

# Coma et corrélats neuronaux de la conscience

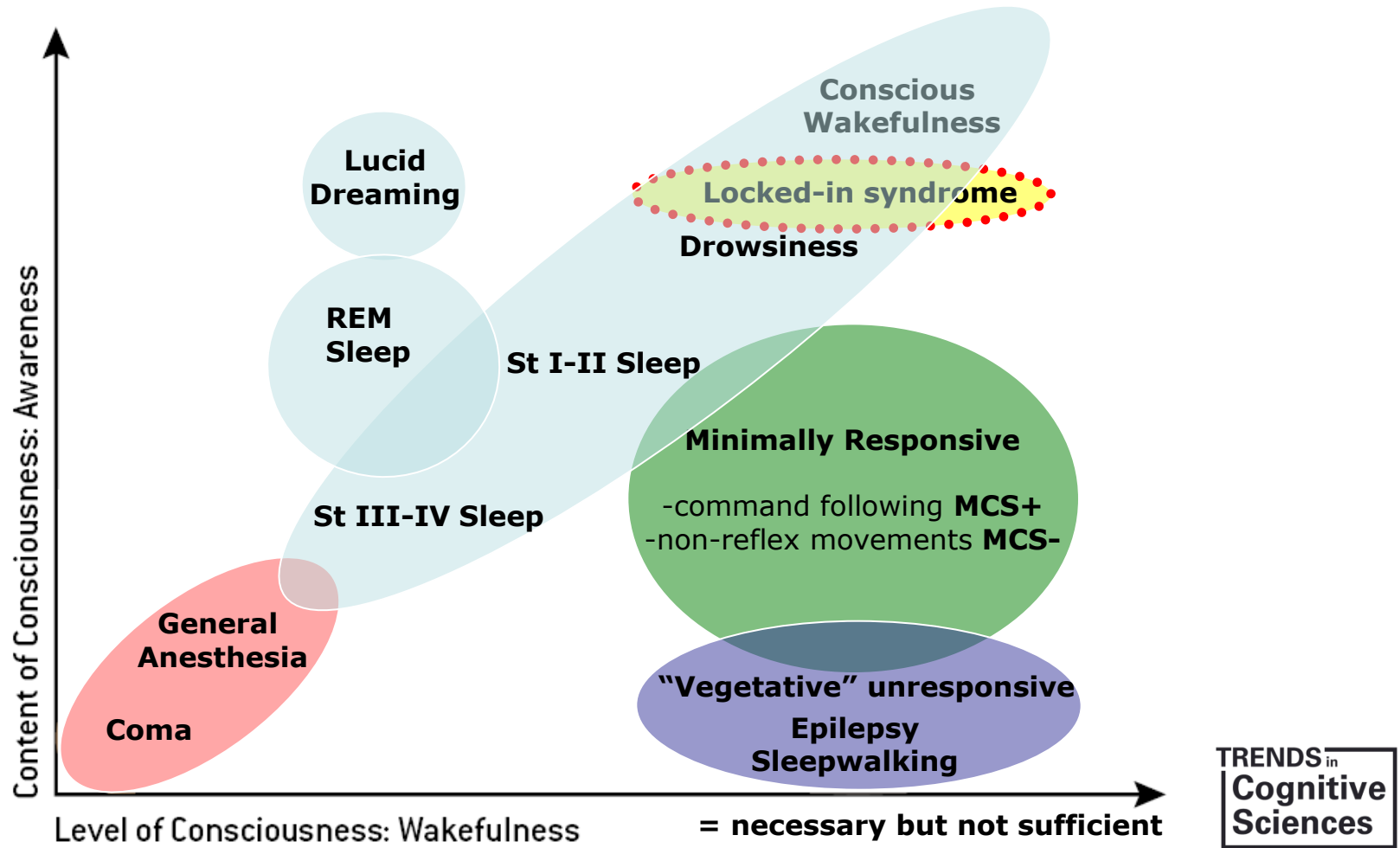
**THIBAUT Aurore**  
Coma Science Group  
Cyclotron Research Centre &  
Neurology Dept  
University & University Hospital of Liège  
Belgium

coma@ulg.ac.be

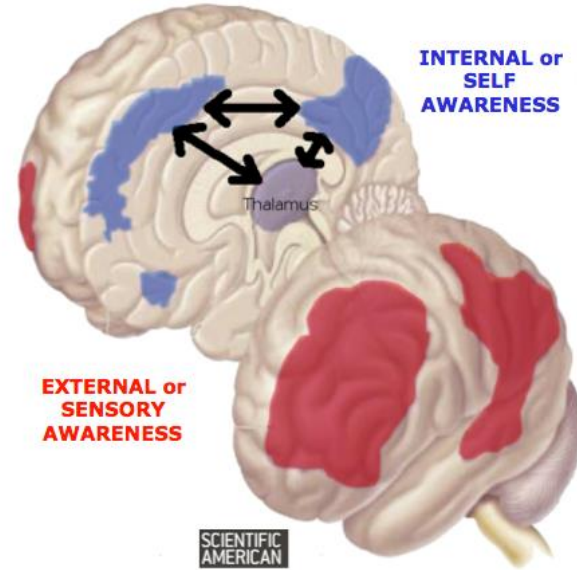
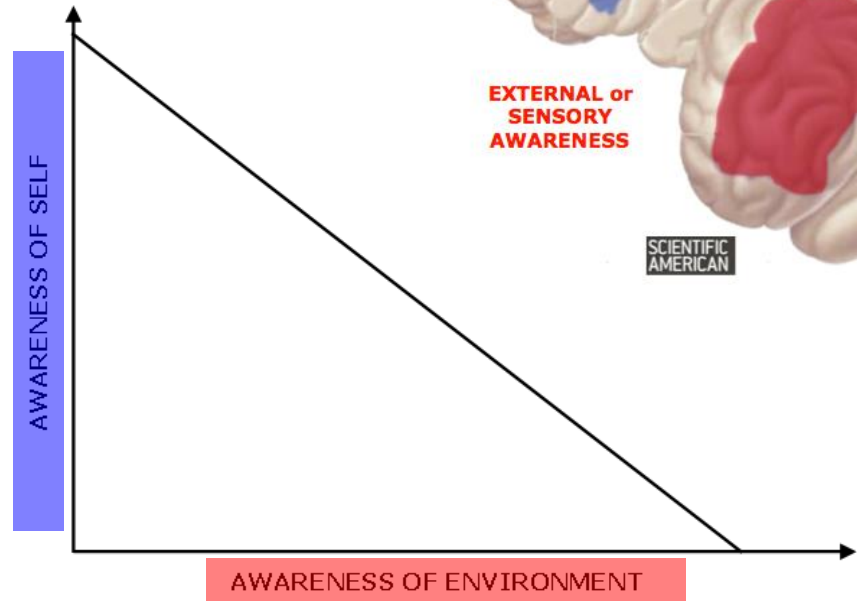
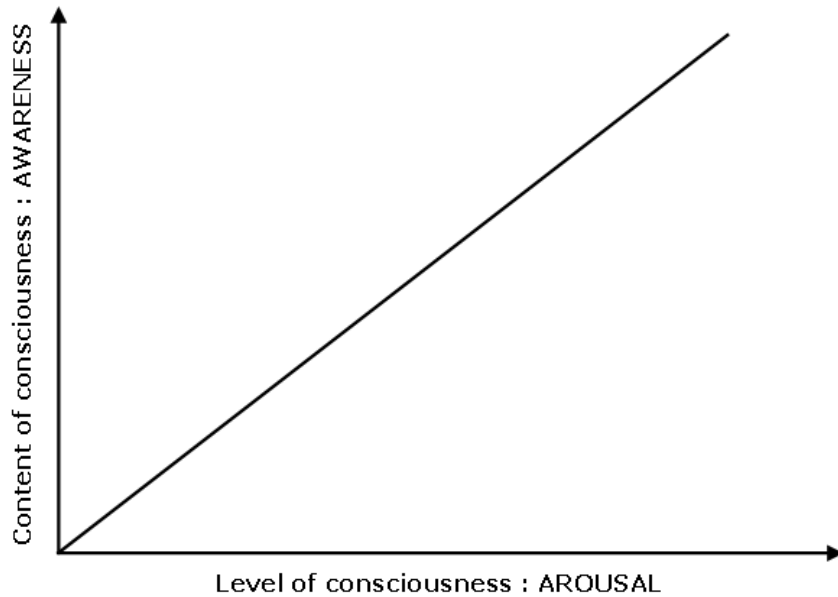


[www.comascience.org](http://www.comascience.org)

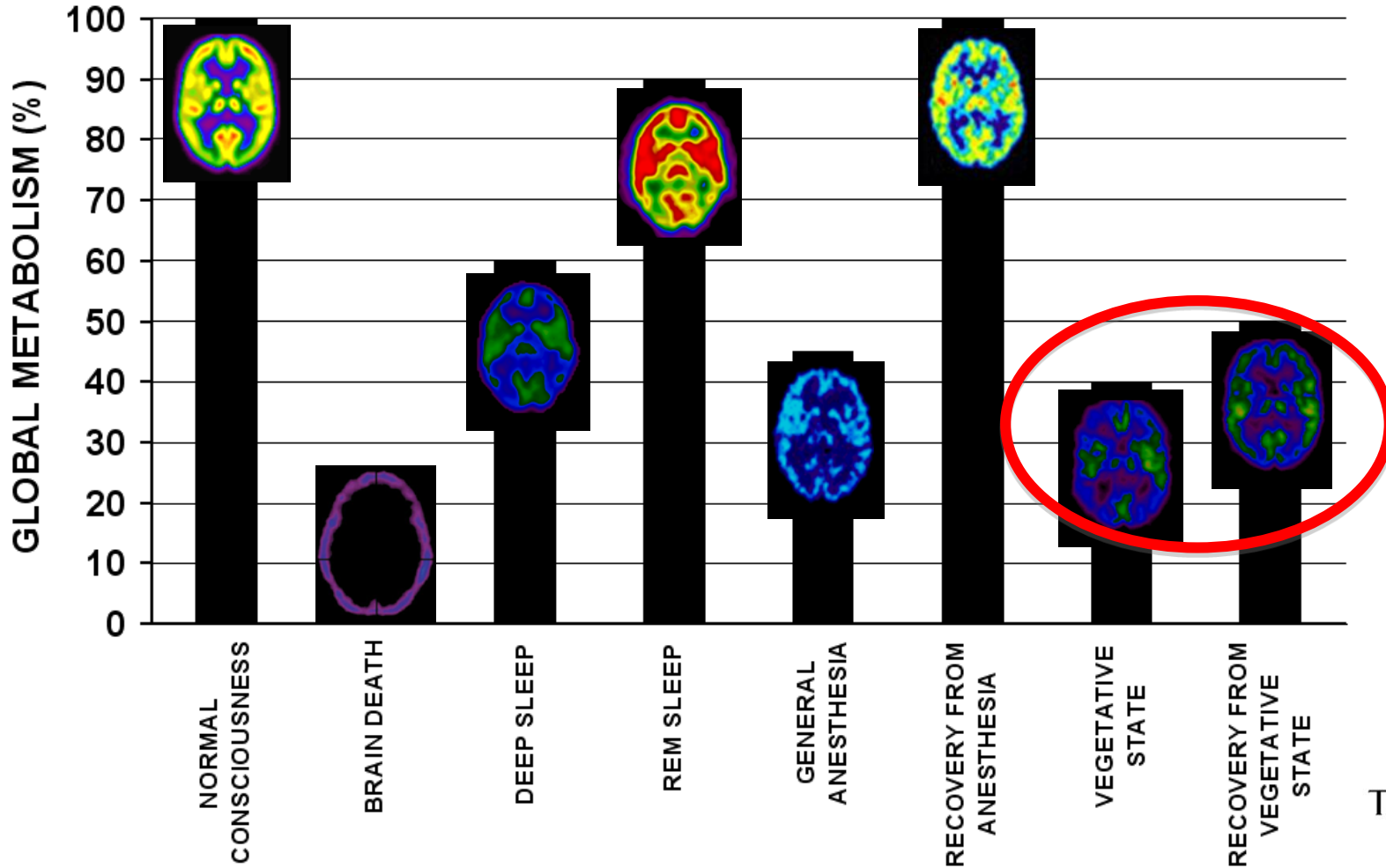
# Reducing consciousness to 2D



# Reducing awareness to 2D



# Consciousness $\neq$ global brain function

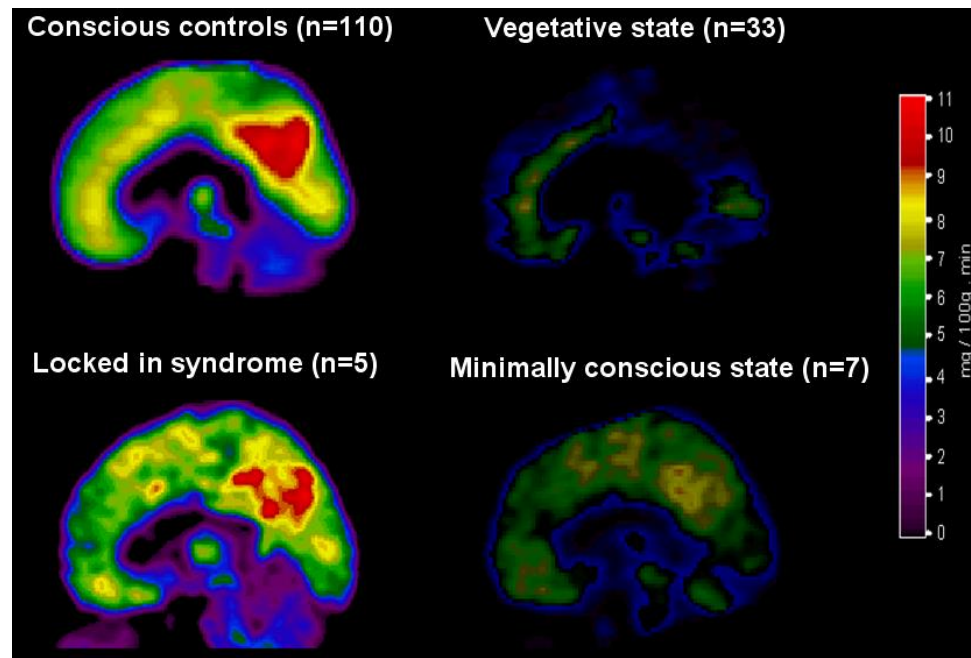
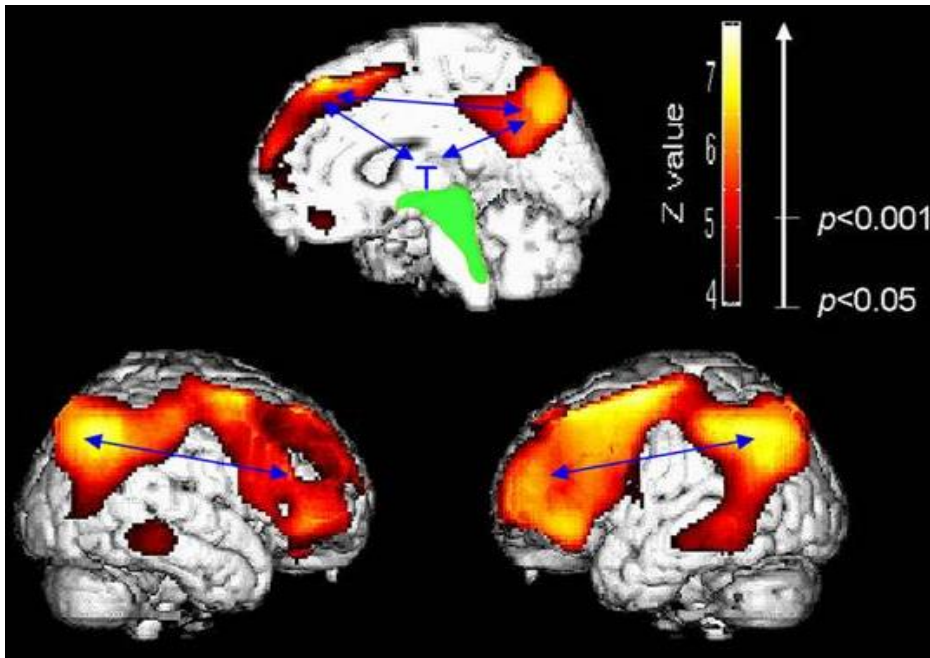


THE LANCET  
Neurology

# Consciousness $\approx$ frontoparietal

Areas systematically dysfunctional in “vegetative” state & recovering activity after recovery of consciousness

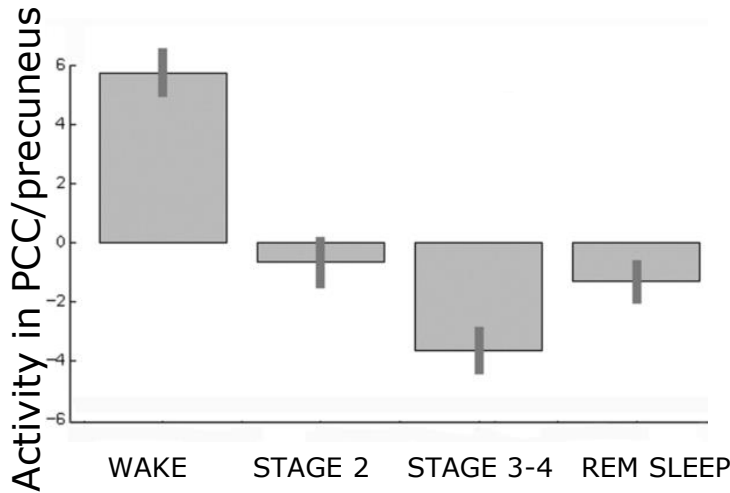
Precuneus is critical hub in fronto-parietal connectivity



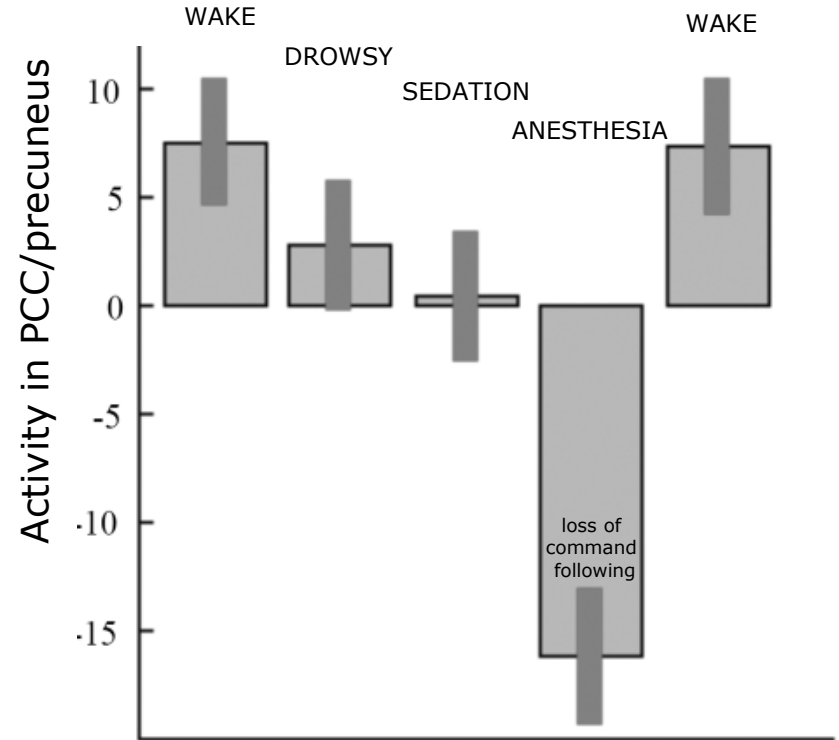
# Precuneus $\approx$ hub in the network

## SLEEP

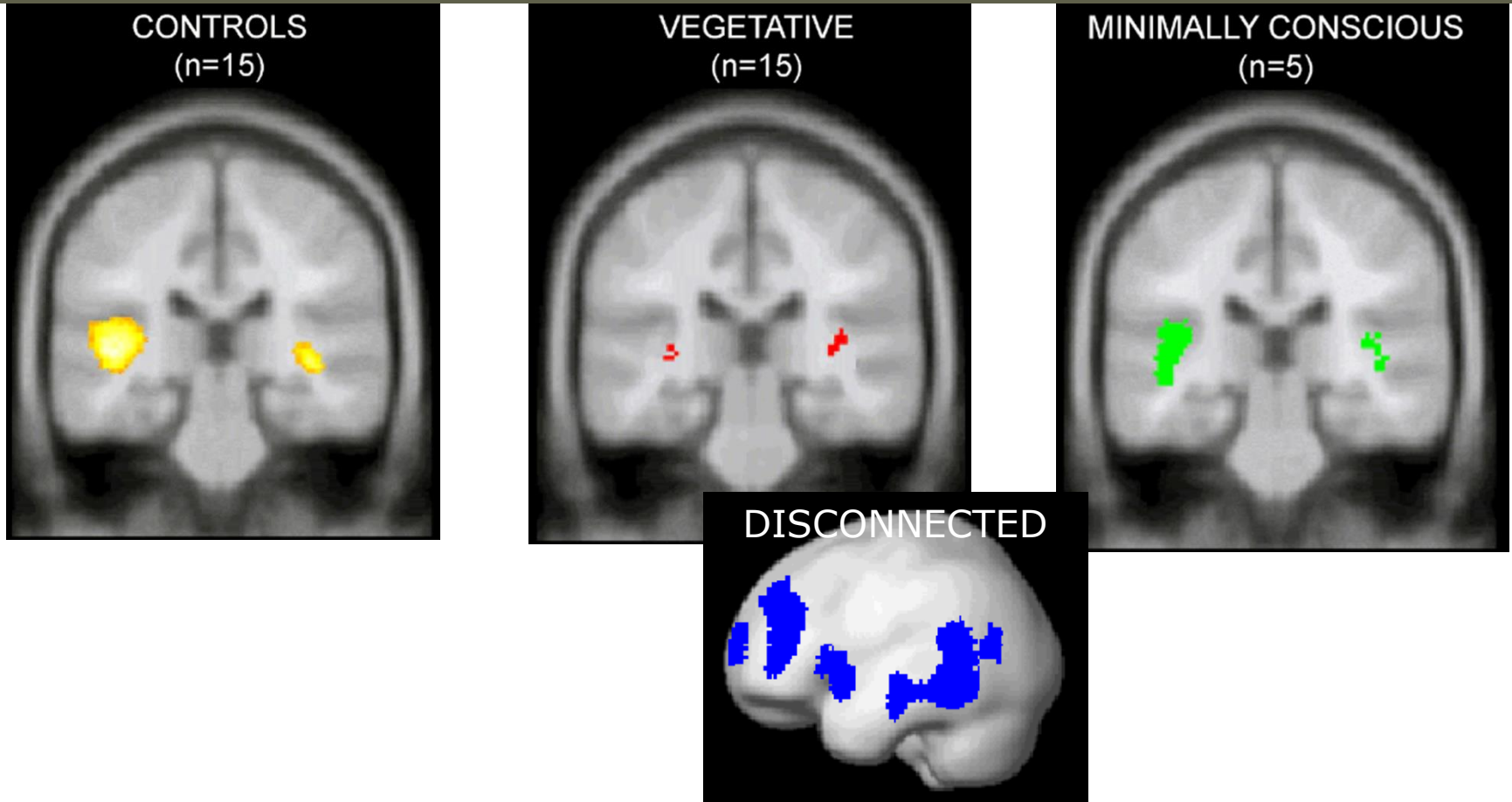
Activity in PCC/precuneus



## ANESTHESIA

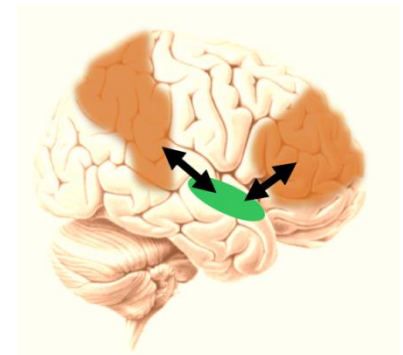
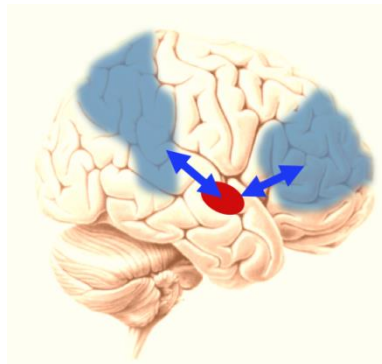
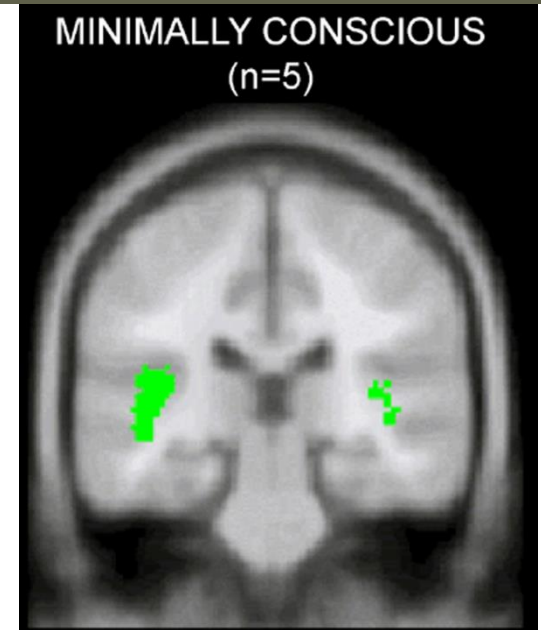
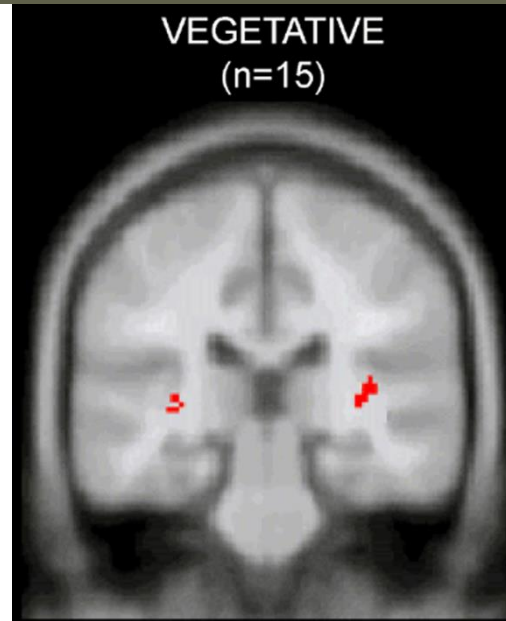
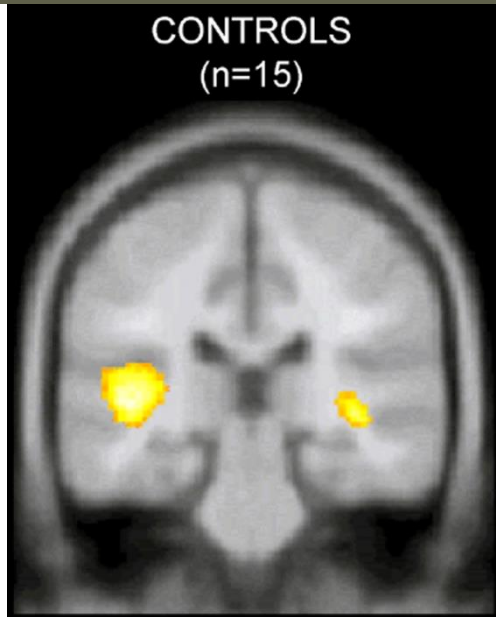


# Consciousness $\neq$ primary cortex



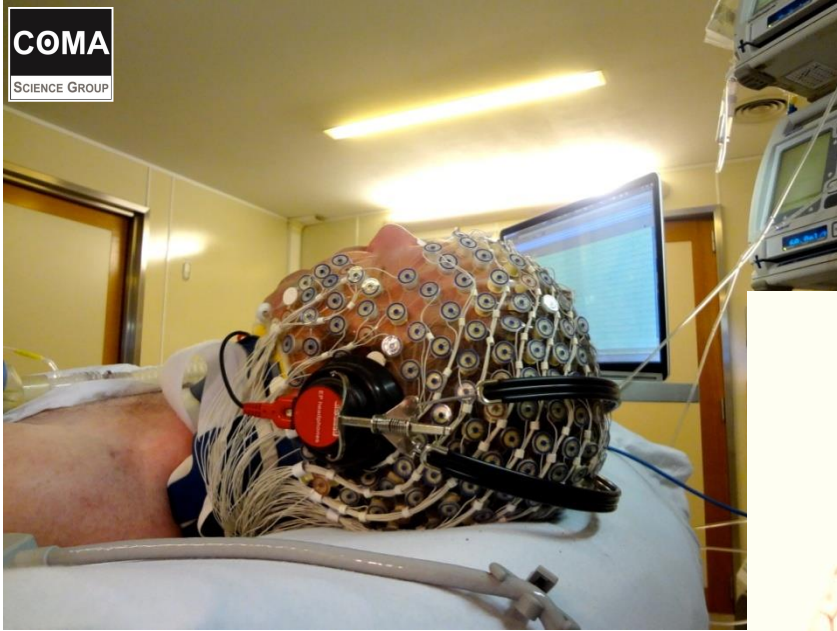


# Consciousness $\neq$ primary cortex

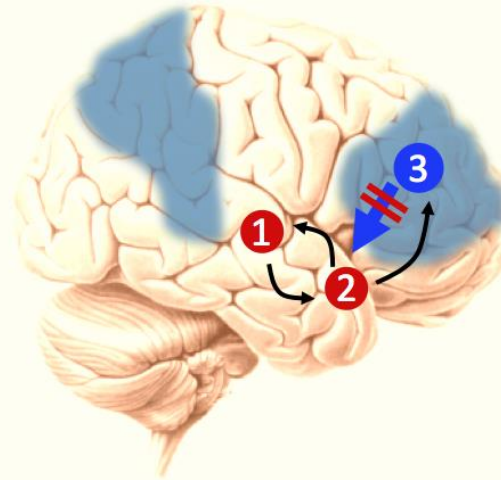




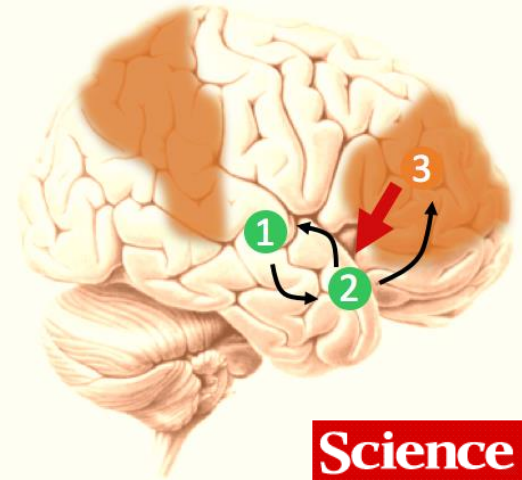
# Consciousness $\approx$ top-down



“VEGETATIVE”  
UNRESPONSIVE



MINIMALLY  
RESPONSIVE



Science

# A new name for « vegetative »

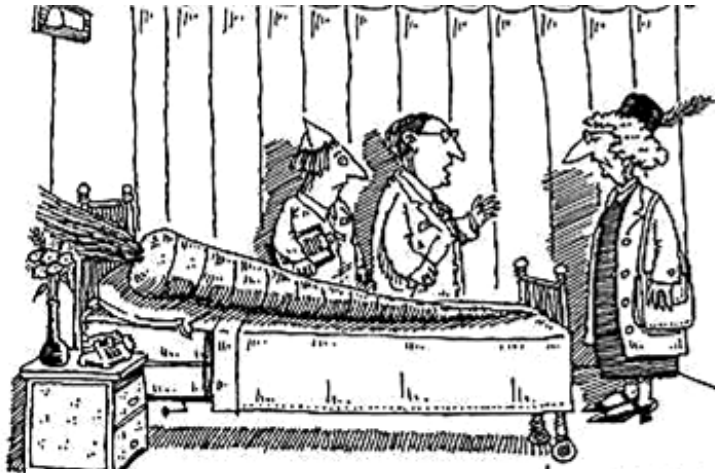


Highly accessed Open Access

## Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome

Steven Laureys<sup>1</sup> ✉, Gastone G Celesia<sup>2</sup> ✉, Francois Cohadon<sup>3</sup> ✉, Jan Lavrijsen<sup>4</sup> ✉, José León-Carrión<sup>5</sup> ✉, Walter G Sannita<sup>6,7</sup> ✉, Leon Szabon<sup>8</sup> ✉, Erich Schmutzhard<sup>9</sup> ✉, Klaus R von Wild<sup>10,11</sup> ✉, Adam Zeman<sup>12</sup> ✉ and Giuliano Dolce<sup>13</sup> ✉ for the European Task Force on Disorders of Consciousness<sup>1</sup> ✉

<http://www.biomedcentral.com/1741-7015/8/68>



“There’s nothing we can do... he’ll always be a vegetable.”

## PERSISTENT VEGETATIVE STATE



# Diagnostic error

n=103 post-comatose patients

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

↪ 40% potential misdiagnosis

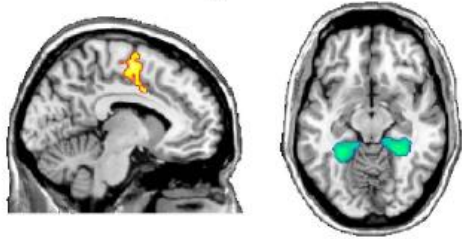
JFK COMA RECOVERY SCALE - REVISED ©2004									
Record Form									
Patient:		Date:							
<b>AUDITORY FUNCTION SCALE</b>									
4 - Consistent Movement to Command *									
3 - Reproducible Movement to Command *									
2 - Localization to Sound									
1 - Auditory Startle									
0 - None									
<b>VISUAL FUNCTION SCALE</b>									
5 - Object Recognition *									
4 - Object Localization: Reaching *									
3 - Visual Pursuit *									
2 - Fixation *									
1 - Visual Startle									
0 - None									
<b>MOTOR FUNCTION SCALE</b>									
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									
<b>OROMOTOR/VERBAL FUNCTION SCALE</b>									
3 - Intelligible Verbalization *									
2 - Vocalization/Oral Movement									
1 - Oral Reflexive Movement									
0 - None									
<b>COMMUNICATION SCALE</b>									
2 - Functional: Accurate †									
1 - Non-Functional: Intentional *									
0 - None									
<b>AROUSAL SCALE</b>									
3 - Attention									
2 - Eye Opening w/o Stimulation									
1 - Eye Opening with Stimulation									
0 - Unarousable									
<b>TOTAL SCORE</b>									



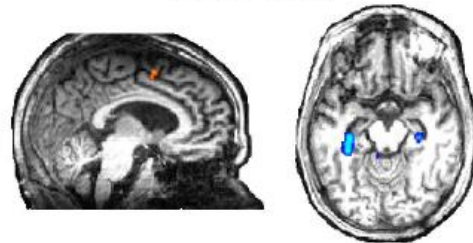
# Yes-No communication with fMRI

The NEW ENGLAND JOURNAL of MEDICINE

Healthy Controls

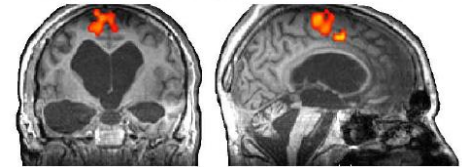


L25 TBI

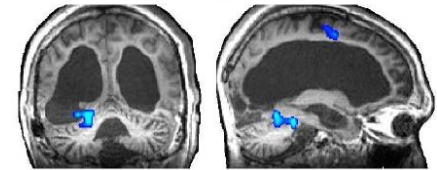


Imagine **Tennis** to answer 'YES'  
Imagine **Navigating** to answer 'NO'

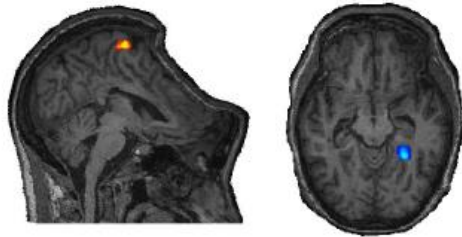
Is your father's name Alexander ?



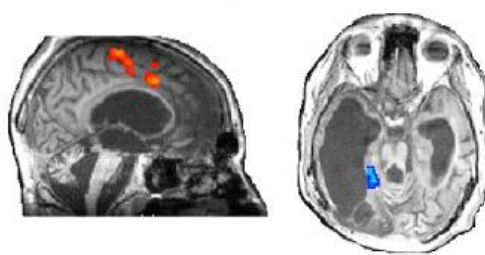
Is your father's name Thomas ?



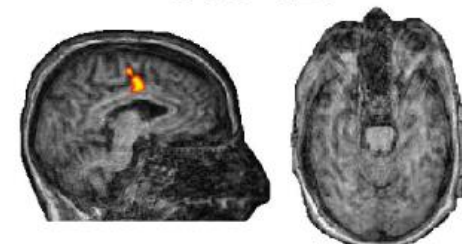
C04 TBI



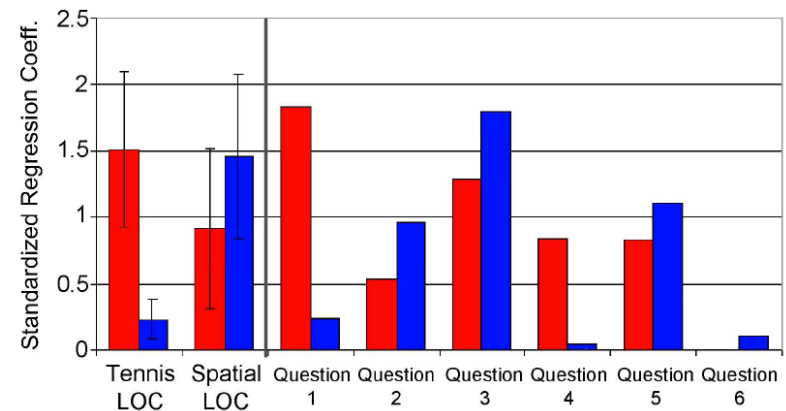
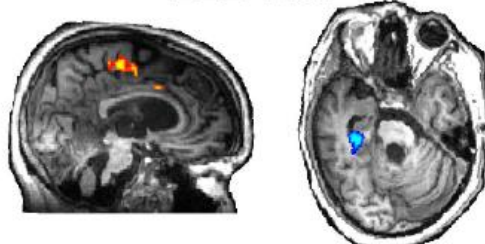
L23 TBI



C06 TBI



L22 TBI





# EEG-based Brain Computer Interfaces

“MOVE YOUR FOOT”

“MOVE YOUR HAND”



HEALTHY  
CONTROL  
SUBJECT



“VEGETATIVE”  
UNRESPONSIVE  
PATIENT



[www.thelancet.com](http://www.thelancet.com)

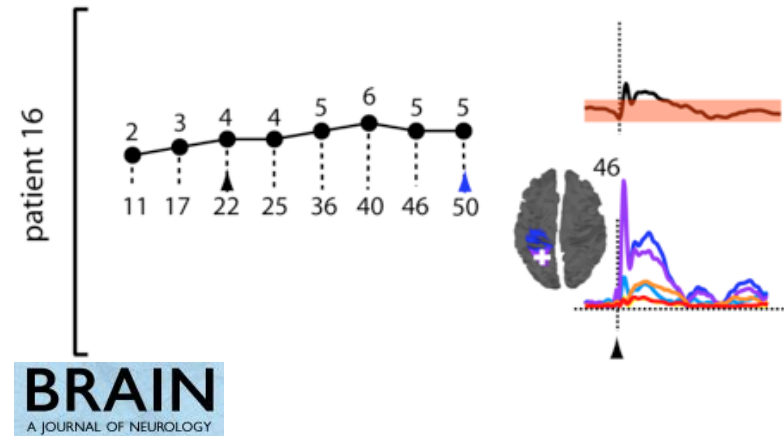
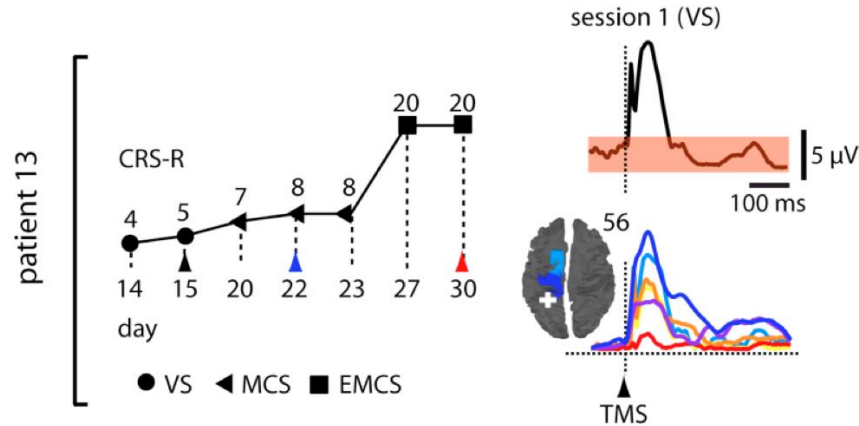


Cruse et al, *Lancet* 2012  
**3/16 VS/UWS (19%)**  
- 2/5 traumatic (40%)  
- 1/11 non-traumatic (9%)

Cruse et al, *Neurology* 2012  
**7/23 MCS (30%)**  
- 7/15 traumatic (49%)  
- 0/8 non-traumatic (0%)

# Consciousness $\approx$ connectivity

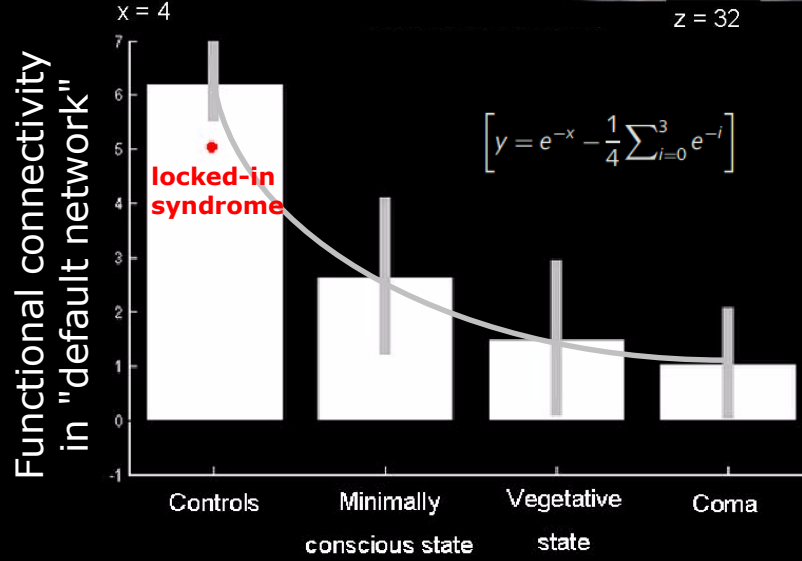
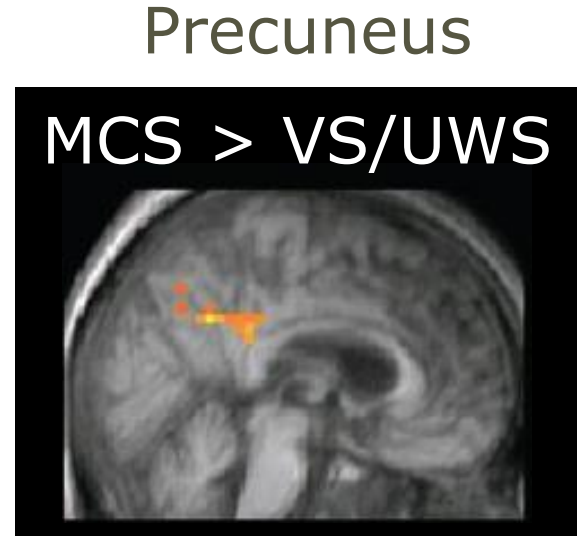
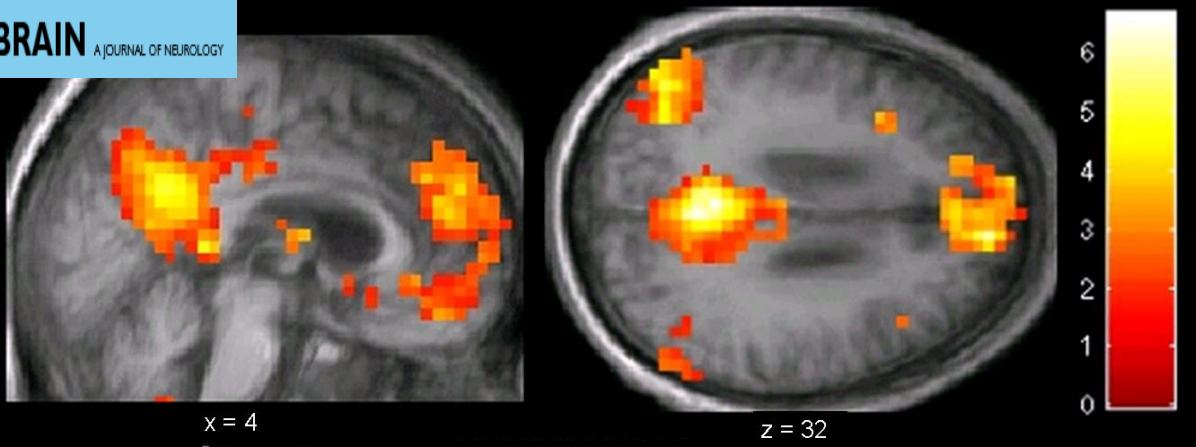
## EEG-TMS





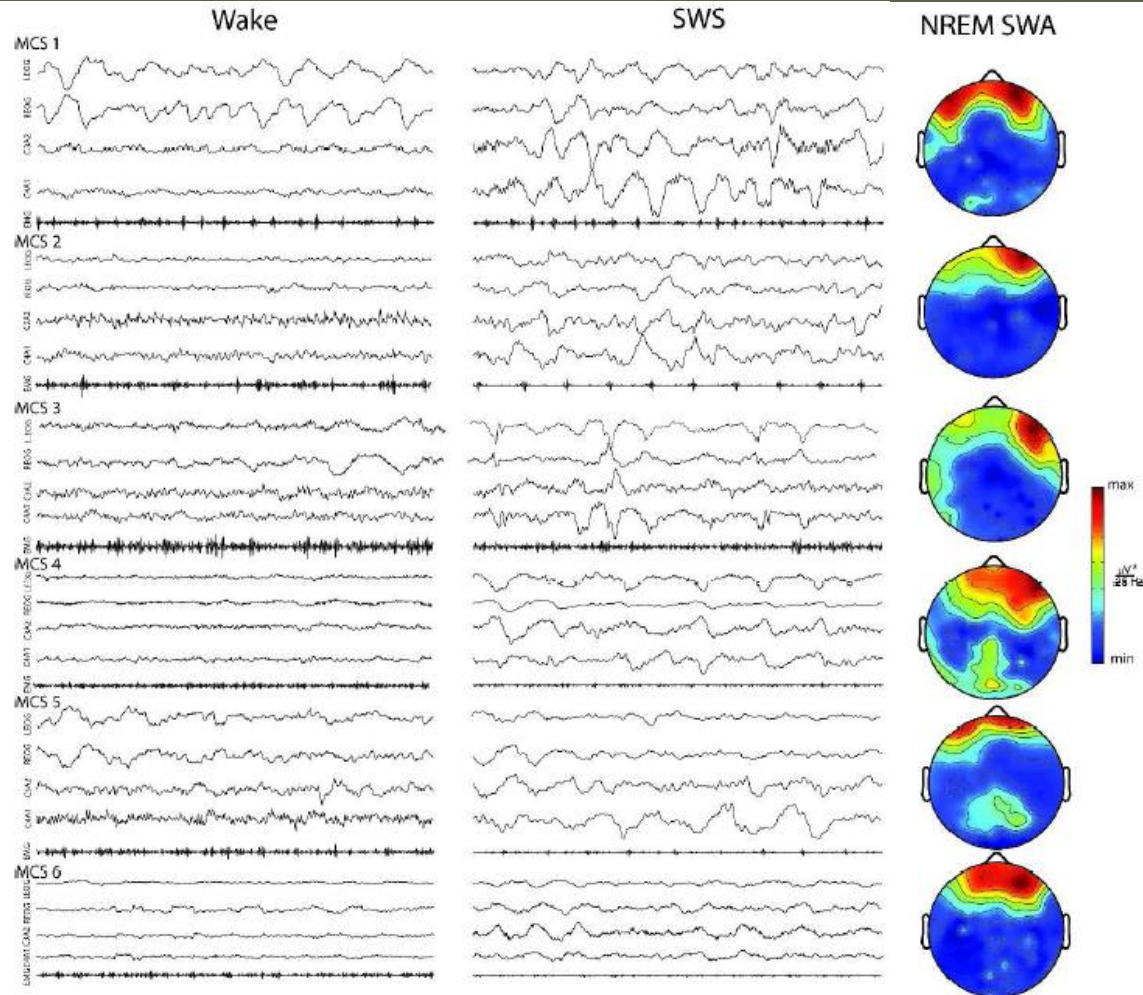
# "Resting" default mode connectivity

**BRAIN**  
A JOURNAL OF NEUROLOGY

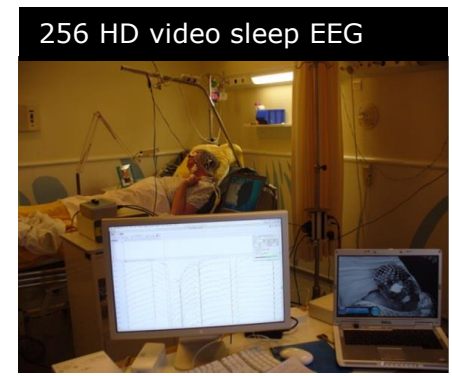


# Understanding plasticity

**BRAIN** A JOURNAL OF NEUROLOGY

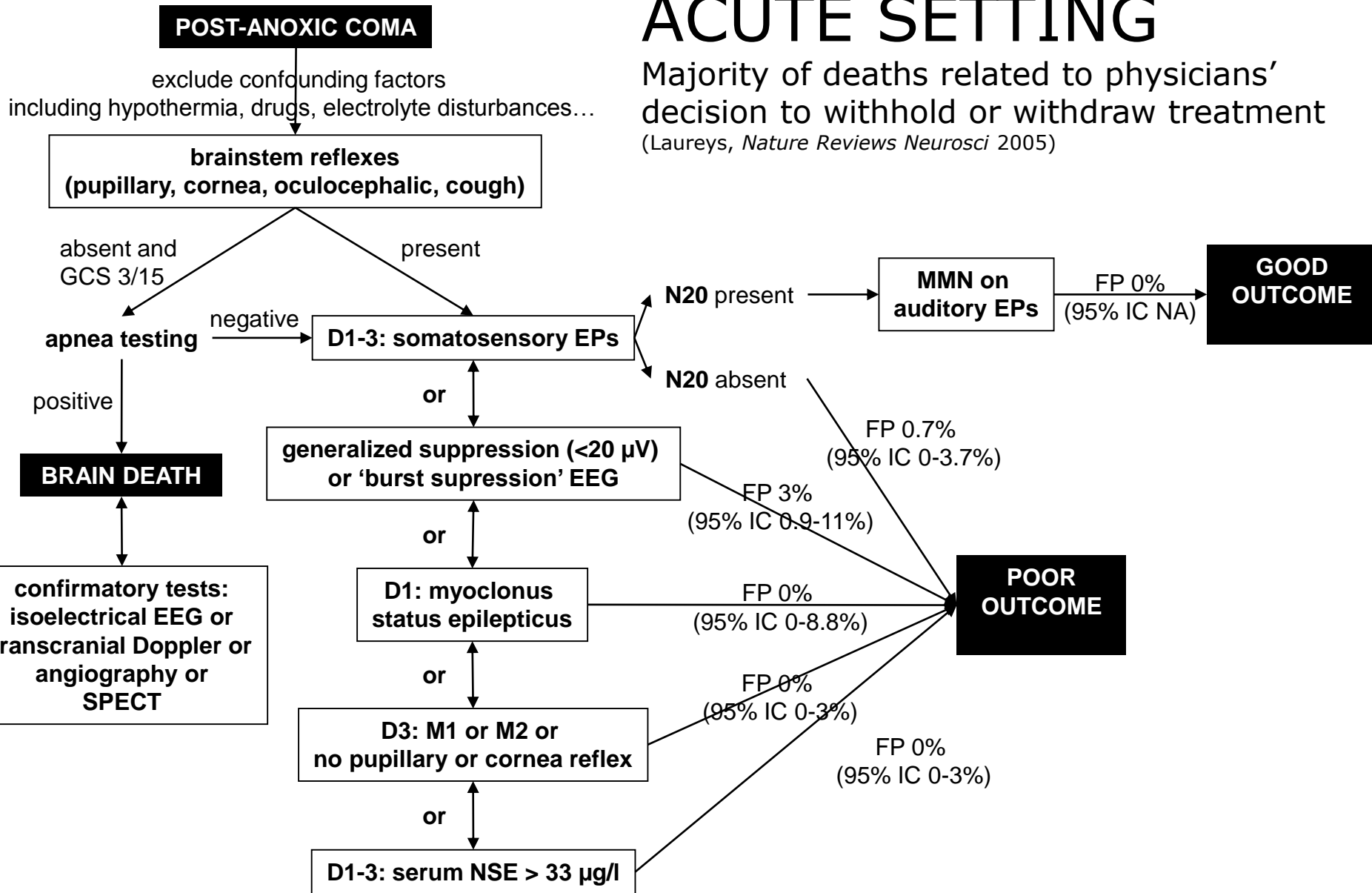


Homeostatic decline SWA  
 $\approx$  plasticity (Tononi)



# ACUTE SETTING

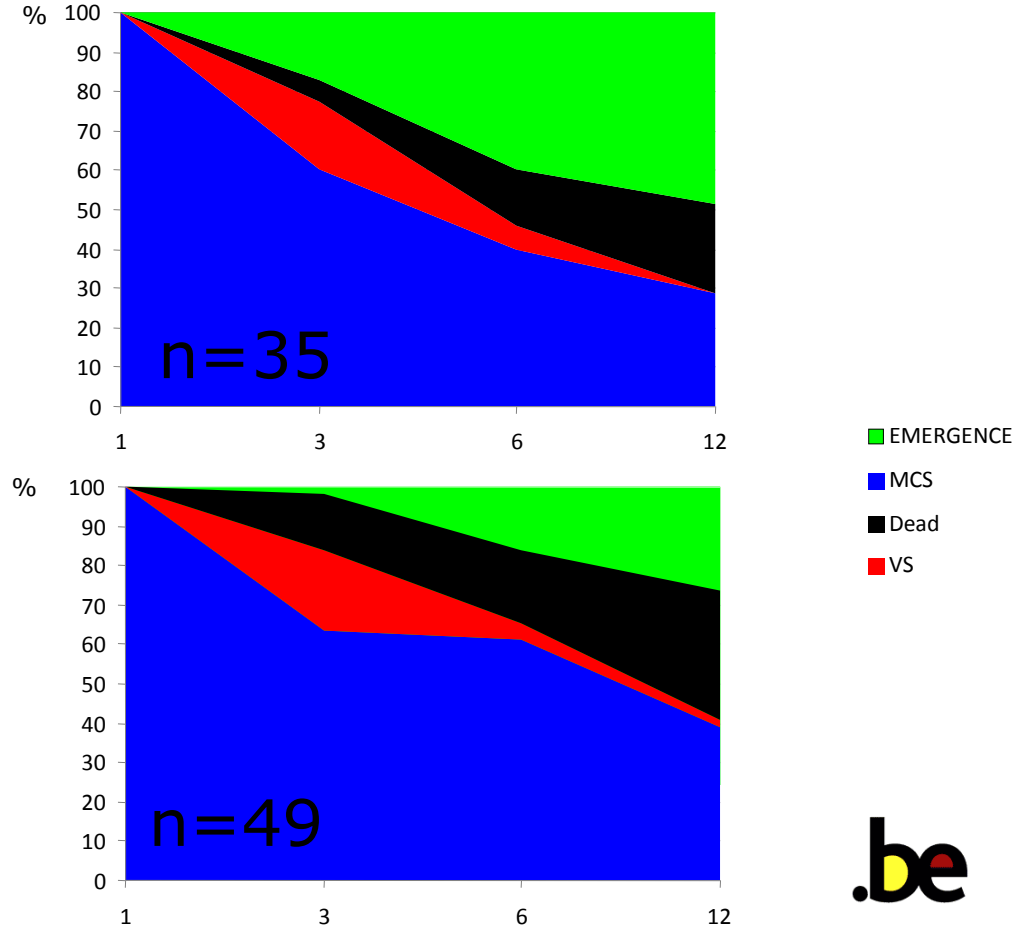
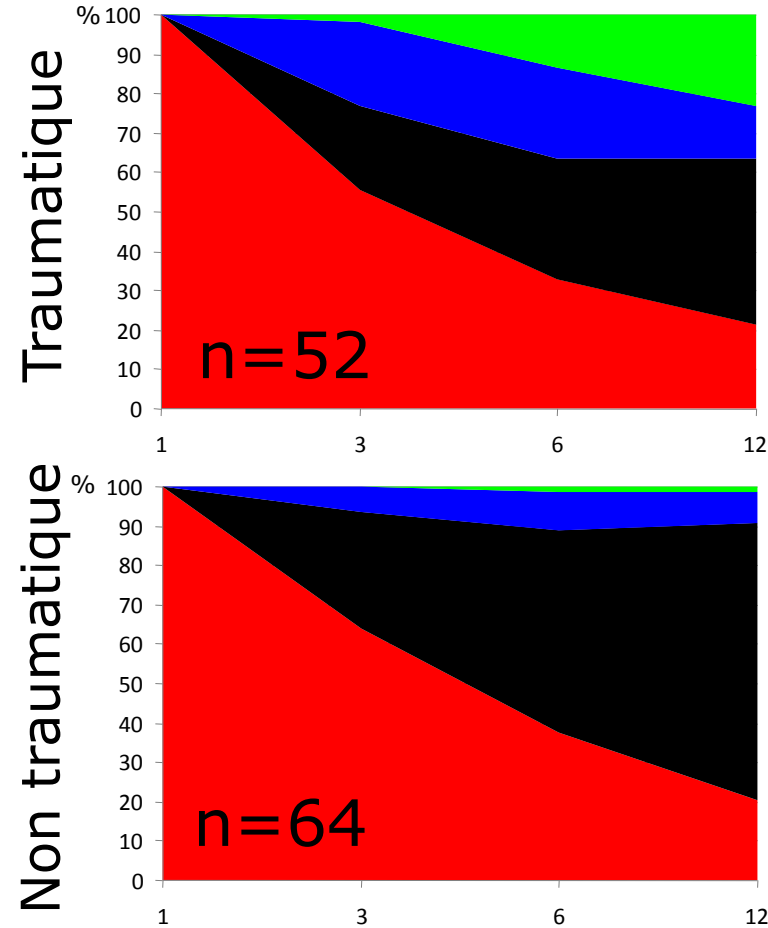
Majority of deaths related to physicians' decision to withhold or withdraw treatment  
(Laureys, *Nature Reviews Neurosci* 2005)



# Pronostic (Projet fédéral Belge, données 2004-07)

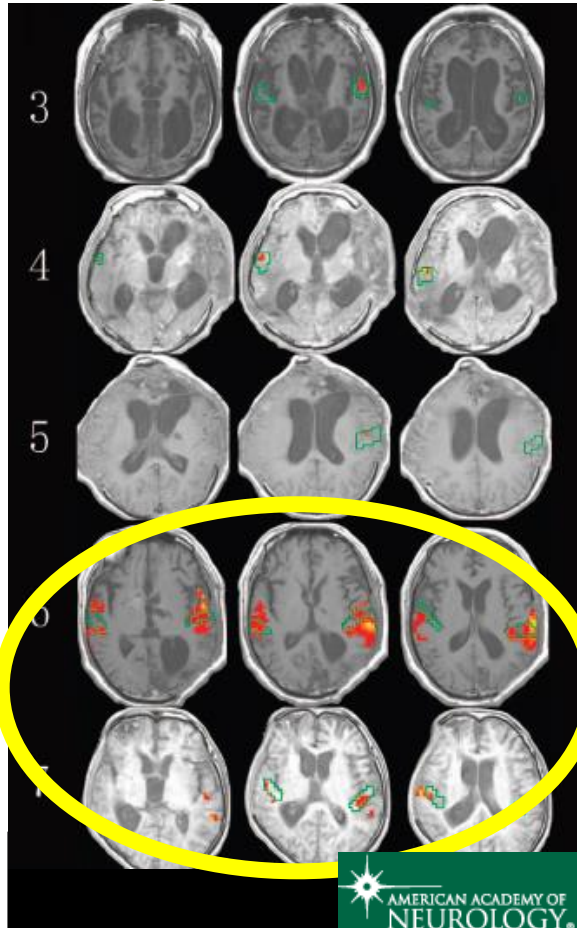
État végétatif (n=116)

État de conscience minimale (n=84)



# Predicting outcome in chronic DOC

vegetative state

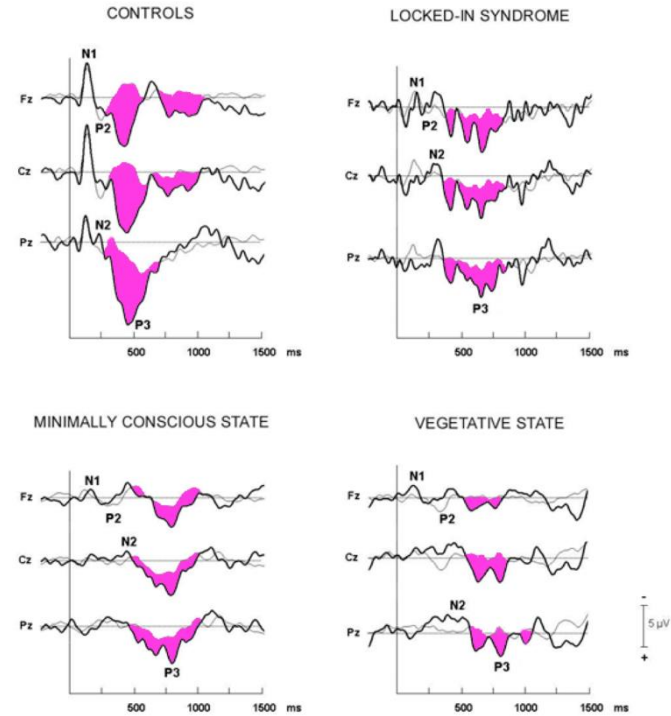


ACTIVATION  
TO THE OWN  
NAME

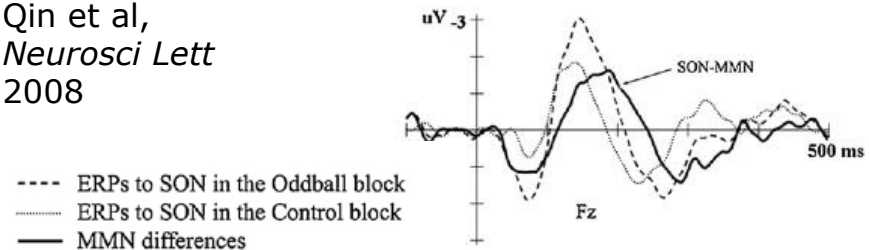
ATYPICAL  
'HIGH LEVEL'  
CORTICAL  
ACTIVATION



Perrin et al  
*Arch Neurol*  
2006



Qin et al,  
*Neurosci Lett*  
2008



- ERPs to SON in the Oddball block
- ..... ERPs to SON in the Control block
- MMN differences



# MRI: DTI & spectroscopy

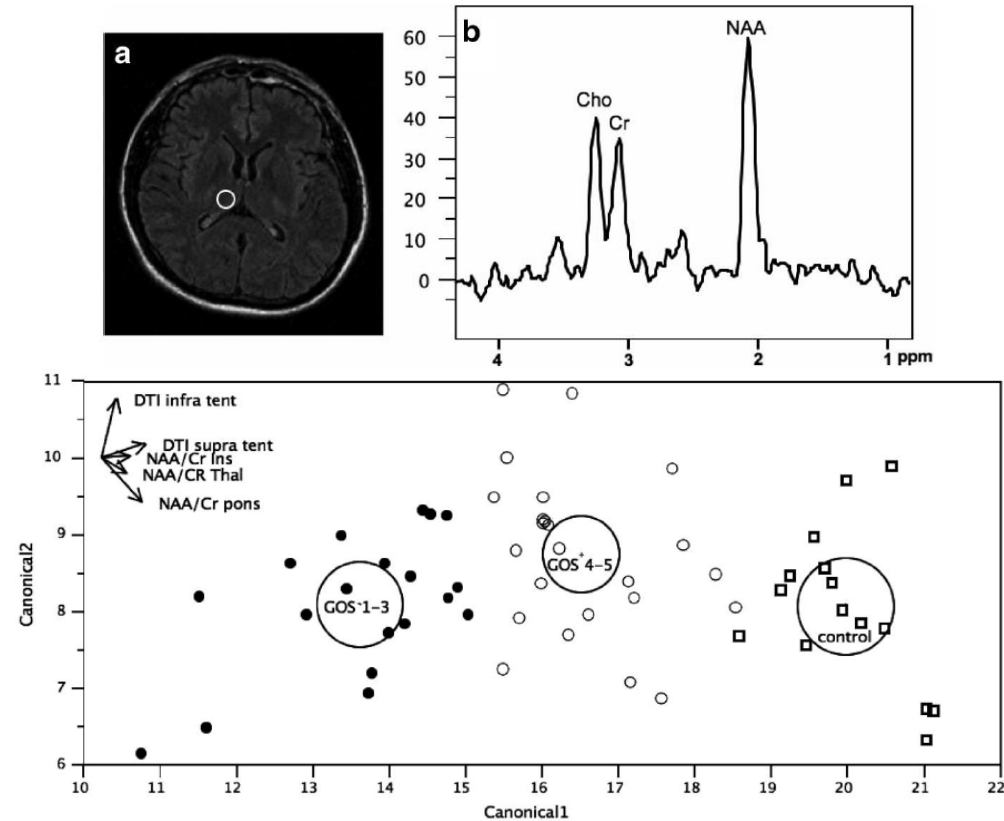
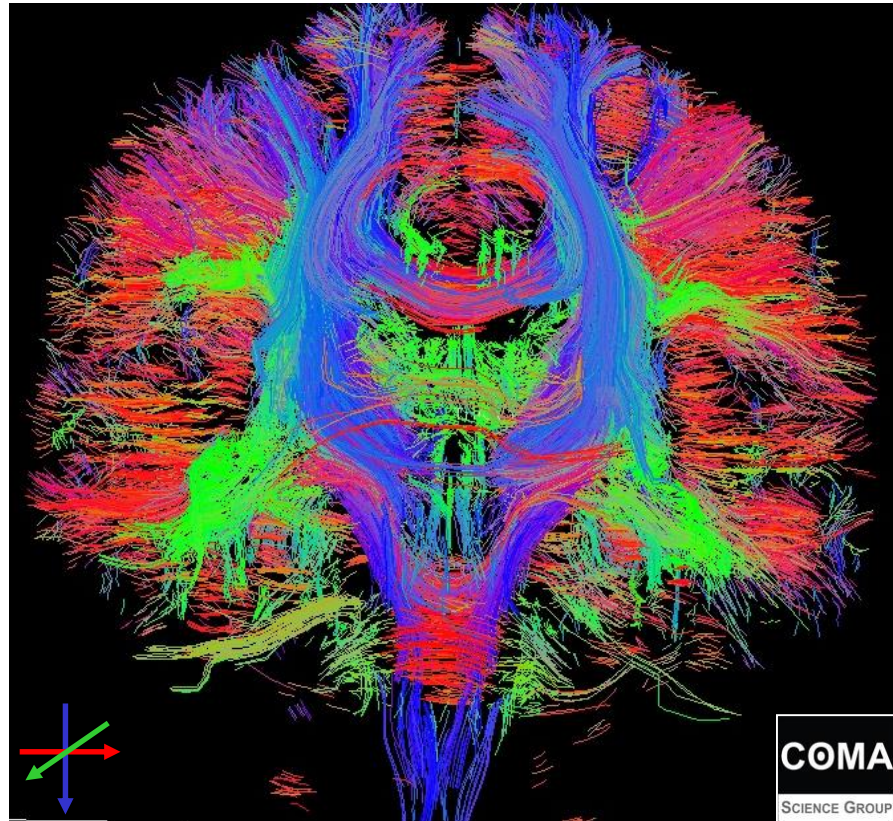
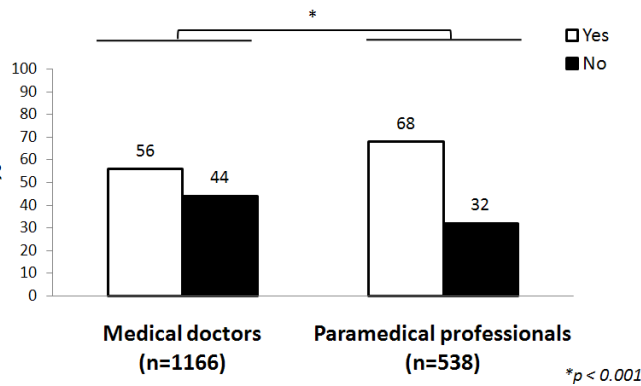


Figure 5. Linear discriminant analysis. Plotting the two discriminant functions (or canonical roots) against each other separated the GOS 1–3 group (unfavorable outcome, *closed circles*), the GOS 4–5 group (favorable outcome, *open circles*), and the control group (*open squares*). NAA, *N*-acetyl aspartate; *Cr*, creatine; *GOS*, Glasgow Coma Scale; *DTI*, diffusion tensor imaging.

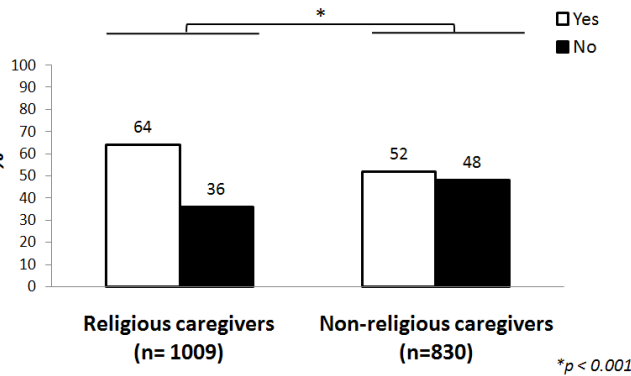


# Nociception and pain

Do you think that patients in a vegetative state can feel pain?



Do you think that patients in a vegetative state can feel pain?



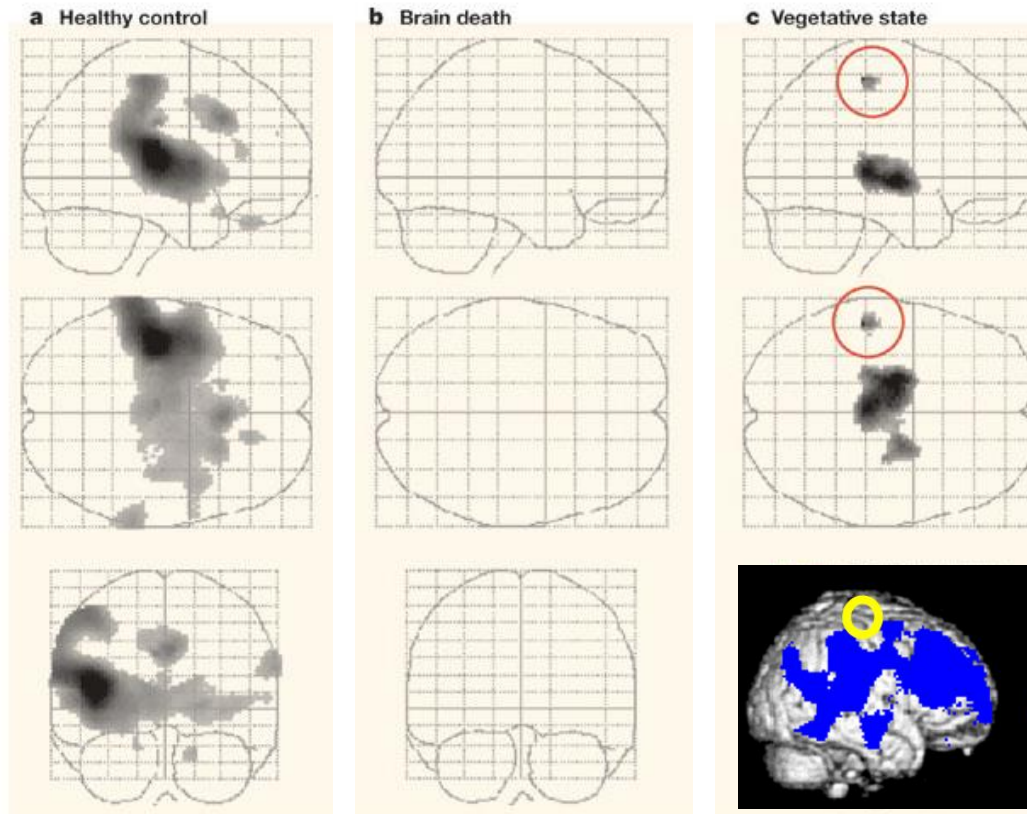
## Nociception Coma Scale - R

Score	Item	Response
<b>MOTOR RESPONSE</b>		
3	<i>Localization to Noxious Stimulation</i>	The non-stimulated limb must locate and make contact with the stimulated body part at the point of stimulation.
2	<i>Flexion Withdrawal</i>	There is isolated flexion withdrawal of at least one limb. The limb must move away from the point of stimulation.
1	<i>Abnormal Posturing</i>	Slow, stereotyped flexion or extension of the upper and/or lower extremities occurs immediately after the stimulus is applied.
0	<i>None/Flaccid</i>	There is no discernible movement following application of noxious stimulation, secondary to hypertonic or flaccid muscle tone.
<b>VERBAL RESPONSE</b>		
3	<i>Intelligible Verbalization</i>	Production of words in response to noxious stimulation. Each verbalization must consist of at least 1 consonant-vowel-consonant (C-VC) triad. For example, « aie » would not be acceptable, but « stop » or « that hurts » would.
2	<i>Vocalization / Oral Movement</i>	At least one episode of non-reflexive oral movement and/or vocalization in response to stimulation (such as « ah » or « aie »)
1	<i>Groans</i>	Groans are observed not spontaneously but in response to noxious stimulation.
0	<i>None</i>	No response to any of the above.
<b>FACIAL EXPRESSION</b>		
3	<i>Cry</i>	Cries are observed not spontaneously but in response to noxious stimulation.
2	<i>Grimace</i>	Grimaces are observed not spontaneously but in response to noxious stimulation.
1	<i>Oral reflexive movement/Startle response</i>	Clamping of jaws, tongue pumping, yawning, chewing movement.
0	<i>None</i>	There is no discernible facial expression following application of noxious stimulation.

Total score >3 / 9  
= analgesic treatment

# Do they feel pain ?

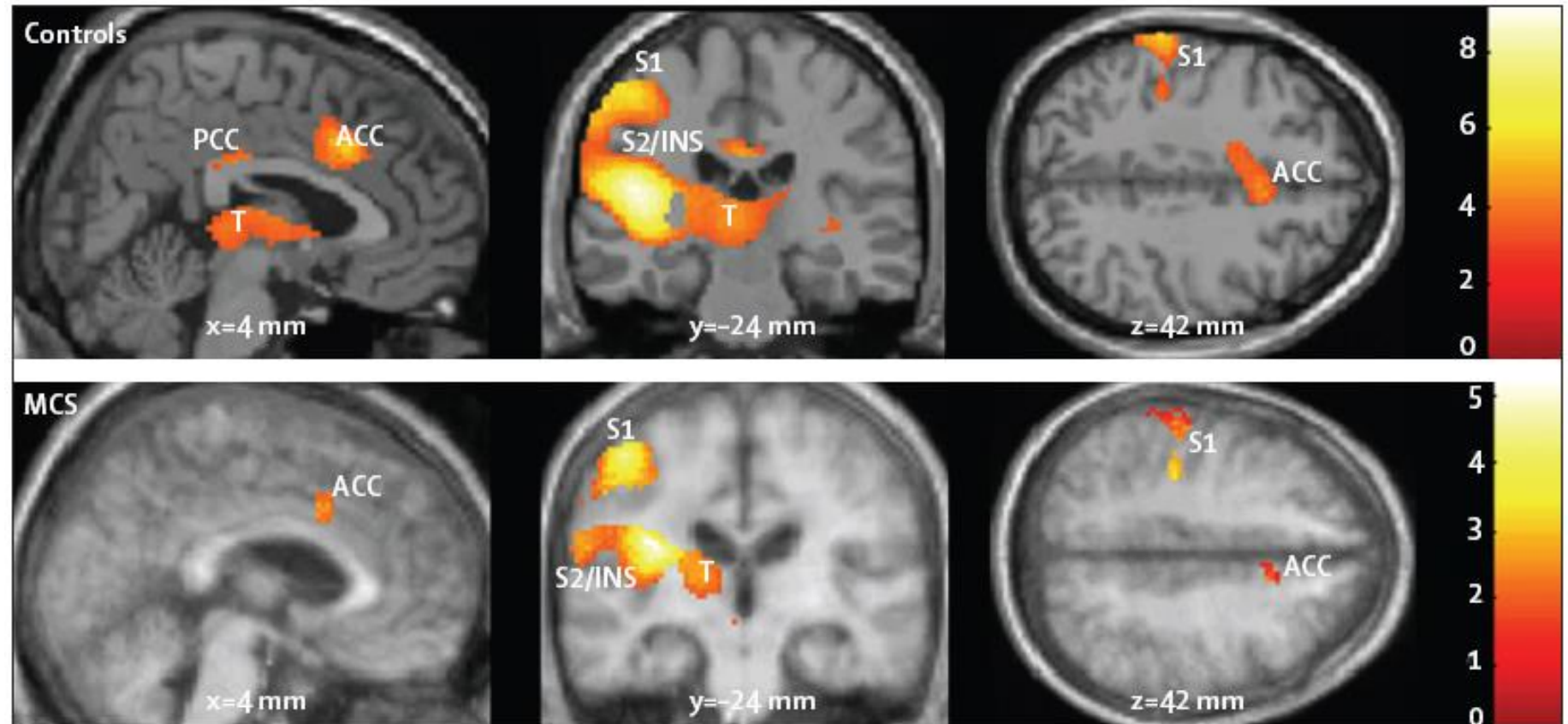
## Noxious electrical stimulation



Low level  
disconnected  
cortical activation

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Nature Reviews | Neuroscience

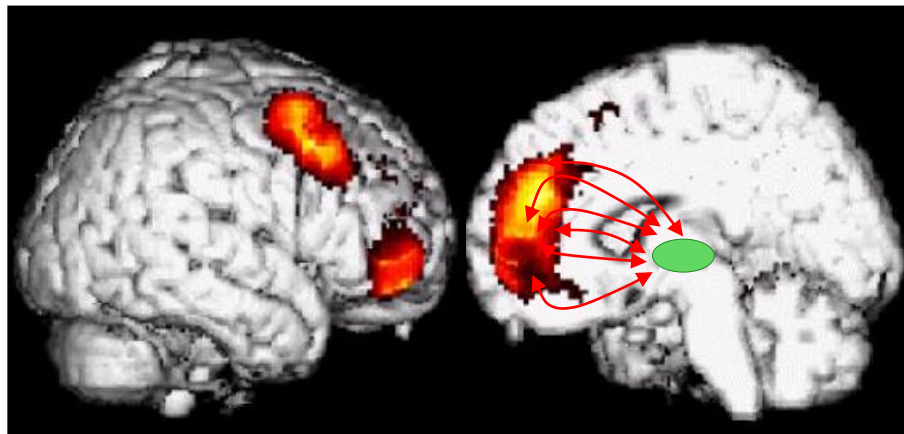
# Pain in minimally conscious state



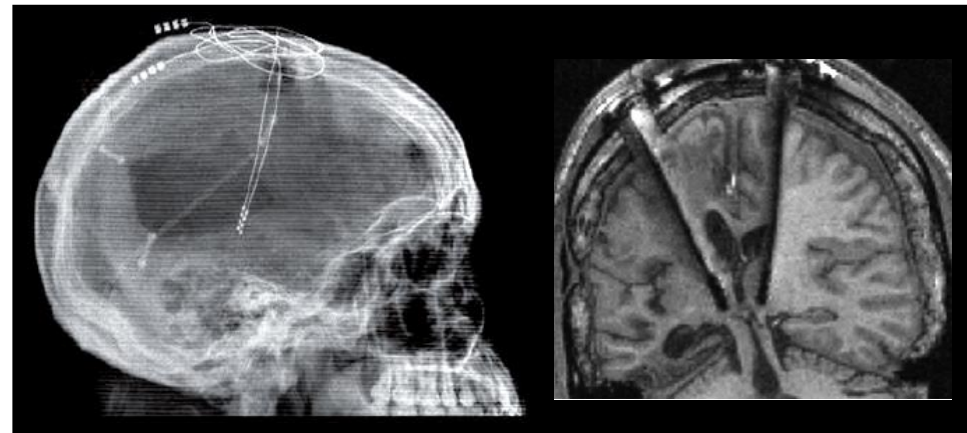
<http://neurology.thelancet.com>

# Consciousness $\approx$ thalamo-cortical

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



Intralaminar nuclei stimulation  
induces “recovery” from  
minimally responsive state



# Curative treatment: Drugs?

Drugs	Study (first author, year)	Number of patients and etiology	Diagnosis	Placebo control	Reported functional outcome
<i>Dopaminergic agents</i>					
Amantadine	Giacino (2012)	184 TBI	MCS/VS	Yes	Positive
	Schnakers (2008)	1 anoxic	MCS	No	Positive
	Patrick (2006)	10 TBI	Low responsive level	No	No effect
	Hughes (2005)	123 TBI	Coma	NA	No effect
	Saniova (2004)	41 TBI	'Persistent unconsciousness'	NA	Positive
	Meythaler (2002)	35 TBI	MCS	Yes	Positive
Bromocriptine	Brahmi (2004)	4 intoxication	Coma	No	Positive
Levodopa	Matsuda (2003)	3 TBI	VS	No	Positive
<i>Nonbenzodiazepine sedative</i>					
Zolpidem	Cohen (2008)	1 anoxic	Lethargic	No	Positive
	Shames (2008)	1 anoxic	MCS	No	Positive
	Singh (2008)	1 TBI	MCS	No	No effect
	Brefel-Courbon (2007)	1 hypoxic	Akinetic mutism	Yes	Positive
	Clauss (2006)	2 TBI, 1 anoxic	VS	No	Positive
	Clauss (2000)	1 TBI	Semi-comatose	No	Positive
<i>GABA agonist</i>					
Baclofen	Sarà (2007)	1 non-TBI	VS	No	Positive



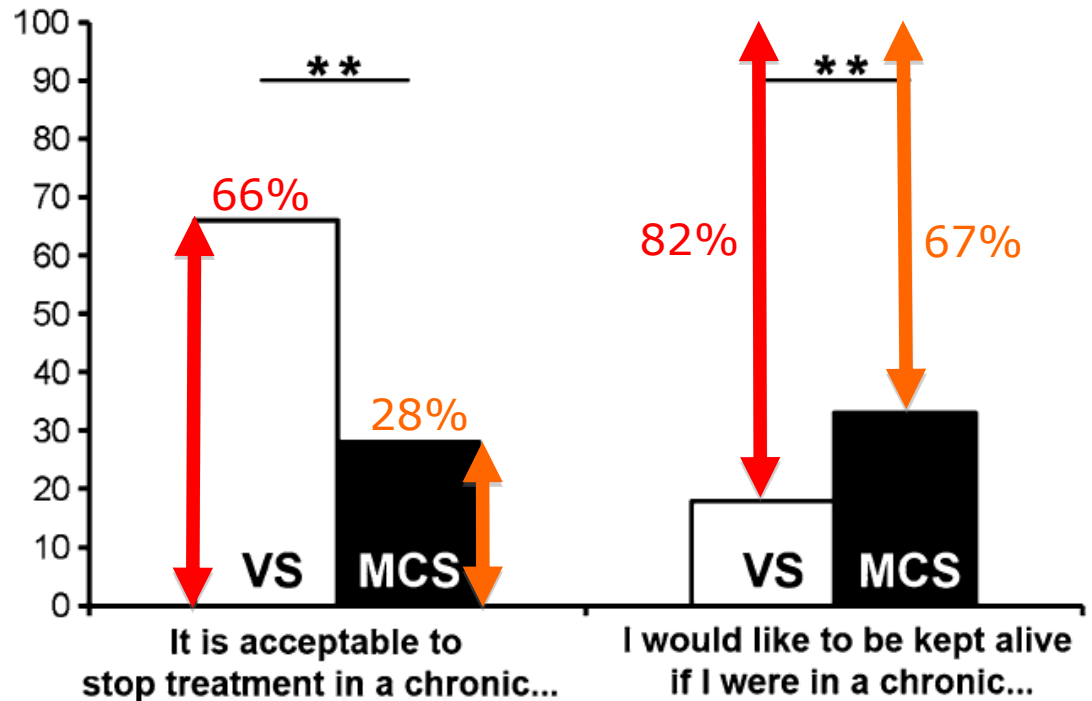
# End-of-life issues

## 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





# Quality of life

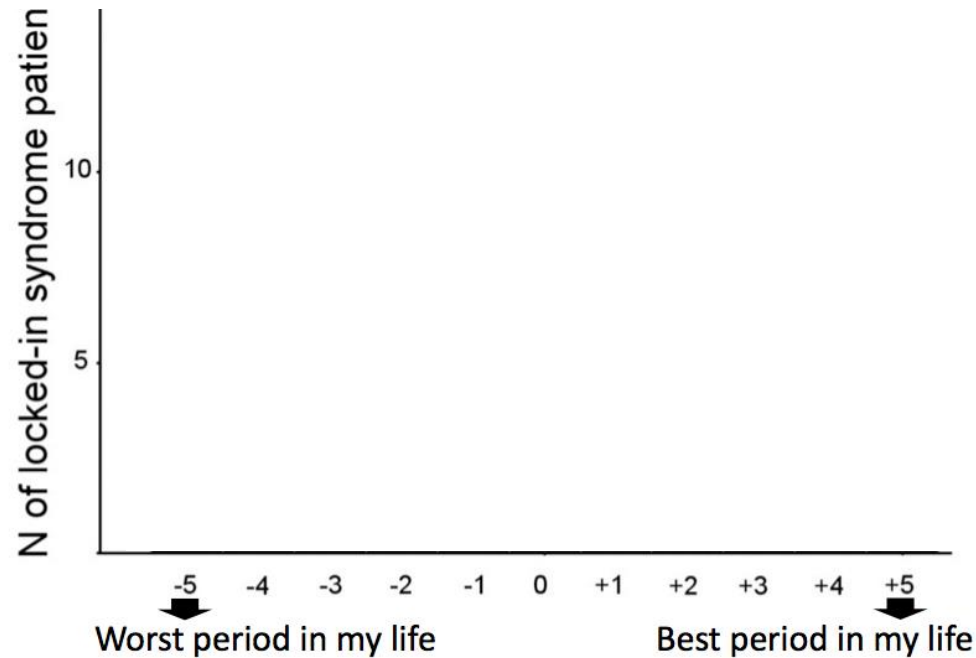
Open Access

Research

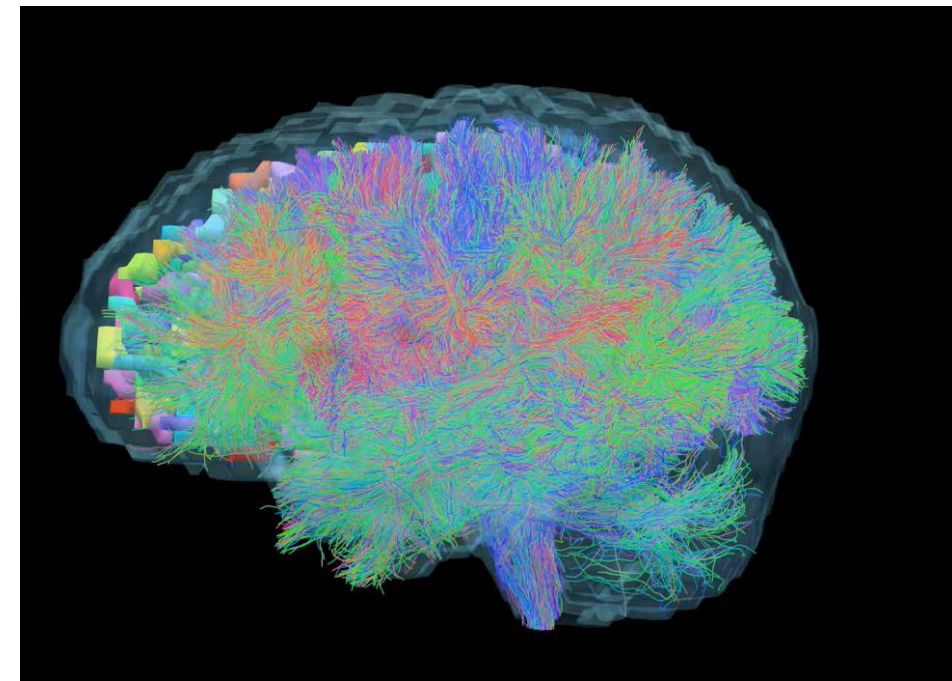
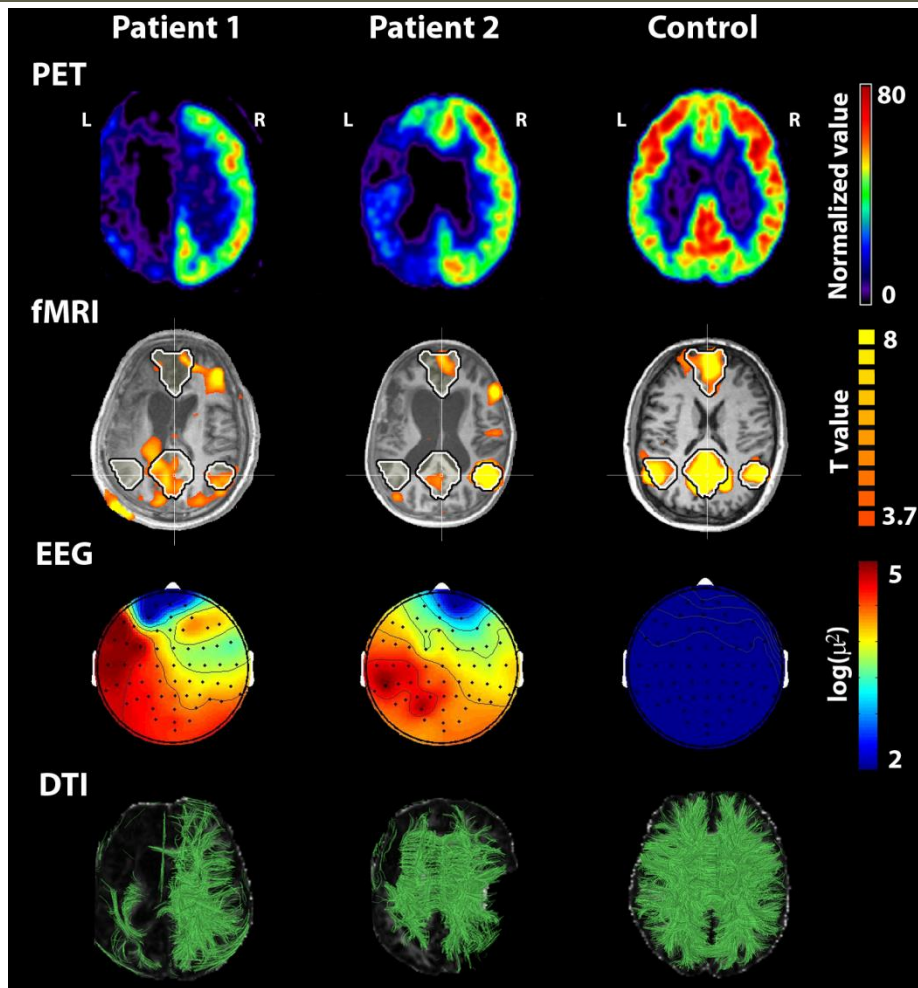


## A survey on self-assessed well-being in a cohort of chronic locked-in syndrome patients: happy majority, miserable minority

Marie-Aur lie Bruno,<sup>1</sup> Jan L Bernheim,<sup>2</sup> Didier Ledoux,<sup>1</sup> Fr d ric Pellas,<sup>3</sup> Athena Demertzi,<sup>1</sup> Steven Laureys<sup>1</sup>



# Conclusion



Erik Ziegler, *Cyclotron Art Committee*



# Conclusion

## Human conscious awareness

≈ emergent property of collective critical neural network dynamics, involving a frontoparietal global workspace

## Diagnostic use

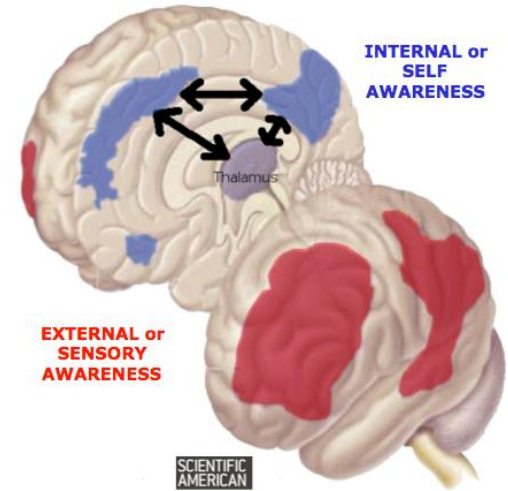
≈ 40% misdiagnosis

## Prognostic use

multimodal imaging

## Therapeutic use

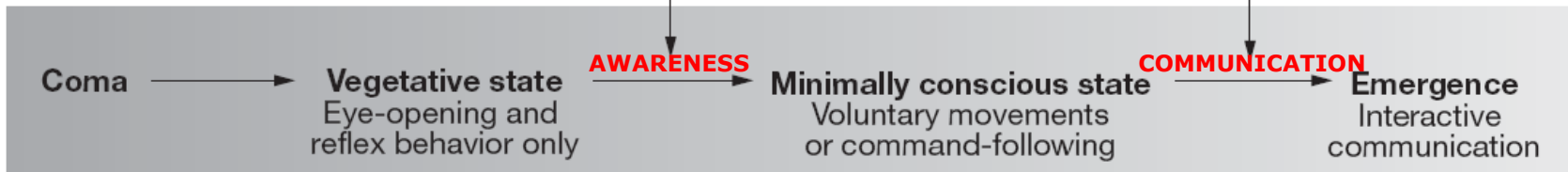
pain treatment / deep brain stimulation thalamus



## Ethical issues

EMG, ERP or fMRI might reveal subclinical command-following

EEG (brain-computer interfaces) or real-time fMRI might enable communication that is not dependent on motor pathways



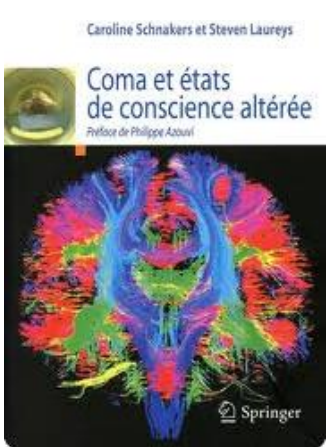
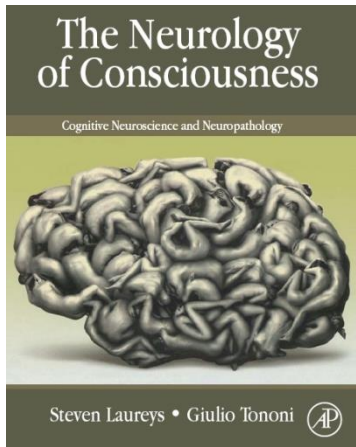
[www.nature.com/clinicalpractice/neuro](http://www.nature.com/clinicalpractice/neuro)

Laureys & Boly, *Nature Clinical Practice*, 2008

Laureys & Schiff, *NeuroImage*, 2012

Sanders et al, *Anesthesiology*, 2012





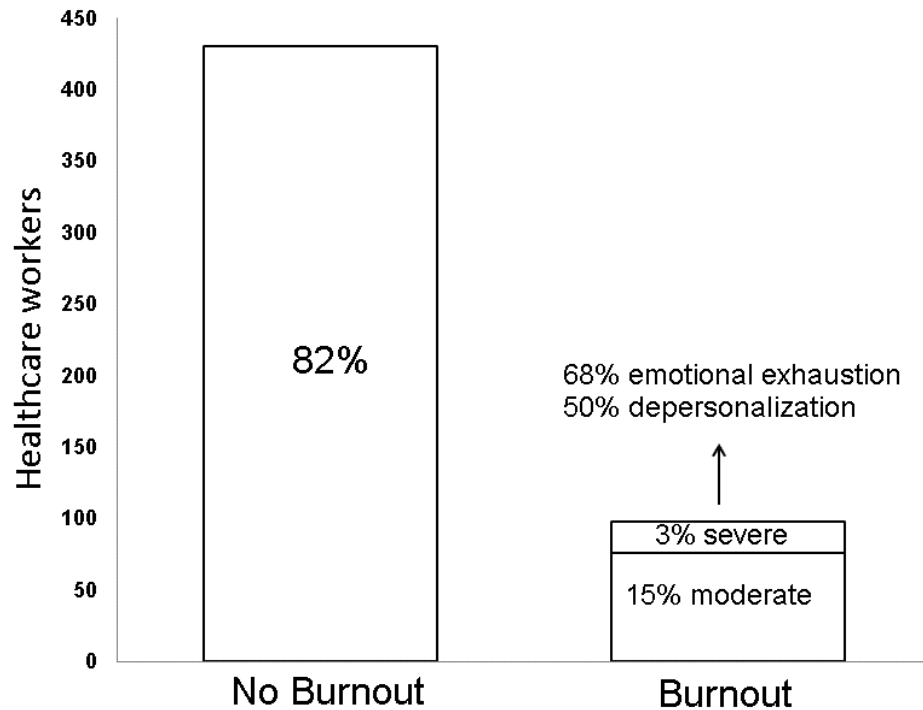
**COMA@ULG.AC.BE**



Université de Liège

# Burnout in caregivers

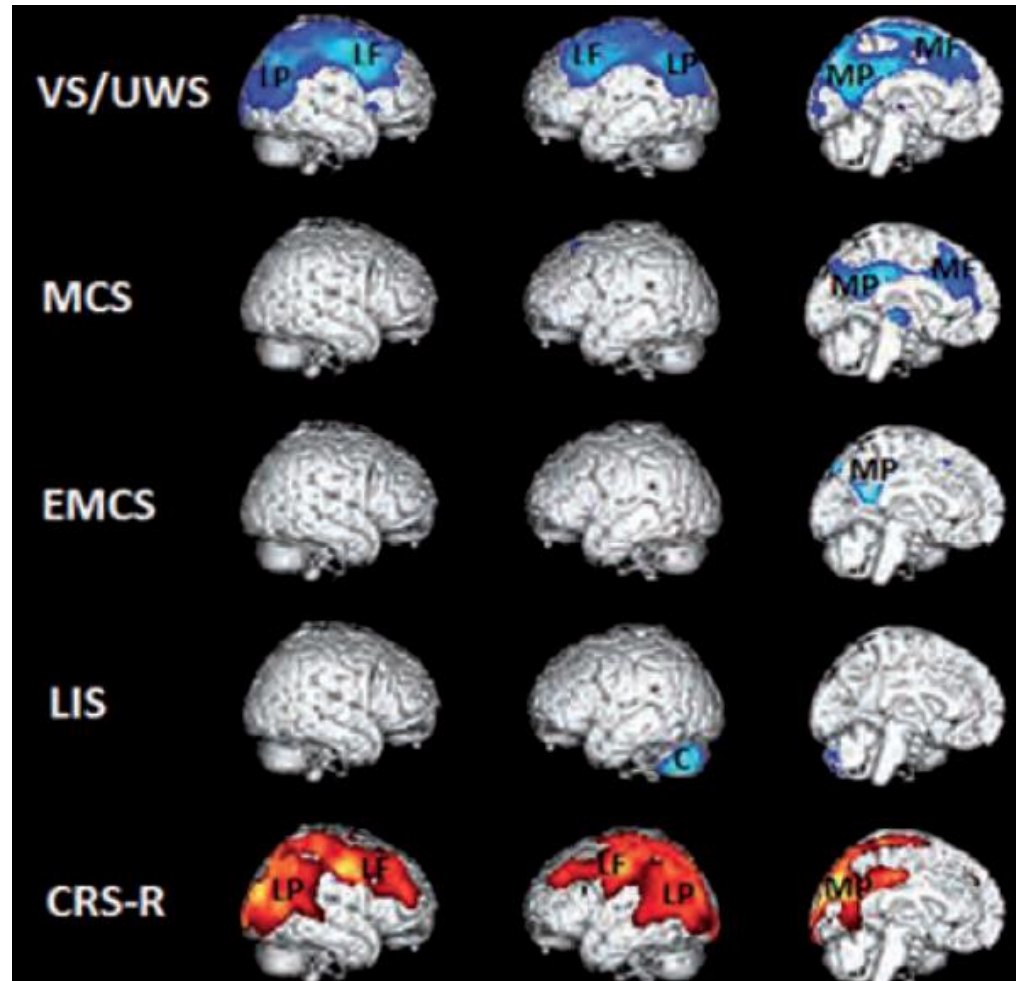
568 health care workers (Maslach Burnout Inventory)



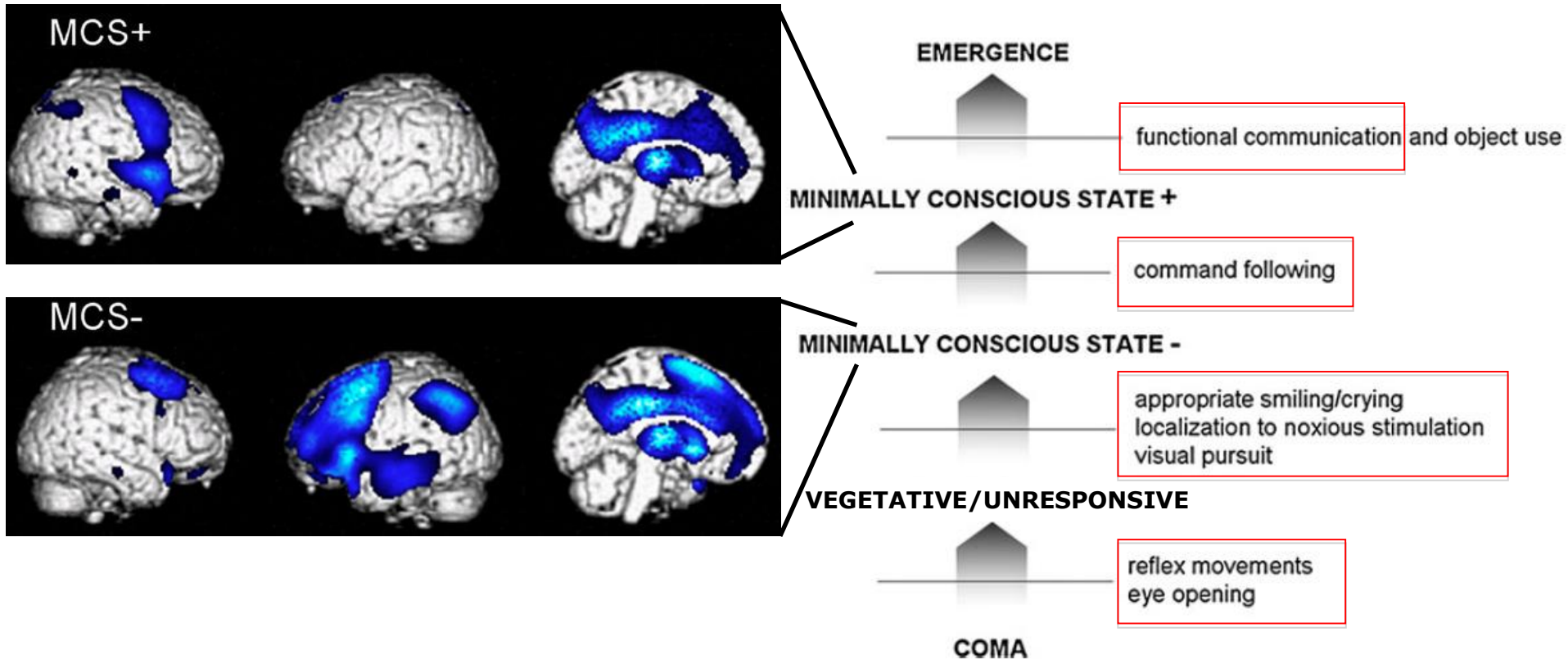
Profession	Burnout
Physician	8%
Nurse	24%
Nursing assistant	23%
Physio-/speech-/ergo-therapist	8%
Psychologist/social worker	10%



# Frontoparietal “global workspace”



# Disorders of consciousness

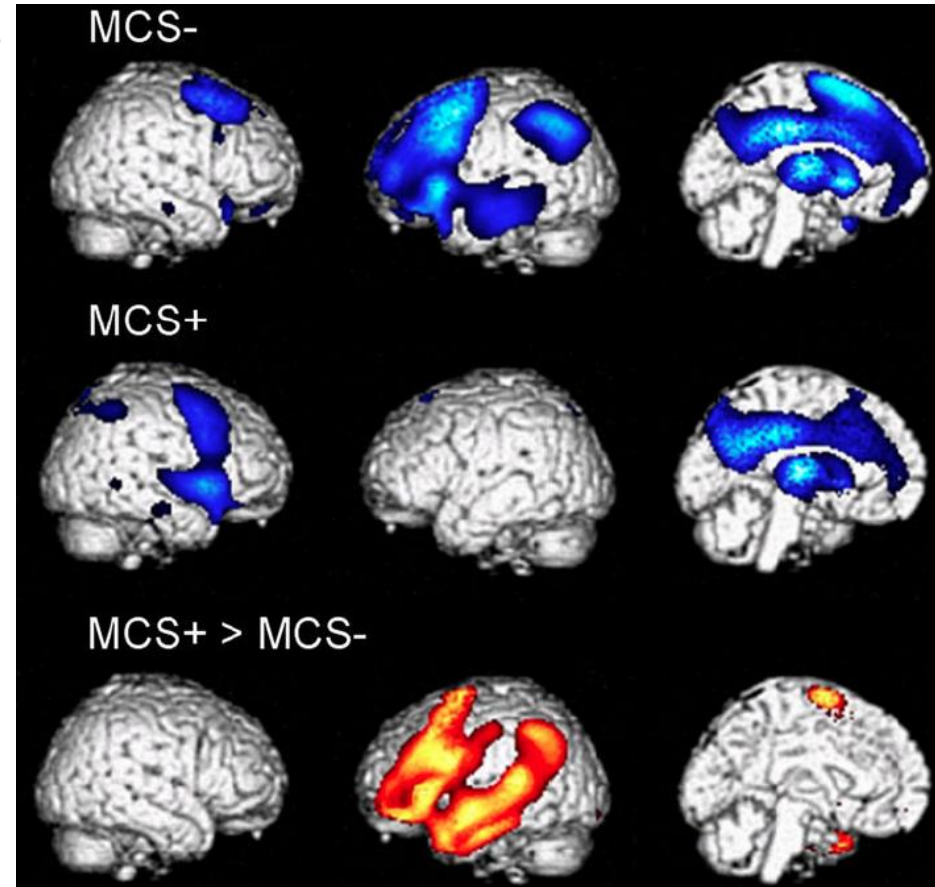
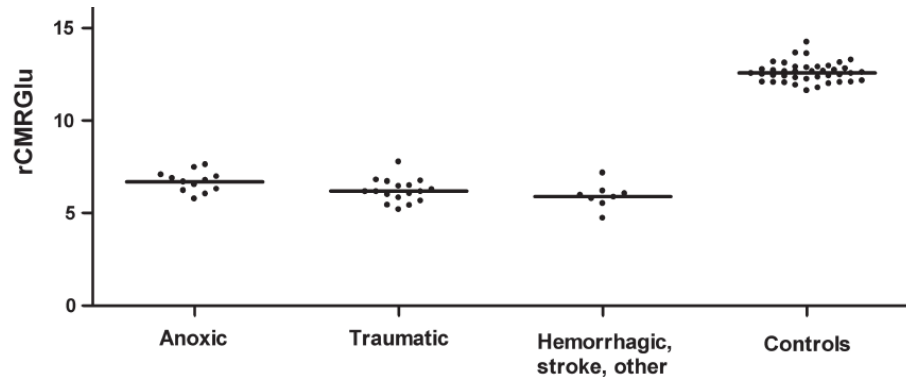


# Aphasia as a confound

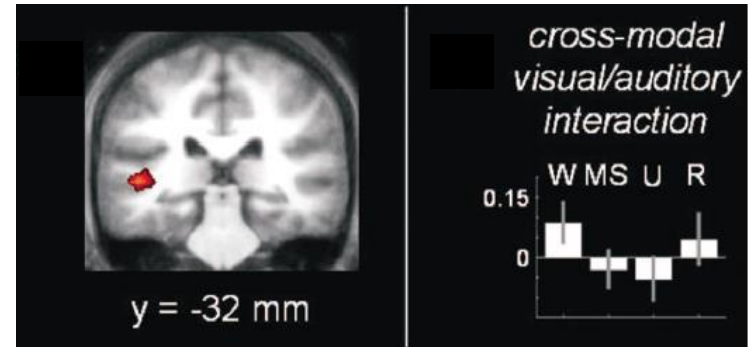
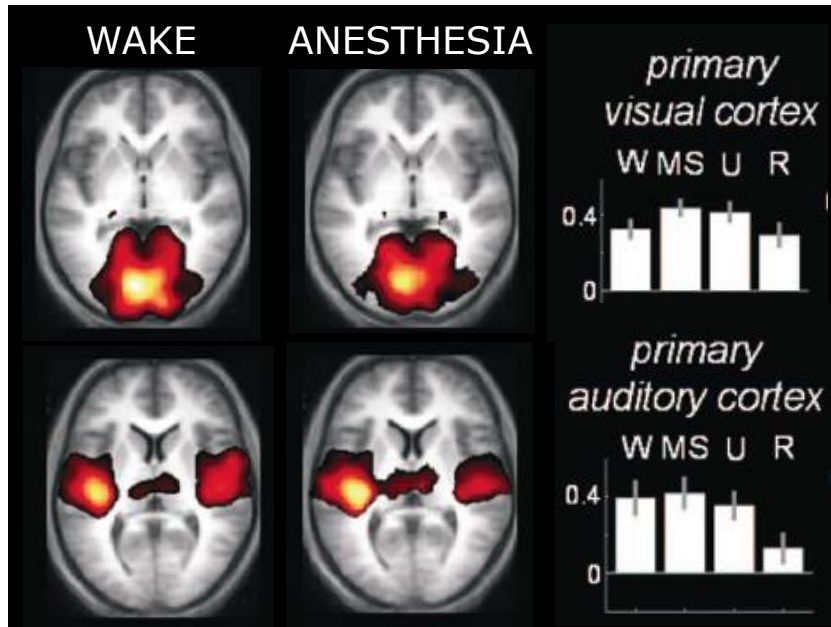
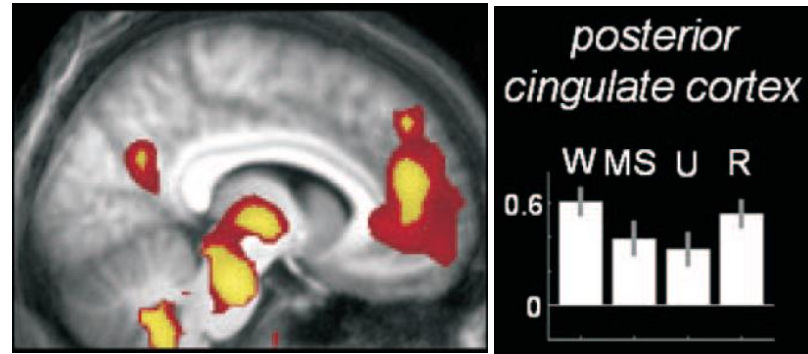
The problem of aphasia in the assessment of consciousness in brain-damaged patients ☆

Steve Majerus<sup>1,3</sup>, Marie-Aurélie Bruno<sup>2,3</sup>, Caroline Schnakers<sup>2</sup>,  
Joseph T. Giacino<sup>4</sup> and Steven Laureys<sup>2,3,\*</sup>

*Progress in Brain Research*, Vol. 177  
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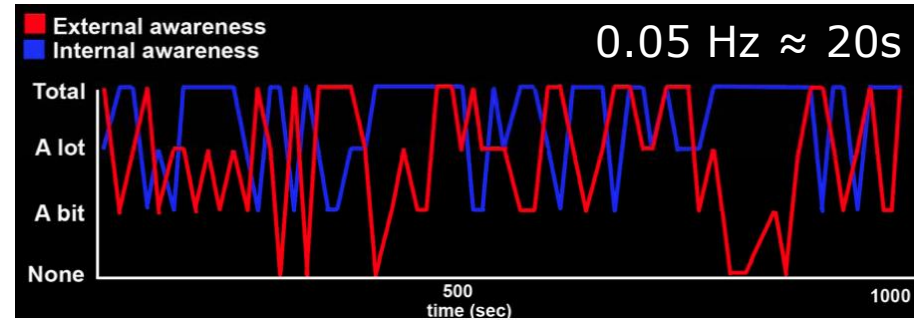
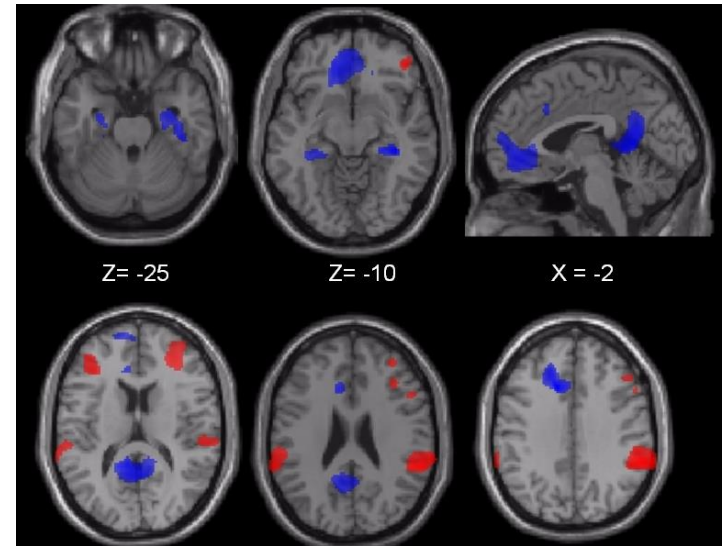
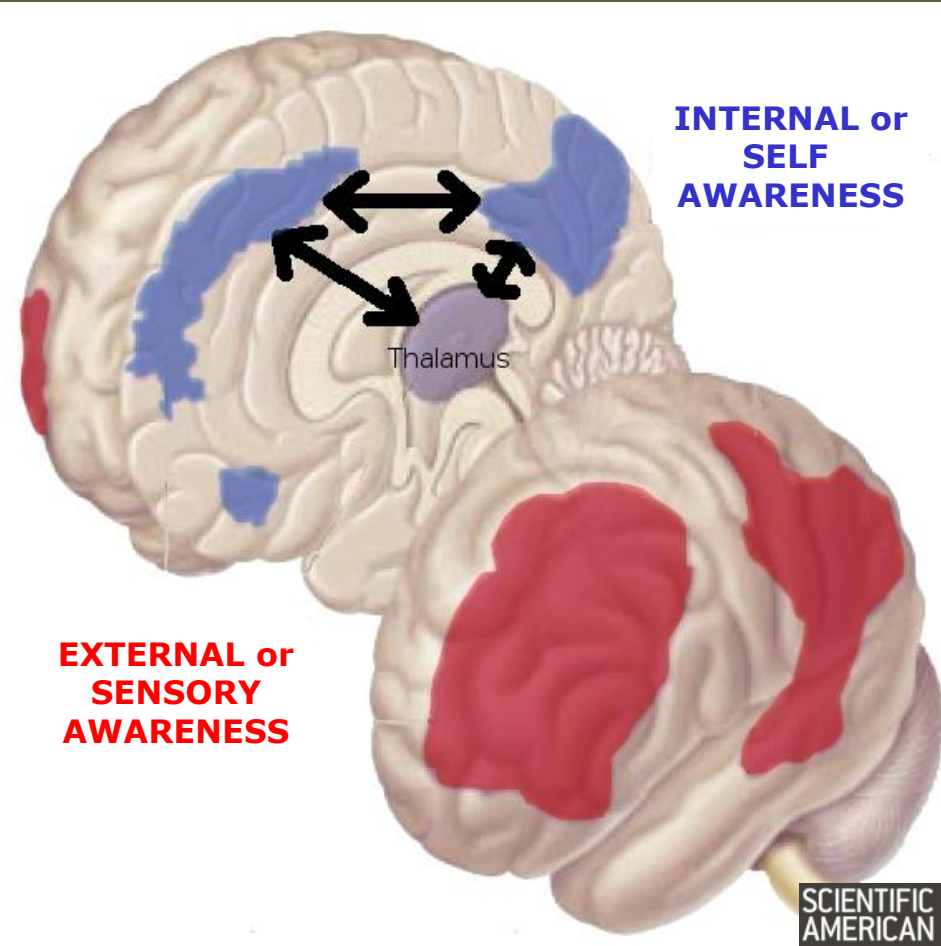


# Default connectivity in anesthesia





# Two awareness networks



Journal of  
Cognitive Neuroscience