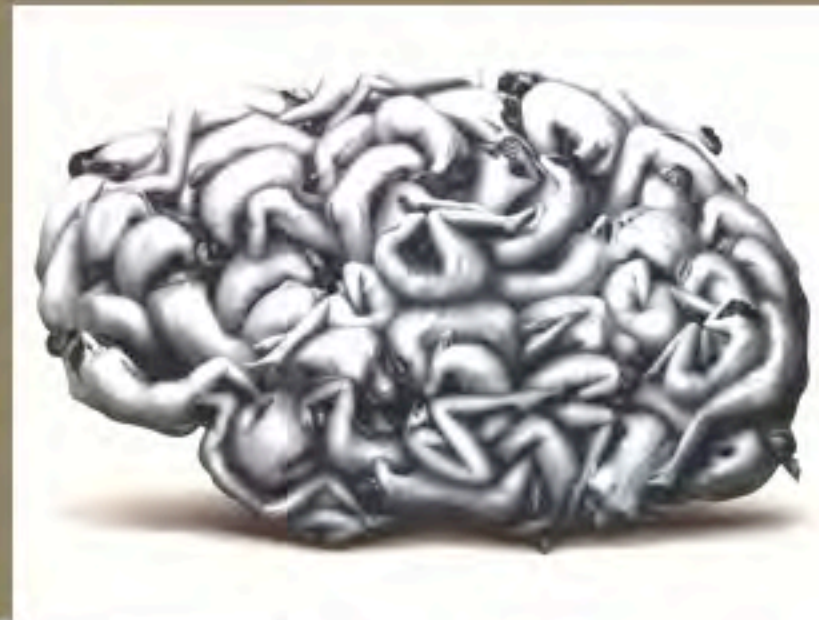


Neurophysiology of “vegetative” unresponsive wakefulness & minimally responsive patients

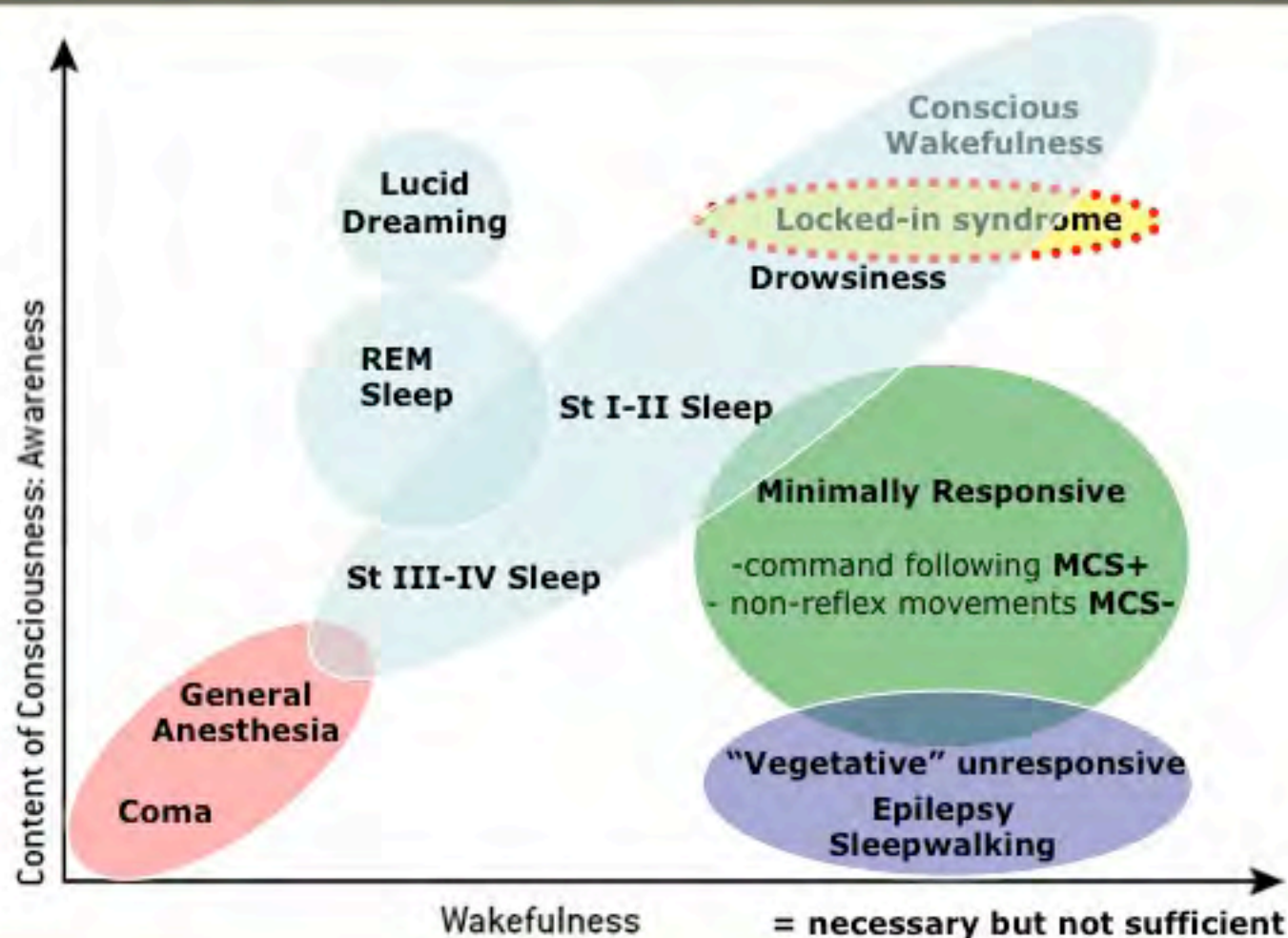
Steven Laureys
Coma Science Group
Cyclotron Research Centre &
Neurology Dept
University & University Hospital of Liège
Belgium

Rome, June 21 2011

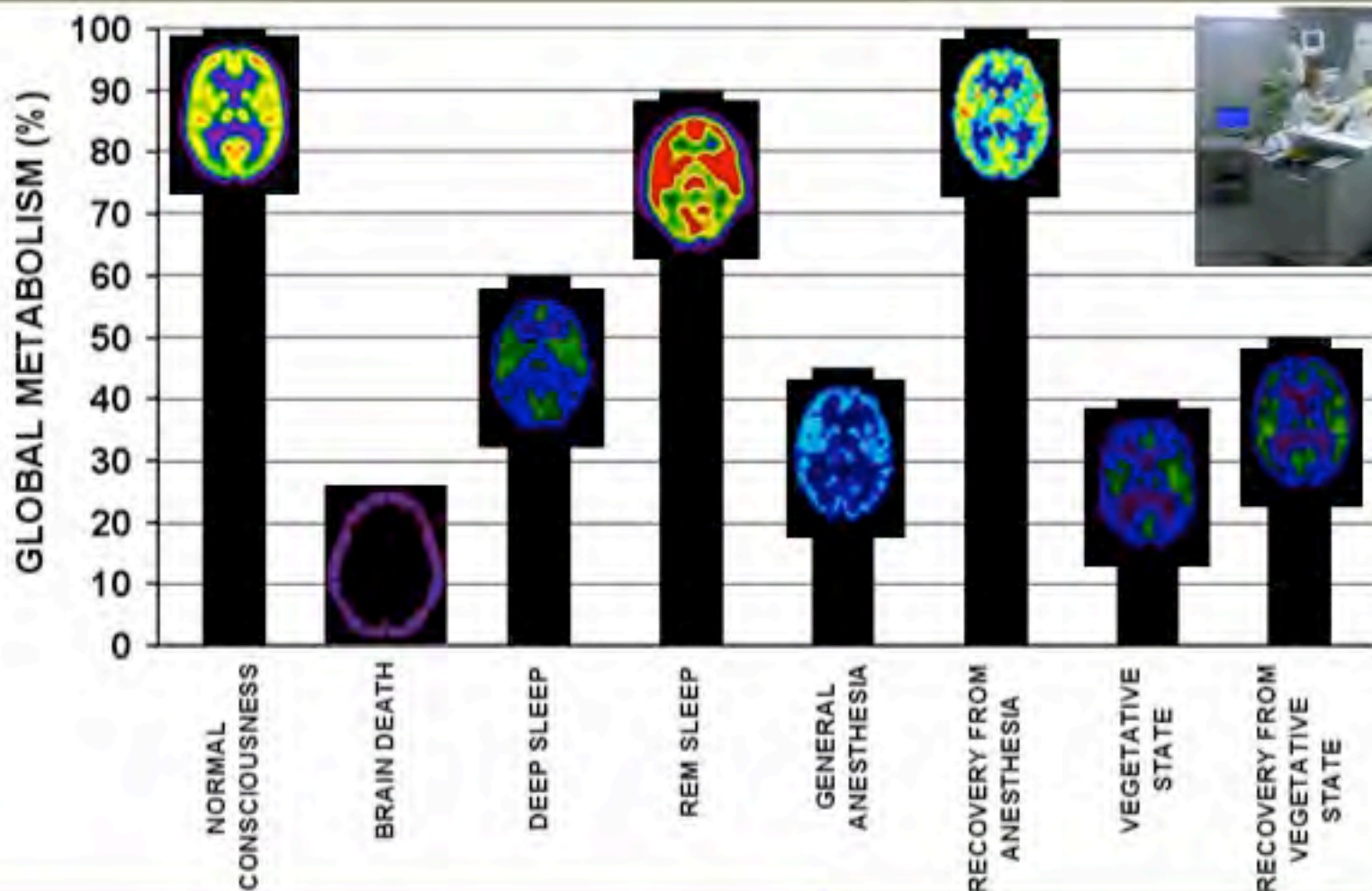


www.comascience.org

Reducing consciousness to 2D

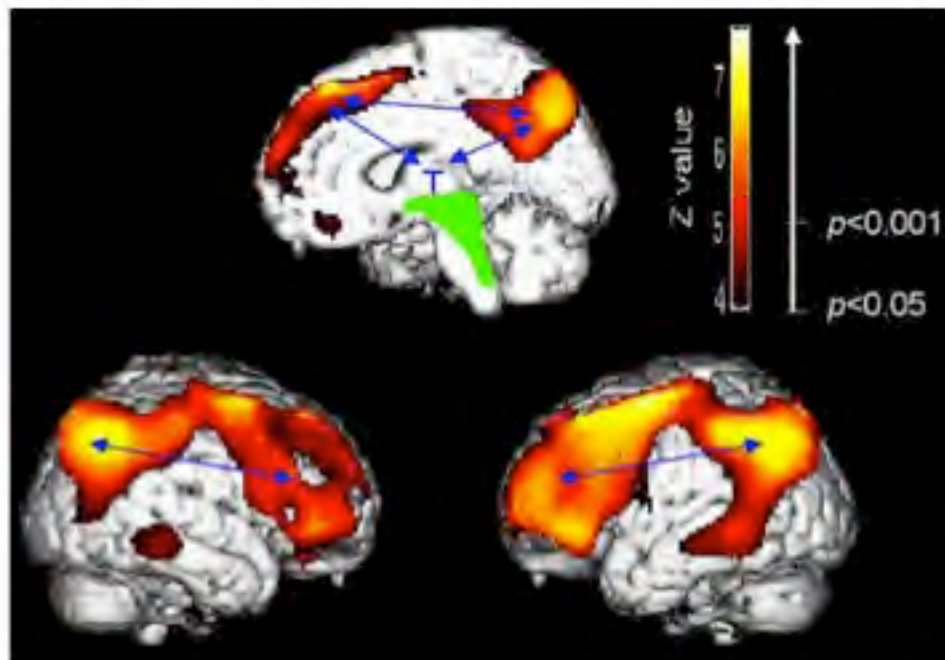


Consciousness \neq whole brain



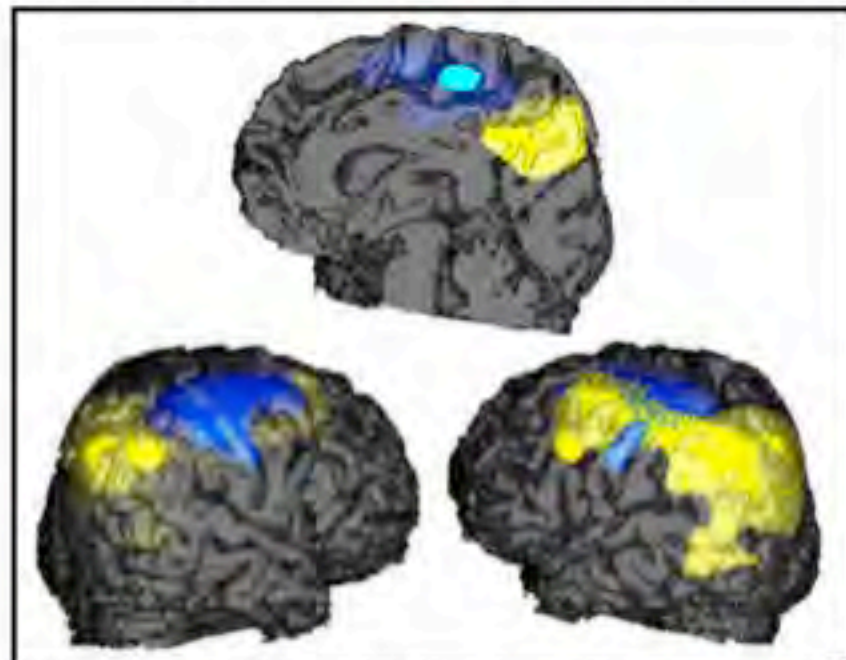
Consciousness \approx frontoparietal

Areas systematically dysfunctional in "vegetative" state



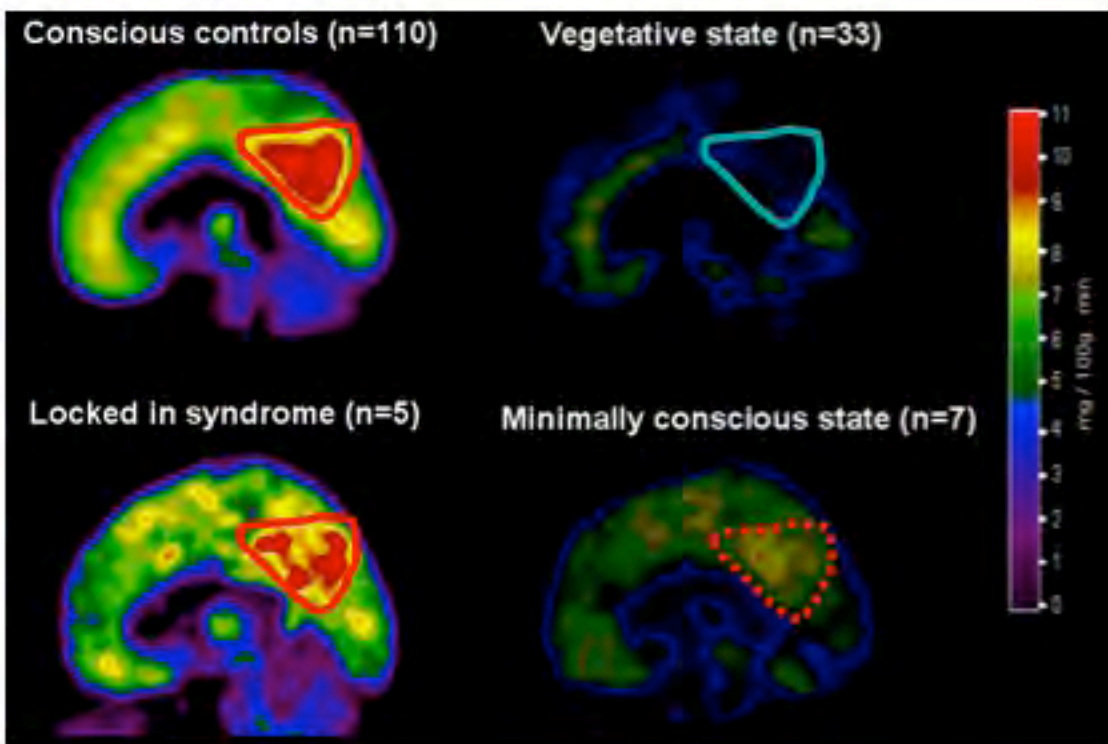
Laureys et al, *Neuroimage* 1999

Areas recovering metabolism after recovery from "vegetative" state



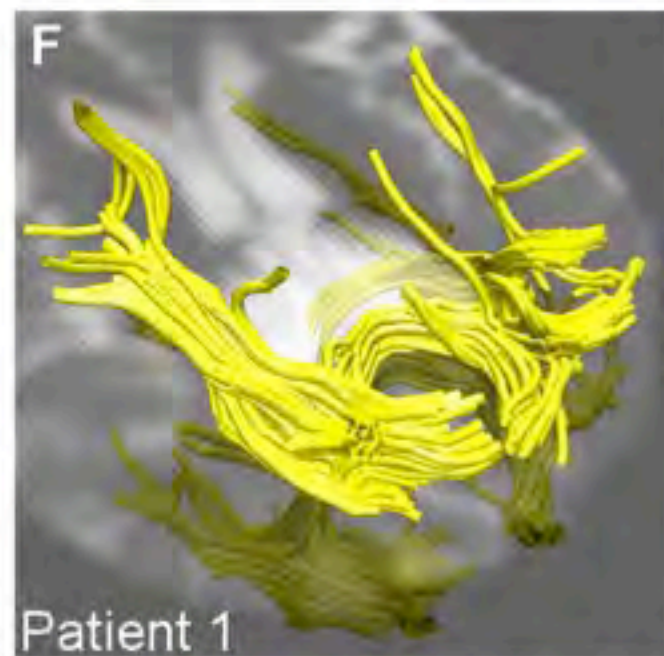
Laureys et al, *J Neurol Neurosurg Psychiatry*, 1999

Precuneus \approx hub in the network



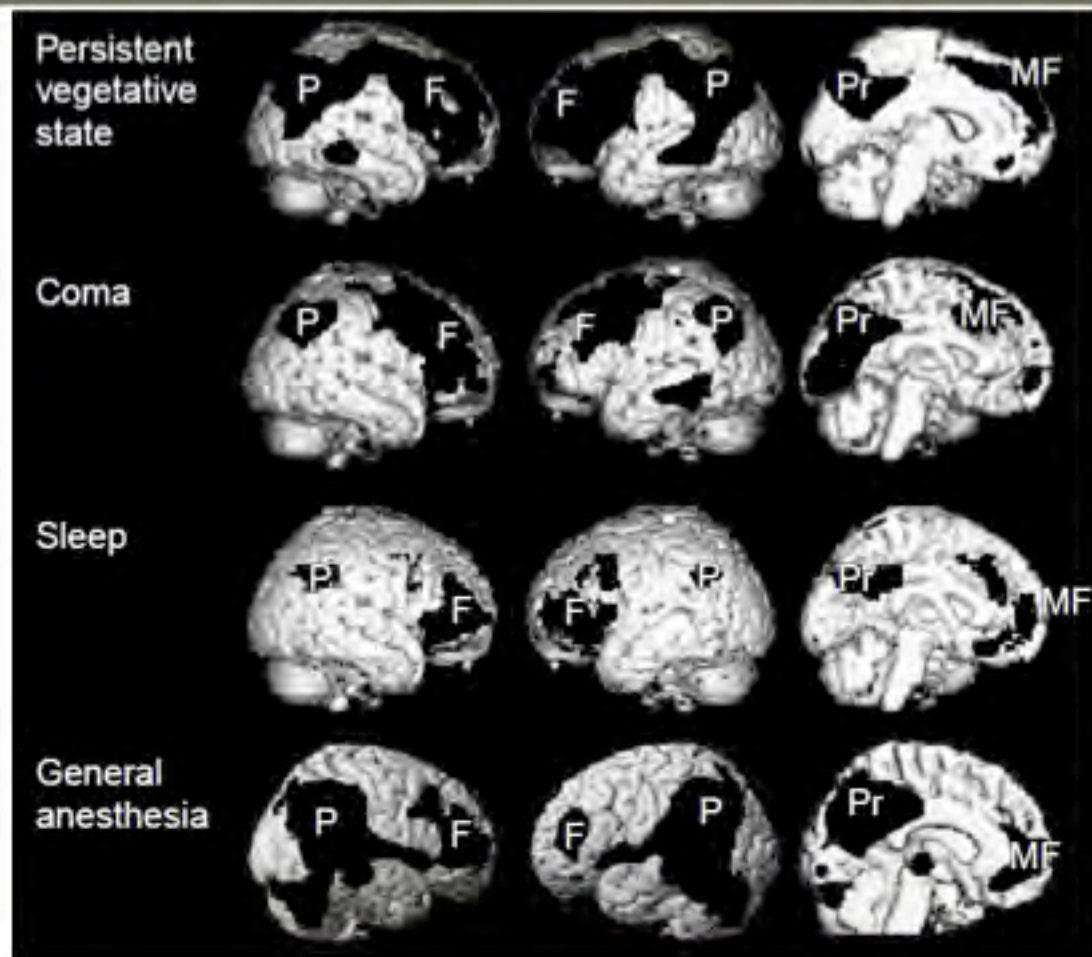
Laureys et al, *Lancet Neurology*, 2004

Axonal re-growth in Terry Wallis



Voss et al, *J Clin Invest*, 2006

Frontoparietal "global workspace"



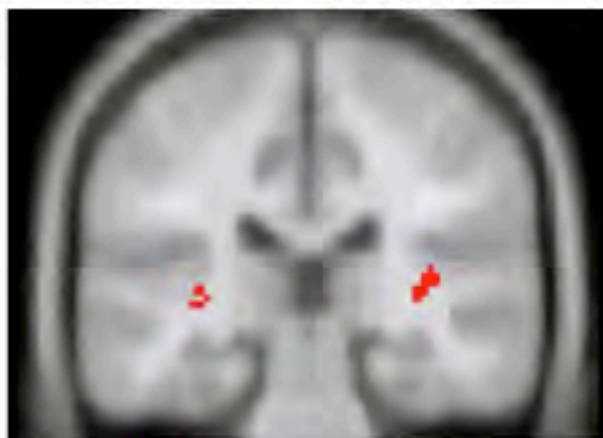
preserved arousal
no awareness

no arousal
no awareness

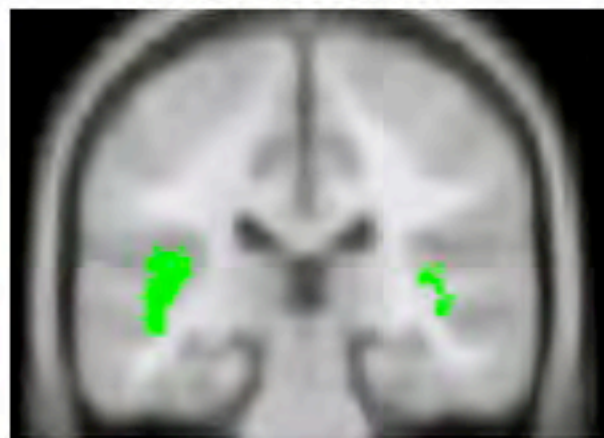
TRENDS in Neurosciences

Consciousness \neq primary cortex

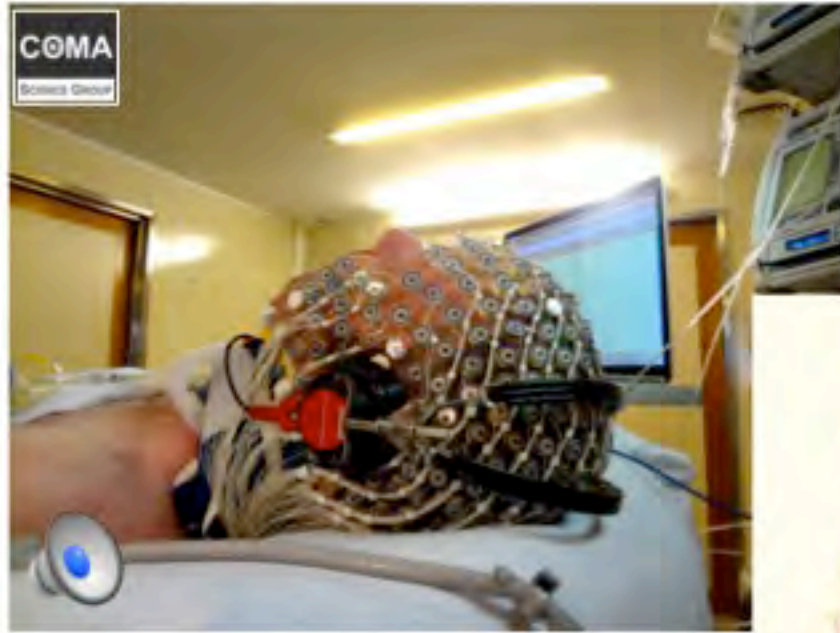
"VEGETATIVE"
UNRESPONSIVE



MINIMALLY
RESPONSIVE



Consciousness \approx top-down



“VEGETATIVE”
UNRESPONSIVE



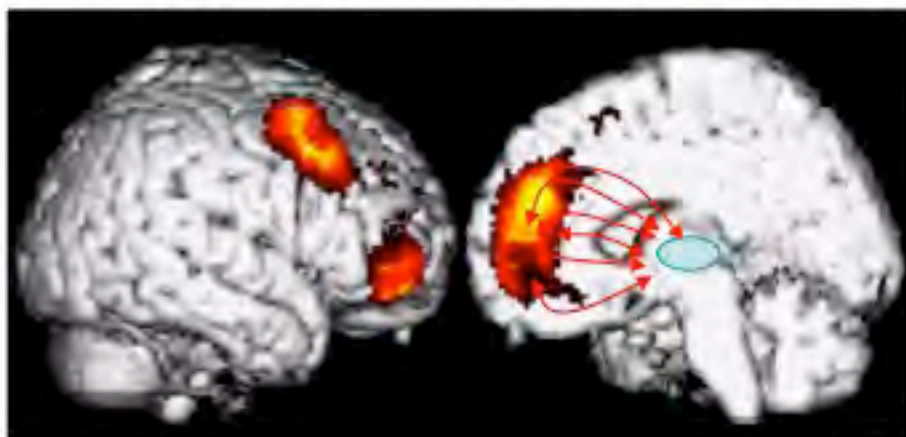
MINIMALLY
RESPONSIVE



Science

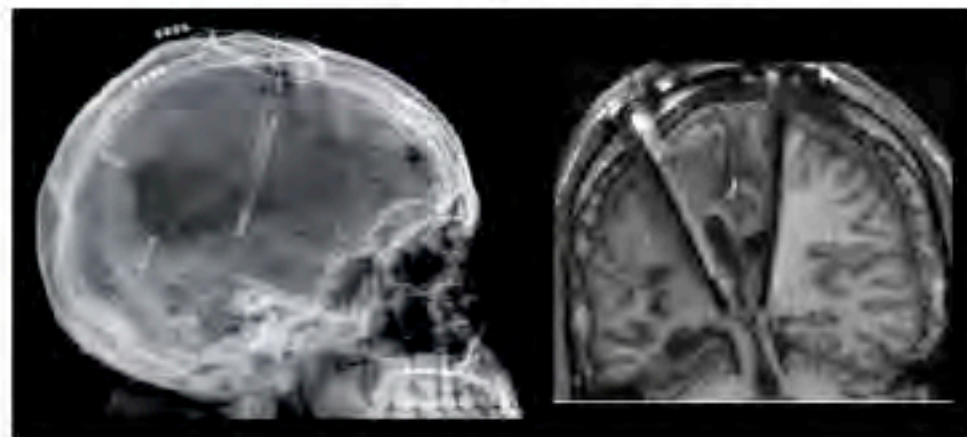
Consciousness \approx thalamo-cortical

Intralaminar nuclei "reconnections"
in spontaneous recovery from
"vegetative" unresponsive state



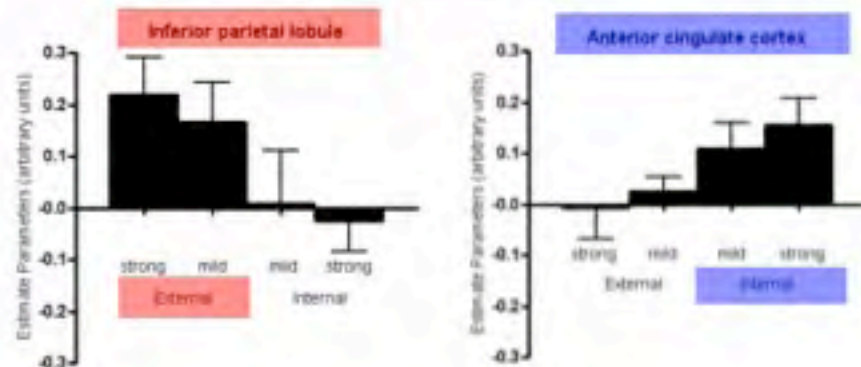
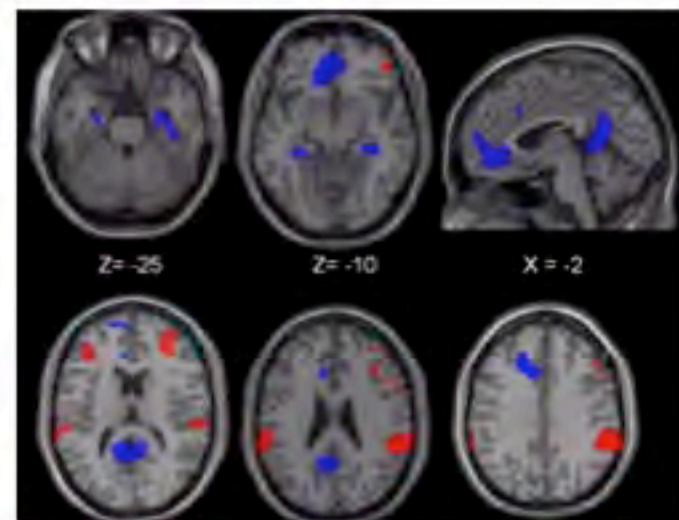
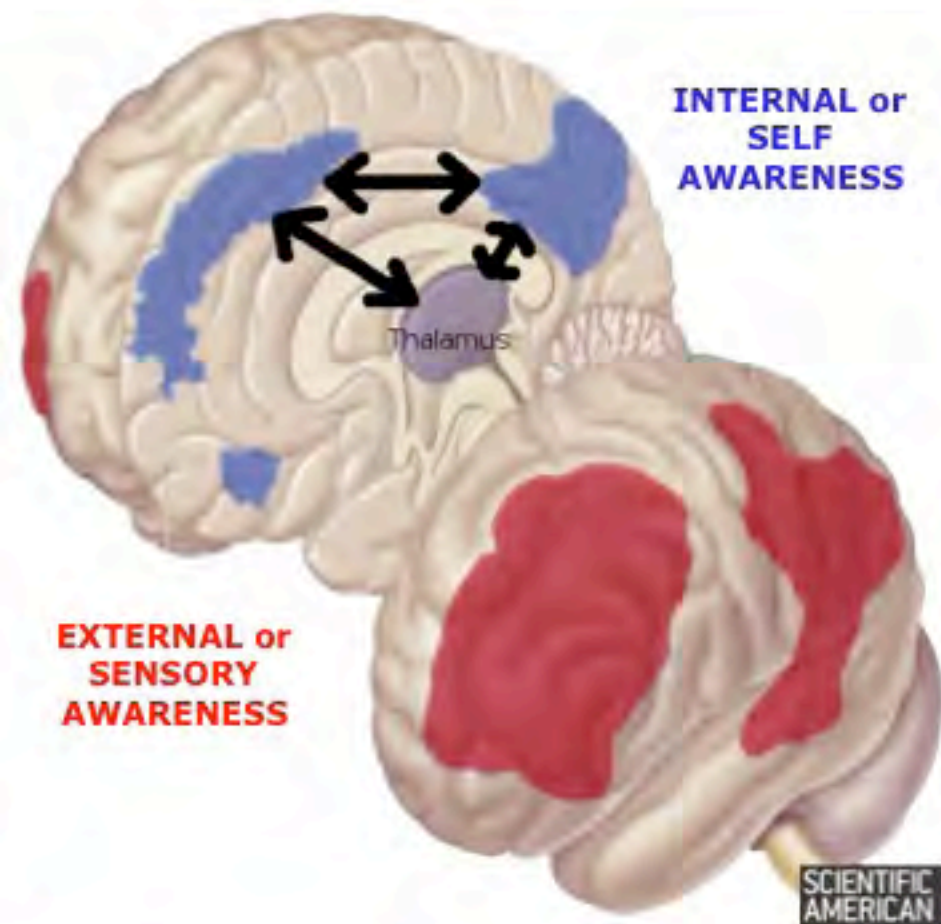
Laureys et al, *Lancet* 2000

Intralaminar nuclei stimulation
induces "recovery" from
minimally responsive state



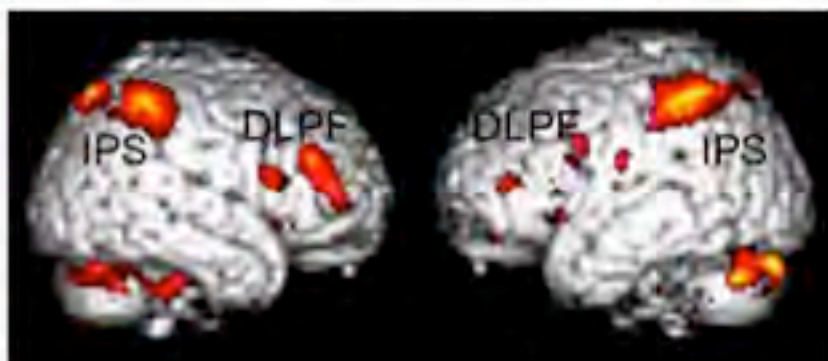
Schiff et al, *Nature* 2007

Two awareness networks



External and internal awareness

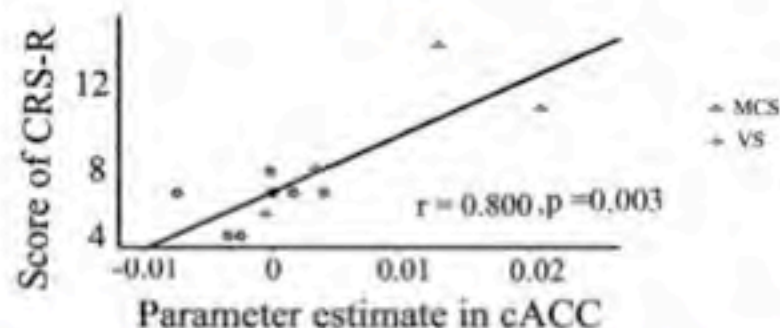
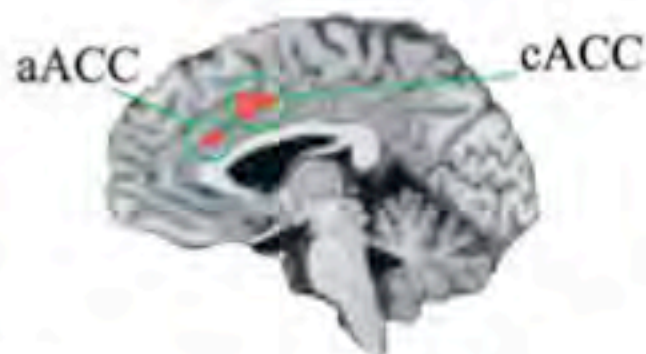
EXTERNAL (SENSORY) AWARENESS (laser stimulation)



perceived (433 ± 23 mJ) >
unperceived (438 ± 21 mJ)

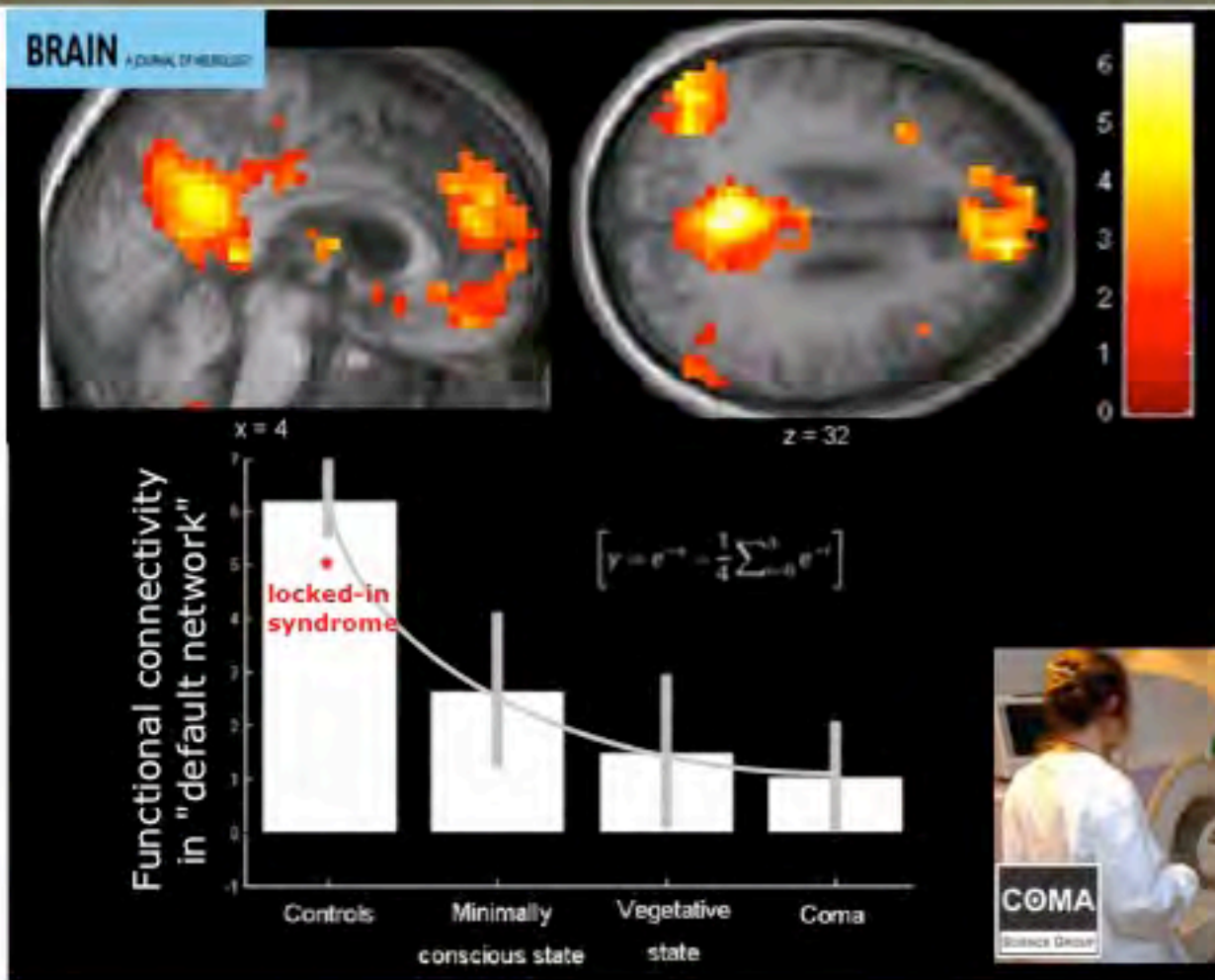
Boly et al, *PNAS* 2007

INTERNAL (SELF) AWARENESS (own name)

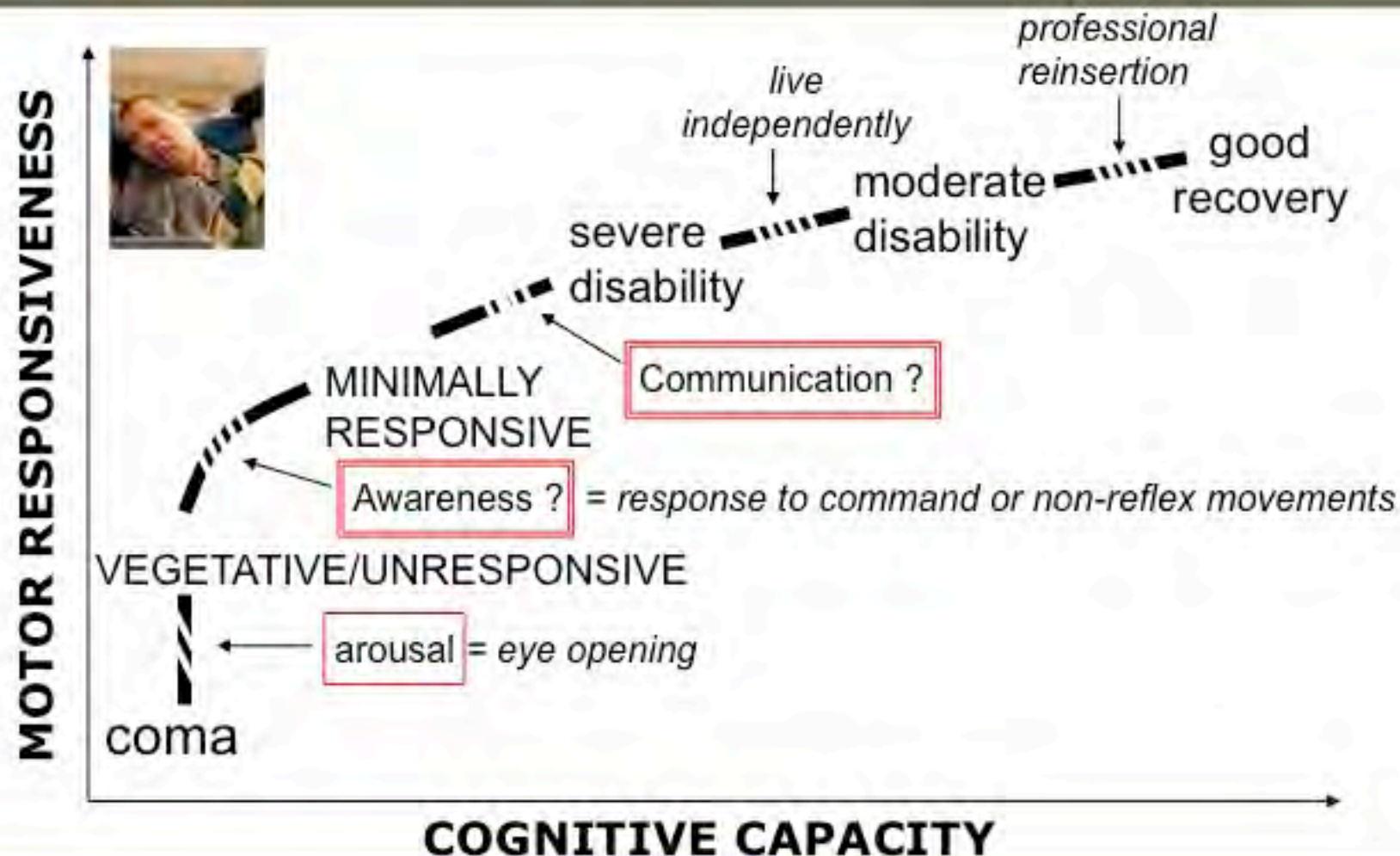


Perrin et al, *Neuropsychologia* 2005
Qin et al, *Human Brain Mapping*, 2010

"Resting" default mode connectivity



Clinical interest



A new name for « vegetative »

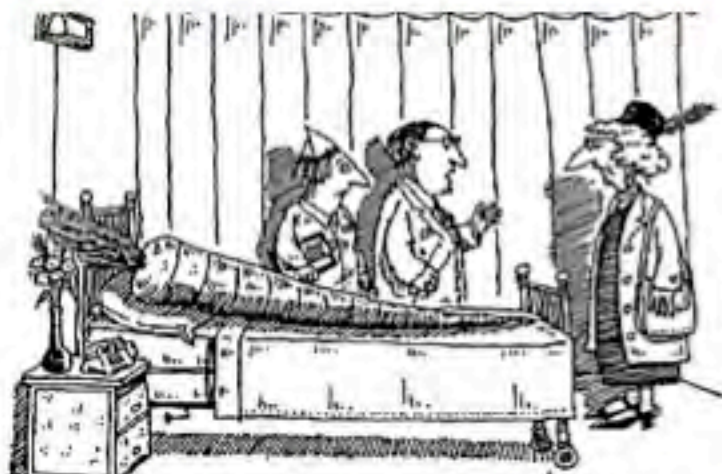


Highly accessed Open access

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

Steven Laureys¹, Gastone G Celesia², Francois Cohadon³, Jan Lavrijsen⁴, José León-Carrión⁵, Walter G Sannita^{6,7}, Leon Szabon⁸, Erich Schmutzhard⁹, Klaus R von Wild^{10,11}, Adam Zeman¹² and Giuliano Dolce¹³ for the European Task Force on Disorders of Consciousness

<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

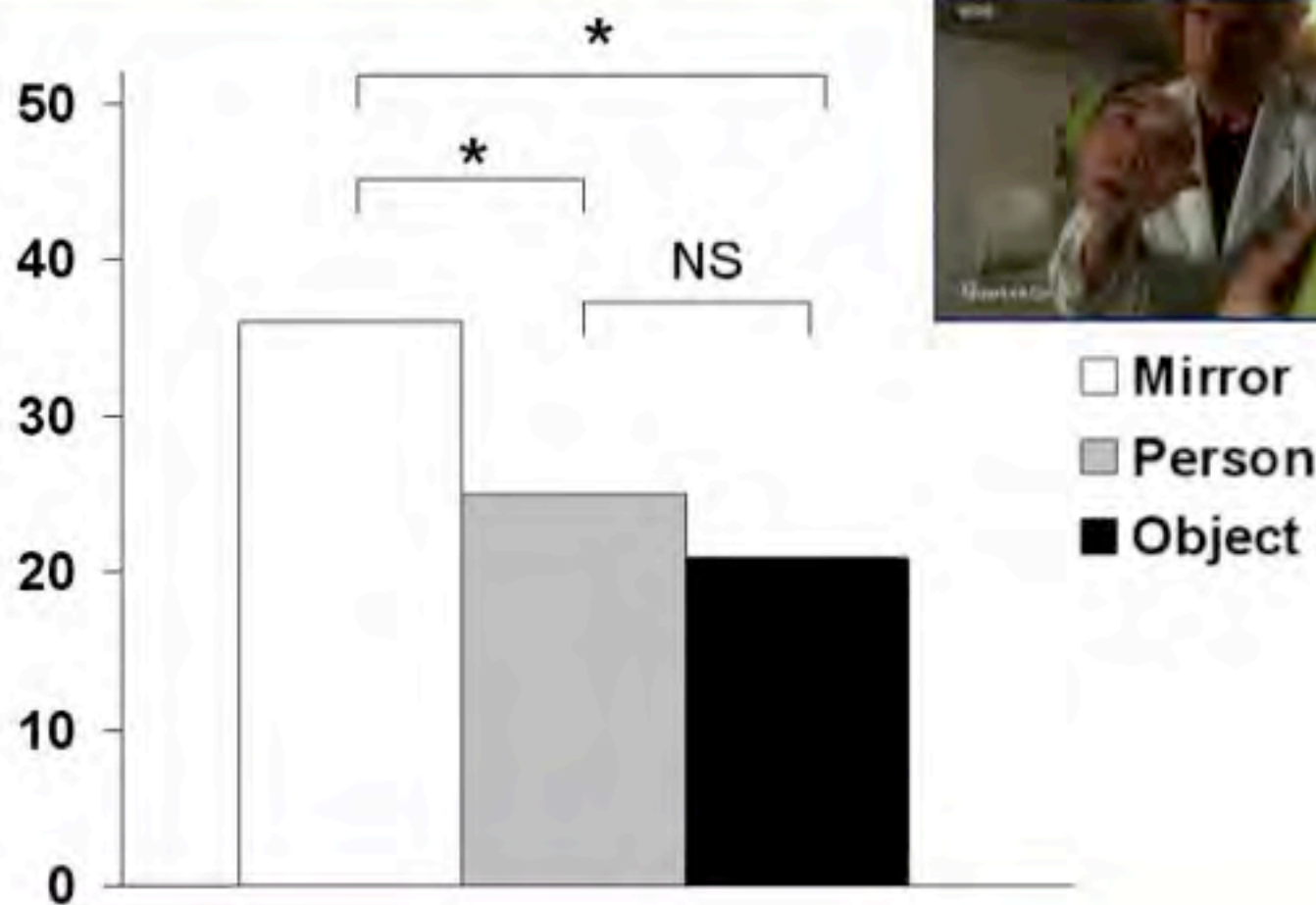
- 45 clinical consensus diagnosis 'vegetative state'
- 18 signs of awareness (Coma Recovery Scale)

 **40% potential misdiagnosis**

ECHELLE DE RECUPERATION DU COMA VERSION REVUE FRANÇAISE (2004) Formulaire de rapport			
Patient :		Date examen clinique :	
ERégle :		Date admission :	
Diagnostic initial :		Date :	
Examineur :			
FUNCTION AUDITIVE			
4 - Mouvement oculo-céphalique sur demande*			
3 - Mouvement répétitif sur demande*			
2 - Localisation de sons			
1 - Réflexe de sursaut au bruit			
0 - Néant			
FUNCTION VISUELLE			
5 - Reconnaissance des objets*			
4 - Localisation des objets - objets*			
3 - Fixation visuelle*			
2 - Fixeur*			
1 - Réflexe de sursaut à la menace			
0 - Néant			
FUNCTION MOTRICIE			
5 - Utilisation fonctionnelle des mains			
4 - Réaction contre indolence*			
4 - Manipulation d'objets*			
3 - Localisation des stimulations tactiles*			
2 - Flexion en volée			
1 - Posture anormale tonico-céphalique			
0 - Néant/Passivité			
FUNCTION COGNITIVE (Niveau 2)			
3 - Production verbale intelligible*			
2 - Production écrite (Mouvements ceps)			
1 - Réflexe ceps			
0 - Néant			
COMMUNICATION			
2 - Fonctionnelle - écrite*			
1 - Non-fonctionnelle - indépendante*			
0 - Néant			
ÉTAT			
2 - Attention			
2 - Ouverture des yeux sans stimulation			
1 - Ouverture des yeux avec stimulation			
0 - Aucun état			
SCORE TOTAL			

Eye tracking : use a mirror!

Number of MCS patients tracking

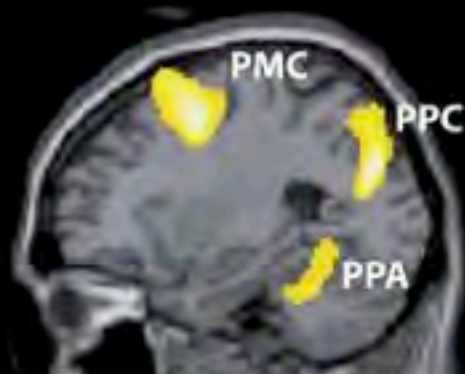


Signs of consciousness on fMRI

Tennis Imagery

Spatial Navigation Imagery

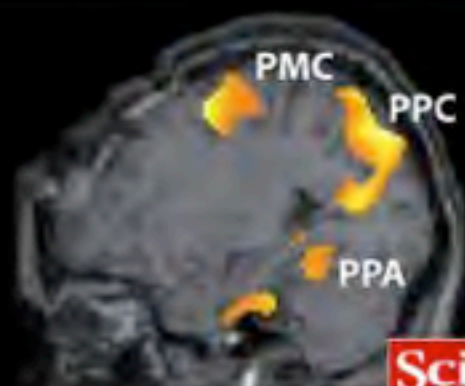
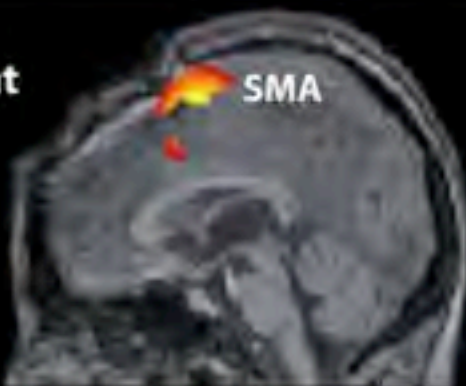
Controls



"He's not in coma...
he's playing tennis!"



Patient



Science

UNIVERSITY OF
CAMBRIDGE

MRC

Université
de Liège



Yes-No communication with fMRI

 THE NEW ENGLAND
JOURNAL of MEDICINE

HEALTHY SUBJECT



Answers « YES »

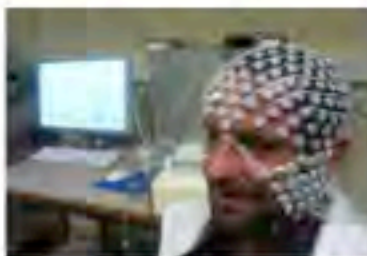
Answers « NO »

« VEGETATIVE STATE »



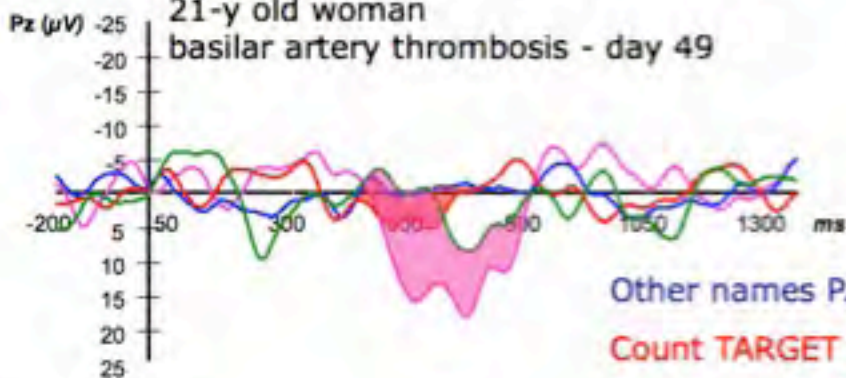
EEG-based Brain Computer Interfaces

www.decoderproject.eu



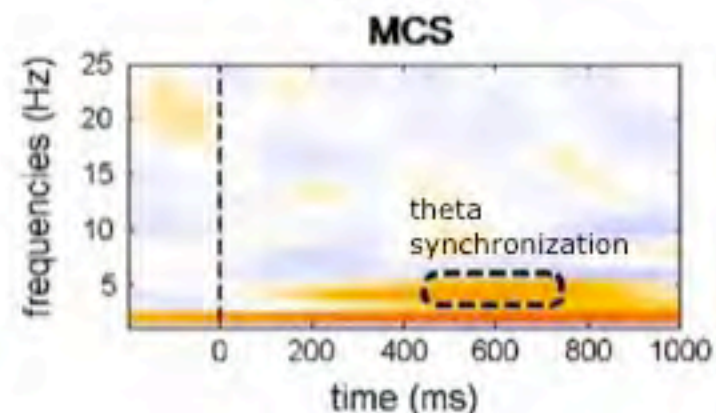
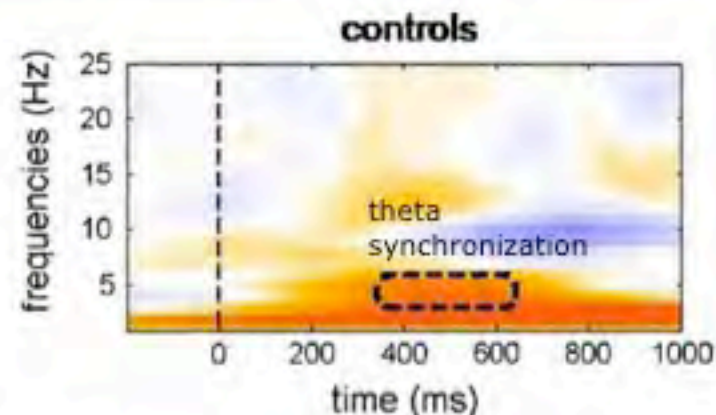
Coma or total locked-in syndrome?

21-y old woman
basilar artery thrombosis - day 49



- Other names **PASSIVE**
- Count **TARGET** (other name)
- Own name **PASSIVE**
- Count **TARGET** (own name)

Schnakers et al, *Neurology*, 2008
Schnakers et al, *Neurocase*, 2009

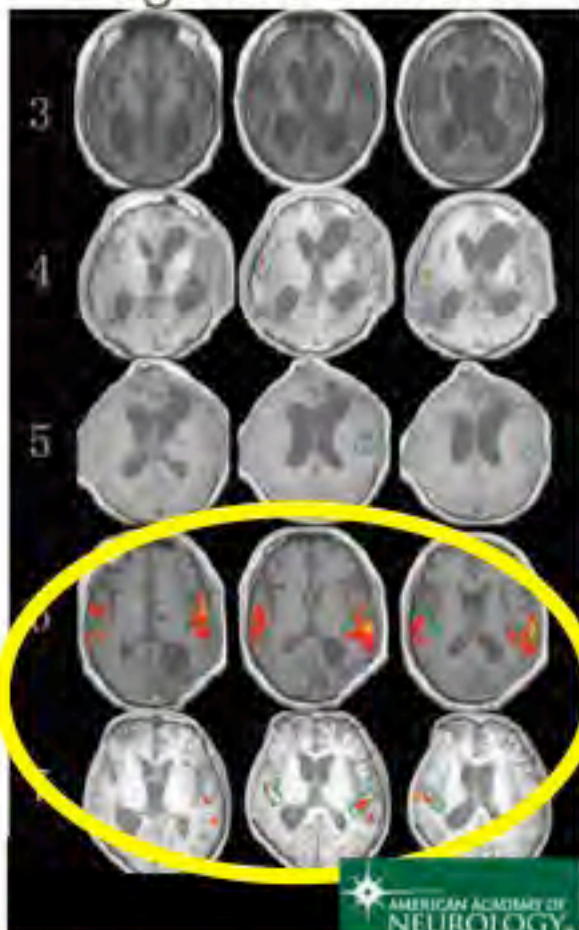


Fellinger et al *Clin Neurophysiol*, 2011

Predicting outcome in chronic DOC

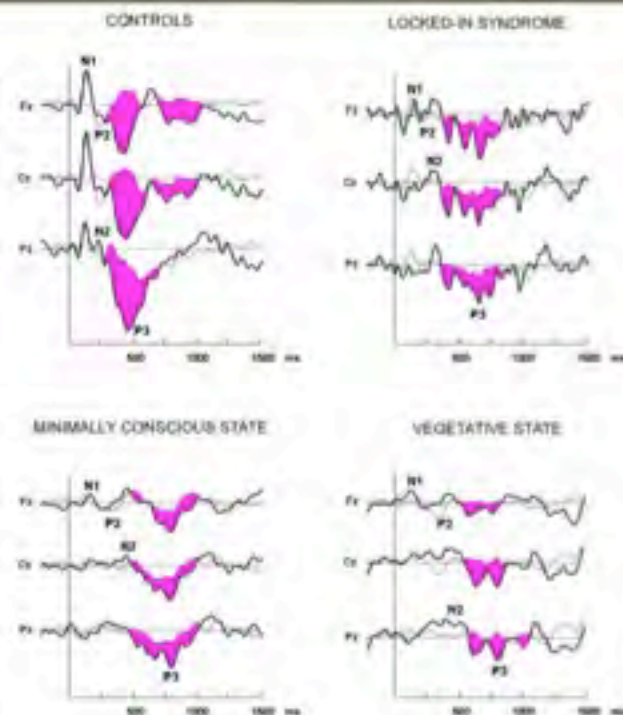
vegetative state

ACTIVATION
TO THE OWN
NAME

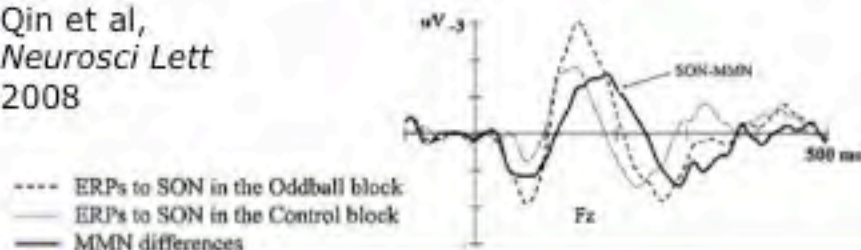


ATYPICAL
'HIGH LEVEL'
CORTICAL
ACTIVATION

Perrin et al
Arch Neurol
2006

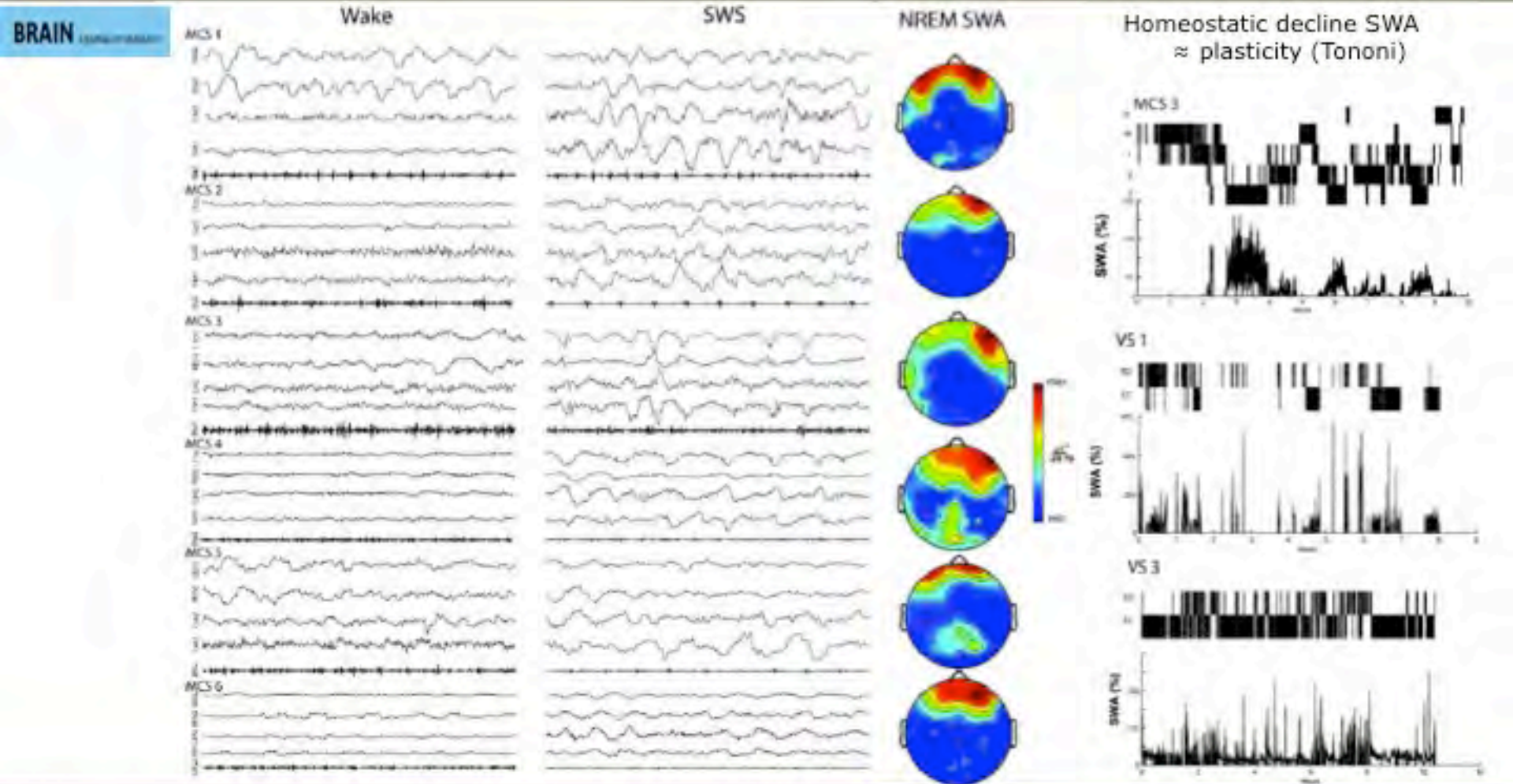


Qin et al,
Neurosci Lett
2008

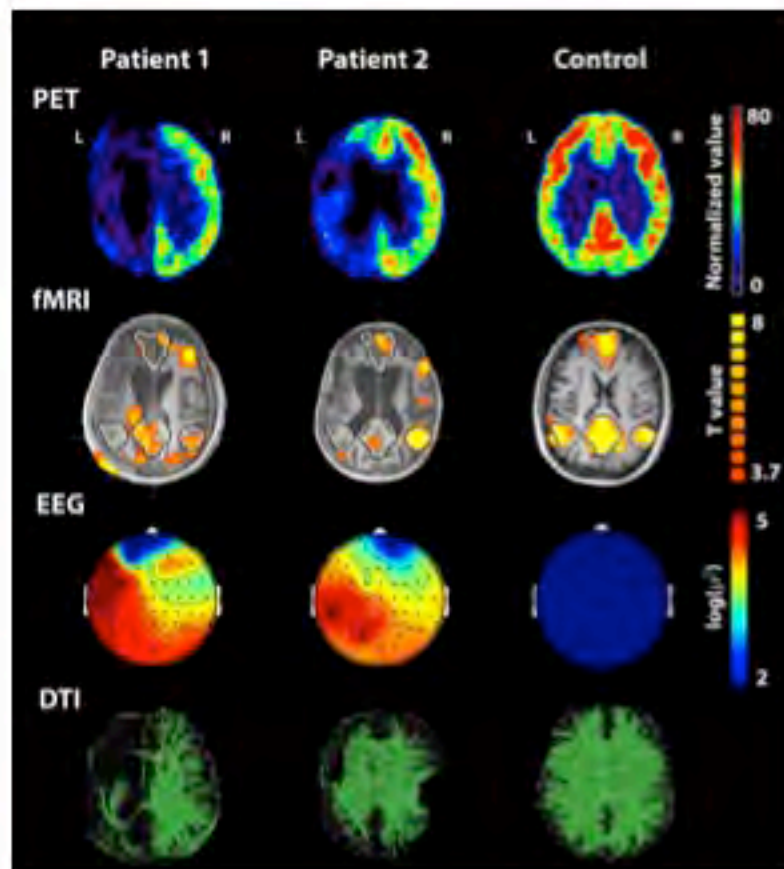
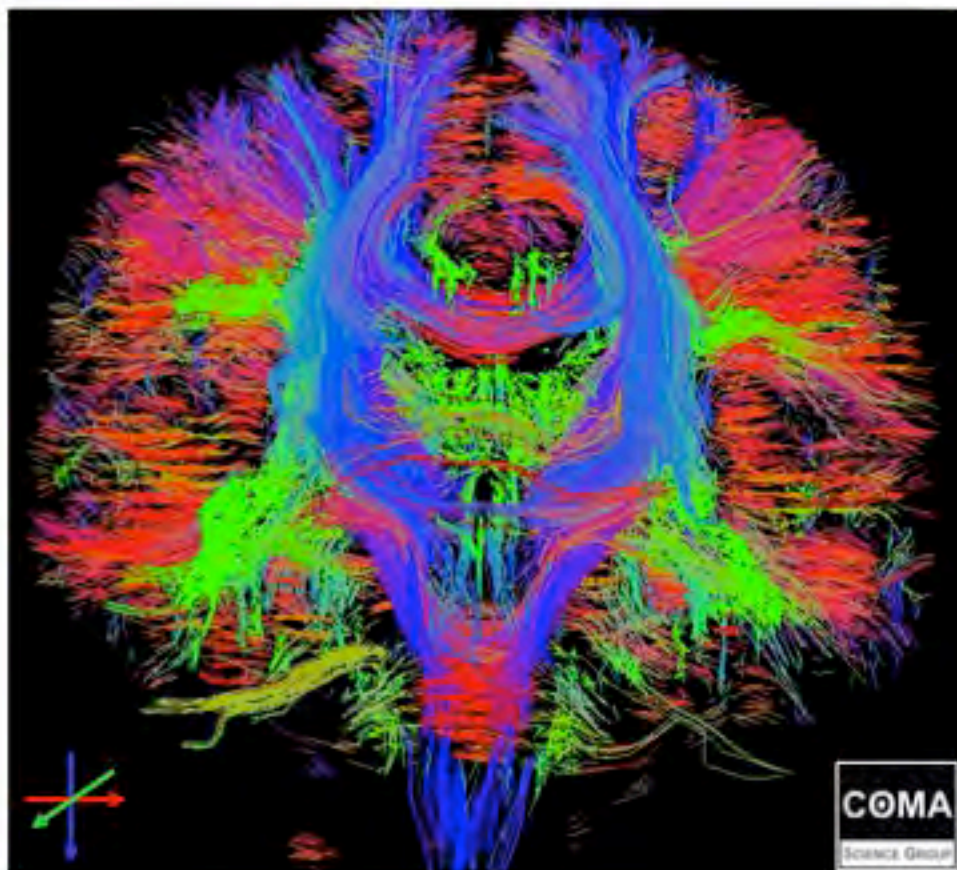


- ERPs to SON in the Oddball block
- ERPs to SON in the Control block
- MMN differences

Understanding plasticity

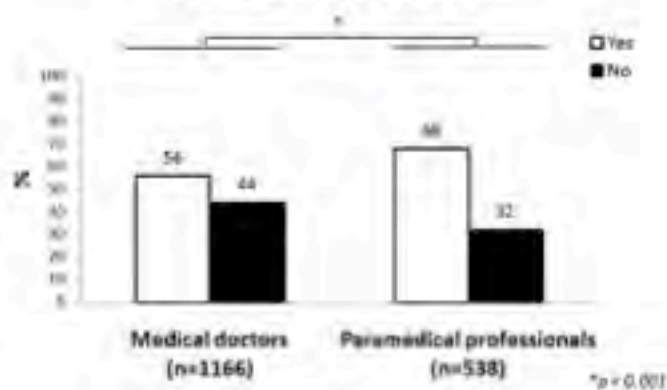


Multimodal imaging

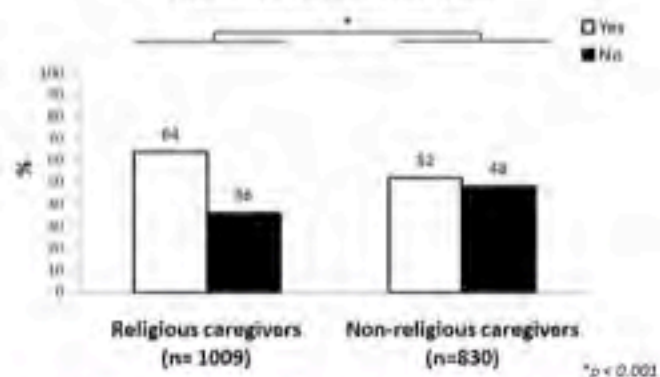


Nociception and pain

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

Score	Item	Response
MOTOR RESPONSE		
3	Localisation to Nocuous Stimulation	The non-stimulated limb never locates and never contact with the stimulated body part at the point of stimulation.
2	Flexion Withdrawal	There is isolated flexion withdrawal of at least one limb. The limb never locates away from the point of stimulation.
1	Abnormal Posturing	Slow, uncoordinated flexion or extension of the upper and/or lower extremities occurs immediately after the stimulus is applied.
0	None/Flaccid	There is no discernible movement following application of nocuous stimulation, secondary to hyporeactive or flaccid muscle tone.
VERBAL RESPONSE		
3	Intelligible Verbalisation	Pro-formation of words in response to nocuous stimulation. Each verbalization must consist of at least 1 consonant-vowel-consonant (CVC) trial. For
2	Focalization / Oral Movement	ocalization is
1	Groans	to nocuous
0	None	
VISUAL RESPONSE		
3	Fixation	ation point
2	Eye movements	
1	Startle	relation
0	No change	There are no discernible changes in response to nocuous stimulation.
FACIAL EXPRESSION		
3	Cry	Cries are observed not spontaneously but in response to nocuous stimulation.
2	Grimace	Grin, or other facial expressions, are observed in response to nocuous stimulation.
1	Clamping of jaws, tongue protrusion, yawning, chattering movements.	
0	None	There is no discernible facial expression following application of nocuous stimulation.

Total score > 7 / 12

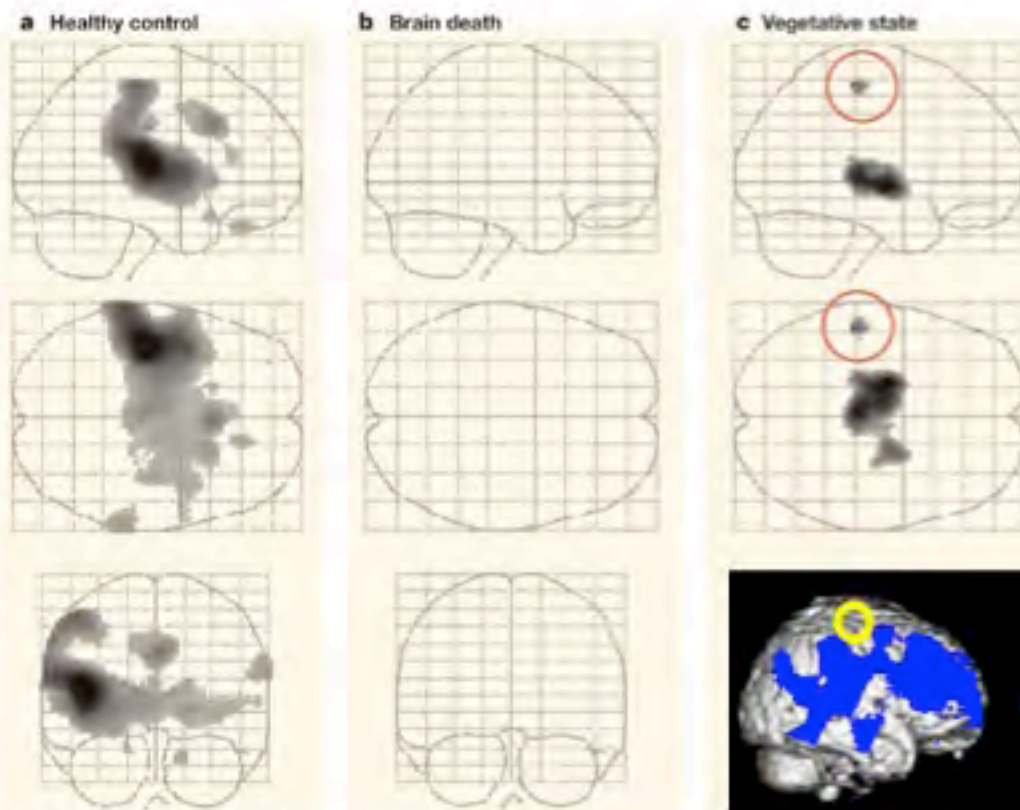
= analgesic treatment

Schnakers et al, *Pain*, 2010

Demertzi et al, *Prog Brain Res*, 2009

Do they feel pain ?

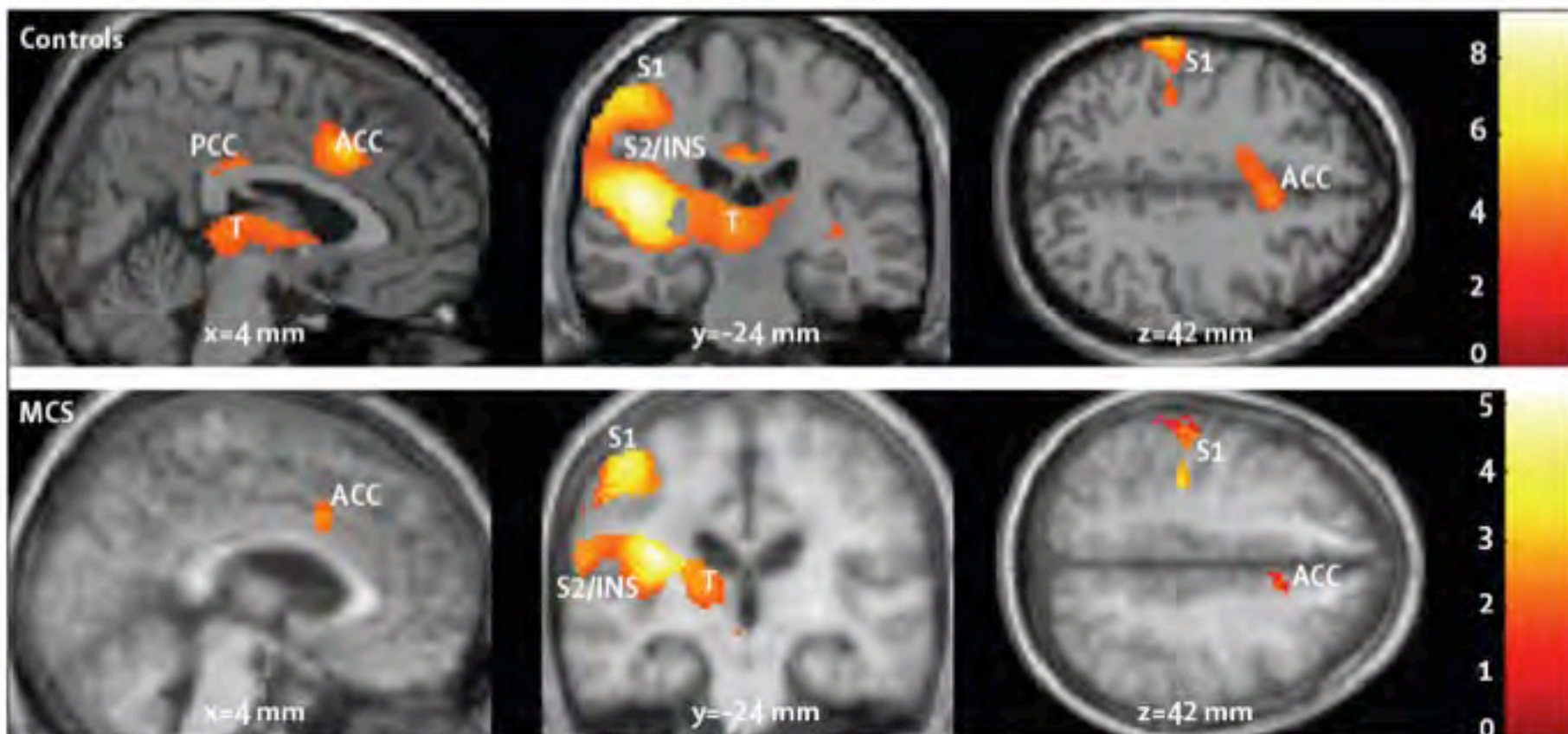
Noxious electrical stimulation



Low level
disconnected
cortical activation

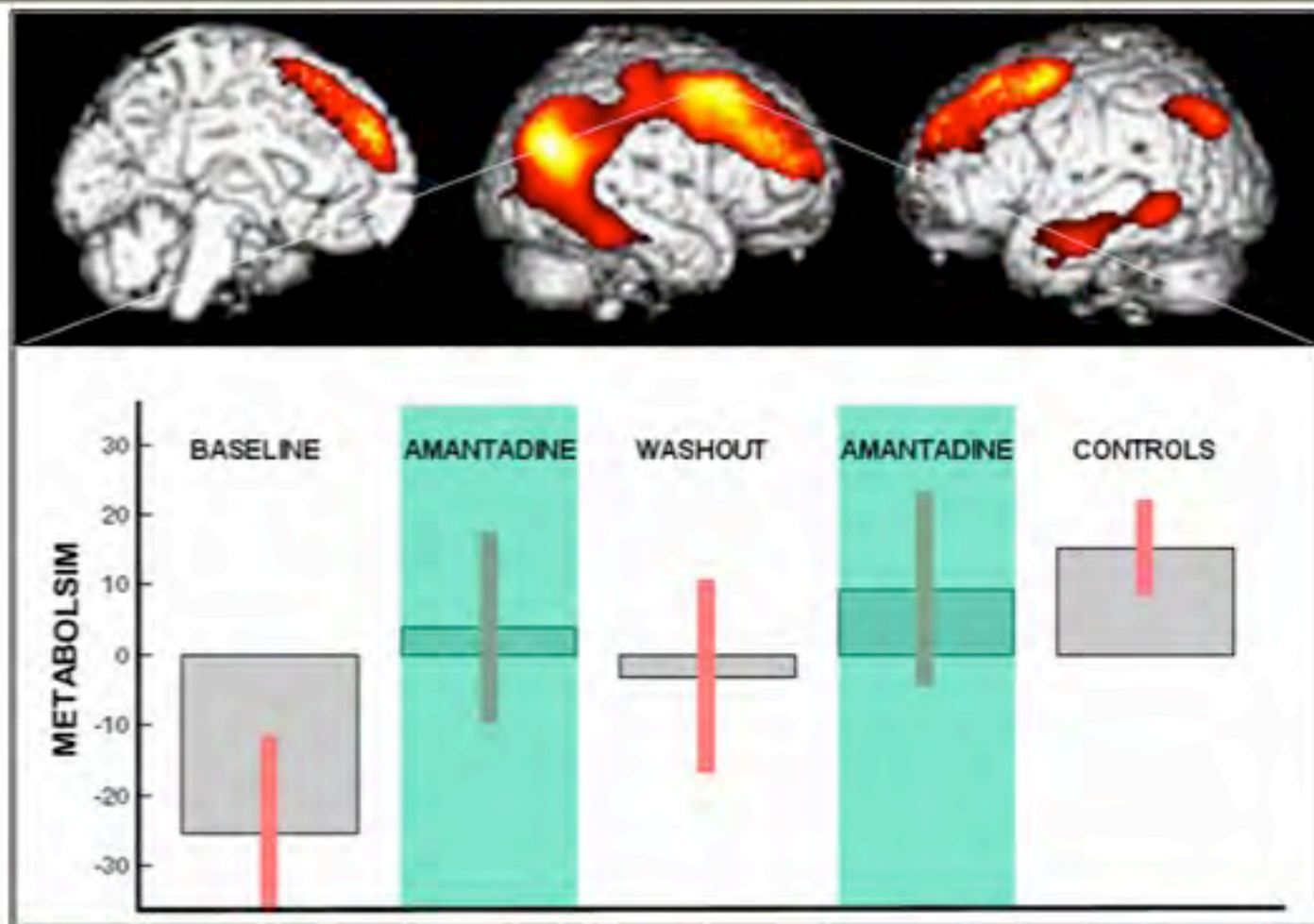
Copyright © 2005 Nature Publishing Group
Nature Reviews | Neuroscience

Pain in minimally conscious state



<http://neurology.thelancet.com>

Curative treatment: Drugs? no evidence based therapy



Ethical 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

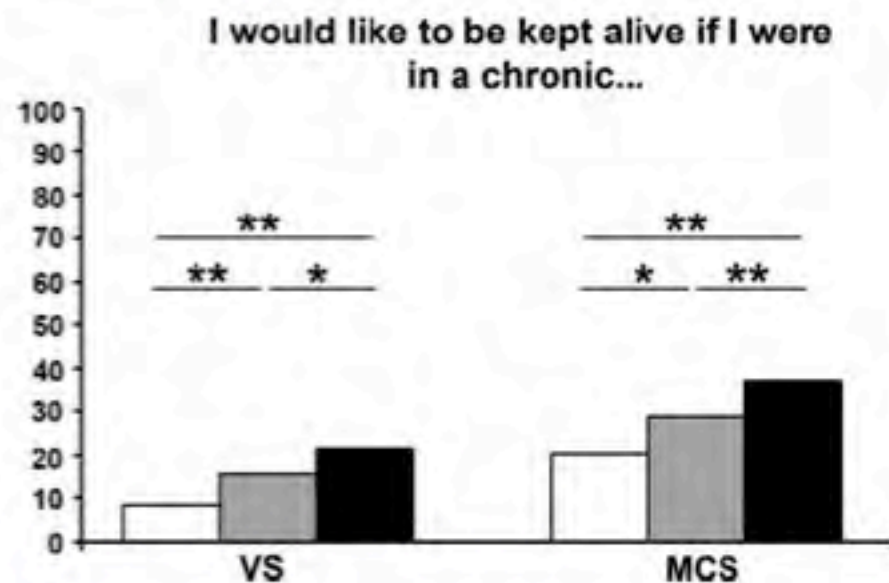


Fig. 2 End-of-life attitudes towards the vegetative state (VS) and minimally conscious states (MCS) depending on geographic region. Bars represent % agreement (white: Northern, grey: Central, black: Southern Europe; * $P < 0.05$, ** $P < 0.001$)

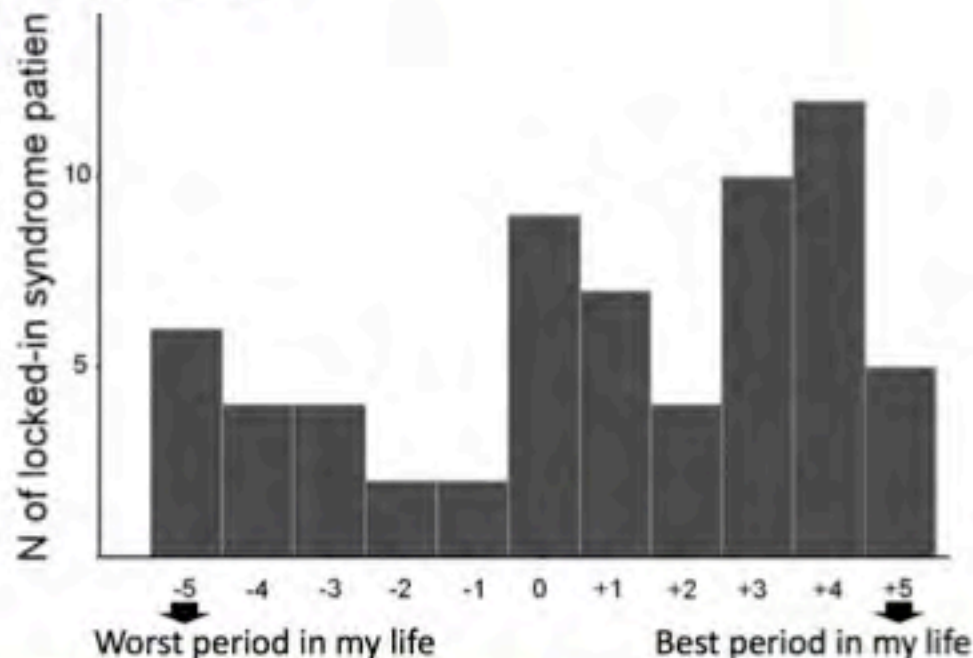
Quality of life

Open Access Research



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

Marie-Aurèle Bruno,¹ Jan L. Bernheim,² Didier Ledoux,¹ Frédéric Pollas,² Athena Demertzi,¹ Steven Laureys¹



Translational research

Neural correlates of conscious awareness

≈ emergent property of widespread fronto-parietal connectivity

Diagnostic use

≈ 40% misdiagnosis

Prognostic use

multimodal MRI

Therapeutic use

pain treatment / deep brain stimulation thalamus



Ethical issues

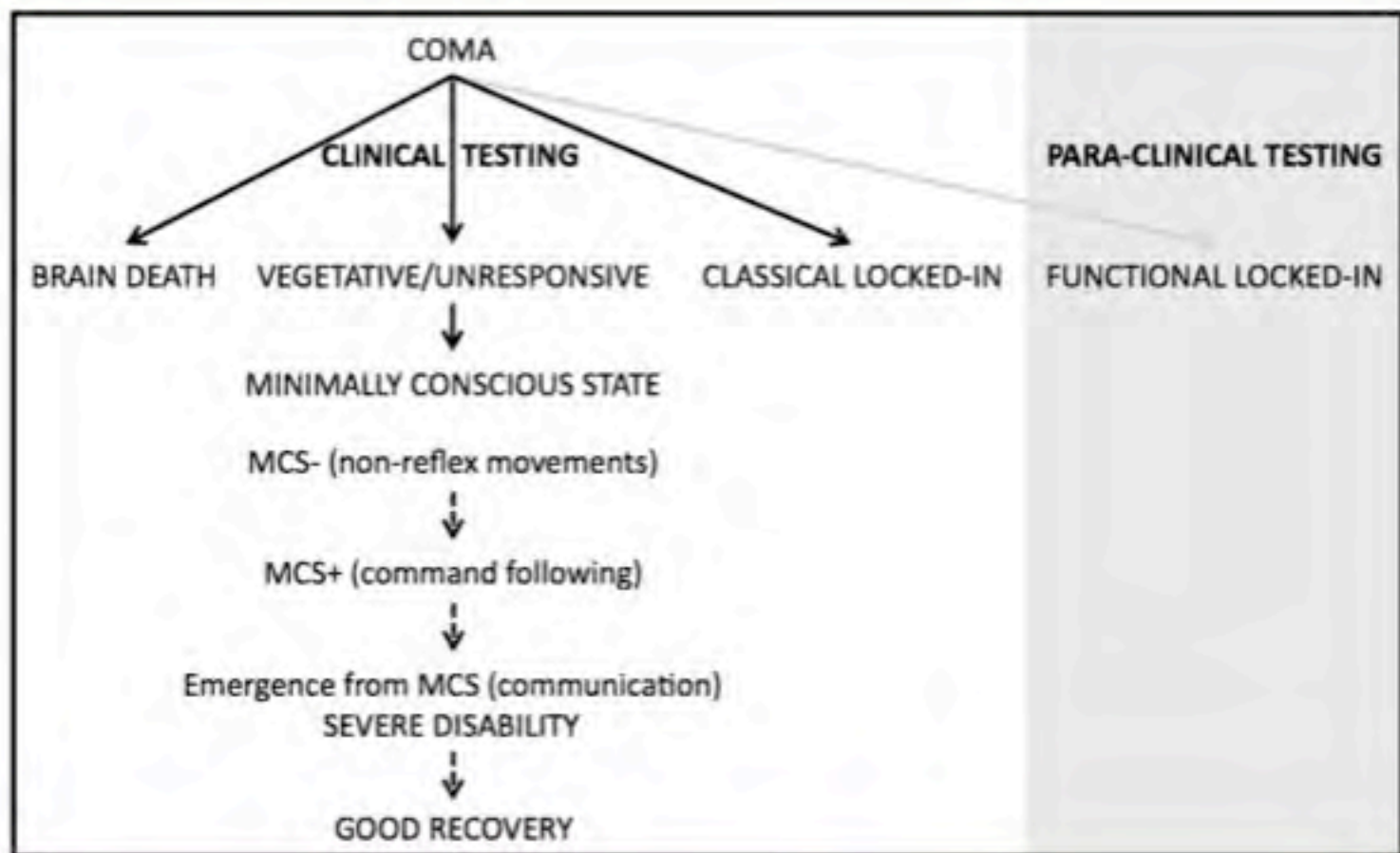
EMG, ERP or fMRI might reveal subclinical command-following

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



www.nature.com/clinicalpractice/neuro

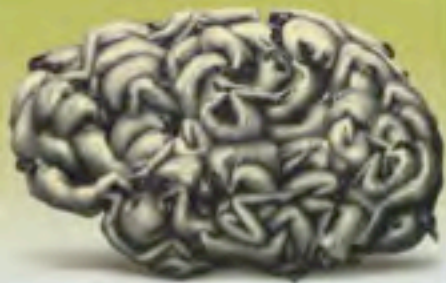
New knowledge, new nosology





The Neurology of Consciousness

Cognitive Neuroscience and Neuropathology



Steven Laureys • Giulio Tononi



THANK YOU



James S. McDonnell Foundation

