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DYNAMICAL ANALYSIS OF BRAIN SEIZURE ACTIVITY FROM EEG SIGNALS

L. Amini¹ C. Jutten^{1,2,3} B. Pouyatos⁴ A. Depaulis^{2,5} C. Roucard⁴

¹GIPSA-LAB, University of Grenoble, Grenoble, France. ²Joseph Fourier University, Grenoble, France.

³Institut Universitaire de France, Paris, France.

⁴SynapCell S.A.S, La Tronche, France. ⁵INSERM, U836, GIN, Grenoble, France.

ABSTRACT

A sudden emergence of seizure activity on a normal background EEG can be seen from visual inspection of the intracranial EEG (iEEG) recordings of Genetic Absence Epilepsy Rat from Strasbourg (GAERS). We observe that most of the recording channels from different brain regions display seizure activity. We wonder if the brain behavior changes within a given seizure. Using source separation methods on temporal sliding windows, we develop a map of dynamic behavior to study this dynamicity. The map is built by computing the correlation functions between the main sources extracted in different time windows. The proposed method is applied on iEEG of four GAERS. We see that the behavior of brain changes about $0.5s - 1.5s$ after onset when the relevant temporal sources become very similar. The corresponding spatial maps for each time window shows that the seizure activity starts from a focus and propagates quickly.

Index Terms— Source Separation, Dynamic Analysis, Intracranial EEG, Seizure, Absence Epilepsy

1. INTRODUCTION

Understanding the mechanisms underlying the absence seizures addresses questions on the origin of the seizure activity, their propagation and their repeatability across different seizures [1, 2, 3, 4]. In [5, 6], researchers wonder if absence epileptic seizures are truly generalized with immediate global cortical involvement. Their research results show that: 1) seizure activity starts from a cortical focus and propagates quickly to other cortical regions, and 2) seizure activity may not involve the whole brain homogeneously.

However, there is a little attention on the change of temporal brain sources during seizures, and its repeatability. By visual inspection, we see that all the iEEG recording channels display similar Spike-Wave Discharges (SWDs) with short delays on normal EEG background at seizure onset (Fig. 1).

In this paper, we wonder if the temporal brain sources are similar during a given seizure, or if they change. To do this dynamic analysis, we consider overlapping sliding time windows. For each sliding window, using blind source sep-

aration methods [7], we estimate the most relevant sources from iEEG channels. Then by quantitatively comparing these source signals, we build a map to show if the shape of the source signals is changing within a given seizure. We call this map: map of dynamic brain behavior (MDB).

In addition to the analysis of temporal changes using MDB, we analyzed the (spatial) contribution of the temporal sources into iEEG channels for each time sliding window: sequences of spatial maps. In each spatial map, we compute the power of all relevant sources estimated in each iEEG channel. Studying this sequence shows the propagation of relevant sources within different iEEG channels.

The rest of paper is organized as follows. In Section 2, the data acquisition, a brief background on blind source separation, and the proposed method are explained. The experimental results are brought in Section 3. The discussion and concluding remarks are reported in Section 4.

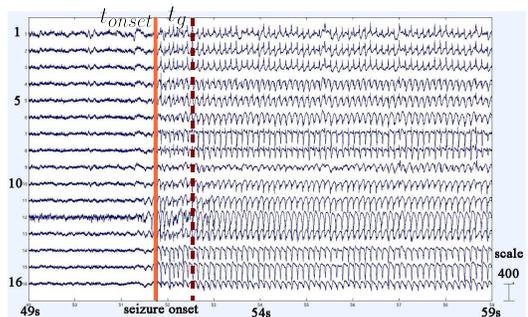


Fig. 1. A typical 10s segment of data for all of channels including background and seizure. The seizure onset is denoted by t_{onset} ; t_g is later explained in Section 3.

2. METHODS

2.1. Data

In this work, we use the iEEG data of four GAERS. This animal model is tested for different criteria such as isomorphism, homology, and pharmacological predictability to be similar to typical absence epilepsy in human [8]. The iEEG data of each

GAERS has 16 channels (Fig. 1) bilaterally recorded from motor cortex, somatosensory cortex and ventroposteromedial thalamus. The sampling rate is $f_s = 5kHz$. The monopolar montage is considered. The 50Hz is removed by a 5-order notch Butterworth filter with 3dB cut-off frequencies equal to 48Hz and 52Hz. For details of iEEG recordings, refer to [9].

2.2. Blind Source Separation (BSS) [7]

Let's assume $\mathbf{X}^k \in \mathbb{R}^{N \times T}$, the matrix of the recorded signals from N iEEG channels and for T samples of window k , in the range of $[t_k - T + 1, \dots, t_k]$, $t_k = t_0 + k(1 - V)T$. V is the overlap ratio between two consecutive sliding windows. We assume that each recorded signal (rows of \mathbf{X}^k), $\mathbf{x}_i^{(k)\top} = [x_i(t_k - T + 1), \dots, x_i(t_k)]$ is the linear instantaneous (based on quasi-static approximation of Maxwell's law) superposition of different electric sources (epileptic and background), $\mathbf{s}_j^{(k)\top} = [s_j(t_k - T + 1), \dots, s_j(t_k)]$, $j = 1, \dots, J$, $i = 1, \dots, N$, $k = 0, \dots, K - 1$. J and K are the number of sources and the number of windows, respectively. Thus, this model is as follows:

$$\mathbf{X}^k = \mathbf{A}^k \mathbf{S}^k \quad (1)$$

where $\mathbf{S}^k \in \mathbb{R}^{J \times T}$ and $\mathbf{A}^k \in \mathbb{R}^{N \times J}$ are defined as:

$$\begin{aligned} \mathbf{S}^k &= [\mathbf{s}_1^{(k)\top}, \dots, \mathbf{s}_J^{(k)\top}]^\top \\ \mathbf{A}^k &= [\mathbf{a}_1^k, \dots, \mathbf{a}_J^k], \quad \mathbf{a}_j^k = [a_{1j}^k, \dots, a_{Nj}^k]^\top \end{aligned} \quad (2)$$

where a_{ij} indicates the contribution of the j th source into the i th observation signal. \top indicates transpose for vectors/matrices. The BSS problem consists in estimating the sources $\hat{\mathbf{S}}^k = \mathbf{B}^k \mathbf{X}^k$ from observations, \mathbf{X}^k . This can be done using independent component analysis (ICA) through estimation of the $N \times J$ invertible mixing matrix \mathbf{A}^k ($\mathbf{B}^k = (\mathbf{A}^k)^{-1}$) such that $\hat{\mathbf{S}}^k$ components are as statistically independent as possible. We assumed (and verified) by mixing matrix that each iEEG recorded signal can be the sum of epileptic and background sources, that can be assumed to be independent. Using ICA, BSS problem is impossible to solve for Gaussian and temporally iid sources [10]. Therefore, we need some imposed diversity between sources by either assuming that (a) sources are non-Gaussian (possibly iid), or (b) sources are non-iid (colored or non-stationary) and possibly Gaussian [7]. In assumption (a), higher order statistics [10] are required and a possible ICA method is the JADE algorithm using fourth-order cumulants [11]. In assumption (b), second order statistics are sufficient and separation can be achieved by joint diagonalization algorithms like SOBI by taking advantage of the temporal structure of sources [7].

2.3. Map of dynamic behavior

Seizure signals have important harmonic oscillations, thus they are non-i.i.d (temporally colored with different spectra), therefore SOBI algorithm is an appropriate method.

The other diversity that can be used is the fact that seizure and background signals have non-Gaussian and Gaussian distributions, respectively, as can be checked by using a Kolmogorov-Smirnov test [12] on 16 seizures and background periods. The result of the test indicates that seizure signals are non-Gaussian with long tails while background signals are mainly Gaussian. By considering this diversity, one can use JADE algorithm where sources are estimated by approximately jointly diagonalizing a set of fourth-order cumulant matrices [11, 7].

In the following, we explain the idea of MDB and how to build it. In the proposed method, there are two steps. In the first step, we use source separation for each temporal sliding window. We assume instantaneous linear mixtures of the sources, i.e. we try to isolate the sources that are electrically propagated from different locations. For each window, we select the most powerful sources. Once the important sources for all sliding windows are estimated, in a second step we would like to know 1) if the sources related to each window are in relation through a neuronal network and 2) if the source signals are changing from one window to another. In this step, we take into account delays induced by neuronal connections. These typical time delays can be around $10ms$. To answer these questions, we use cross-correlation functions of different sources (for different values of time delay, τ), to construct MDB.

For the first step of this dynamic study, we consider overlapping sliding windows, $k = 0, \dots, K - 1$ with window length T and overlap ratio V . For each window, we use either SOBI, or JADE algorithm to estimate the $J < N$ most important sources. To do the dimension reduction from N to J , we use PCA [7]. Once the K sets of sources, $\hat{\mathbf{S}}^k$, $k = 0, \dots, K - 1$, are estimated then in the second step, we quantitatively measure the similarity between them. To calculate this similarity, we can consider different measures, based on normalized covariance or mutual information. Since the two measures provide similar MDB, we decided to use the simplest measure based on normalized covariances between source signals as a function of time delay, τ . The maximum of this function over τ is considered as the measure of similarity. More precisely, the maximum of absolute value of covariance between each signal pair j_1 and j_2 ($j_1, j_2 = 1, \dots, J$) from windows k_1 and k_2 ($k_1, k_2 = 0, \dots, K - 1$) are calculated as follows:

$$\mathbf{E}_{j_1 j_2}(k_1, k_2) = \max_{\tau} | \widehat{cov}(\hat{\mathbf{s}}_{j_1, \tau}^{(k_1)\top}, \hat{\mathbf{s}}_{j_2}^{(k_2)\top}) | \quad (3)$$

where $\hat{\mathbf{s}}_{j_1, \tau}^{(k_1)\top} = [\hat{s}_{j_1}(t_{k_1} - T + 1 + \tau), \dots, \hat{s}_{j_1}(t_{k_1} + \tau)]$. $\hat{\mathbf{s}}_{j_2}^{(k_2)\top}$ correspond to $\tau = 0$. Samples go beyond window-borders are omitted from shifted signal. The values obtained in (3) are normalized by division with the standard deviations:

$$\mathbf{C}_{j_1 j_2}(k_1, k_2) = \mathbf{E}_{j_1 j_2}(k_1, k_2) / (\sigma_{\hat{\mathbf{s}}_{j_1}^{k_1}} \sigma_{\hat{\mathbf{s}}_{j_2}^{k_2}}) \quad (4)$$

where $\sigma_{\hat{\mathbf{s}}_j^k}$ is the standard deviation of signal $\hat{\mathbf{s}}_j^{(k)\top}$. For each

comparison between the J source signals of two windows k_1 and k_2 , we obtain a $J \times J$ block matrix, $\mathbf{C}(k_1, k_2)$. The (j_1, j_2) entry of $\mathbf{C}(k_1, k_2)$ is $\mathbf{C}_{j_1 j_2}(k_1, k_2)$. The values of $\mathbf{C}_{j_1 j_2}(k_1, k_2)$, i.e. the maxima of absolute value of correlation functions are in the range $[0, 1]$. By constructing the matrix \mathbf{C} of size $JK \times JK$ using all K^2 matrices $\mathbf{C}(k_1, k_2)$, we can study the change of behavior during K windows considering J sources for each window. The values of matrix \mathbf{C} are thresholded at a predefined value, th , giving $\bar{\mathbf{C}}$: values larger than th are kept unchanged and the rest are zeroed. We called this matrix, map of dynamic behavior (MDB).

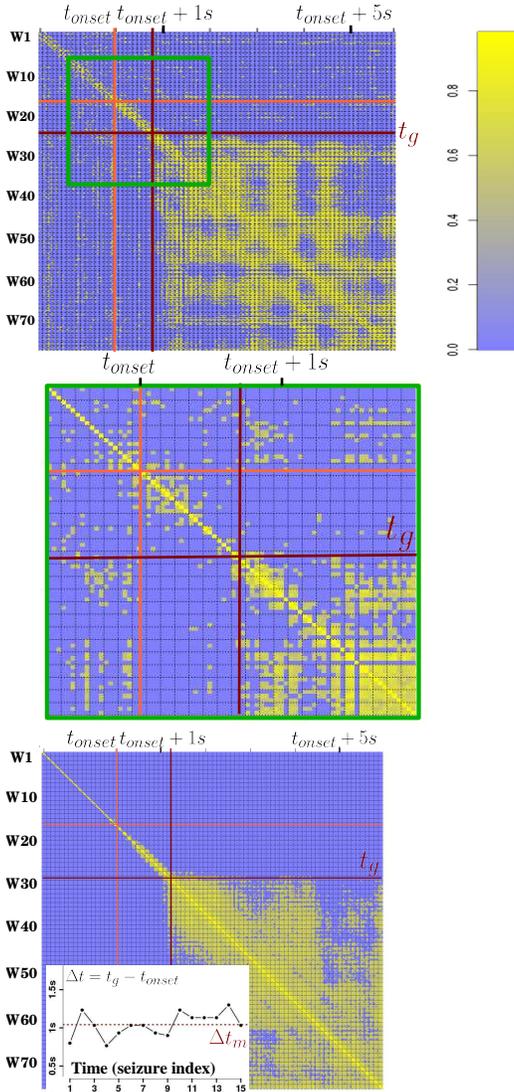


Fig. 2. From top to bottom, 1) MDB for a typical seizure from a typical rat data for $[t_{onset} - 1.5s, t_{onset} + 6s]$, 2) the zoom on green square marked on previous MDB for $[t_{onset} - 0.5s, t_{onset} + 2s]$ and 3) the averaged MDB over 13 seizures from the same rat data and $\Delta t = t_g - t_{onset}$ versus seizures. t_{onset} , t_g , Δt_m indicate the seizure onset, start of period when the sources become similar and the mean of Δt , respectively.

3. EXPERIMENTAL RESULTS

We measure the temporal similarity between the most relevant sources extracted in each time sliding window providing MDB. In MDB, we see if there is a change between temporal sources through the sliding windows. Thus, in MDB only temporal effects can be seen and it cannot inform the questions about spatial effects. For spatial effects, later in this section, we explain briefly about spatial maps related to temporal sources.

MDB: In Fig. 2, MDBs using JADE algorithm are shown. The top image shows the MDB for a typical seizure from a typical rat data for time interval from 1.5s before till 6s after seizure onset (t_{onset}). The shift between two sliding windows is 100ms ($V = 0.8$) and $T = 0.5s$. The middle MDB shows a zoom on the green square marked on the top MDB, i.e. for $[t_{onset} - 0.5s, t_{onset} + 2s]$. Matrix $\bar{\mathbf{C}}$ is symmetric with $J \times K$ rows (each row is built by K symmetric $J \times J$ squares). In the top and the middle MDB, $\bar{\mathbf{C}}$ has $J \times K = 228$ ($J = 3$, $K = 76$), and $J \times K = 78$ ($J = 3$, $K = 26$) rows, respectively. We set experimentally $th = 0.5$. The choice of th is not critical since the general shape of the map is not too much influenced by this parameter.

The onset of each seizure, t_{onset} , is detected automatically. By assuming different distributions for seizure and background and by using Bayesian decision theory on temporal sliding windows, we detect spike discharges and eventually, we determine the seizure onset.

In MDB, the more yellow (blue), the more similar (dissimilar) source signals. We remind that in the first step of source separation, we separate the sources that are electrically propagated (zero time delay) from different locations. Then, in the second step, we would like to know if the relevant sources within and between different windows are similar for non-zero time delays (related to a neuronal propagation). If the sources within a window are similar, it means that probably these sources are involved in a neuronal network. During background, the diagonal blocks, $\mathbf{C}(k, k)$, or the small 3×3 squares are yellow for diagonal entries and blue for off-diagonal ones (middle MDB of Fig. 2). This means that the most relevant (background) sources are different within each window. During seizure, most of the diagonal blocks are yellow for off-diagonal as well as diagonal entries. This shows that the relevant sources are similar (up to a delay) probably due to neuronal interactions. Up to know, we only interpreted the 3×3 diagonal blocks of MDB, i.e. the similarity between the estimated sources within each window. Now, we would like to know if the relevant sources are similar between different windows: this is done by using the off-diagonal blocks of MDB, $\bar{\mathbf{C}}(k_1, k_2)$, $k_1 \neq k_2$. In Fig. 2, we see that during background and even in the beginning of the seizure, $\bar{\mathbf{C}}(k_1, k_2) \simeq 0$, i.e. the sources are changing from one window to another (this part of map is mostly blue). In contrast, after a latency (Δt), $\bar{\mathbf{C}}(k_1, k_2) \neq 0$: the relevant

sources have similar temporal regime, i.e. they become stationary. We call the time at which the source signals become similar, the time of generalization of seizure: t_g (dark red bars on the MDBs of Fig. 2).

To see the repeatability of this result across different seizures, we calculate the averaged MDB as follows. Let's indicate the matrix \mathbf{C} for each of N_s seizures as \mathbf{C}^n , $n = 1, \dots, N_s$. We estimate the average of \mathbf{C}^n matrices giving $\mathbf{C}_m = (1/N_s) \sum_{n=1}^{N_s} \mathbf{C}^n$. By thresholding this average matrix, we estimate the averaged MDB, $\bar{\mathbf{C}}_m$. In the bottom image of Fig. 2, the averaged MDB for the same rat data for $N_s = 13$ seizures is demonstrated. It can be seen that a similar result as for individual MDB is obtained, i.e. the sources become similar and stationary after a latency. Similar averaged MDBs are obtained for the other 3 rat datasets.

To detect t_g automatically, we calculate the sum of columns of matrix $\bar{\mathbf{C}}$ giving $b(t)$, $t = 1, \dots, J \times K$. $b(t)$ has an 'S' shape which has small (near zero) values for background and increases for seizure. Using a sigmoid model for $b(t)$, t_g is detected as the time at which $b(t)$ values reach to the middle of the increasing slope. We study the intra and inter variability of the latency ($\Delta t = t_g - t_{onset}$) between different rats. As an example, Δt values for 13 seizures for the same rat data are overlaid on the bottom MDB in Fig. 2. The mean \pm standard deviation of Δt values over 13 seizures, for rat dataset 1-4 are respectively $0.85s \pm 0.3s$, $1.05s \pm 0.17s$, $0.72s \pm 0.2s$, and $0.66s \pm 0.16s$. The mean \pm standard deviation of Δt over 52 seizures (4 rats \times 13 seizures) is $0.82s \pm 0.26s$.

We computed MDBs for different number of components ($J = 2$ to 5) and as we got similar results, for simplicity, we kept $J = 3$. We also used PCA to estimate the number of components for each window k by keeping 95% of energy ratio. We again got similar results. However, in this case, since J may vary for each window k , the correspondence between size of squares in $\bar{\mathbf{C}}$ matrix and time scale is not linear which makes the interpretation more complicated. We also checked that sources provided by PCA are different from sources provided by JADE.

We also used other measures for comparing quantitatively the estimated sources. We tested the normalized maximum mutual information over τ between the estimated source signals [13] for taking into account the probable non-linearities, and we obtain similar MDB. We tested different values of T and V . The window length is considered long enough ($T = 0.5s$) to see at least a couple of biphasic signals (SWDs) and to provide significant statistic results. We can increase V from 80% to higher values which may increase the temporal resolution, however this is not critical for the general shape of MDB.

Spatial map: Up to here, we explained about the change of temporal relevant signals and we saw that in the beginning of seizure the source signals are typical, but non-stationary, while at t_g , their temporal regime becomes very stationary.

Now, one can wonder what happens spatially, i.e. if these sources have important contributions into some particular iEEG channels. To study about this issue, we analyzed the columns of matrix \mathbf{A}^k (2). For each window k , the total power of the $J = 3$ relevant sources in iEEG channel i can be calculated as $p_i(k) = \sum_{j=1}^J (a_{ij}^k)^2$ since JADE provides normalized power sources. Let's call the representation of $p_i(k)$ values for $i = 1, \dots, N$ as the spatial map related to time window k . In Fig. 3, 3 spatial maps related to time windows ending at respectively t_{onset} plus 0.1s, 0.6s and 1.1s are shown. The parameters are the same as the former results for MDB. The dots show the channel locations. The blue scale represents the values of $p_i(k)$: the more blue, the more important power of the sources in iEEG channels. It can be seen that in map 1, where the related time window ends at $t_{onset} + 0.1s$, the temporal sources have important contributions in right somatosensory channels. The power values of map 1 are lower than spatial maps 2-3 since its related window is not entirely in seizure. After propagation of SWDs, the contribution of sources can change from one window to another one which can be seen in the example spatial maps shown in Fig. 3.

We also calculated the angle between each column pair of the different time windows. These angles are about 20 – 30 degrees which shows that there is not a spatially stable origin of the epileptic sources, conversely, a rapid change of most active areas in many possible locations in the whole brain.

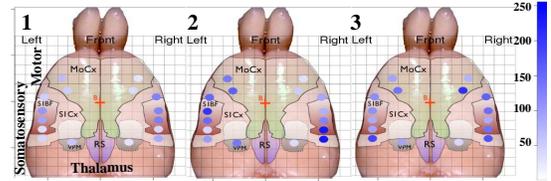


Fig. 3. Three spatial maps 1-3 related to 3 time windows ending at t_{onset} plus 0.1s, 0.6s and 1.1s, respectively. The dots represent the channel locations. The blue scale represents $p_i(k)$ values.

4. DISCUSSION AND CONCLUSION

In this work, we wonder if the brain behavior remains the same or if it changes during a given seizure in a rat model of absence epilepsy (GAERS). We use source separation methods to estimate the most relevant temporal sources from iEEG recordings for sliding windows within a given seizure. We measure the temporal similarity between the sources extracted on different windows to examine the change of behavior giving a map of dynamic behavior (MDB). Based on MDB, we observe that at the beginning of the seizure, high amplitude oscillations appear but with strong temporal/frequential fluctuations, while after a latency (about 0.5s – 1.5s after onset), the temporal sources (related to epileptic oscillations) become stationary. This change of

brain behavior cannot be seen visually from iEEG recordings (Fig. 1). This can show the importance of the analysis compared to visual inspection of recordings. The time at which the sources start to become stationary (t_g) is studied for its inter and intra variability between four rat datasets. Over 52 seizures (4 rats \times 13 seizures), mean \pm standard deviation of $\Delta t = t_g - t_{onset}$ is $0.82s \pm 0.26s$. About 1s after seizure onset we often see on iEEG recordings the involvement of the thalamus. Since this deep structure is connected with wide areas of the cortex, it could probably exert a “synchronizing” action on cortical channels, and as a consequence might reduce the source variability across time. This may explain the latency after onset before generalization of seizure.

In this paper, our focus was mostly on temporal effects of source signals. For the spatial point of view, for each time window, we compute the total power of all relevant temporal sources in each iEEG channel. The location of the most active channels evolves over time, affecting preferentially somatosensory cortex of both hemispheres but also many neighboring regions without special regularity. It seems that this is related to the typicality of absence epilepsy which invades the whole brain without very accurate localization except for onset. For completing this analysis, we also computed the dynamic functional connectivity using differential connectivity graph [14] for focusing on spatial effects. This study is out of the scope of this paper, but preliminary results confirm that the seizure activity starts from right/left somatosensory cortex and then propagates rapidly to other regions.

Further investigations include in depth interpretation with neuroscientists of periodicities and inhomogeneities of the MDB and study of changes in the spatial localization of sources during the seizures. From methodological point of view, the proposed method is the first attempt on dynamical EEG analysis for absence epileptic seizure using blind source separation, and it requires more advances in this perspective.

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