The neural basis of Consciousness

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KU Leuven
May 7 2020
Consciousness in real-life

Terri Schiavo °1963, cardiac arrest, vegetative 1990, † 2005 USA
Laureys et al, *Curr Opin Neurol* 2005

Behavioural signs of Consciousness

- **Cognitive Capacity**
- **Motor Responsiveness**

Vegetative/Unresponsive

- Coma

Minimally Responsive

- Communication?
  - Awareness?
  - Arousal = eye opening

Moderate Disability

- Severe disability
- Live independently
- Good recovery
- Professional reinsertion

Severe Disability

- Moderate disability

- Good recovery
- Professional reinsertion

- Communication?
Not everyone agrees with guidelines

Demertzi et al, *J Neurol* 2011

Demertzi et al, *Prog Brain Res* 2009
Demertzi & Racine et al, *Neuroethics* 2012

2,475 medical professionals

<table>
<thead>
<tr>
<th></th>
<th>VS</th>
<th>MCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is acceptable to</td>
<td>66%</td>
<td>28%</td>
</tr>
<tr>
<td>stop treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>in a chronic...</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>VS</th>
<th>MCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>I would like to</td>
<td>82%</td>
<td></td>
</tr>
<tr>
<td>be kept alive</td>
<td></td>
<td>67%</td>
</tr>
<tr>
<td>if I were in a chronic...</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Feel pain</th>
<th>Do not feel pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>VS/UWS</td>
<td>59</td>
<td>77</td>
</tr>
<tr>
<td>(n=2259)</td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>Treatment can be</td>
<td>29</td>
<td>38</td>
</tr>
<tr>
<td>stopped in chronic...</td>
<td>**p&lt;.001</td>
<td>NS</td>
</tr>
</tbody>
</table>

Demertzi et al, *Prog Brain Res* 2009
Demertzi & Racine et al, *Neuroethics* 2012
We cannot always trust behavior

**Standardized assessment**

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


---

<table>
<thead>
<tr>
<th>JFK COMA RECOVERY SCALE - REVISED 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Record Form</strong></td>
</tr>
<tr>
<td>This form should only be used in association with the &quot;CRS-R ADMINISTRATION AND SCORING GUIDELINES&quot; which provide instructions for standardized administration of the scale.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient:</th>
<th>Diagnosis:</th>
<th>Etiology:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Onset:</td>
<td>Date of Admission:</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date of Admission:</th>
<th>Week (ADM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
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<tr>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>15</td>
<td>16</td>
</tr>
</tbody>
</table>

**AUDITORY FUNCTION SCALE**
- 4: Consistent Movement to Command *
- 3: Reproducible Movement to Command *
- 2: Localization to Sound
- 1: Auditory Startle
- 0: None

**VISUAL FUNCTION SCALE**
- 5: Object Recognition *
- 4: Object Localization: Reaching *
- 3: Visual Pursuit *
- 2: Fixation *
- 1: Visual Startle
- 0: None

**MOTOR FUNCTION SCALE**
- 6: Functional Object Use*
- 5: Automatic Motor Response *
- 4: Object Manipulation *
- 3: Localization to Noxious Stimulation *
- 2: Flexion Withdrawal
- 1: Abnormal Posturing
- 0: None/Flaccid

**OROMOTOR/VERBAL FUNCTION SCALE**
- 3: Intelligible Vocalization *
- 2: Vocalization/Oral Movement
- 1: Oral Reflexive Movement
- 0: None

**COMMUNICATION SCALE**
- 2: Functional: Accurate 1
- 1: Non-Functional: Intentional *
- 0: None

**AROUSAL SCALE**
- 3: Attention
- 2: Eye Opening with Stimulation
- 1: Eye Opening with Stimulation
- 0: Un arousable

**TOTAL SCORE**
- Denotes emergence from MCS
- Denotes MCS *

Giacino et al, *Neurology* 2002
To be conscious, we need a brain

(all of it?)
To be conscious, we need a functional brain.
Neuroimaging paradigms

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

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 stream of consciousness

William James (1842-1910)

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

• The human brain is approximately 2% of body’s weight

• 80% of this energy for neuronal signalling → most of consumed energy used for function

• Stimulus & performance-evoked changes in brain energy consumption are surprisingly small (typically <5%)

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

Task performance - Rest (fixation/eyes closed) → Deactivations

The brain’s default mode at rest

Demertzi & Whitfield-Gabrieli, in: Neurology of Consciousness 2nd ed. 2015
Demertzi, Soddu, Laureys, Curr Opin Neurobiology 2013
Demertzi et al, Front Hum Neurosci 2013
Raichle et al, PNAS 2001
Default mode network in DOC

Vanhaudenhuyse & Noirhomme et al, Brain 2010
DMN anticorrelations

Fox et al, PNAS 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, Soddu, Laureys, Curr Opin Neurobiology 2013
Demertzi et al, Front Hum Neurosci 2013
Cognitive-behavioral relevance

Vanhaudenhuyse*, Demertzi* et al, J Cogn Neurosci 2011
Anticorrelations and awareness

- Normal consciousness
- Autobiographical mental imagery
- Hypnosis

Demertzi, Soddu, Faymonville et al, *Prog Brain Res* 2011
Anticorrelations and wakefulness

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 Jillings³, Paul M. Parize⁶, Stefan Sunaert⁴, Paul H. Van de Heyning¹, Vincent Dousset⁵, Steven Laureys⁶ & Athena Demertzï⁶,⁷
Anticorrelations and environment

Van Ombergen ... and Demertzi, Sci Reports 2017
Demertzi et al, Brain Str Funct 2015
Anticorrelations and pathology

Vanhaudenhuyse et al, *Brain* 2010
Many resting state networks

Biswal et al., Magn. Reson. Med. 19

Smith et al, PNAS 2009
Long-range system connectivity disrupted

Number of subjects (%) with neuronal networks

Single-patient classification

<table>
<thead>
<tr>
<th>Performance measures</th>
<th>Accuracy</th>
<th>TPR healthy</th>
<th>TPR patients</th>
<th>Selected RSNs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Healthy vs. all patients</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuronal</td>
<td>85.3</td>
<td>.82</td>
<td>.87</td>
<td>Auditory, DMN</td>
</tr>
</tbody>
</table>

Demertzi & Gómez et al, Cortex 2014
Heine et al, Front Psychol 2012; Smith et al, PNAS 2009; Beckmann et al, Phil. Trans. R. Soc. B 2005
MCS> VS/UWS

<table>
<thead>
<tr>
<th>Network</th>
<th>Feature selection criterion (t-test)</th>
<th>Single-feature classification</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>t value</td>
<td>Rank</td>
</tr>
<tr>
<td>Auditory</td>
<td>8.32</td>
<td>1</td>
</tr>
<tr>
<td>Visual</td>
<td>7.79</td>
<td>2</td>
</tr>
<tr>
<td>Default mode</td>
<td>6.95</td>
<td>3</td>
</tr>
<tr>
<td>Frontoparietal</td>
<td>6.82</td>
<td>4</td>
</tr>
<tr>
<td>Salience</td>
<td>6.21</td>
<td>5</td>
</tr>
<tr>
<td>Sensorimotor</td>
<td>5.87</td>
<td>6</td>
</tr>
</tbody>
</table>

FWE p<0.05 (cluster-level)
Crossmodal connectivity classifies DOC

- 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
RS stationary connectivity:

- is linked to behavior and task performance (Laird et al., J Cogn Neurosci 2011)
- reflects physiological & pathological unconsciousness (Heine et al, Front Psychol 2012)
- permits single-patient automatic diagnosis (Demertzi & Antonopoulos et al, Brain 2015)

But

it remains unclear to what extent it provides a representative estimate of cognition (Peterson et al, NeuroImage Clin 2015)

Ongoing interactions among distinct brain regions (Hutchison et al, NeuroImage 2013)
From stationarity to dynamics

Stationary fc

Time-varying fc

Dynamic

\[ x_t = A \cdot x_{t-1} + e_t \]
**Brain dynamics and cognition**

**Typical wakefulness:** significance for performance, emotion and cognition

**Unconsciousness:** rigid spatiotemporal organization, less metastable dynamics

- **anesthesia**

The brain cannot map the complexity of the internal and external world
Patterns of recurrent coordinated activity

Demertzi & Tagliazucchi, Dehaene, Deco, Barttfeld, Raimondo, Martial, Fernández-Espejo, Rohaut, Voss, Schiff, Owen, Laureys, Naccache, Sitt. Science Advances 2019
Markov Process

- stochastic process that has no memory
- selection of next state depends only on current state, and not on prior states
- process is fully defined by a set of transition probabilities $\pi_{ij}$
  $\pi_{ij} =$ probability of selecting state $j$ next, given that presently in state $i$.
  Transition-probability matrix $\Pi$ collects all $\pi_{ij}$

Consciousness-level dependent

Transition-Probability Matrix

- Example
  - system with three states
  $\Pi = \begin{pmatrix} \pi_{11} & \pi_{12} & \pi_{13} \\ \pi_{21} & \pi_{22} & \pi_{23} \\ \pi_{31} & \pi_{32} & \pi_{33} \end{pmatrix} = \begin{pmatrix} 0.1 & 0.5 & 0.4 \\ 0.9 & 0.1 & 0.3 \\ 0.3 & 0.3 & 0.4 \end{pmatrix}$

- If in state 1, will stay in state 1 with probability 0.1
- If in state 1, will move to state 3 with probability 0.4
- Never go to state 3 from state 2

Demertzi & Tagliazucchi, Dehaene, Deco, Barttfeld, Raimondo, Martial, Fernández-Espejo, Rohaut, Voss, Schiff, Owen, Laureys, Naccache, Sitt. *Science Advances* 2019
Why does it matter?
### 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>
Quality of Life

Continuity of self-image


Nizzi, Blandin, Demertzi *NeuroEthics* 2018

Interpersonal attitudes impact experienced personhood

Prevalence of different attitudes among LIS patients and healthy controls.

- Lack of communication: 97%
- Objectification: 77%
- Lack of consideration: 63%

N=30
BRAIN

BRAIN-BODY INTERACTIONS
Cognition and somatic markers

Auditory oddball paradigm

Cardiac cycle phase acceleration only in MCS

Electrocardiographic markers carry independent information from EEG

Post interval

<table>
<thead>
<tr>
<th>VS/UWS</th>
<th>MCS</th>
<th>Healthy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (ms)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Federico Raimondo,1,2,3,4 Benjamin Rohaut, MD, PhD,5,6
Athena Demertzis, PhD,3,5 Melanie Valente,3,5 Denis A. Engemann,3,5,7,8
Moti Salti, PhD,9 Diego Fernandez Sleza, PhD,1,2
Lionel Naccache, MD, PhD,3,4,5,6,10 and Jacobo D. Sitt, MD, PhD,3,5
Warm water caloric irrigation

Baseline EOG
(eyes closed)

Nystagmus

amplitude
duration
Conclusions

Consciousness needs a brain which:
• is intrinsically organized
• shows complexity
• shows dynamic flexibility

Consciousness from brain-body interactions

Consciousness as a collective consensus

Consciousness ….
a.demertzi@uliege.be

ADemertzi