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Characterizing dynamics of absence seizure EEG with spatial-temporal permutation entropy

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ABSTRACT

Characterizing transient brain dynamics prior to seizures is a main challenge in absence epilepsy study. As brain is a chaos dynamical system, many complexity based methods have been used to track the dynamical changes of absence seizure EEG. However, most of these methods treat multichannel EEG recordings as a set of individual time series, which will inevitably lead to the loss of crucial cross-channel correlation in the epileptic network. Recently, a spatial-temporal permutation entropy method called multivariate multiscale permutation entropy (MMPE) was proposed to measure the complexity of multichannel data. In this study, MMPE was applied to multichannel EEG for characterizing dynamics of absence seizure. It was found that the pre-ictal EEG exhibited a significant lower MMPE value than interictal EEG, and a significant higher MMPE value than the ictal EEG, indicating that the complexity of multichannel EEG decreased in the transition of brain activities. This finding confirmed the existence of a pre-seizure state in absence epilepsy. The identification ability of MMPE was tested against its original univariate complexity measures: permutation entropy (PE) and multiscale permutation entropy (MSPE), and another multivariate multiscale entropy: multivariate multiscale sample entropy (MMSE). After evaluating the performance by four classifiers (Decision Tree, *K*-Nearest Neighbor, Discriminant Analysis, Support Vector Machine), MMPE can achieve accuracy of 87.2% at least, which is about 15%, 12%, and 10% higher than that of PE, MSPE and MMSE. Hence, this work supports the view that EEG has a detectable change prior to an absence seizure, and MMPE could be considered as a candidate precursor of the impending absence seizures.

1. Introduction

Absence epilepsy is predominantly a disease of childhood. Absence seizures are temporally short, and may recur over 100 times a day, which would have significant impact on the daily life of sufferers [1]. Lots of effort have been devoted to investigate the dynamic changes of EEG, and attempt to find suitable indicators that can quantify dynamic characteristics of seizure [2,3]. However, there still exists a debate about whether the epileptogenic process in absence seizures corresponds to a model of abrupt transition or gradual and detectable transition [4]. Hence, it is challenging to understand the transition of brain activities towards an absence seizure and look for some precursor that can aid in the diagnosis of epilepsy and open new therapeutic possibilities.

It is well known that brain is a chaos dynamical system, and the brain data often exhibit complex fluctuations that contain information about the underlying dynamics [5,6]. It was recently shown that measures of statistical or structural complexity are necessary for a better understanding of chaotic time series because they are able to capture their organizational properties [7]. Hence, complexity-related metrics may have potentially important applications to extract information useful to distinguish different brain states. Sample entropy (SE), as one of the most widely used complexity measures, have been introduced to analyze physiological time series [8]. SE reflects the likelihood that "similar" patterns of observations will not be followed by additional "similar" observations. However, there are major pitfalls involving in tracking the dynamics of absence seizure EEG with SE. First of all, SE is very sensitive to parameter selections, especially the tolerance threshold (r) for accepting similar patterns [9]. Moreover, SE is amplitude dependent method, which would make SE vulnerable to the effect of artifacts in EEG and the selection of reference

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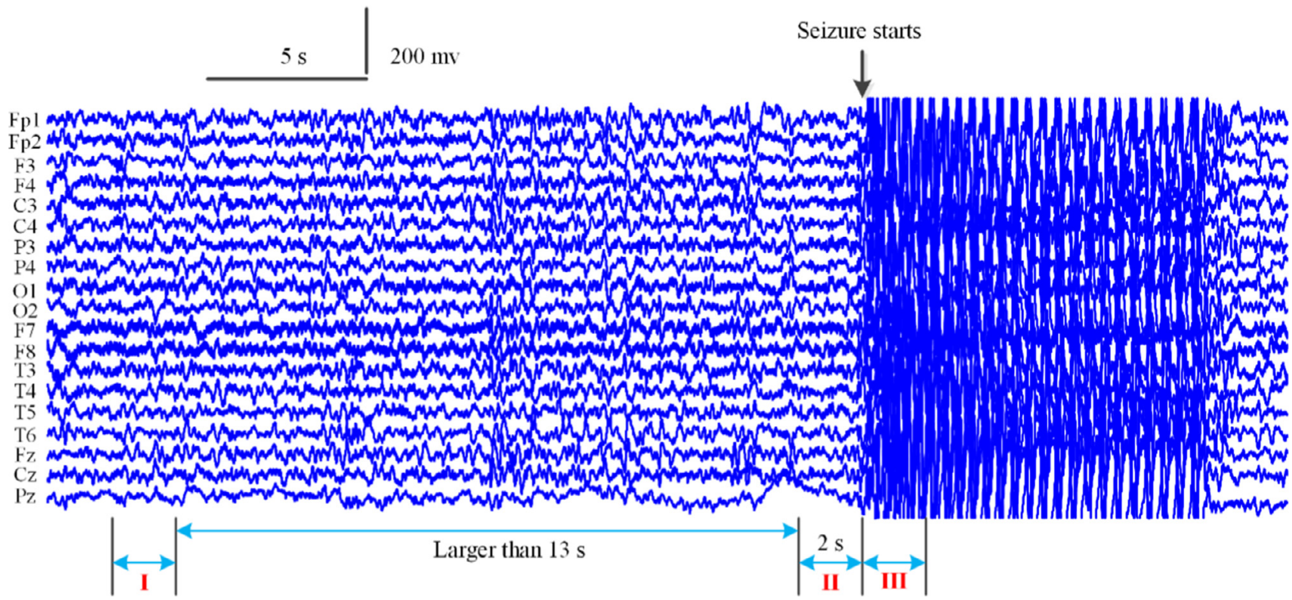

Fig. 1. The continuous 19-channel EEG recordings with an absence seizure, and segments corresponding to interictal, pre-ictal, and ictal EEG are denoted by I, II, and III, respectively.

electrode. In addition, SE is heavily dependent on the data length and may diverge from their analysis for short data sets [10]. While absence seizure is often very temporally short, the sensitivity to data length would inevitably limit SE to effectively capture transient dynamics of absence seizure EEG.

To address these issues, permutation entropy (PE) was introduced as an alternative measure of complexity for absence seizure EEG [11,12]. The concept of PE is based on the measure of the relative frequencies of different ordinal patterns in time series, which means that there is no need to choose the tolerance threshold. Since the PE is a symbolic methodology that does not depend on the amplitude of the signal, it will be robust to noise and avoid the effect of the selection of reference electrode. As an invariant measure, PE can discern the subtle change of complexity from limited amount of data. These advantages make PE extremely suitable for tracking the transient dynamics in one-dimensional signal. Our previous analysis found that PE can successfully detect preictal-state in 169 of 314 seizures (54%), which was higher than SE (21%) [13]. However, there are often evident or underlying structural correlations over multiple temporal scales in physical time series, while permutation entropy at single scale cannot reflect the inherent multiple time scales. To quantify the interdependence between complexity and time scales, multiscale permutation entropy (MSPE) was proposed to analyze the absence seizure EEG in our previous work [14]. It was found that the MSPE can more accurately track the dynamics of absence seizure compared to the single-scale PE.

Although interesting results can be obtained, application of PE/MSPE for absence seizure EEG still suffers from the following defects. Firstly, as a univariate analysis method, PE/MSPE can only reflect the complexity changes in single channel EEG recordings. According to the International League Against Epilepsy (ILAE), childhood absence epilepsy is a generalized type of epilepsy and does not have a localized source [15]. Hence, it needs to be further explored which channel should be considered as the representative channel to track brain state. Furthermore, PE/MSPE treats multichannel time series as individual time series and analyzes them separately. This leads to a result that they cannot account for spatial relationship among channels and only suite for multivariate signals that are statistically independent. However, epileptic seizures are thought to be generated and to evolve through an underlying anomaly of synchronization in the activity of groups of neuronal populations [16]. When analyzing the absence seizure EEG with PE/MSPE, the relevant cross-channel correlation will inevitably be lost. Hence, there is a need to explore some complexity measures that can track the dynamical changes in both temporal and spatial spaces.

To capture the spatial-temporal dynamical changes, multivariate multiscale permutation entropy (MMPE) [17] is applied to analyze the multichannel absence seizure EEG in this work. The MMPE deals with multichannel neural data simultaneously over multiple time scales in a rigorous and unified way. This method can be used to cater for within- and cross-channel correlations as well as for complex dynamical couplings and various degrees of synchronization over multiple scales, thus allowing for direct analysis of multichannel data. The focus of this paper is twofold: (1) to show that the transient dynamics of EEG data prior to the absence seizures can be identified by MMPE, thus suggesting the existence of a pre-seizure state in absence epilepsy; (2) to show the advantages of MMPE over other complexity measures in distinguishing seizure state.

2. Materials and methods

2.1. Subjects and data acquisition

EEG recordings were obtained from 9 patients (5 males and 4 females) aged from 8 to 21 years old with absence epilepsy. The study protocol had taken consent from the ethics committee of Peking University People's Hospital and the patients had signed informed consent that their clinical data might be used and published for research purposes. The EEG data were recorded by the Neurofile NT digital video EEG system from a standard international 10–20 international system (Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, T6, Fz, Cz, and Pz). EEG data was obtained at a sampling rate of 256 Hz using a 16-bit analogue-to-digital converter and filtered within a frequency band from 0.5 Hz to 35 Hz.

To investigate the characteristics of absence seizure EEG, interictal, pre-ictal, and ictal EEG segments were selected from the EEG recordings of 9 patients. The timing of onset and offset in spike-wave discharges (SWDs) was identified by an epilepsy neurologist (XZL), and these SWDs were defined as large-amplitude rhythmic 3–4 Hz discharges with typical spike-wave morphology lasting >1.0 s. As illustrated in the Fig. 1, the first 2 s segment