The Neural Correlate of Consciousness: Lessons from Coma and Related States

Audrey Vanhaudenhuyse PhD
Neuropsychologist
Coma Science Group
Cyclotron Research Centre
CHU Sart-Tilman
Liège

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Disorders of consciousness

• Defining consciousness
• Scientific perspective
  • Neural correlates of consciousness
• Clinical perspective
  • Diagnosis
  • Prognosis
  • Treatment
• Locked in Syndrome & Ethical issues
• Conclusion
Defining consciousness
Reducing consciousness to 2D

Laureys, *Trends in Cognitive Sciences*, 2005

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Consciousness ≠ whole brain

Laureys et al, Lancet Neurology, 2004

www.comascience.org
Thalamo-cortical loop

Laureys et al, Neuroimage 1999
Reducing awareness to 2D

Consciousness | Diagnosis | Prognosis | Treatment | LIS & Ethics | Conclusion

Boly... Laureys, Ann NY Acad Sci 2009

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External and internal awareness

**NEURAL CORRELATE OF EXTERNAL (SENSORY) AWARENESS**

Peri-luminal laser stimulation on the hand (24 subjects)

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

Boly et al, PNAS 2007
(also Dehaene et al, Nat Rev Neuroci 2001; Rees et al, Nat Rev Neuroci 2001)

**NEURAL CORRELATE OF INTERNAL (SELF) AWARENESS**

Auto-referential stimuli

Laureys et al, Consciousness & Cognition 2007
(also Mason et al, Science, 2007; Golland et al, Neuropsychologia 2008)
External vs internal awareness

Vanhaudenhuyse & Demertzi et al, J Cogn Neurosci, 2010

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“Resting state” default brain activity

Anti-correlation of internal and external awareness networks

Spontaneous brain fluctuations predict conscious perception of external stimuli

Boly et al, Ann NY Acad Sci 2009

Boly et al, PNAS 2007
Clinical interest & Diagnosis
Consciousness, arousal & awareness

Laureys et al, Lancet Neurology, 2005
Misdiagnosis of vegetative state

n=103 post-comatose patients

45 clinical consensus diagnosis ‘vegetative state’
18 signs of awareness (Coma Recovery Scale)

⇒ 40% potential misdiagnoses

Schnakers et al, *BMC Neurology* 2009

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Eye tracking: use a mirror!

Vanhaudenhuyse et al
*J Neurol Neurosurg Psychiatry 2008*

Without mirror: 29% VS

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**Consciousness** | **Diagnosis** | **Prognosis** | **Treatment** | **LIS & Ethics** | **Conclusion**

- **n=52**
- Without mirror:
  - 29% VS

**Number of MCS patients tracking**

- Mirror
- Person
- Object
P300 to the own name
‘Self’ processing in MCS

- Meaningless Noise
- Acoustically Matched Cries
- Patient’s Own Name

Laureys et al., Neurology, 2004
Signs of consciousness on fMRI

Yes-No communication with fMRI

Monti & Vanhaudenhuyse, Coleman, Boly, Pickard, Tshibanda, Owen, Laureys
New England J Med 2010

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Brain Computer Interfaces

Cognitive ERPs

Coma or total locked-in syndrome?
21-y old woman
basilar artery thrombosis - day 49

Schnakers et al, Neurology, 2008
Schnakers et al, Neurocase, 2009

Other names PASSIVE
Count TARGET (other name)

Own name PASSIVE
Count TARGET (own name)

pH salivary based

Schnakers et al, Neurology, 2008
Schnakers et al, Neurocase, 2009

Vanhaudenhuyse et al. BBS 2007

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

Steve Majerus², Marie-Aurélie Bruno², Caroline Schnakers², Joseph T. Giacino³ and Steven Laureys²,³,∗

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Metabolism in language network
“Resting state” default brain activity

"Resting state" default brain activity

Vanhaudenhuyse et al, *Brain*, 2010
Automated awareness classifier

linear “Support Vector Machine” classifiers

Phillips et al, NeuroImage, 2010
Prognosis

Laureys & Boly
What is it like to be vegetative or minimally conscious?

Consciousness | Diagnosis | Prognosis | Treatment | LIS & Ethics | Conclusion
POST-ANOXIC COMA

- exclude confounding factors including hypothermia, drugs, electrolyte disturbances…
- brainstem reflexes (pupillary, cornea, oculocephalic, cough)
- apnea testing
- present
- negative
- GCS 3/15
- absent and
- present

BRAIN DEATH

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

ORGAN PROCUREMENT ORGANIZATION

POST-ANOXIC COMA

MMN on auditory EPs N20 present

MMN on auditory EPs N20 absent

GCS 3/15

apnea testing

absent and cornea, oculocephalic, cough)

D1: myoclonus status epilepticus

D3: M1 or M2 or no pupillary or cornea reflex

D1-3: serum NSE > 33 µg/l

D1-3: somatosensory EPs

generalized suppression (<20 µV) or ‘burst supression’ EEG

POOR OUTCOME

GOOD OUTCOME

ORGAN PROCUREMENT ORGANIZATION

Pittsburgh Protocol non-heart-beating donor

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

Adapted from Wijdicks et al, Neurology, 2006
Boveroux et al, Réanimation, 2008 (French)
Pronostic  (Belgian Federal Project 2004-07)

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Bruno et al., in preparation

www.comascience.org
MRI: DTI & spectroscopy

Tshibanda et al, Prog Brain Res, 2009
Tshibanda et al, Neuroradiology, in press
fMRI predictor of outcome?

ATYPICAL 'HIGH LEVEL' CORTICAL ACTIVATION

Di et al, Neurology, 2007
Coleman et al, Brain, 2008

www.comascience.org
Treatment

- symptomatic
- curative

"...a (woman’s) brain is a mystery... and even more so in this state”

Pedro Almodovar - Hable con ella

Consciousness | Diagnosis | Prognosis | Treatment | LIS & Ethics | Conclusion
Nociception and pain

Demertzi et al, Prog Brain Res, 2009

Schnakers et al, Pain, in press

Nociception Coma Scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No response</td>
</tr>
<tr>
<td>1</td>
<td>Blink to pain</td>
</tr>
<tr>
<td>2</td>
<td>Vocalization</td>
</tr>
<tr>
<td>3</td>
<td>Head turning</td>
</tr>
<tr>
<td>4</td>
<td>Screen avoidance</td>
</tr>
<tr>
<td>5</td>
<td>Painful stimulus</td>
</tr>
</tbody>
</table>

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

Medical doctors (n=1166) vs Paramedical professionals (n=538) vs Religious caregivers (n=1009) vs Non-religious caregivers (n=830)

www.comascience.org
Do they feel pain?

Noxious electrical stimulation

Low level disconnected cortical activation

Laureys et al, Neuroimage, 2002
Laureys, Nature Reviews Neuroscience, 2006

www.comascience.org
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
Curative treatment: Deep brain stimulation?

Locked-In Syndrome
&
Ethical challenges
Pseudo coma
Ethical framework
Quality of life in LIS

LIS condition is worth than vegetative state or minimally conscious state?

![Bar Chart]

- Medical (n=561)
  - Oui: 57%
  - Non: 35%
  - Pas de réponse: 8%

- Paramedical (n=194)
  - Oui: 61%
  - Non: 32%
  - Pas de réponse: 7%

Bruno et al., RMLg 2008
Quality of life in LIS

Anamnestic Comparative Self Assessment (Bernheim et al)

-5 -4 -3 -2 -1 0 +1 +2 +3 +4 +5

worst period in my life

best period in my life

X Locked-in patients n=70
X Matched healthy controls n=70
Belgian survey (n=748)

Age 38±16 years (range 16-83)
Profession: medical =310 (41%), paramedical= 141 (19%), other=247 (33%), missing n=51 (7%)

Laureys et al, unpublished
End-of-life decisions

LETTER TO THE EDITOR

Organ donation after physician-assisted death

Olivier Detry1, Steven Laureys1, Marie-Élisabeth Faymonville2, Arnaud De Roover1, Jean-Paul Squifflet1, Maurice Lamp3 and Michel Meurisse1

1 Department of Abdominal Surgery and Transplantation, 2 Coma Science Group, Cyclotron Research Centre, Department of Neurology, 3 Department of Anaesthesiology and Intensive Care Medicine, CHU de Liège, University of Liège, Sart Tilman B93, B4000 Liège, Belgium


Organ Procurement After Euthanasia: Belgian Experience


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Conclusion
Neural correlates of conscious awareness
≈ emergent property of the collective behavior
of fronto-parietal neuronal ‘global workspace’
≈ cortico-thalamo-cortical functional connectivity

Diagnostic use
≈ 40% signs of consciousness in vegetative state

Prognostic use
(f)MRI prospective multicenter studies

Therapeutic use
symptom & pain treatment / curative thalamic DBS

Ethical issues

Tononi & Laureys, The Neurology of Consciousness, 2009
Laureys & Boly, Nature Clinical Practice, 2008
Owen, Schiff & Laureys, Prog Brain Res, 2009
THANK YOU
slides can be downloaded on website
EU funded positions open

PhD candidates:
Marie-Aurélie Bruno
Olivia Gosseries
Athena Demertzi
Camille Chatelle
Marie Thonnard
Victor Cologan
Jean-Floris Tshibanda MD
Pierre Boveroux MD
Muriel Kirsch MD
Audrey Maudoux MD
Isabelle Lutte MD

PhDs:
Audrey Vanhaudenhuysse
Melanie Boly MD
Didier Ledoux MD
Caroline Schnakers
Quentin Noirhomme Engineering
Andrea Soddu Physics
Betina Sorger Maastricht
Dorothée Lulé Tubingen

Collaborations:
NY N Schiff, J Fins, J Giacino
Cambridge A Owen et al
Milano M Massimini et al
Wisconsin G Tononi et al
Tubingen & Wurzburg A Kübler
Paris L Puybasset et al
Hangzhou China H Di
Salzburg M Schabus
Lyon F Perrin
Weizmann R Malach et al
Naples M Papa

Visiting fellows: Natalia Lapitskaia, Remy Lehembre, Jonathan Orban,
Francisco Gomez...