Sleep and residual cognitive processing in disorders of consciousness

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Overview

I. Background - Sleep and Brain Plasticity

II. Disorders of Consciousness – Recent data
   - Quest for neuronal markers for diagnosis and prognosis in (i) sleep and (ii) waking

III. Summary & Discussion

I. Introduction to Sleep

Sleep spindle (12-15Hz burst) is the electrographic landmark for the transition from waking to sleep with loss of perceptual awareness.

Memory Related Areas

Hippocampus

Mesial Prefrontal Cortex

Postcentral Gyrus

Precentral Gyrus


Schabus et al., PNAS, 2007
In the sleep laboratory…

**Spindles and General Cognitive Abilities**

- General Cognitive Ability ("g") measured with Raven's Advanced Progressive Matrices (APM)

**Finding 2**


**Finding 3**

Alzheimer's disease and spindle decrease

- More pronounced fast spindles decrease in AD than matched elderly controls.
- Even ipsilateral deviations after hemispheric strokes (e.g., Gottselig et al., 2002)

Disorders of Consciousness

- In cooperation with the
  - Albert-Schweitzer-Klinik (OA Dr. Pichler, Graz)
  - "Apalliker Care Unit" im Geriatriezentrum am Wienerwald (Prim. Dr. Domis, Wien)
  - Universitätsklinik für Neurologie, PMU (Prof. Dr. Trinka; PD Dr. Golaszewski; Dr. Kronbichler, Salzburg)
Consciousness' 2 components

**Vegetative State**
- CRS-R Coma Recovery Scale-Revised
- Minimally Conscious State

- Auditory Function Scale
  - 4: Consistent Movement to Command
  - 3: Reproducible Movement to Command
  - 2: Localization to Sound

- 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

- Behavioral assessment remains the gold standard to monitor level of consciousness in patients with DOC.
- Therefore, high rate of misdiagnosis (41%, Schnakers et al., 2009) for the vegetative state (VS).

**Minimally Conscious State** (VS without SWS, REM, Spindles, Circadian Rhythm)

**Autom State (MCS with SWS, REM, Spindles and high arousal index)**

Ongoing Project

**Quest for diagnostic and prognostic markers...**

- Motor Imagination & Linguistic Tasks
- PSG: Sleep/Wake Cycles, Spindles...

- "The opposite of black is white."

Ca. 15+10 min

Ca. 25+15 min

Ongoing Project

Sleep/Wake Cycles, Spindles...
Coma-Sleep Results
- CRC analysis -

<table>
<thead>
<tr>
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<th>VS</th>
<th>MCS</th>
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<tr>
<td>Circadian</td>
<td>8/15</td>
<td>5/9</td>
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<td>Cortical desynchr. arousal</td>
<td>4/19</td>
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<td>Spindles</td>
<td>2/19</td>
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<td>Slow wave sleep</td>
<td>17/19</td>
<td>9/9</td>
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<td>REM sleep</td>
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Complexity of sleep architecture appeared higher in MCS than VS.
- Especially, REM sleep, sleep spindles and cortical desynchronization arousals appear to differentiate.

- Preliminary SBG analysis -

More complex sleep architecture appears to be present in MCS (n=15) as compared to VS (n=19) patients (Chi² = 5.87, p = .053).

Coma-Sleep Results
CRS-R x Sleep Spindles

CRS-R (global score) is associated with spindle intensity at central and frontal recordings sites (e.g. C4, r² = .34, p < .05).

Brain response to the patient’s first name

Sequences of 8 equiprobable first names: the own name and 7 non familiar first names

Helmut Simon Patrick Hector Helmut Victor

Perrin, Schnakers, Schabus et al, Arch Neurol, 2006
"Active" EEG paradigm
(extended analyses from Schnakers, Perrin, Schabus et al., 2008)

12 controls (CO)
13 minimally conscious patients (MC)
8 vegetative state patients (VS)

Event-related theta synchronisation to counted own vs. other names even in VS patients, yet delayed!!

Fellinger, Schnakers, & Schabus, in revision

Theta (3.5-6.5Hz) phase locking

Controls
MCS
VS

Own Name (ON)
passive listening
• residual activation of frontal networks in MCS during appearance of the subject’s own first name

MCS
VS

Target unfamiliar name (TUN)
active counting
• residual activation of frontal networks in MCS patients while counting of an unfamiliar name

Linguistic Paradigm - sentence comprehension

Antonym sentence paradigm
Auditory presentation of 3 different word pairs embeded in the sentence
“The opposite of X is Y”

20 x antonym pairs (e.g. black – white)
20 x pairs of related words (e.g. black – yellow)
20 x pairs of unrelated words (e.g. black – nice)

Antonym vs. unrelated sentence endings - Time-frequency differences

MCS patients showed upper-alpha (10-12Hz) ERD (0-400ms) after the presentation of the antonym. Post-hoc semantic integration rather than predictive processing.

Controls revealed significant upper alpha ERS (0-600ms) in response to critical antonyms as well as a small alpha ERD in response to the semantic violation (unrelated words).

Schabus et al. (2011)
Observation and imagination of a simple motor behaviour

a) Theta band (4-7Hz) activation. Note the strong evoked response in the early time window (0-500ms after video onset) in controls, but also MCS patients.

b) Lower alpha band (8-10Hz) desynchronization is strongest in controls during video observation. Again a similar response in MCS patients can be observed.

c) While SMR (12-15Hz) frequency desynchronizes in control subjects, MCS patients synchronize.

Lower alpha + SMR topography

Strong desynchronization during observation of a motor behaviour "Mirroring"

Occipital desynchronization in the lower alpha band attention-modulated visual processing?

Central synchronization in the SMR band integration of somatosensory information? (cf. Beta synchronization in imagery)

Overall Conclusion

Residual cognitive processing in DOC can be identified using EEG, which would be undetected using classical behavioral assessments (ethical relevance; diagnosis/prognosis)

Sleep in DOC might be a potential tool to distinguish VS from MCS.

Yet to-date very hard to do reliably statements on a single subject level…
Recent Joint COST Publications


THE END.