SPATIAL AND TEMPORAL IDENTIFICATION OF SEIZURE PRECURSOR DYNAMICS: A PHASE MODELING APPROACH

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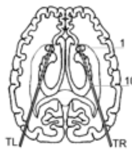
INTRODUCTION / AIM OF STUDY

Recent studies have indicated a significant predictive performance for bivariate EEG analysis techniques, allowing one to discriminate the pre-ictal from the inter-ictal epoch above chance level [1]. In addition, some studies reported that the site selected as best for prediction was not in close vicinity to the epileptic focus but could be located in remote or even contralateral brain structures. These prima facie counterintuitive finding may indicate the importance of regions outside of the ictal-onset zone but within the *epileptic network* in generating clinical seizures. Addressing this issue we studied coupling strength and directional relationships in multi-day, multi-channel invasive EEG using two bivariate measures, which are based on the concept of phase synchronization.
The aim of this study is to identify structures corresponding to the epileptic foci and additional regions with seizure precursor dynamics, which allows one to discriminate the pre-ictal from the inter-ictal period.

METHODS

EEG Data

- intracranial EEG recordings
  - 6 patients: 5 with unilateral focal TLE
    1 with bilateral TLE
  - total recording duration about 44 days
  - total number of seizures: 43
- assumed duration of pre-ictal period: 4h
- inter-ictal recordings excl. 4h before and 30min after seizure onset



Bivariate Measures

- Moving window approach (window length: 4096 data points = 20s, no overlap).
  For each window and each channel combination:
  - discrete phase $\Phi_n(t_k)$ with $t_k = k\Delta t$ from Hilbert transform
  - strength of synchronisation via mean phase coherence [2] defined as:

$$R_{1,2} = \left| \frac{1}{N} \sum_{k=0}^{N-1} e^{i(\phi_1(t_k) - \phi_2(t_k))} \right|$$

$R \to 1$, completely phase synchronized systems
$R \to 0$, unsynchronized systems

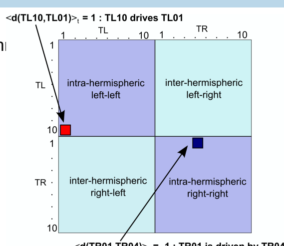
- directional relationship (in a driver-responder sense) calculated via a phase modeling approach [3] using Fourier series $F_{1,2}(\Phi_{1,2}, \Phi_{2,1})$ of phase increments:

$$c_{1,2} = \left\langle \left(\frac{\partial F_{1,2}}{\partial \phi_{2,1}} \right)^2 \right\rangle = 2\pi^2 \sum_{m,l} l^2 A_{m,l}^{1,2} \qquad d^{(1,2)} = \frac{c_2 - c_1}{c_1 + c_2}$$

$c_{1,2}$ reflect influence off the systems on each other
In case of a clear asymmetric influence from system 2 on system 1: $d^{(1,2)} = -1$.
Avoid directional misinterpretation due to complete phase synchronised systems: discard values of $d^{(1,2)}$ if $R > 0.9$ (cf. [4,5])

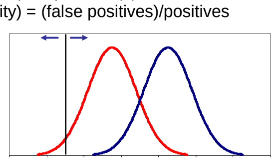
Focus Localization Statistics

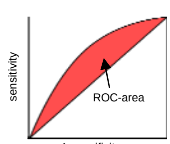
- spatial identification of directional relations:
  - averaged $d^{(1,2)}$ for each patient and each chan combination over inter-ictal data: $\langle d^{(1,2)} \rangle_t$
  - colour-coded directional matrix (***Fig. 1***);
- statistics to quantify asymmetry of directional matrices:
  - inter-hemispheric: $I^{\text{inter}}_{\text{left}\to\text{right}} = \sum_{i\,\text{left},\, j\,\text{right},\, i<j} \langle d^{(i,j)} \rangle$
  - intra-hemispheric: $I^{\text{intra}}_{\text{left}} = \sqrt{\sum_{i,j\,\text{left}} (\langle d^{(i,j)} \rangle)^2}$
  - directional relation of each channel: $C(i) = \sum_{j, i \neq j} \langle d^{(i,j)} \rangle$



Receiver Operating Characteristic (ROC)

- ROC-area: quantifies the separability of two distributions
  - sensitivity = (true positives)/positives
  - (1-specificity) = (false positives)/positives





CONCLUSION

- Phase modeling approach allows identification of epileptic foci
- Driver-responder relationship between epileptic focus and other brain structures ambiguous

- Results indicate relevance of brain regions outside the epileptic focus in ictogenesis:
  Mean phase coherence: best performing channel combination (discrimination of pre-ictal / inter-ictal periods) often located in remote or contralateral structures.
  Mean phase coherence / phase modeling approach: best performing channel combination exhibits predominantly symmetric driving.

- Findings indicate a complex *epileptic network*

RESULTS

I. Lateralization / Detection of focal structures

Inter-ictal temporal means of $d^{(1,2)}$:
Driver responder relationship of each channel combination $\langle d^{(1,2)} \rangle_t$
Exemplary matrices for 4 patients (***Fig. 1***)

Results:
1. No clear structures in case of bilateral epilepsy (***Fig. 1***; PAT 3)
2. Intra-hemispheric asymmetry (I^{intra}):
   more pronounced in focal hemisphere (4 patients)
3. Channel with highest asymmetry r ($C(r)=max$): recording site close to the epileptic focus (4 patients)
4. Ambiguous result: focal hemisphere quantified (I^{inter}) as driving (3 patients) or as driven (2 patients)

II. Identification of seizure precursor dynamics

- Prediction performance via ROC for both measures (cf. ***Fig. 2***):
  positive value = pre-ictal decrease
  negative value = pre-ictal increase

Results of prediction performance :
1. Mean phase coherence R (***Fig. 2*** left)
   Best channel combinations
   - located in remote or contralateral structures (4 patients)
   - exhibit symmetric driver-responder relationships (4 patients)
2. Driver-responder relationship $d^{(1,2)}$ (***Fig. 2*** right)
   No clear-cut relationship to side of epileptic focus and symmetry of driving

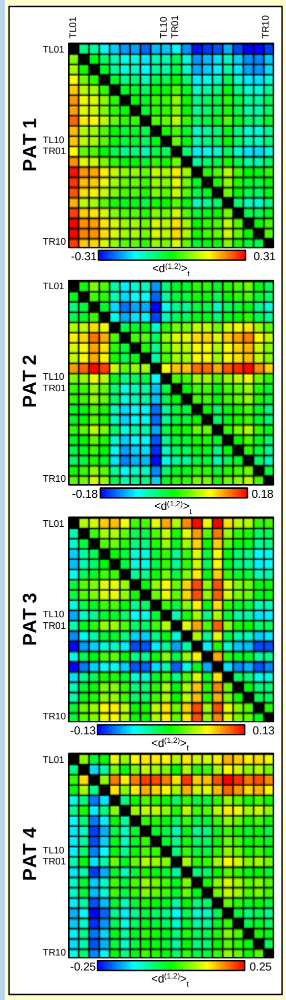


Fig. 1: spatial distribution of driver-responder relationship

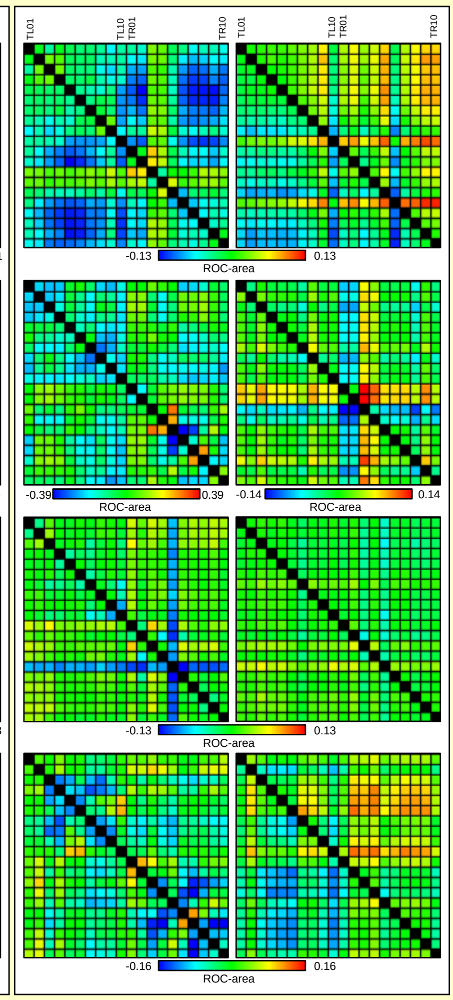


Fig. 2: ROC values for mean phase coherence (left) and for driver-responder relationship (right)

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