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

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Altered states of consciousness

- Consciousness
- Coma
- General Anesthesia
- Locked-in syndrome
- Minimally Conscious State
- Vegetative state
- Somnambulism
- Epilepsy

- Wakefulness
- Drowsiness
- Light sleep
- Deep Sleep
- REM Sleep

- Conscious Wakefulness
- Locked-in syndrome
- Drowsiness

- 40% misdiagnosis!

Laureys & Boly, Current Opinion in Neurology 2007
Laureys & Boly, Nature Clinical Practice 2008
Schnakers et al., BMC Neurology 2009
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Introduction | Brain metabolism | External awareness | Self awareness | Voluntary brain activity | Conclusions

Laureys & Boly, Current Opinion in Neurology 2007
Laureys & Boly, Nature Clinical Practice 2008
Vanhaudenhuyse et al., JNNP 2008
Altered states of consciousness

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Ambiguous sign: Blink to visual threat

Does not herald consciousness in VS
Altered states of consciousness

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Laureys, Scientific American 2007
Brain metabolism studies

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www.comascience.org
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
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”
“Awareness network”
External awareness:

Brain responses to sensory stimuli
Persistent vegetative state

*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

Median nerve electrical stimulation

PET scan
Pain perception in VS

Laureys et al., Neuroimage 2002
External awareness correlates in healthy volunteers
Pain perception in MCS

Healthy controls (n=15)

Minimally Conscious State (n=5)
Auditory perception

CONTROLs (n=15)  VEGETATIVE (n=15)  MINIMALLY CONSCIOUS (n=5)

Boly et al., Archives of Neurology 2004, Neuropsychological Rehabilitation 2005
Areas with more efficient connectivity with auditory cortex in MCS compared to PVS

Boly et al, Archives of Neurology, 2004
Emotional processing

Meaningless Noise

Acoustically Matched Cries

Patient’s Own Name

Laureys et al., Neurology, 2004
fMRI precedes the clinic

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

Introduction | Brain metabolism | External awareness | Self awareness | Voluntary brain activity | Conclusions

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
Default network in VS and brain death

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

- Posterior cingulate cortex
- Temporoparietal junction
- Medial prefrontal cortex
- Parahippocampal gyrus

x = 4 mm
y = -60 mm
z = 32 mm

Vanhaudenhuyse, Noirhomme et al., Brain 2010
Self awareness in the minimally conscious state?

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

Boveroux et al, Anesthesiology, accepted for publication
Anticorrelations between default network and lateral frontoparietal cortices

Boly et al., Ann NY Ac Sci 2008
Anticorrelations between frontoparietal networks vanish with unconsciousness
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

Boveroux et al, Anesthesiology, accepted for publication
“Awareness network”
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, Gossieres et al., in preparation
TMS-EEG during sleep, coma and anesthesia

Massimini et al., Science 2005
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Ferrarelli et al., PNAS 2009
Boly, Rosanova et al., in preparation; Rosanova, Gosseries et al., in preparation
Searching for voluntary brain activity:

‘Tennis playing’
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
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
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
Real time fMRI communication

**Sample Question Scans**

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

<table>
<thead>
<tr>
<th>Question</th>
<th>Patient</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Is your father's name Alexander?</td>
<td><img src="image1" alt="Brain Image A" /></td>
<td><img src="image2" alt="Brain Image B" /></td>
</tr>
<tr>
<td>b) Do you have any brothers?</td>
<td><img src="image3" alt="Brain Image C" /></td>
<td><img src="image4" alt="Brain Image D" /></td>
</tr>
<tr>
<td>c) Is your father's name Thomas?</td>
<td><img src="image5" alt="Brain Image E" /></td>
<td><img src="image6" alt="Brain Image F" /></td>
</tr>
<tr>
<td>d) Do you have any sisters?</td>
<td><img src="image7" alt="Brain Image G" /></td>
<td><img src="image8" alt="Brain Image H" /></td>
</tr>
</tbody>
</table>
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
ERP active paradigms

Schnakers et al., Neurology 2008; Boly et al., Neuroimage 2007; Owen, Coleman, Boly et al., Science 2006
Imaging consciousness: Perspectives

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- 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)
We thank the participating patients and their families