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Fluctuating EEG coherence in chronic brain injury

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ABSTRACT

Chronic, severe disturbances of consciousness and cognitive function consequent to brain injury is a major public health concern with enormous economic and social consequences. Affected patients typically have structural damage to cortex, subcortical regions, and their interconnections. However, the presence of regions of anatomically spared cortex with preserved metabolic activity, and episodic evidence of fragments of behavior appropriate to those regions, suggests that functional disturbances in thalamocortical and corticocortical interactions likely play a key role. Our ability to assess these interactions, especially over extended periods of time, is severely limited.

Here, we present a new approach to this problem. Our strategy uses the standard, accessible, EEG, along with a novel approach to its analysis. The approach is motivated by a rigorous dynamical-systems study of a population model of thalamocortical dynamics. The population model is an extension of the model of the thalamocortical module developed by Robinson and coworkers. As Robinson and coworkers showed, this model provides a concise account of the normal EEG, but does not display spontaneous state transitions. When two such modules are coupled together by a shared reticular population, we found (Drover et al. CoSyNe, 2009) that the combined system shows spontaneous transitions between multiple dynamical modes, distinguished by the coherence of activity between the modeled cortical populations. This observation supports the notion that the reticular thalamus is key to coordinating the activity of multiple cortical regions, and suggests that the existence of multiple modes of coherence constitutes a fingerprint of normal thalamocortical and corticocortical interactions.

Motivated by these observations, we analyzed EEG/CCTV recordings in three patients with severe chronic brain injury, as evidenced by metabolic (resting PET) and anatomical (MRI, DTI) studies. We calculated EEG spectra and coherence from 30 segments of artifact-free EEG (total 300 sec), and determined time-localized spectra and coherences. For coherences calculated from pairs of channels over the frontal lobes bilaterally, we found spontaneous alternation between two modes; for coherences calculated from pairs of channels within one hemisphere, this dynamical feature was absent. These preliminary findings indicate that time-varying patterns of coherence can be reliably identified in brain-injured patients, and suggest that their presence or absence may correlate with recovery of function.

RATIONALE AND APPROACH

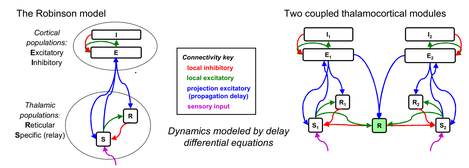
Importance of understanding thalamocortical dynamics in brain injury

- Cognitive function (e.g., visuomotor behavior, working memory) relies on changing patterns of corticocortical interactions
- The central thalamus likely plays a major role in enabling these patterns
  - fan-out connectivity at the population level
  - matrix projections to superficial layers
- Disruption of thalamocortical dynamics is prominent in brain injury
  - diffuse axonal injury, ischemia, hemorrhage
  - functional deafferentation of the thalamus
- Behavioral function in traumatic brain injury can be modulated by central thalamic stimulation (Schiff et al. 2007)

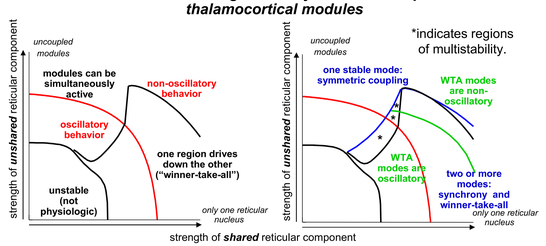
Strategy: identifying distinctive fingerprints of thalamocortical interactions in the EEG

- The EEG is noninvasive and easily recorded in severely compromised patients. It has high temporal resolution – but it is not a direct measure of thalamic function
- We therefore use a model-based approach to suggest indirect manifestations of thalamocortical circuitry in the EEG (Panel A)
  - Starting point: the Robinson model (Robinson et al. 2002)
  - Allow two modules to be coupled by shared reticular nuclei
  - **Distinctive dynamics emerge (Drover et al. 2009): multistable modes of corticocortical coherence and power** (panel B)
- **This motivates a signal-processing strategy to identify multiple modes of coherence and power: time-localized spectral analysis, followed by simple clustering**

A. Population-based model of thalamocortical dynamics



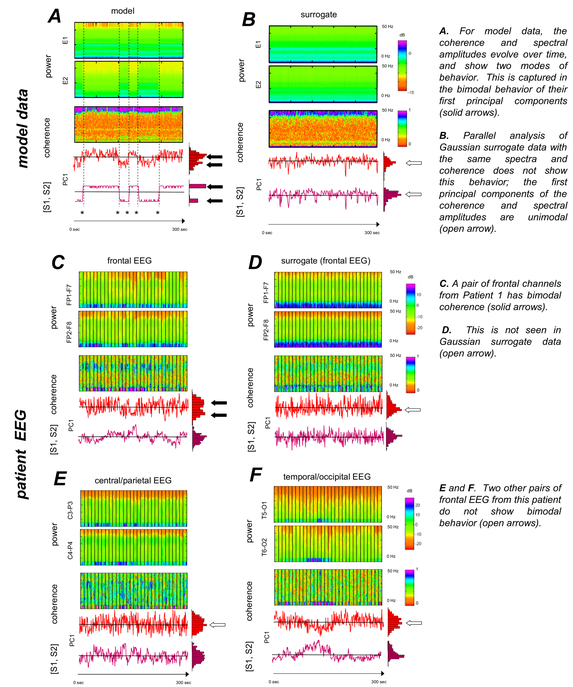
B. Bifurcation diagram for dynamics of coupled thalamocortical modules



Signal processing

Goal: identify changing modes of coherence over time

- Digitized at 200 Hz (XLTEK)
- 30 artifact-free segments, 10 sec each, eyes open resting state
- Multitaper spectrograms and coherograms (1.28 s window, 9 tapers, 3.9 Hz bandwidth)
- Principal components analysis of coherence and joint spectral amplitudes ([S1, S2])
- Examine distribution of first principal component for multimodality (Hartigan dip test)
- Significance testing: Gaussian surrogates matched for power and coherence



A. *For model data, the coherence and spectral amplitudes evolve over time, and show two modes of behavior. This is captured in the bimodal behavior of their first principal components (solid arrows).*

B. *Parallel analysis of Gaussian surrogate data with the same spectra and coherence does not show this behavior; the first principal components of the coherence and spectral amplitudes are unimodal (open arrow).*

C. *A pair of frontal channels from Patient 1 has bimodal coherence (solid arrows).*

D. *This is not seen in Gaussian surrogate data (open arrow).*

E *and* ***F.*** *Two other pairs of frontal EEG from this patient do not show bimodal behavior (open arrows).*

RESULTS

Patient characteristics and recording methods

Three patients with chronic brain injury and evidence of partial recovery of function:

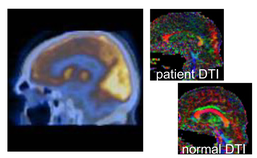
- Recordings obtained during hospitalization for multimodal evaluation (imaging, behavioral, electrophysiological)
- Informed consent from family
- 32 -channel EEG, augmented 10-20 montage
- 24+ hours of recording, with video, per patient
- Selection of artifact-free segments based on visual inspection of EEG and video
- Eyes open resting state

Patient 1 ID: IN-356W

40 yr old man
emerged from minimally conscious state (EMCS)
traumatic brain injury at age 19, motor vehicle accident
evaluated 21 years later

Behavior: coma for 6 weeks, then in minimally conscious state (MCS) for 18 years, then spontaneous recovery of language

MR: enlarged ventricles
PET: frontal hypometabolism
DTI: reduced interhemispheric connectivity

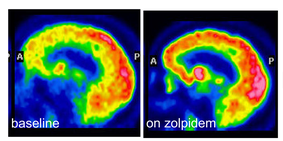


Patient 2 ID: IN-301M

32 year old man
emerged from minimally conscious state (EMCS)
hypoxia at age 23
evaluated 9 years later

Behavior: marked improvement in speech, motor control, chewing, and swallowing with zolpidem

MR: diffuse cortical injury, left thalamic lesion
PET: bilateral hypometabolism, increases with zolpidem

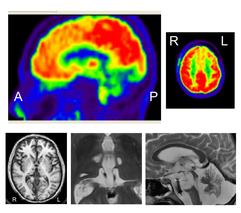


Patient 3 ID: IN-316W

24 year old woman
minimally conscious state (MCS)
basilar artery occlusion with brainstem infarct at age 22
evaluated 2 years later

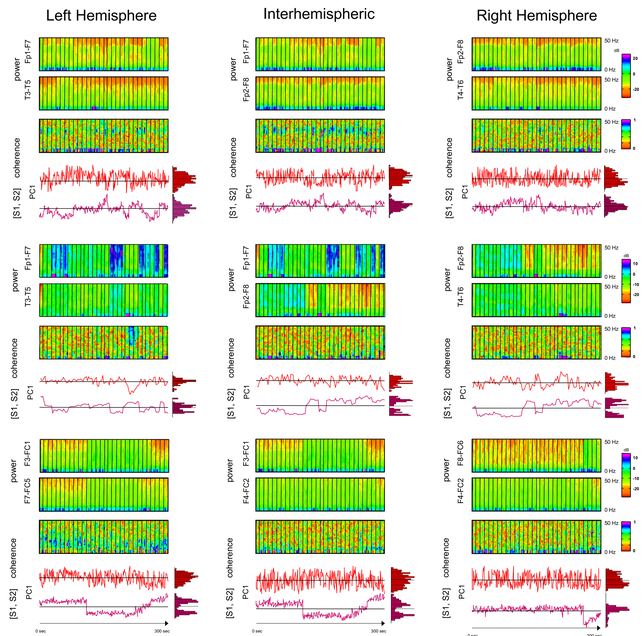
Behavior: opens left eye; preserved vertical gaze; has intact language processing and severely impaired motor function

MR: bilateral infarction of ventral and tegmental pons, midbrain, and central thalamus, right lateral geniculate nucleus infarct
PET: left frontotemporal hypometabolism, bilateral superior mesial frontal downregulation; right calcarine hypometabolism
fMRI: intact auditory and language processing



Sample EEG analyses

Each panel shows analysis of a pair of EEG to detect the presence of multiple modes of activity. Data consist of 30 swatches of 10 sec of EEG on each of two channels, concatenated into a 300-sec record. ***Step 1:*** *Spectrograms and coherograms are calculated (pseudocolor plots). The spectrograms indicate how the power at each frequency on the two channels varies over time; the coherogram indicates how the coherence (the frequency-specific correlation between the channels) varies over time.* ***Step 2:*** *Principal component analysis is applied, and the loading of the first principal component is plotted over time (red trace: coherence; and purple trace: joint spectral amplitudes [S1, S2]).* ***Step 3:*** *A histogram is constructed from the principal component loadings. If coherences and spectra varied randomly, then these histograms would be expected to be approximately Gaussian. But in many cases, bimodality is observed, suggesting that EEG patterns spontaneously fluctuate between two (or more) modes.*



Summary and clinical correlation of EEG analyses

This summarizes the number of channel pairs manifesting bimodality for ***coherence*** *and* ***power.*** *Each triplet indicates the number of bimodal pairs found by visual inspection, by significance testing (p<0.01), and number of channel pairs analyzed.*

Patient 1 had late spontaneous recovery of language; evidence of bimodal cortical coherence patterns is strongest in the left hemisphere.

Left Hemisphere	Interhemispheric	Right Hemisphere
3/1/8	1/1/8	1/0/8
1/0/8	0/1/8	1/0/8

Patient 2 had a left thalamic lesion; evidence of bimodal cortical coherence patterns is strongest in the right hemisphere.

Left Hemisphere	Interhemispheric	Right Hemisphere
0/0/8	0/0/8	2/0/8
5/2/8	1/1/8	6/6/8

Patient 3 had evidence of bimodal activity patterns in the right hemisphere based on coherence, and in the left hemisphere based on amplitude. The clinical correlate of this mixed pattern is as yet unclear.

Left Hemisphere	Interhemispheric	Right Hemisphere
1/0/14	1/0/13	3/0/14
6/6/14	3/2/13	1/1/14

CONCLUSIONS

- Population models of thalamocortical dynamics predict fluctuating patterns of cortical coherence and power.
- Multitaper spectral analysis, combined with principal components analysis, provides a rigorous means to identify these fluctuations.
- These fluctuations are present, to varying degrees, in three patients with chronic brain injury, and appear to correlate with the integrity of thalamocortical networks.

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