Detecting signatures of consciousness in cortical dynamics

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15 November 2018

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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

Functional connectivity in rest

Stationary

Allen et al, Cereb Cortex 2014
Stationary rs functional 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)
Dynamic functional connectivity in rest

Objectives | Methods | Results | Discussion

Stationary fc

Dynamic fc

Allen et al, Cereb Cortex 2014
Typical wakefulness: significance for performance, emotion and cognition
(Alavash, et al, Neuroimage, 2016; Shine et al., Neuron, 2016; Friston, Neuroimage, 1997;
Thompson et al., Hum. Brain Mapp, 2013)

Unconsciousness: rigid spatiotemporal organization, less metastable dynamics

• sleep (Tagliazucchi et al., PNAS 2013; Wang, et al, PNAS (2016;
Wilson et al., Neuroimage 2015; Chow et al., PNAS 2013)

• anesthesia
  ○ in humans (Tagliazucchi et al, J. R. Soc. Interface. 2016;
  ○ in animals (Barttfeld PNAS . 2014); Grandjean et al.,

The brain cannot map the complexity of the internal and external world
The aim:

to use spontaneous brain dynamics to detect signatures of consciousness in wakeful noncommunicating conditions
Disorders of Consciousness

- Coma
- General Anesthesia
- St I-II Sleep
- St III-IV Sleep
- Conscious Wakefulness
- Drowsiness
- Minimally Conscious state
- “Vegetative” unresponsive

Demertzi, Boly, Laureys. Encyclopedia of Consciousness 2009
Behaviour

Terry Schiavo °1963, vegetative 1990, † 2005 USA
### 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

<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>
</tbody>
</table>

- \( n = 23 \)

#### CMD

<table>
<thead>
<tr>
<th></th>
<th>VS/UWS-</th>
<th>VS/UWS+</th>
</tr>
</thead>
<tbody>
<tr>
<td>ONTARIO</td>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>

- \( n = 11 \)

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**Grant Type:** Collaborative Activity Award, Phase I & II (2008-2017)
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)
Diffusion Spectrum Imaging
Patterns (all sites)

Objectives | Methods | Results | Discussion

Pattern 1

Pattern 2

Pattern 3

Pattern 4

KW = 8e-13  UWS/MCS = 0.001

KW = 0.008  UWS/MCS = 0.8

KW = 0.4  UWS/MCS = 0.2

KW = 2e-9  UWS/MCS = 0.007

Rate of pattern occurrence (prob)

Rate of pattern occurrence (prob)

Rate of pattern occurrence (prob)

Rate of pattern occurrence (prob)
Patterns (different k)

| Objectives | Methods | Results | Discussion |

A

3 patterns

5 patterns

6 patterns

7 patterns

KW: 8e-10
Rho: -0.8, p = 9e-13
UWS/MCS = 0.001

KW: 4e-13
Rho: -0.7, p = 1e-17
UWS/MCS = 0.005

KW: 4e-15
Rho: -0.7, p = 2e-21
UWS/MCS = 0.002

KW: 8e-14
Rho: -0.7, p = 1e-18
UWS/MCS = 0.005
Patterns (per site)

A

Objectives | Methods | Results | Discussion

Training in Paris dataset

Pattern 1

Pattern 2

Pattern 3

Pattern 4

Training in Liège dataset

Pattern 1

Pattern 2

Pattern 3

Pattern 4

Training in NY dataset

Pattern 1

Pattern 2

Pattern 3

Pattern 4
**Structure-function correlation**

**Objectives | Methods | Results | Discussion**

\[ KW = 4 \times 10^{-11} \quad \text{UWS/MCS} = 0.007 \]

<table>
<thead>
<tr>
<th>Pattern 1</th>
<th>Pattern 2</th>
<th>Pattern 3</th>
<th>Pattern 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>R = 0.24</td>
<td>R = 0.34</td>
<td>R = 0.42</td>
<td>R = 0.67</td>
</tr>
</tbody>
</table>

- UWS
- MCS
- HC

\[ \times 10^{−1} \]

- ACC
- PCG
- PCG R
- STG L
- STG R
- ITG L
- ITG R
- LPC
- LPC R
- MPC
- PCG
- AG
- DLPC R
- DLPC C
- IPL R
- IPL C
- PMC L
- PMC R
- STA R
- STA L
- SMA R
- SMA L
- Oper L
- Oper R
- ParCing
- TempPol L
- TempPol R
- VLPFC
- dACC
- dACC R
- DLPC L
- DLPC C
- AssocVis R
- AssocVis L
- SecVis R
- SecVis L
- PrimVis R
- PrimVis L
The pattern exploration differs with respect to state of consciousness (1)

A. Between-pattern transition probabilities

Consciousness-level dependent

- Pattern 1 to Pattern 2: Rho=0.53
- Pattern 2 to Pattern 3: Rho=-0.33
- Pattern 3 to Pattern 4: Rho=-0.56
- Pattern 4 to Pattern 1: Rho=0.56

MCS vs. UWS

- Pattern 1 to Pattern 2: p=0.02
- Pattern 2 to Pattern 1: p=0.05
- Pattern 3 to Pattern 4: p=0.03
- Pattern 4 to Pattern 3: p=0.03

MCS > UWS
MCS < UWS
The pattern exploration differs with respect to state of consciousness (2)

B. Duration of pattern occupation

<table>
<thead>
<tr>
<th>Pattern 1</th>
<th>Pattern 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>KW=1.8e-6</td>
<td>KW=0.3</td>
</tr>
<tr>
<td>UWS/MCS=0.01</td>
<td>UWS/MCS=0.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean duration (s)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Paris</td>
<td>Liège</td>
</tr>
<tr>
<td>UWS</td>
<td>MCS</td>
</tr>
<tr>
<td>UWS</td>
<td>MCS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pattern 3</th>
<th>Pattern 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>KW=0.05</td>
<td>KW=6.1e-6</td>
</tr>
<tr>
<td>UWS/MCS=0.02</td>
<td>UWS/MCS=0.1</td>
</tr>
</tbody>
</table>

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<thead>
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<th>Mean duration (s)</th>
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We measure consciousness?

Pattern prediction in cognitive-motor dissociation

Pattern prediction in anesthesia

Objectives | Methods | Results | Discussion
Rs-fMRI dynamics:

- reveal complex inter-regional communication as compared to stationary fc
- differentiate states of consciousness uniformly across centers
- may reflect cognitive processing (str-funct corr)
- align with theoretical frameworks on the mechanisms of consciousness
--------- Forwarded message --------
From: Kevin LaBar <scienceadvanceseditorial@aaas.org>
Date: Thu, Nov 15, 2018 at 5:43 AM
Subject: Science Advances aat7603: Accept-Technical Hold
To: <tagliazucchi.enzo@googlemail.com>, <jacobositt@inserm.fr>, <a.demertzialiege.be>

Ref.: Ms. No. aat7603
Title: Human consciousness is supported by dynamic complex patterns of brain signal coordination

Dear Dr. Tagliazucchi, Sitt, Demertz,

We are pleased to inform you that our editors are preparing to accept your manuscript, referenced above. However, your paper cannot be formally accepted until some issues related to author paperwork and/or file types have been addressed.
Defining Consciousness

WHICH SELF IN UNCONSCIOUSNESS?

- social
  - COMMON VIEW: no self
  - HYPOTHESIS: yes self
- narrative
  - MODEL: Embodiment
  - HOW: Probe balance
- minimal
Thank you for your attention!

a.demertzi@uliege.be

ADemertzi
The Hilbert transform

Phase coherence
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 $\pi_{ij}$
  \[
  \pi_{ij} = \text{probability of selecting state } j \text{ next, given that presently in state } i.
  \]
  Transition-probability matrix $\Pi$ collects all $\pi_{ij}$

### Transition-Probability Matrix

#### Example

- system with three states

\[
\Pi = \begin{pmatrix}
\pi_{11} & \pi_{12} & \pi_{13} \\
\pi_{21} & \pi_{22} & \pi_{23} \\
\pi_{31} & \pi_{32} & \pi_{33}
\end{pmatrix} = \begin{pmatrix}
0.1 & 0.5 & 0.4 \\
0.9 & 0.1 & 0.0 \\
0.3 & 0.3 & 0.4
\end{pmatrix}
\]

- 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

#### Requirements of transition-probability matrix

- all probabilities non-negative, and no greater than unity
- sum of each row is unity
- probability of staying in present state may be non-zero