Disorders of consciousness and Locked-In Syndrome after Stroke

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Neuropsychologist

IRISH HEART FOUNDATION COUNCIL ON
16th ANNUAL STROKE STUDY DAY
April 12th 2013
Consciousness

Consciousness | Definition | Diagnosis | Prognosis | Ethics | Conclusion
Reducing consciousness to 2D

Laureys, *Trends in Cognitive Sciences*, 2005

TRENDS in Cognitive Sciences

Consciousness | Definition | Diagnosis | Prognosis | Ethics | Conclusion

Level of Consciousness: Wakefulness

= necessary but not sufficient

Content of Consciousness: Awareness

Lucid Dreaming

REM Sleep

St I-II Sleep

St III-IV Sleep

General Anesthesia

Coma

Conscious Wakefulness

Locked-in syndrome

Drowsiness

Minimally Responsive
- command following MCS+
- non-reflex movements MCS-

Bruno & Vanhaudenhuysen et al., 2011

Vegetative State

Epilepsy

Sleepwalking

Unresponsive Wakefulness Syndrome

Laureys et al., 2010

"There’s nothing we can do... he’ll always be a vegetable."

www.comascience.org
Consciousness ≠ global brain function

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

Areas systematically dysfunctional in “UNRESPONSIVE” state

Areas recovering metabolism after recovery from “UNRESPONSIVE” state

Laureys et al, Neuroimage 1999

Laureys et al, J Neurol Neurosurg Psychiatry, 1999
Precuneus ≈ hub in the network

Conscious controls (n=110)  Vegetative state (n=33)

Locked in syndrome (n=5)  Minimally conscious state (n=7)

Laureys et al, Lancet Neurology, 2004

Terry Wallis wakes from 19-year coma

Voss et al, J Clin Invest, 2006
Clinical definitions
States of consciousness

- **NORMAL CONSCIOUSNESS**
  - Arousal: High
  - Awareness: High

- **COMA**
  - Arousal: Low
  - Awareness: Low

- **VEGETATIVE/UNRESPONSIVE STATE**
  - Arousal: Low
  - Awareness: Low

- **MINIMALLY CONSCIOUS STATE**
  - Arousal: Low
  - Awareness: Low

- **LOCKED IN SYNDROME**
  - Arousal: Low
  - Awareness: Low

**Laureys, Owen and Schiff, Lancet Neurology, 2005**
Locked-in syndrome (LIS)

- Presence of sustained eye opening
- Quadriplegia or quadriparesis
- Aphonia or severe hypophonia
- Occular mode of communication
- Preserved cognitive abilities

The **LIS** can be **subdivided** on the basis of motor impairments:

- **Classical**: quadriplegia, aphonia, vertical eye movements/ blinking
- **Incomplete**: voluntary motions other than vertical eye movements
- **Total**: complete immobility including all eye movements

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American Congress of Rehabilitation Medicine, 1995
Laureys et al, Prog in Brain Resc, 2005
Bauer et al, J Neurol, 1979

www.comascience.org
Cognition in LIS

- Presence of sustained eye opening
- Quadriplegia or quadriparesis
- Aphonia or severe hypophonia
- Ocular mode of communication
- Preserved cognitive abilities

*N=10 (1 to 6y after insult)*

**Adapted neuropsychological tests**
# Communication

<table>
<thead>
<tr>
<th>1</th>
<th>E</th>
<th>A</th>
<th>N</th>
<th>R</th>
<th>C</th>
<th>V</th>
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<tr>
<td>2</td>
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<td>6</td>
<td>Q</td>
<td>Y</td>
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</table>

<table>
<thead>
<tr>
<th>Chair</th>
<th>Bed</th>
<th>Book Thx!</th>
<th>Radio</th>
<th>Music</th>
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</thead>
<tbody>
<tr>
<td>Television</td>
<td>Plus</td>
<td>Minus</td>
<td>I'm hungry</td>
<td>I'm thirsty</td>
</tr>
<tr>
<td>Can I have a pen?</td>
<td>Can I have my computer?</td>
<td>Eye-coded alphabetical system</td>
<td>Eyeglasses</td>
<td>Don't understand</td>
</tr>
<tr>
<td>Can you repeat?</td>
<td>Mum</td>
<td>Dad</td>
<td>Time</td>
<td>Day</td>
</tr>
<tr>
<td></td>
<td>Again</td>
<td>Urinary</td>
<td>I'm cold</td>
<td>I'm hot</td>
</tr>
</tbody>
</table>

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*Bruno et al., Pediatric Neurology, 2009*
Diagnosis: behavioural assessment
Diagnosis

First person who realized that the patient was conscious

- Physicians: 62%
- Relative: 33%
- Others: 5%

Average time elapsed between insult and LIS diagnosis:

<table>
<thead>
<tr>
<th>Group</th>
<th>Average Time Elapsed</th>
</tr>
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<tbody>
<tr>
<td>Adults (N=44)</td>
<td>79 days (from hours to 4 years)</td>
</tr>
<tr>
<td>Children (N=5)</td>
<td>41 days (from hours to 6 months)</td>
</tr>
</tbody>
</table>

- Misdiagnosis explain by:
  - Rarity of LIS
  - Recognize signs of consciousness
  - Fluctuation of vigilance
  - Cognitive/sensory deficits

Laureys et al., Prog Brain Res, 2005
Bruno et al., Pediatric Neurology, 2009
Behavioral scales

Full Outline of UnResponsiveness

Wijdicks et al., Ann Neurol, 2005
Behavioral scales

Full Outline of UnResponsiveness

n=171 post-comatose patients
71 “vegetative state” (Glasgow Coma Scale)
8 visual pursuit
(Full Outline of UnResponsiveness)

11% potential misdiagnosis

Wijdicks et al., Ann Neurol, 2005
Bruno et al., Neurocrit Care, 2011
Behavioral scales

Full Outline of UnResponsiveness

n=103 post-comatose patients

45 clinical consensus “vegetative state”
18 signs of awareness
(Coma Recovery Scale-Revised)

≫ 40% potential misdiagnosis

Wijdicks et al., Ann Neurol, 2005
Bruno et al., Neurocrit Care, 2011
Schnakers et al., BMC Neurology, 2009
Eye tracking: use a mirror!

Vanhaudenhuyse et al., J Neurol Neurosurg Psychiatry, 2008
Diagnosis: paraclinical assessments
Yes-No communication with fMRI

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

www.comascience.org
EEG-based BCIs: motor imagery

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%)
EEG-based BCIs: active ERPs

Complete Locked-in syndrome

Passive Other Name
Active Other Name
Passive Own Name
Active Own Name

Schnakers et al, Neurology, 2008
Other tools: Active pH paradigm

Imagery of lemon & milk

Vanhaudenhuyse, Bruno et al, Behav Brain Sci 2007
Wilhelm, Jordan, Birbaumer, JNNP 2006
Sniffing enables communication and environmental control for the severely disabled

Anton Plotkin\textsuperscript{a,1}, Lee Sela\textsuperscript{a,1}, Aharon Weissbrod\textsuperscript{a}, Roni Kahana\textsuperscript{a}, Lior Haviv\textsuperscript{a}, Yaara Yeshurun\textsuperscript{a}, Nachum Soroker\textsuperscript{b, c}, and Noam Sobel\textsuperscript{a,2}

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Edited* by Brian A. Wandell, Stanford University, Stanford, CA, and approved June 24, 2010 (received for review May 13, 2010)
“Resting” default mode connectivity

Vanhaudenhuyse & Noirhomme et al, Brain 2010
Consciousness ≈ connectivity

EEG-TMS

Rosanova and Gosseries et al, Brain 2012
Consciousness ≈ connectivity

EEG-TMS

Rosanova and Gosseries et al, Brain 2012
Automated consciousness classifier

"Relevance Vector Machine" on FDG-PET

Phillips et al, NeuroImage, 2011
Prognosis
POST-ANOXIC COMA

exclude confounding factors including hypothermia, drugs, electrolyte disturbances...

brainstem reflexes
(pupillary, cornea, oculocephalic, cough)

absent and
GCS 3/15

apnea testing

positive

absent

BRAIN DEATH

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

ORGAN PROCUREMENT ORGANIZATION

MMN on auditory EPs

N20 present

FP 0% (95% IC NA)

GOOD OUTCOME

N20 absent

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

ORGAN PROCUREMENT ORGANIZATION

Pittsburgh Protocol non-heart-beating donor

POOR OUTCOME

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

D1: myoclonus status epilepticus

D1-3: somatosensory EPs

or

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

FP 0% (95% IC 0.8-8.8%)

or

D3: M1 or M2 or no pupillary or cornea reflex

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

D1-3: serum NSE > 33 µg/l

D1-3: serum NSE > 33 µg/l

Adapted from Wijdicks et al, Neurology, 2006
Boveroux et al, Réanimation, 2008 (French)

Majority of deaths related to physicians’ decision to withhold or withdraw treatment
(Laureys, Nature Reviews Neurosci 2005)
Vegetative state (n=403)

Minimally conscious state (n=437)

Non-Traumatic

Traumatic

Bruno & Ledoux et al., in preparation
Survivance & prognosis in LIS

Age at insult versus survival time of 250 locked-in patients registered in the ALIS

- **Adults LIS - N=95**
  - 92% head movement
  - 65% upper limbs
  - 74% lower limbs
  - 50% speech production
  - 95% vocal/intelligible sounds

- **Pediatric LIS - N=33**
  - 26% “good recovery”
  - 35% motor recovery
  - 16% quadriplegic/anarthric
  - 23% died

Laureys et al., Prog Brain Res, 2005
Bruno et al., Pediatric Neurology, 2009
Ethics and Quality of Life
Belgian survey (n=750)

Treatment can be stopped in...

- VS: 70
- MCS: 30
- LIS: 22

I would like euthanasia if I were in...

- VS: 77
- MCS: 63
- LIS: 58

Age 38±16 years (range 16-83)
Profession: medical & paramedical

Bruno, Laureys et al., in preparation
BEING IN A CHRONIC LOCKED-IN SYNDROME IS WORSE THAN BEING IN A VEGETATIVE STATE

Belgian survey (n=750)

- Medical (n=561)
  - Yes: 57%
  - No: 35%
  - No response: 8%

- Paramedical (n=194)
  - Yes: 61%
  - No: 32%
  - No response: 7%
ALIS QUESTIONNAIRE 2007

Questionnaire ALIS – juillet 2007

Ces données sont confidentielles et à but purement statistique ; elles contribuent à informer le monde médical comme le public sur le LIS.

Nom : ............................................................................................................ Prénom : ........................................................................................................

Adresse : ........................................................................................................

Email : ...........................................................................................................

Date de naissance : ......................................................................................

Lieu de naissance : ......................................................................................

Complications : ...........................................................................................

Date de survenue de la condition : ..............................................................

Quel service hospitalier ? ...........................................................................

Vous est-ce arrivé après un accident de la route ou un traumatisme crânien ?

Pas de traumatisme crânien : ........................................................................

Pas d'accident de la route : ...........................................................................

Date de LIS : .................................................................................................

Divers :

Le premier à découvrir que vous étiez conscient (et pas en coma ou végétatif) était :

☐ le médecin ☐ la famille ☐ autre.................................................................

Parviennent-vous à une communication efficace ?

☐ Oui ☐ Non

Par rapport à votre condition de LIS vous avez reçu :

☐ Gastrostomie ☐ Trachéotomie

☐ Jamais eu ☐ équipé actuellement ☐ enlevé le .... / .... / ....

Communication :

A un moment la communication principale passait via les mouvements des yeux (nécessaire au diagnostic LIS) :

☐ Oui ☐ Non

Etude sur la qualité de vie :

Identifiez le moment le moins heureux de votre vie avant ou après votre période LIS (sur l'échelle, ce moment vaut -5) et ensuite le moment le plus heureux de votre vie avant votre période LIS (ce moment vaut +5 sur l'échelle). Indiquez sur cette échelle votre degré de bien-être durant les deux dernières semaines. Evitez que l'entourage vous influence dans votre choix.

plus mauvaise période de ma vie ................................................................. meilleure période de ma vie
Epidemiological data

- Men/Women ratio: 43/20
- Mean age: 49±11y (24 – 75y)
- LIS duration: 8y (5 – 10y)
Consciousness | Definition | Diagnosis | Prognosis | Ethics | Conclusion

ACSA and RNLI

SWB → Anamnestic Comparable Self-Assessment scale

| Best period in my former life | 5 | As well as the best period in my life |
|-----------------------------  | 4 | Almost as well as in the best period in my life |
|                             3 | Very well |
|                             2 | Well |
|                             1 | Somewhat to the good side |
|                             0 | Neither well nor bad |
|                           -1 | Somewhat to the bad side |
|                           -2 | Bad |
|                           -3 | Very bad |
|                           -4 | Almost as bad as in the worst period in my life |
| Worst period in my life     | -5 | As bad as the best period in my life |

11 questions:
- Mobility
- Self-care
- Recreational/work activities
- Family/relationship

Bernheim et al., Bioethics, 1999
Wood-Dauphinee & Williams, Chron Dis, 1987
Daneski et al., Clin Reha, 2003
A CSA scores distribution

Worst period of my life

Best period of my life

Bruno & Bernheim et al, BMJ open, 2011
A CSA and RNLI

Unable to move around in community
Limited recreational activities
Absence of language production
Pain

63%
12%
45%
46%

Bad QoL (p=0.042)
Bad QoL (p=0.028)
Bad QoL (p=0.049)
Bad QoL (p=0.071)

Bruno & Bernheim et al, BMJ open, 2011
ACSA and Emotional state

- Difficulty to deal with life of events: 22%
- Depression: 13%
- Anxiety: 67%

Bad QOL (p=0.022)
Bad QOL (p=0.040)
Bad QOL (p=0.015)

Bruno & Bernheim et al, BMJ open, 2011
End-of-life decisions

- Reanimation in case of cardiac arrest: 42% Bad QoL (p=0.011)
- Euthanasia: 53% Bad QoL (p=0.032)
- Suicidal thoughts: 32% Bad QoL (p=0.040)

Presence of suicidal thoughts:
- 46% Bad QoL
- 26% Good QoL
Burnout in caregivers

568 health care workers (Maslach Burnout Inventory)

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

<table>
<thead>
<tr>
<th>Profession</th>
<th>Burnout</th>
</tr>
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<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>

Gossieres, Demertzi et al, *Brain Injury* 2012
Conclusion
Conclusion

Human conscious awareness
≈ frontoparietal global workspace

Disorders of Consciousness ≠ Locked-In Syndrome

Diagnosis
≈ 40% misdiagnosis → Adapted behavioral scale
≈ paraclinical tools

Prognosis
≈ Need of studies to better orient the rehabilitation care

Quality of Life
≈ Don’t judge a book by its cover

Laureys & Schiff, *NeuroImage*, 2012
Sanders et al, *Anesthesiology*, 2012
Thank you for your attention!

Slides on comascience.org

MSc & PhD positions open
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