2015 International Symposium on Nonlinear Theory and its Applications
NOLTA2015, Kowloon, Hong Kong, China, December 1-4, 2015

Information processing and analysis in real time in brain-computer interface for prediction and suppression of epileptic seizures

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Abstract—This report is devoted to information processing and real-time analysis of EEG signals in brain-computer interface for prediction and suppression of epileptic seizures. Our subject under study is the genetic WAG/Rij rat model for childhood absence epilepsy which becomes instrumental in developing theories on the origin of absence epilepsy, the evaluation of new and experimental treatments, as well as in developing new methods for automatic seizure detection, prediction and or interference of seizures. Here the novel method for automated online analyses of EEG is developed for the special brain-computer interface for SWD interference by different types of electrical deep brain stimulation.

1. Introduction

Visual analyzes of the electroencephalograms (EEGs) reveal that the electroencephalographic hallmark of absence seizures, spikewave discharges (SWDs), appears abruptly from a normal background activity. Forerunners of SWDs cannot be easily detected in EEG, there are also no clinical signs from which absence seizures could be predicted. SWDs are known to be produced in an interconnected cortico-thalamo-cortical neuronal network, in which the cortex interacts with an intact thalamus.

The classical description of the spike-wave discharges in the multi-channel EEG is that the SWD appear abruptly from a normal background activity [1]. However, a gradual increase in power in the low frequencies at frontal but also at other cortical locations toward the beginning of the SWD has been found in patients in both EEG and MEG studies [2, 3]. Whether precursor activity could also be reliably found in frontal cortex and thalamus (in the genetic absence models was investigated in WAG/Rij rats. It is obvious that the reliable detection of precursor activity, in combination with different forms of electrical stimulation, may not only open new research tools, but also the possibility to investigate whether the prevention of SWD might be possible. The development of on-line SWD detection methods gives new possibilities for understanding the absence epileptic brain, the origin of SWDs, the consequences of seizures, but also to investigate whether new and different interventions, dependent on real-time seizure detection might be putative effective treatment options. Examples are neuro feedback training in WAG/Rij rats [4] and deep brain stimulation, both can be given contingent upon the real-time detection of SWDs [5, 6, 7, 8].

In this report we discuss the results of the information processing and real-time analysis of EEG signals for prediction and suppression of epileptic seizures. We develop the novel method and corresponding experimental setup for the automated on-line analyses of EEG for the special brain-computer interface for SWD interference by different types of electrical deep brain stimulation.

2. WAG/Rij rat model of absence epilepcy

WAG/Rij rats were used as model of absence epilepsy [9]. Animals were born and raised at the laboratory of the Center for Cognition, Donders Institute of Brain, Cognition and Behavior of Radboud University Nijmegen (The Netherlands). They were kept in pairs in standard cages with food and water available ad libitum under a 12–12 h lightdark cycle, with white lights on at 18:00 at a constant environment temperature of 21 C. After surgery, housing conditions were the same except that rats were housed individually. Distress and suffering of animals was kept to a minimum. The experiments were conducted in accordance with the legislations and regulations for animal care and were approved by The Ethical Committee on Animal Experimentation of the Radboud University Nijmegen.

Animals were equipped with six stainless steel electrodes (two pairs of MS 333/2A, Plastic One Inc., Roanoke, VI, USA) for monopolar recordings. Three EEG electrodes were placed epidurally over the cortex in the frontal cortical areas, skull flat. Four depth electrodes were implanted into the thalamus (ANT, PO, VPM and caudial RTN) (see for details [7]). Ground and reference electrodes were placed symmetrically over both sides of the cerebellum. Electrodes were permanently attached to the rats skull with dental cement. EEG signals were fed into a multi-channel differential amplifier via a swivel contact, band-pass filtered between 1 and 500 Hz, digitized with 1024 samples/s/channel (Data Acquisition Hardware and Software, DATAQ Instruments Inc., Akron, OH).

3. Network analyses of cortico-thalamo-cortical seizure-precursors at the frequency band of SWDs

To consider and predict SWD precursor activity we have applied both time-frequency and network analyses of EEG multichannel recordings.

To time-frequency analysis of automatically identified SWD we have used continuous wavelet transform (CWT) with complex Morlet mother wavelet, which would provide an optimal timefrequency resolution and allow to localize precisely different oscillatory patterns in the EEG [10, 11, 12]. Earlier, based on wavelet time-frequency analysis we have found [13] that SWDprecursors are observed in EEG recordings in cortex and thalamus. This precursor activity consists of several frequency components in the range from 2 to 12 Hz. The two most powerful rhythmic components in frequencies $3 \div 5$ Hz (Delta precursor) and $7 \div 12$ Hz (Theta/alpha precursor) immediately preceded the onset of SWD, considering their predominance and close proximity in time to the onset of SWD. Theta/alpha precursor activity was found in the cortex and thalamus at the same time. However, the delta events appeared first in the cortex and it was followed by a small but significant delay by delta precursor activity in the thalamus.

The discovered Delta– and Theta/alpha– precursors might be difficult to detect considering the low spatial resolution of having only single cortical and single thalamic EEG recording electrodes. Moreover, there is some variation in the exact location of the focal region. The thalamus is heterogeneous regarding projections to and from the cortex. Therefore, analysis of multi-channel EEG might be more promising for efficient and accurate diagnostics of the EEG activity preceding SWDs. In addition, it allows a better spatial resolution for mainly the contribution of the various thalamic nuclei in SWD generation and maintenance.

Under the assumption that SWD represent synchronous activity in the cortico-thalamo-cortical network, it was proposed a network approach to establish a measure of synchronization along the frequency domain. The pre-ictal $\mapsto$ ictal transition periods of 6 s duration were selected for 12 laboratory WAG/Rij rats. Epochs of non-epileptic activity were used as control data: for each rat 30 epoch of 10 s duration were randomly selected during passive wakefulness distant (by at least 5 min) to SWD. A major proportion of SWD tends to emerge during this state of vigilance (Drinkenburg et al., 1991).

The wavelet spectra of the pre-ictal $\mapsto$ ictal transition periods of each of the considered EEG channels were calculated and the local maxima at the each time moment was extracted. In other words, the ‘skeletons’ of wavelet surface was constructed. If maxima of wavelet spectra (points of skeletons) of the different channels in one time-point in one place on frequency f axis are observed, then it can be concluded that these EEG oscillations corresponding to different points of registration in the brain demonstrate synchronous dynamics because their fundamental frequencies coincide [14]. So, before the SWD a set of unordered points are present in the skeleton representation. This indicates that oscillations in each channel are characterized by its own frequencies which are not correlated with other channel frequencies. In other words, there is no inter-channel synchronization. This situation is observed both in the cortex and thalamus.

In the time period before SWD the time-frequency dynamics of multi-channel EEG dramatically changes. The maxima of wavelet surfaces begin to cluster in this time interval, demonstrating the presence of synchronization between EEG channels. Two clusters were found: one with typical frequency about $8 \div 10$ Hz (corresponding to Theta/alpha–precursor) and a second one $3 \div 4$ Hz (Delta precursor) before SWD. Analysis of the sets of SWDs (10 epochs per each of 8 animals) showed that Delta precursor activity was more pronounced in the thalamus than in the somatosensory cortex. Conversely, the Theta/alpha–precursors were more clearly expressed in the channels from the somatosensory cortex. Immediately prior to SWD onset he destruction of synchronization between channels was observed. It corresponds to the uncorrelated set of different channel oscillations frequencies. A well-pronounced inter-channel synchronization in the frequency band $8 \div 11$ Hz (main rhythm of SWD oscillations in WAG/Rij rats) and occasionally in Delta-range where a synchronous cluster is formed and destroyed the irregularly. It illustrates how SWD emerge.

So, we can conclude that in contrast to a long lasting view that SWD are sudden and unpredictable events (Panayioutopoulos, 1997; ref), SWD generation is a gradual process which already starts more than a second prior to the onset of a full blown SWD. Such early changes might open the possibility for SWD prediction. The obtained results obtained received with both time-frequency and network analyses demonstrate the possibility to detect SWD preceding activity. It is by no means clear which of the methods is preferable, and most robust. The well-pronounced synchronous cluster at the frequency band of SWDs ($8 \div 11$ Hz) suggests that synchronization in the cortico-thalamo-cortical network at the $8 \div 11$ Hz range might be a possible candidate to act as a biomarker of the subsequent formation of SWD in cortex and thalamus.

4. The design of brain-computer interface for the automatic seizure prediction system based on the multi-channel EEG set

The network algorithm described in Section 3 may be implemented with the help of the interface for the automatic seizure prediction shown in Fig. 1. Typically, there is no need to analyze a lot of channels of ECoG to detect

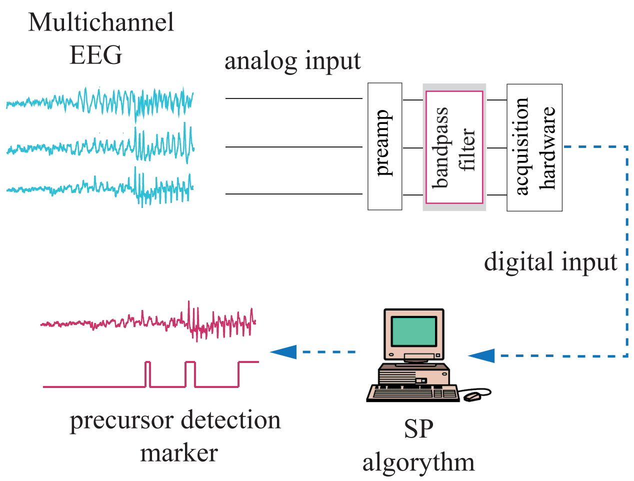

Figure 1: The brain–computer interface for the automatic seizure prediction system based on the multichannel EEG set

the precursor, especially, in the real-time regime. ECoG channels based on properties of skeletons of wavelet surfaces corresponding to different ECoG channels were chosen. The selection of the channels for the effective analysis should be based on the skeletons that reflect the most different time-frequency dynamics. Usually, all cortical channels show the same frequency dynamics, therefore only one cortical channel (Layer 5) was included. Frequency dynamics of thalamic recordings is significantly different from the cortex dynamics. Among thalamic channels the largest difference in frequency dynamics holds for the anterior nucleus (ATN) and posterior nucleus of thalamus (PO). Therefore these three channels, namely, Cortex 5 channel (ctx5), Anterior nucleus of thalamus (ATN) and Posterior nucleus of thalamus (PO) were used.

In this case the expression for the resulting product of the wavelet energy values of the different EEG channels may be written as

$$R(t) = \langle|W_{ctx5}(t)|\rangle_f \times \langle|W_{ATN}(t)|\rangle_f \times \langle|W_{PO}(t)|\rangle_f, \qquad (1)$$

where $\langle|W_{ctx5}(t)|\rangle_f$ is the wavelet energy calculated in the considered $8 \div 11$ Hz SWD frequency band for Cortex 5 channel, $\langle|W_{ATN}(t)|\rangle_f$ and $\langle|W_{PO}(t)|\rangle_f$ are the energy values obtained for ATN, and PO, respectively.

The example of typical dependence of the characteristic (1) on time before and during the onset of the seizure is given in Fig. 2. It can be seen that before the onset of SWD the value of $R(t)$ starts to increase; it witnesses the simultaneous increase of the wavelet energy within the frequency range corresponding to SWD oscillations for all examined channels of EEG. The time intervals when the value of the energy product exceeds the threshold are the markers of the precursor activity. So, we can conclude that the analysis of the wavelet energy in the frequency range corresponding to SWD dynamics allows not only to recognize automatically the seizure event but also predict it by means of the well-known threshold method [10, 11, 12].

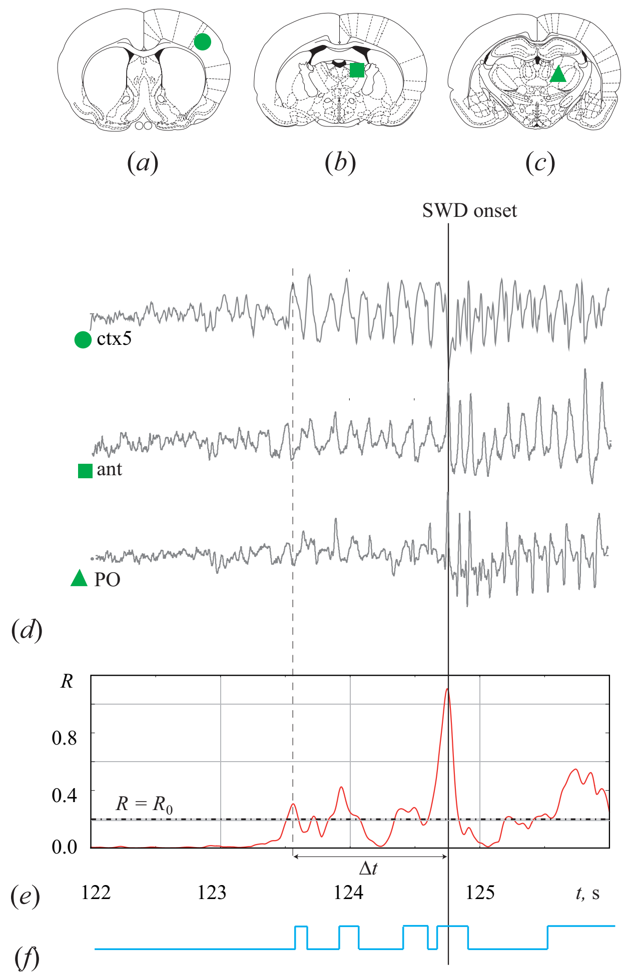

Figure 2: The ECoG recordings electrodes location in the brain (a,b,c), ECoG recordings corresponded to different ECoG channels (d), the dependency of the considered characteristics $R(t)$ on time (e). The moments of time, considered as the precursor and the onset of seizure (the point of clinical attack is marked as “SWD onset”) are shown by the dashed and solid lines, respectively). (f) The result of prediction, based on the use of threshold value $R_0 = 0.2$

According to the results concerning the online SWD prediction, based on the considered wavelet-based method, we can find the high (up to 90%) percent of predicted seizures (high sensitivity of the algorithm). But at the same time it comes with the large amount of false detections, which are caused by the appearance of any other oscillatory patterns on EEG during light-slow wave sleep. Mean value of false detection during light-slow wave sleep time intervals is close to 20 events per minute. Whether these precursors are only present in these genetic epileptic rats, or whether these precursors a marker of a process of synchronization of cortical brain activity in general during the process of the transition from passive wakefulness to drowsiness and light slow wave sleep, needs further analyses. In this regard, the future development of algorithms for seizure prediction is connected with the achievement of a good balance between their sensitivity (number of predicted epochs) and specificity (the relation between the number of predicted SWDs and number of false alarms). The combination of our algorithm with a light-slow wave sleep detection system will already reduce quite a number of false alarms.

5. Conclusion

Based on both time-frequency and network analyses we can conclude that absence seizures are preceded by short lasting delta and theta precursor oscillatory activity in cortex and thalamus and that the combination rarely occurs during control periods. Our studies show that the well-pronounced synchronous cluster at the frequency band of SWDs observed in the pre-ictal–ictal transition period suggests that synchronization in the cortico-thalamo-cortical network at the $8 \div 11$ Hz range can be considered as a possible candidate to act as a biomarker of the subsequent formation of SWD in cortex and thalamus. We have proposed effective wavelet-based method of identification of precursor synchronous cluster in the cortico-thalamo-cortical network by means of multi-channel EEG recording.

The successful detection of a pre-seizure state before clinical onset gives a possibility of special brain computer interfaces development for the automatic on-line identification of absence seizure and chance for a therapist to prevent seizure by means of new treatment techniques, such as the delivery of an electric impulses series or transcranial stimulation to avoid an oncoming seizure.

Acknowledgments

This work has been supported by the Russian Science Foundation (grant 14–12–00224).

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