Physics Letters A 380 (2016) 1419–1425

Contents lists available at ScienceDirect

Physics Letters A

www.elsevier.com/locate/pla

Evaluation of selected recurrence measures in discriminating pre-ictal and inter-ictal periods from epileptic EEG data

Eulalie Joelle Ngamga [a], Stephan Bialonski [b], Norbert Marwan [a,*], Jürgen Kurths [a,c,d], Christian Geier [e,f], Klaus Lehnertz [e,f,g]

[a] Potsdam Institute for Climate Impact Research, Telegraphenberg A 31, 14473 Potsdam, Germany
[b] Max-Planck-Institute for the Physics of Complex Systems, Nöthnitzer Straße 38, 01187 Dresden, Germany
[c] Department of Physics, Humboldt University Berlin, 12489 Berlin, Germany
[d] Institute for Complex Systems and Mathematical Biology, University of Aberdeen, Aberdeen AB24 3UE, United Kingdom
[e] Department of Epileptology, University of Bonn, Sigmund-Freud-Straße 25, 53105 Bonn, Germany
[f] Helmholtz Institute for Radiation and Nuclear Physics, University of Bonn, Nussallee 14–16, 53115 Bonn, Germany
[g] Interdisciplinary Center for Complex Systems, University of Bonn, Brühler Straße 7, 53175 Bonn, Germany

ARTICLE INFO

Article history:
Received 9 November 2015
Received in revised form 15 February 2016
Accepted 16 February 2016
Available online 20 February 2016
Communicated by C.R. Doering

Keywords:
Recurrence plot
Recurrence quantification analysis
Recurrence network
EEG
Pre-seizure state
Epilepsy

ABSTRACT

We investigate the suitability of selected measures of complexity based on recurrence quantification analysis and recurrence networks for an identification of pre-seizure states in multi-day, multi-channel, invasive electroencephalographic recordings from five epilepsy patients. We employ several statistical techniques to avoid spurious findings due to various influencing factors and due to multiple comparisons and observe precursory structures in three patients. Our findings indicate a high congruence among measures in identifying seizure precursors and emphasize the current notion of seizure generation in large-scale epileptic networks. A final judgment of the suitability for field studies, however, requires evaluation on a larger database.

1. Introduction

Recurrence plots (RPs) are graphical representations of times during which two states of a system are neighbors in phase space [1]. They have been widely used over the last 25 years as a tool to study changes and transitions in the dynamics of a system (even high-dimensional), or to detect synchronization and coupling [2–4]. This has been achieved by using the visual aspects of structures encountered in RPs as well as different statistical quantification approaches [2,3]. One important and widely used approach is *recurrence quantification analysis* (RQA), which is based on diagonally and vertically aligned recurrence points in the RP [5,6]. These lines characterize the temporal interdependences between individual observations or segments of the phase-space trajectory. Several substantial measures of complexity (MOC) have been defined on the base of these temporal structures of the RP and are related to predictability, stationarity, or intermittency. RQA has demonstrated its potential through many successful applications in different fields [7]. Among others, they were applied to electroencephalographic (EEG) data from epilepsy patients as well as from epileptic rats. For example, Acharya and colleagues [8] have used RQA measures to classify EEG data from normal, during seizures (ictal), and between seizures states (inter-ictal). Further, RQA measures have been reported to exhibit sudden abrupt changes occurring up to some minutes before seizure onsets [9–12]. The latter findings can contribute to better understand this neurological disorder that affects about 65 million individuals worldwide [13] as well as to develop alternative therapies, e.g. based on the prediction of seizures [14–20], particularly for the 20–30% of patients that remain poorly treated or untreated [21]. It remains elusive, however, whether the described phenomena can be regarded as seizure precursors, since their statistical validity has not sufficiently or not at all been investigated, and since the analyzed EEG recordings were of rather short duration.

Recently, another quantification approach has been introduced that combines time series recurrence with complex networks [22–24]. Here, the recurrence matrix is considered as the adja-

* Corresponding author.
E-mail address: marwan@pik-potsdam.de (N. Marwan).

http://dx.doi.org/10.1016/j.physleta.2016.02.024

cency matrix of an undirected and unweighted complex network. The resulting *recurrence network* (RN) can be characterized with well-known network measures, i.e., further diagnostic tools become available for time series analysis [25,26]. In contrast to RQA, where the MOC characterize the *dynamical properties* of the system, these network-based measures capture the *geometric properties* associated with a trajectory in phase space [24]. Such complementary information can be useful when studying regime changes [25], characterizing different dynamics [27,28], or even for the detection of coupling directions [29]. First applications in different scientific disciplines have demonstrated the usefulness of these additional characteristics. Very promising findings have been discussed, e.g., by Lang and colleagues [30] in a RN-analysis of synchronous EEG time series from normal subjects and from epilepsy patients. Among other findings, the authors observed that RNs of normal subjects exhibited a sparser connectivity and a smaller clustering coefficient compared to those of epilepsy patients (cf. [31]). These findings have been confirmed by another study, reporting an increasing degree of structural complexity in the EEG of normal subjects compared to the EEG from epilepsy patients [32].

It has been suggested that the conceptual difference between RQA and RN measures may allow to capture complementary aspects of the underlying dynamics under investigation, and that the combined use of both quantification approaches may improve the detection of dynamical changes [24]. In certain applications, however, a higher performance of RN measures in comparison to that of RQA measures has been observed. For example, this has been reported in Ref. [33] where a classification of healthy women and preeclamptic patients based on cardiovascular time series has been performed with the aim of performing early prediction of preeclampsia. Another example is found in Ref. [27], where a classification of periodic and chaotic behavior is performed using short time series of observables from continuous-time dynamical systems.

We observed a lack of literature describing such a comparison of performance between RQA and RN measures when applied to time series from complex systems such as the brain, and in particular in the analysis of EEG data. In the present work, we compare selected RQA and RN measures for a specific problem of multivariate EEG data analysis. In particular, we investigate the suitability of these measures for an identification of pre-seizure states in multi-day, multi-channel, invasive EEG (iEEG) recordings.

2. Data and methods

2.1. Patient characteristics and data

We analyze iEEG recordings from five epilepsy patients (see Table 1 and Fig. 1) who underwent presurgical evaluation of drug-resistant epilepsy at the University of Bonn Epilepsy Program [34]. The patients signed informed consent that their clinical data might be used and published for research purposes. Further, the study protocol had received prior approval by the ethics committee of the University of Bonn.

The iEEG data was recorded from chronically implanted intrahippocampal depth and/or subdural grid and strip electrodes (on average of 54 contacts) with a total recording time of 929 h during which 32 seizures (five to seven seizures per patient) occurred. The data was band-pass-filtered between 0.1 and 70 Hz, sampled at 200 Hz using a 16 bit analog-to-digital converter, and referenced against the average of two recording contacts outside the focal region. Reference contacts were chosen individually for each patient. Some recording gaps have been encountered and they were mainly due to diagnostic procedures that required the patient to be temporarily disconnected from the recording system.

Table 1
Clinical data. ID: patient identification number; age (yrs.) and gender: female (f), male (m); D_{epi}: duration of epilepsy (yrs.); FH: focal hemisphere, left (L), right (R); FR: focal region, MT mesial aspects of temporal lobe, LT lateral aspects of temporal lobe; N_{rs}: number of recording sites; N_{sz}: number of seizures; D_{rec}: duration of iEEG recording (hrs).

ID	age/gender	D_{epi}	FH	FR	N_{rs}	N_{sz}	D_{rec}
1	37/f	5	R	MT	70	7	169
2	55/m	10	L	LT	20	6	232
3	44/f	44	L	LT	52	5	220
4	22/m	19	L	LT	62	7	167
5	35/f	6	R	LT	70	7	141

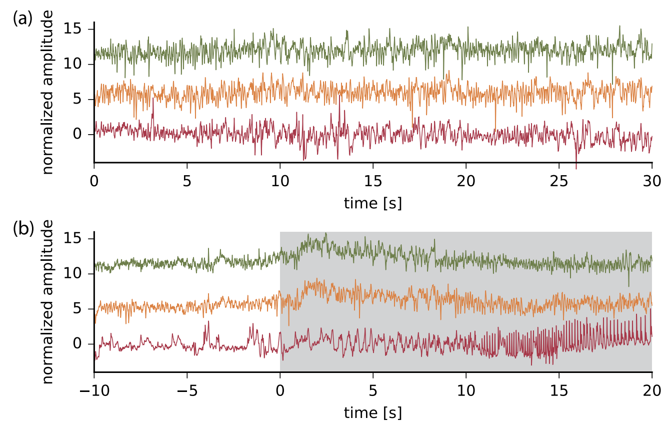

Fig. 1. Example of iEEG data from an inter-ictal (a) and a pre-ictal/ictal period (b) of patient 3 from recording sites within the epileptic focus (red), from its neighborhood (orange), and from a remote brain region (green). The latter two time series were shifted to enhance readibility, and amplitude values were normalized to zero mean and unit variance. The gray-shaded area marks the initial phase of the seizure. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

2.2. RQA- and RN-based measures of complexity

The basis of the MOC that we here used to characterize the iEEG is the recurrence plot (RP). It was introduced to visualize the time-dependent behavior of the dynamics of a system and particularly the recurrences of the phase-space trajectory to a certain state [1,2]. Let us consider x as an exemplary univariate time series with T sampling points and let x_i denote the value of x at discrete time i. In order to observe the recurrences of states from this time series, we compute the $T \times T$ matrix

$$\mathbf{R}_{i,j} = \Theta(\varepsilon - |x_i - x_j|), \qquad i, j = 1, \ldots, T \tag{1}$$

where $\Theta(\cdot)$ is the Heaviside function, ε is a predefined threshold, and $|\cdot|$ denotes absolute value. In general, Eq. (1) can be applied on phase-space trajectories in $\mathbb{R}^m$ (where m is the dimensionality and the absolute value is replaced by a norm [2]), but here we apply it on time series directly (i.e., without embedding of time series in the phase space, similarly to Ref. [35]). This choice is motivated by the fact that several recurrence properties are invariant under embedding [36] and by the highly non-stationary character of brain dynamics [37–39], which complicates the choice of appropriate embedding parameters. Moreover, embedding can cause spurious correlations which affect mainly the recurrence analysis of stochastic signals [40].

An RP is a graphical representation of the above defined matrix $\mathbf{R}$. For the coordinate (i, j) of an RP we choose black color to plot a point if $\mathbf{R}_{i,j} = 1$, i.e., in the recurrent case, and white color otherwise. An example is shown in the left part of Fig. 2 for 10.24 s of an iEEG recording. The white and black points can form different lines and structures, which are related to the properties of the underlying dynamics.