Tracking consciousness in minimal behavioural responsiveness

School of Psychology
University of Birmingham, UK

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Athena Demertzi, PhD
FNRS Research Associate
GIGA Consciousness
GIGA Research Institute & Neurology Department
University & University Hospital of Liège
Belgium
Patients cannot express themselves

Hable con ella 2002, Pedro Almodóvar
What is Consciousness?

Materialism

Functionalism

Dualism

Edinburgh survey (n=250)

Liège survey (n=1858)

Defining Consciousness
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

Demertzi et al, Prog Brain Res 2009
Demertzi & 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%

2,475 medical professionals

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

Laureys et al, Curr Opin Neurol 2005
Gold standard?

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>Coma Recovery Scale-Revised results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UWS</strong></td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>VS/UWS</td>
</tr>
<tr>
<td>MCS</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

UWS = unresponsive wakefulness syndrome. MCS = minimally conscious state.

Table 2: Diagnostic results by modality

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

Passive paradigms
“Imagine visiting the rooms of your house”
Boly et al, Lancet Neurol 2008

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

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

Consciousness  |  Moral significance  |  Assessing Consciousness  |  Conclusions
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
--- | ---
![](image1.png)


Smith et al, *PNAS* 2009

Consciousness | Moral significance | **Assessing Consciousness** | Conclusions
Default mode network (DMN)
DMN anticorrelations

Fox et al, *Proc N Acad Sci* 2005
External awareness
or anticorrelated network

Internal awareness
or Default mode network

DMN anticorrelations

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: 0.05Hz (range: 0.01-0.1)

Effect of awareness

- Normal consciousness
- Autobiographical mental imagery
- Hypnosis

<table>
<thead>
<tr>
<th>Consciousness</th>
<th>Moral significance</th>
<th>Assessing Consciousness</th>
<th>Conclusions</th>
</tr>
</thead>
</table>

**Consciousness**

**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. Wuyts², Ben Jeurissen², Jan Sijbers², Floris Vanhevel³, Steven Jillings¹, Paul M. Parizel³, Stefan Sunaert⁴, Paul H. Van de Heyning¹, Vincent Dousset⁵, Steven Laureys⁶ & Athena Demertzι⁶,⁷
Effect of environment

Consciousness | Moral significance | Assessing Consciousness | Conclusions

Post – Pre flight

Van Ombergen ... and Demertzi, Sci Reports 2017
Effect of pathology

Vanhaudenhuyse et al, Brain 2010
Systems-level organization

Heine, … & Demertz, *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

Demertzi & Antonopoulos et al, *Brain* 2015
Sanity check: generalization on healthy

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

N=159

Consciousness | Moral significance | Assessing Consciousness | Conclusions

Grant Type: Collaborative Activity Award, Phase I & II (2008-2017)

Demertzi*, Tagliazucchi*, Dehaene, Deco, ... Schiff, Owen, Laureys, Naccache, Sitt. under review
Patients cannot express *themselves*
SELF

CONSCIOUSNESS
WHICH SELF IN UNCONSCIOUSNESS?

social

COMMON VIEW: no self

HYPOTHESES: yes self

MODEL: Embodiment

narrative

HOW: Probe balance

minimal
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

- Consciousness:
  - needs to be inferred: framework for used technologies? (Demertzi, Sitt, Sarasso, Pinxten, Neurosci Consciousness 2017)
  - carries a moral significance
  - is not out there to capture
  - a matter of social consensus? (Nizzi, Blandin, Demertzi, NeuroEthics 2018)

Consciousness concerns us all
Thank you for your attention!

a.demertzi@uliege.be

@ADemertzi
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)

<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>
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</table>

n = 125

<table>
<thead>
<tr>
<th></th>
<th>EMCS</th>
<th>MCS</th>
<th>UWS</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIEGE</td>
<td>3</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>ONTARIO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VS/UWS-</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VS/UWS+</td>
<td>5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

n = 23

n = 11

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

Demertzi & Van Ombergen et al, Brain Structure and Function 2015
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
Validation in congenitally deaf
Validation in congenitally blind
Validation in propofol anesthesia
Clinical evolution

Kaplan–Meier estimation

n=67

Faugeras, Rohaut, Valente, Sitt, Demeret, Bolgerta, Weiss, Grinea, Marois, Quirins, Demertzi, Raimondo, Galanaud, Haberm, Engemann, Puybasse, Naccache, *Brain Inj* in press
Why does it matter?
The American Journal of Bioethics, 8(9): 3–12, 2008

**Target Article**

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

Benefit for patients?

Consciousness   |   Moral significance |   Assessing Consciousness

Continuity of self-image

Healthy controls (n=20)

LIS patients (n=44)


Nizzi & Demertzi et al, Conscious & Cogn 2012
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

Gosseries, Demertzi et al, Br Inj 2012
Methodological challenges

Heine, … & Demertzi, *Front Psychol* 2012
Consciousness  |  Moral significance  |  Assessing Consciousness  |  Ethics  |  Conclusions

How?

Demertzi & Gómez et al, *Cortex* 2014