

EEG-based Detection of Covert Awareness in Disorders of Consciousness

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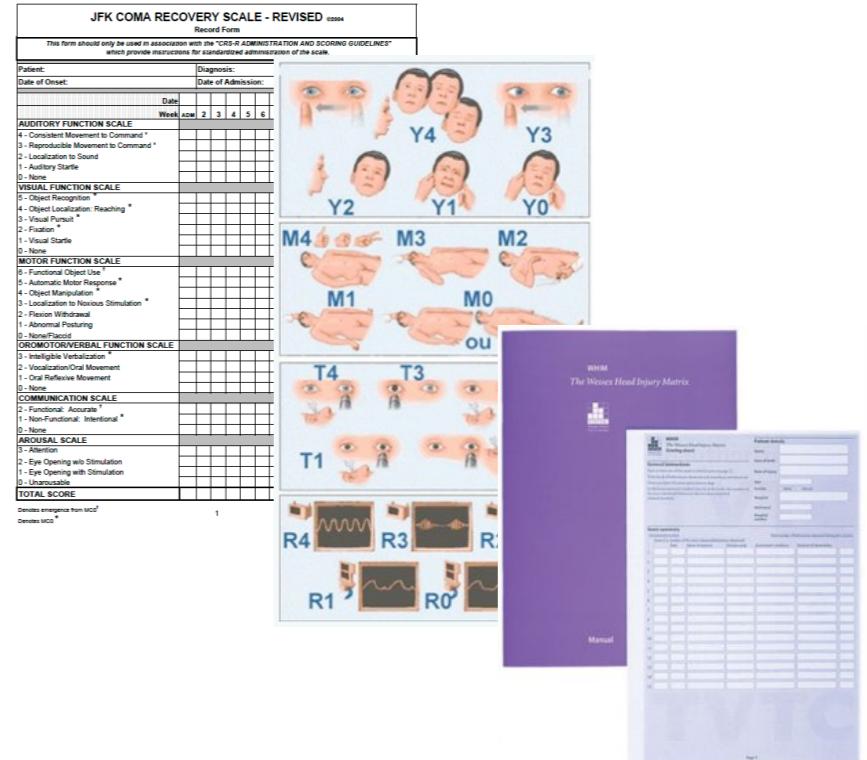
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Consciousness and Its Disorders

	Wakefulness	
Awareness	Awake	Not Awake
Aware	You?	REM Sleep
Not Aware	Vegetative State	Coma

Behavioural Assessment

- FOUR / GCS / WHIM / SMART;
- Coma Recovery Scale-Revised (CRS-R) – Giacino et al., 2004;



- **Patients in the Vegetative State**: Retain autonomic functions with variable preservation of cranial and spinal reflexes; Exhibit no evidence of sustained, reproducible, purposeful, or voluntary behavioural responses to multi-sensory stimulation; No evidence of language comprehension or expression; No response to command.

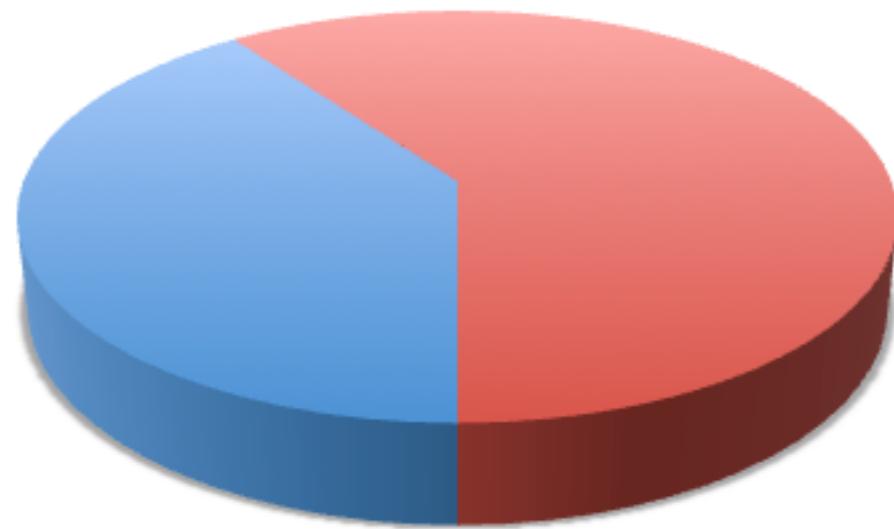
The Problem of Subjectivity

- Ultimately, diagnosis depends on the response to verbal commands;
 - Consistency?
 - Volitional or spontaneous?
- Up to 40% of VS patients have been misdiagnosed;
 - Schnakers et al., 2009; Childs et al., 1993;



Considered to be Vegetative

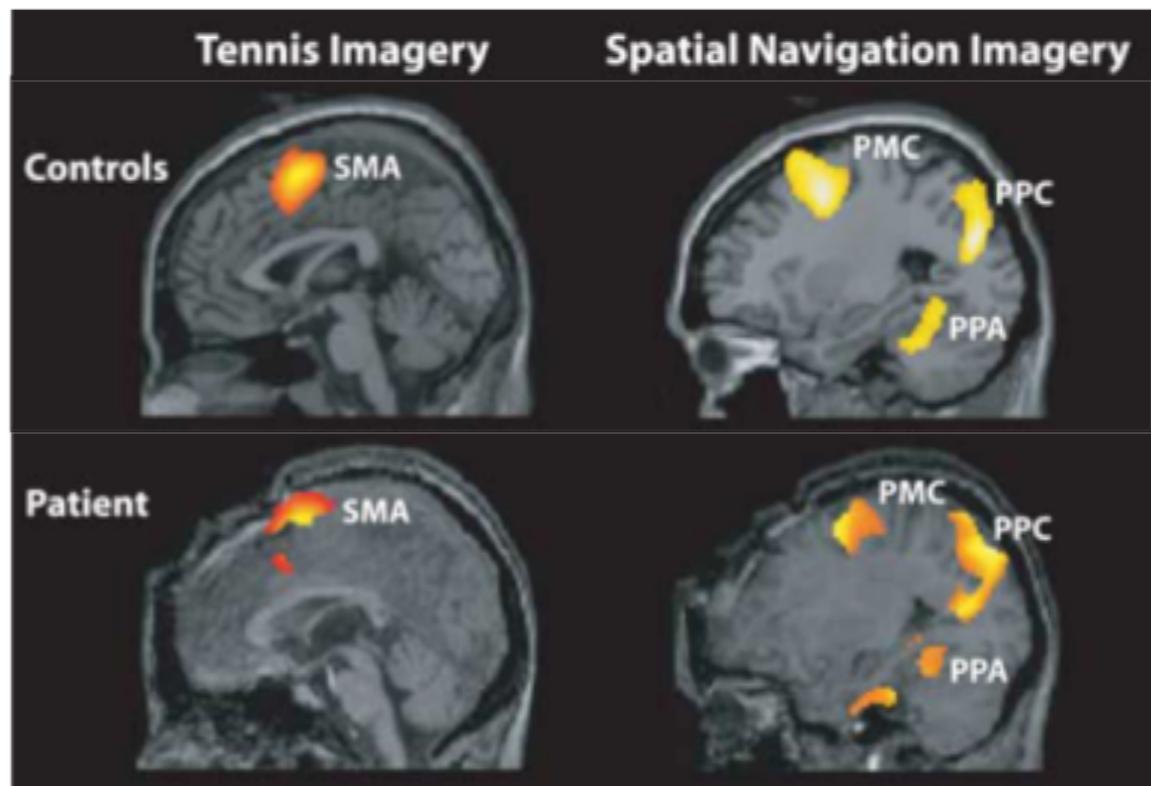
**Minimally-
Conscious**



**Truly
Behaviourally
Vegetative**

Volition as a Marker of Awareness

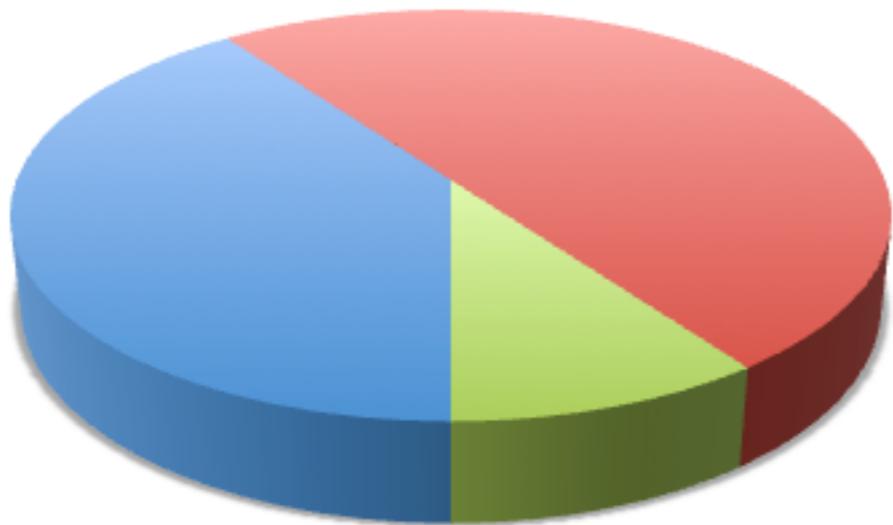
- **Owen et al., 2006, Science**
- Neural manifestation of command-following in a vegetative patient in the MRI scanner;



- **Monti et al., 2010, NEJM** 17% of patients thought to be VS show similar signs of awareness.

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**Something
else?**

- Diagnosis of 'vegetative' required before end-of-life legal proceedings;
- Caregiver expectations, everyday medical decisions (e.g. pain-relief).

fMRI vs EEG

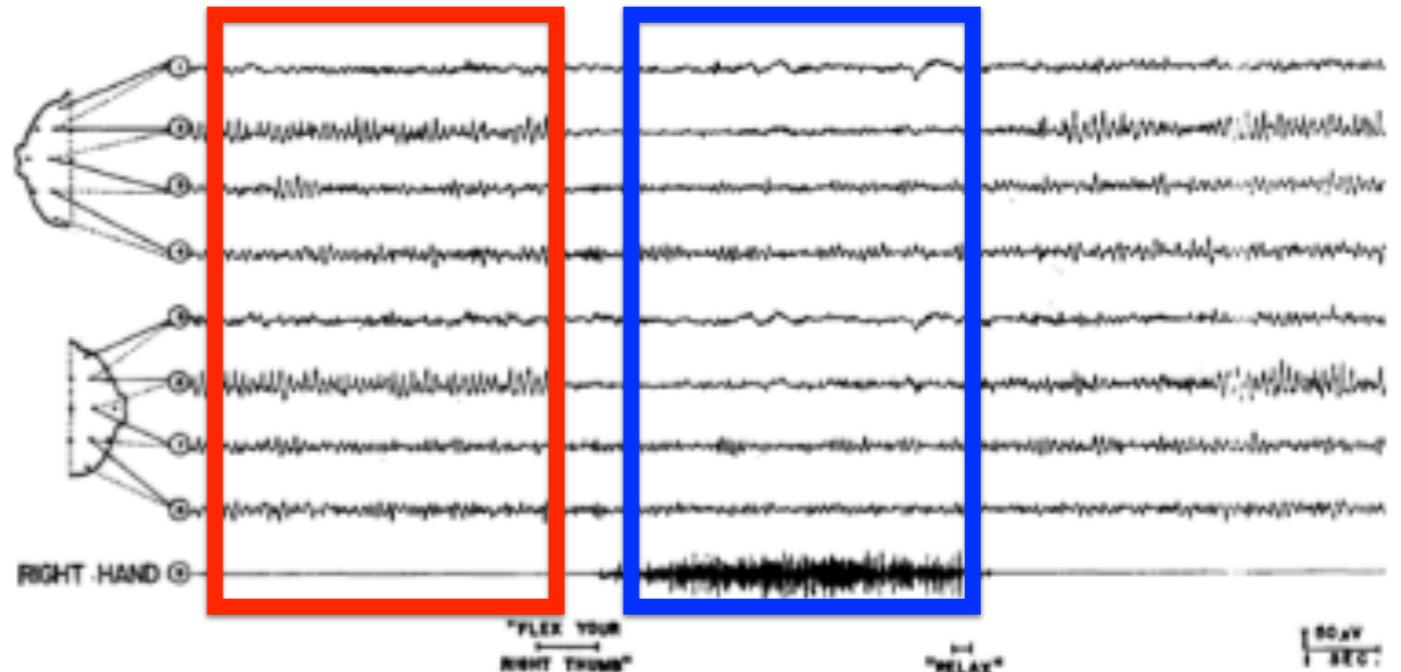
- **fMRI accessibility issues for patients**
- Expense / Availability;
- Metallic implants – plates/pins;
- Physical stresses;
- Movement artefacts in analyses.



- **Benefits of EEG** Relatively inexpensive; Can be used at the bedside; Greater number of measurements

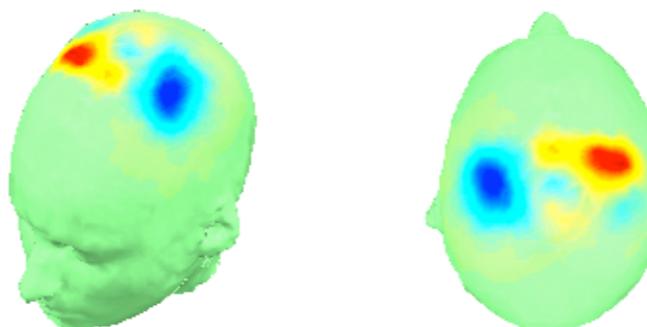
Motor movements in EEG

- Reduction in power of mu/beta bands (7-30Hz) of the EEG signal across the motor area;



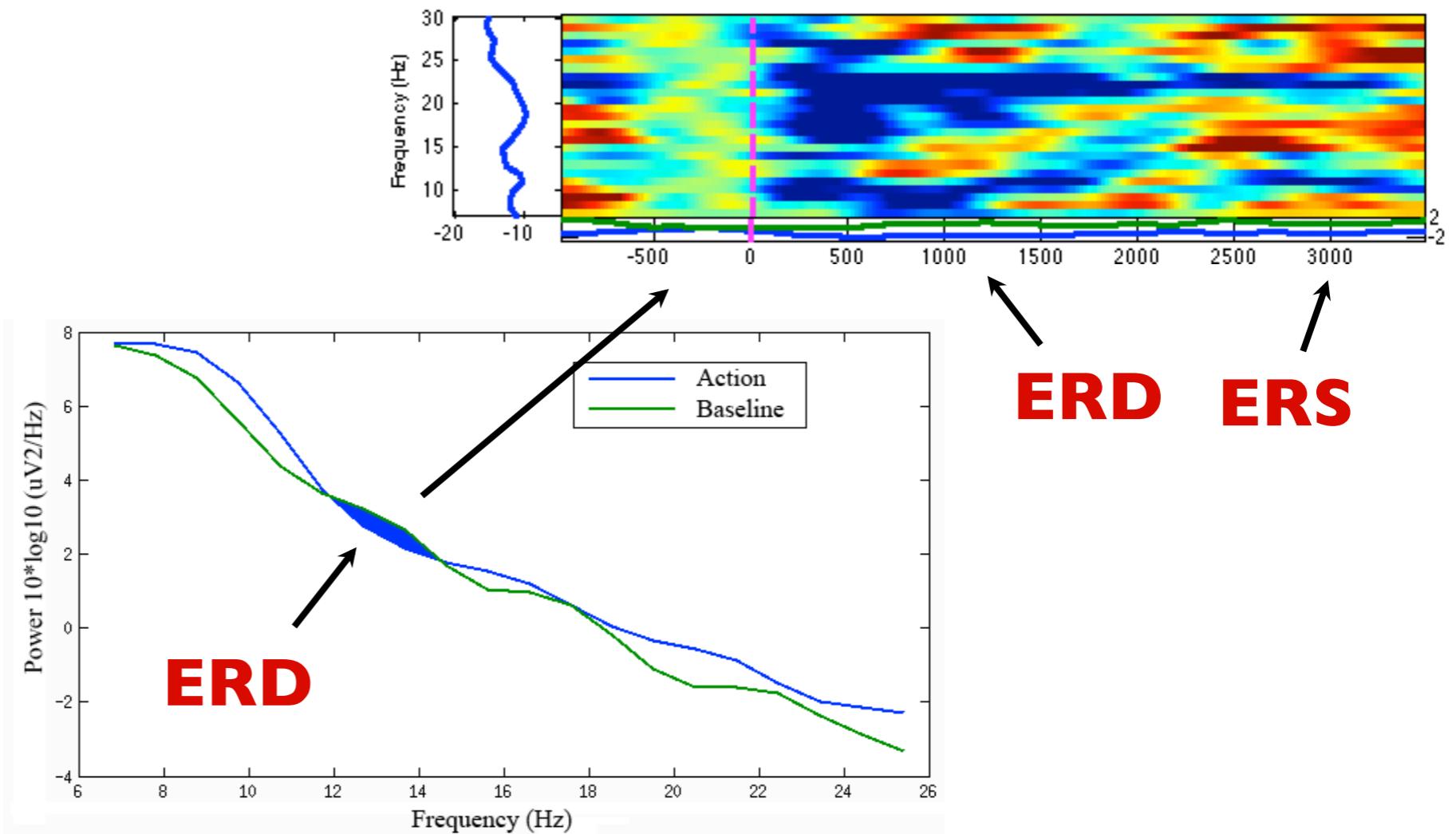
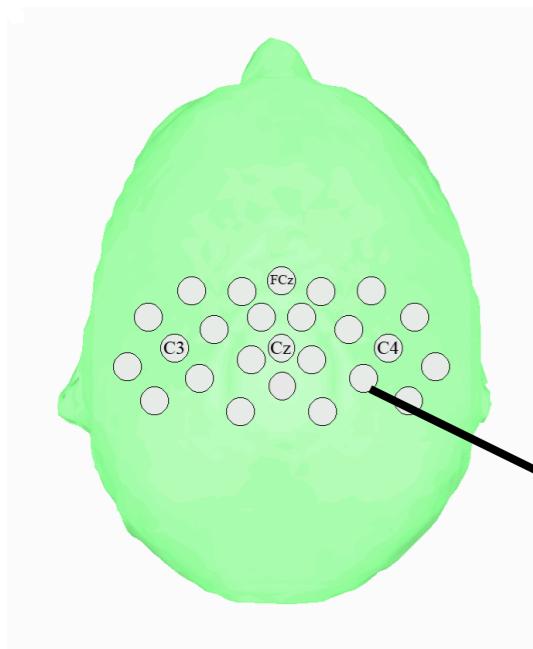
from Chatrian et al., 1958

- Mu/beta bands are an idling rhythm of the sensorimotor cortex; A reduction in power – **event-related desynchronisation (ERD)** – reflects activation of the underlying cortex;
- Topographically distributed.



Motor Imagery and EEG

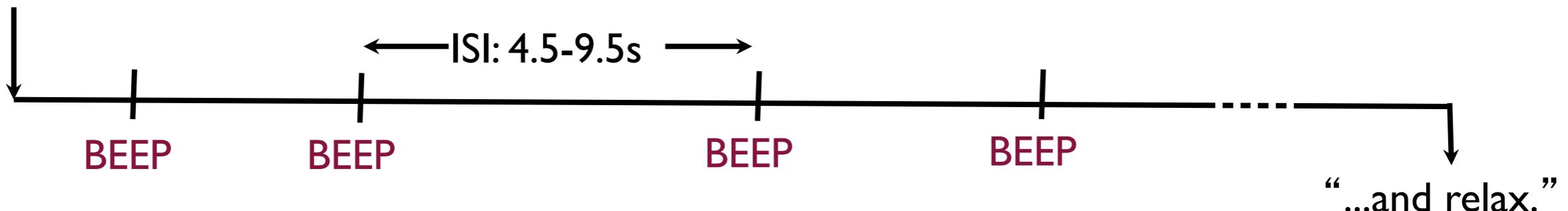
- Used extensively in Brain-Computer Interfacing applications



- In healthy individuals, with machine learning, these responses can be classified and translated into output:
 - e.g. moving a cursor, driving a wheelchair, playing a video game.
 - Showing you can follow commands?**

The Motor Imagery Task

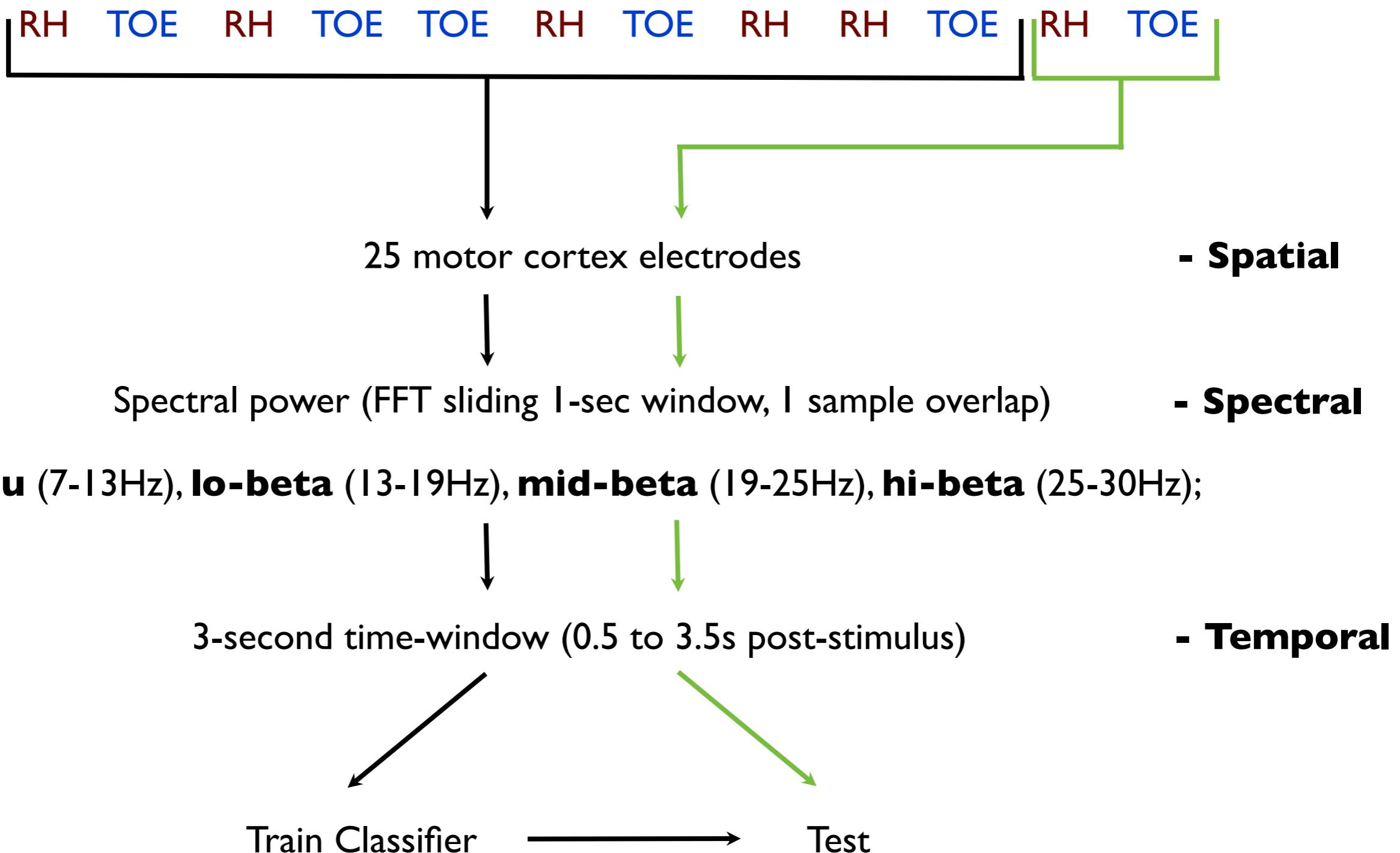
- “Every time you hear a beep, imagine that you are **squeezing your right-hand into a fist // wiggling all of your toes**, and then relaxing. Concentrate on the way the muscles would feel if you were really doing this. Try to do this as soon as you hear each beep.”



- 4-6 blocks of 15 tones each - **same tone** every time; **different instruction**
- EEG recorded from **129-channel** Electrical Geodesic Inc. electrolytic net:
- Quick application; No skin abrasion required; No gel residue
- 25 electrodes** over motor cortex analysed (1-40 Hz filtering, local average reference)
- Cross-validated classification of spectral power in **mu** (7-13Hz), **lo-beta** (13-19Hz), **mid-beta** (19-25Hz), **hi-beta** (25-30Hz) in ‘right-hand’ vs. ‘toe’ trials

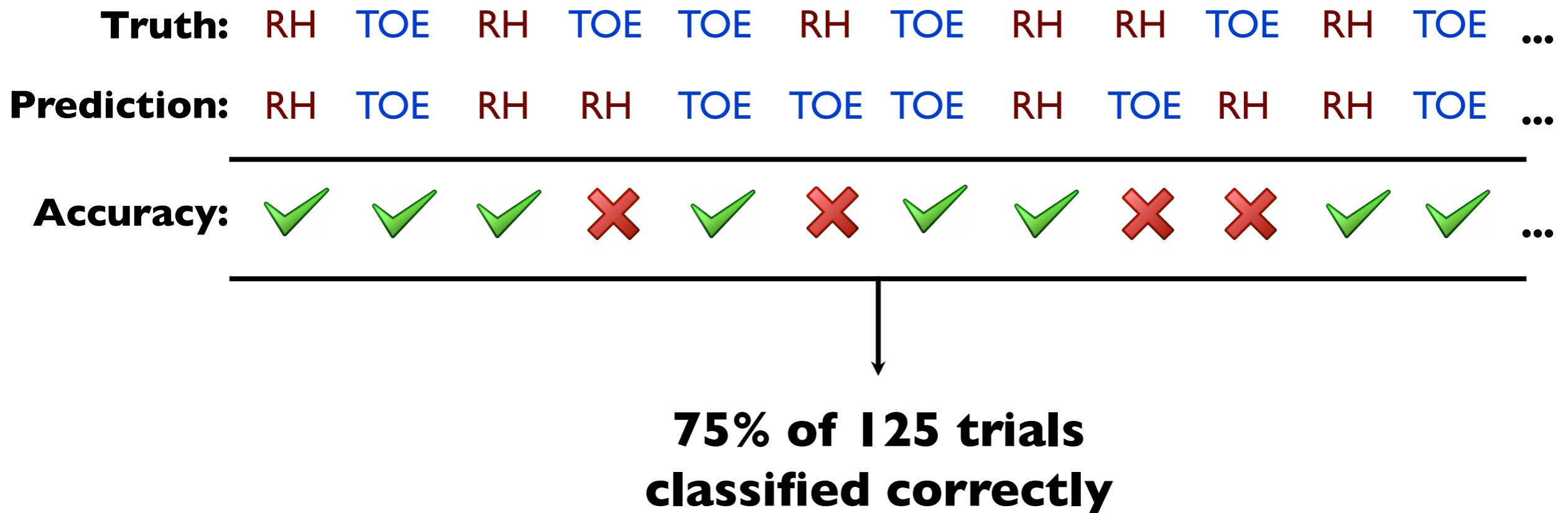
The Analysis Pipeline

- Block-wise cross-validation:



- Repeat so every block is tested exactly once;

The Analysis Pipeline



- Binomial test that classification is above chance ($\alpha = .01$):
- i.e. the spatio-temporal characteristics of the EEG spectra are consistent within Right-Hand trials and within Toe trials;
- The commands were successfully followed.

Healthy Participants

- 12 healthy participants (aged 21-31);
- **75%** of the group returned positive results
 - i.e. significantly above chance classification of command-following;
- Mean Classification accuracy of **68%** (range **60-91%**);



Feature Weight Plot

- The same participants asked **not** to follow the commands:
 - None returned a positive EEG result;
 - A positive EEG result requires a volitional decision to follow the given commands.



Patient Assessment

- **16** patients (**5** traumatic) assessed at two centres;
- Age: **14** to **63**-years (median 38.5-years);
- Time post-ictus: **1** to **94**-months (median 22-months);
- Behaviourally assessed with Coma Recovery Scale-Revised across 4-5 days admission;
- Maximum CRS-R scores: **3** to **7** (median **6**).



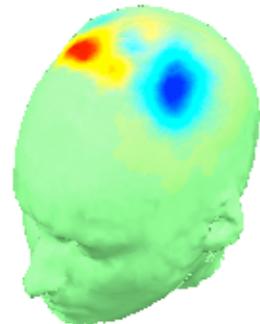
Addenbrooke's Hospital, Cambridge, UK



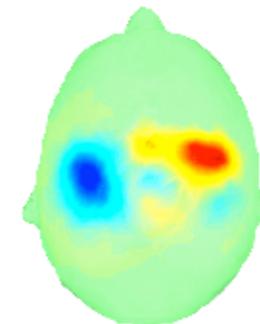
University Hospital of Liège, Belgium

Command-following in the Vegetative State

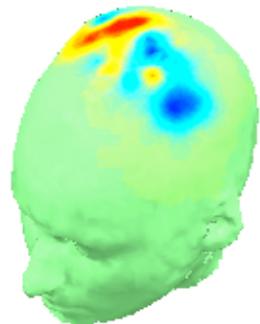
- 3 of 16 patients returned positive EEG command-following results ($p < .01$);



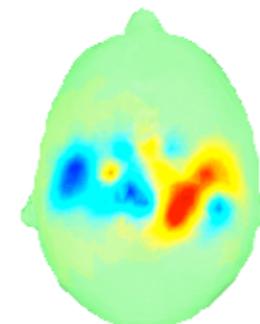
91%



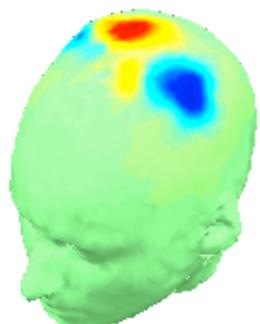
- Healthy Control.



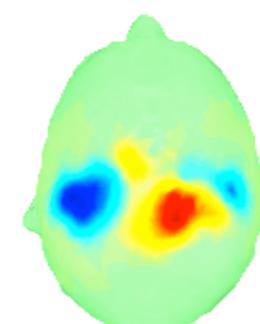
61%



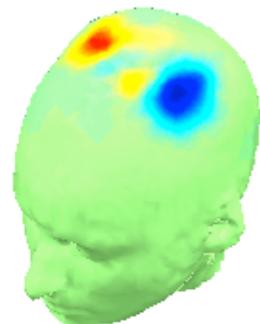
- 35-year old male, 9-months post-ictus, **anoxia**.



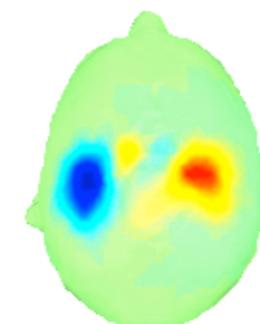
71%



- 45-year old male, 23-months post-ictus, **trauma**.



78%



- 29-year old male, 3-months post-ictus, **trauma**.

What is the Correct Diagnosis?

- **Behavioural examination was not sufficient to accurately describe the level of awareness in 19% of our sample.**
- We cannot draw strong conclusions about their inner worlds...
- However, successfully following-command across >100 trials requires:
 - working memory;
 - response selection;
 - language comprehension;
 - sustained attention;
- Key aspects that characterise awareness.

Patients who follow command might be relatively more 'aware'.

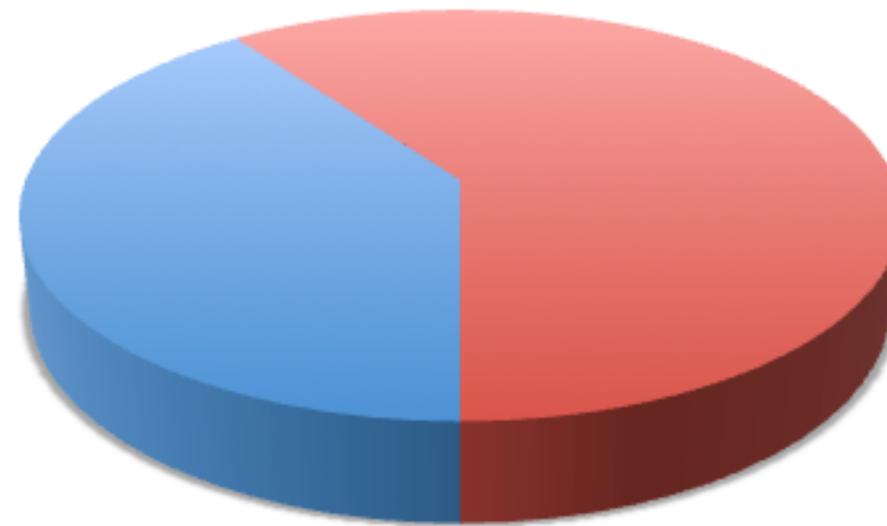
*But what are they aware **of**?*



The Problem of the Minimally-Conscious State

**Considered to be
Vegetative**

**Minimally-
Conscious**

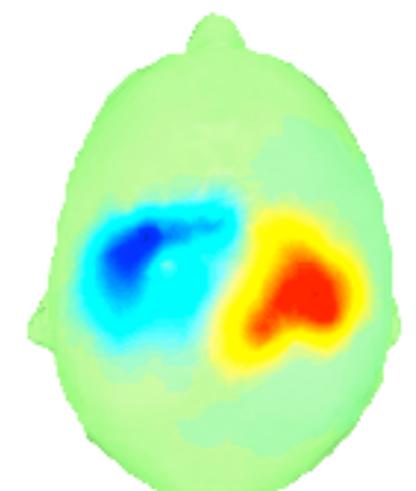
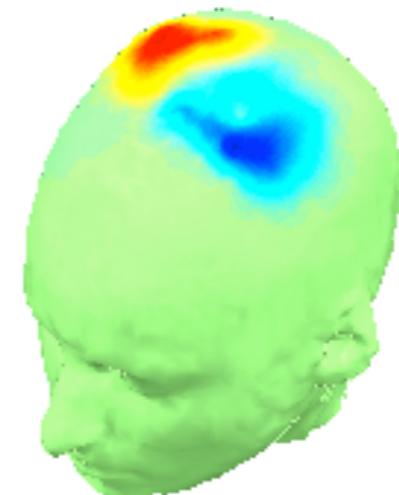


**Truly
Behaviourally
Vegetative**

- 40% of patients considered ‘vegetative’, are actually in the minimally-conscious state (e.g. Schnakers et al., 2009; Childs et al., 1993);
- Minimally-conscious patients produce **inconsistent but reproducible** signs of awareness.
 - What can our EEG assessments of command-following tell us about this state?

Command-following in the Minimally-Conscious State

- **23** patients (15 traumatic);
- Age: **11** to **79**-years (median 36-years);
- Time post-ictus: **1** to **109**-months (median **18**-months);
- Behaviourally assessed with Coma Recovery Scale-Revised across 4-5 days admission.
- Maximum CRS-R scores: **7** to **16** (median **11**);
- **7 MCS patients (30%) followed commands significantly with their EEG response**



Command-following in the Minimally-Conscious State

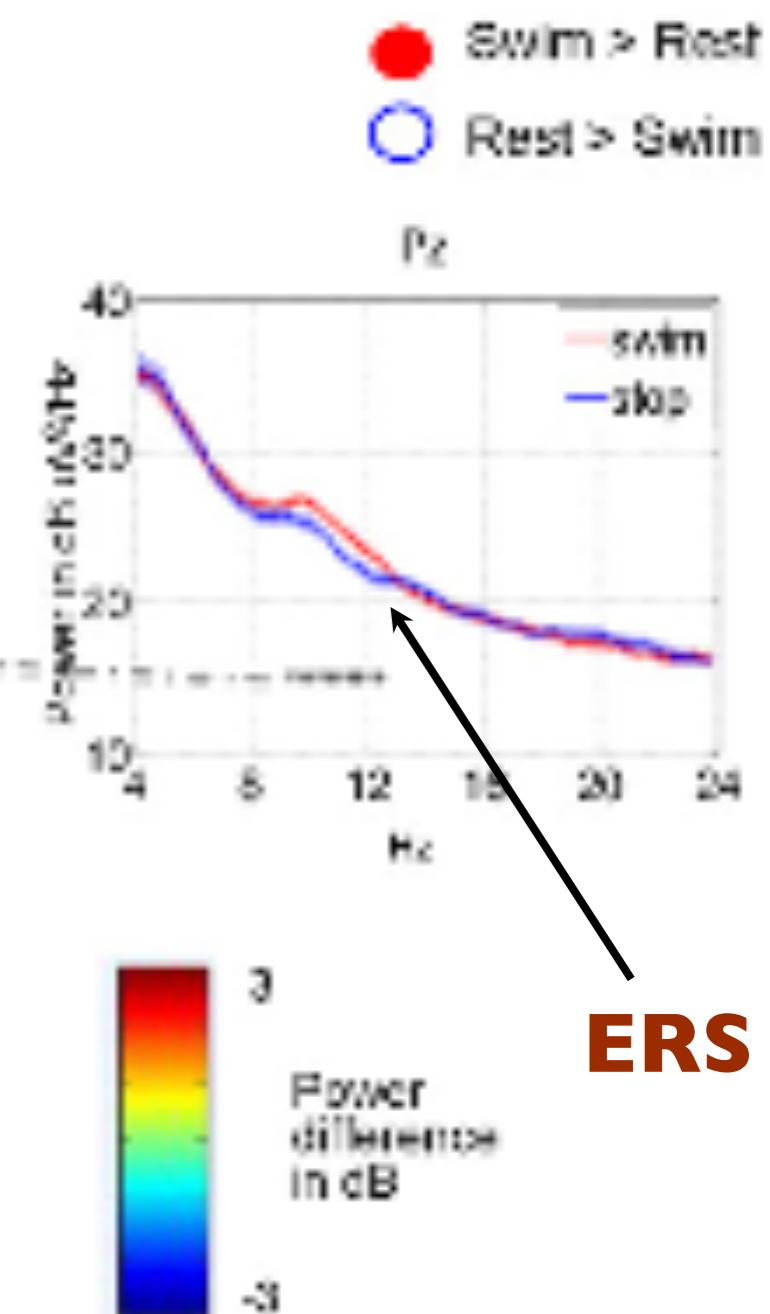
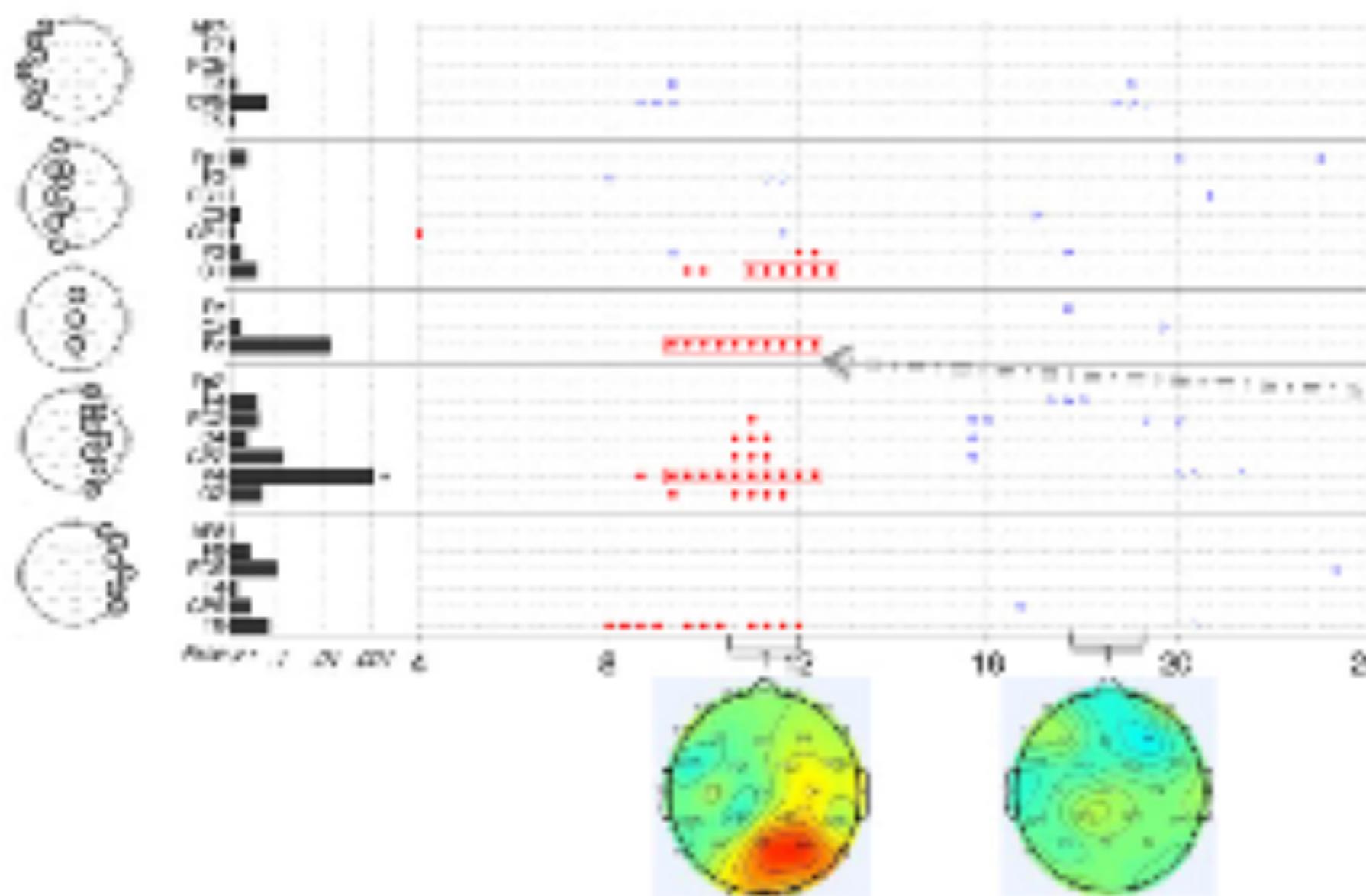
EEG Command-Following	
Traumatic	33% (5/15)
Non-Traumatic	0% (0/8)

Fisher's Exact Test, p<.05

- Non-traumatic MCS patients are less likely to produce evidence of high-level cognitive functions than traumatic patients
- Other factors like age, time post-ictus do not explain pattern.
- All 3 traumatic MCS patients who could not follow commands with their behaviour, were able to with this EEG assessment.

Related Research

- 19-year old MCS patient, 6 months post-ictus, Trauma.
- Asked to imagine swimming or rest



Critiques



“Command following does not tell us anything about self-awareness”

We cannot make claims about subjective conscious experience of patients. But command following is commonly used in standard clinical practice to test for awareness. So we are doing no worse.



“Your patients weren’t really vegetative”

If so, this is despite repeated behavioural assessment on standardised scales by clinical experts. This only serves to highlight the challenges inherent in basing awareness solely on behaviour.



“Your methodology is not robust enough to be sure either way”

Various controls in place to limit false positives....

Could this be done without awareness?

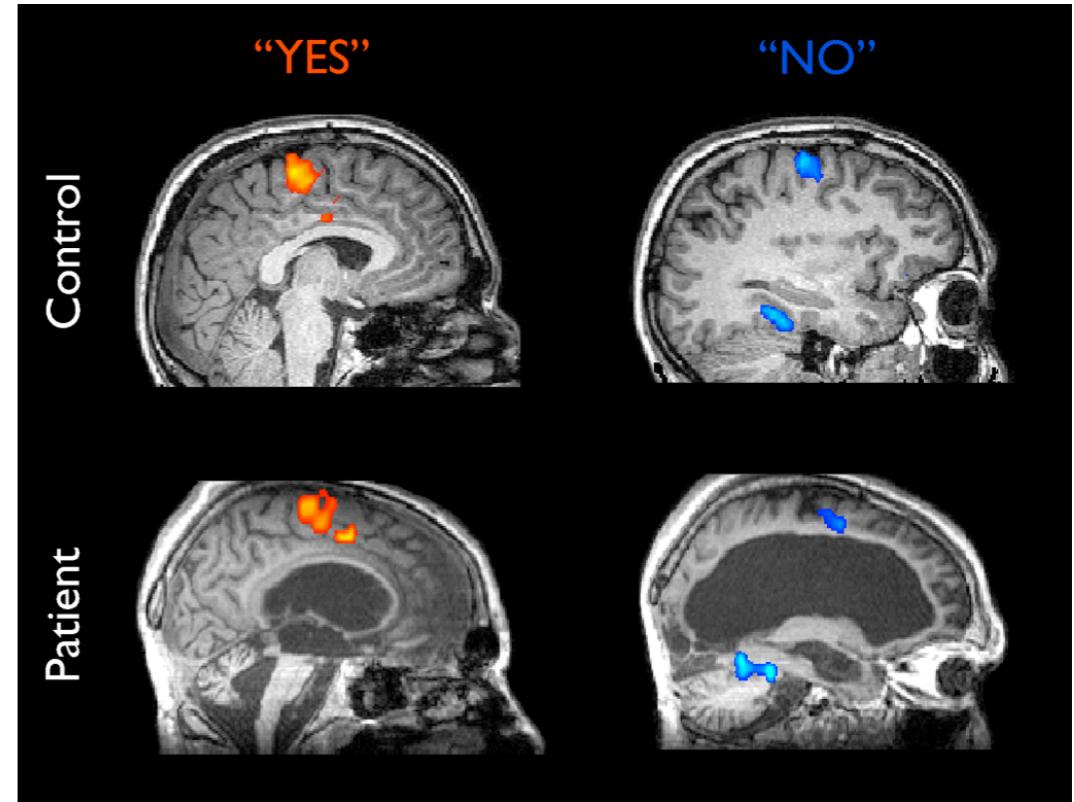
- Unlikely. Task instructions delivered once at the beginning of each randomised block of 15 tones;
- Identical tones regardless of imagery type, at random intervals;
- Significantly higher classifiability in post-tone time w.r.t. pre-tone
- **Healthy Controls**
 - 75% of healthy controls told **to follow commands** returned positive results;
 - **None** of the same controls told **not to follow commands** returned positive results;
- **Patients**
 - Topographically sensible modulation of EEG
 - In over 100 trials of imagery



Future Potential - Communication

- Monti et al., 2010, NEJM:

- Used fMRI BCI to allow a VS patient to answer yes/no questions.



- EEG provides many possibilities for this challenging patient group:
 - Functional communication and its implications for family, medical care
 - Measuring cognitive processes and inner worlds of these patients

Future Challenges



“How do we account for the significant variability in arousal?”

Patients (especially MCS) often have continual variation in arousal. Both tests and analysis techniques should be sensitive to this.



“What questions might we want to ask?”

Ones with independently verifiable answers? Questions affecting their clinical care needs? Questions to test their self-awareness?



“What do we do with the answers?”

Clear ethical guidelines should direct the use of these techniques

Summary

- Motor Imagery and EEG can detect awareness in patients thought to have none;
 - First time this has been done outside the fMRI scanner;
 - Improves diagnostic accuracy compared with behavioural assessment alone;
 - EEG makes large-scale studies possible:
 - e.g. prevalence, effects of aetiology, age, time post-ictus;
 - Future potential for EEG-based communication devices.



Thanks!

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