Tracking longitudinal spectral changes in wake and sleep EEG in severe brain injury

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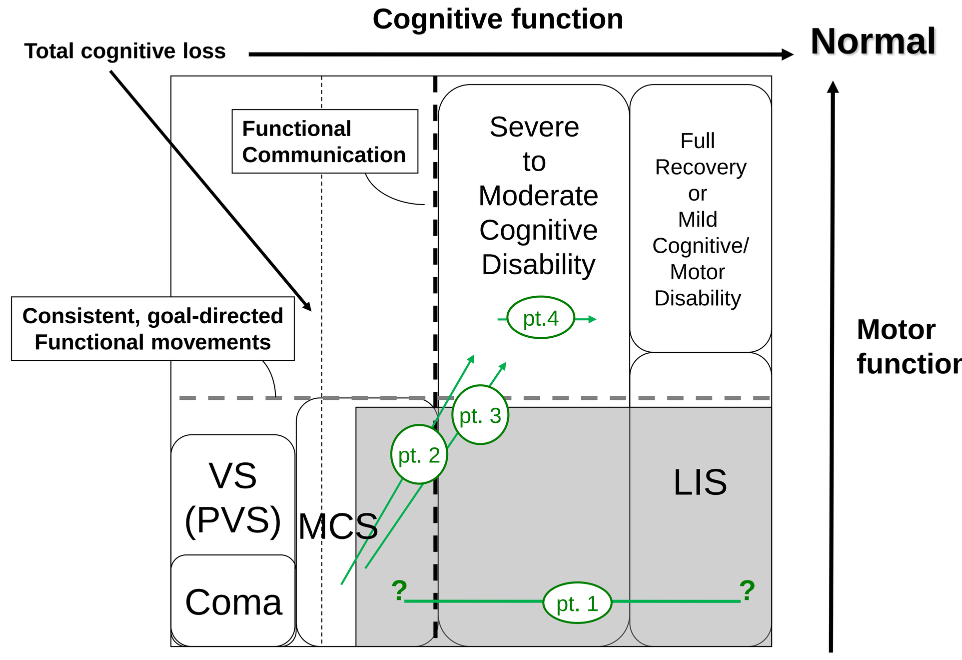
MOTIVATION

- Spectral analysis of the electroencephalogram (EEG) of patients with disorders of consciousness can identify features that may indicate abnormal cortical dynamics.
- Few prior clinical studies have identified EEG changes in sleep or wakefulness as potential indicators of a recovery process.
- Focusing on the sleep EEG recorded in a longitudinal study of patients with traumatic brain injury, we apply quantitative methods (power spectra and coherence) to identify potential biomarkers of the recovery process.

PATIENTS

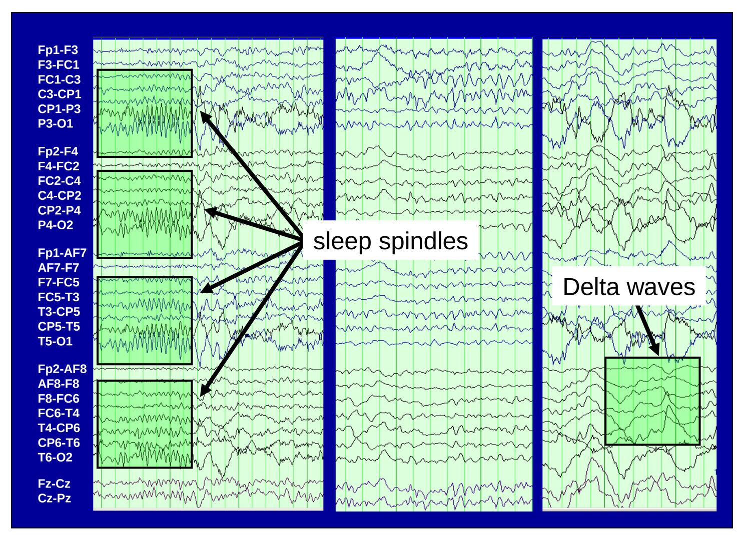


Schiff, N.D. (2010) Recovery of consciousness after brain injury: a mesocircuit hypothesis. *Trends in Neurosciences*. 33(1). 1-9

EEG METHODS

Recording and Analysis

- 32+ hrs of recording with video at each time point
- Augmented longitudinal bipolar recording montage (International 10/10 system)
- 200 to 256 Hz sampling rate via XLTEK (Ontario, CN LH65S1) system
- Segments of artifact-free, slow wave sleep (SWS) selected from consecutive nights of each EEG record based on visual review and video.
- Power spectra and coherence (bandwidth 1Hz, 0.05 confidence limits) estimated using multi-taper methods (MATLAB with Chronux toolbox)



Elements of Sleep Architecture

EEG waves in sleep can be described in terms of their shape and structure. Sleep in normal subjects consists of four stages of NREM sleep and REM. The onset of sleep (Stage 1) is characterized by drowsiness and a transition from alpha waves (8-13 Hz) to theta waves (4-8 Hz). Stage 2 is characterized by sleep spindles (12-14 Hz) and K-complexes. During these stages, conscious awareness of the external environment disappears. Delta waves (high voltage, <4 Hz) are the dominant feature of slow wave sleep (SWS) and are present during Stage 3. Note, though, that normal sleep architecture was generally not present in these patients.

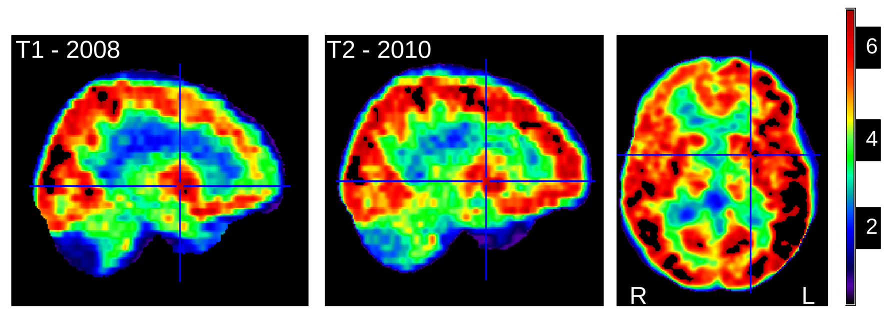
RESULTS

Novel features of power and coherence spectra

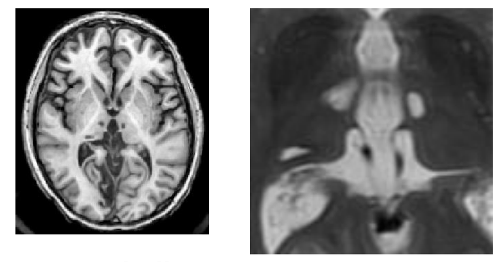
Patient 1

- Female; 22 yo at time of injury
- Stroke due to basilar artery occlusion with brainstem infarct
- Severely impaired motor function

- Visit 1 (T1) = 2 yrs post injury
- Visit 2 (T2) = 32 months post T1

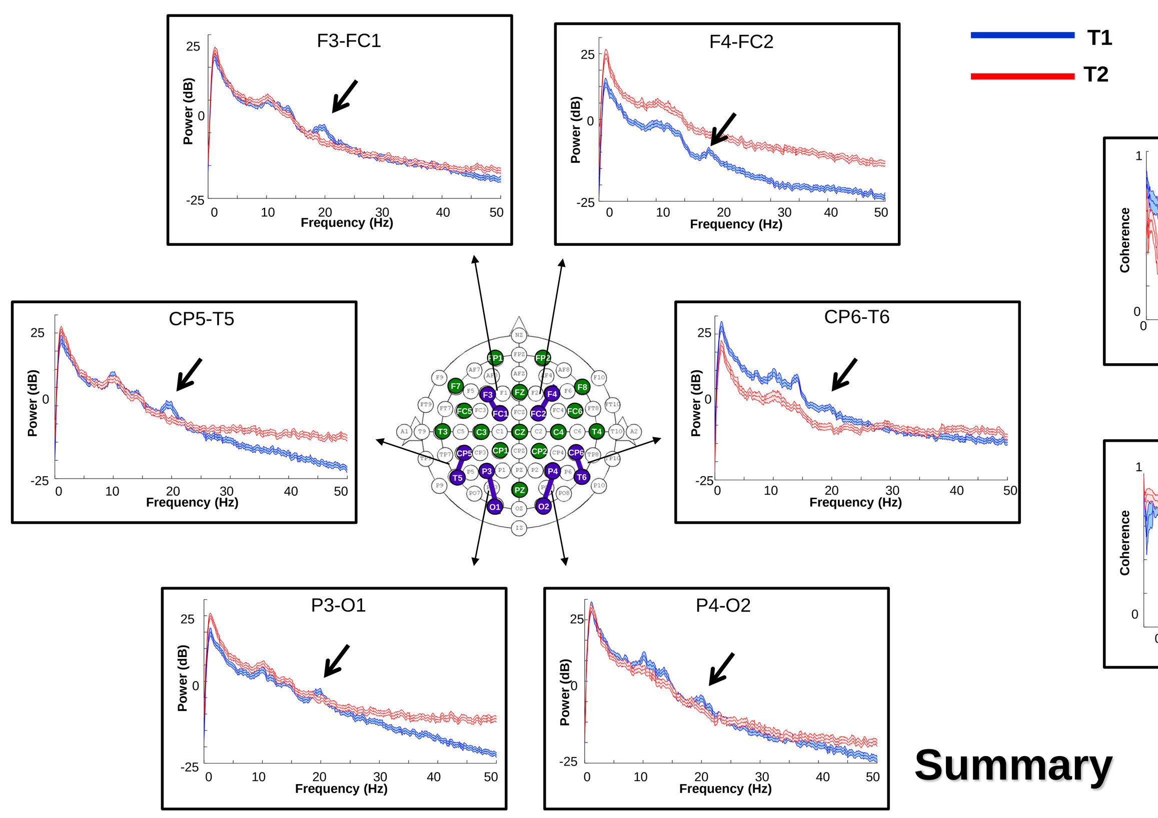


[18]**FDG-PET :** Hypometabolism in left hemisphere at visit 2

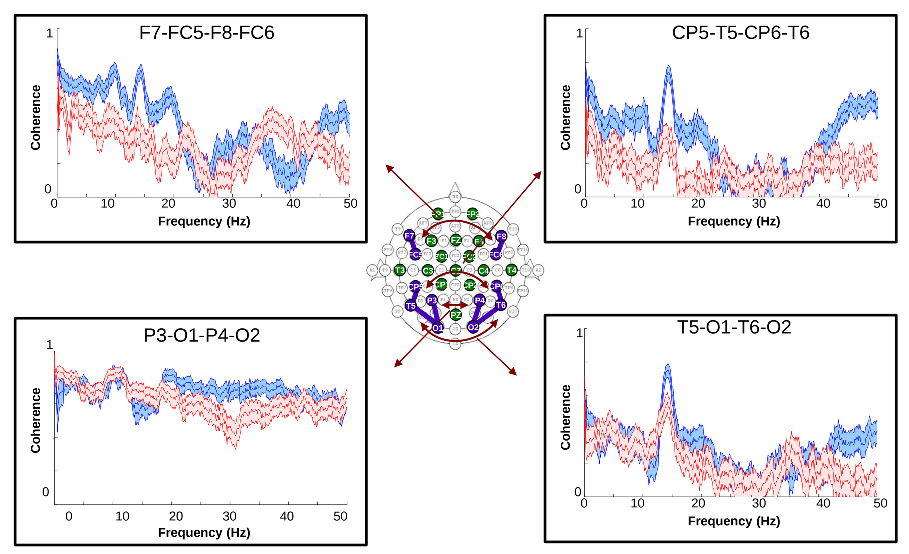


MR Findings preserved cortex; bilateral infarctions of central thalami, ventral and tegmental pons & midbrain; Infarct to R LGN

Spectra in the Sleep State



Coherence



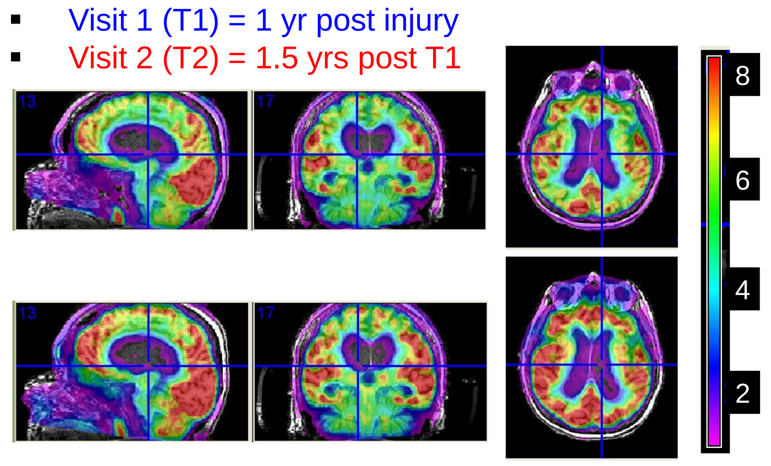
Summary

- Visual inspection of the EEG shows primarily stage 2 sleep at the 1st visit (T1). A bilateral increase in low-frequency (< 4 Hz) power at the 2nd visit (T2) may reflect a shift towards stage 3 sleep.
- Comparison of spectra between the two visits shows a prominent peak in power around 18-20 Hz across all channels in first study (T1) that is absent in spectra calculated in the second study (T2).
- The 18 Hz peak is accompanied by greater *intra*-hemispheric and *inter*-hemispheric coherence at T1 than at T2, suggesting an abnormal globally coherent process not present in the T2 assessment.

Patient 2

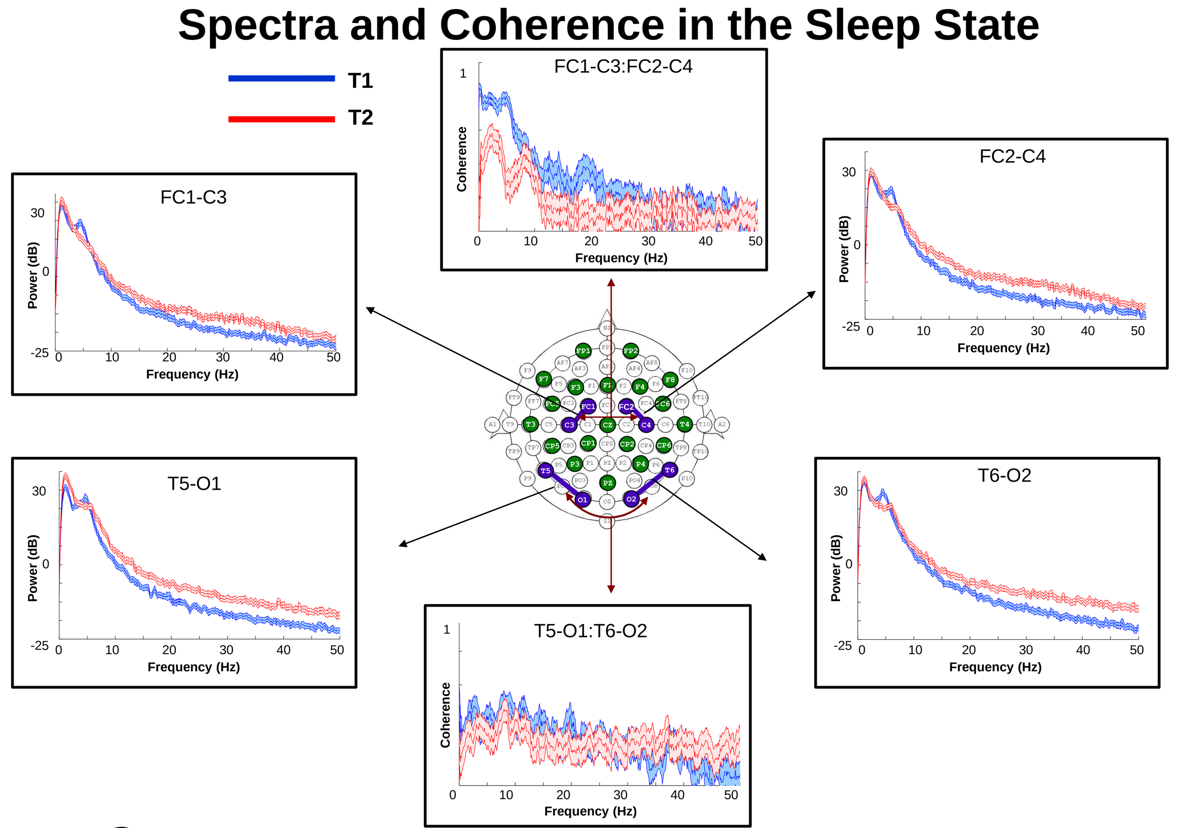
- Female; 58 yo at time of injury
- Hypoxic ischemic encephalopathy, secondary to diffuse fat emboli.
- Initially, unresponsive with visual tracking (T1); recovery of fluent speech and elements of executive function (T2).

- Visit 1 (T1) = 1 yr post injury
- Visit 2 (T2) = 1.5 yrs post T1



[18]**FDG-PET :** Global increase in metabolism observed between visit 1 and visit 2

Spectra and Coherence in the Sleep State



Summary

- Visual inspection of the EEG record shows largely stage 2 sleep during the first visit (T1); a combination of sleep stages 2 and 3 are seen across the second visit (T2).
- There is a prominent peak in power at ~4-6 Hz across all channels in T1 but not at T2.

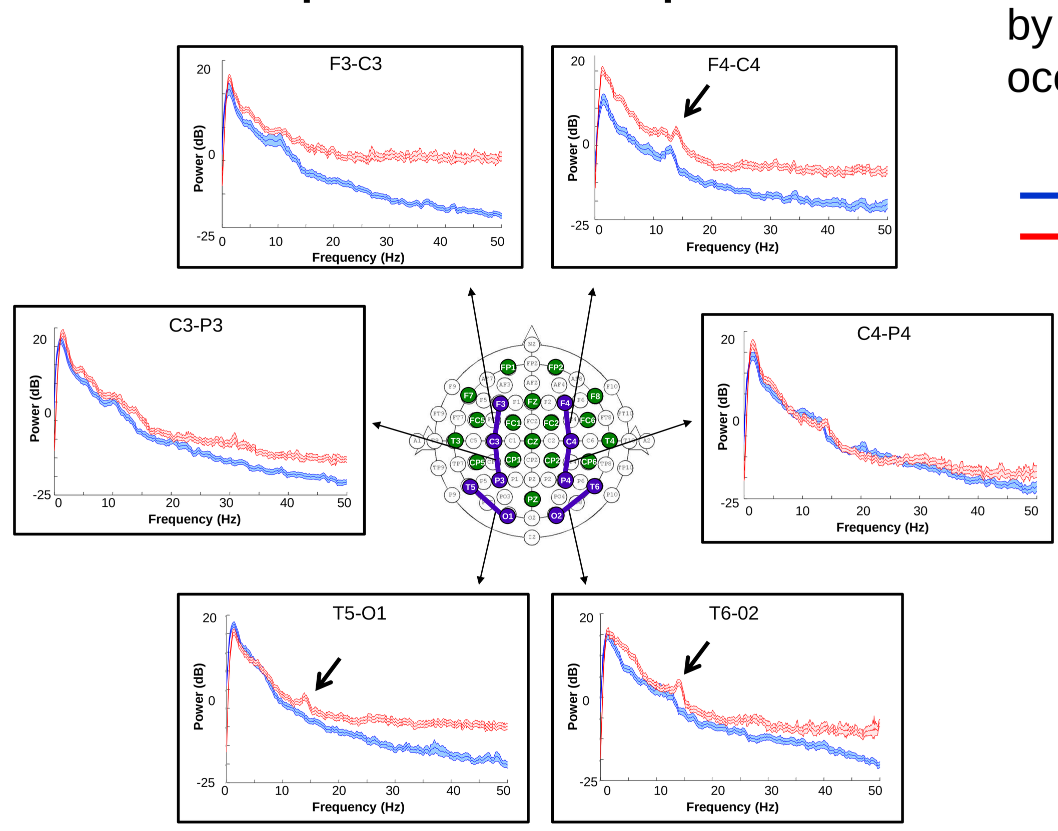
Changes in the spindle frequency range

Patient 3

- Male; 20 yo at time of injury
- Left temporoparietal intra-cerebral hemorrhage
- Initially in MCS with limited command following (T1), recovers to confusional state with fluent speech (T2)

- Visit 1 (T1) = 1 yr post injury
- Visit 2 (T2) = 10 yrs post T1

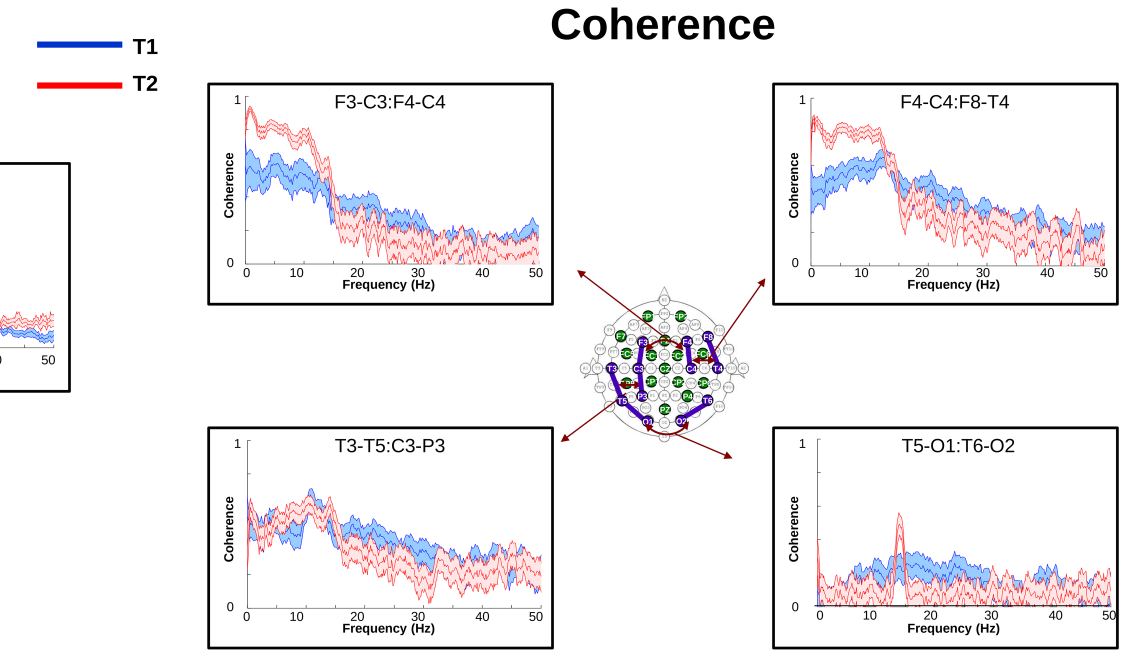
Spectra in the Sleep State



Summary

- Visual inspection of the EEG shows that at T2, spindles appear in the occipital regions.
- Spectral shape is generally similar at visit 1 and visit 2.
- The EEG at T2 shows an increase in power in the occipital regions at the spindle frequencies at ~15 Hz, accompanied by an increase in inter-hemispheric coherence across the occipitoparietal regions in the beta band.

Coherence

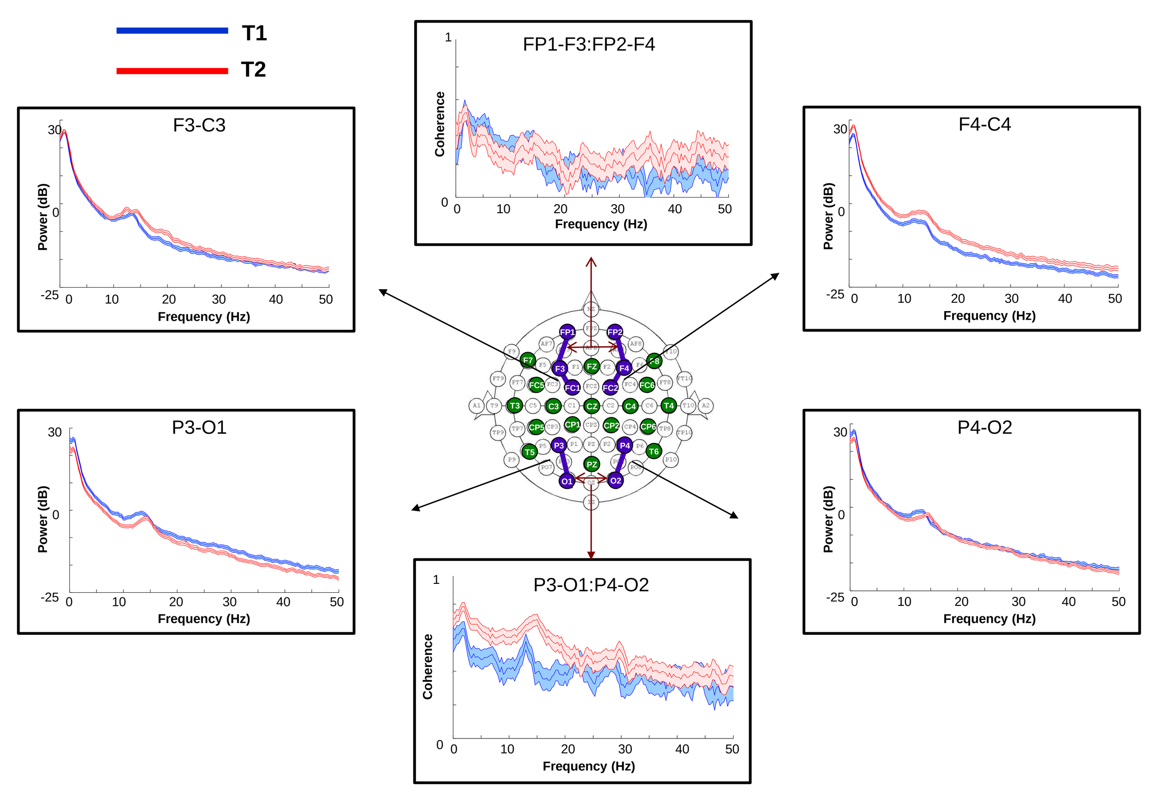


Patient 4

- Male; 19 yo at time of injury
- Severe closed head injury - TBI
- On testing across examination period subject demonstrated increased motor control and improved impulse control

- Visit 1 (T1) = 20 yrs post injury
- Visit 2 (T2) = 18 months post T1

Spectra and Coherence in the Sleep State



Summary

- Visual inspection of the EEG record reveal an increase in spindle activity in the second visit (T2) during NREM sleep.
- Comparison of spectra between the two visits shows a slight increase in peak frequency within the spindle range (12-14 Hz) most prominent in posterior channels and an increase in inter-hemispheric coherence across the temporal-occipitoparietal regions at ~14 Hz.

CONCLUSIONS

- Spectral analysis of the EEG reveals longitudinal changes in power spectra and coherence associated with behavioral recovery and metabolic change in all subjects.
- In Patients 1 and 2, the sleep records from the first visit reveal globally coherent oscillations (5 Hz and 18 Hz), atypical of normal sleep. These are not present in the second visit. The change over time suggests the dissolution of aberrant pathological processes, and correlates with recovery of normal sleep as assessed by visual inspection in both subjects.
- In Patients 3 and 4, the overall shape of the power spectrum is preserved across both time points in the frontal, temporal and parietal regions. Both show a slight increase in frequency of the peak within the spindle range.
- The presence of ~14 Hz peak in the second visit of Patient 3 accompanied by an increase in *intra*-hemispheric coherence in the spindling frequency at ~14 Hz in the intact hemisphere and inter-hemispheric coherence in the occipital regions suggest the reappearance of features typical of normal sleep.

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