Assessing consciousness in the absence of communication

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France
What is Consciousness?

Materialism

Functionalism

Dualism

Consciousness

| Moral significance | Assessing Consciousness | Conclusions |

A clinical definition

Demertzi, Boly, Laureys. Encyclopedia of Consciousness 2009
Do they feel pain?

Do you think patients in a ... can feel pain?

Unresponsive wakefulness syndrome

Healthy controls UWS patients

Minimally conscious state

Healthy controls MCS patients

Demertz et al, Prog Brain Res 2009
Demertz & Racine et al, Neuroethics 2012

Laureys et al., Neuroimage 2002

Boly et al, Lancet Neurol 2008
End-of-life?

- VS worse than death for the patient: 55%
- VS worse than death for their families: 80%

- MCS worse than VS for the patient: 54%
- MCS worse than VS for their families: 42%

Demertzí et al, *J Neurol* 2011
Behavioural signs of C

**Consciousness | Moral significance | Assessing Consciousness | Conclusions**

Laureys et al, *Curr Opin Neurol* 2005
Standardized assessment

- n=103 post-comatose patients
- 45 Clinical diagnosis of VS
- 18 Coma Recovery Scale MCS
- 40% misdiagnosed

Schnakers et al, Ann Neurol 2006; BMC Neurol 2009

PET Neuroimaging

<table>
<thead>
<tr>
<th></th>
<th>VS/UWS</th>
<th>MCS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>UWS</td>
<td>24 (21%)</td>
<td>5 (4%)</td>
<td>29 (26%)</td>
</tr>
<tr>
<td>MCS</td>
<td>12 (11%)</td>
<td>71 (63%)</td>
<td>83 (74%)</td>
</tr>
<tr>
<td>Total</td>
<td>36 (32%)</td>
<td>76 (68%)</td>
<td>112 (100%)</td>
</tr>
</tbody>
</table>

Stender & Gosseries et al, Lancet 2014
Neuroimaging paradigms

Owen et al, Science 2006
Monti & Vanhaudenhuyse et al, NEJM 2010
Boly et al, Lancet Neurol 2008

Active paradigms

“Imagine playing tennis”

“Imagine visiting the rooms of your house”

Passive paradigms

median nerve

Heine, Di Perri, Soddu, Laureys, Demertzi
In: Clinical Neurophysiology in Disorders of Consciousness, Springer-Verlag 2015

Demertzi & Laureys, In: I know what you are thinking: brain imaging and mental privacy, Oxford University Press 2012
The mind at rest

William James (1842-1910)

The stream of thought (Chapter IX)
The principles of psychology 1890
Some numbers

- The human brain is approximately 2% of the weight of the body
- 80% of this energy consumption is used to support neuronal signaling
- Stimulus and performance-evoked changes in brain energy consumption <5%

While conscious awareness is energetically inexpensive, it is dependent upon a very complex, dynamically organized, non-conscious state of the brain that is achieved at great expense

Intrinsic functional organization

Task

Rest


Smith et al, *PNAS* 2009
Default mode network (DMN)
DMN anticorrelations

Fox et al, *Proc N Acad Sci* 2005
DMN anticorrelations

External awareness
or anticorrelated network

Internal awareness
or Default mode network

Demertzi & Whitfield-Gabrieli. in: Neurology of Consciousness 2nd ed. 2015
Demertzi et al, Front Hum Neurosci 2013
Demertzi, Soddu, Laureys. Curr Opin Neurobiology 2013
Cognitive-behavioral relevance

External-internal: $r = -0.44$, $p < .02$
Mean switch: $0.05$Hz (range: $0.01$-$0.1$)

Effect of awareness

- Normal consciousness
- Autobiographical mental imagery
- Hypnosis

Consciousness   |   Moral significance
Assessing Consciousness   |   Conclusions

Demertzi, Soddu, Faymonville et al, *Prog Brain Res* 2011
Effect of arousal

Boveroux et al, Anesthesiology 2010
Effect of environment

Parabolic flight

Parabolic flight trajectory

Angelique Van Ombergen¹, Floris L. Wuyts¹, Ben Jeurissen², Jan Sijbers², Floris Vanhevel³, Steven Jillings¹, Paul M. Parizel³, Stefan Sunaert⁴, Paul H. Van de Heyning¹, Vincent Dousset⁵, Steven Laureys⁶ & Athena Demertzis⁶,⁷
Effect of environment

Consciousness   |   Moral significance   |   Assessing Consciousness   |   Conclusions

Van Ombergen … and Demertzis, *Sci Reports* 2017
Effect of pathology

Di Perri, ..., Demertzi*, Laureys*, Soddu*, Lancet Neurol 2017
Vanhaudenhuyse et al, Brain 2010
Intrinsic Connectivity Networks

Heine, ... & Demertzi, *Front Psychol* 2012
Networks are disrupted in low consciousness states

Demertzi & Gómez et al, Cortex 2014
Which network discriminates best?

### MCS > VS/UWS

<table>
<thead>
<tr>
<th>Network</th>
<th>t value</th>
<th>Rank</th>
<th>p value</th>
<th>TP</th>
<th>TN</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auditory</td>
<td>8.32</td>
<td>1</td>
<td>&lt;.001</td>
<td>25</td>
<td>18</td>
<td>43/45</td>
</tr>
<tr>
<td>Visual</td>
<td>7.79</td>
<td>2</td>
<td>&lt;.001</td>
<td>23</td>
<td>15</td>
<td>38/45</td>
</tr>
<tr>
<td>Default mode</td>
<td>6.95</td>
<td>3</td>
<td>&lt;.001</td>
<td>23</td>
<td>15</td>
<td>38/45</td>
</tr>
<tr>
<td>Frontoparietal</td>
<td>6.82</td>
<td>4</td>
<td>&lt;.001</td>
<td>23</td>
<td>15</td>
<td>38/45</td>
</tr>
<tr>
<td>Salience</td>
<td>6.21</td>
<td>5</td>
<td>&lt;.001</td>
<td>24</td>
<td>15</td>
<td>39/45</td>
</tr>
<tr>
<td>Sensorimotor</td>
<td>5.87</td>
<td>6</td>
<td>&lt;.001</td>
<td>24</td>
<td>13</td>
<td>37/45</td>
</tr>
</tbody>
</table>

*FWE p<0.05 (cluster-level)*

Demertzi & Antonopoulos et al, *Brain* 2015
Single-patient classification

- Training set: 45 DOC (26 MCS, 19 VS/UWS)
  - 14 trauma, 28 non-trauma, 3 mixed
  - 34 patients assessed >1m post-insult

- Test set: **16 MCS, 6 VS/UWS** (M_{age}: 43y, 15 non-trauma; all chronic), from 2 different centers
Sanity check: generalization on healthy

Demertzi & Antonopoulos et al, *Brain* 2015
Consciousness is supported by cortical dynamics

Demertzi*, Tagliazucchi*, Dehaene, Deco, Barttfeld, Raimondo, Rohaut, Schiff, Owen, Laureys, Naccache, Sitt. *in prep*
Conclusions

fMRI resting state connectivity
• carries information about cognitive function
• can be used in the clinical setting
• needs clinical translation
• illuminates the dynamic structure of consciousness

Need of a framework for applying techniques balancing:
• availability
• sensitivity
• specificity
Coma Science Group & PICNIC Lab
The departments of Neurology and Radiology in Liège and Paris

...and mostly patients and their families!

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### Analysis pipeline

**EPI acquisition**
- Slice-time correction
- Realignment
- Segmentation
- Normalization
- Smoothing
- Motion outliers (ART)
- aCompCor
- Regressing out realignment parameters and ART outliers
- Bandpass filtering [0.008-0.09Hz]

**Preprocessing**

**Brain parcellation**
(Sphere ROIs)

**ROI timeseries extraction**

**Phase analysis**
(Hilbert transform)

**Unsupervised clustering**
(k-means)

**State identification**
(cluster centroids)
### Study cohort (N=159)

#### Main dataset

<table>
<thead>
<tr>
<th></th>
<th>VS/UWS</th>
<th>MCS</th>
<th>CTR</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIEGE</td>
<td>17</td>
<td>23</td>
<td>21</td>
</tr>
<tr>
<td>PARIS</td>
<td>13</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>NY</td>
<td>6</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
<td>42</td>
<td>47</td>
</tr>
</tbody>
</table>

**n = 125**

#### Validation datasets

- **sedated**
  - LIEGE:
    - EMCS: 3
    - MCS: 14
    - UWS: 6
  - ONTARIO:
    - VS/UWS-: 6
    - VS/UWS+: 5

**n = 23**

- **CMD**

**n = 11**

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Grant Type: Collaborative Activity Award, Phase I & II (2008-2017)
44-year-old male cosmonaut
First long-duration mission (169 days) to the ISS in 2014
fMRI protocol pre-flight: 30 days, post-flight: 9 days after Earth re-entry

Hypothesis-free

Hypothesis-driven
Behavior is modified in hypnosis.

Demertzi, Vanhaudenhuyse, Noirhomme, Faymonville, Laureys, J Physiol Paris 2015
Awareness is modified in hypnosis.

Demertzi, Vanhaudenhuyse, Noirhomme, Faymonville, Laureys, J Physiol Paris 2015
Awareness is modified in hypnosis

Demertzi, Vanhaudenhuyse, Noirhomme, Faymonville, Laureys, J Physiol Paris 2015
Crossmodal interaction in consciousness

The local-global paradigm

Local effect

Global effect

Intracerebral LFP Voltage (μV)
Validation in congenitally deaf
Validation in congenitally blind
Validation in propofol anesthesia
Faugeras, Rohaut, Valente, Sitt, Demeret, Bolgerta, Weiss, Grineau, Marois, Quirins, Demertzi, Raimondo, Galanaud, Haberm, Engemann, Puybasse, Naccache, *Brain Inj* in press
Why does it matter?
Neuroimaging and Disorders of Consciousness: Envisioning an Ethical Research Agenda

Joseph J. Fins, Weill Medical College of Cornell University*
Judy Illes, University of British Columbia*
James L. Bernat, Dartmouth Medical School**
Joy Hirsch, Columbia University**
Steven Laureys, University of Liege**
Emily Murphy, Stanford Law School**

*Co-lead authors.
**Equal authors in alphabetical order.
### Balancing costs-benefits

<table>
<thead>
<tr>
<th>Results of Tests</th>
<th>Beneficial Effects</th>
<th>Harmful Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>- brain activity than neurological examination</td>
<td>Relatives: decisions to limit life-sustaining treatment</td>
<td>Relatives: may lose hope, purpose, and meaning in life</td>
</tr>
<tr>
<td>+ brain activity than neurological examination</td>
<td>Clinical management: may be intensified by the chance of further recovery</td>
<td>Relatives: false hopes</td>
</tr>
<tr>
<td>Same as neurological examination</td>
<td>Clinicians &amp; relatives: may be affirmed in their decision about the level of treatment</td>
<td>Clinicians &amp; relatives: may be disappointed &amp; treatment cost/effectiveness may be poor</td>
</tr>
</tbody>
</table>
Benefit for science

Consciousness | Moral significance | Assessing Consciousness | Ethics | Conclusions


- 1924: EEG
- 1970: PET
- 1977: MRI
- 1992: fMRI
- 2002: MCS
- 2010: UWS

MCS +/- Functional LIS
Cognitive-motor dissociation
Benefit for patients?

Consciousness | Moral significance | Assessing Consciousness | Ethics | Conclusions

Continuity of self-image

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

Worst period
-5

Anamnestic Comparative Self Assessment Ratings


<table>
<thead>
<tr>
<th>LIS patients (n=44)</th>
<th>Healthy controls (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>29</td>
<td>7</td>
</tr>
</tbody>
</table>
Benefit for caregivers?

Table III. Percentage of healthcare workers presenting a burnout.

<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>

n=523

Gossieres, Demertzi et al, Br Inj 2012
Methodological challenges

Heine, … & Demertz, Front Psychol 2012
How?

Demertzi & Gómez et al, *Cortex* 2014