PREICTAL STATE DETECTION OF ABSENCE SEIZURES USING MUTUAL INTERDEPENDENCE MEASURE

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Abstract : In this paper we present a novel automated method based on joint entropy to characterize dynamical interdependence between different cortical regions using EEG recordings for detecting preictal state of the absence seizures. To this end, based on interchannel joint entropies, average mutual interdependence measure (AMIM) is derived to quantify the synchrony of multichannel EEGs, recorded from three patients with absence seizures. To assess the variability of interchannel synchrony, the standard deviation of overall interdependence between EEG channels is investigated as well. Using these criteria, four states, interictal, preictal, ictal and postictal states could be distinguished from each other. Abnormal synchronization of neurons during seizure was detected by a significant rapid increase of AMIM. In contrast, preictal period was identified by a considerable decrease in AMIM showing desynchronization of cortical regions. The preictal drop occurred before seizure onset and after a polymorphic transient. Interchannel synchrony persisted for postictal periods with AMIM values relatively less than those observed for ictal periods. During interictal periods, the decrease in the degree of interdependence between EEG channels was significantly observed relative to ictal periods. The quantifying of such states by AMIM would facilitate investigations of mechanisms leading to seizure initiation and evolution.

Introduction

Providing good temporal resolution, multichannel EEG signal is an efficient non-invasive tool to detect abnormalities in the electrical activity of the brain especially epilepsy. However the complexity of the interictal and ictal states of the seizures make the visual inspection of the raw EEG difficult for the electroencephalographers. Therefore further analysis is required to trace temporal transient patterns of the ictal and interictal brain activities.

Absence seizure is a form of generalized seizure which is associated with spike-and-wave complexes. These abnormal synchronized oscillatory rhythms are characterized in human by ~ 3Hz oscillations in the EEG and believed to develop in thalamo-cortical pathways which activate the entire cerebral cortex simultaneously [1]. Although it is believed that the onset of absence is sudden and the seizures usually occur in quiet wakefulness or drowsiness. During the transition from wakefulness to drowsiness or sleep, the firing pattern of the thalamo-cortical neurons shifts to an oscillatory, rhythmic, synchronized state of the EEG [2]. This type of seizure is initiated by abnormally discharging neurons that recruit and entrain neighboring neurons into a critical mass. This process manifests itself as an increasing synchronization of neuronal activity accompanied by a loss of inhibition. Instead, the interactions between neurons, that play a crucial role in seizure generation, probably take place on different spatial and temporal scales and are known to be nonlinear in nature. Thus, by analyzing the linear and nonlinear interdependence of the signals recorded from different regions of the cortex, it is possible to reflect the strength of coupling between functionally different regions. We derive an Average Mutual Interdependence Measure (AMIM) based on Interchannel Joint Entropy (IJE) to quantify linear and nonlinear interdependencies of cerebral activities between different regions of the brain. We aim to address the questions whether transient states can be distinguished between interictal and ictal periods.

Materials and Methods

Block diagram of our nonlinear EEG state analyzer is shown in Figure 1.

EEG Recordings and Preprocessing

Three patients suffering from generalized epilepsy with absence seizure were included.

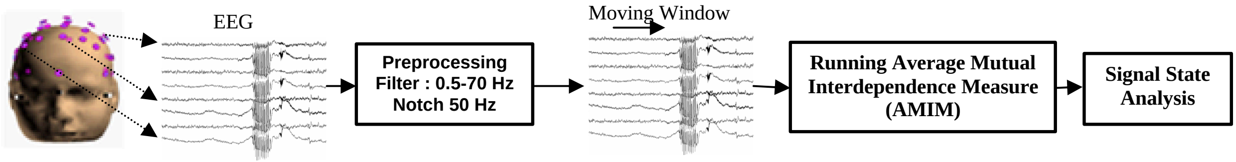

Figure 1: Block diagram of nonlinear EEG state analyzer.

Their EEG signals were recorded by eleven electrodes positioned on Fp1, C3, T3, O1, Fp2, C4, T4, O2, Fz, Cz and Pz according to the international 10–20 system at the North Hospital of Amiens. EEG signals were sampled at a sampling rate of 256 Hz, digitized with 12-bit resolution, bandpass filtered between 0.5 and 70 Hz and analyzed in longitudinal bipolar montage. A 50 Hz notch filter was also used to eliminate possible line noise. For every patient, all seizures were examined, including pre-seizure EEG data of at least 30 seconds duration. These data sets were used to calculate mutual interdependence of EEG channels.

EEG Nonlinear Analysis

Entropy as the mean or expected value of the information was defined for the first time by Shannon [3]. The joint entropy measures the average uncertainty or information between two signals. In this study, the mutual interdependence between channel pairs is measured through the evaluation of the joint entropy of the segmented EEG. Based on this criterion, an average mutual interdependence measure is derived to quantify the interdependence of EEG channels.

Joint Entropy

Between two variables S_X and S_Y, the degree of uncertainty or information can be measured by the joint entropy even when there is no a priori knowledge of either their individual characteristics or their dynamical interdependence. $H(S_X,S_Y)$, the joint entropy between S_X and S_Y, is defined as [4]:

$$H(S_X,S_Y)=-\sum_{m,n=1}^{M,N} s_{mn}\log_2 s_{mn} \qquad (1)$$

where $\{s_{mn}\}_{m,n=1}^{M,N}$ is the joint probability distribution of S_X and S_Y. The relation between the individual entropies $H(S_X)$ and $H(S_Y)$ and their joint entropy is given as :

$$H(S_X, S_Y) = H(S_X) + H(S_Y) \qquad (2)$$

It expresses the fact that the joint entropy is always smaller than the sum of the individual entropies. The equality holds only when the two variables are independent or uncorrelated. One of the advantages of the joint entropy is its independence of absolute scales such as the amplitude or the frequency of the signals. In this paper we used the method proposed in [5] to compute the joint entropy between two signals.

Average Mutual Interdependence Measure

As pointed out, the joint entropy is a description of average uncertainty or information between two signals. It is not usable for nonstationary signals. To make this measure applicable for nonstationary signal analysis, the recorded EEGs were segmented by a moving window, which represents a common way of handling large amounts of data, especially for long-term EEG recordings. For this purpose we have chosen a window length of 1 second, with 1 sample distance in time between two consecutive windows. This window length was regarded as a compromise between the number of points needed for entropy computation and approximate stationarity within a window's length.

To determine the overall average of all interchannel joint entropies, the spatial averaging over the joint entropy values has been computed between the *i*th segment on the *l*th channel and the same segment of all other channels. The spatial averaging allows extracting transient events within the context of the global dynamics of the brain. Based on this procedure, then, the average mutual interdependence measure over channels is defined as:

$$AMIM(l,i)=\frac{1}{N_c-1}\sum_{k=1,k\neq l}^{N_c} H(S(l,i-M:i+M),S(k,i-M:i+M))$$
$$i=1,\dots,N_s,\ l=1,\dots,N_c \qquad (3)$$

where AMIM(l,i) is the average mutual interdependence between the EEG segment *i* (of width of $2\times M+1$ samples) of the channel *l* and other channels at instant i. N_c and N_s are the number of channels and segments, respectively. A large AMIM value indicates high degree of synchronization between EEG channels. To measure variability in the interdependence of EEG channels, the standard deviation of mutual interdependences between channels, $AMIM_{std}$, is defined as:

$$AMIM_{std}(l,i)=\left(\frac{1}{N_c-1}\sum_{k=1,k\neq l}^{N_c}[H(S(l,i-M:i+M),S(k,i-M:i+M)) - AMIM(l,i)]^2\right)^{1/2}$$
$$i=1,\dots,N_s,\ l=1,\dots,N_c \qquad (4)$$

This measure can be thought of as a rough measure of the average amount by which each interchannel joint entropy deviate on either side of the mean. A large $AMIM_{std}$ value indicates that the interchannel joint entropies are far from the mean. To eliminate aberrations and reveal the real trend in AMIM and $AMIM_{std}$, we used a moving average filter of width 300 msec for each channel.

Figure 2 shows the procedure developed to compute AMIM. It consists of the subsequent computing of:

(I) The interchannel joint entropies between the EEG channels for each segment;
(II) AMIM by spatial averaging of IJEs;
(III) Time averaging of AMIM computed at the previous step.

Accordingly, AMIM can be referred to as a spatio-temporal measure of exchange of information between different cortical regions. The most straightforward concept is to evaluate the hypothesis that this measure is capable to discriminate an interictal state from an ictal one. The existence of assumed preictal and postictal periods can be also verified.

From a vanishing AMIM we can conclude that there is desynchronization between different cortical regions. Conversely, higher AMIM value shows a relatively higher cortical synchronization. On the other hand, AMIM$_{std}$ values close to zero reflect less variability between interchannel joint entropies. For two significantly different states, the AMIM$_{std}$ determines the confidence interval for them to be considered as different states.

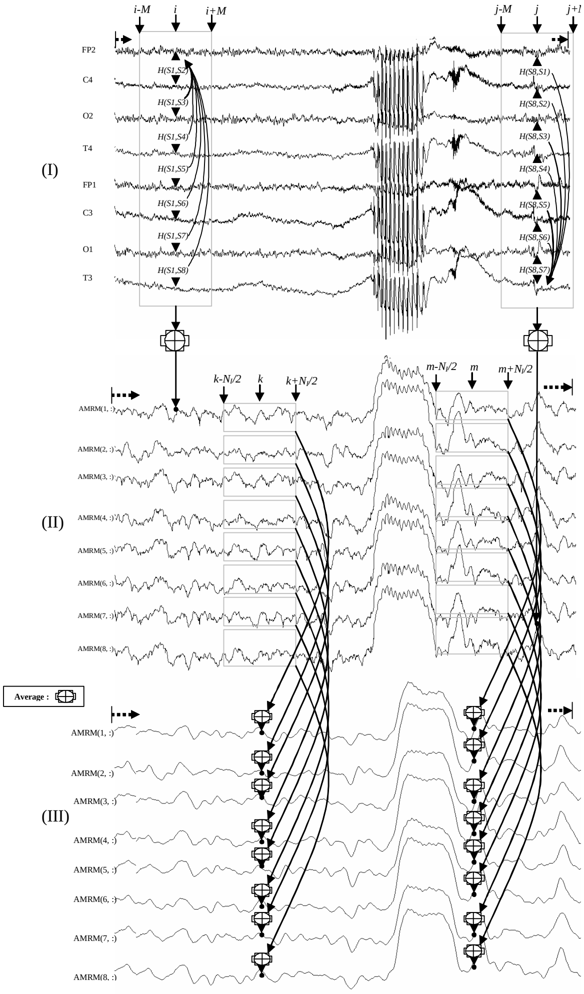

Figure 2. Schematic representation of the three-level procedure: (I) computing the joint entropy between the EEG channels for each segment, (II) computing AMIM by spatial averaging of interchannel joint entropies, (III) time averaging of AMIM computed in the previous step.

Results

We use AMIM and AMIM$_{std}$ to asses the synchrony embedded in the EEG data with seizure. A typical absence seizure is shown in Figure 3. It presents multichannel EEG and the spectrogram of all EEG channels. In Figure 3(a), the arrow is placed on the polymorphic transient where the disappearance of alpha activity occurs. On the spectrogram (Figure 3(b)) this event happens on all channels while the increase in the power of the delta activity remained undetermined. Figure 4 shows 3D representation of EEG and AMIM and AMIM$_{std}$ calculated from EEG recorded from the same seizure.

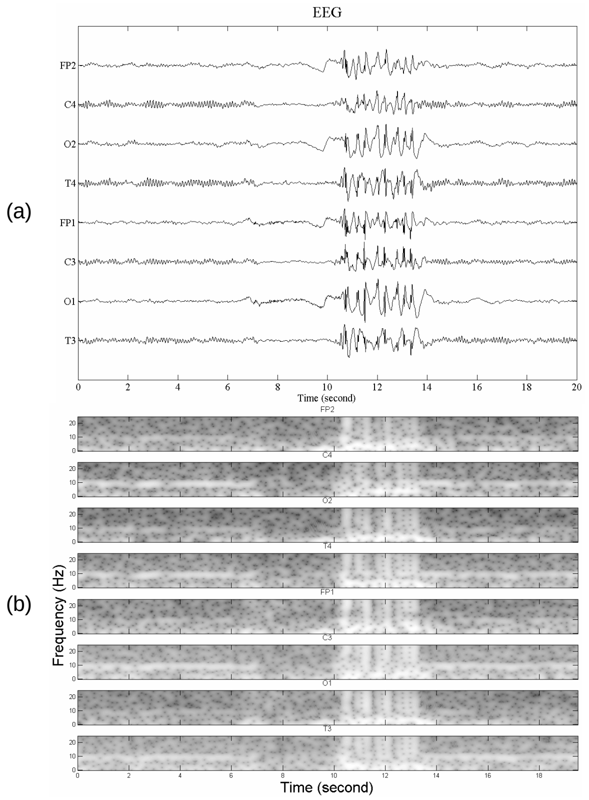

Figure 3. A typical absence seizure. (a) Multichannel EEG, (b) Spectrogram of the EEG channels. The arrow is placed where the alpha activity disappears.

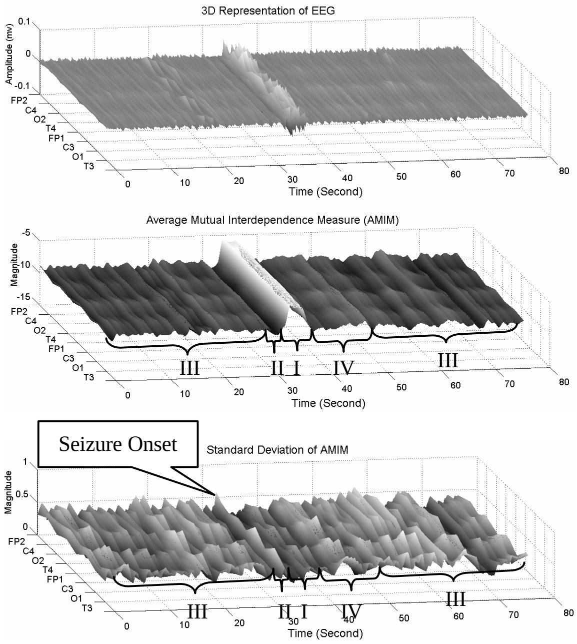

Figure 4. 3D Representation of multichannel EEG and AMIM and AMIM$_{std}$ computed from EEG recorded from the patient with absence seizure. The second plot reveals four states of the ictal (the phase used as the reference state, I), the preictal (desynchronization phase: II), the interictal (moderate synchronization phase: III) and the postictal (high synchronization : IV) states.

Table 1
Overall Mean and standard error of AMIM over each state for all states and patients that permit to differentiate significantly the four states.

Patient	Interictal III	Preictal II	Ictal I	Postictal IV
1	9.1803±0.0173	9.8801±0.0326	6.6478±0.0843	9.0887±0.0269
2	6.0155±0.0301	6.1020±0.0541	2.5653±0.0727	5.4261±0.0150
3	10.1161±0.0436	10.5397±0.0588	8.0804±0.1212	9.8911±0.0401

As shown, we observe four states as the following:

(I) *Ictal state:* During the ictal activity, a steep increase in interchannel synchronization is found by a significant increase in AMIM values. In this period, the maximum of AMIM occurs always shortly after the onset of the seizure. This reflects the high synchrony between channels during seizure. In this period, low AMIM$_{std}$ values show high degree of dependency and synchrony between different cortical regions. This period is used as the reference for identifying other states.

(II) *Preictal state:* Low values of AMIM before the seizure onset and after the polymorphic transient with duration of less than 200 msec (see Figure 3(a)) are the characteristics of this phase. This demonstrates the preictal desynchronization of cortical regions. Like the ictal period, AMIM$_{std}$ values are low in the preictal phase. The desynchronization indirectly may suggest a transitional period to higher degree of complexity of cortical networks. The duration of preictal state varies in different seizures, ranged from several milliseconds up to a few seconds.

(III) *Interictal state:* The relatively low values of AMIM in the interictal period with respect to the ictal period reflect much less synchronization than the ictal period. Conversely during this phase, high values of AMIM$_{std}$ show higher degree of independence of cortical networks in comparison to the ictal state.

(IV) *Postictal state:* Postictal state is reflected by AMIM values lower than those observed in the ictal period. In this phase the degree of synchronization is less than the one found in the ictal and higher than the ones observed in the interictal and the preictal states. On the other hand, high values of AMIM$_{std}$ show high variation in the synchrony between cortical regions.

The results of AMIM$_{std}$ demonstrate that the variability of interdependence of EEG channels decreases during the preictal and the ictal periods but not in the interictal and postictal intervals. As shown in Figure 4, at the onset of the seizure, the marked increase in AMIM$_{std}$ is associated with the rapid transition from the preictal to the ictal states. To investigate the efficiency of our analysis for all states and patients, the overall means and standard deviations of AMIM over each state were calculated and listed in Table 1. All states show statistically significant different AMIM values which show the reliability of this method in differentiating different states of EEG before, during and after seizures.

Discussion

Results show that in all analyzed absence seizures, the preictal period preceding the seizure is characterized by a decrease in synchronization between all areas of the brain. Using this representational mathematical analysis, a hypothesis can be proposed for the preictal state. The preictal desynchronization might be due to the thalamocortical inhibition which blockades local cortical neuronal networks, in this case what are recorded as EEG are mostly desynchronized background activities. We hypothesize that the existence of the polymorphic transients, happening at the transition between the interictal and preictal states, may be due to a cortical or deep subcortical trigger. Therefore this can modify the excitability of the thalamus which leads to eyes opening. For the majority of seizures a certain discrimination of the interictal and preictal period could be achieved based on a preictal decrease in AMIM values.

Conclusions

The degree of synchronization between EEG signals from different recording sites has been analyzed, and a distinct desynchronization before seizures, and a distinct high synchronization after seizures, which were usually not found during the interictal periods, has been demonstrated to characterize the preictal and postictal states. This study demonstrates how non-linear interdependence measure can disclose information difficult to obtain by visual inspection.

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