Coma et corrélats neuronaux de la conscience

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Reducing consciousness to 2D

Laureys, *Trends in Cognitive Sciences*, 2005
Reducing awareness to 2D

Content of consciousness: AWARENESS

Level of consciousness: AROUSAL

Awareness of self

Awareness of environment

INTERNAL or SELF AWARENESS

EXTERNAL or SENSORY AWARENESS


Consciousness ≠ global brain function

Laureys et al., Lancet Neurology, 2004
Consciousness ≈ 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
Laureys et al, Lancet Neurology, 2004
Precuneus \approx hub in the network

**SLEEP**

Activity in PCC/precuneus

**ANESTHESIA**

Activity in PCC/precuneus

Consciousness ≠ primary cortex

Laureys et al, *Brain*, 2000
Boly et al, *Archives of Neurology*, 2004
Consciousness ≠ primary cortex

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

"VEGETATIVE" UNRESPONSIVE

MINIMALLY RESPONSIVE

A new name for « vegetative »

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

Laureys et al., BMC Medicine 2011

There's nothing we can do... he'll always be a vegetable.
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
Yes-No communication with fMRI

Healthy Controls

L25 TBI

C04 TBI

L23 TBI

C06 TBI

L22 TBI


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

Is your father’s name Alexander?

Is your father’s name Thomas?
**EEG-based Brain Computer Interfaces**

**“MOVE YOUR FOOT”**

**HEALTHY CONTROL SUBJECT**

**“MOVE YOUR HAND”**

**“VEGETATIVE” UNRESPONSIVE PATIENT**

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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%)
Consciousness ≈ connectivity

EEG-TMS

Rosanova and Gosseries et al, Brain 2012
“Resting” default mode connectivity

**Brain**

Vanhaudenhuyse et al, *Brain* 2010

MCS > VS/UWS

Precuneus

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Vanhaudenhuyse et al, *Brain* 2010
Understanding plasticity

Homeostatic decline SWA \approx \text{plasticity (Tononi)}

Landness and Bruno et al, *Brain*, 2011
POST-ANOXIC COMA

exclude confounding factors including hypothermia, drugs, electrolyte disturbances…

brainstem reflexes
(pupillary, cornea, oculocephalic, cough)

absent and GCS 3/15

apnea testing

D1-3: somatosensory EPs

or

generalized suppression (<20 µV)

or ‘burst supression’ EEG

D1: myoclonus status epilepticus

D3: M1 or M2 or no pupillary or cornea reflex

D1-3: serum NSE > 33 µg/l

N20 present

MMN on auditory EPs

FP 0% (95% IC NA)

N20 absent

FP 0.7% (95% IC 0-3.7%)

FP 3% (95% IC 0.9-11%)

FP 0% (95% IC 0-8.8%)

FP 0% (95% IC 0-3%)

FP 0% (95% IC 0-3%)

BRAIN DEATH

confirmatory tests: isoelectrical EEG or transcranial Doppler or angiography or SPECT

GOOD OUTCOME

POOR OUTCOME

Majority of deaths related to physicians’ decision to withhold or withdraw treatment (Laureys, Nature Reviews Neurosci 2005)

ACUTE SETTING

Adapted from Wijdicks et al, Neurology, 2006
Boveroux et al, Réanimation, 2008

www.comascience.org
**Pronostic** (Projet fédéral Belge, données 2004-07)

Bruno et al., in preparation

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**Conclusion**
Predicting outcome in chronic DOC

ACTIVATION TO THE OWN NAME

ATYPICAL ‘HIGH LEVEL’ CORTICAL ACTIVATION

Perrin et al, *Arch Neurol* 2006


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.
Nociception and pain

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

<table>
<thead>
<tr>
<th>Medical doctors (n=1166)</th>
<th>Paramedical professionals (n=538)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>56</td>
<td>44</td>
</tr>
<tr>
<td>68</td>
<td>32</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=1009)</th>
<th>Non-religious caregivers (n=830)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>64</td>
<td>36</td>
</tr>
<tr>
<td>52</td>
<td>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>Localization to Noxious 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>Flenon Withdrawal</td>
<td>There is isolated finger withdrawal of at least one limb. The limb must move away from the point of stimulation.</td>
</tr>
<tr>
<td>3</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>4</td>
<td>None/Flaccid</td>
<td>There is no discernible movement following application of noxious stimulation, secondary to hypotonic or flaccid muscle tone.</td>
</tr>
</tbody>
</table>

**MOTOR RESPONSE**

**VERBAL RESPONSE**

**Intelligible Verbalization**

Production of words in response to noxious stimulation. Each verbalization must consist of at least 1 consonant-vowel-consonant (CVC) word. For example, "no" would not be acceptable, but "stop" or "that hurts" would.

**Vocalization / Oral Movement**

At least one episode of non-reflexive oral movement and/or vocalization in response to stimulation (such as "no", "ah", or "ahh").

**Grimace**

Grimaces are observed not spontaneously but in response to noxious stimulation.

**None**

No response to any of the above.

**FACIAL EXPRESSION**

**Gry**

Eye are observed not spontaneously but in response to noxious stimulation.

**Grimace**

Grimaces are observed not spontaneously but in response to noxious stimulation.

**Oral reflexive movement/Sneer response**

Clamping of jaws, tongue-pumping, yawning, or chewing movement.

**None**

There is no discernible facial expression following application of noxious stimulation.

Total score >3 / 9 = analgesic treatment

Chatelle et al, *JNNP*, 2012
Do they feel pain?

Noxious electrical stimulation

Pain in minimally conscious state

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


http://neurology.thelancet.com

www.comascience.org
Consciousness ≈ thalamo-cortical

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

Intralaminar nuclei stimulation induces “recovery” from minimally responsive state

Laureys et al, Lancet, 2000
Curative treatment: Drugs?

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Study (first author, year)</th>
<th>Number of patients and etiology</th>
<th>Diagnosis</th>
<th>Placebo control</th>
<th>Reported functional outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopaminergic agents</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amantadine</td>
<td>Giacino (2012)</td>
<td>184 TBI</td>
<td>MCS/VS</td>
<td>Yes</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>Schnakers (2008)</td>
<td>1 anoxic</td>
<td>MCS</td>
<td>No</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>Patrick (2006)</td>
<td>10 TBI</td>
<td>Low responsive level</td>
<td>No</td>
<td>No effect</td>
</tr>
<tr>
<td></td>
<td>Hughes (2005)</td>
<td>123 TBI</td>
<td>Coma</td>
<td>NA</td>
<td>No effect</td>
</tr>
<tr>
<td></td>
<td>Saniova (2004)</td>
<td>41 TBI</td>
<td>‘Persistent unconsciousness’</td>
<td>NA</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>Meythaler (2002)</td>
<td>35 TBI</td>
<td>MCS</td>
<td>Yes</td>
<td>Positive</td>
</tr>
<tr>
<td>Bromocriptine</td>
<td>Brahmi (2004)</td>
<td>4 intoxication</td>
<td>Coma</td>
<td>No</td>
<td>Positive</td>
</tr>
<tr>
<td>Levodopa</td>
<td>Matsuda (2003)</td>
<td>3 TBI</td>
<td>VS</td>
<td>No</td>
<td>Positive</td>
</tr>
<tr>
<td>Nonbenzodiazepine sedative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zolpidem</td>
<td>Cohen (2008)</td>
<td>1 anoxic</td>
<td>Lethargic</td>
<td>No</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>Shames (2008)</td>
<td>1 anoxic</td>
<td>MCS</td>
<td>No</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>Singh (2008)</td>
<td>1 TBI</td>
<td>MCS</td>
<td>No</td>
<td>No effect</td>
</tr>
<tr>
<td></td>
<td>Brefel-Courbon (2007)</td>
<td>1 hypoxic</td>
<td>Akinetic mutism</td>
<td>Yes</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>Clauss (2006)</td>
<td>2 TBI, 1 anoxic</td>
<td>VS</td>
<td>No</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>Clauss (2000)</td>
<td>1 TBI</td>
<td>Semi-comatose</td>
<td>No</td>
<td>Positive</td>
</tr>
<tr>
<td>GABA agonist</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baclofen</td>
<td>Sara (2007)</td>
<td>1 non-TBI</td>
<td>VS</td>
<td>No</td>
<td>Positive</td>
</tr>
</tbody>
</table>

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. Gossieres · A. Soddu · C. Schnakers · G. Moonen · S. Laureys

2,475 medical professionals

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-Aurélie Bruno, Jan L Bernheim, Didier Ledoux, Frédéric Pellas, Athena Demertzi, Steven Laureys

Bruno et al, BMJ Open, 2011
Conclusion


Erik Ziegler, *Cyclotron Art Committee*
Conclusion

Human conscious awareness
≈ emergent property of collective critical neural network dynamics, involving a frontoparietal global workspace

Diagnostic use
≈ 40% misdiagnosis

Prognostic use
multimodal imaging

Therapeutic use
pain treatment / deep brain stimulation thalamus

Ethical issues
Burnout in caregivers

568 health care workers (Maslach Burnout Inventory)

- 82% No Burnout
- 68% emotional exhaustion
- 50% depersonalization
- 3% severe
- 15% moderate

<table>
<thead>
<tr>
<th>Profession</th>
<th>Burnout</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician</td>
<td>8%</td>
</tr>
<tr>
<td>Nurse</td>
<td>24%</td>
</tr>
<tr>
<td>Nursing assistant</td>
<td>23%</td>
</tr>
<tr>
<td>Physio-/speech-/ergo-therapist</td>
<td>8%</td>
</tr>
<tr>
<td>Psychologist/social worker</td>
<td>10%</td>
</tr>
</tbody>
</table>

Gosseries, Demertzi et al, *Brain Injury* 2012
Frontoparietal “global workspace”

Thibaut et al, J Rehabil Med 2012
Disorders of consciousness

Aphasia as a confound

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

Steve Majerus¹,³, Marie-Aurélie Bruno²,³, Caroline Schnakers², Joseph T. Giacino⁴ and Steven Laureys²,³,*

*Progress in Brain Research, Vol. 177
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Bruno et al, J Neurology, 2012
Default connectivity in anesthesia

Boveroux et al, *Anesthesiology* 2010
Two awareness networks

EXTERNAL or SENSORY AWARENESS

INTERNAL or SELF AWARENESS