Brain, behavior and cognitive interplay in disorders of consciousness: A multiple case study

BAPS meeting
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UGent

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GIGA Consciousness
University of Liège

www.comascience.org
1. Introduction
Altered states of consciousness and diagnostic issues

Introduction

| Material and method | Results | Discussion |

- n=126 post-comatose patients
- Clinical consensus diagnosis:
  - 51 ‘vegetative state’
  - 18 signs of awareness
- Coma Recovery Scale - Revised

эм 30-40% potential misdiagnosis

Bodart, Gossedies & Laureys, Semin Neurol, 2013
Schnakers et al, BMC Neurology, 2009
Stender & Gossedies et al, Lancet, 2014
1) To study the behavioral, cognitive and neuroimaging profile of 5 different patients in MCS and EMCS

→Hypothesis: association between patients’ structural and functional brain damage and their behavioral/cognitive profile, consistent with previous studies establishing neural correlates of behavior, language and cognition.

2) To highlight the importance to develop new assessment tools to refine the cognitive profile of post-comatose patients
2. Material and method
Coma Recovery Scale-Revised (CRS-R; Giacino & al, 2004)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Date</th>
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</thead>
<tbody>
<tr>
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</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 Verbalization *
- 2 - Vocalization/Oral Movement
- 1 - Oral Reflexive Movement
- 0 - None

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

**AROUSAL SCALE**
- 3 - Attention
- 2 - Eye Opening w/o Stimulation
- 1 - Eye Opening with Stimulation
- 0 - Unarousable

**TOTAL SCORE**
Cognitive Assessment by Visual Election (CAVE; Murphy, 2018)

Cut-off score = 8/10
Cognitive profile in comparison with neuroimaging data

- **PET scan**
  - Injection of fluorodeoxyglucose
  - SPM12
  - FWE-corrected $p < 0.05$

- **Structural MRI – Voxel-based morphometry**
  - SPM8
  - FWE-corrected $p < 0.05$
3. Results
Case 1

Introduction | Material and method | Results | Discussion

**Male**

26 years old

16 months post-TBI

Right-handed

EEG ➔ slow theta dysrhythmia on posterior and temporal derivations of left hemisphere

### CRS-R: EMCS (functional communication)

- **CAVE Score**
  - Real objects: 9/10
  - Numbers: 9/10
  - Words: 9/10
  - Letters: 10/10
  - Pictures: /
  - Colors: /
  - No left/right differences
Case 2

Introduction | Material and method | Results | Discussion

Male
66 years old
30 months post-stroke and epilepsy
Right-handed
Male

**CAVE** | **Score**
--- | ---
Real objects | 7/10
Numbers | 9/10
Words | 6/10
Letters | 5/10
Pictures | 10/10
Colors | 7/10
Left/right differences

CRS-R: EMCS (functional use of objects)

EEG → significant left hemispheric damage with a nascent encephalopathy
**Case 3**

**Introduction**

Material and method

**Results**

- **Age:** 20 years old
- **Follow-up:** 13 months post-TBI
- **Handedness:** Right-handed
- **Gender:** Male
- **EEG:** Biased by abundant movement artifacts

**CAVE Score**

<table>
<thead>
<tr>
<th>CAVE</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Real objects</td>
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<tr>
<td>Numbers</td>
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<tr>
<td>Words</td>
<td>1/10</td>
</tr>
<tr>
<td>Letters</td>
<td>7/10</td>
</tr>
<tr>
<td>Pictures</td>
<td>9/10</td>
</tr>
<tr>
<td>Colors</td>
<td>5/10</td>
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</tbody>
</table>

No left/right differences

**CRS-R:** MCS+ (command-following)
Case 4

Introduction | Material and method | Results | Discussion

21 years old

3 years post-hypoglycemia

Female

Right-handed

CRS-R: MCS-
(visual + motor functions)

21 years old

3 years post-hypoglycemia

Right-handed

Female

EEG → significant encephalopathy with no sign of lateralization

<table>
<thead>
<tr>
<th>CAVE</th>
<th>Score</th>
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</thead>
<tbody>
<tr>
<td>Real objects</td>
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<tr>
<td>Numbers</td>
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<td>Words</td>
<td>2/10</td>
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<tr>
<td>Letters</td>
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<td>Pictures</td>
<td>NA</td>
</tr>
<tr>
<td>Colors</td>
<td>0/10</td>
</tr>
<tr>
<td>No left/right differences</td>
<td></td>
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</tbody>
</table>

No left/right differences
Case 5

Introduction | Material and method | Results | Discussion

Male
64 years old
13 months post-stroke

CRS-R: MCS-(visual + motor functions)

64 years old

13 months post-stroke

Right-handed

Male

CAVE | Score
---|---
Real objects | 4/10
Numbers | 3/10
Words | 1/10
Letters | 1/10
Pictures | 3/10
Colors | 2/10

Left/right differences

EEG → symmetrical slow dysrythmia with no paroxysm
4. Discussion
Patients’ general profile

- % of success on the CAVE // CRS-R total score
  → Consistent behavioral cognitive profile

- Highest scorer on bedside assessments: less extended hypometabolism

- Cognitive profile // structural/functional neuroimaging
### Specific functions

<table>
<thead>
<tr>
<th>Case</th>
<th>Behavior/cognition</th>
<th>Grey matter damage</th>
<th>Hypometabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>EMCS</td>
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<tr>
<td></td>
<td>CRS-R total score: 19</td>
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<tr>
<td></td>
<td>CAVE: 92.5%</td>
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<td>Case 2</td>
<td>EMCS</td>
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<tr>
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<td>CRS-R total score: 19</td>
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<tr>
<td></td>
<td>CAVE: 73%</td>
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<tr>
<td>Case 3</td>
<td>MCS plus</td>
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<tr>
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<td>CRS-R total score: 15</td>
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<td></td>
<td>CAVE: 67%</td>
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<tr>
<td>Case 4</td>
<td>MCS minus</td>
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<tr>
<td></td>
<td>CRS-R total score: 14</td>
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<td></td>
<td>CAVE: 23%</td>
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<tr>
<td>Case 5</td>
<td>MCS minus</td>
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<td></td>
<td>CRS-R total score: 12</td>
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<tr>
<td></td>
<td>CAVE: 23%</td>
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</tbody>
</table>

- **Visual fixation/pursuit // preserved occipital areas**
- **Spatial neglect**
  In both patients with left GM damage +++
- **Residual motor abilities**
  +++ in cases 1, 2 & 4
- **Residual language and executive functions**
  Yes/no code in case 1 // frontal lobules ok
  +++ in cases 1, 2 & 3
5. Take home message
Take home message

• Preliminary study!

• CRS-R & CAVE → Consistent behavioral/cognitive profile

• Brain-behavior relationships might be observed even in severely brain-injured patients

• Importance of the development of behavioral assessment tools, such as the CAVE
  – for clinical work (to refine patients’ profile)
  – for scientific interest (neural correlates in patients with severe brain injury)
Thank you!

For supplementary information:
caubinet@uliege.be
### GREY MATTER DAMAGE

<table>
<thead>
<tr>
<th>Case 1 &lt; CTR</th>
<th>L hippocampus</th>
<th>0</th>
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<tbody>
<tr>
<td>Case 2 &lt; CTR</td>
<td>L fusiform cortex</td>
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<td></td>
<td>L medial orbitofrontal cortex</td>
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<tr>
<td></td>
<td>R superior temporal cortex</td>
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<td></td>
<td>L calcarine</td>
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<td></td>
<td>R cerebellum</td>
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<td>Case 3 &lt; CTR</td>
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<td>L precentral cortex</td>
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<tr>
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<td>L hippocampus</td>
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<tr>
<td>Case 4 &lt; CTR</td>
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<tr>
<td>Case 5 &lt; CTR</td>
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<td>R supplementary motor area</td>
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### HYPOMETABOLISM

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<th>Case 1 &lt; CTR</th>
<th>L angular gyrus</th>
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<td></td>
<td>L thalamus</td>
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<td>Case 2 &lt; CTR</td>
<td>L inferior parietal</td>
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<td>Case 3 &lt; CTR</td>
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<td>R middle frontal cortex</td>
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<td>R middle cingulate cortex</td>
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