Identifying the brain’s awareness system: lessons from coma and related states

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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

Boly et al, Ann NY Acad Sci 2009
Vanhaudenhuysse & Demertzi et al, J Cogn Neursoci 2011
Consciousness ≠ global brain function

Laureys et al., Lancet Neurology, 2004
Consciousness ≈ frontoparietal

Areas systematically dysfunctional in “vegetative” state

Laureys et al, Neuroimage 1999

Terry Schiavo °1963, vegetative 1990, † 2005
Consciousness $\approx$ frontoparietal

Areas systematically dysfunctional in "vegetative" state

Areas recovering metabolism after recovery from "vegetative" state

Laureys et al, *Neuroimage* 1999

Laureys et al, *J Neurol Neurosurg Psychiatry*, 1999
Absence seizure

Laufs et al, Epilepsia 2006

www.comascience.org
Complex partial seizures

Seizure without loss of awareness

Seizure with loss of awareness

HMPAO-SPECT
Ictal-interictal P<0.01

Blumenfeld et al, *Cerebral Cortex* 2004
Somnambulism

Patient compared to 24 controls


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Frontoparietal “global workspace”

- Preserved arousal, no awareness
- No arousal, no awareness


www.comascience.org
Precuneus ≈ hub in the network

Conscious controls (n=110)  Vegetable state (n=33)
Locked in syndrome (n=5)  Minimally conscious state (n=7)

Laureys et al, Lancet Neurology, 2004
Voss et al, J Clin Invest, 2006

Terry Wallis wakes from 19-year coma

www.comascience.org
Precuneus ≈ hub in the network

**SLEEP**
Activity in PCC/precuneus

- WAKE
- STAGE 2
- STAGE 3-4
- REM SLEEP

**ANESTHESIA**
Activity in PCC/precuneus

- WAKE
- DROWSY
- SEDATION
- ANESTHESIA

Two awareness networks

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

INTERNAL or SELF AWARENESS

EXTERNAL or SENSORY AWARENESS

Laureys, Scientific American 2007
Vanhaudenhuyse, Demertzi et al, J Cogn Neurosci 2011
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
Qin et al, Human Brain Mapping, 2010
Modulation by hypnosis

Demertzi et al, Prog Brain Res 2011
Consciousness ≠ primary cortex

"VEGETATIVE" UNRESPONSIVE

MINIMALLY RESPONSIVE

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

Consciousness ≈ thalamo-cortical

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

Intralaminar nuclei stimulation induces “recovery” from minimally responsive state


Clinical interest

"Miracle recovery"
Rom Houben

COGNITIVE CAPACITY

MINIMAL RESPONSIVE
Awareness?
= non-reflex movements or response to command

VEGETATIVE/UNRESPONSIVE
Arousal = eye opening - only reflex movements

MOTOR RESPONSIVENESS

Coma

"Live independently"
Professional reinsertion
good recovery

Severe disability
Moderate disability

Laureys et al., Current Opinion in Neurology, 2005
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!

Vanhaudenhuyse et al
*J Neurol Neurosurg Psychiatry 2008*
A new name for «vegetative»

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

“Theres nothing we can do... he'll always be a vegetable.”

Laureys et al, BMC Medicine 2011
Yes-No communication with fMRI

Answers « YES »

Answers « NO »

« VEGETATIVE STATE »
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%)

Cruse et al, *Neurology* 2012
7/23 MCS (30%)
- 7/15 traumatic (49%)
- 0/8 non-traumatic (0%)

www.thelancet.com

www.comascience.org
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
Aphasia as a confound

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

Steve Majerus\textsuperscript{1,3}, Marie-Aurélie Bruno\textsuperscript{2,3}, Caroline Schnakers\textsuperscript{2}, Joseph T. Giacino\textsuperscript{4} and Steven Laureys\textsuperscript{2,3,*}

*Progress in Brain Research, Vol. 177
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Bruno et al, J Neurology, 2012
Automated consciousness classifier

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


www.comascience.org
Frontoparietal “global workspace”
Visual fixation is a reflex

Bruno et al, *BMC Neurology* 2010
Consciousness $\approx$ connectivity

EEG-TMS

Rosanova and Gossieres et al, *Brain* 2012
“Resting state” default brain activity

Boly et al, Human Brain Mapping 2009
Automated default mode analysis

Soddu et al. *Hum Brain Mapp.* 2012
Default connectivity in anesthesia

Boveroux et al, *Anesthesiology* 2010
“Resting” default mode connectivity

Vanhaudenhuyse et al, Brain 2010
EEG entropy

Predicting outcome in chronic DOC

Vegetative state

ATYPICAL 'HIGH LEVEL' CORTICAL ACTIVATION

ACTIVATION TO THE OWN NAME

Perrin et al, *Arch Neurol* 2006


www.comascience.org
Understanding plasticity

Homeostatic decline SWA ≈ plasticity (Tononi)

Landnes and Bruno et al, *Brain*, 2011
“Dreaming” in MCS?

Landnes and Bruno et al, *Brain*, 2011

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%

Nociception Coma Scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Item</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MOTOR RESPONSE</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>Flexion Withdrawal</td>
<td>There is isolated flexion 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 lower extremities occurs immediately after the stimulus is applied.</td>
</tr>
<tr>
<td>0</td>
<td>None-Placed</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>VERBAL RESPONSE</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Inaudible 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. Failure to produce such verbalization should not be considered an insensitivity to pain.</td>
</tr>
<tr>
<td>2</td>
<td>Vocalization / Oral Movement</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Grunts</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td></td>
<td>VISUAL RESPONSE</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Fixation</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Eye movements</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Stare</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>No change</td>
<td></td>
</tr>
<tr>
<td></td>
<td>FACIAL EXPRESSION</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Cry</td>
<td>Cracks are observed not spontaneously but in response to nociceptive stimulation.</td>
</tr>
<tr>
<td>2</td>
<td>Grimace</td>
<td>The patient grimaces and shows other signs of discomfort or possible pain in response to nociceptive stimulation.</td>
</tr>
<tr>
<td>1</td>
<td>Oral reflexive movement / Stare response</td>
<td>Nipping of jaws, tongue pumping, yawning, chewing movement.</td>
</tr>
<tr>
<td>0</td>
<td>None</td>
<td>There is no discernible facial expression following application of nociceptive stimulation.</td>
</tr>
</tbody>
</table>

Total score > 7 / 12 = analgesic treatment

Demertzi et al, Prog Brain Res, 2009

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

Noxious electrical stimulation


www.comascience.org
Pain in minimally conscious state

http://neurology.thelancet.com


www.comascience.org
Curative treatment: amantadine

Schnakers et al
*J Neurol Neurosurg Psychiatry* 2008

www.comascience.org
Ethical framework

The American Journal of Bioethics, 8(9): 3–12, 2008

Neuroimaging and Disorders of Consciousness: Envisioning an Ethical Research Agenda

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Judy Illes, University of British Columbia*
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Steven Laureys, University of Liege**
Emily Murphy, Stanford Law School**

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

2,475 medical professionals

It is acceptable to stop treatment in a chronic...

Demertzi et al, J Neurology 2011
Demertzi et al, Neuroethics in press
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 Pellas, Athena Demertzi, Steven Laureys

Conclusion

Erik Ziegler, Cyclotron Art Committee

Bruno et al, Prog Brain Res, 2011
Conclusion

Neural correlates of conscious awareness
≈ emergent property of collective widespread fronto-parietal connectivity

Diagnostic use
≈ 40% misdiagnosis

Prognostic use
multimodal imaging

Therapeutic use
pain treatment / deep brain stimulation thalamus

Ethical issues

Laureys & Boly, Nature Clinical Practice, 2008
Laureys & Schiff, NeuroImage, 2012
Sanders et al, Anesthesiology, 2012

www.comascience.org
Slides on website
MSc & PhD positions open
coma@chu.ulg.ac.be