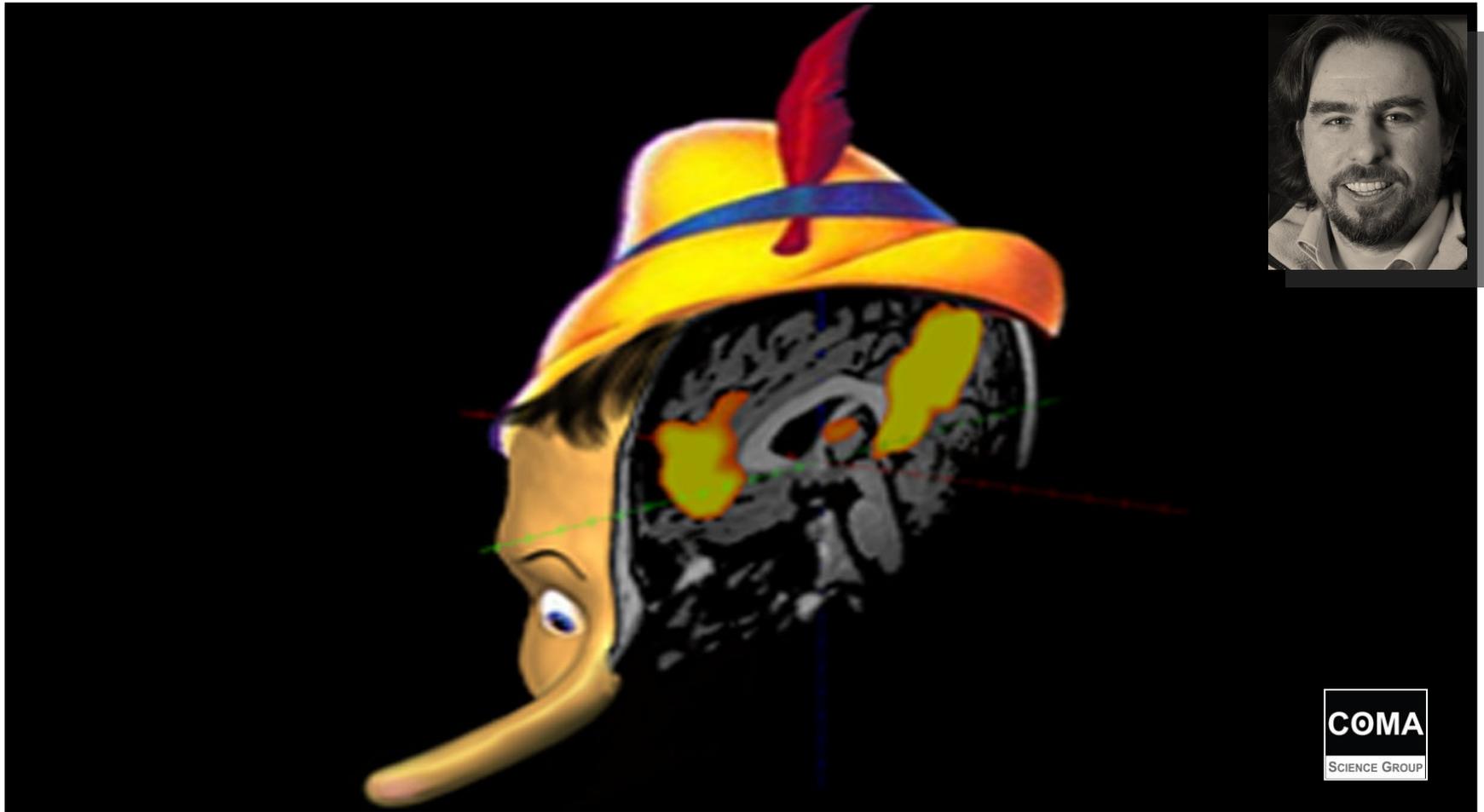
It is acceptable to stop treatment
in a chronic...



Functional MRI in “resting state”



Should we trust the test?



Credit : A Soddu

Near death experiences (n=190)



99% positive
1% negative

140 coma
- anoxic (45)
- traumatic (30)
- other (65)

50 non-coma

