Brain function in locked-in, minimally conscious & vegetative/unresponsive wakefulness syndrome

Vanessa CHARLAND-VERVILLE
Steven LAUREYS
Coma Science Group
University & University Hospital of Liège
Belgium

Merano, Oct 20th, 2011
Reducing consciousness to 2D

Laureys, *Trends in Cognitive Sciences*, 2005
Consciousness ≠ whole brain

Laureys et al, Lancet Neurology, 2004
Consciousness \( \approx \) 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
Precuneus $\approx$ hub in the network


Axonal re-growth in Terry Wallis

Frontoparietal “global workspace”

preserved arousal
no awareness

no arousal
no awareness

(sleep data: Maquet et al 2000; anesthesia: Kaisti et al 2002)
Consciousness ≠ primary cortex

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

“VEGETATIVE” UNRESPONSIVE

MINIMALLY RESPONSIVE
Consciousness $\approx$ top-down

Consciousness ≈ thalamo-cortical

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


Intralaminar nuclei stimulation induces “recovery” from minimally responsive state

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

Two awareness networks

EXTERNAL or SENSORY AWARENESS

INTERNAL or SELF AWARENESS

Laureys, *Scientific American* 2007

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External and internal awareness

EXTERNAL (SENSORY) AWARENESS
(laser stimulation)

perceived (433 ± 23 mJ) >
unperceived (438 ± 21 mJ)


INTERNAL (SELF) AWARENESS
(own name)

Perrin et al, *Neuropsychologia* 2005
“Resting” default mode connectivity

Vanhaudenhuyse et al, *Brain* 2010
Clinical interest

- **COGNITIVE CAPACITY**
  - MINIMALLY RESPONSIVE
    - Awareness?
      - = response to command or non-reflex movements
  - VEGETATIVE/UNRESPONSIVE
    - arousal = eye opening

- **MOTOR RESPONSIVENESS**
  - COMA
  - VEGETATIVE/UNRESPONSIVE
  - MINIMALLY RESPONSIVE
  - COMMUNICATION
    - good recovery
    - professional reinsertion
  - moderate disability
  - live independently
  - severe disability
  - moderate disability
  - severe disability

Laureys et al., *Current Opinion in Neurology*, 2005
"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
Eye tracking: use a mirror!
Signs of consciousness on fMRI

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

Owen, Coleman, Boly, Davis, Laureys & Pickard, Science, 2006
Yes-No communication with fMRI

HEALTHY SUBJECT

Answers « YES »

« VEGETATIVE STATE »

Answers « NO »
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
Predicting outcome in chronic DOC

Vegetative state

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
Understanding plasticity

Landsness and Bruno et al, *Brain*, 2011
Understanding plasticity

Homeostatic decline SWA $\approx$ plasticity (Tononi)

Landsness and Bruno et al, *Brain*, 2011
Multimodal imaging

Bruno et al, Prog Brain Res, 2011
Tshibanda et al, Neuroradiology, 2010
Nociception and pain

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

**Demertzi et al, Prog Brain Res, 2009**

<table>
<thead>
<tr>
<th>Medical doctors (n=1166)</th>
<th>Yes (%)</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>56</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Paramedical professionals (n=538)</td>
<td>Yes (%)</td>
<td>No (%)</td>
</tr>
<tr>
<td>68</td>
<td>32</td>
<td></td>
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</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Religious caregivers (n=1009)</th>
<th>Yes (%)</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>64</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Non-religious caregivers (n=830)</td>
<td>Yes (%)</td>
<td>No (%)</td>
</tr>
<tr>
<td>52</td>
<td>48</td>
<td></td>
</tr>
</tbody>
</table>

Nociception Coma Scale

Total score >7 / 12 = analgesic treatment

Schnakers et al, Pain, 2010

<table>
<thead>
<tr>
<th>Score</th>
<th>Item</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Localisation to Noxious Stimulation</td>
<td>The non-affected limb must move towards the stimulated limb.</td>
</tr>
<tr>
<td>2</td>
<td>Flexion Withdrawal</td>
<td>The limb must move away from the noxious stimulation.</td>
</tr>
<tr>
<td>1</td>
<td>Abnormal Posturing</td>
<td>The limb must move away from the noxious stimulation.</td>
</tr>
<tr>
<td>0</td>
<td>None</td>
<td>There is no discernible movement following noxious stimulation.</td>
</tr>
</tbody>
</table>

**VERBAL RESPONSE**

- **Intelligible Verbalization**
- **Vocalization / Oral Movement**
- **Grunts**
- **None**

**FACIAL EXPRESSION**

- **Complete**
- **Partial**
- **None**

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

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Do they feel pain?

Noxious electrical stimulation

Low level disconnected cortical activation

Pain in minimally conscious state


http://neurology.thelancet.com
Curative treatment: Drugs? no evidence based therapy

Demertzi et al *Expert Rev Neurotherapeutics* 2008
Schnakers et al *J Neurol Neurosurg Psychiatry* 2008
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

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)

2,475 medical professionals

Quality of life

Translational research

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
New knowledge, new nosology

Bruno, Vanhaudenhuyse et al *J Neurology*, 2011

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