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Modelling of intracerebral network interactions that co-occur with interictal epileptic discharges

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Introduction

Interictal epileptic discharges (IEDs) that occur in stereoelectroencephalography (SEEG) recordings are difficult to interpret due to the abundance of such discharges and the complex nature of network interactions \([1,2]\). An analysis framework was developed to unravel the dynamic interactions of the brain regions involved and to provide the clinician with a 3D-view of the spatiotemporal pattern of the region that initiates the IEDs, which is most likely related to the seizure onset zone (SOZ).

Methods

The framework should first of all answer the question whether the brain activity underlying the IEDs is synchronized (Fig. 1, top row). To this end, the non-linear correlation \((h^2_{ij})\) between EEG signals recorded with the depth electrodes is calculated for each possible combination of these signals \([3]\). A regularization procedure is introduced to robustly estimate the delay between the EEG signals by maximizing the average correlation of all IEDs while enforcing smoothness in the estimated delay between spatially neighboring EEG signals.

Secondly a general linear model (GLM) analysis is applied to answer the question which brain regions are significantly involved in the IEDs (Fig. 1, bottom row). The GLM models the likelihood of a region to generate epileptiform activity \([4]\) by considering the variation in correlation over time and the IED density function. The delay estimation is taken into account and filtering is applied to retain only the symmetric results within the GLM matrix. The EEG signals with significant GLM outcome (false discovery rate (FDR); \(q<0.01\)) are considered to be involved in the epileptic network and are further analyzed.

Finally, in order to evaluate the interdependency of the sources underlying the IEDs, spatiotemporal independent component analysis (stICA) is applied for each individual IED \([5]\). Hierarchical clustering \([6]\) of the spatial pattern of the independent components (ICs) along the EEG contact points is applied to investigate whether independent focal regions can be identified (see for example the results presented in Fig. 2C). To estimate the maximal number of independent regions involved the gap statistic \([7]\) is employed.
Results

The SEEG recordings were analyzed retrospectively for patients (N=5) who underwent successful epilepsy surgery (Engel class I-II). The selected depth electrode EEG recordings of the patients studied contained on average 439±260 IED’s, manually detected by EEG technicians. The results of the analysis for one of the patients studied are illustrated in Fig. 2, indicating independent focal regions targeted by the depth electrodes RH (hippocampus) and RO and RP (insula). The 3D-view of the complete epileptic network underlying the IEDs (Fig. 2D) is visualized using the in-house developed depth electrode navigation software [8]. The location in the right hippocampus with initial spiking and subsequent rapid propagation towards distant depth electrodes is concordant with the SOZ. The analysis procedures for 3 other patients resulted in a single focal region coinciding with the SOZ targeted by either one or two depth electrodes involved. The most complex interactions occurred for a patient with alternating involvement of two depth electrodes targeting the right parietal brain region and additionally with independent involvement of the right and left hippocampus. The findings were concordant with the electroclinical hypotheses of each of the five patients studied and with successful outcome of epilepsy surgery.

Conclusions

The results presented indicate that the framework for dynamic connectivity mapping developed in this study describes the complex epileptic network interactions underlying the IEDs, and thereby is able to identify the focal region which is most likely related to the SOZ.

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References


Figure 1: Flowchart of the SEEG analysis applied to an example patient. Top row: The non-linear correlation is computed for windows centered around IEDs (left) from which the time lag can be estimated (middle). Correlation and delay matrices are computed by considering the SEEG recordings for all contact points, and regularization is applied in order to obtain physiologically plausible delay values (right). Shown are the correlation and delay estimation matrices obtained for 843 IEDs occurring in the SEEG recording during the first 24 hours of the depth electrode recordings of this patient. Bottom row: A sliding window analysis is performed (left) in which the changes in non-linear correlation over time are computed (middle). The result of the General Linear Model analysis reveals which brain regions are involved in the epileptic network (right). For this patient, three distinct depth electrodes (located in two separate brain regions) are indicated to be involved in the generation of epileptiform activity.
Figure 2: Example of results of the SEEG analysis for a patient. A) A SEEG epoch of 10 seconds indicating the occurrence of IEDs at the electrode RH (placed in the right hippocampus) and at the electrodes RO and RZ (placed in the insula of the right hemisphere). B) The output of the General Linear Model displaying which brain regions are involved in the epileptic network. C) Independent Component Analysis followed by a clustering procedure shows the spatiotemporal pattern for several focal regions. The ‘RH’ electrode is shown to be individually active, and the ‘RO’ and ‘RP’ electrodes appear to be active simultaneously. The location of the ictal onset zone determined by neurologists is shown by the yellow box. D) The model of the network organization which shows the depth electrodes that are a part of the epileptic network after analysis with GLM and ICA. The $h^2$ correlation ratios are denoted in percentage and the delay is given in milliseconds. Abbreviations: RH = right hippocampus, RO=right occipital, RP=right parietal, RT=right temporal.