Ethical challenges in disorders of consciousness

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

coma@chu.ulg.ac.be

European Neurological Society

ENS

AMERICAN ACADEMY OF NEUROLOGY

Cyclotron research centre

COMA SCIENCE GROUP

Université de Liège

CHU de Liège

www.comascience.org

A new name for « vegetative »

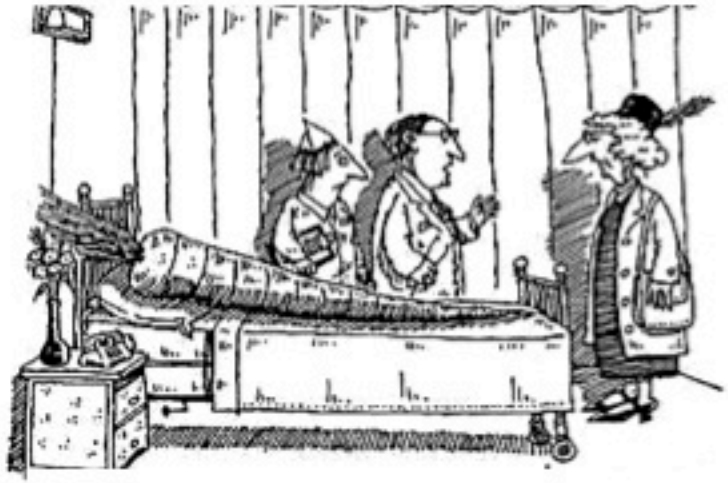
BMC Medicine

Highly accessed Open Access

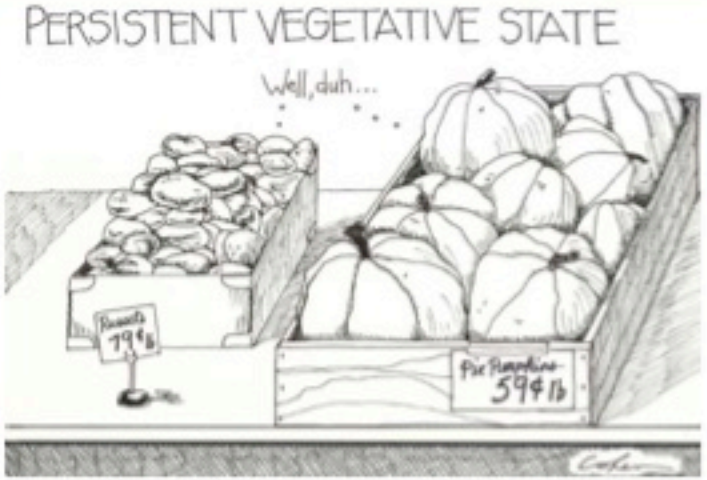
Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome

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

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



"There's nothing we can do... he'll always be a vegetable."



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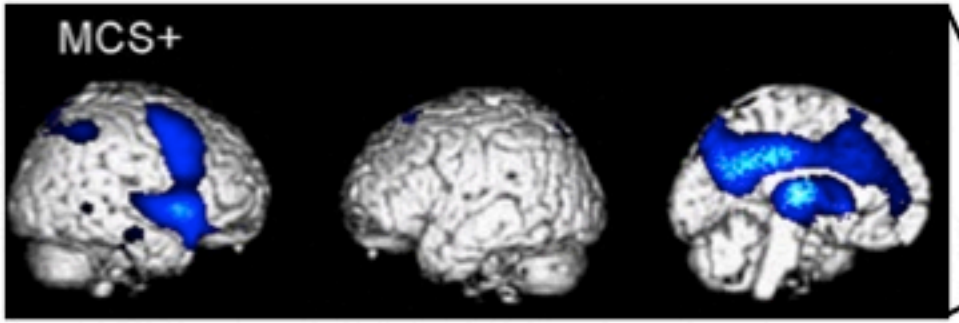
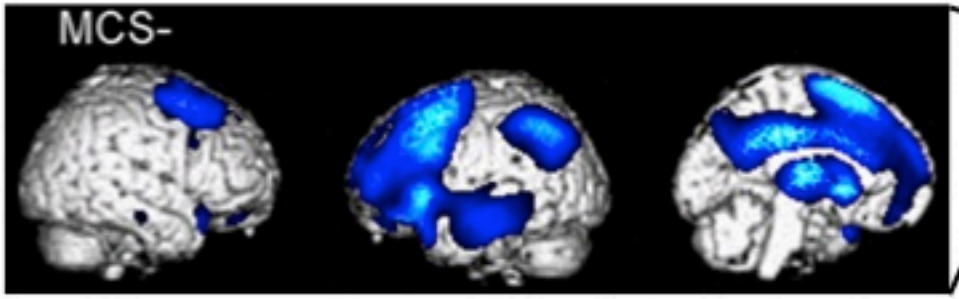
Disorders of consciousness





EMERGENCE

functional communication and object use

MINIMALLY CONSCIOUS STATE +

command following

MINIMALLY CONSCIOUS STATE -

appropriate smiling/crying
localization to noxious stimulation
visual pursuit

VEGETATIVE/UNRESPONSIVE

reflex movements
eye opening

COMA

Bruno et al, *J Neurology*, 2011

A new era for the study of DOC

Coma and consciousness: Paradigms (re)framed by neuroimaging

Steven Laureys [a,*,1], Nicholas D. Schiff [b,**,1]

[a] Coma Science Group, Cyclotron Research Centre and Neurology Department, University and University Hospital of Liège, 4000 Liège, Belgium
[b] Department of Neurology and Neuroscience, LC-803, Weill Cornell Medical College, 1300 York Ave., New York, NY 10065, USA

1970-90s

COMA → PVS → SEVERE DISABILITY FUNCTIONALLY APPROXIMATING PVS

→ DEATH

2010s-future

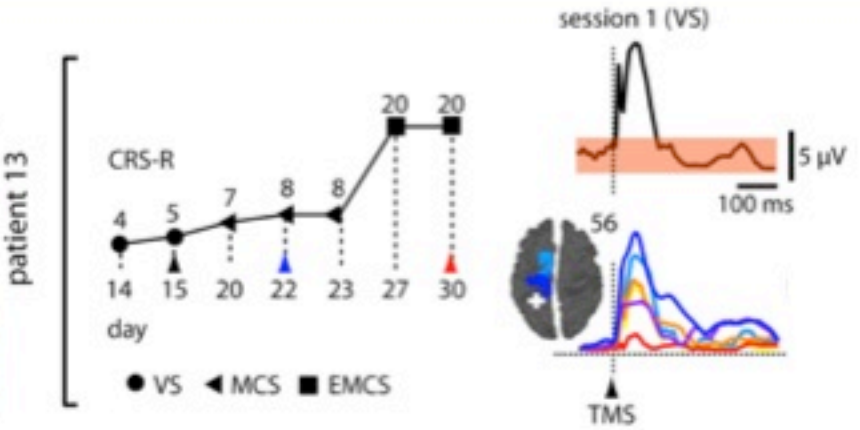
COMA → VS UWS → MCS- → MCS+ → CONFUSIONAL STATE

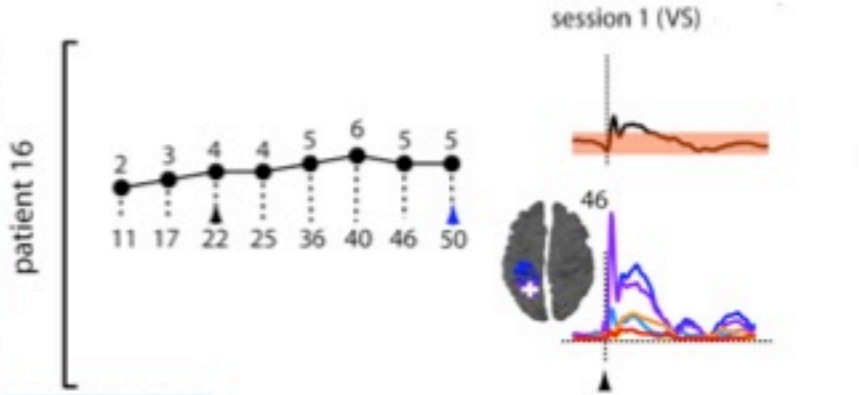
- RECOVERY OF NORMATIVE COGNITIVE FUNCTION
- LOCKED-IN STATE
- FUNCTIONAL LIS

Laureys and Schiff, *NeuroImage*, 2012

Consciousness ≈ connectivity

EEG-TMS





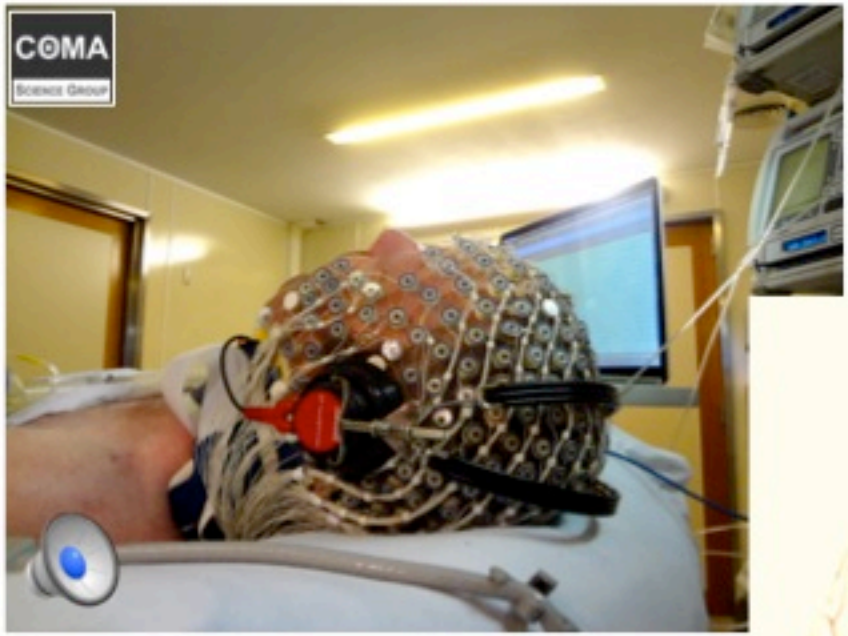
BRAIN
A JOURNAL OF NEUROLOGY

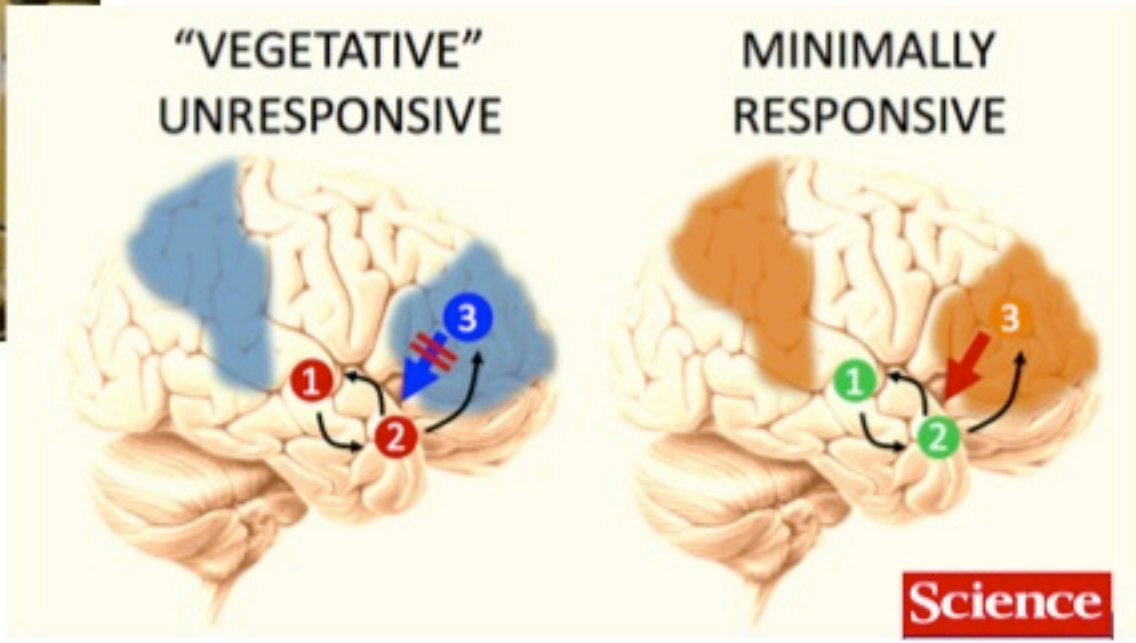
CHU de Liège

UNIVERSITÀ DEGLI STUDI DI MILANO

Rosanova and Gosseries et al, *Brain* 2012

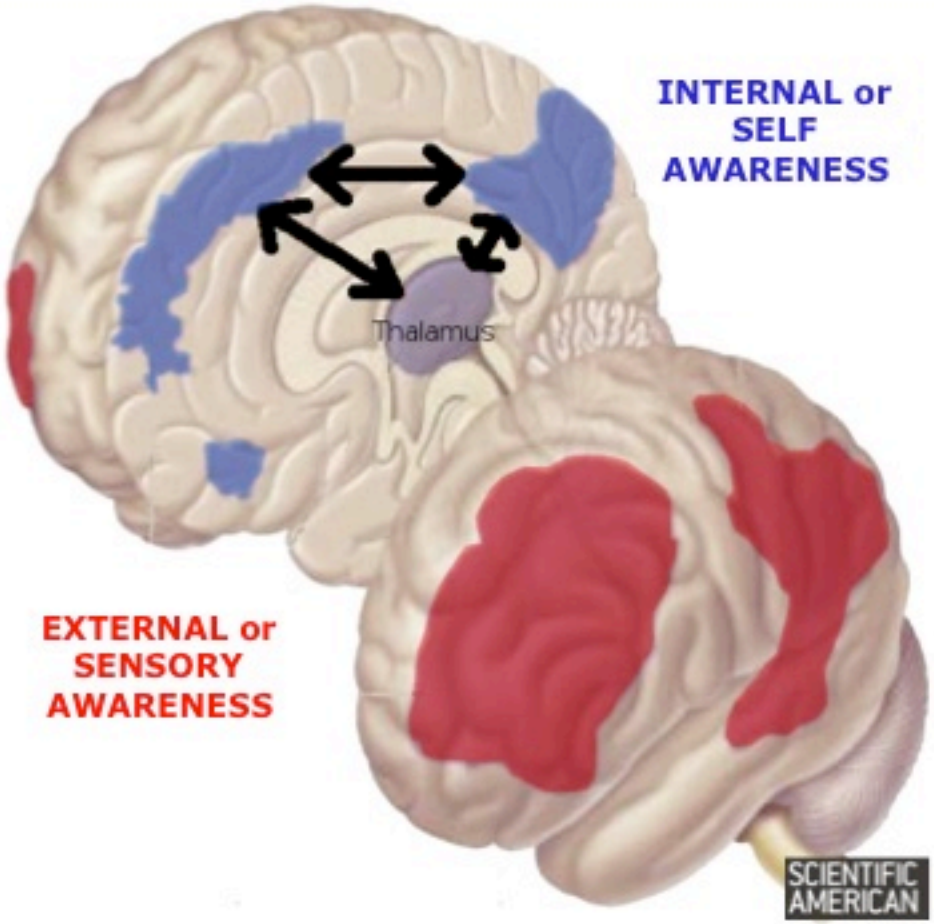
Consciousness ≈ top-down

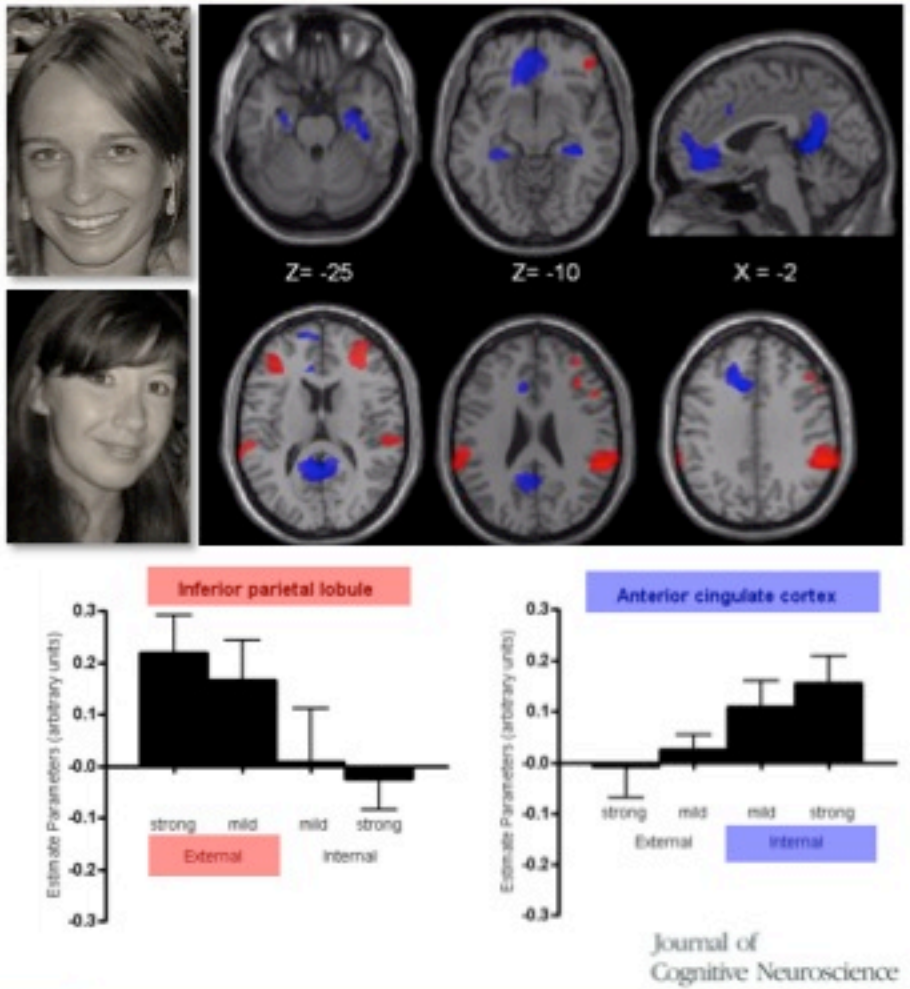




Boly, Garrido, Gosseries, Bruno, Schnakers, Massimini, Litvak, Laureys, Friston, *Science*, 2011

Two awareness networks

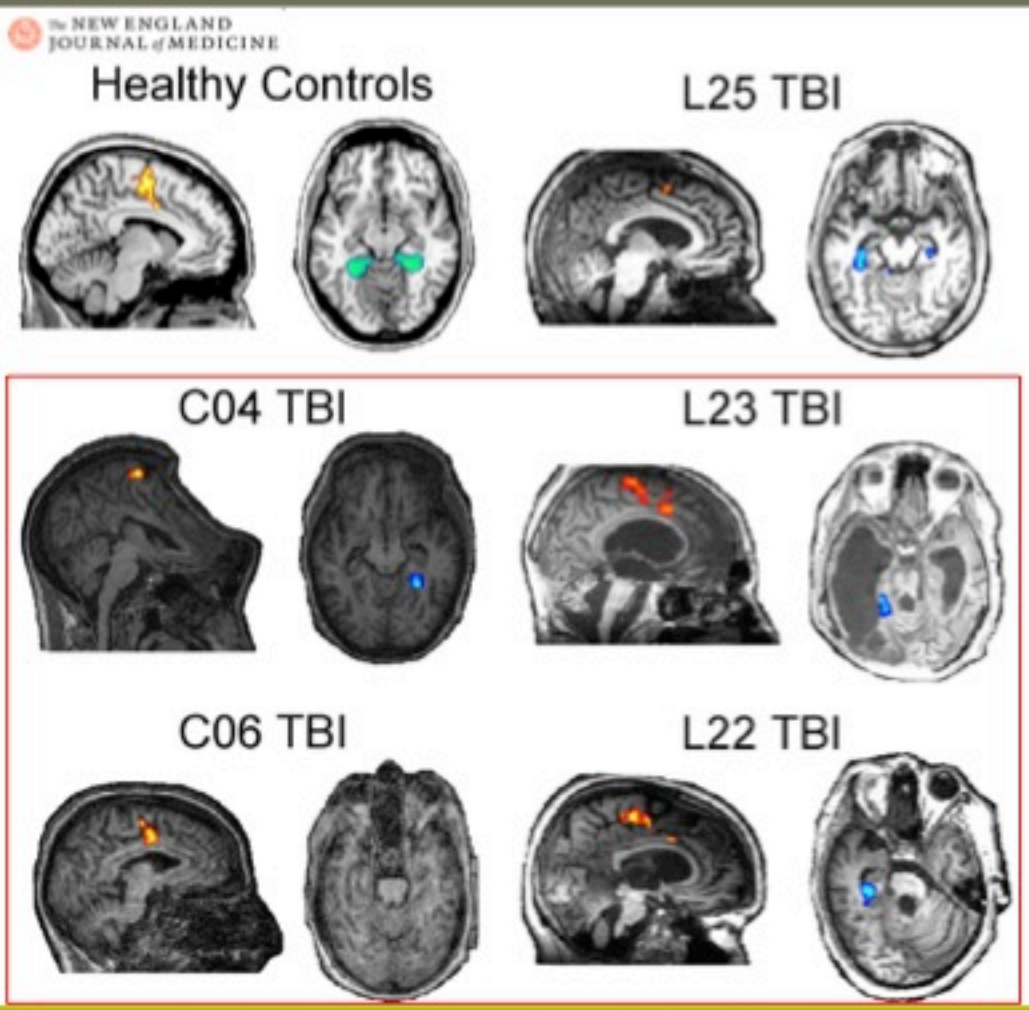


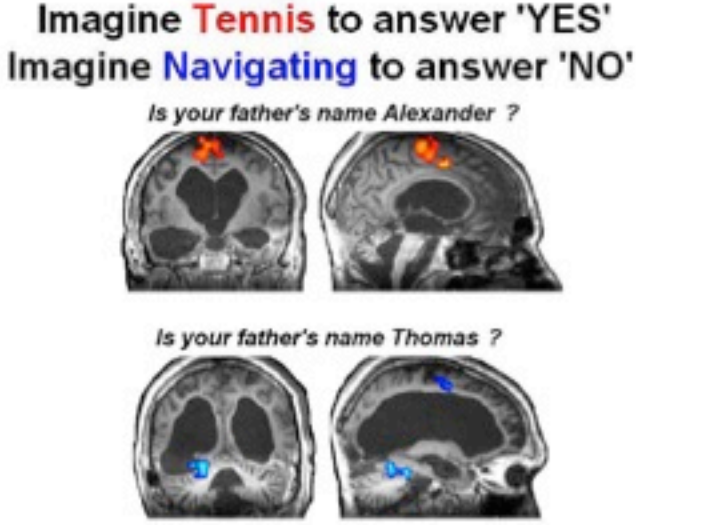


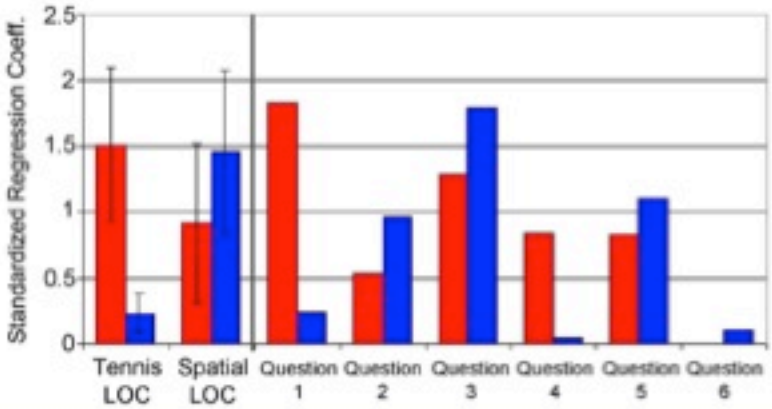
Laureys, *Scientific American* 2007
Vanhaudenhuyse, Demertzi et al, *J Cogn Neursoci* 2011

Communication with fMRI

The NEW ENGLAND JOURNAL of MEDICINE

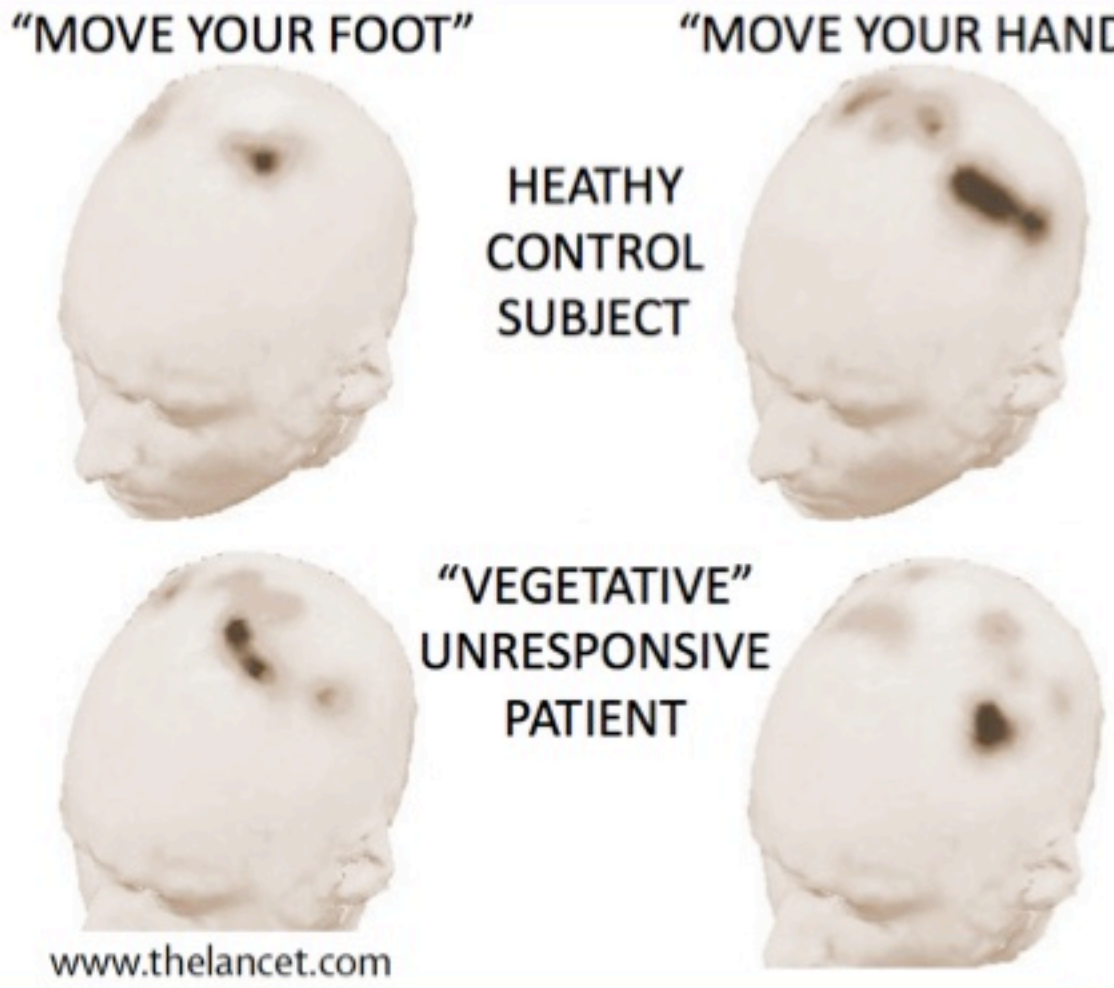






Monti & Vanhaudenhuyse, Coleman, Boly, Pickard, Tshibanda, Owen, Laureys
New England J Med 2010

EEG-based Brain Computer Interfaces



Cruse et al, *Lancet* 2012

3/16 VS/UWS (19%)
- 2/5 traumatic (40%)
- 1/11 non-traumatic (9%)

Cruse et al, *Neurology* 2012

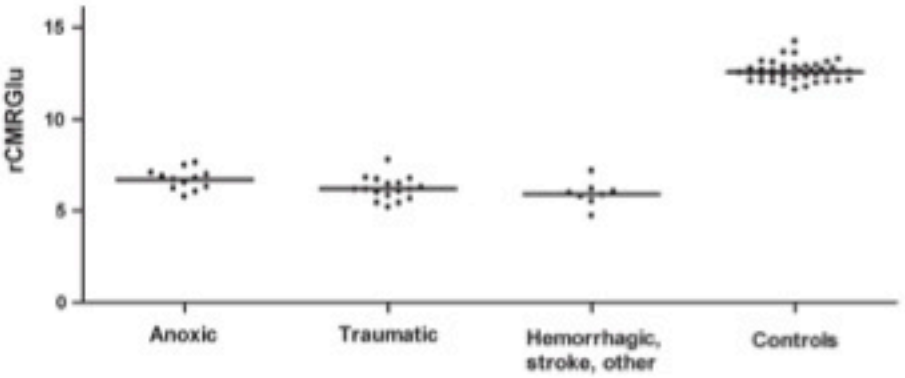
7/23 MCS (30%)
- 7/15 traumatic (49%)
- 0/8 non-traumatic (0%)

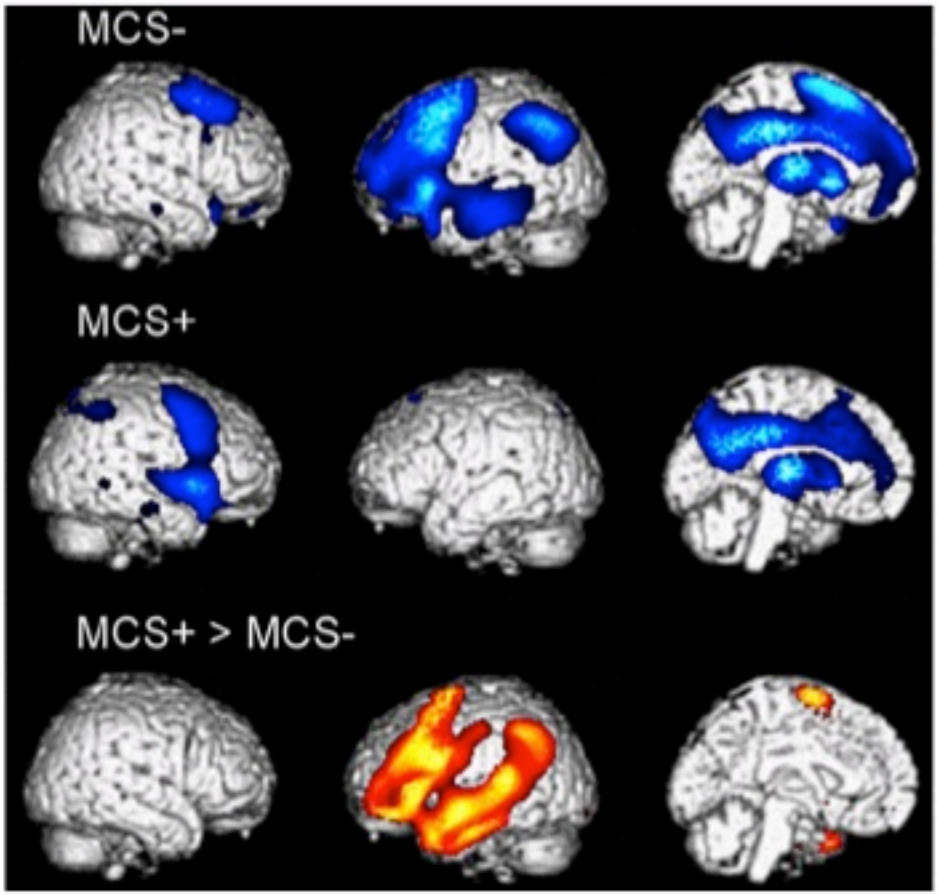
Aphasia as a confound

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

Steve Majerus[1,3], Marie-Aurélie Bruno[2,3], Caroline Schnakers[2], Joseph T. Giacino[4] and Steven Laureys[2,3,*]

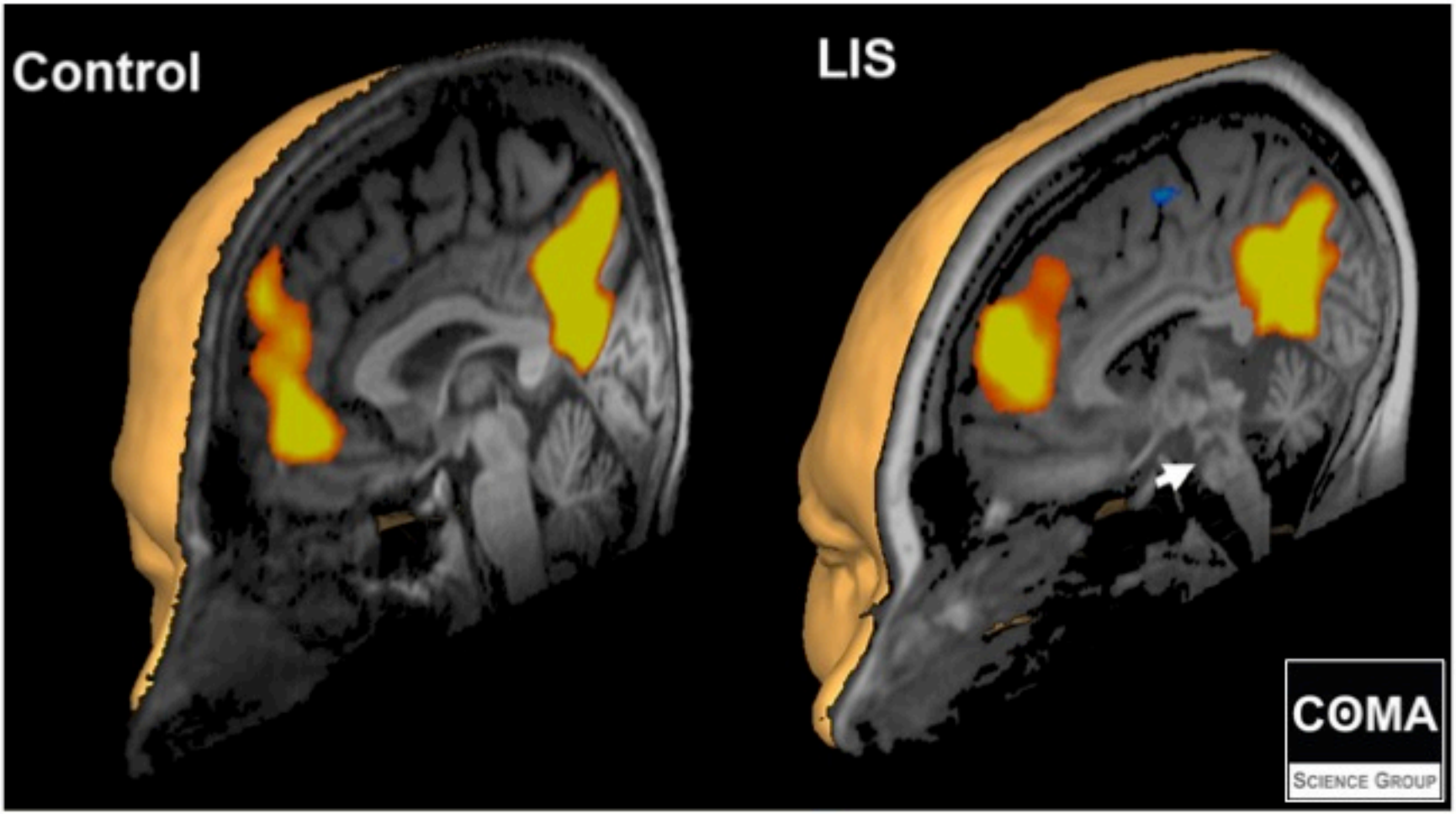
Progress in Brain Research, Vol. 177





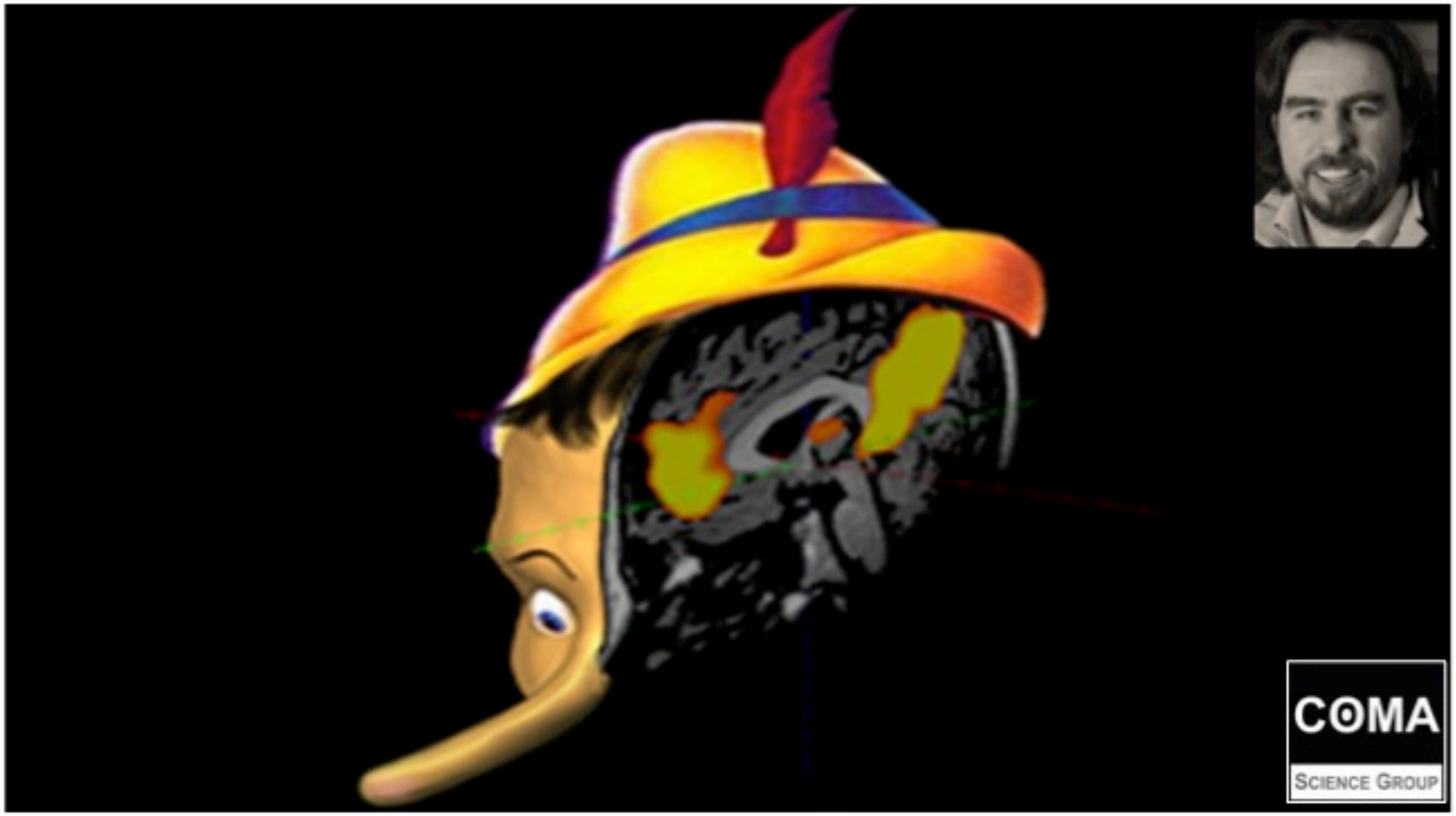
Bruno et al, *J Neurology*, 2012

Functional MRI in "resting state"



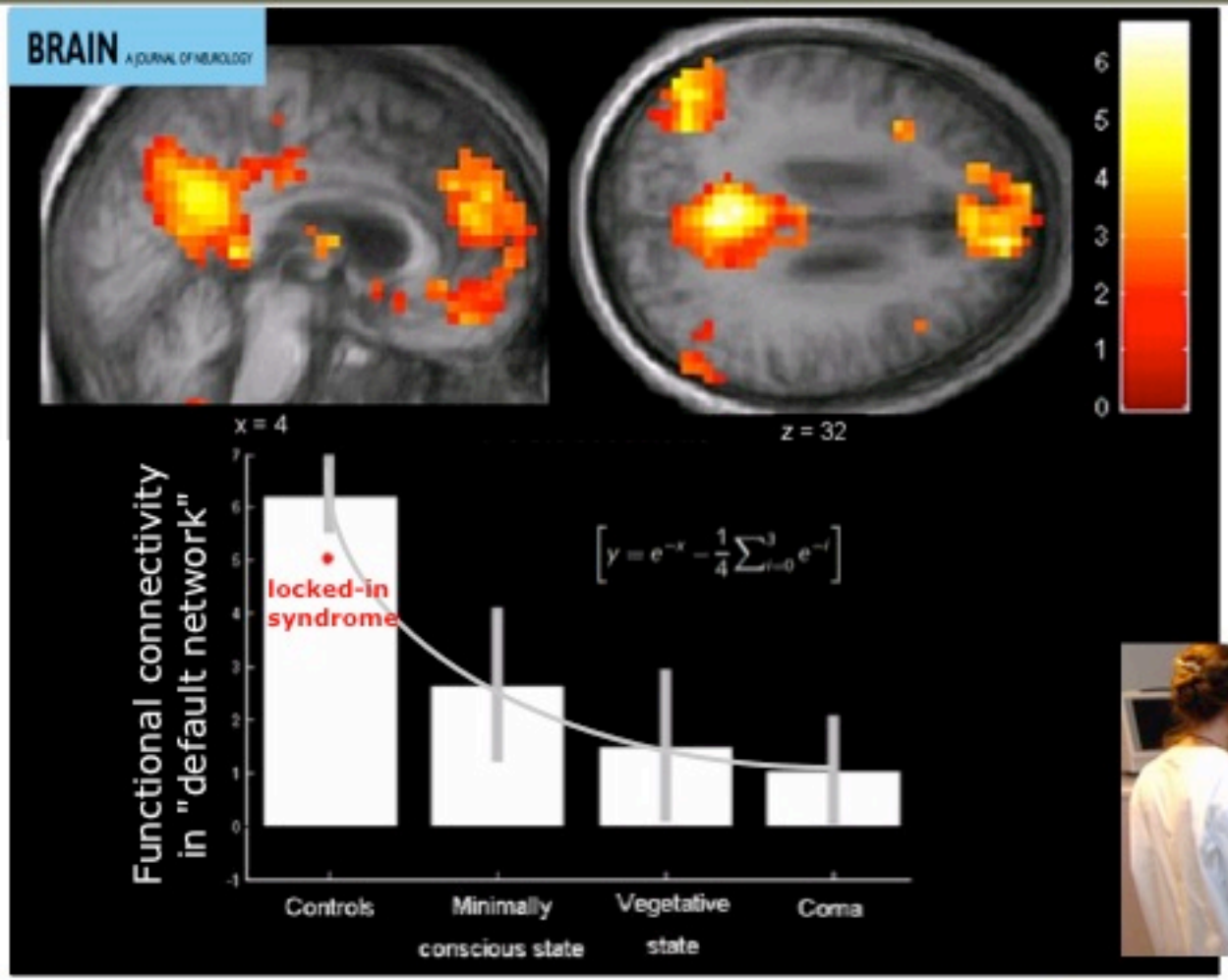
Jox, Bernat, Laureys, Racine, submitted

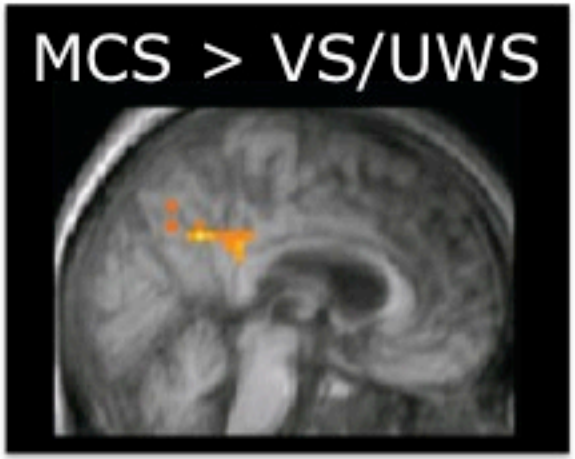
Should we trust the machine?



Jox, Bernat, Laureys, Racine, submitted

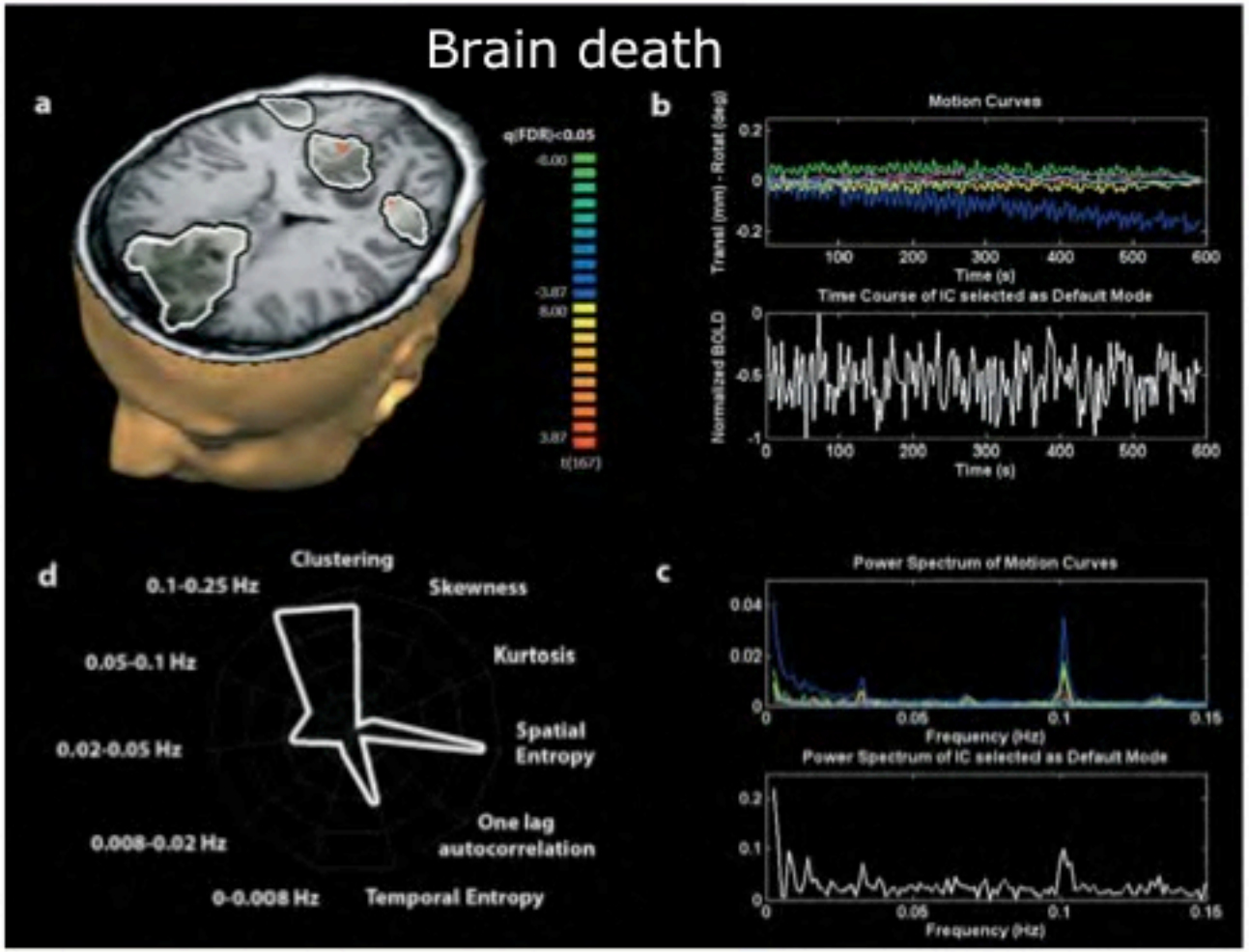
"Resting" default mode connectivity





Vanhaudenhuyse et al, *Brain* 2010

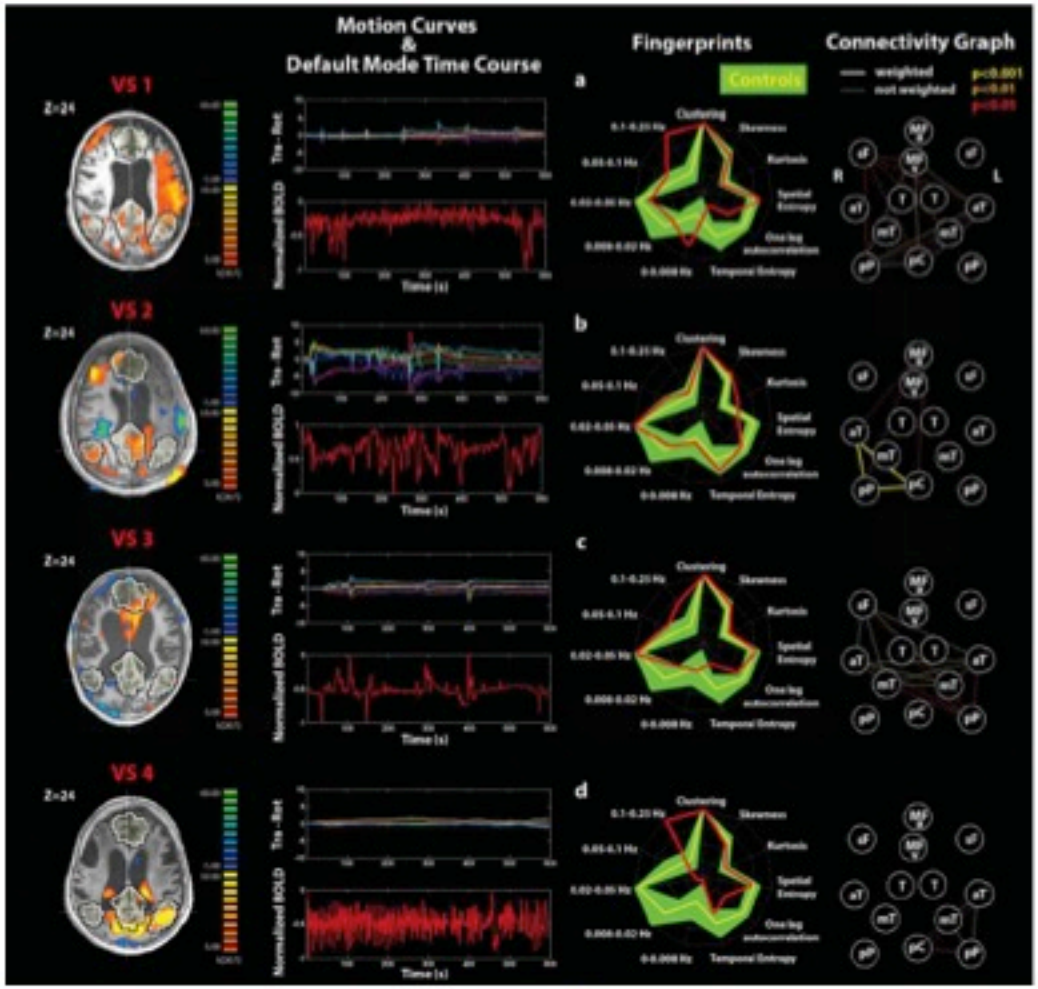
Movement artifacts



Resting state activity in patients with disorders of consciousness
Soddu et al, *Functional Neurology* 2011; 26: 1-7

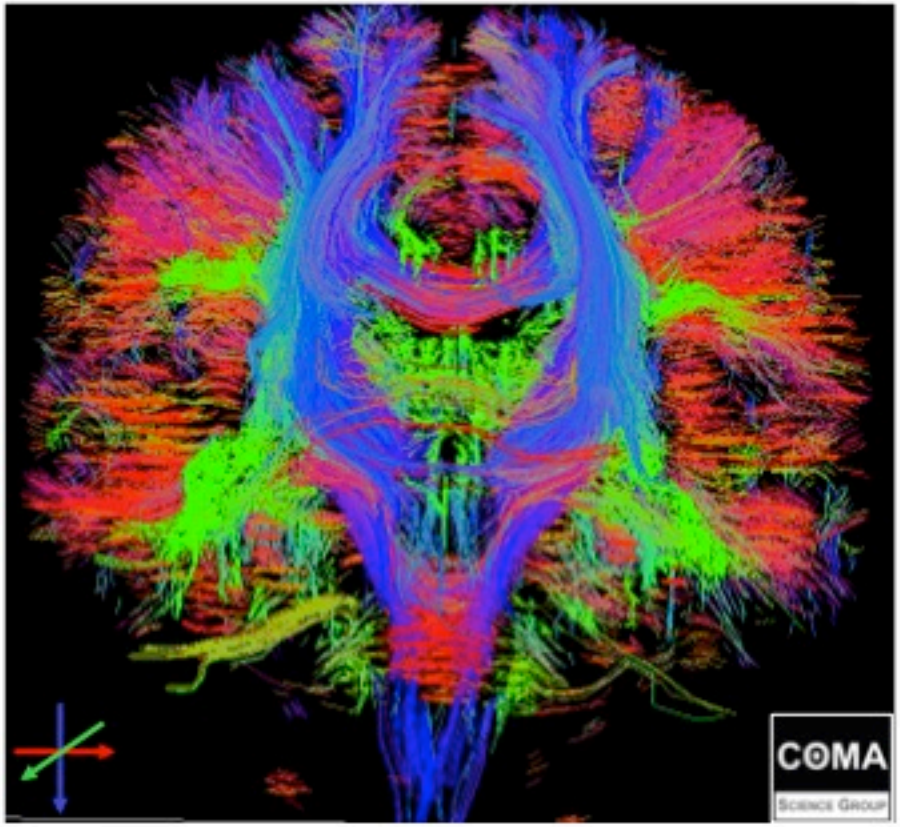
False positives / false negatives

"resting state" default mode fMRI studies



Identifying the default-mode component in spatial IC analyses of patients with disorders of consciousness Soddu et al *Hum Brain Mapp.* 2012

MRI: DTI & spectroscopy



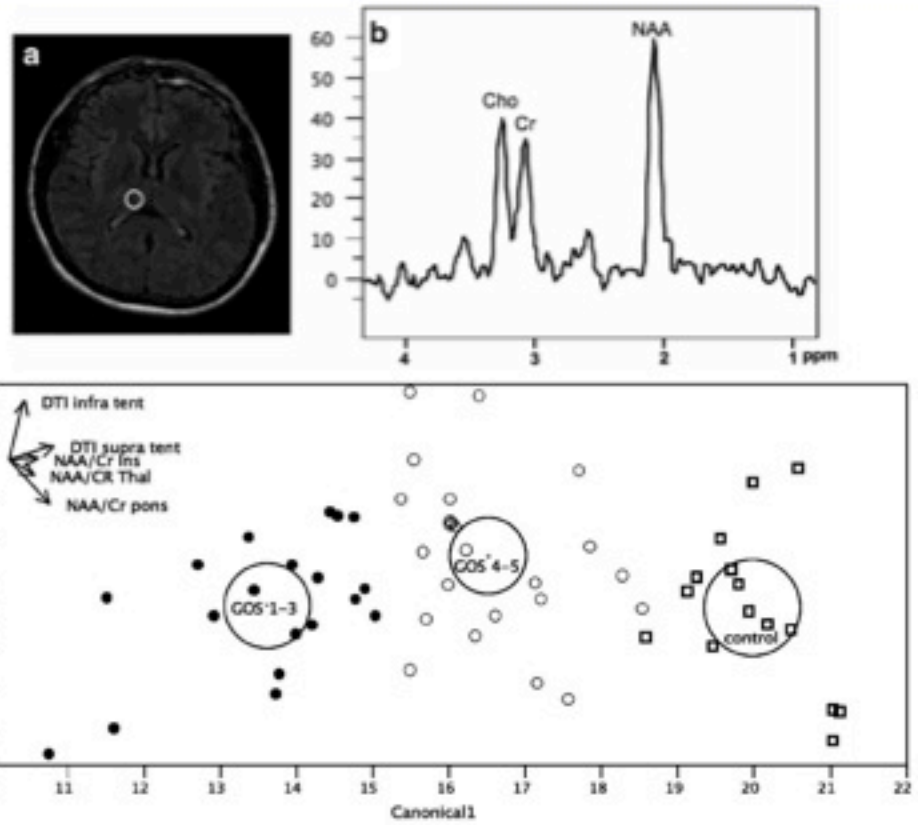
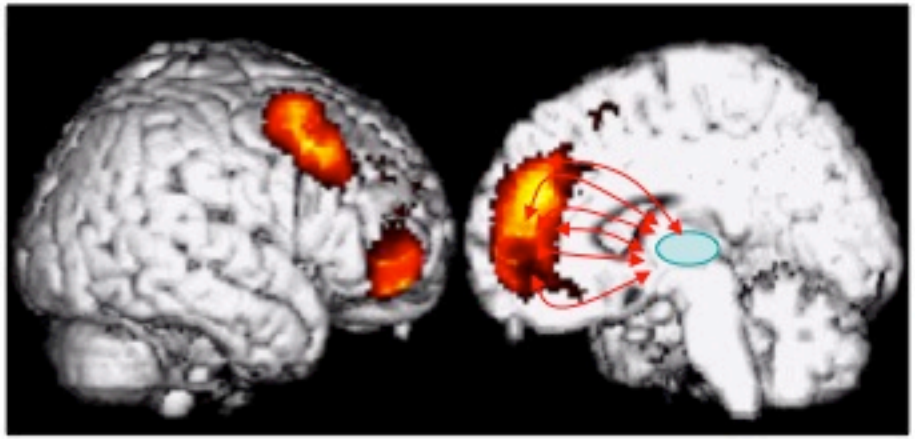


Figure 5. Linear discriminant analysis. Plotting the two discriminant functions (or canonical roots) against each other separated the GOS 1–3 group (unfavorable outcome, *closed circles*), the GOS 4–5 group (favorable outcome, *open circles*), and the control group (*open squares*). NAA, *N*-acetyl aspartate;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

Tshibanda *et al, Prog Brain Res*, 2009
Tshibanda *et al, Neuroradiology*, 2010

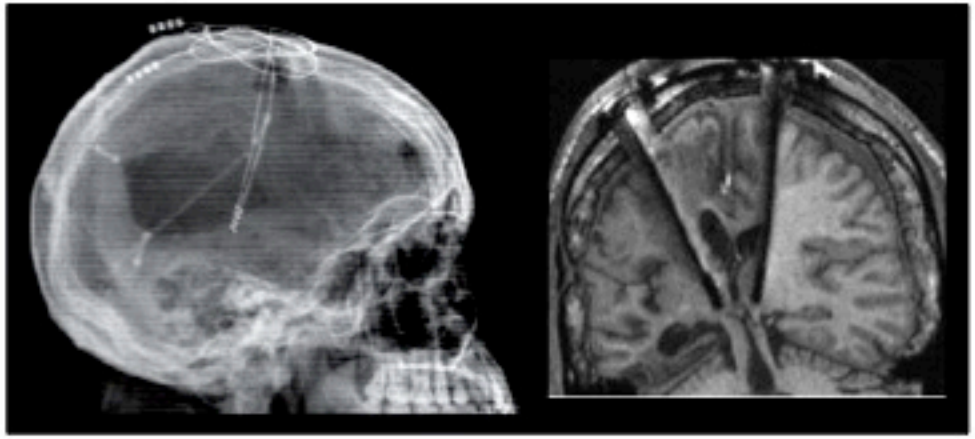
Deep brain stimulation

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



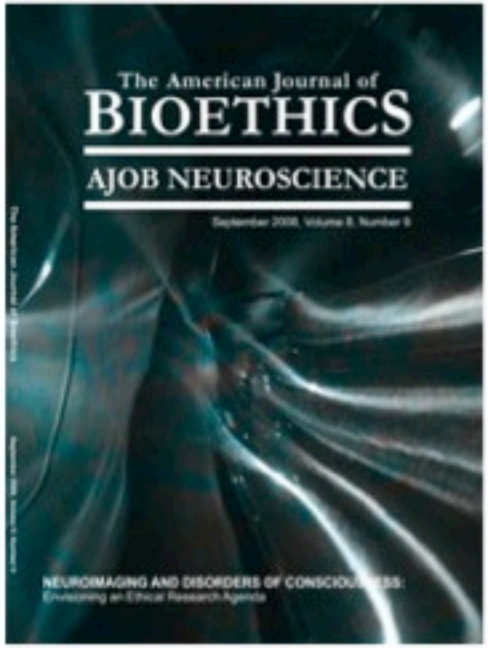
Laureys et al, *Lancet* 2000

Intralaminar nuclei stimulation induces "recovery" from minimally responsive state



Schiff et al, *Nature* 2007

Ethical framework



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

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**

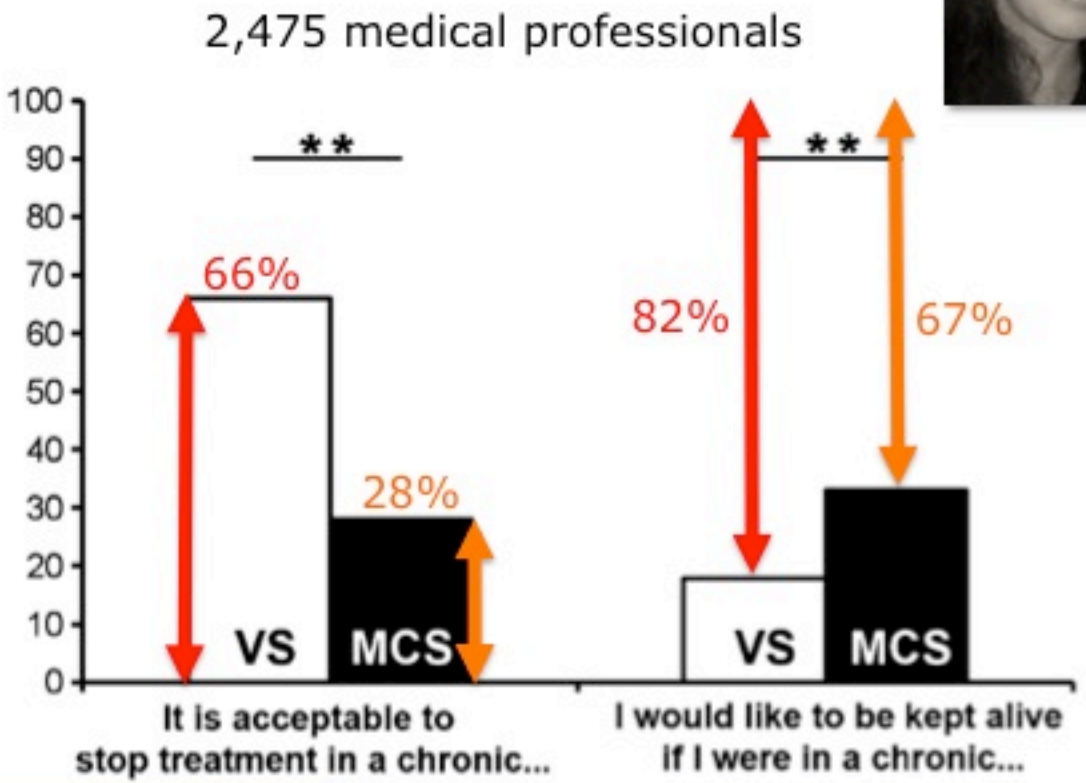
*Co-lead authors.
**Equal authors in alphabetical order.

Fins et al, *Am J BioEthics* 2008

End-of-life issues

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

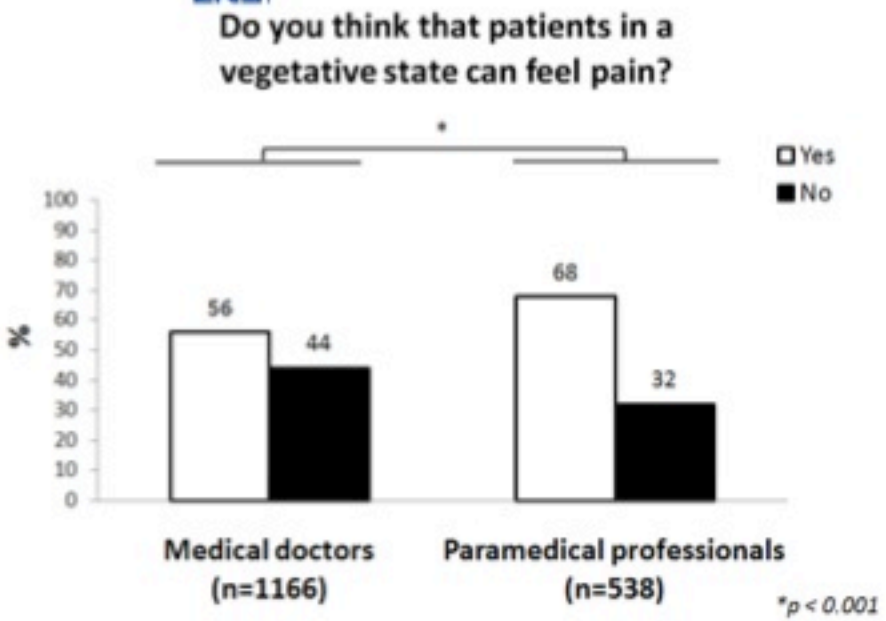
A. Demertzi · D. Ledoux · M.-A. Bruno · A. Vanhaudenhuyse · O. Gosseries · A. Soddu · C. Schnakers · G. Moonen · S. Laureys



Demertzi et al, *J Neurology* 2011

Do they feel pain?

European Neurological Society



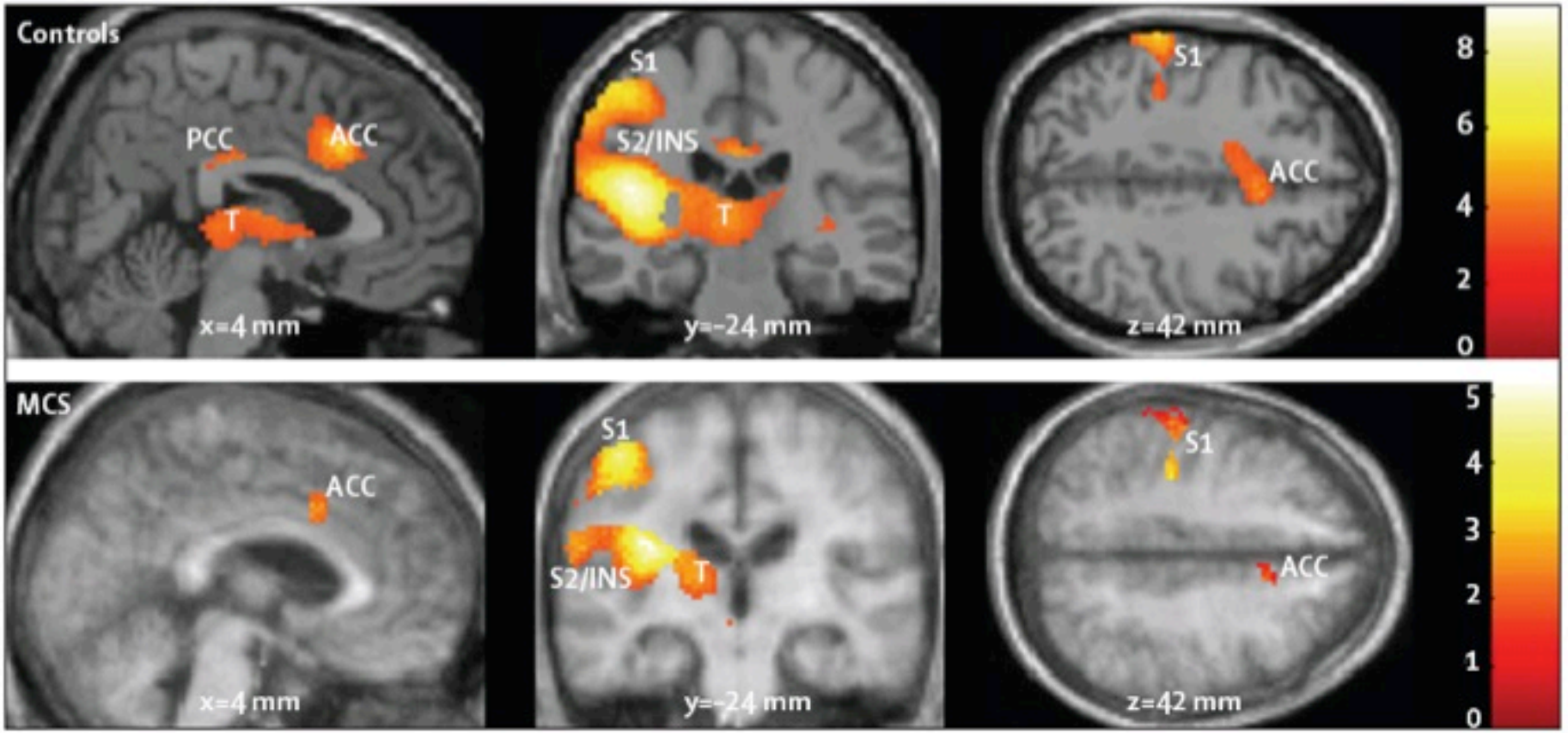
Nociception Coma Scale

Score	Item	Response
MOTOR RESPONSE		
3	*Localization to Noxious Stimulation*	The non-stimulated limb must locate and make 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 must move away from the point of stimulation.
1	*Abnormal Posturing*	Slow, stereotyped 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 noxious stimulation, secondary to hypotonic or flaccid muscle tone.
VERBAL RESPONSE		
3	*Intelligible Verbalization*	Production of words in response to noxious stimulation. Each verbalization must consist of at least 1 consonant-vowel-consonant (C-VC) triad. For example, [illegible] that hurts»
2	*Vocalization / Oral Movement*	[illegible] calization in
1	*Groans*	[illegible] to noxious
0	*None*	
VISUAL RESPONSE		
3	*Fixation*	[illegible] ication point
2	*Eyes movements*	
1	*Startle*	[illegible] mulation.
0	*No change*	There are no discernible changes in response to noxious stimulation.
FACIAL EXPRESSION		
3	*Cry*	Cries are observed not spontaneously but in response to noxious stimulation.
2	*Grimace*	[illegible]
1	*Oral reflexive movement/Startle response*	Clamping of jaws, tongue pumping, yawning, chewing movement.
0	*None*	There is no discernible facial expression following application of noxious stimulation.

Total score >7 / 12
= analgesic treatment

Demertzi et al, *Prog Brain Res*, 2009
Schnakers et al, *Pain*, 2010

Pain in minimally conscious state



http://neurology.thelancet.com

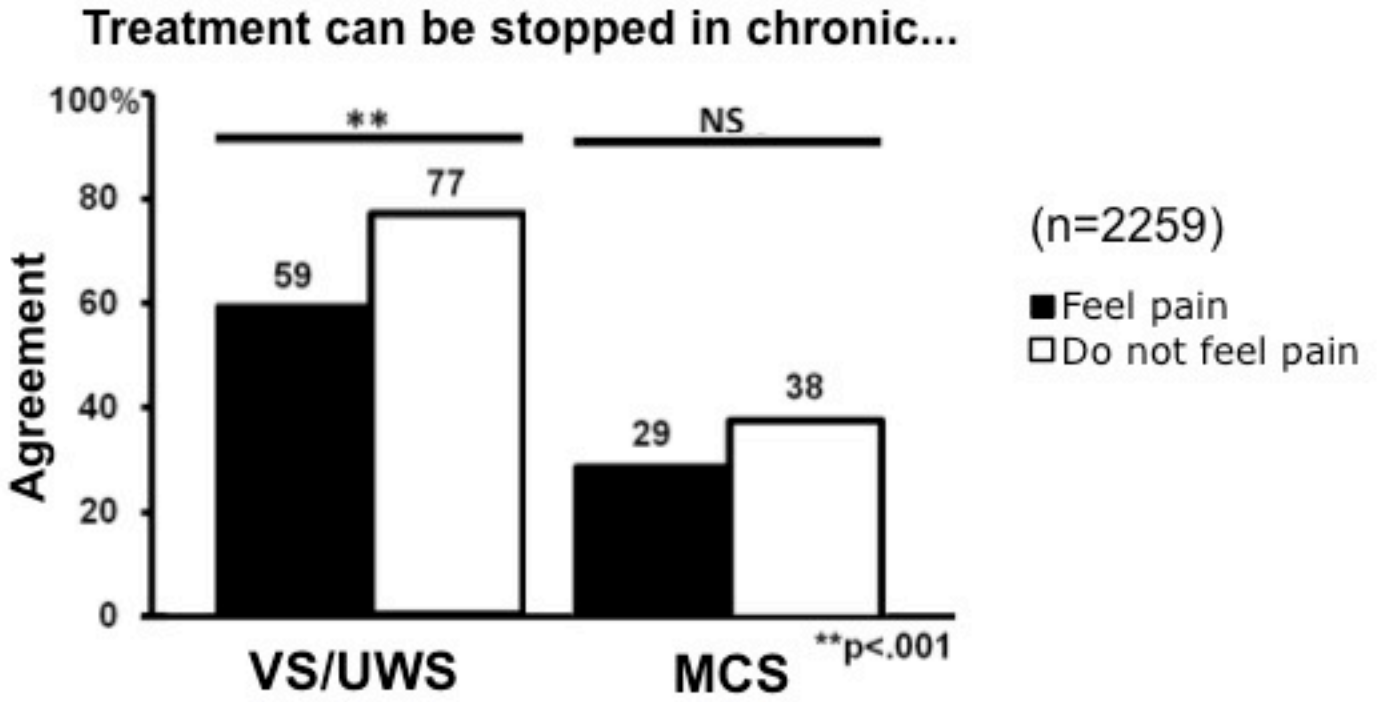
Boly et al *Lancet Neurology*, 2008

Attitudes towards pain & end-of-life

Pain Perception in Disorders of Consciousness: Neuroscience, Clinical Care, and Ethics in Dialogue

A. Demertzi · E. Racine · M-A. Bruno · D. Ledoux · O. Gosseries · A. Vanhaudenhuyse · M. Thonnard · A. Soddu · G. Moonen · S. Laureys

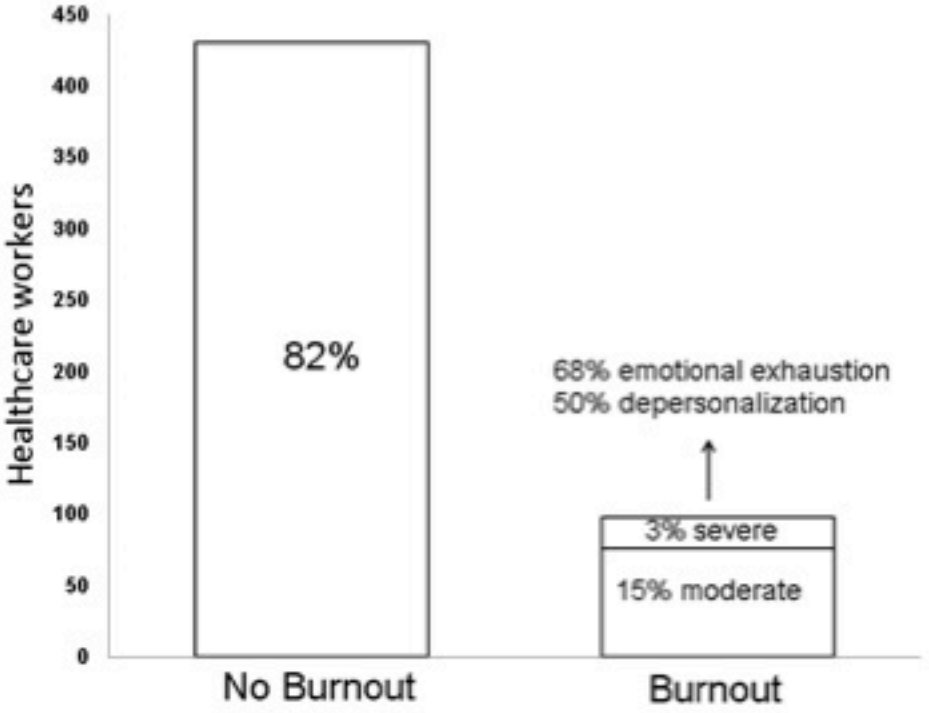
European Neurological Society



Demertzi & Racine et al, *Neuroethics* 2012

Burnout in caregivers

568 health care workers (Maslach Burnout Inventory)



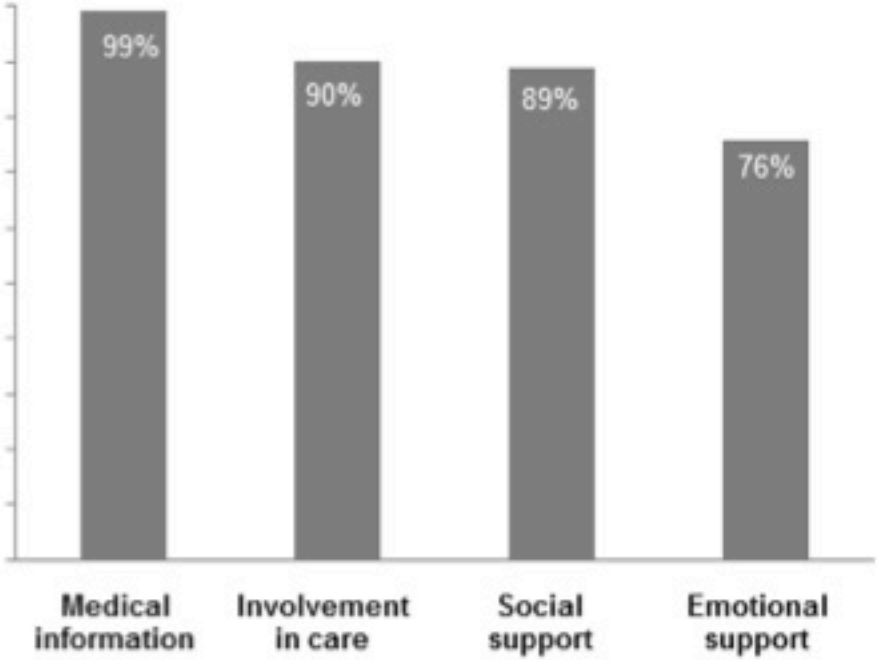
Profession	Burnout
Physician	8%
Nurse	24%
Nursing assistant	23%
Physio-/speech-/ergo-therapist	8%
Psychologist/social worker	10%

Gosseries, Demertzi et al, *Brain Injury* in press

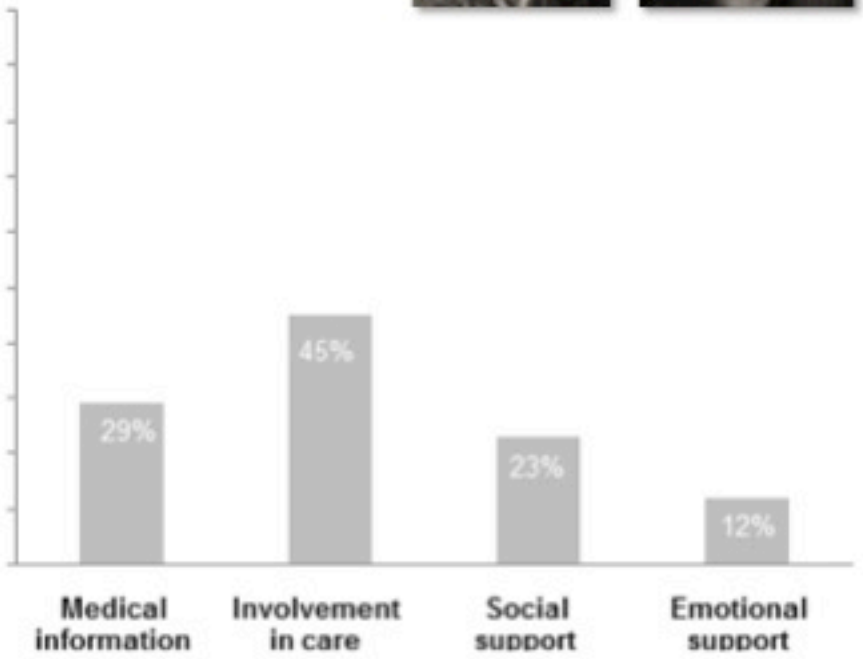
Family needs

- 193 families of DOC patients
- 82% depression, 73% anxiety, 19% wished to stop treatment

a) Importance



b) Satisfaction



Gosseries, Demertzi et al,

J Head Trauma Rehabilitation, under revision

Quality of life

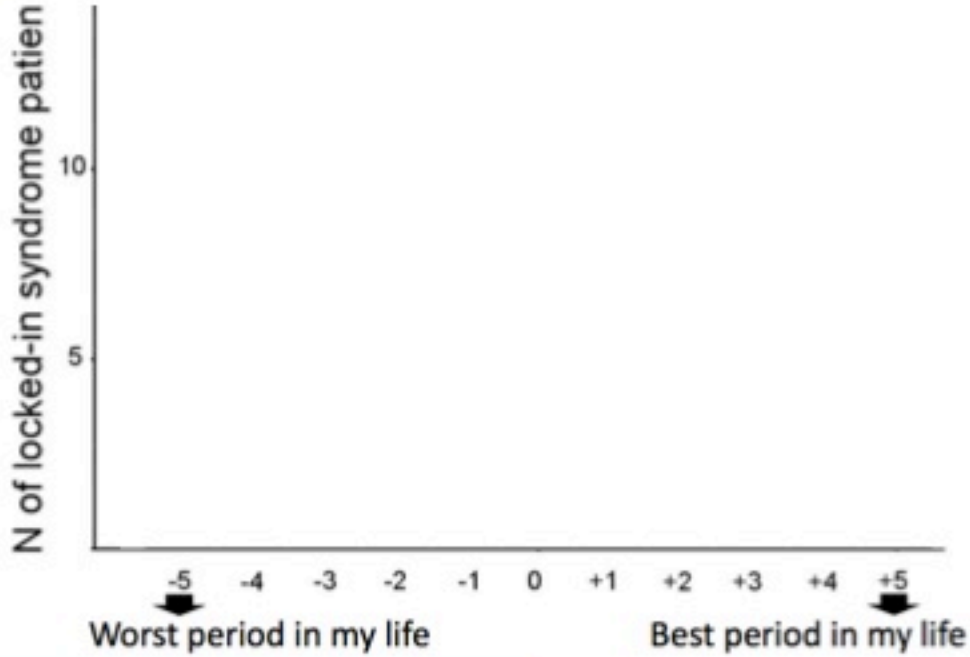
Open Access Research

BMJ open

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

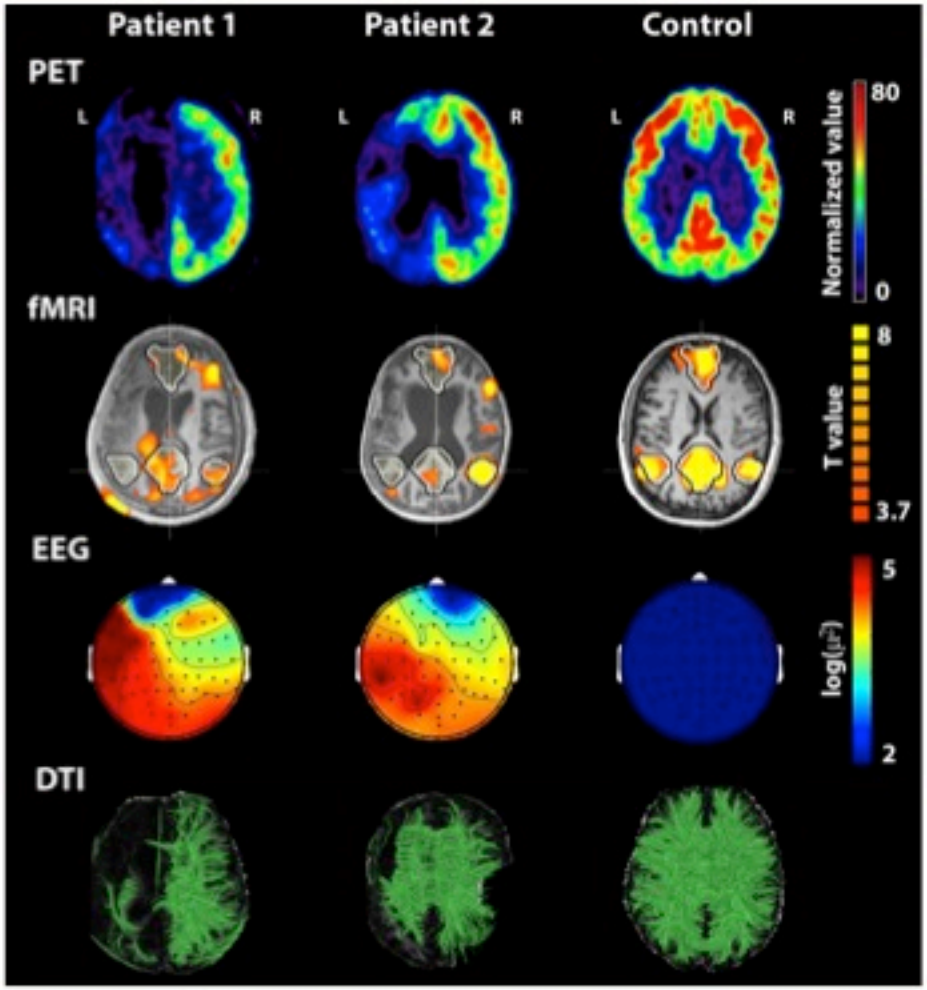
Marie-Aurélie Bruno,[1] Jan L Bernheim,[2] Didier Ledoux,[1] Frédéric Pellas,[3] Athena Demertzi,[1] Steven Laureys[1]

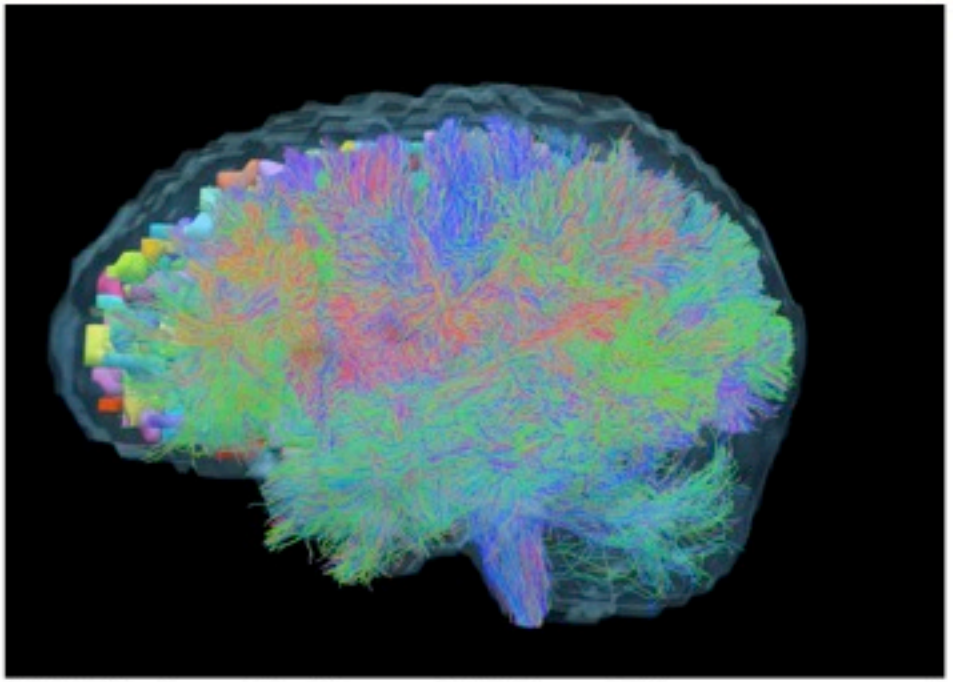
ALIS
Association du Locked-in Syndrome



Bruno et al, *BMJ Open*, 2011

New diagnostic & prognostic tests





Erik Ziegler, *Cyclotron Art Committee*

Bruno et al, *Prog Brain Res*, 2011

Results of additional diagnostic testing and their possible ethically relevant effects

Results of Tests	Beneficial Effects	Harmful Effects
Tests show *less brain activity than* neurological examination	Relatives may better cope with the decision to withdraw life-sustaining treatment	Relatives may lose hope, purpose, and meaning in life
Tests show *more brain activity than* neurological examination	Clinical management may be intensified by the chance of further recovery	False hopes may be nurtured, leading to long-term harm, disappointment & suffering
Tests show the *same level of brain activity* as neurological examination	Clinicians and relatives may be affirmed in their decision about the level of treatment	Clinicians and relatives may be disappointed & treatment cost/effectiveness may be poor

Jox, Bernat, Laureys, Racine, *Lancet Neurology*, in press

Responding to requests for interventions

Diagnosis

- Recognize the value and limitations of new technology
- Clarify hopes and expectations, taking into account the strain on family
- Acknowledge the complex relationship between patient awareness and decision making

Prognosis and treatment

- Communicate prognosis in an area of uncertainty
- Involve patients and their families in research studies
- Approach treatment decision making by focusing on goals of treatment

Challenges

1. Epidemiology
   - centralized database
2. Diagnosis
   - standardized validated assessments (CRS-R)
3. Prognosis
   - objective validated tests (fMRI, PET, EEG, ERP, EEG-TMS)
4. Treatment
   - amantadine, zolpidem, deep brain stimulation, sensory stimulation
5. Adapted network of care for VS/UWS-MCS
   - rationalize & improve medical care & scientific understanding

FERB UET