World Federation of Neurology Teaching course:
Severe brain damage & disorders of consciousness

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World Congress of Neurology
Marrakesh, November 2011
Coma, consciousness, self, mind & soul

1858 participants attending scientific meetings on consciousness

- Mind and brain are two separate things: 49% religious, 32% non-religious
- Mind is fundamentally physical: 39% religious, 47% non-religious
- Some spiritual part of us survives after death: 63% religious, 16% non-religious
- Each of us has a soul which is separate from the body: 57% religious, 20% non-religious

Reducing consciousness to 2D

Laureys, *Trends in Cognitive Sciences*, 2005

www.comascience.org
Consciousness ≈ 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
Frontoparietal “global workspace”

- Persistent vegetative state: preserved arousal, no awareness
- Coma: no arousal, no awareness
- Sleep: no arousal, no awareness
- General anesthesia: no arousal, no awareness

Baars, Ramsoy, Laureys, Trends in Neurosciences 2003
Frontoparietal “global workspace”

Vegetative state

Absence seizure

Complex partial seizure

Sleepwalking

Laureys, *Trends in Cognitive Sciences* 2005

Salek-Haddadi et al, 2000

Blumenfeld et al, 2004

Bassetti et al, 2000
Precuneus ≈ hub in the network

Conscious controls (n=110)  
Vegetative state (n=33)

Locked in syndrome (n=5)  
Minimally conscious state (n=7)

Axonal re-growth in Terry Wallis

Laureys et al, Lancet Neurology, 2004

Voss et al, J Clin Invest, 2006
Precuneus ≈ hub in the network

**SLEEP**
Activity in PCC/precuneus

**ANESTHESIA**

Consciousness ≠ primary cortex

“VEGETATIVE” UNRESPONSIVE

MINIMALLY RESPONSIVE

Laureys et al, *Brain*, 2000
Boly et al, *Archives of Neurology*, 2004
Consciousness ≈ top-down

Consciousness $\approx$ thalamo-cortical

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

Intralaminar nuclei stimulation induces “recovery” from minimally responsive state


Two awareness networks

Laureys, Scientific American 2007
Vanhaudenhuyse et al, J Cogn Neursoci 2011
Two awareness networks

![Graph showing two awareness networks with a frequency of 0.05 Hz (20 sec/cycle)]

- **External awareness:** stimulus related, sensory perceptions
- **Internal awareness:** stimulus independent, mental imagery, inner speech

Modulation by hypnosis

Demertzi et al, Prog Brain Res, 2011
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 state” default brain activity

Boly et al, Human Brain Mapping 2009
Default connectivity in anesthesia

Boveroux et al, Anesthesiology 2010

www.comascience.org
"Resting" default mode connectivity

Vanhaudenhuyse et al, Brain 2010

www.comascience.org
Clinical interest

MINIMALLY RESPONSIVE

Communication?

Awaresness?

= response to command or non-reflex movements

VEGETATIVE/UNRESPONSIVE

arousal = eye opening

COMA

COGNITIVE CAPACITY

Consciousness | Neural correlates | Diagnosis | Prognosis | Treatment | Ethics | Conclusion

Laureys et al., Current Opinion in Neurology, 2005

www.comascience.org
A new name for «vegetative»

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

Steven Laureys, Gastone G Celesia, Francois Cohadon, Jan Lavrijsen, Jose Leon-Carrion, Walter G Sannita, Leon Sazbon, Erich Schmutzhard, Klaus R von Wild, Adam Zeman and Giuliano Diclo 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.”

Laureys et al, BMC Medicine 2011
Diagnostic error

n=103 post-comatose patients
- 45 clinical consensus diagnosis ‘vegetative state’
- 18 signs of awareness (Coma Recovery Scale)

40% potential misdiagnosis

Schnakers et al, BMC Neurology 2009
Eye tracking: use a mirror!

Graph showing the number of MCS patients tracking different categories:
- Mirror
- Person
- Object

Significance levels:
- * indicates statistical significance
- NS indicates nonsignificant results

Reference:
Vanhaudenhuyse et al. *J Neurol Neurosurg Psychiatry* 2008
Functional MRI
PET scan
High-density EEG
Transcranial magnetic stimulation
Visual fixation is a reflex

Bruno et al, *BMC Neurology* 2010
Signs of consciousness on fMRI

Tennis Imagery

Spatial Navigation Imagery

Controls

Patient

SMA

PMC

PPC

PPA

“He’s not in coma... he’s playing tennis!”

≠ “automatic” brain response

Soddu et al, *Prog Brain Res* 2009
Yes-No communication with fMRI

Healthy Subject

Answers « YES »

Answers « NO »

« VEGETATIVE STATE »

EEG-based Brain Computer Interfaces

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
EEG-based Brain Computer Interfaces

“MOVE YOUR FOOT”
HEATHY CONTROL SUBJECT

“MOVE YOUR HAND”

“VEGETATIVE” UNRESPONSIVE PATIENT

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

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\(^{2,3,\dagger}\)

*Progress in Brain Research, Vol. 177
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Automated consciousness classifier

"Relevance Vector Machine" on FDG-PET data in DOC

EEG entropy

Gossières et al, *Functional Neurology*, 2011
Predicting outcome in chronic DOC

**ACTIVATION TO THE OWN NAME**

**ATYPICAL 'HIGH LEVEL' CORTICAL ACTIVATION**

Perrin et al, *Arch Neurol* 2006


www.comascience.org
Understanding plasticity

Homeostatic decline SWA ≈ plasticity (Tononi)

Landnes and Bruno et al, Brain, 2011

www.comascience.org
“Dreaming” in MCS?
Multimodal imaging

Bruno et al, Prog Brain Res, 2011
Tshibanda et al, Neuroradiology, 2010

www.comascience.org
Nociception and pain

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

- Medical doctors (n=1166)  
  - Yes: 56%  
  - No: 44%

- Paramedical professionals (n=538)  
  - Yes: 68%  
  - No: 32%

* p < 0.001

**Nociception Coma Scale**

<table>
<thead>
<tr>
<th>Score</th>
<th>Item</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>MOTOR RESPONSE</strong></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Localization to Nociceptive Stimulation</td>
<td>The non-stimulated limb must locate and make contact with the stimulated body part at the point of stimulation.</td>
</tr>
<tr>
<td>2</td>
<td>Flaccid Withdrawal</td>
<td>There is isolated flaccid withdrawal of at least one limb. The limb must move away from the point of stimulation.</td>
</tr>
<tr>
<td>1</td>
<td>Abnormal Posturing</td>
<td>Slow, stereotyped flexion or extension of the upper and/or lower extremities occurs immediately after the stimulus is applied.</td>
</tr>
<tr>
<td>0</td>
<td>None-Flaccid</td>
<td>There is no discernible movement following application of nociceptive stimulation, secondary to hypotonic or flaccid muscle tone.</td>
</tr>
<tr>
<td></td>
<td><strong>VERBAL RESPONSE</strong></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Intelligible Verbalization</td>
<td>Production of words in response to nociceptive stimulation. Each verbalization must consist of at least 1 consonant-vowel-consonant (C-V-C) triad. For example,  “Lift up,” “Help,” etc.</td>
</tr>
<tr>
<td>2</td>
<td>Vocalization / Oral Movement</td>
<td>Calm in response to nociceptive stimulation. For example, “Grimace”</td>
</tr>
<tr>
<td>1</td>
<td>Groans</td>
<td>Calm in response to nociceptive stimulation. For example, “Wheeze”</td>
</tr>
<tr>
<td>0</td>
<td>None</td>
<td>There are no discernible changes in response to nociceptive stimulation.</td>
</tr>
<tr>
<td></td>
<td><strong>VISUAL RESPONSE</strong></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Fixation</td>
<td>There are no discernible changes in response to nociceptive stimulation.</td>
</tr>
<tr>
<td>2</td>
<td>Eye movement</td>
<td>There are no discernible changes in response to nociceptive stimulation.</td>
</tr>
<tr>
<td>1</td>
<td>Stare</td>
<td>There are no discernible changes in response to nociceptive stimulation.</td>
</tr>
<tr>
<td>0</td>
<td>No change</td>
<td>There are no discernible changes in response to nociceptive stimulation.</td>
</tr>
<tr>
<td></td>
<td><strong>FACIAL EXPRESSION</strong></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Cry</td>
<td>There are no discernible changes in response to nociceptive stimulation.</td>
</tr>
<tr>
<td>2</td>
<td>Grimace</td>
<td>There are no discernible changes in response to nociceptive stimulation.</td>
</tr>
<tr>
<td>1</td>
<td>Oral reflexive movement</td>
<td>There are no discernible changes in response to nociceptive stimulation.</td>
</tr>
<tr>
<td>0</td>
<td>None</td>
<td>There are no discernible changes in response to nociceptive stimulation.</td>
</tr>
</tbody>
</table>

**Total score >7/12 = analgesic treatment**


Schnakers et al, *Pain*, 2010
Do they feel pain?

Noxious electrical stimulation


www.comascience.org
Pain in minimally conscious state

Controls

MCS

http://neurology.thelancet.com

Curative treatment: Drugs? no evidence based therapy

Schnakers et al. *J Neurol Neurosurg Psychiatry* 2008
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.

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. Gosselies • A. Soddu • C. Schnakers • G. Moonen • S. Laureys

2,475 medical professionals

I would like to be kept alive if I were in a chronic...

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)

Demertzi et al, J Neurology 2011
Quality of life

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

Marie-Aurèle Bruno, Jan L Bernheim, Didier Ledoux, Frédéric Pellias, Athena Demertzi, Steven Laureys

New knowledge, new nosology

Conclusion

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

Owen, Schiff & Laureys, *Prog Brain Res*, 2009
THANK YOU