Contribution of neuroimaging studies to the physiopathology and diagnosis of patients with disorders of consciousness

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Functional Imaging Laboratory, Wellcome Trust Centre for Neuroimaging, University College London, UK

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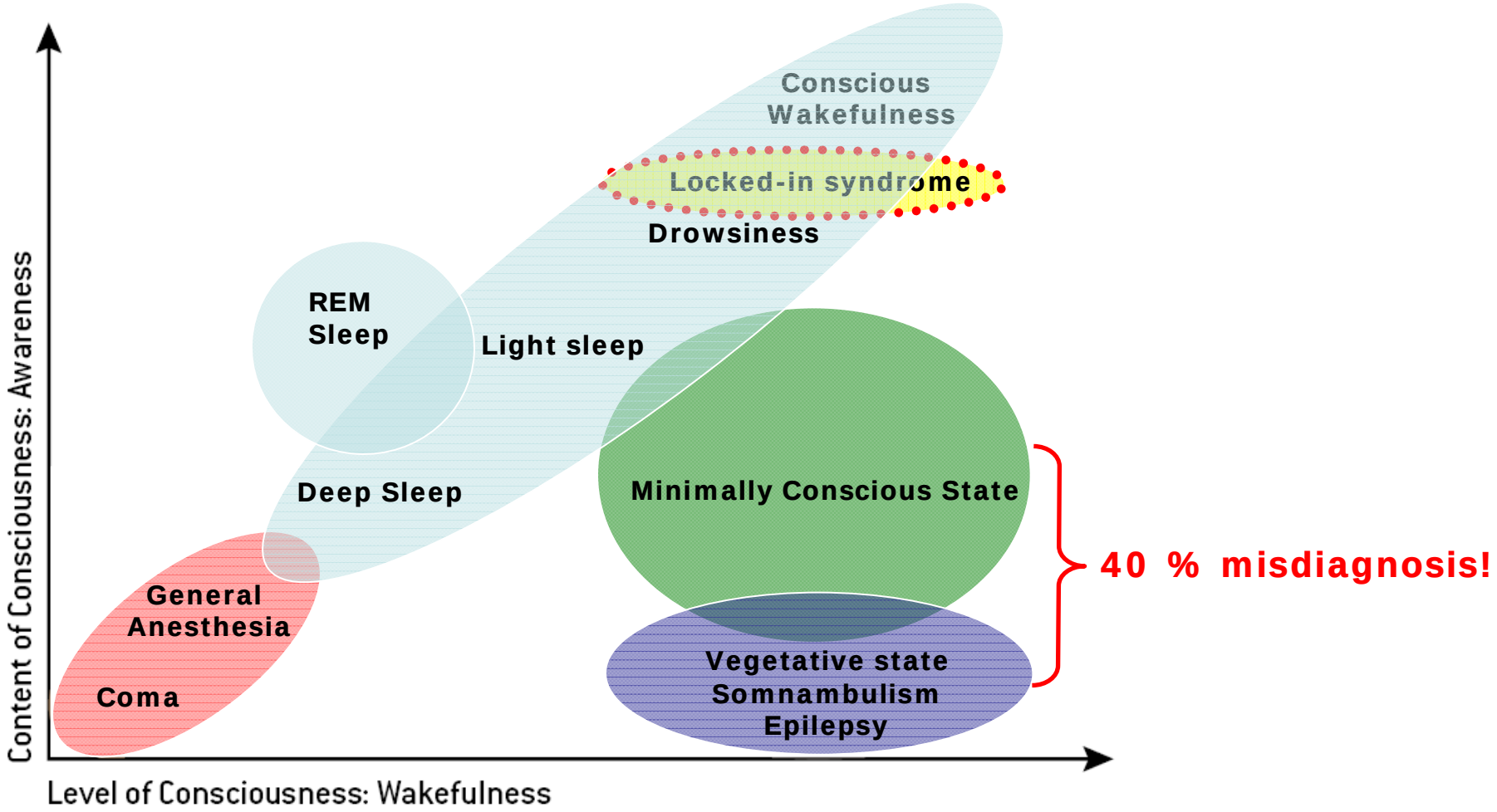
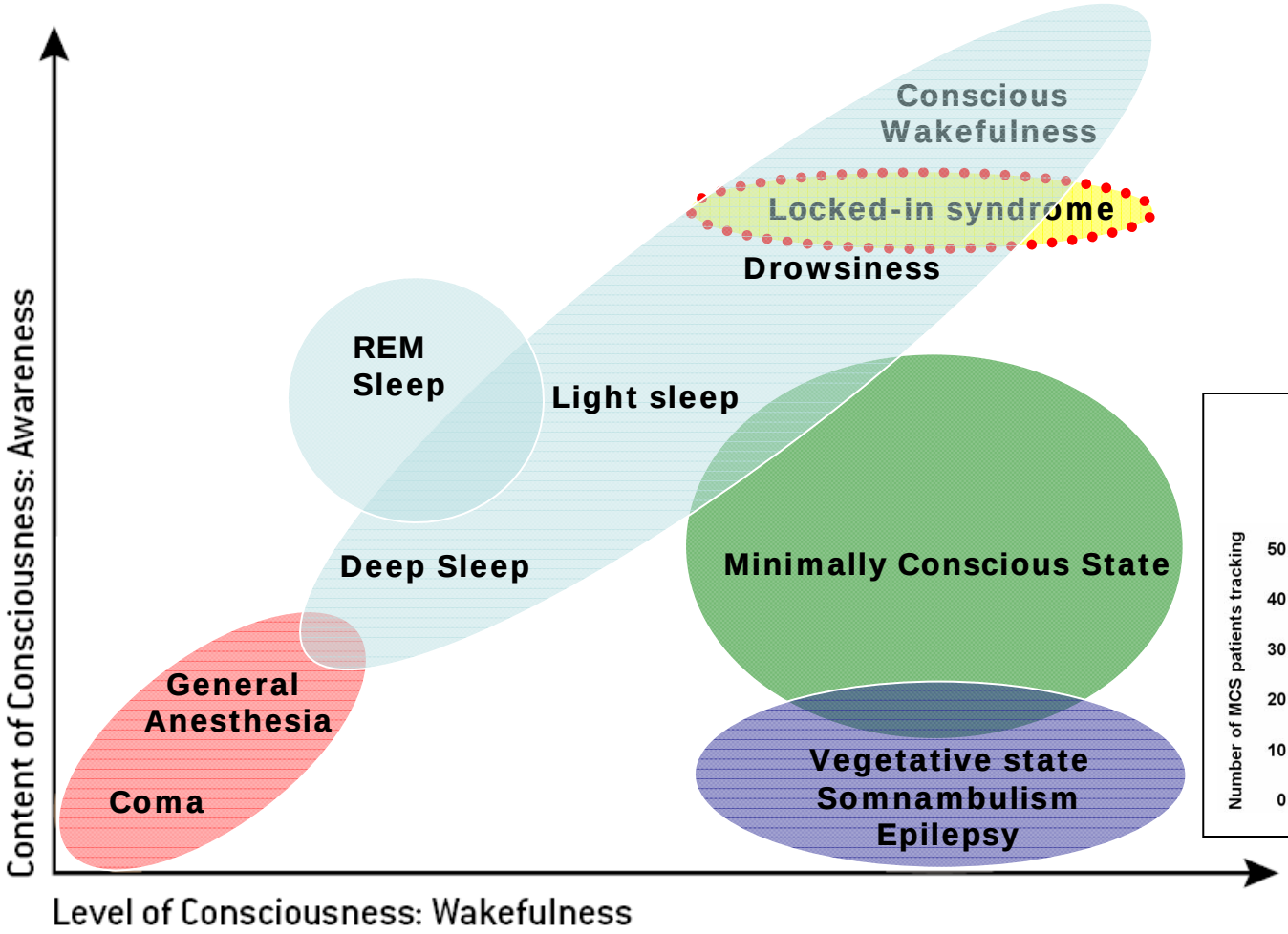
Altered states of consciousness

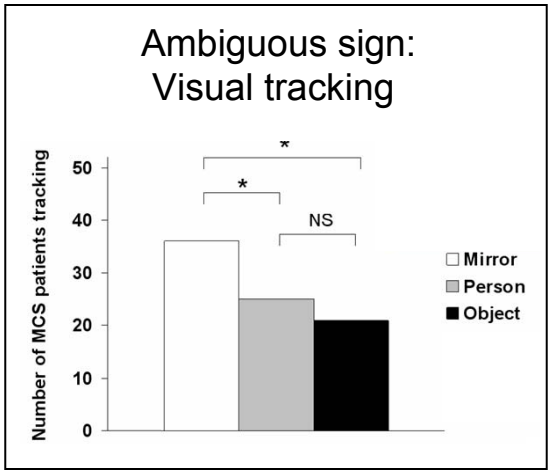


Laureys & Boly, Current Opinion in Neurology 2007
Laureys & Boly, Nature Clinical Practice 2008

Schnakers et al., BMC Neurology 2009

Altered states of consciousness

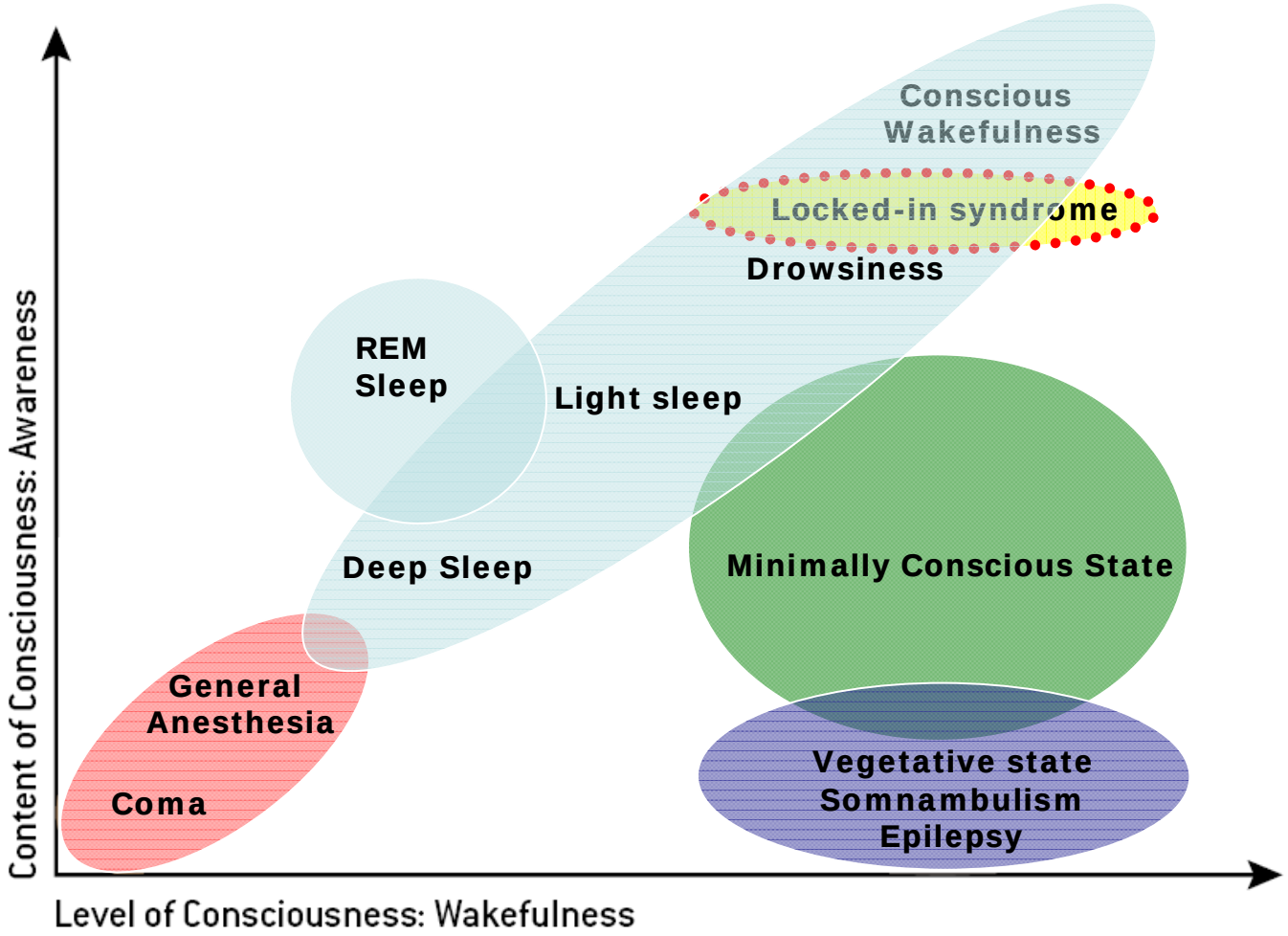




Laureys & Boly, Current Opinion in Neurology 2007
Laureys & Boly, Nature Clinical Practice 2008

Vanhaudenhuyse et al., JNNP 2008

Altered states of consciousness



Ambiguous sign:
Blink to visual threat

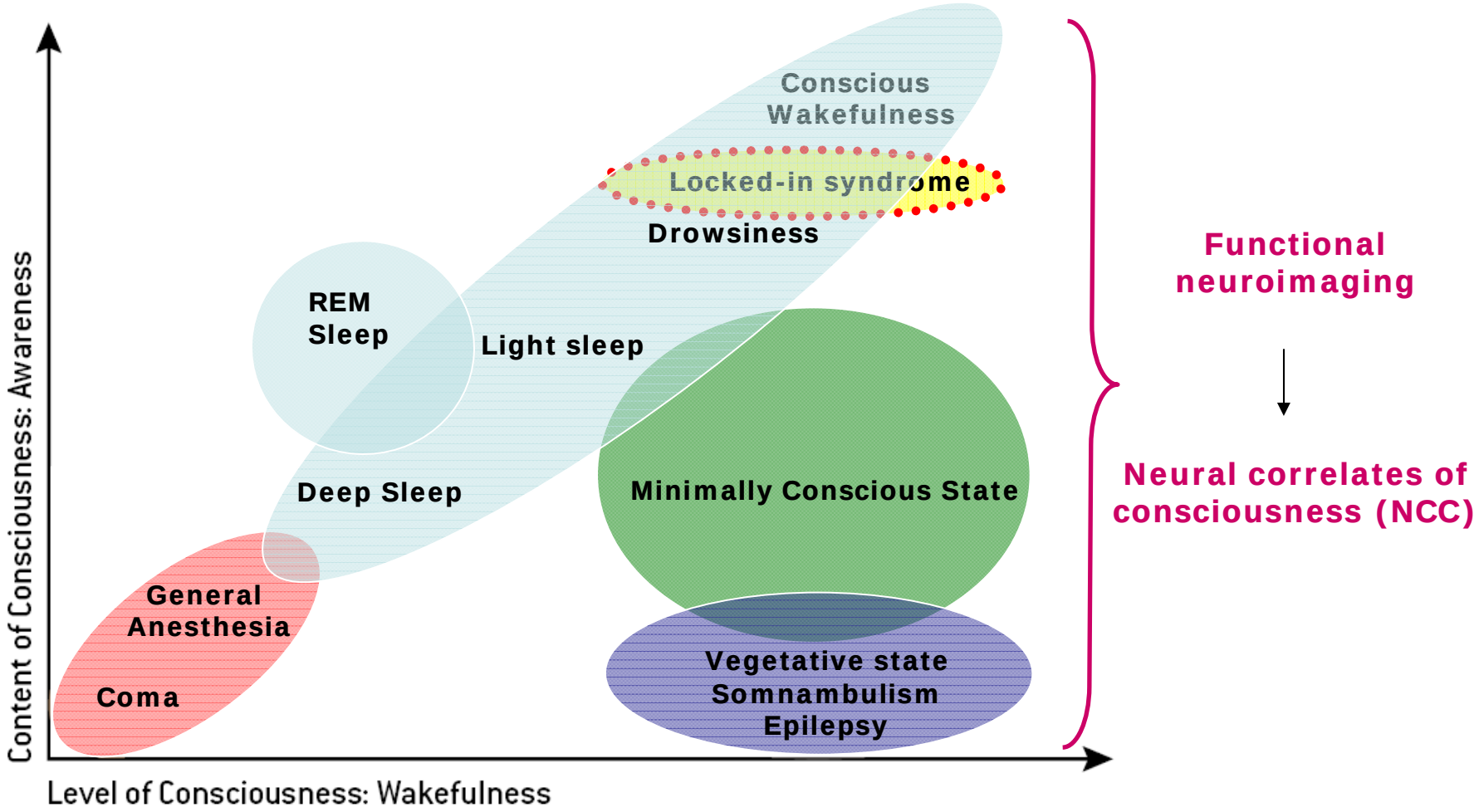
↓

Does not herald consciousness in VS

Laureys & Boly, Current Opinion in Neurology 2007
Laureys & Boly, Nature Clinical Practice 2008

Vanhaudenhuyse et al., Neurology 2008

Altered states of consciousness



Laureys, Scientific American 2007
Laureys & Boly, Current Opinion in Neurology 2007, Nature Clinical Practice 2008

Brain metabolism studies

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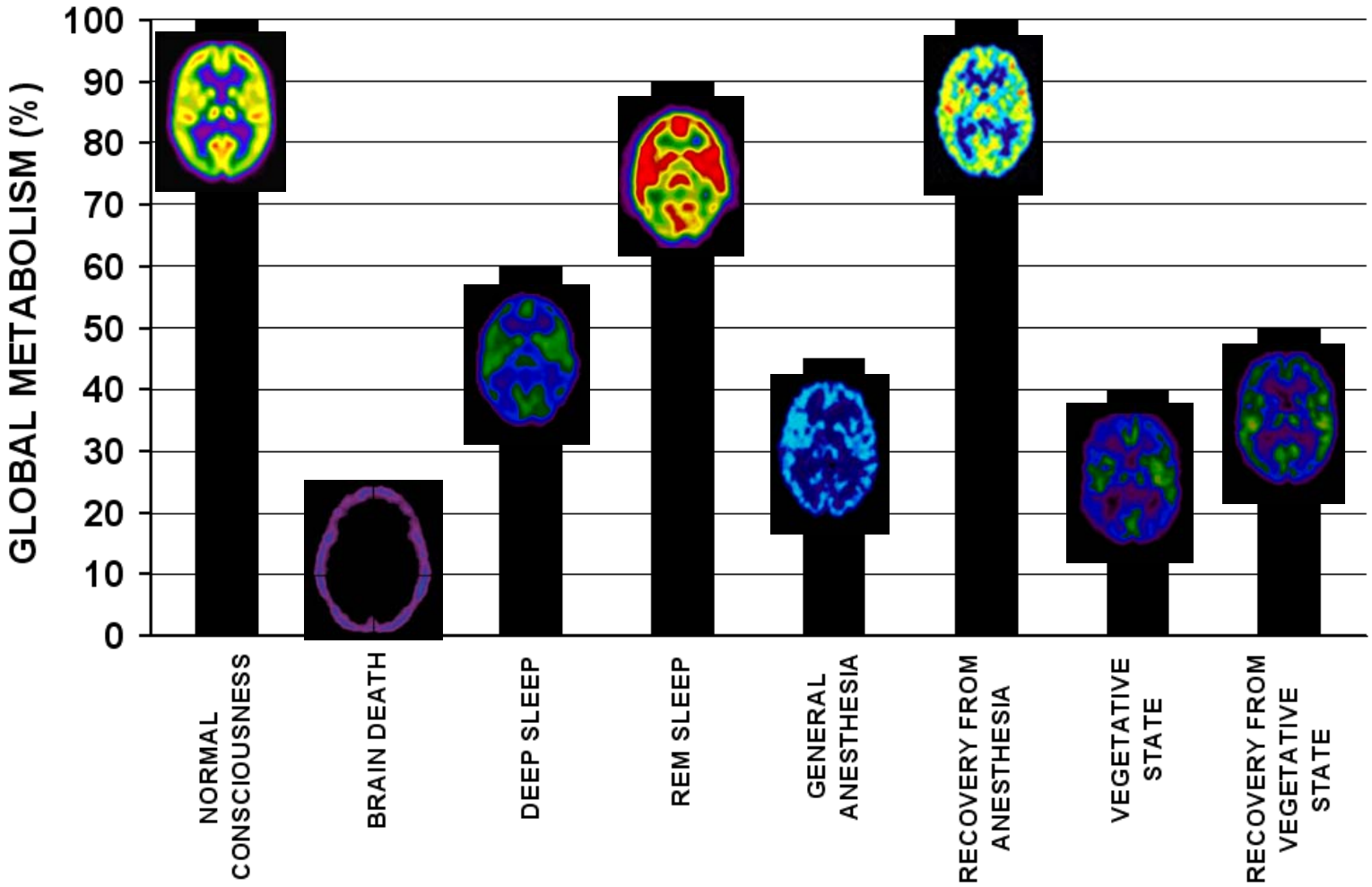
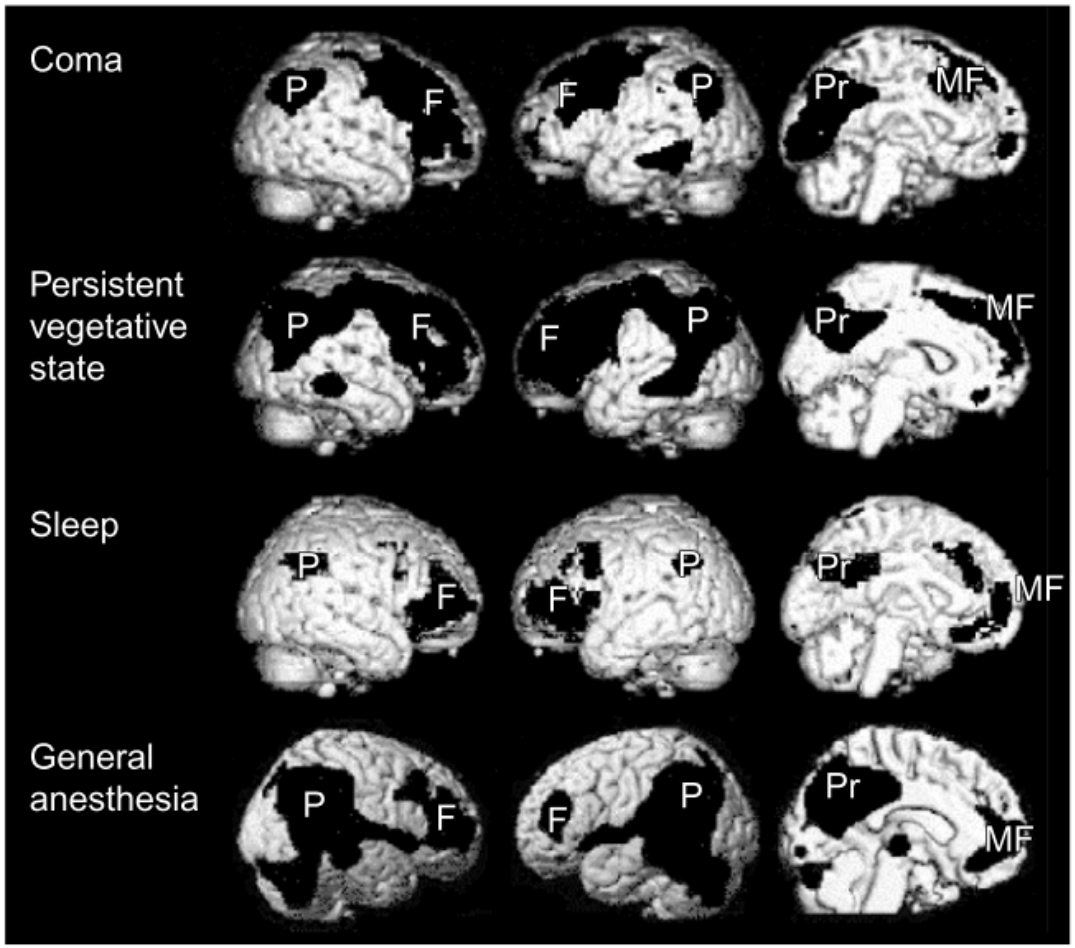
Global brain metabolism ≠ consciousness



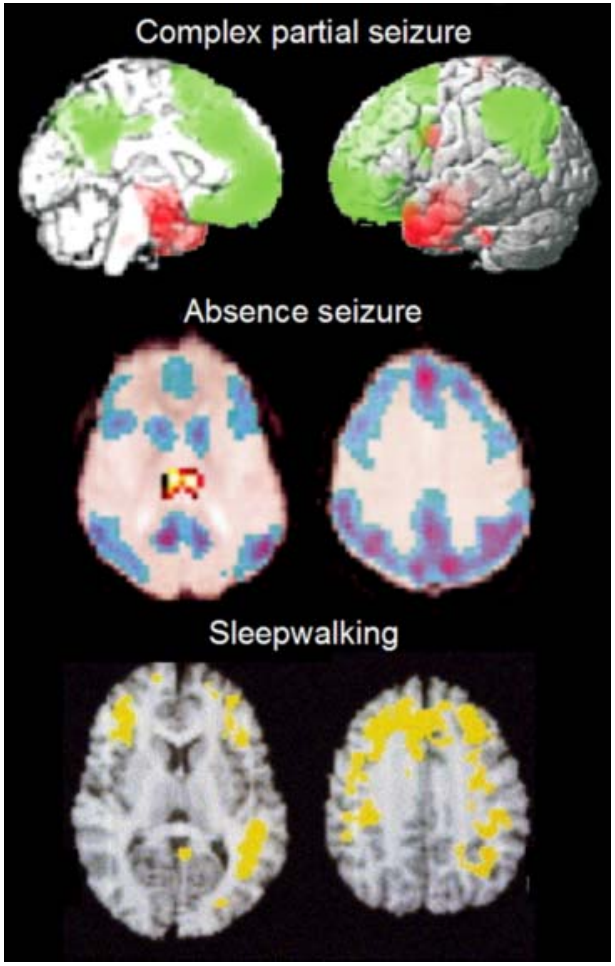
Laureys et al., Lancet Neurology, 2004 (sleep data from Pierre Maquet; anesthesia data from Mike Alkire)

Regional brain metabolism and consciousness



Baars, Ramsoy & Laureys, Trends in Neuroscience 2003

Transient “vegetative” states

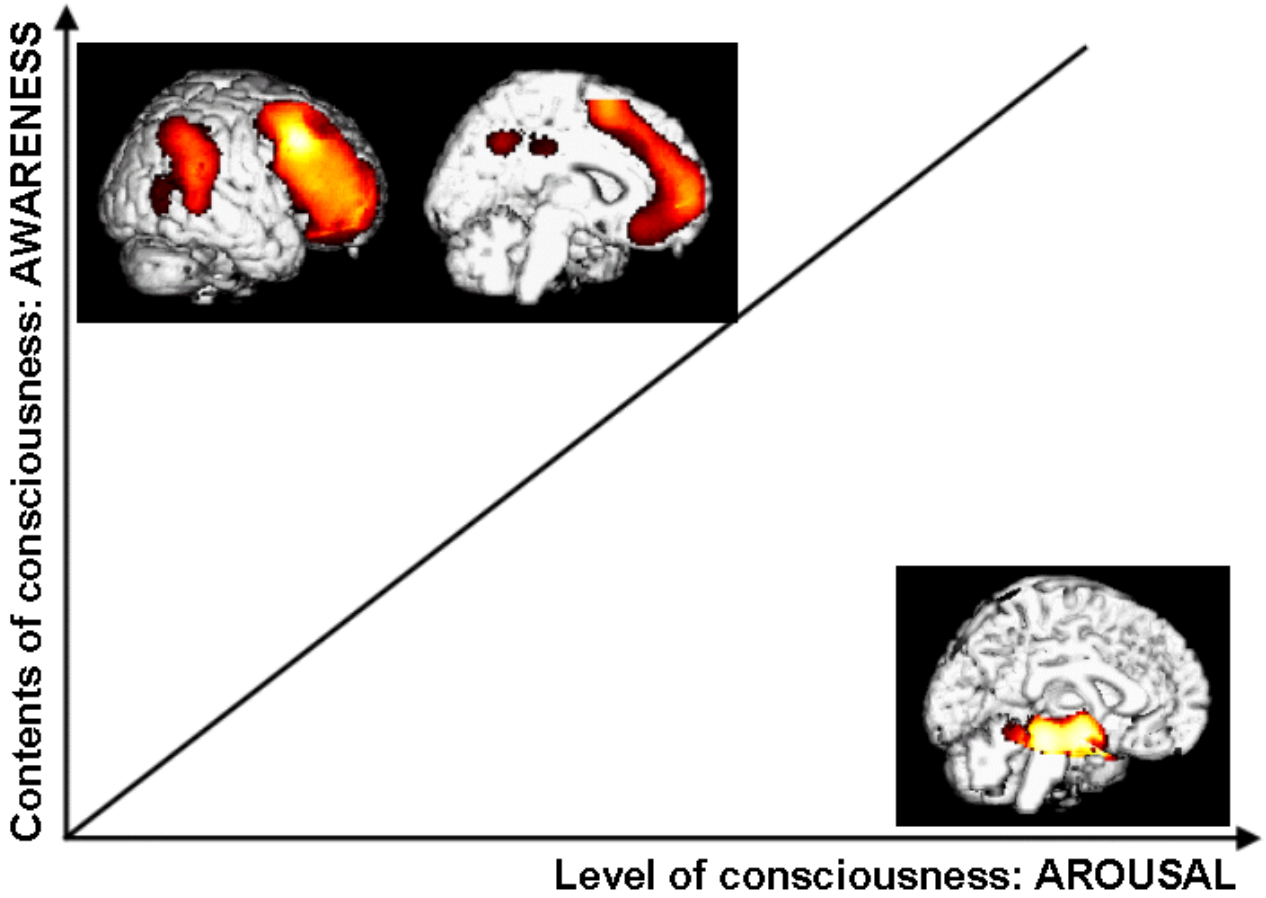


SPECT data from
Hal Blumenfeld (n=6)

fMRI data from
Salek-Haddadi (n=1)

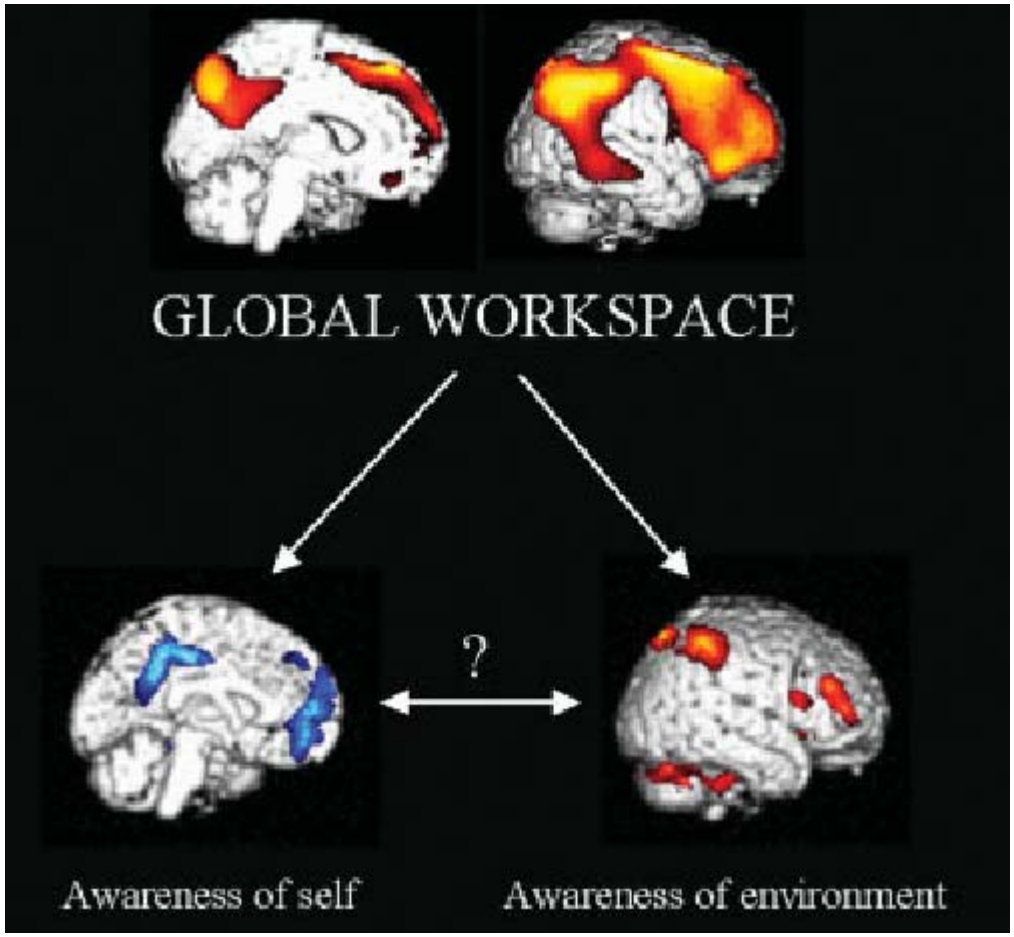
SPECT data from
Claudio Bassetti (n=1)

Neuroanatomy of consciousness



Boly et al., Annals of the New York Academy of Sciences 2008

“Awareness network”



Boly et al., Human Brain Mapping 2008
Boly et al., PNAS 2007

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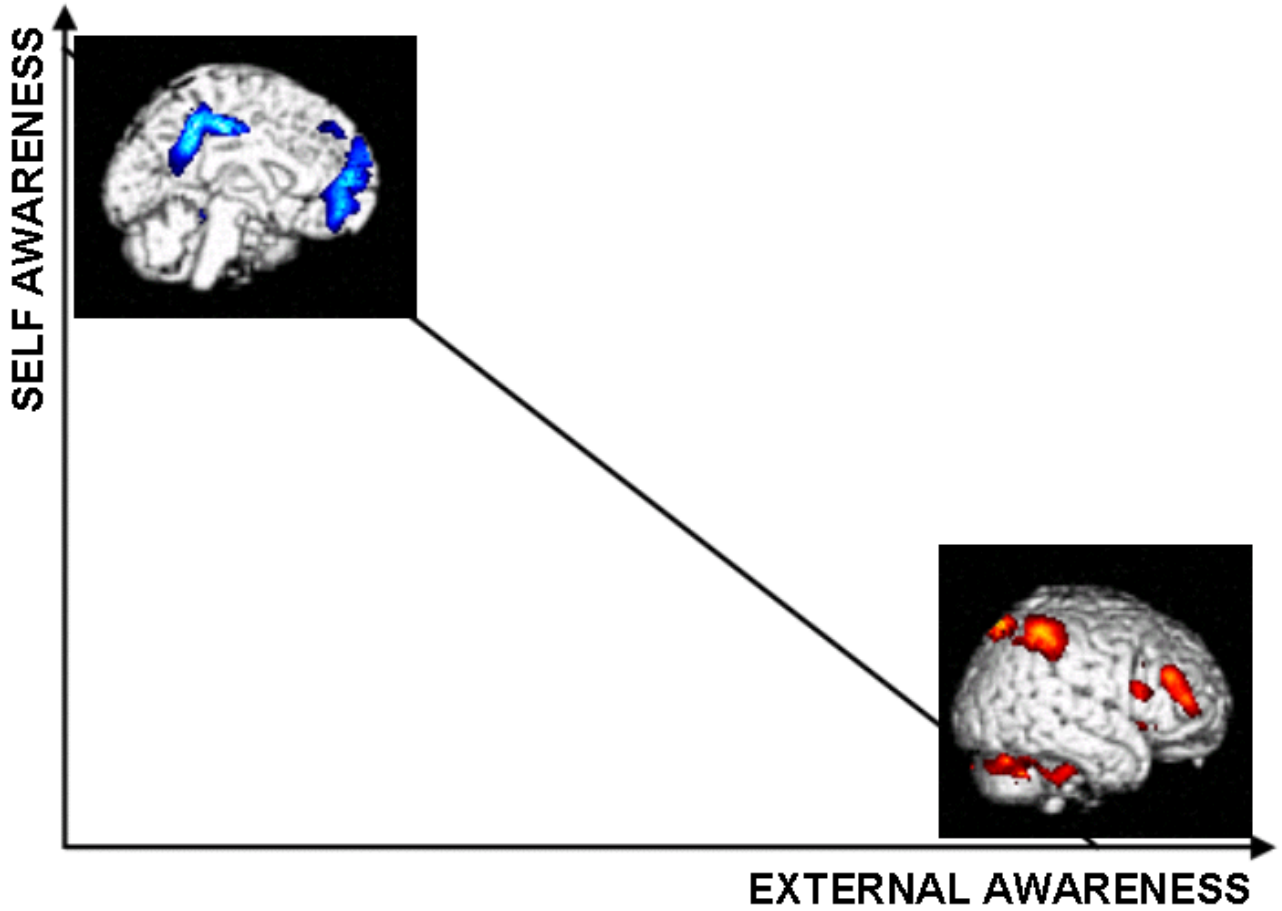

Boly et al., Annals of the New York Academy of Sciences 2008

External awareness:

Brain responses to sensory stimuli

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DO THEY FEEL PAIN ?

THE LANCET

Seminar

Vol 350 • September 13, 1997

Persistent vegetative state

Adam Zeman

Lingering doubt

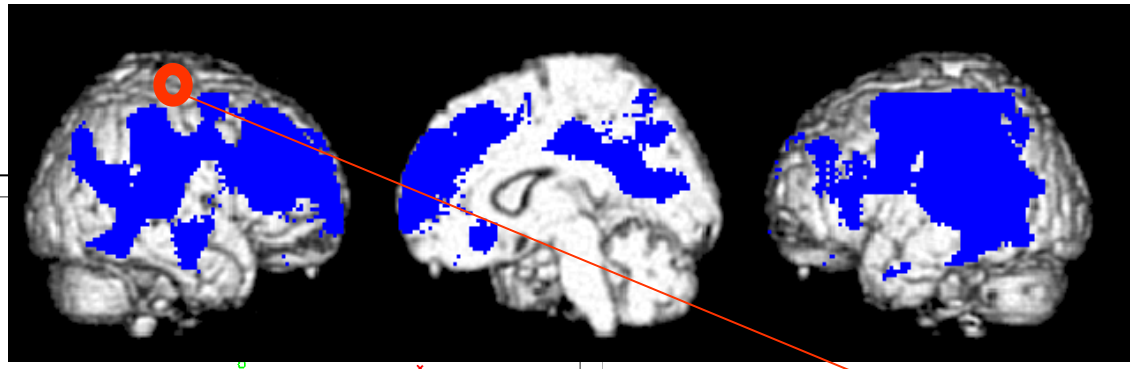
Can we be absolutely certain that patients in a vegetative state cannot experience anything? Might a grimace in response to pain not indicate a glimmer of awareness?

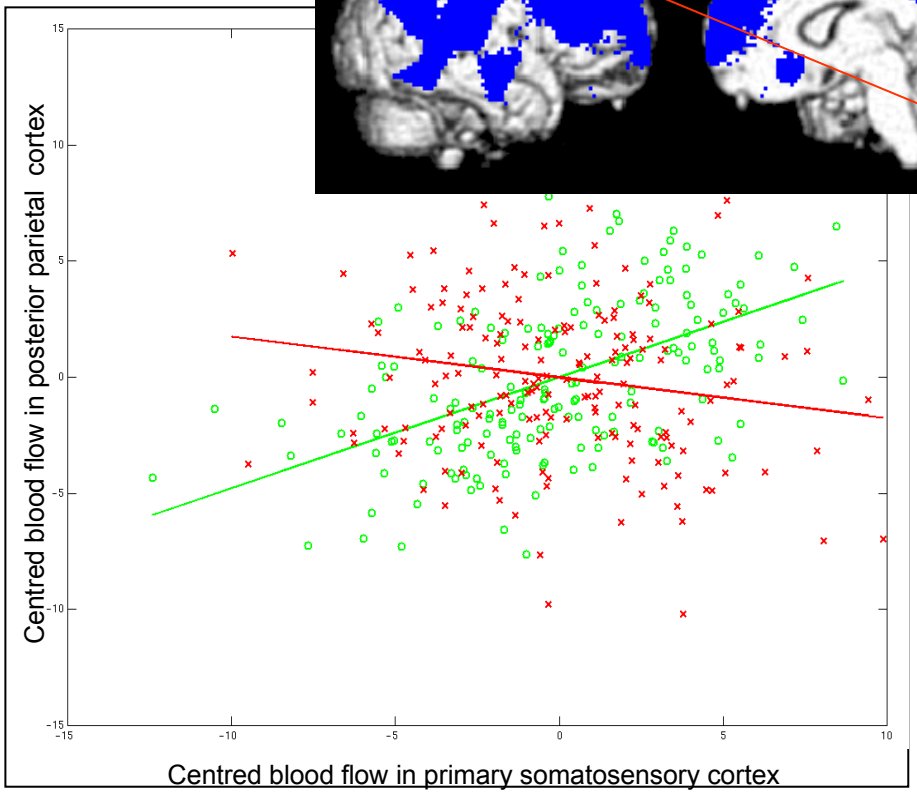
Noxious processing

PET scan

Median nerve electrical stimulation

Pain perception in VS



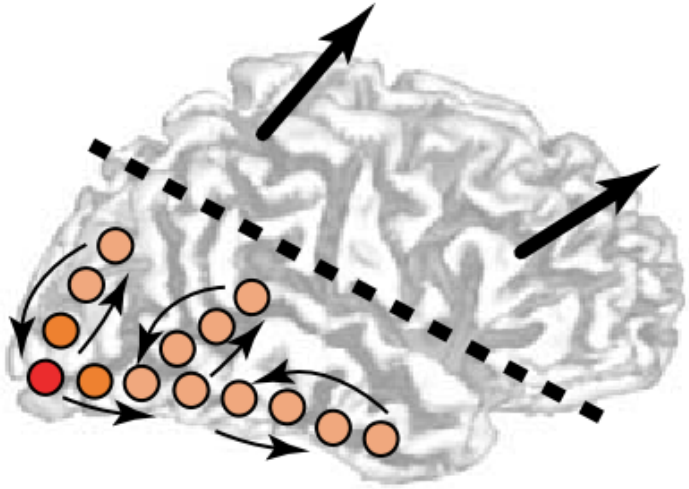


Primary somatosensory cortex SI

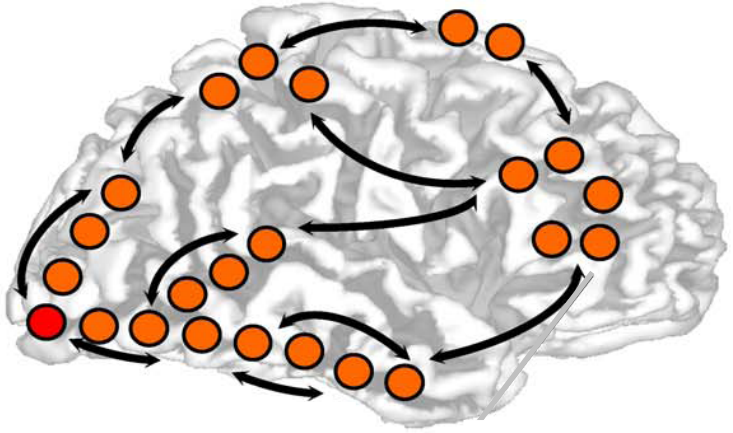
Laureys et al., Neuroimage 2002

External awareness correlates in healthy volunteers

subliminal

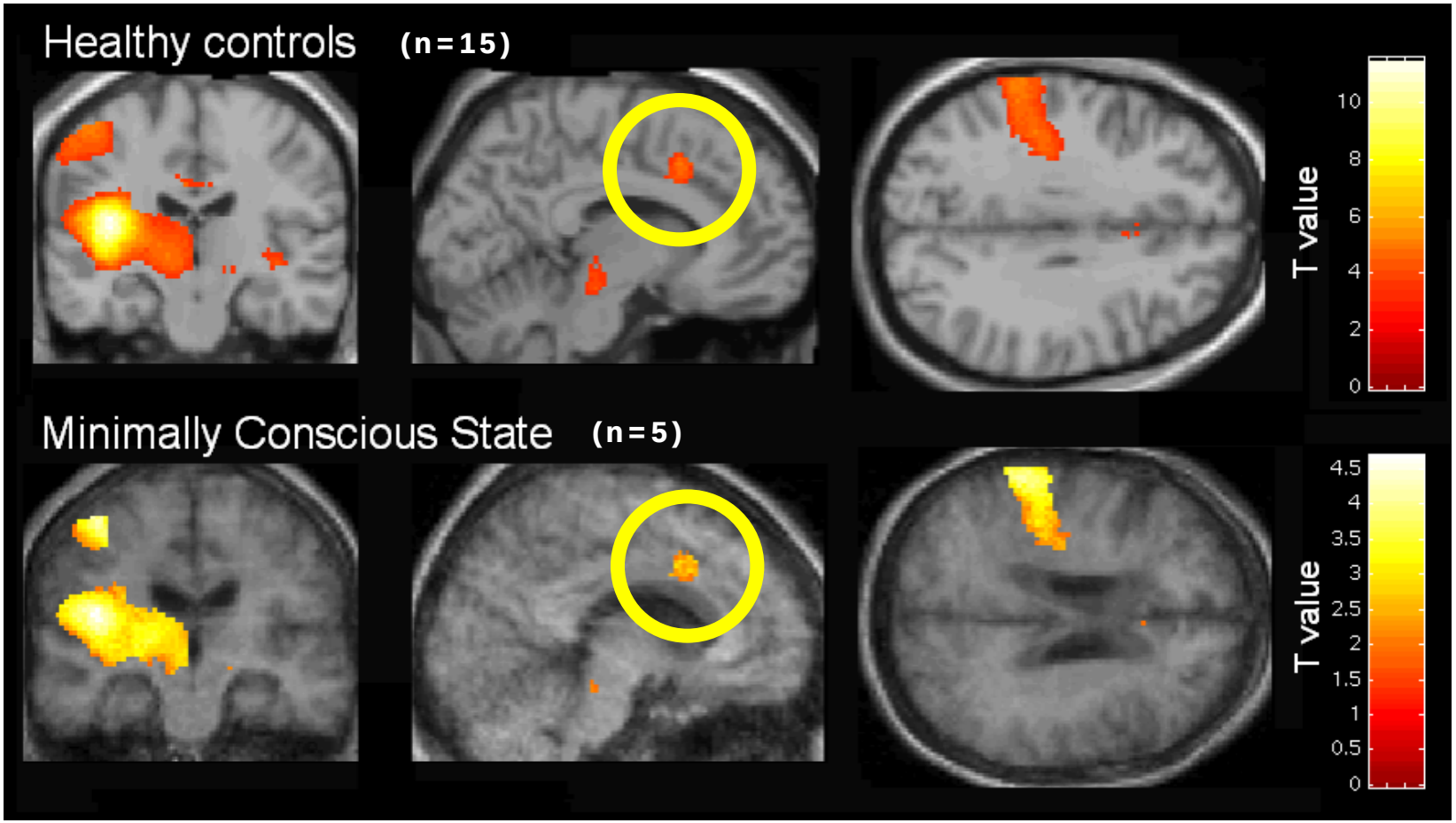


conscious



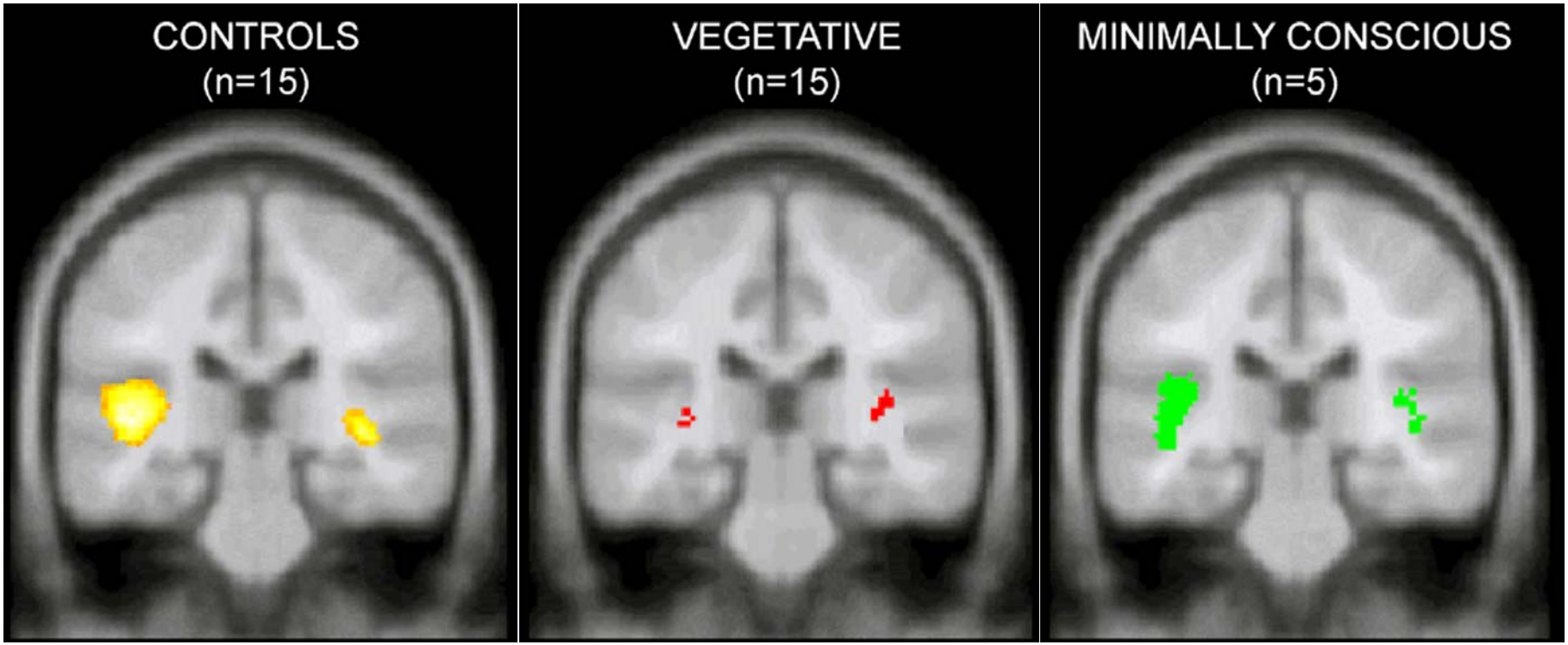
Dehaene et al., Trends in Cognitive Sciences 2006

Pain perception in MCS



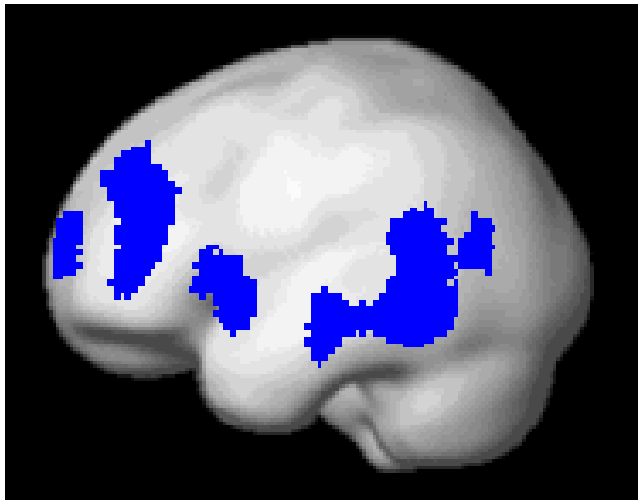
Boly et al., Lancet Neurology 2008

Auditory perception

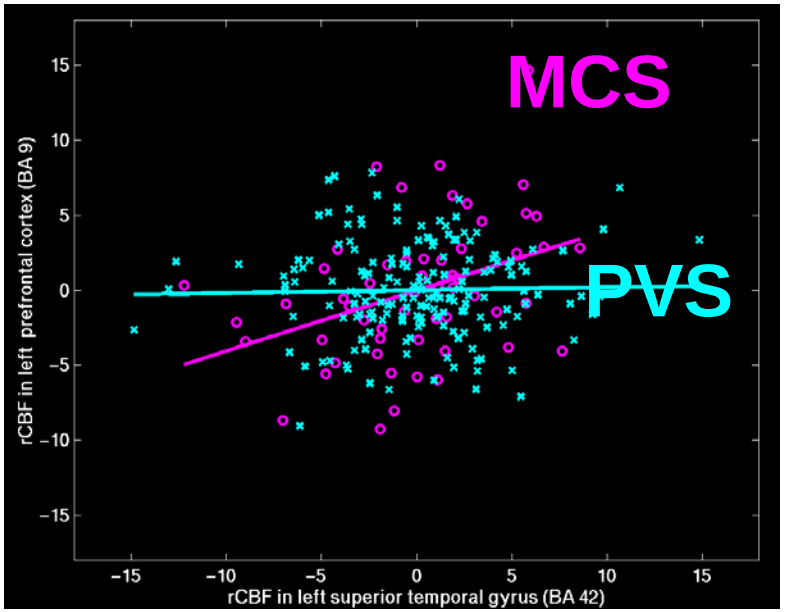


Boly et al., Archives of Neurology 2004, Neuropsychological Rehabilitation 2005

Auditory perception

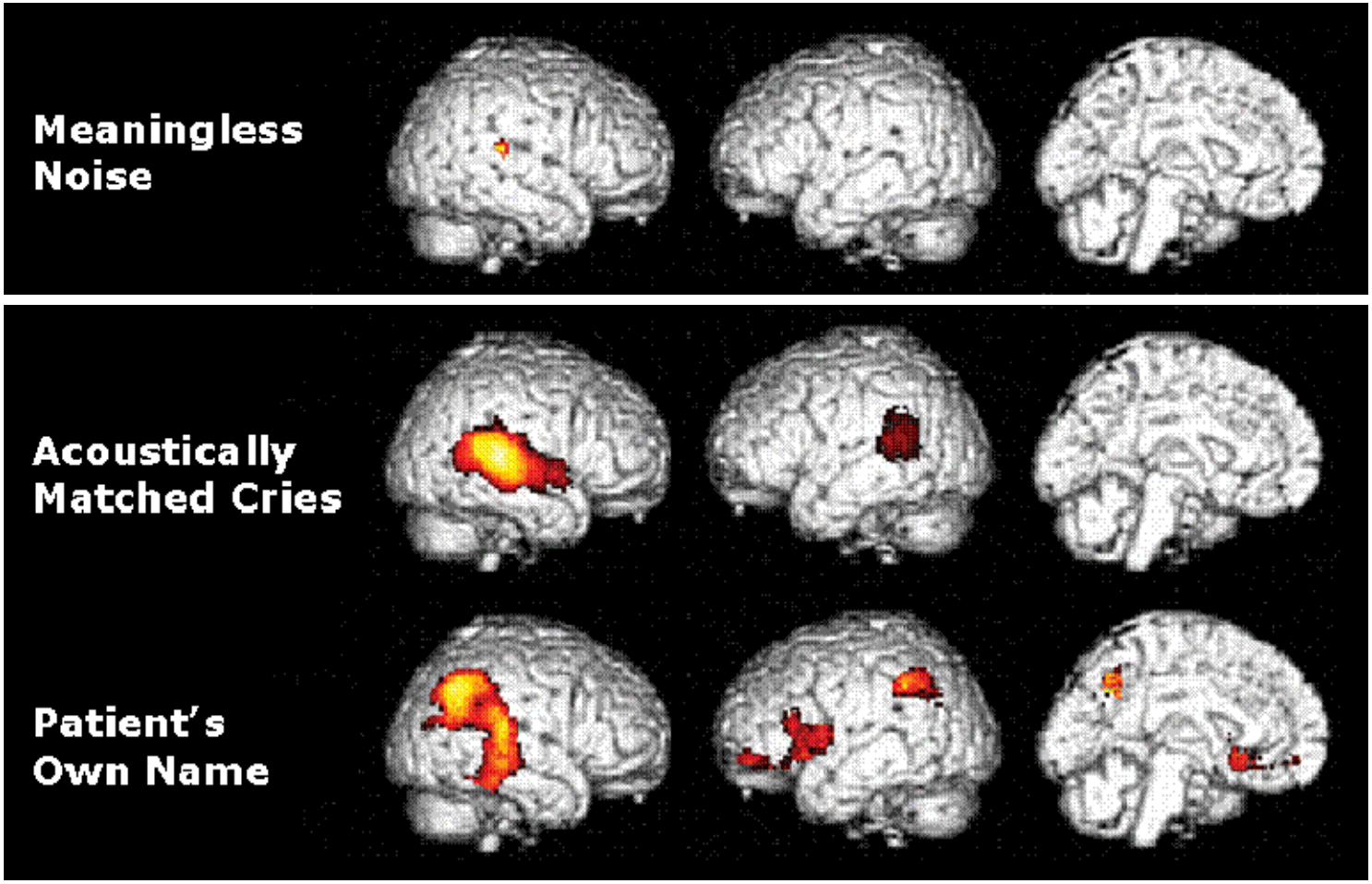


Areas with more efficient connectivity with auditory cortex in MCS compared to PVS



Boly et al, Archives of Neurology, 2004

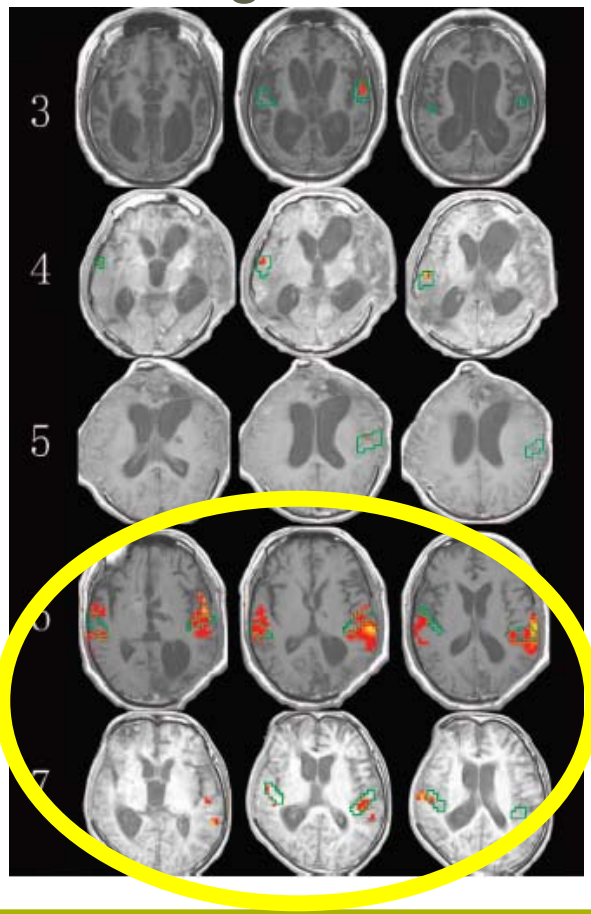
Emotional processing



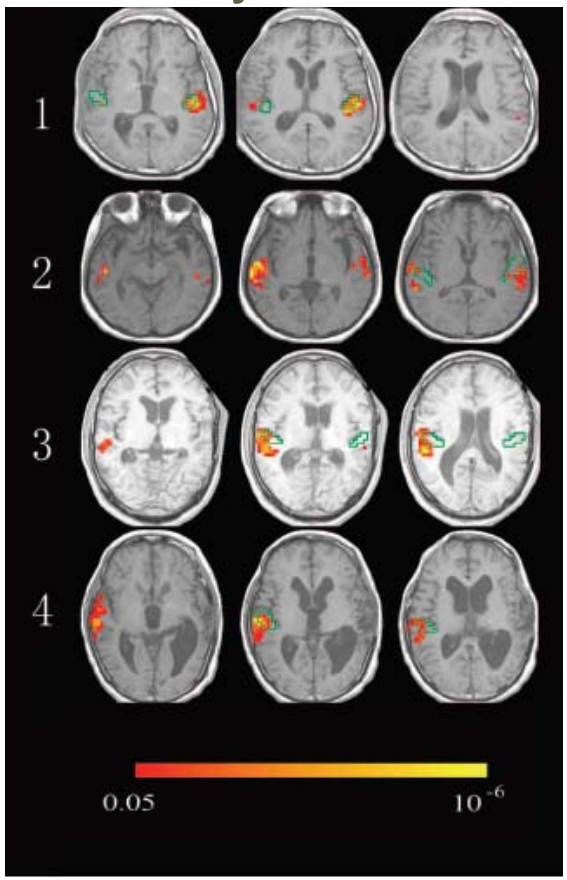
Laureys et al., Neurology, 2004

fMRI precedes the clinic

vegetative



minimally conscious



Di, Yu, Weng, Laureys et al, Neurology, 2007

Self awareness:

Functional connectivity studies

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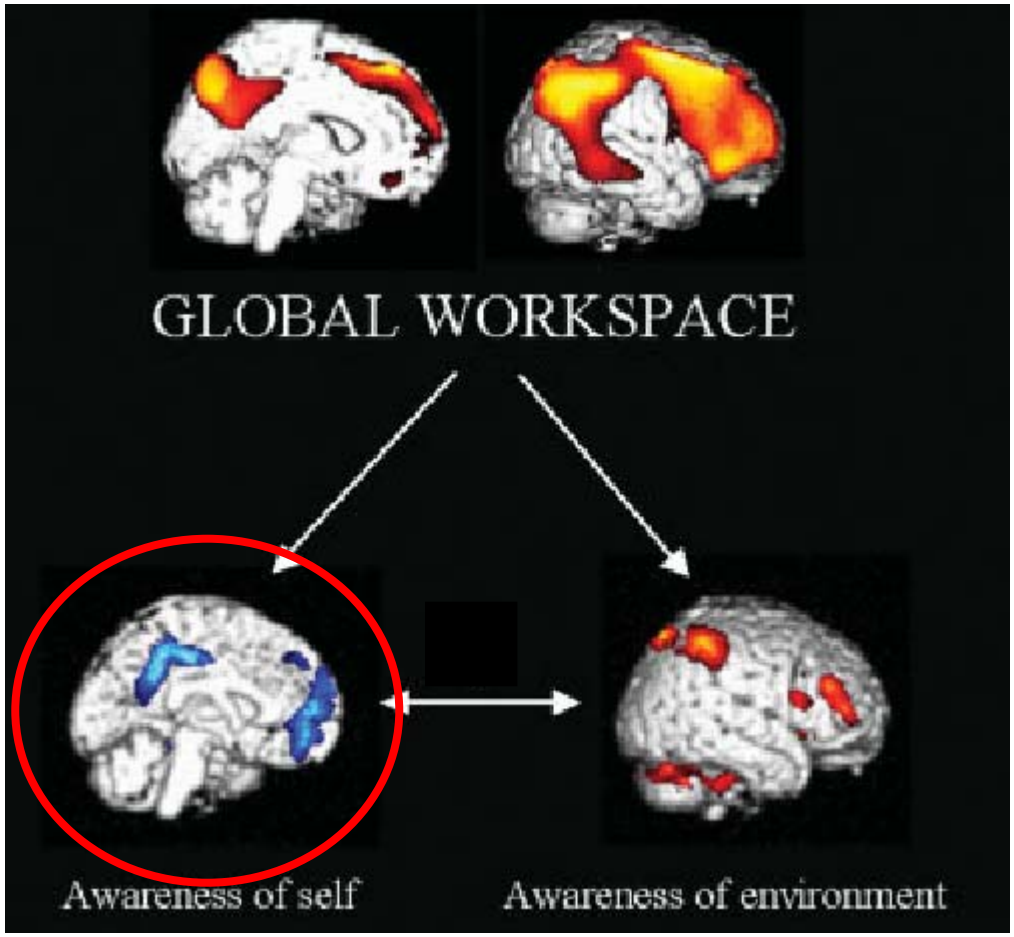
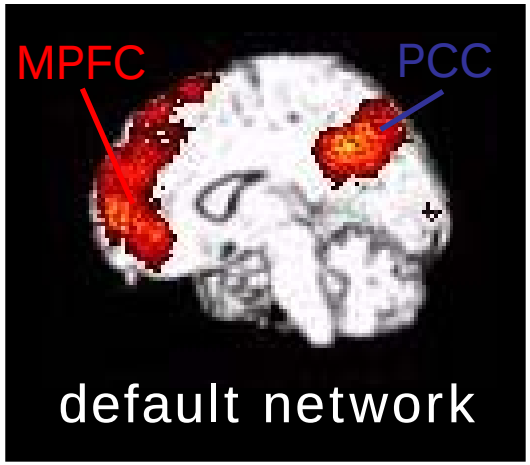
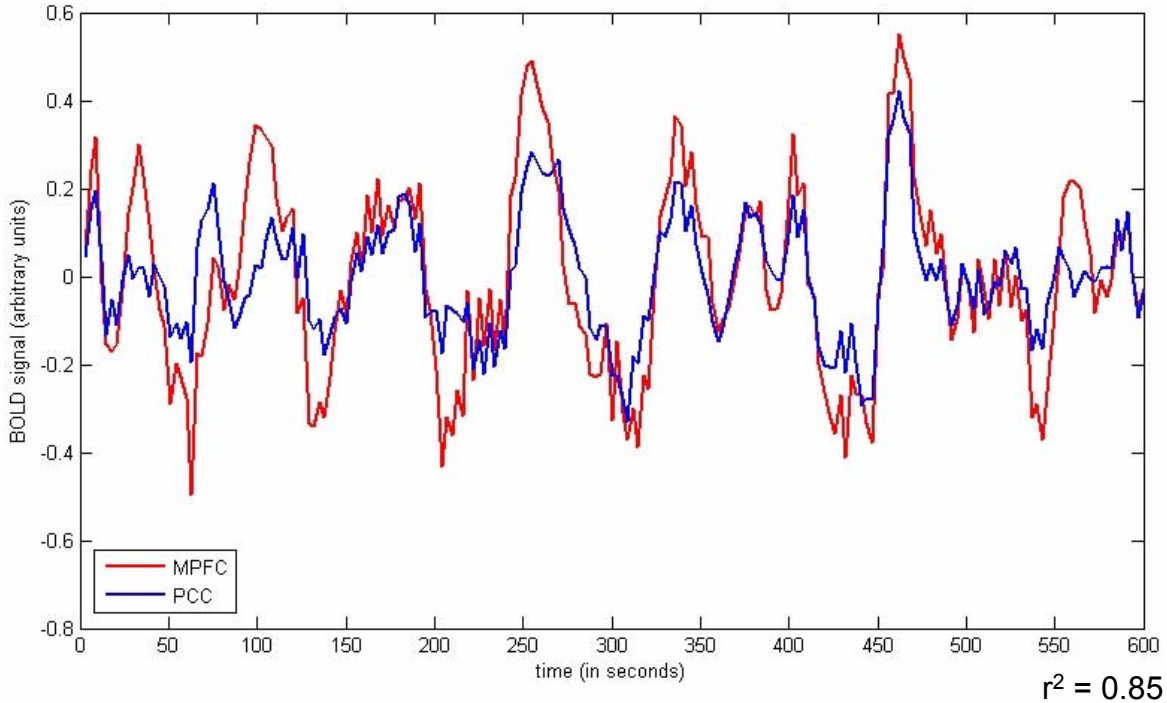
“Awareness network”



Boly et al., Human Brain Mapping 2008
Boly et al., PNAS 2007

Coherent spontaneous brain activity fluctuations

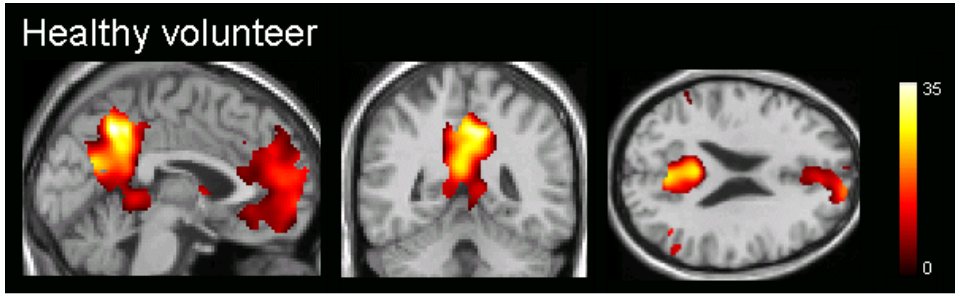




$r^2 = 0.85$

Boly et al., Annals of the New York Academy of Sciences 2008

Default network in VS and brain death



Boly et al., Hum Brain Map 2009

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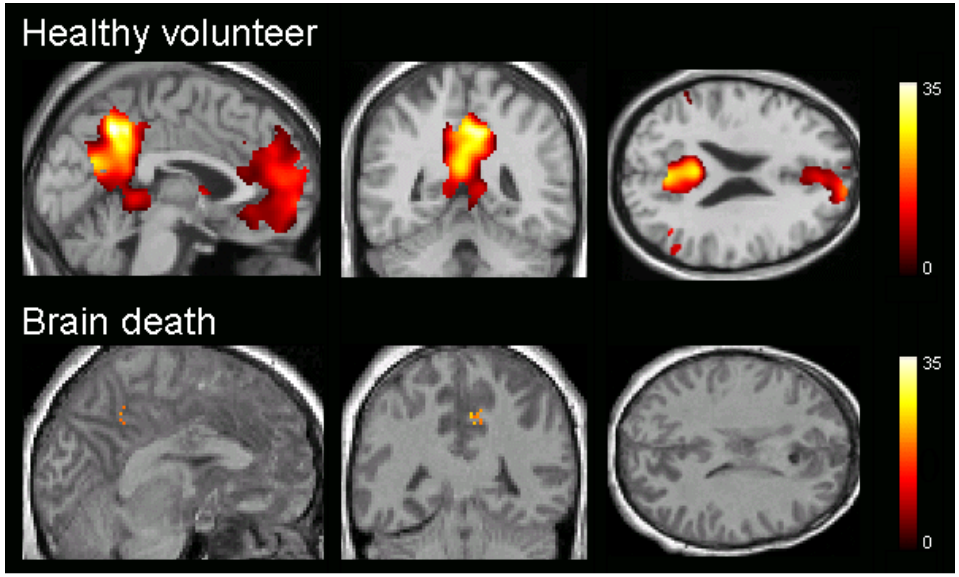
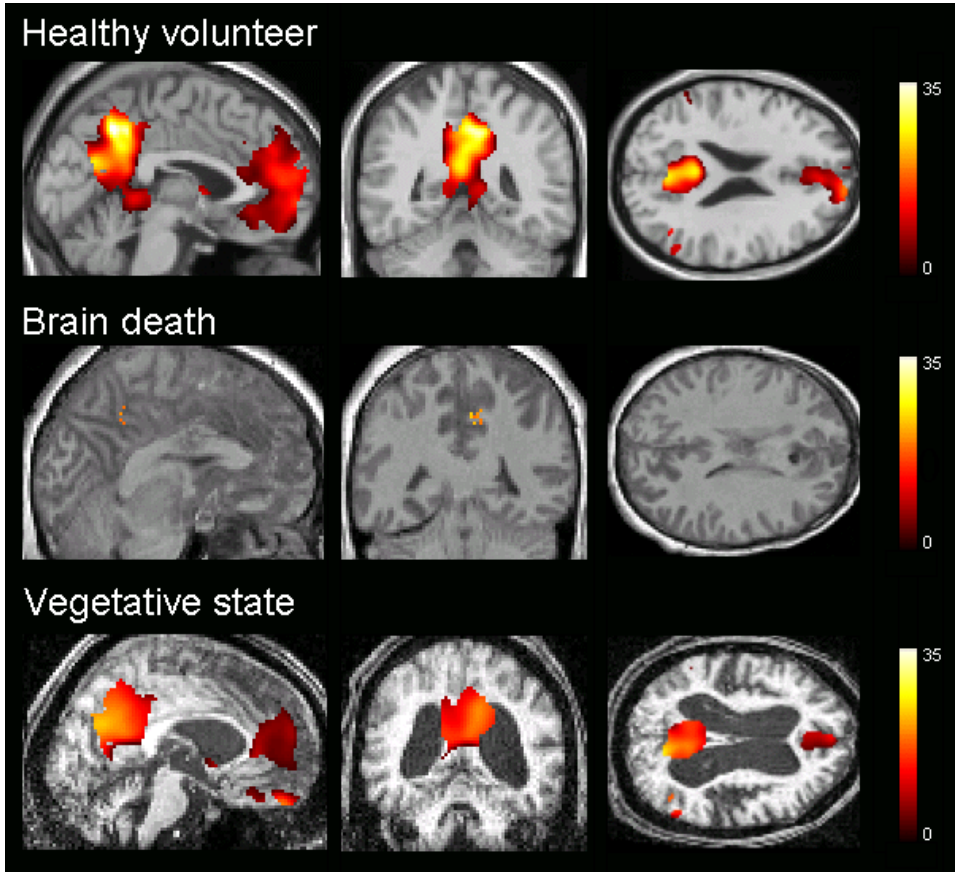


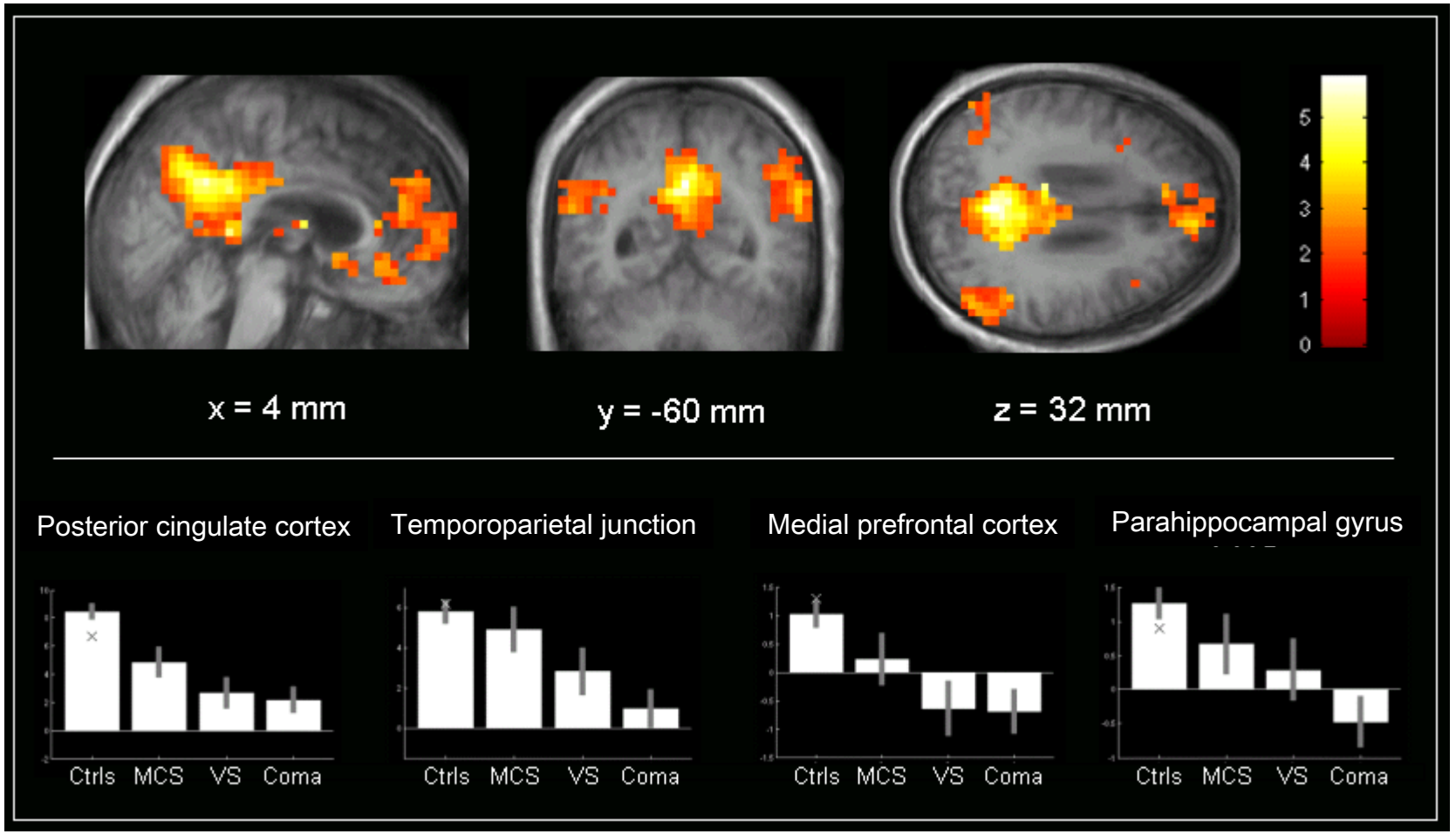
Boly et al., Hum Brain Map 2009

Default network in VS and brain death



Boly et al., Hum Brain Map 2009

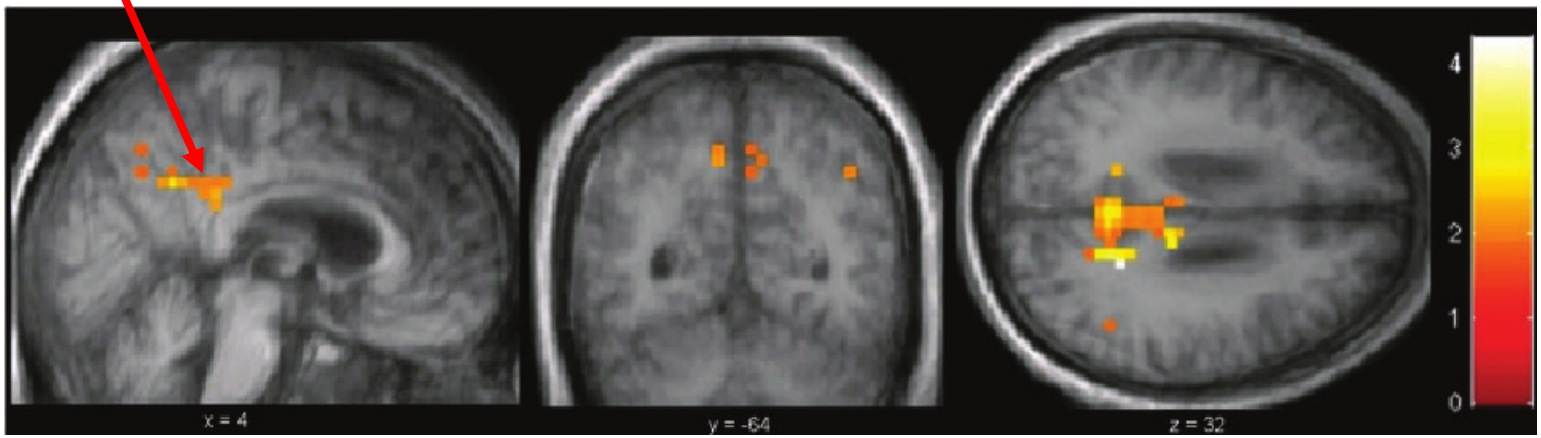
Default network in coma, VS, MCS and locked-in syndrome



Vanhaudenhuyse, Noirhomme et al., Brain 2010

Self awareness in the minimally conscious state?

Precuneus

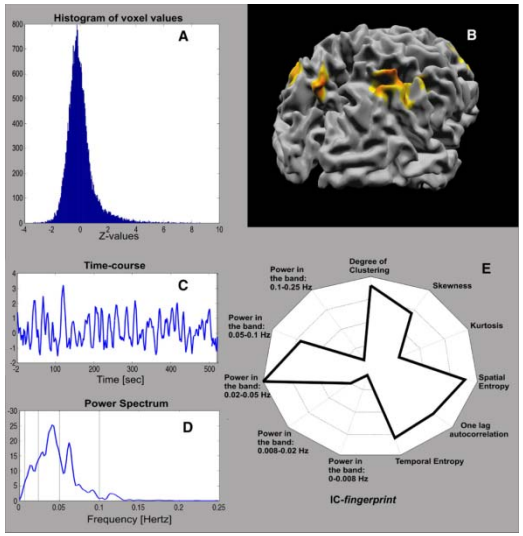


Default network connectivity is higher in MCS compared to coma and vegetative state

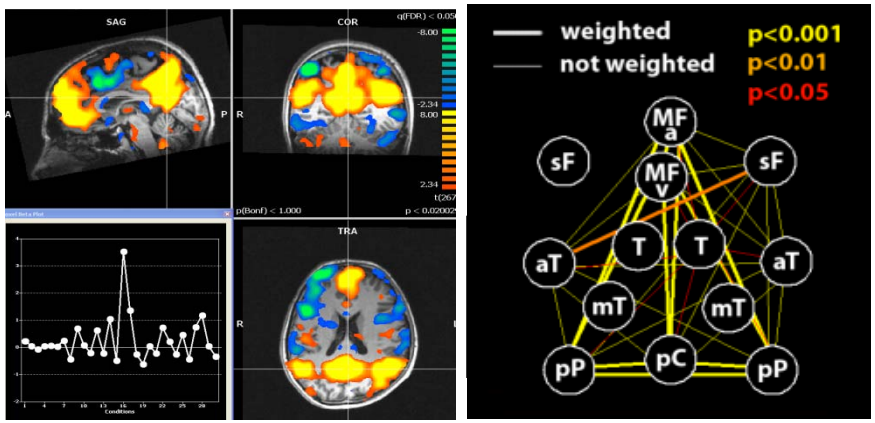
Vanhaudenhuyse, Noirhomme et al., Brain 2010

Improving single subject measures in patients

Component selection – ICA fingerprints

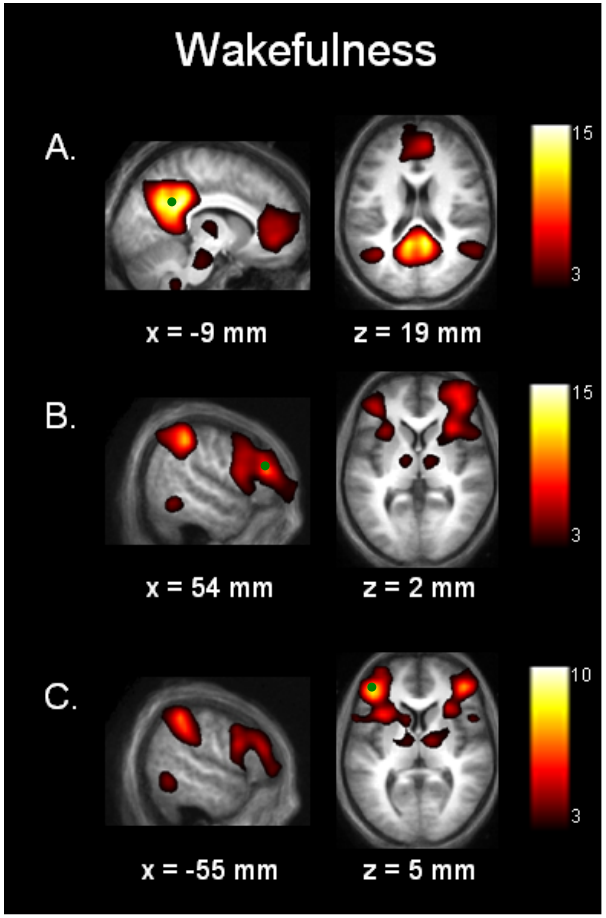


Global indexes - Connectivity graphs



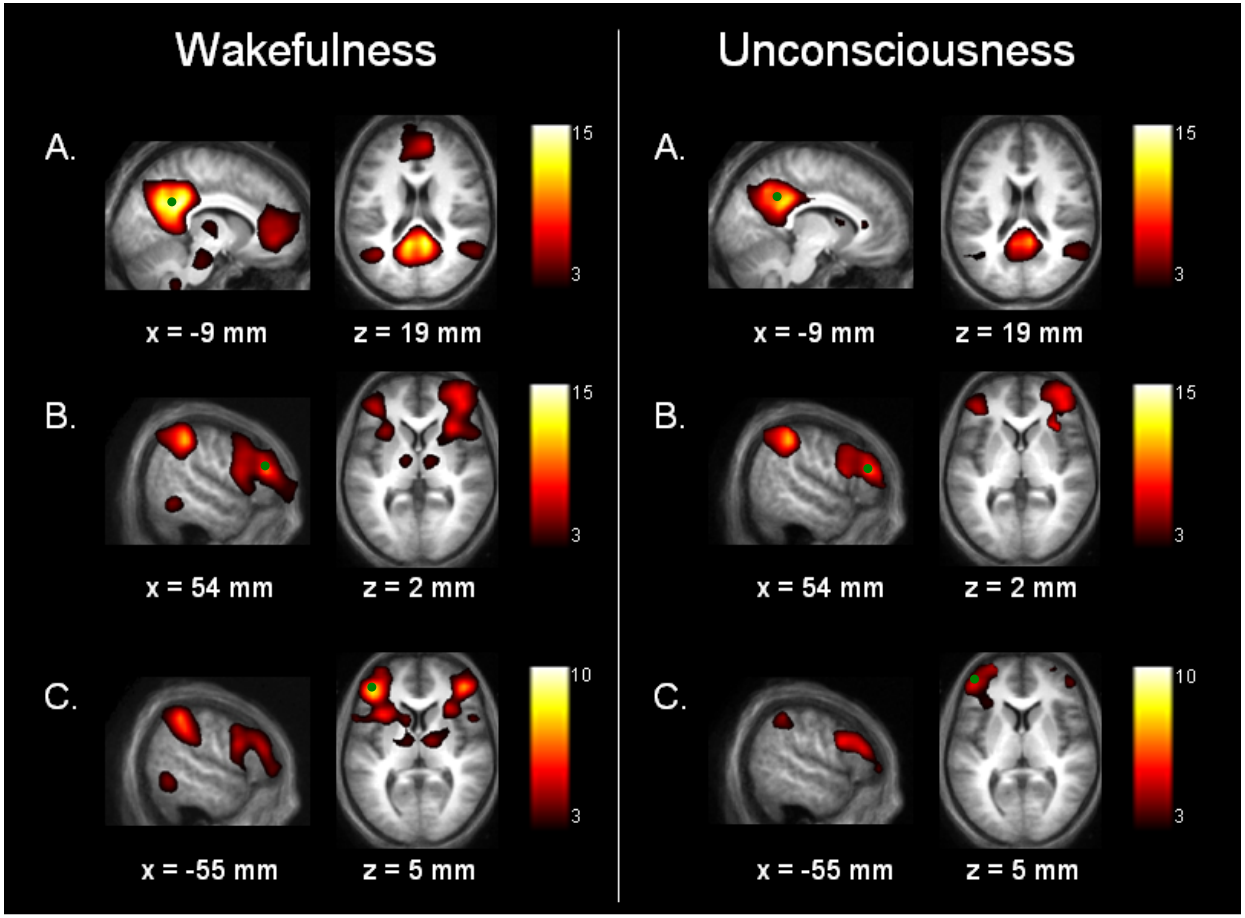
DeMartino et al., Neuroimage 2007; Soddu et al., submitted

Functional connectivity during propofol-induced loss of consciousness



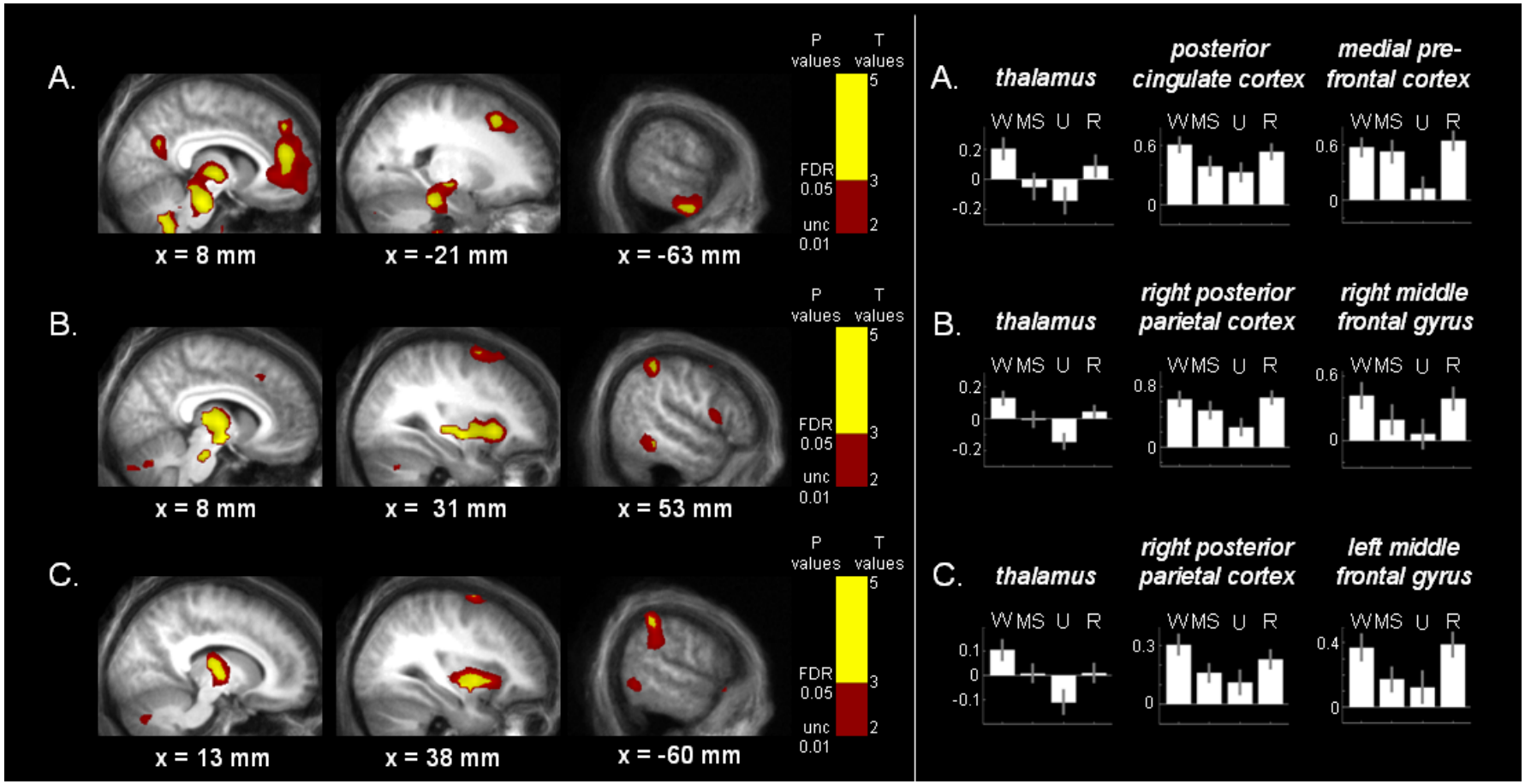
Boveroux et al, Anesthesiology, accepted for publication

Functional connectivity during propofol-induced loss of consciousness

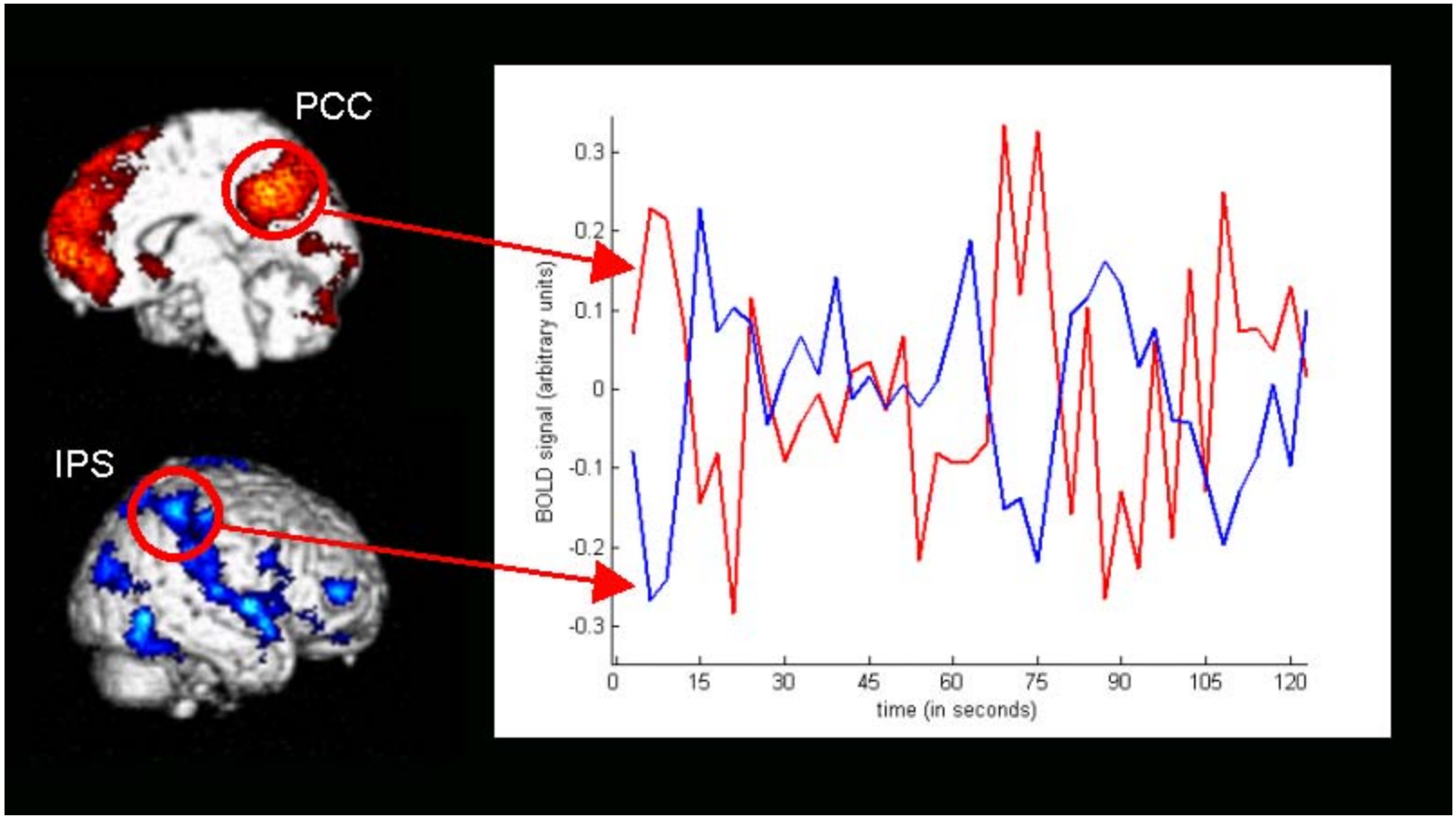


Boveroux et al, Anesthesiology, accepted for publication

Consciousness // connectivity in default network and in lateral frontoparietal cortices

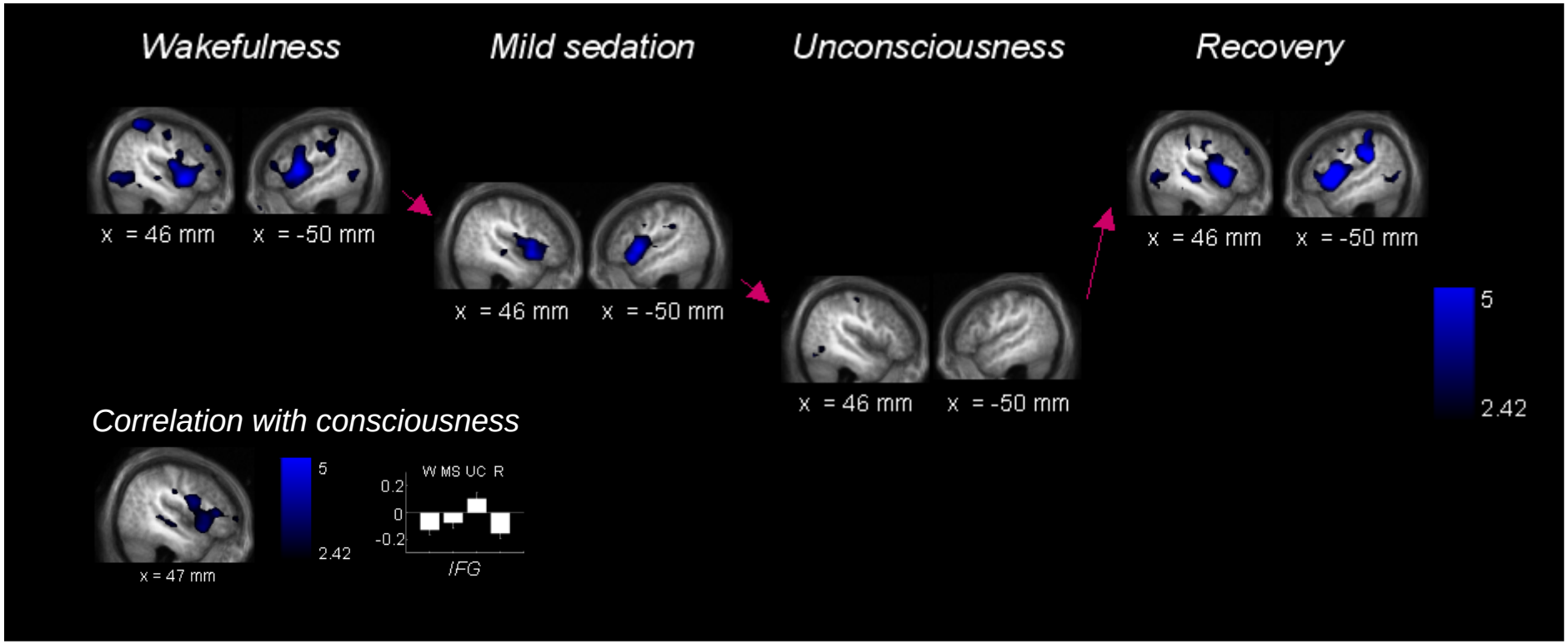


Anticorrelations between default network and lateral frontoparietal cortices



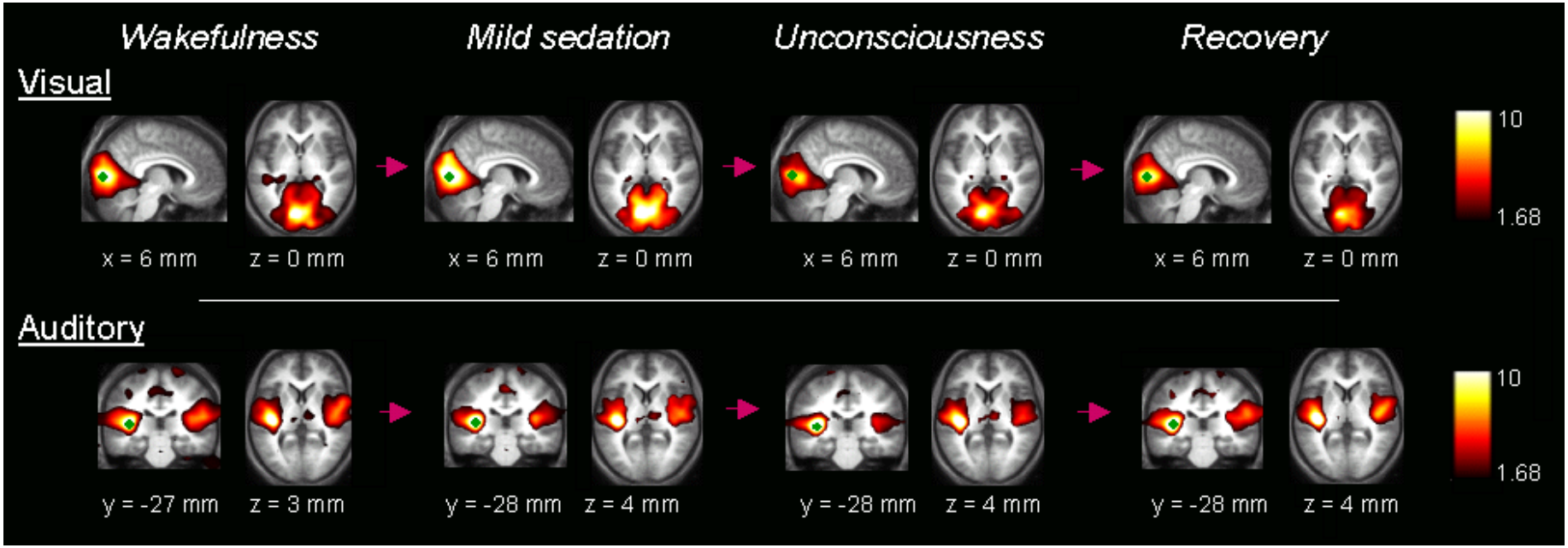
Boly et al., Ann NY Ac Sci 2008

Anticorrelations between frontoparietal networks vanish with unconsciousness



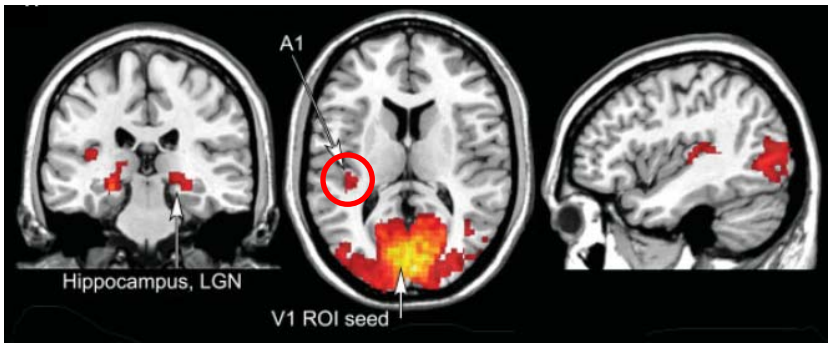
Boveroux et al, Anesthesiology, accepted for publication

Visual and auditory networks connectivity remain stable across sedation stages

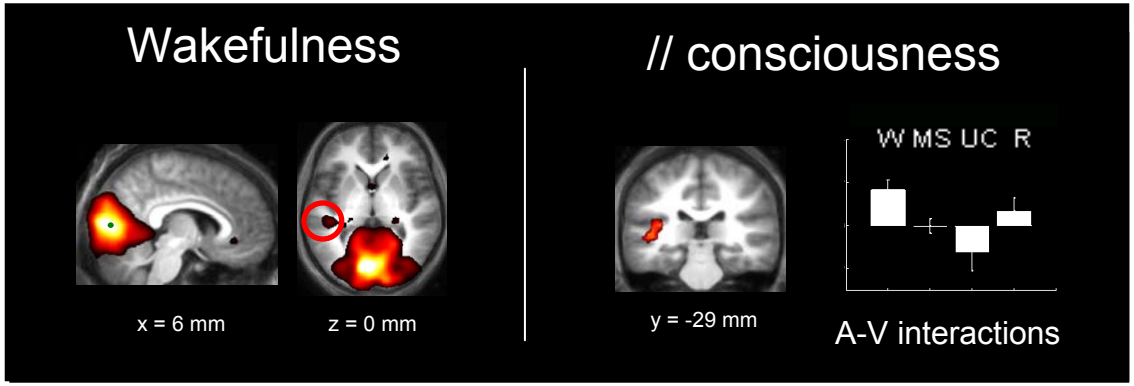


Boveroux et al, Anesthesiology, accepted for publication

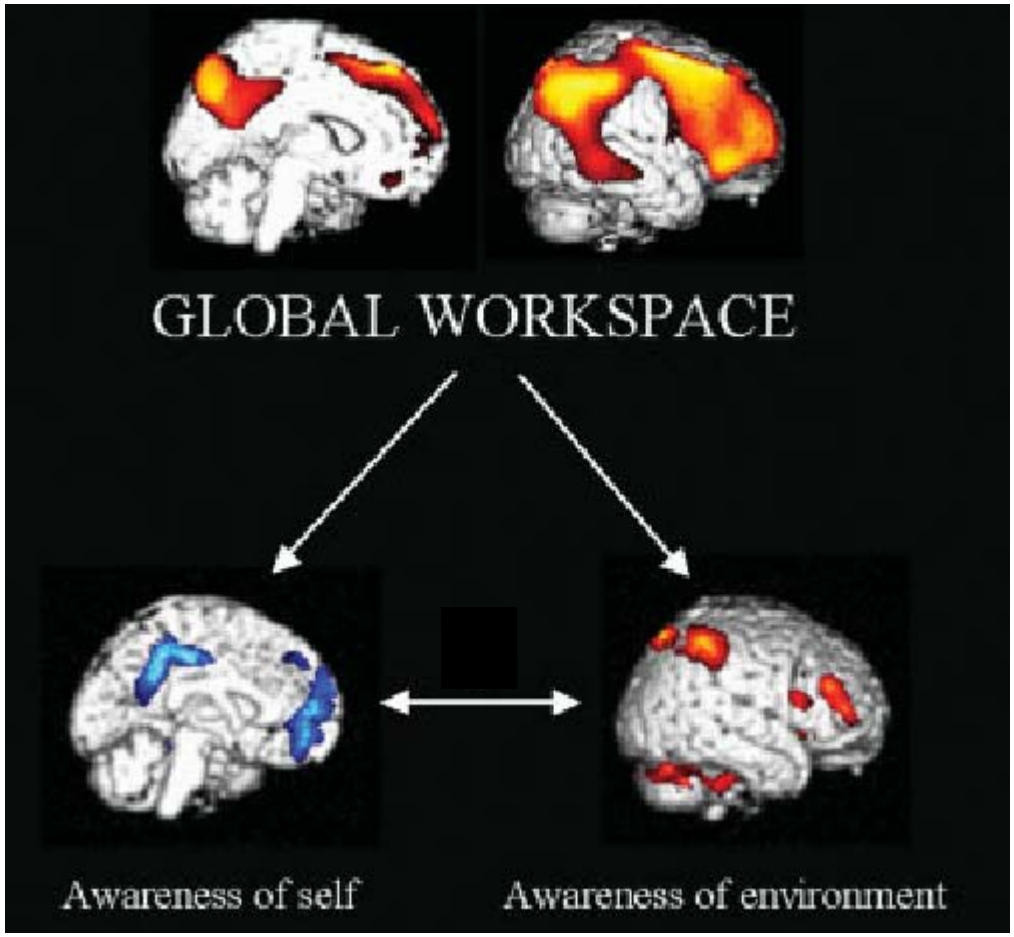
Cross-modal auditory-visual interactions vanish with unconsciousness



Eckert et al., Hum Br Map 2008

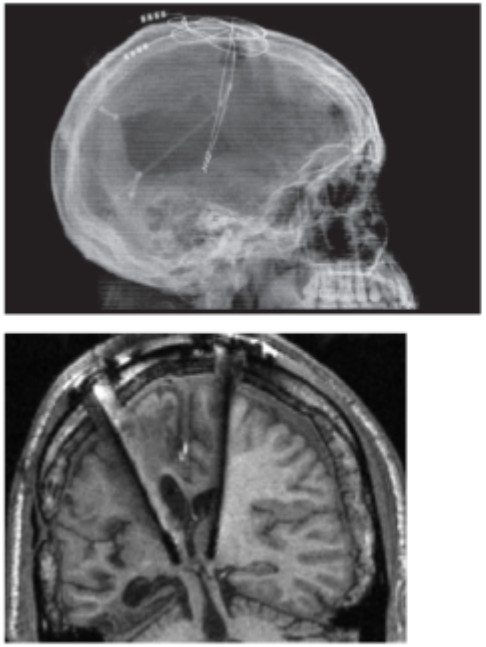


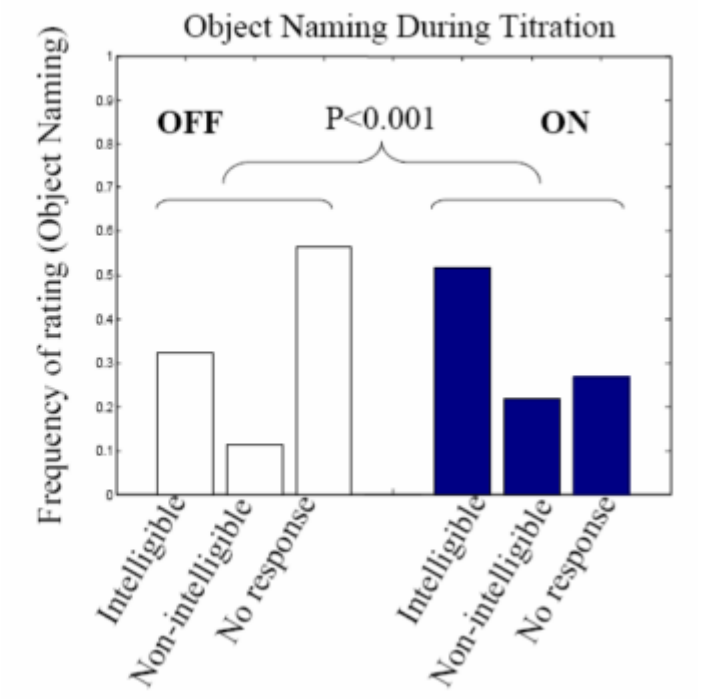
“Awareness network”



Boly et al., Human Brain Mapping 2008
Boly et al., PNAS 2007

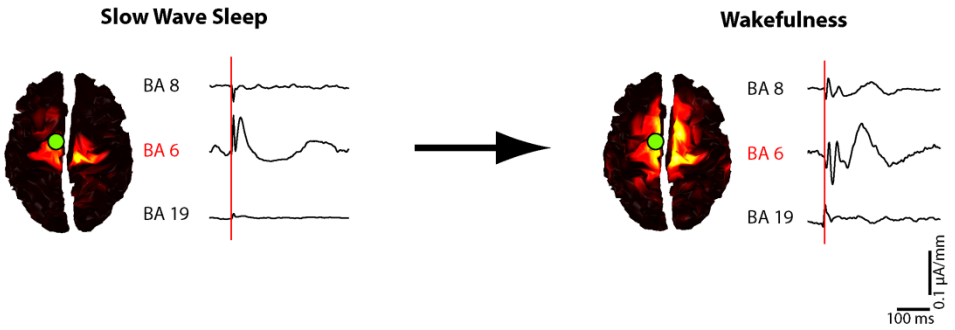
Thalamo-cortical connectivity





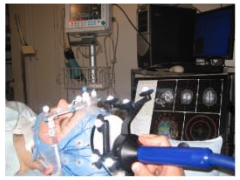
Schiff et al., Nature 07

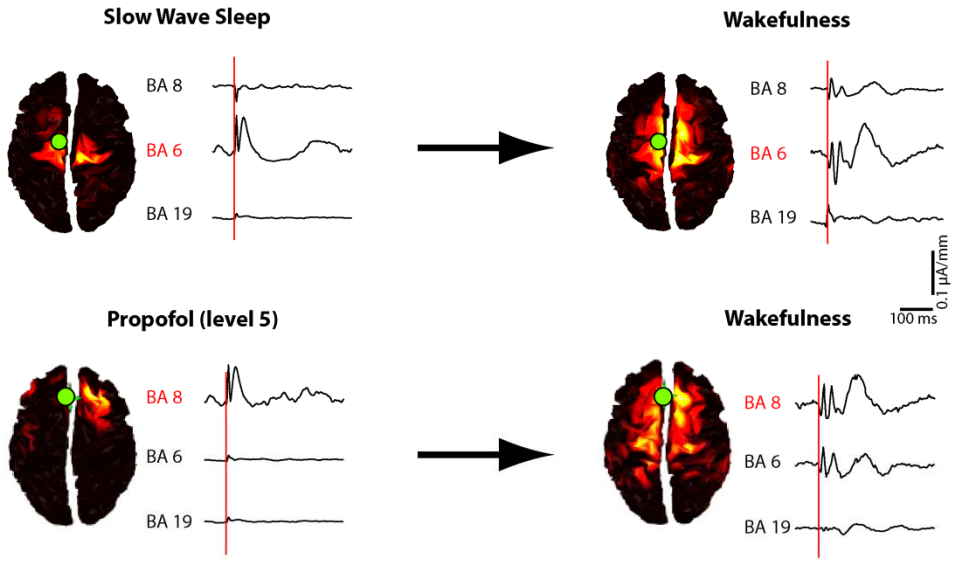
TMS-EEG during sleep, coma and anesthesia



Massimini et al., Science 2005
Ferrarelli et al., PNAS 2009
Boly, Rosanova et al., in preparation; Rosanova, Gosseries et al., in preparation

TMS-EEG during sleep, coma and anesthesia





Massimini et al., Science 2005
Ferrarelli et al., PNAS 2009
Boly, Rosanova et al., in preparation; Rosanova, Gosseries et al., in preparation

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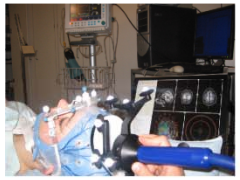

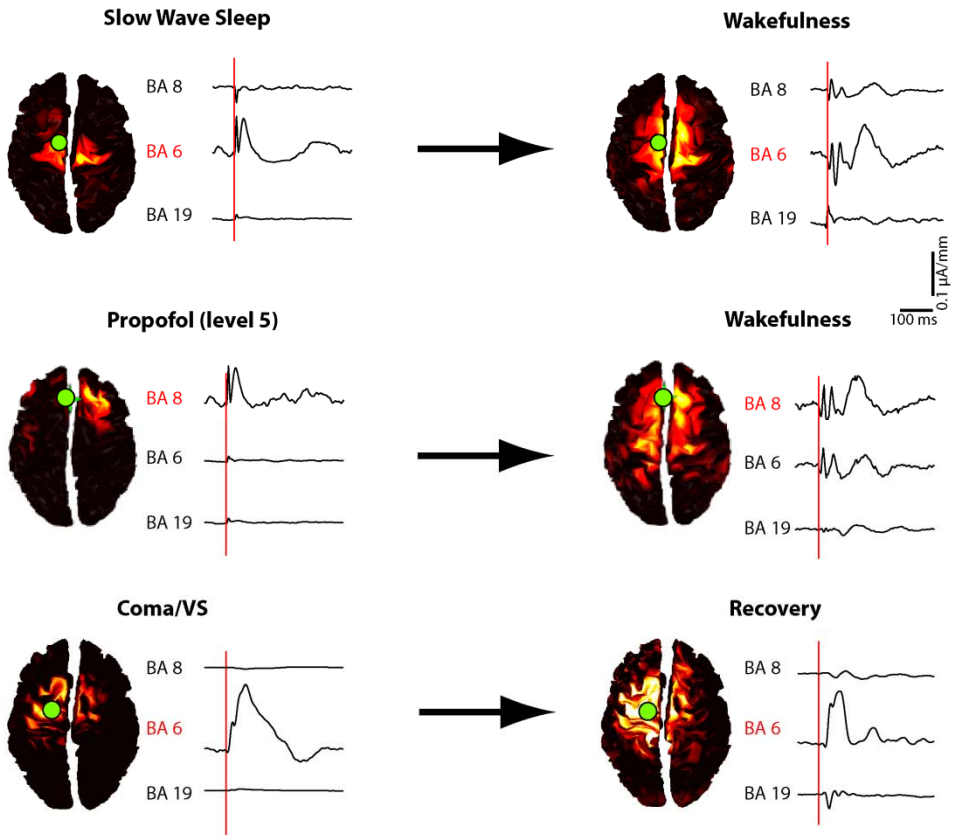

Massimini et al., Science 2005
Ferrarelli et al., PNAS 2009
Boly, Rosanova et al., in preparation; Rosanova, Gosseries et al., in preparation

Searching for voluntary brain activity:

‘Tennis playing’

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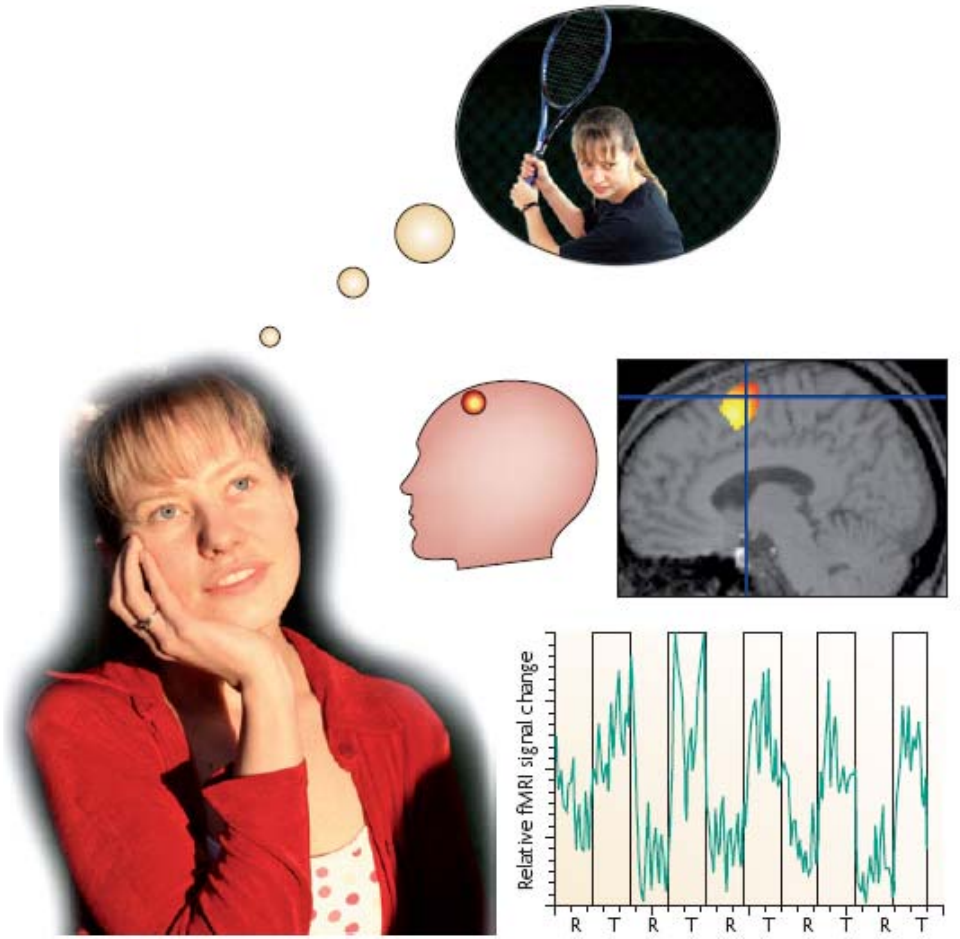
Mental imagery tasks

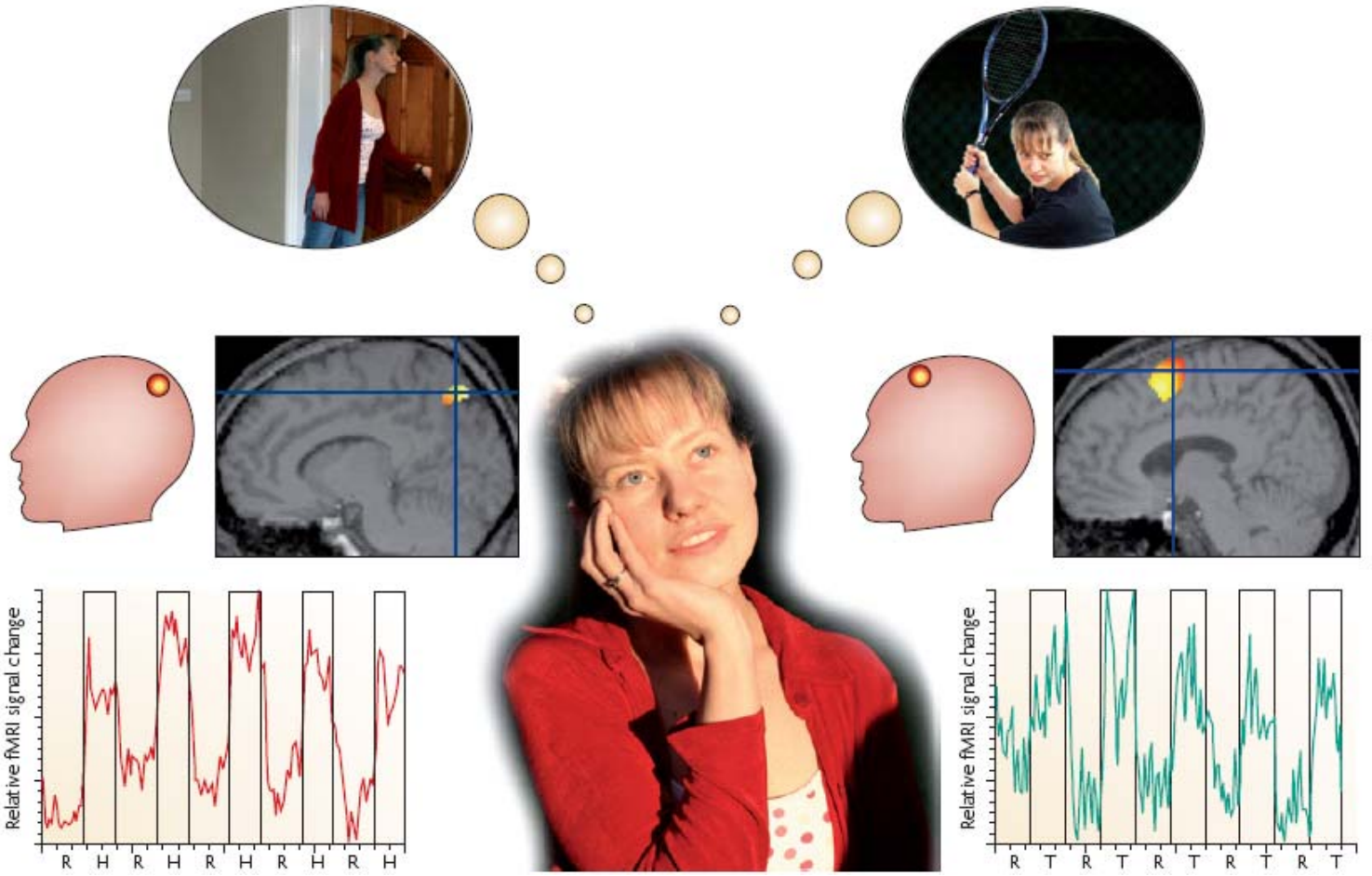
Boly et al., Neuroimage 2007
Owen et al., Nature Reviews Neuroscience 2008

Mental imagery tasks



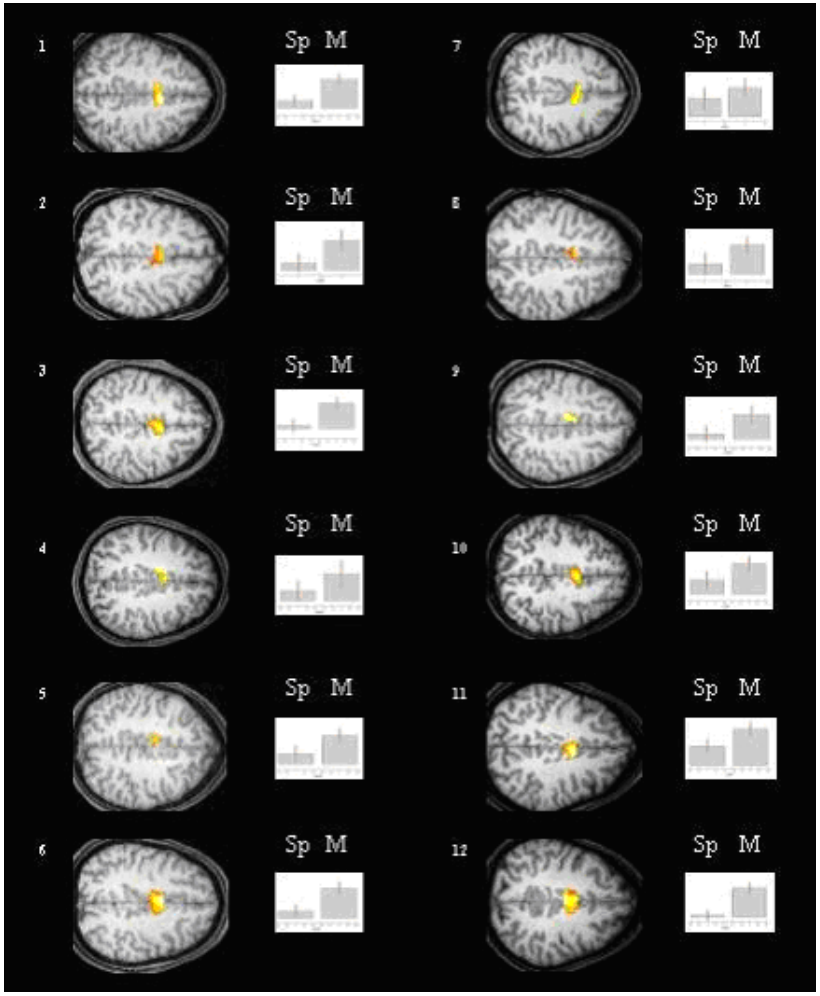
Boly et al., Neuroimage 2007
Owen et al., Nature Reviews Neuroscience 2008

Mental imagery tasks



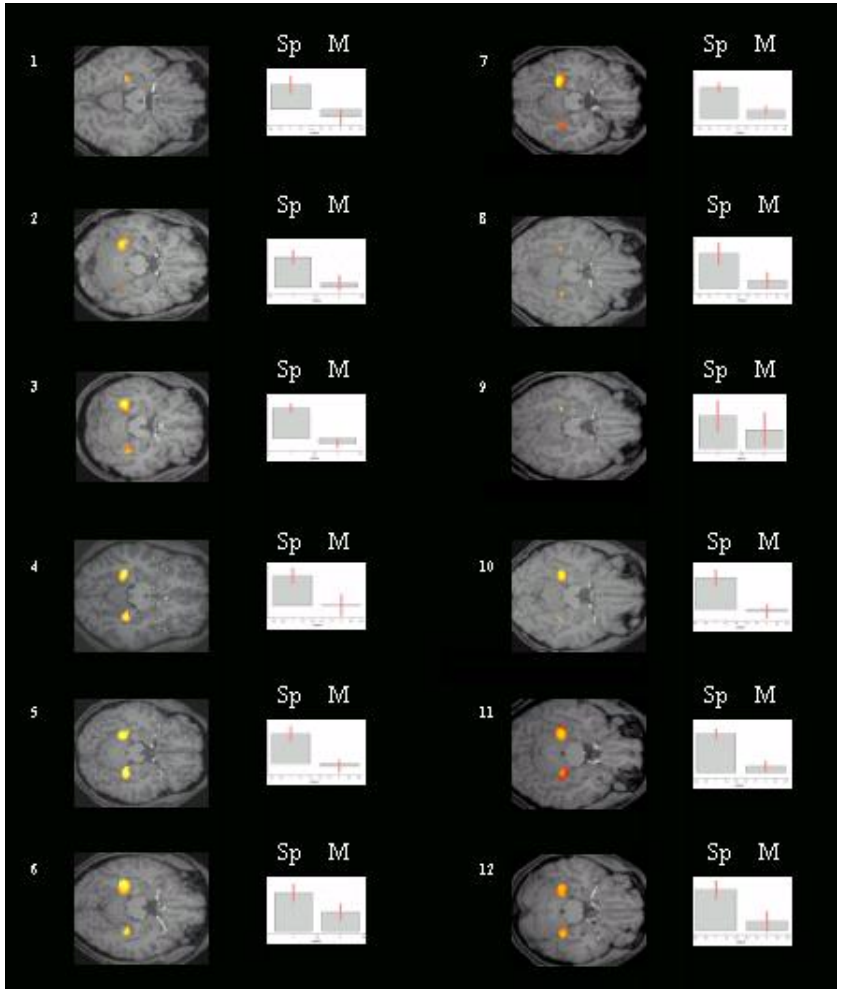
Boly et al., Neuroimage 2007
Owen et al., Nature Reviews Neuroscience 2008

Mental imagery: tennis



Boly et al., Neuroimage 2007

Mental imagery: spatial navigation



Boly et al., Neuroimage 2007

Detecting awareness in vegetative state

23 year-old woman

Severe traumatic brain injury in July 2005

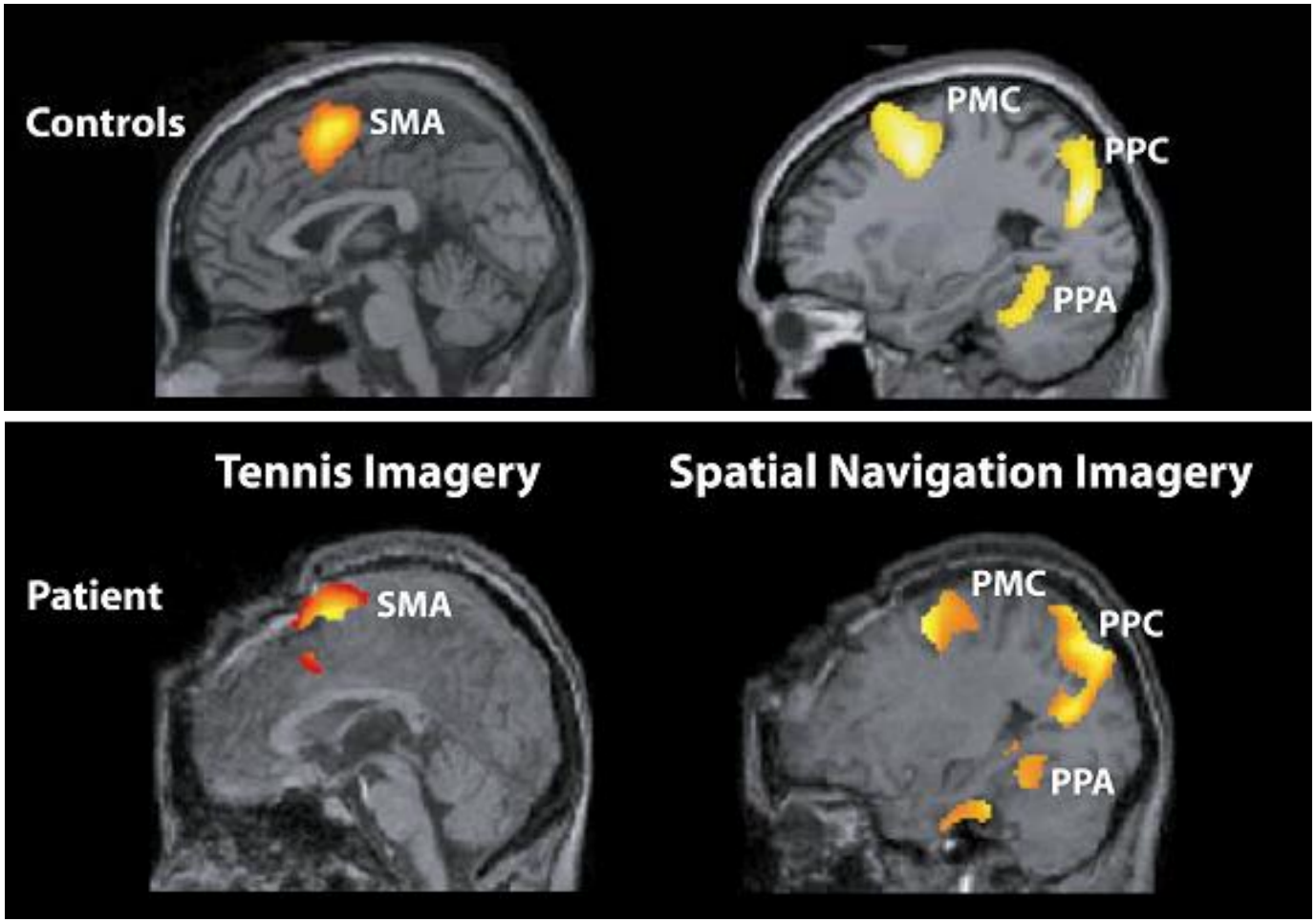
CT scan: brain swelling and frontal-lobe contusions

Between the time of the accident and the fMRI scan in January 2006, the patient's behaviour was consistent with international guidelines defining the vegetative state:

- Open her eyes spontaneously
  - Sleep/wake cycles preserved
  - Preserved reflexive behaviour (startle, noxious, threat, tactile, olfactory)
  - No evidence of orientation, fixation more than 5 seconds or tracking to visual or auditory stimuli
  - No overt motor responses to command

Owen, Coleman, Boly, Davis, Laureys & Pickard, Science 2006

Detecting awareness in vegetative state



Owen, Coleman, Boly, Davis, Laureys & Pickard, Science 2006
Boly et al., Neuroimage 2007

Real time fMRI communication

22 year-old man

Severe traumatic brain injury in July 2003

CT scan: severe and diffuse cortico-sous-cortical atrophy predominant in the left hemisphere

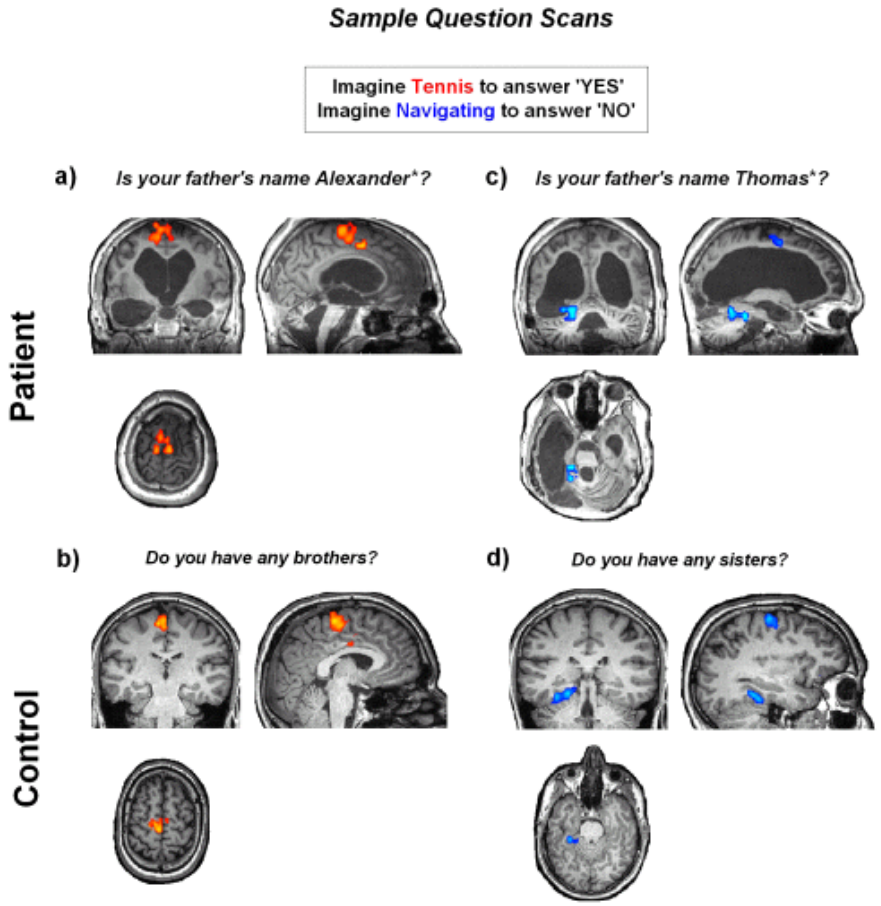
Admitted to the CHU Sart Tilman (Liège) in September 2008 with a diagnosis of persistent vegetative state present since 5 years.

Repeated clinical assessment evidenced the presence of inconsistent response to command => clinical diagnosis of minimally conscious state

No possibility of communication of any kind at the bedside

Monti, Vanhaudenhuyse, Coleman, Boly, Pickard, Tshibanda,Owen & Laureys,
New England Journal of Medicine 2010

Real time fMRI communication



Monti, Vanhaudenhuyse, Coleman, Boly, Pickard, Tshibanda,Owen & Laureys,
New England Journal of Medicine 2010

Active paradigms at the population level

Works only in a minority of patients:

54 patients scanned between 2005 and 2009
in Liège and Cambridge

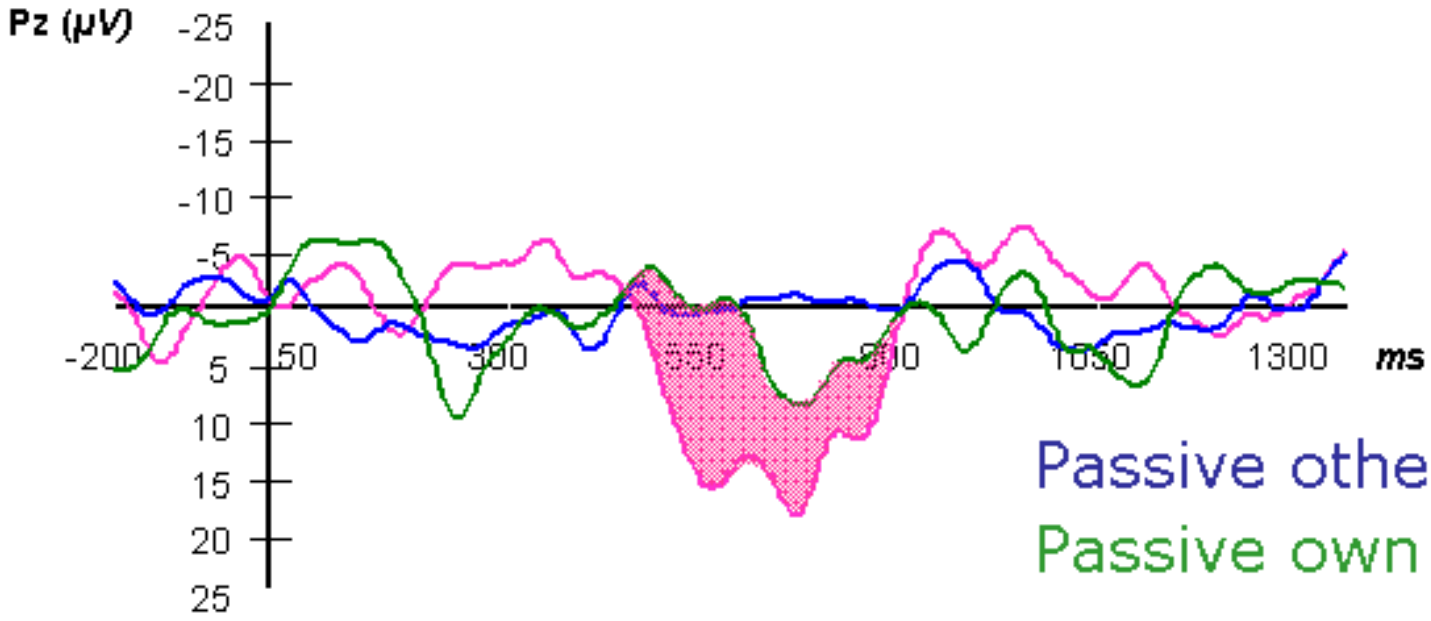
In 10%, a significant response was detected:

2/20 patients in a vegetative state

3/31 patients in a minimally conscious state

Monti, Vanhaudenhuyse, Coleman, Boly, Pickard, Tshibanda,Owen & Laureys,
New England Journal of Medicine 2010

ERP active paradigms



Passive other name

Passive own name

Count own name

9/14 MCS

Schnakers et al., Neurology 2008; Boly et al., Neuroimage 2007; Owen, Coleman, Boly et al., Science 2006

Imaging consciousness:

Perspectives

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Imaging consciousness: perspectives

- Active paradigms:

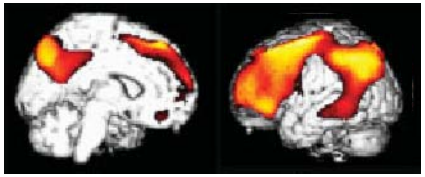
  - direct applicability – further develop (EEG-based) brain computer interfaces
  - but helpful in only a minority of patients (5/54 or ~10%)

- Passive paradigms:

  There is a need to integrate current knowledge about current neural correlates of consciousness into a unifying diagnostic framework

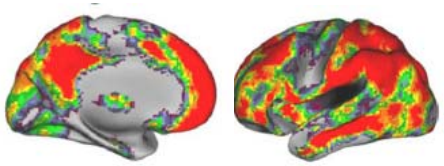
  ⇒ Explanatory correlates of consciousness: bring theoretical neuroscience closer to the patient's bedside (Boly et al., Progress in Brain Research 2009)

Impairment in unconsciousness

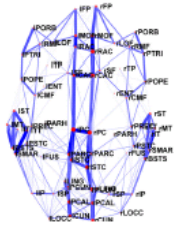


?

Hierarchy of brain connectivity



functional



structural

Boly, Massimini & Tononi, Progress in Brain Research 2009
Monti, Vanhaudenhuyse et al., NEJM 2010

Buckner et al., J Neurosci 2009
Hagmann et al., PLOS Biology 2008

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