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Spectral signatures of brain networks in disorders of consciousness and sedation

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INTRODUCTION

OVERVIEW

Impaired states of consciousness are characterised by distinct signatures of brain networks. These signatures often reflect the level of behavioural responsiveness, thus giving us insight into how the brain subserves consciousness. Furthermore, brain network patterns can reveal covert processes that differentiate between conditions of impaired consciousness.

CLINICAL SIGNIFICANCE

Understanding the mechanics of consciousness impairment would have multifaceted clinical benefits. Up to 42% of patients with disorders of consciousness are misclassified[1], 1 in 1000 individuals remain inadvertently aware during anaesthesia[2], and current behavioural measures for prognosis after severe brain injury are insufficiently informative[3].

A BETTER SOLUTION?

Graph theory can quantify key properties of connectivity networks of the brain at various organization scales. Thus, it can potentially inform about brain states of patients with disorders of consciousness or under sedation, patients, thus aiding in clinical diagnostics and prognosis.

SUMMARY

We present three studies that use electroencephalographic (EEG) data recorded at the bedside to investigate patterns and dynamics of functional brain networks during three conditions of pharmacologically and pathologically impaired consciousness.

METHODS

Samples used from populations with impaired consciousness

Sedation

20 healthy subjects; Sedative: propofol; 7 min recordings at baseline, mild sedation, moderate sedation and recovery.

Disorders of consciousness

Traumatic coma

No wakefulness, no awareness

16 patients; Bedside overnight recordings early after injury (acute phase); CRS-R outcome scores recorded after 2 months.

Vegetative state

Wakefulness without awareness

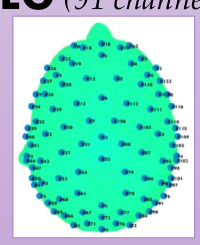
Minimally conscious state

Wakefulness with partial awareness

32 chronic patients (13 VS, 19 MCS); 64 healthy controls; 10 min of resting state data.

EEG ANALYSIS

High-density EEG *(91 channels)*



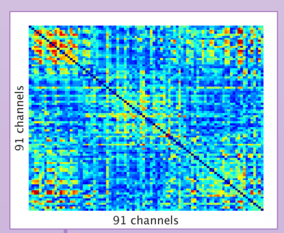
Cross-spectral analysis

Canonical frequencies:

- *Delta: 1-4 Hz*
- *Theta: 4-8 Hz*
- *Alpha: 8-13 Hz*

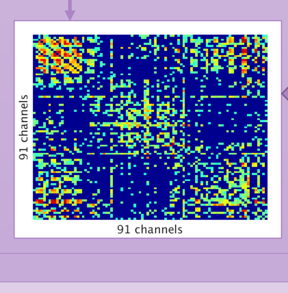
Connectivity networks

WPLI matrix

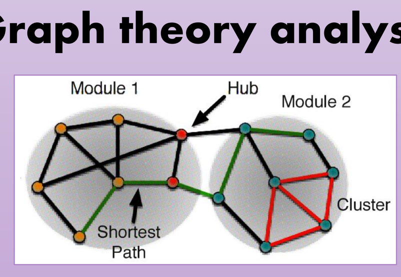


Threshold

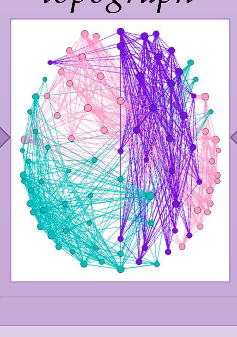
Keep 10-50% strongest connections



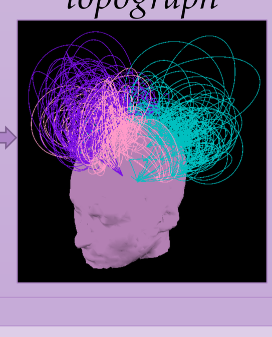
Graph theory analysis



Flattened topograph



3D topograph



CONNECTIVITY NETWORKS

The **Weighted Phase Lag Index (WPLI)**[4] estimates functional connectivity between pairs of nodes (here, scalp electrodes). It uses cross-spectral analysis to compute phase differences between signals and it corrects for volume conduction.

ASSESSING RESPONSIVENESS

During sedation: **drug level in blood** and **hit rate** during a simple button press auditory discrimination task.

In disorders of consciousness: the **CRS-R (Coma Recovery Scale Revised)**[5], which measures the degree of visual, auditory and motor response, communication ability, and wakefulness.

What network properties can graph theory discover?[6]

Segregation

The presence of local, specialised groups of nodes at micro- and mesoscale level: *node clustering coefficient, modularity.*

Integration

The facility of long-range information exchange across nodes in the network at macroscale level: *characteristic path length, global efficiency.*

Node centrality

Nodes involved in information exchange between modules: *betweenness, participation coefficient.*

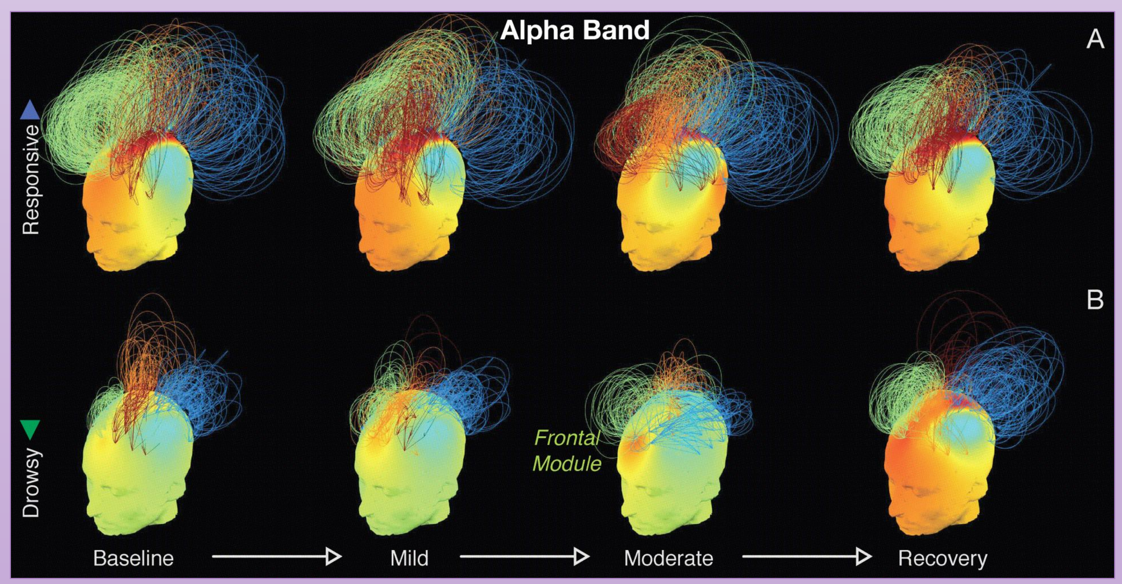
RESULTS

SEDATION[7]

Subjects were split into 2 groups:

Responsive: *Subjects who remained responsive during moderate sedation.*

Drowsy: *Subjects who stopped responding during moderate sedation, at the same blood level of drug.*

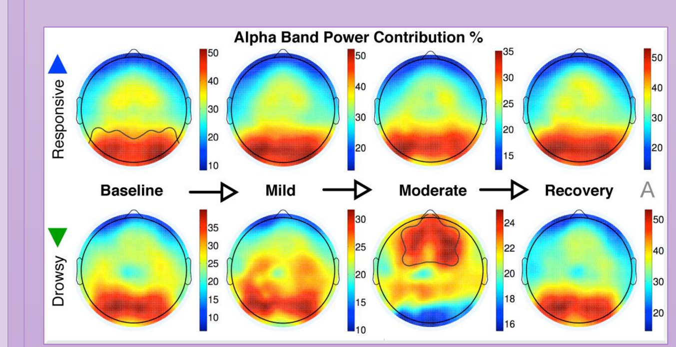


Alpha band connectivity networks predict behaviour under similar anaesthetic blood level.

The responsive group showed a stable fronto-centro-occipital pattern of connectivity, whereas drowsy group networks altered significantly.

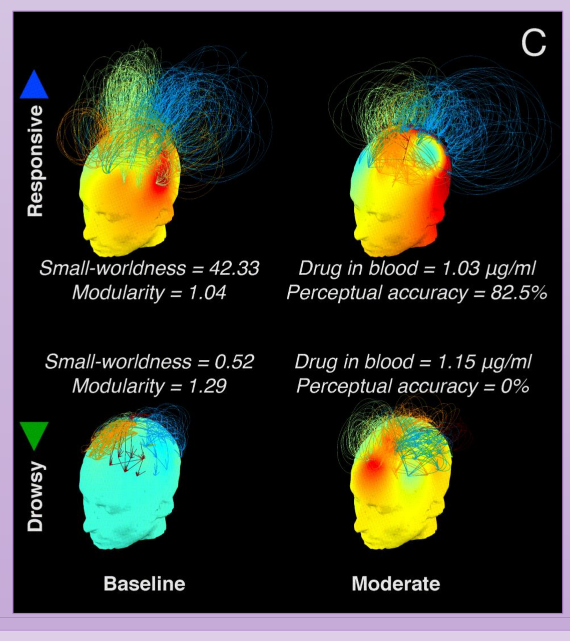
Alpha band power changes as a function of sedation.

Alpha network connectivity changes mirror alpha power changes during sedation.



Alpha network properties *before* sedation predict susceptibility to propofol.

Despite no differences in alpha power strength or topography before sedation, small-world-ness properties of alpha networks predicted whether subjects stopped responding during moderate sedation.



COMA

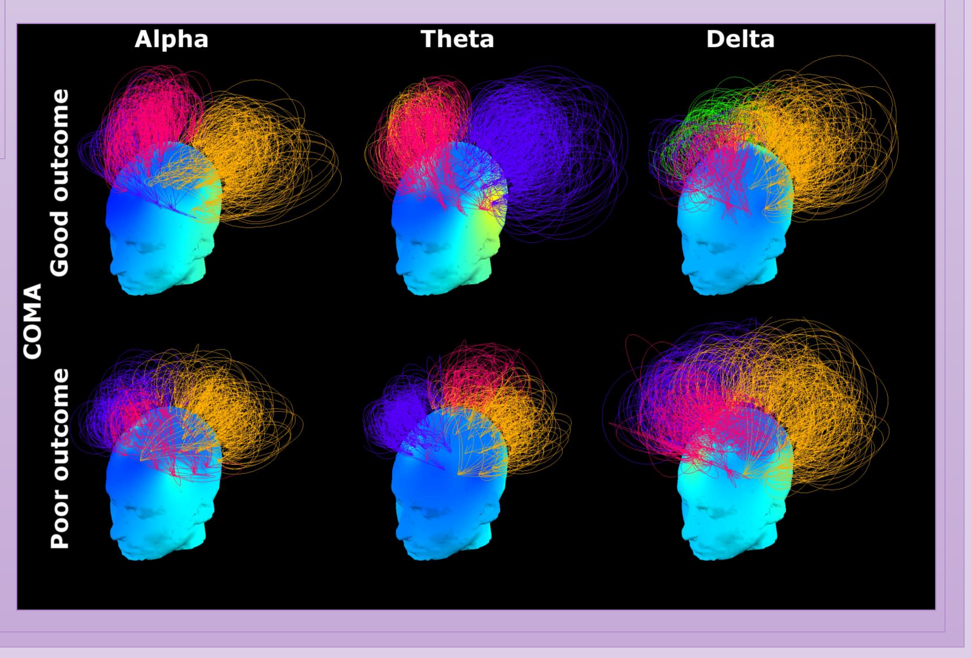
Patients were split into 2 groups:

Good outcome: *CRS-R score >= 10*

Poor outcome: *CRS-R score < 10.*

Network topography discriminates between good and poor long-term outcome in acute comatose patients.

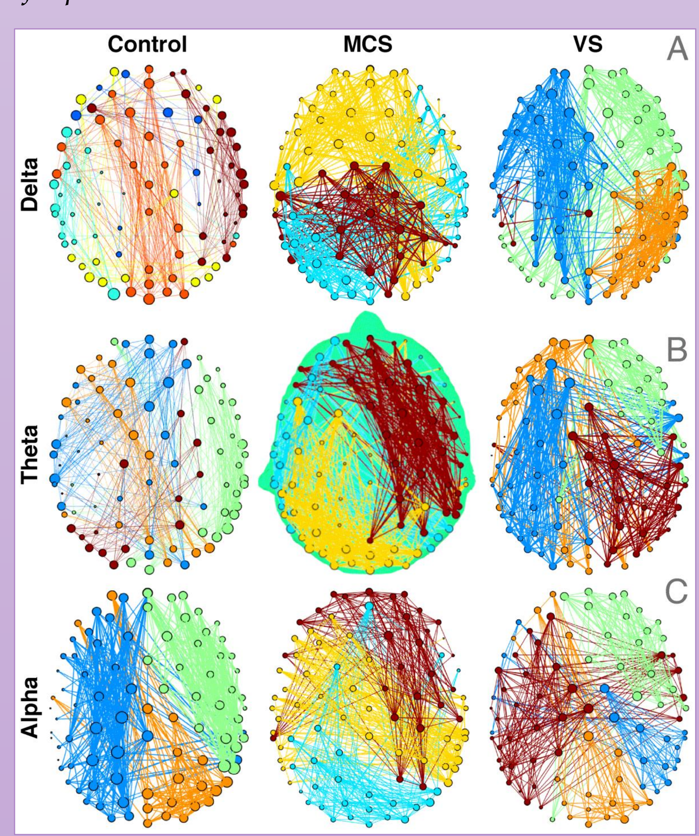
At the same levels of behavioural responsiveness early after traumatic brain injury, patients with good eventual outcome showed robust fronto-parietal connectivity in alpha and theta networks, whereas patients with poor outcome showed stronger connectivity in delta networks.



CHRONIC DISORDERS OF CONSCIOUSNESS[8]

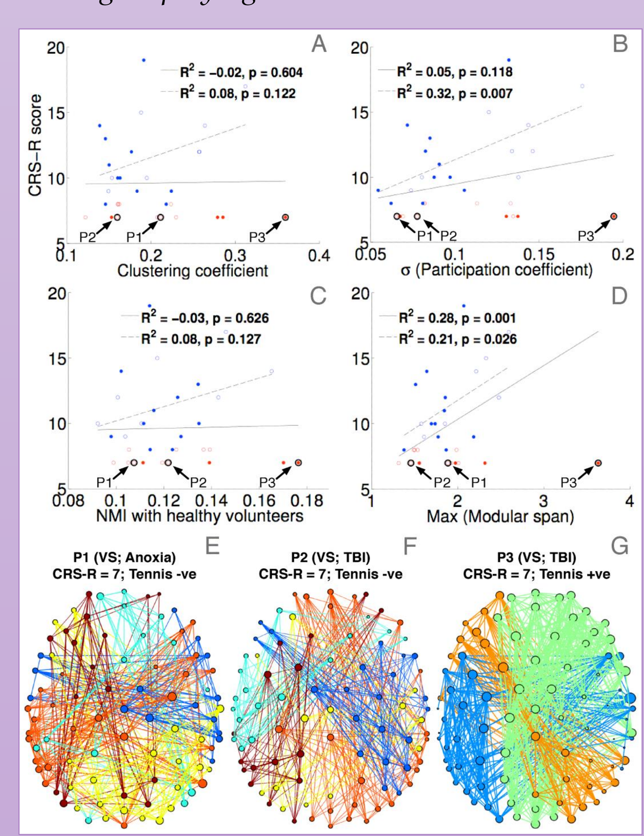
Connectivity network topology varies across healthy controls and patients.

Alpha networks in healthy brains display a balance between strong local interactions and robust interconnectivity. Patients with impaired consciousness show stronger connectivity at lower frequencies.



Alpha network metrics predict CRS-R scores and suggest covert awareness.

Good scores in MCS patients are predicted by alpha network metrics. Alpha network topography also discriminates between patients with the same clinical classification who are able or unable to imagine playing tennis.



SUMMARY

- Functional brain connectivity, conveniently assessed using EEG, is helpful in explicating and predicting behaviour in conditions of impaired consciousness.
- The presence of a robust **frontoparietal module in alpha networks** predicts **preserved alertness** during moderate sedation, **higher CRS-R scores** in chronic disorders of consciousness, and **better long-term clinical outcomes** from coma.
- On the contrary, stronger structured connectivity in lower frequency **delta networks** suggests states of **impaired consciousness**.
- Our findings inform the development of clinically valuable tools for bedside **diagnostics and monitoring** in intensive care units and in the operating theatre.

REFERENCES

[1]Schnakers, C. et al. *Brain Injury* 22, 786-792 (2008) | [2]Sebel, P. et al. *Anesth Analg* 99, 833-839 (2004) | [3]Grote, S., et al. *J Neurotraum* 28, 527-534 (2011) | [4]Vinck, M., et al. *NeuroImage* 55, 1548-1565 (2011) | [5]Giacino, J., et al. *Arch Phys Med Rehab* 85, 2020-2029 (2004) | [6]Bullmore, E. & Sporns, O. *Nat Rev Neurosci* 10, 186-198 (2009) | [7]Chennu, S. et al. *PLoS Comp Biol* (in press) | [8]Chennu, S. et al. *PLoS Comp Biol* 10, e1003887 (2014).