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Analysis of variations of correlation dimension and nonlinear interdependence for the prediction of pediatric myoclonic seizures – A preliminary study

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ABSTRACT

In this preliminary study, we evaluated the predictive ability of Correlation Dimension (CD) and Nonlinear Interdependence (NI) for seizures in pediatric myoclonic epilepsy patients. Scalp EEG recordings of eight diagnosed cases of myoclonic epilepsy were analyzed using Receiver Operating Curve (ROC) for discriminating the preictal period from interictal period. Furthermore, based on clinical seizure characteristics and EEG data, the spatiotemporal patterns of measures in clinically relevant areas of the brain were compared with other areas for each patient. CD showed a dominant increasing behavior in both all of the individual channels and channels of clinical interest for 75% of patients. For NI, the dominant direction was also increasing in 62.5% of patients for all of the individual channels and in 75% of patients for channels of clinical interest. However, there was no consistent general behavior in the timing of the preictal change amongst patients and within individual patient. Nonlinear measures of CD and NI can differentiate the preictal phase from the corresponding interictal phase. However, due to high variability, patient-wise tuning of possible automated systems for seizure prediction is suggested. This is the first study to employ nonlinear analysis for seizure prediction in pediatric myoclonic epilepsy.

1. Introduction

Myoclonic epilepsy in children comprises up to 10% of all epilepsies and is characterized by simple seizures with nonrhythmic fast contractions of muscles in short periods of time occurring at variable intervals. These seizures are often combined with other types of generalized seizures (Camfield et al., 2013; Genton et al., 2013; Noachtar and Peters, 2009). Due to its specific etiopathology, neurophysiological and clinical features and associated disorders, appropriate treatment and management of myoclonic epilepsies in children pose special problems for the physician and the family of patients (Crespel et al., 2013; Koepp et al., 2014; Serafini et al., 2013; Wolf et al., 2015).

Various techniques for automated analysis of EEG signal based on time domain (Lin et al., 2016), frequency domain (Bandarabadi et al., 2015) and time-frequency (Tzallas et al., 2007) analysis have been used in seizure detection and prediction studies. These techniques offer rapid detection of ictal and interictal events and play important role in developing new treatment methods and improving the quality of life of patients (Kannathal et al., 2013; Litt and Echauz, 2002; Mormann and Andrzejak, 2016; Paternoster et al., 2013; Shorvon et al., 2011).

EEG signals of normal brain have several characteristics of nonlinear systems, including limit cycles, instances of bursting behavior, hysteresis and amplitude-dependent frequency behavior (Carney et al., 2011). In addition, EEG signal recorded from patients with epilepsy is nonlinear and shows chaotic behavior (Mormann et al., 2005; Osorio et al., 1998; Rogowski et al., 1981). These observations suggest the possibility of detection of preictal state by dynamically monitoring minute variations of specific nonlinear measures that can signal the impending seizure before its onset.

Nonlinear dynamics for characterizing epileptic EEG signals employ various univariate and bivariate nonlinear measures for the detection of preictal state such as correlation dimension (Lehnertz and Elger, 1998),

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correlation density (Martinerie et al., 1998), largest Lyapunov exponent (Iasemidis et al., 1990), Kolmogorov entropy (van Drongelen et al., 2003), nonlinear interdependence (Arnhold et al., 1999) and phase synchrony (Mormann et al., 2000). These nonlinear measures provide different information about the underlying process leading to a seizure (Lehnertz et al., 2001). Therefore, automated algorithms designed to detect preictal state usually employ both univariate and bivariate measures (Brinkmann et al., 2016).

Application of nonlinear measures for seizure prediction shows different spatiotemporal characteristics including the direction and timing of variations in different areas of the brain during assumed preictal period. Studies have reported either marked decrease in the dimension of EEG signals using correlation dimension (Elger and Lehnertz, 1998), or both increase and decrease in amplitude of correlation dimension during preictal period (Aarabi and He, 2012). Similarly nonlinear interdependence shows either a decrease in epileptogenic zones seconds to minutes prior to seizure (Arnhold et al., 1999), or various patterns of synchrony in different areas (Aarabi and He, 2012; Mormann et al., 2005). These variations have also been observed in the durations of preictal state ranging from seconds to hours (Bandarabadi et al., 2015; Mormann et al., 2003b). Furthermore, depending upon the type of algorithm used for the detection of preictal state, best possible results can be obtained by the placement of electrodes either over seizure onset zones (Gadhoumi et al., 2012), or over remote areas (Kuhlmann et al., 2010; Mormann et al., 2003b).

Automated seizure prediction systems are designed for specific predictive measures (Gadhoumi et al., 2016) and sometimes lead to contradicting results. This calls for further investigation of spatiotemporal characteristics of nonlinear measures extracted from epileptic EEG signals. For this purpose, our study focuses on two nonlinear measures: Correlation dimension as the univariate measure, and nonlinear interdependence as the bivariate measure. The application of these measures in predicting pediatric myoclonic seizures is analyzed based on their performance in discriminating the preictal period from the interictal period. Although some studies have used accelerometry for the detection of myoclonic seizures (Ramgopal et al., 2014), to our knowledge, this is the first study that employs nonlinear EEG analysis for the prediction of myoclonic seizures. We narrowed our focus on pediatric patients as they are one of the most challenging to manage (Jerger et al., 2001; Meyer-Lindenberg, 1996; Paternoster et al., 2013; van Drongelen et al., 2003). Application of nonlinear techniques for pediatric patients needs a specific and discrete treatment (van Dijkman et al., 2016b) (van Dijkman et al., 2016a). In this preliminary study, EEG recordings of a single seizure from eight diagnosed cases of myoclonic epilepsy were analyzed for the amplitude distribution of each of these nonlinear measures during interictal and preictal periods. Also, the spatiotemporal patterns of nonlinear measures in clinically relevant areas of the brain were compared with the other areas.

2. Methods

2.1. Subjects

We carried out a retrospective study using EEG data of patients who underwent long term Video-EEG monitoring due to unknown type of epilepsy or intractable seizure focus at the Shefa Neuroscience Research Center, Khatam al Anbia Hospital, Tehran, I.R. Iran. Subjects' demographic data, including seizure characteristics and corresponding clinically relevant regions/EEG channels were obtained from their medical records (Table 1). The study sample comprised of eight patients from 2010 to 2015. This study was approved by the medical research ethics committee of the Baqiyatallah University of Medical Sciences. The patients' medical records and EEG data were accessed with permission of the director of Shefa Neuroscience Research Center. According to the declaration of Helsinki, the confidentiality of patients was maintained throughout the data acquisition and analysis and each

Table 1
Patients' demographic and seizure data and EEG recording characteristics.

Patient #	Age (years)/ Gender	Epilepsy (years)	Duration of observation period (day)/ No. of Seizures	Drugs	Seizure Characteristics	Relevant EEG Channels/Regions
1	4/M	3	3/5	Acetazolamide, Depakine, Phenytoin Compound (Phenytoin and Phenobarbital)	Myoclonic jerk, head drop, tonic, tonic clonic	Left side parietal and temporal regions
2	9/M	9	1/5	Clobazam, Phenobarbital, Acetazolamide, Primidone	Tonic, head drop, left side clonic movements, dialeptic, staring	Right side of skull
3	9/M	9	1/Frequent	Carbamazepine, Primidone	Myoclonic, LGS	All regions
4	17/M	17	4/2	Clonazepam	Myoclonic jerk, generalized atonic, psychomotor	Left side frontal and temporal regions
5	12/M	4	1/21	Vigabatrin, Topiramate	Intractable mixed type (CPS, myoclonic and GTC)	Left side frontal, central, parietal and temporal regions
6	11/F	1	5/125	Carbamazepine, Levetiracetam	Myoclonic jerks on right side of face and right hand, staring	Left side frontal, central regions
7	19/F	15	1/2	Lamotrigine, Sertraline	Jerky movements of upper extremity, staring	Right frontal region
8	10/M	NA	2/Frequent	NA	Myoclonic, partial, clonic, GTCS	All regions

LGS: Lennox-Gastaut Syndrome; CPS: Complex Partial Seizure; GTC: Generalized Tonic Clonic.