Coma, consciousness & the brain

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Disorders of consciousness

NORMAL CONSCIOUSNESS

AROUSAL

AWARENESS

COMA

AROUSAL

AWARENESS

UNRESPONSIVE WAKEFULNESS

MINIMALLY RESPONSIVE

LOCKED-IN SYNDROME

AROUSAL

AWARENESS

AROUSAL

AWARENESS

AROUSAL

AWARENESS

Reducing awareness to 2D


www.comascience.org
Consciousness $\approx$ frontoparietal

Laureys, *Trends in Cognitive Sciences*, 2005
Frontoparietal "global workspace"

- Persistent vegetative state
  - Preserved arousal
  - No awareness

- Coma
  - No arousal
  - No awareness

- Sleep
  - No arousal
  - No awareness

- General anesthesia

Consciousness $\approx$ frontoparietal

Areas systematically dysfunctional in “vegetative” state & recovering activity after recovery of consciousness

Precuneus is critical hub in fronto-parietal connectivity

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

Consciousness ≠ primary cortex

"VEGETATIVE" UNRESPONSIVE

MINIMALLY RESPONSIVE

Laureys et al, *Brain*, 2000
Boly et al, *Archives of Neurology*, 2004

www.comascience.org,
Consciousness ≈ top-down

Two awareness networks

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

Laureys, *Scientific American* 2007

www.comascience.org
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
Modulation by hypnosis

Demertzì et al, Prog Brain Res 2011
Disorders of consciousness

Yes-No communication with fMRI

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

Is your father's name Alexander?
Is your father's name Thomas?

Monti & Vanhaudenhuyse, Coleman, Boly, Pickard, Tshibanda, Owen, Laureys
New England J Med 2010
EEG-based Brain Computer Interfaces

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%)

HEATHY CONTROL SUBJECT

“MOVE YOUR FOOT”

“MOVE YOUR HAND”

“VEGETATIVE” UNRESPONSIVE PATIENT

www.thelancet.com

www.comascience.org
“Resting state” default brain activity

Boly et al, Human Brain Mapping 2009
Functional MRI in “resting state”

Control vs. LIS

http://neurology.thelancet.com

Jox, Bernat, Laureys, Racine, Lancet Neurology 2012
Should we trust the machine?

Jox, Bernat, Laureys, Racine, Lancet Neurology 2012
Default connectivity in anesthesia

Boveroux et al, Anesthesiology 2010
"Resting" default mode connectivity

Vanhaudenhuyse et al, *Brain* 2010
EEG entropy

Gosseries et al, Functional Neurology, 2011

www.comascience.org
Consciousness $\approx$ connectivity

EEG-TMS

Rosanova and Gossieres et al, *Brain* 2012
Predicting outcome in chronic DOC

ACTIVATION TO THE OWN NAME

ATYPICAL 'HIGH LEVEL' CORTICAL ACTIVATION

Perrin et al, Arch Neurol 2006

Qin et al, Neurosci Lett 2008

Di et al, Neurology, 2007
Di et al, Clinical Medicine, 2008
MRI diffusion tensor imaging

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.

Galanaud et al, Anesthesiology, 2012
Luyt et al, Anesthesiology, 2012
Nociception and pain

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

- Yes
- No

<table>
<thead>
<tr>
<th>Medical doctors (n=1166)</th>
<th>Paramedical professionals (n=536)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes 64%</td>
<td>Yes 82%</td>
</tr>
<tr>
<td>No 36%</td>
<td>No 18%</td>
</tr>
</tbody>
</table>

*p < 0.001

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

<table>
<thead>
<tr>
<th>Religious caregivers (n=1090)</th>
<th>Non-religious caregivers (n=830)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes 64%</td>
<td>Yes 52%</td>
</tr>
<tr>
<td>No 36%</td>
<td>No 48%</td>
</tr>
</tbody>
</table>

*p < 0.001

Nociception Coma Scale -R

<table>
<thead>
<tr>
<th>Score</th>
<th>Item</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Localisation to Pressure 1</td>
<td>The non-responding limb must locate and make contact with the stimulated body part at the point of stimulation.</td>
</tr>
<tr>
<td>2</td>
<td>Fluorescence Withdrawal</td>
<td>There is delayed, partial withdrawal of at least one limb. The limb must move away from the point of stimulation.</td>
</tr>
<tr>
<td>3</td>
<td>Abnormal Positioning</td>
<td>Gigantism, non-normal, or extension of the upper arm and/or lower extremities occurs immediately after the stimulus is applied.</td>
</tr>
<tr>
<td>4</td>
<td>Noted Flaccid</td>
<td>There is an observable movement following application of non-noxious stimulation, necessary or inappropriate, or facial muscle tone.</td>
</tr>
</tbody>
</table>

VERBAL RESPONSE

<table>
<thead>
<tr>
<th>Score</th>
<th>Item</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Involuntary Verbalisation</td>
<td>Production of words in response to non-noxious stimulation. Each verbalisation must consist of at least 1 consonant-vowel-consonant (CVC) sound.</td>
</tr>
<tr>
<td>2</td>
<td>Auditory-Occlusion</td>
<td>Patient perceives at least 1 arousing environmental stimulus.</td>
</tr>
<tr>
<td>3</td>
<td>No</td>
<td>None.</td>
</tr>
</tbody>
</table>

VISUAL RESPONSE

<table>
<thead>
<tr>
<th>Score</th>
<th>Item</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fixation</td>
<td>A conscious patient attempts to fixate vision on a stimulus.</td>
</tr>
<tr>
<td>2</td>
<td>Eye Movement</td>
<td>Eye movement in response to non-noxious stimulation.</td>
</tr>
<tr>
<td>3</td>
<td>Stere</td>
<td>Patient attempts to move eyes or head towards the stimulus.</td>
</tr>
<tr>
<td>4</td>
<td>No</td>
<td>No change.</td>
</tr>
</tbody>
</table>

FACIAL EXPRESSION

<table>
<thead>
<tr>
<th>Score</th>
<th>Item</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Effort</td>
<td>Patient shows effort in response to non-noxious stimulation.</td>
</tr>
<tr>
<td>2</td>
<td>Grimace</td>
<td>Patient shows grimacing in response to non-noxious stimulation.</td>
</tr>
<tr>
<td>3</td>
<td>Oral Response</td>
<td>Patient shows open movement, tongue protrusion, yawning, chewing movements.</td>
</tr>
<tr>
<td>4</td>
<td>No</td>
<td>None.</td>
</tr>
</tbody>
</table>

Total score > 3 / 9 = analgesic treatment

Demertzi et al, Prog Brain Res, 2009

Schnakers et al, Pain, 2010, JNPP 2012

www.comascience.org
Do they feel pain?

Noxious electrical stimulation

Laureys et al, Neuroimage, 2002
Laureys, Nature Reviews Neuroscience, 2005
Pain in minimally conscious state

http://neurology.thelancet.com

Consciousness $\approx$ thalamo-cortical

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

Intralaminar nuclei stimulation induces “recovery” from minimally responsive state


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.


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Quality of life

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

Marie-Aurélie Bruno, Jan L Bernheim, Didier Ledoux, Frédéric Pellia, Ahtina Demertzis, Steven Laureys

Bruno et al, BMJ Open, 2011
Conclusion

Erik Ziegler, Cyclotron Art Committee

Bruno et al, Prog Brain Res, 2011
Conclusion

Human conscious awareness
\[ \approx \text{emergent property of collective critical neural network dynamics, involving a frontoparietal global workspace} \]

Diagnostic use
\[ \approx 40\% \text{ misdiagnosis} \]

Prognostic use
multimodal imaging

Therapeutic use
pain treatment / deep brain stimulation thalamus

Ethical challenge

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Laureys & Schiff, *NeuroImage*, 2012
Sanders et al, *Anesthesiology*, 2012

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