On the Calculation of Entropy of EEG Transients

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Abstract

In order to characterize abnormal behaviours related to epileptic seizures and other neurological disorders, in this paper it is described a methodology and fundaments to find an optimum tolerance criterion r to estimate the entropy of abnormal transients with a duration of two seconds from electroencephalograms (EEG) recordings of patients diagnosed with partial epilepsy, attention deficit/hyperactivity disorder (ADHD), and conduct disorder (CD). The considered EEG signals come from patients with different ages diagnosed with these cerebral disorders in order to investigate the possibility of identifying each of them using approximate entropy (ApEn) and sampling entropy (SampEn) of the transients, which lead to the determination of an appropriate value for the parameter r. With the present approach it is possible to obtain an accurate identification of abnormal transients in EEG signals of short duration and reliable estimations of their entropies.

Keywords: *EEG recordings, approximate entropy, sampling entropy, abnormal transients, Epilepsy, ADHD, conduct disorder.*

1. Introduction

Some cerebral disorders from several etiologies may affect people from all ages. Epilepsy is characterized by recurrent seizures due to excessive electric discharges from groups of brain cells. This disease is the most common neurological cause of death. Only 70% of patients with epilepsy adequately respond to drug-based treatments. Epilepsy accounts for 0.6% of the global burden of disease. In 2012 epilepsy was responsible for approximately 20.6 million disability-adjusted life years (DALYs) lost (World Health Organization, 2018).

Other common neurodevelopmental disorders that can be diagnosed during childhood are attention deficit/hyperactivity disorder (ADHD), and conduct disorders (CD). Patients with ADHD can be overly active thereby it could be difficult for them to pay attention, or to control some impulsive behaviours. In this sense, children with ADHD may act without thinking about the possible consequences of their actions (Centers for Disease

Control and Prevention, 2018a). Just to mention, ADHD is a condition that affects approximately 9.5% of children in USA with ages ranging from 4 to 17 years old (Centers for Disease Control and Prevention, 2018b). ADHD would last until adulthood in children diagnosed with this disease.
Regarding CD, it is a mental condition diagnosed when children show an increasingly aggressive behaviour as well as serious violations of social norms and rules in public places. Children with CD are more likely to get injured, and may have difficulties of gettingalong with peers (Centers for Disease Control and Prevention, 2019).

Electroencephalography is a technique used in neurology that registers and measures the electrical activity of the cerebral cortex. This has been used as a clinical standard procedure to evaluate the central nervous system. Electric waves measured in electroencephalograms (EEG) are provoked by changes of potential between electrodes located at standardized places over the patient's scalp. EEG signals are the key tool in the diagnosis and treatment of some neurological disorders.

EEG recordings on average last 30 minutes. A wave that presents particular features of EEG activity is called a pattern. Patterns can be classified into three types: 1) attenuation, signals of low amplitude; 2) transients, which are isolated waves or complexes clearly distinguished from the background activity that suddenly appear; and 3) repetitions, which are transients that repeat several times without interruption by the background activity (Stern, 2010; Kane, 2017).

Some EEG patterns are related to certain mental diseases, and these can be used to identify some events of epileptic seizures as well as other cerebral diseases related to behaviour problems. Patterns can be classified as normal or abnormal, depending on the patient's characteristics. For example, the delta activity pattern that can be abnormal in adults, in three-years old patients is considered normal (Stern, 2010, Chap. 10). Another example is the transient K-complex found in EEG signals of patients of all ages that is considered as a normal event in the stages II and III of sleep (Boostani, 2017; Camilleri, 2014; Stern, 2010, Chap.15). However, some events are considered as abnormal patterns regardless the patients' characteristics, such as the transients of paroxysmal fast activity, interictal epileptiform discharge, benign epileptiform transient of sleep, and others (Stern, 2010).

A way to identify abnormal patterns in transients during the diagnosis is by means of the medical consensus of specialists, expressed in the form of clinical guidelines. Transients can be also characterized by measuring their characteristics such as frequency content,
amplitude, energy, etc. We highlight that besides the classical techniques, there exist other techniques based on analysing the complexity of the signals.

Approximate entropy (ApEn) and sampling entropy (SampEn) are algorithms that estimate the entropy to classify complex systems even if

their data include both deterministic chaotic and stochastic processes, regardless the length of the data (Pincus, 1991; Richman, 2000).

Among the different applications of entropy, it has been employed to characterize physiological pathologies or abnormal conditions in biological signals. For instance, Rajendra et al. (Rajendra, 2012) employed four parameters of entropies, namely ApEn, SampEn, and phase entropies S1 and S2, to develop a methodology to identify epileptic seizures. The resulting parameters extracted from the EEG signals were fed to seven different classifiers. In that work they found that all entropy parameters except the phase entropy (S1 and S2) indicate lower values for pre-ictal and ictal classes due to the periodicity or rhythmicity. Similarly, (El-Kishky, 2012) implemented the Shannon entropy, and two techniques of fractal dimension (namely Higuchi method, and Hurst exponent) in intracranial EEG recordings of patients diagnosed with epilepsy. These parameters were proposed as discriminants for detecting epileptic seizures in EEG signals. They found that Shannon entropy provided the strongest differentiation between ictal and inter-ictal intervals in the considered cases.

Regarding the ApEn and SampEn parameters, these depend on four inputs, namely: 1) the length N of the time series, 2) the length m of the subseries or the embedding dimension, 3) the delay τ, and 4) a tolerance parameter r. Concerning these input parameters, (Kaffashi, 2008) concluded that for signals created by non-linear dynamics whose autocorrelation function decays sufficiently fast, taking $\tau = 1$ is enough to provide a good estimation of the complexity of the signal. However, for signals with long range correlation, taking similar to time occurrence of the first zero-crossing of the autocorrelation function can provide additional information.

On the other hand, there exist several works where entropy has been employed to characterize physiological signals, for instance, (Castiglioni, 2008), based on their results from HRV, concluded the $ApEn_{max}$, i.e., the maximum value of ApEn*(m; r;N*), with fixed *m* and *N*, provides reasonable results and allows a better description of the complexity of the signals. Besides, (Restrepo, 2014) asserted that, as well as $ApEn_{max}$, the estimator r_{max}, i.e. the value of *r* at which ApEn(*m; r;N*) = $ApEn_{max}$, can also be used to discern between dynamics even in the presence of noise. The parameter r involves enough information for an optimal representation of either a specific event or a group of them. Since the parameter of tolerance *r* depends on the standard deviation of the data distribution, it is possible to obtain several estimations of entropy from the same time series, therefore a question stands on which is an appropriate value of r to obtain a reliable estimate of the entropy in EEG signals of different pathologies.

As mentioned above, the works [7] and [9] used ApEn and SampEn to characterize and classify different conditions in biological signals. Accordingly, this paper presents a technique to automatically identify abnormal transients in EEG signals over the whole recordings, and a methodology to obtain an appropriate value of the parameter *r*. Hence, in

order to characterize these EEG transients, the proposed methodology gives a reliable estimation of their entropy.

The outline of this work is the following: In Section 2, the research and design implied in this work is highlighted, in Section 3, the techniques ApEn and SampEn to estimate the entropy of signals are described. In Section 4, the characteristics of both the EEG recordings and the device to acquire them are presented. In Section 5, a technique to identify abnormal transients in EEG signals, and the methodology to obtain an optimal parameter *r* to estimate the signals' entropy are shown, furthermore, the results obtained with this methodology applied to EEG signals from three neurological disorders are considered. Finally, in Sections 6 and 7 the discussion and conclusions are presented, respectively.

2. Research and Design

The automatic extraction of the characteristics of the biological signals, in addition to providing information on the structure of the data, is also used as a set of auxiliary techniques in the diagnosis. Therefore, several techniques have been studied in order to analyze their suitability in different disorders where the EEG signal is a standard para-clinical technique that may help experts make decisions in diagnosis. The research consists then of designing the methodology and to find the segments of signals that differentiate physical conditions and to verify that the analysis of these segments are according to clinical meaning.

In order to aim this objective, four main topics were considered: 1) The knowledge of the EEG signal and its typical waveforms related to physical conditions;2) The expertise in signal processing techniques that extract information; 3) The ability to design and implement the algorithms and 4) The preparation of the database that contains patients with different disease conditions. The former three areas were analyzed and implemented by the engineer with close collaboration with the neurology specialist because it is essential the continuous feedback during the design, research, and interpretation of results. The last topic considered was that the recording protocol and clinical condition of the EEG signal sets were previously diagnosed by the neuropediatrician using the standard procedure. Finally, this information was used as a tag into the database in order to evaluate the algorithms.

To acquire the knowledge of the EEG wave morphology, it was necessary to consult the expert, as well as to review several books and manuals of clinical interpretation of EEG waveforms. These sources describe the graph-elements in amplitude, duration, frequency and characteristic morphology associated with the pathological condition are represented with graphical examples. Furthermore, according to the position of the electrode in the scalp and the age of the patient, the metrics obtained could be considered as normal or abnormal waveforms. Once the metrics

were obtained, expert review the false positives and false negatives to make sure that the interpretation of several cases was correct.

The selection of the signal processing techniques is the result of investigating from previously published works into state of the art. Then, the study of those selected techniques is carried out in order to understand them and analyze the scope of its use. The implementation of them in an algorithm and the test with known signals was performed using MATLAB® as a tool of programming. Therefore, the proficiency of this language must also be considered as a previous requirement. Once the algorithms have been implemented and tested, different clinical cases of
each disease were used, and the results were commented with the clinical expert. Finally, a large-scale automatic analysis was performed along the entire database.

In this research work, a question arises as to whether it is possible to obtain a reliable measurement of the complexity of EEG transients that could lead to their characterization and could differentiate between several neurological disorders. We found that the entropy of EEG signals is a way to answer this question.

The first step was to prove that entropy is a suitable method to obtain a complexity measurement of transients, since these events are short duration segments. Then, the second step consisted in finding the appropriate tolerance parameter, *r*, that allows extracting an accurate estimation of entropy to characterize the transients from different pathologies. The r parameter definition is the main issue of this work, further explained in the methodology and results section.

3. Methods

Entropy is a well-known technique to measure the complexity of signals, and for the analysis of time series. In the literature there exist several works where entropy has been used to characterize different events or to identify patterns related to the physiological states, pathologies, or abnormal conditions (Pincus, 1991; Richman, 2000; Rajendra, 2012; El-Kishky, 2012). In this work we consider only two methods to estimate the entropy of EEG recordings, namely, approximate entropy (**ApEn**) and sampling entropy (**SampEn**).

3.1. ApEn

ApEn was introduced in (Pincus, 1991) as a measure to quantify the regularity of a time series, even if they are noisy or their lengths are small. ApEn depends on three parameters: the length N of the time series; the length m of an embedded pattern to be compared; and the parameter r, which is also called the similitude criterion. The procedure to calculate the ApEn is the following:

Let $X = x_1, x_2, \dots, x_N$ be a time series of length N. Let us construct a set of subsignals $\{X_1, X_2, \dots, X_{N-m+1}\}$ each of which is specified by a vector $X_i = (x_i, x_{i+1}, \dots, x_{i+m-1}),\ \ i = 1, 2, \dots, N-m+1$ of m consecutives values of X, starting at the i-th entry. The distance between X_i and X_j, denoted by $d[X_i, X_j]$, is defined as the maximum of the absolute difference between corresponding components of the vectors X_i, X_j, that is,

$$d[X_i, X_j] := \max_{k=1,2,\dots,m}(|x_{i+k-1} - x_{j+k-1}|).$$

For each X_i and a fixed $r > o$, let $N_m(i)$ be the number of subsignals $X_j (j = 1, \dots, N-m+1)$ such that $d[X_i, X_j] \leq r$. Then, for each $i = 1, \dots, N-m+1$, calculate a statistical parameter $C_i^m(r)$, defined by the expression

$$C_i^m(r) := \frac{N_m(i)}{N-m+1},$$

and compute the formula

$$\varphi^m(r) = \frac{1}{N-m+1} \sum_{i=1}^{N-m+1} \ln C_i^m(r),$$

where $\varphi^m(r)$ represents the prevalence of repetitive patterns of length m. In the next step m is increased to $m+1$, and the previously described process is repeated to obtain $C_i^{m+1}(r)$ and $\varphi^{m+1}(r)$. Finally, ApEn is calculated by the expression

$$ApEn(m, r, N) = \varphi^m(r) - \varphi^{m+1}(r).$$

3.2. SampEn

Similarly to ApEn, SampEn is a parameter that measures the regularity of signals but, unlike ApEn, self-matches are not counted when $C_i^m(r)$ is calculated. In addition, only the first $N-m$ vectors are considered. According to (Richman, 2000), the process to calculate the SampEn is the following:

Construct a set of subsignals $\{X_1, X_2, \dots, X_{N-m}\}$ of the length m. For each $X_i = (x_i, x_{i+1}, \dots, x_{i+m-1})$, and a fixed $r > 0$, let b_i be the number of subsignals $X_j (j = 1, \dots, N-m; j \neq i)$ such that $d[X_i, X_j] \leq r$. Let us calculate a parameter $B_i^m(r)$, defined by the expression

$$B_i^m(r) := \frac{1}{N-m-1} b_i,$$

and compute the formula

$$B^m(r) := \frac{1}{N-m}\sum_{i=1}^{N-m} B_i^m\,(r)\,,$$

Now, let m be increased to $m+1$ and calculate the statistical parameter $A_i^{m+1}(r)$, defined by the expression

$$A_i^{m+1}(r) := \frac{1}{N-m-1}\,a_i\,,$$

where a_i is the number of subsignals $X_j^{(m+1)}(j=1,\dots,N-m; j\neq i)$ of length $m+1$ such that $d\left[X_i^{(m+1)}, X_j^{(m+1)}\right] \leq r$. Finally, compute the formula

$$A^m(r) := \frac{1}{N-m}\sum_{i=1}^{N-m} A_i^{m+1}\,(r),$$

from which SampEn follows according to the expression

$$SampEn(m,r,N) = -\ln\left(\frac{A^m(r)}{B^m(r)}\right).$$

In this case, the term $B^m(r)$ represents the probability that two sequences of m points would match, while $A^m(r)$ is the probability that two sequences of $m+1$ points would match.

4. Material and Data

In this work six EEG recordings with duration of 28 to 45 minutes from six patients were analyzed. Two of them were diagnosed with partial epilepsy, two with CD, and two with ADHD. The ages of the patients range from 4 to 24 years. The recordings were taken according to tenets of the Declaration of Helsinki (World Medical Association, 2018). The recordings were obtained with a Comet-PLUS® Portable EEG-Recording & Review System from Grass Technologies®, with a sampling frequency of 200 Hz. The distribution of the electrodes was according to the 10–20 standard under an average assembly in which the amplitudes of the signals are the potential differences between the electrodes, and the average of the rest of the channels. Finally, the algorithms and the statistical analysis were implemented in MATLAB®.

5. Methodology and Results

The whole EEG recordings were split in segments of one second duration to facilitate the identification of abnormal transients associated to neurological disorders. For this aim a methodology based on a previous

work was implemented to detect abnormal events, and to identify the EEG channels with the highest occurrence of these.

Transients are isolated waves or complexes whose ends are not easily identified. In the methodology described in (Ramirez-Fuentes, 2018), abnormal events are detected without their tails, but in the present work the tails are considered so that the duration of the events will be greater than one second.

On considering the tails, the abnormal transients consist of 400 samples, at a sampling frequency of 200 S/s, that is, 200 samples correspond to a segment of 1 second duration corresponding to the abnormal event; 100 samples correspond to a tail of 0.5 seconds duration before the event; and 100 samples correspond to a tail of 0.5 seconds duration after the event, as is shown in Figure 1.

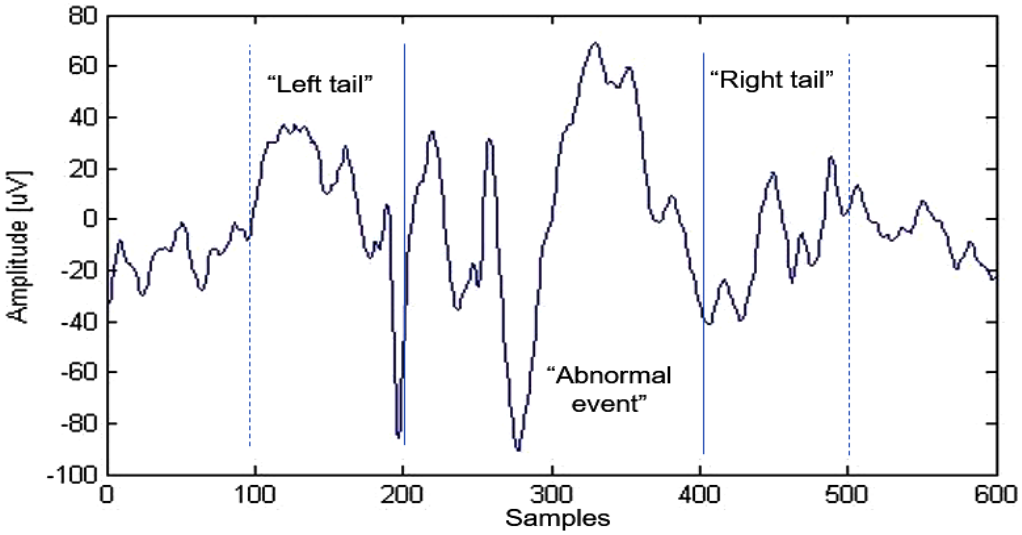

Figure 1: Segment of EEG signal with abnormal behavior.

The number of data of the considered transients (including their tails) is appropriate to estimate their entropy by using ApEn and SampEn algorithms, see, e.g. , (Pincus, 1991; Richman, 2000). For implementing the algorithms the parameter r is allowed to take values from 0.05 to 1, in steps of 0.05. For each value of r, ApEn and SampEn were calculated. These quantities, as functions of the parameter r, were simultaneously plotted in the same graph to see their behaviors (cf. (Richman, 2000)). In the first place both algorithms ApEn(N,m,r) and SampEn(N,m,r) with N = 400 and m = 3 were applied to a uniform random signal. This signal is characterized by its non-correlative feature, that is, as the time increases the signal takes values independently of the previous, and its power spectral density is uniform. Next, the algorithms were applied to the EEG signals from the patients with the three neurological disorders.

Figure 2 shows the plots of ApEn and SampEn as functions of r for a random time series with uniform distribution. We can see that both plots

tend to approach each other from r = 0.65, as it was expected according to (Richman, 2000).

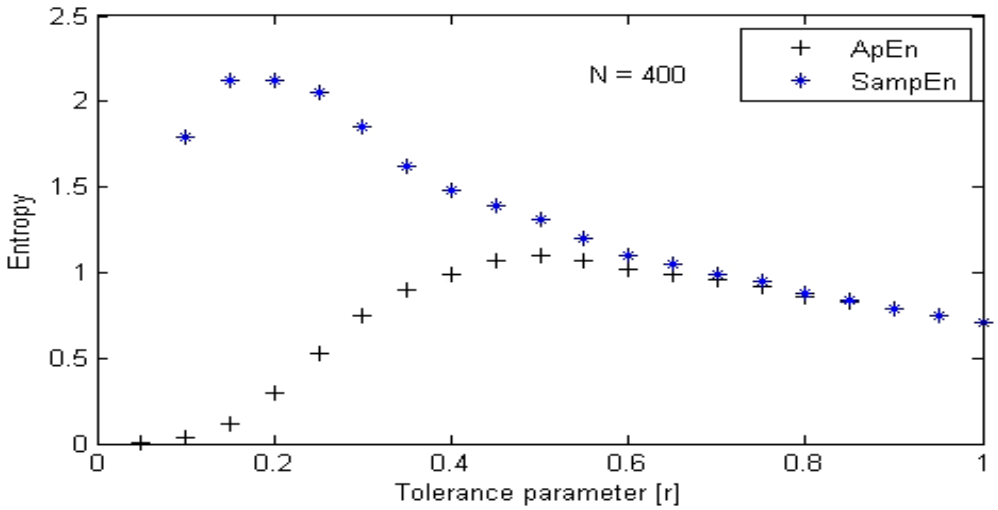

Figure 2: ApEn and SampEn of a random time series with uniform distribution.

Next, the EEG recordings of the six patients were analyzed, but only the results from three patients are shown below since these are the most representative. The channels with the greater number of abnormal events were identified, and then, all abnormal transients were segmented to estimate their entropy, and to identify an optimum parameter r for each recording. Figures 3, 4 and 5 show the plots of the entropy as a function of the parameter r. These plots were obtained on considering the channels with the highest occurrence of abnormal events.

Figure 3 shows the entropy and the standard deviation obtained from 109 transients detected in the channel 17 of an EEG recording, from a patient diagnosed with partial epilepsy. This channel corresponds to the front-central zone in the cerebral cortex. In Figure 3a it is observed that ApEn and SampEn have a similar statistical tendency from r = 0.15. This agrees with the sudden reduction of the slope of the standard deviation at r = 0.15 as is shown in Figure 3b.

Figure 4 shows the entropy and the standard deviation obtained from 81 transients detected in channel 5 of an EEG recording of a patient diagnosed with ADHD. This signal corresponds to the left front-polar zone in the cerebral cortex. In Figure 4a it is observed that ApEn and SampEn not only have a similar statistical tendency but also a strong convergence from r = 0.2. In Figure 4b it is observed that the rate of change of the standard deviation suddenly decreases from r = 0.2.

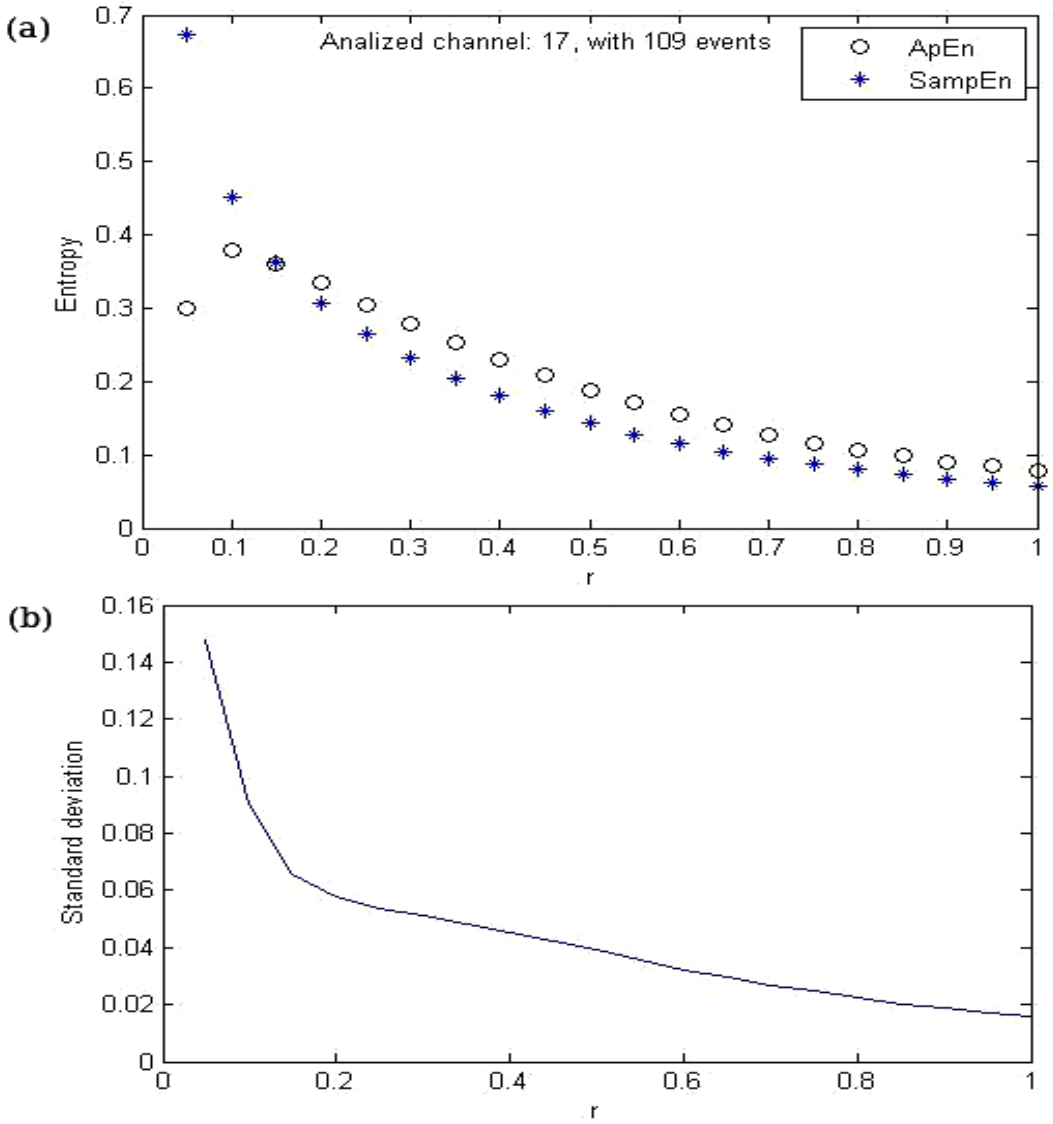

Figure 3: ApEn and SampEn from EEG transients of a patient diagnosed with partial epilepsy

Figure 5 shows the entropy and the standard deviation obtained from 28 transients detected in channel 5 of an EEG recording of a patient diagnosed with CD. Like in Figure 3a, we observe in Figure 5a that both ApEn and SampEn have a similar statistical tendency from r = 0.15. This tendency agrees with the rate of change of the standard deviation that rapidly decreases from r = 0.15.

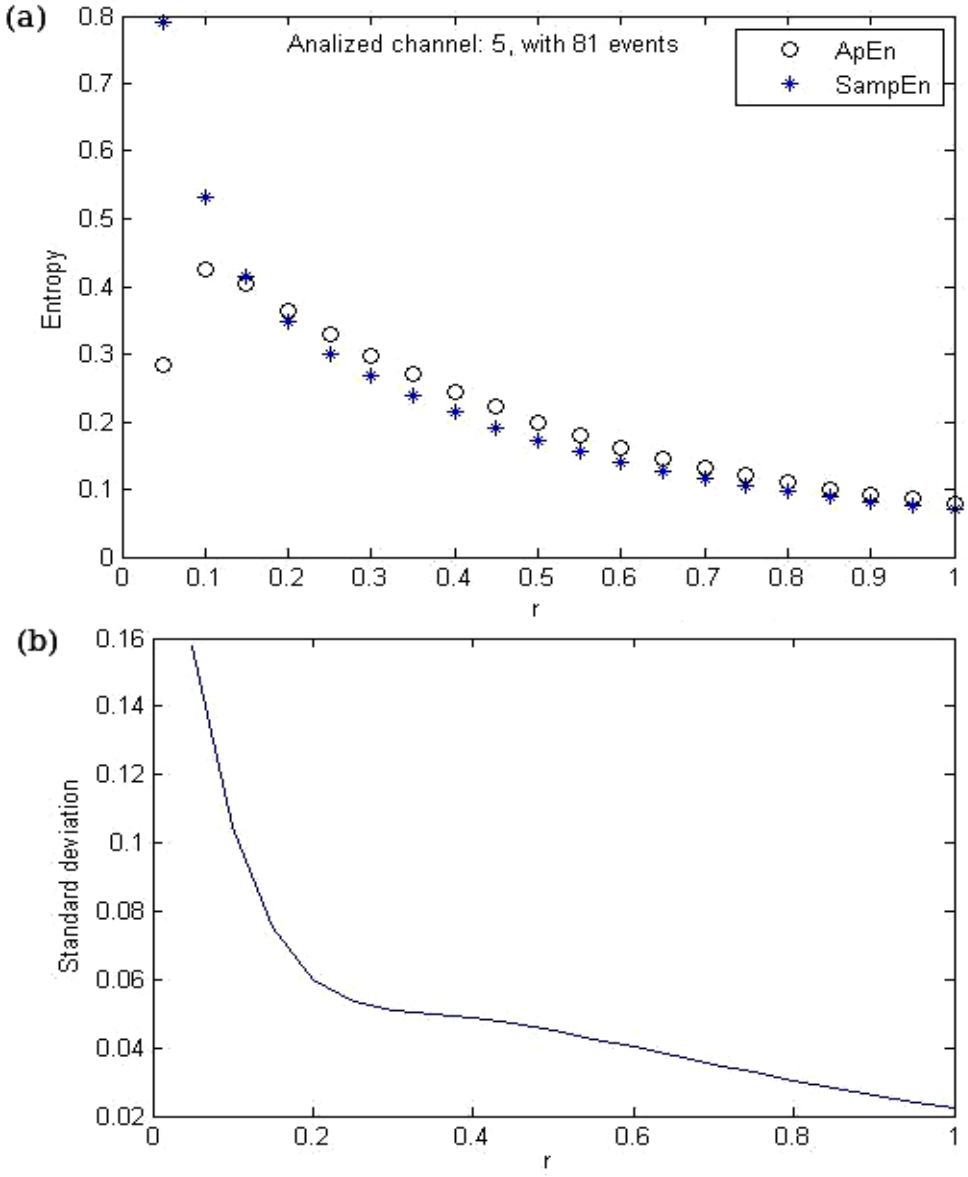

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Figure 4: ApEn and SampEn obtained from EEG transients of a patient diagnosed with ADHD

6. Discussion

It is worth mentioning that in this work it has been used time series corresponding to real EEG signals of three different pathologies of patients diagnosed with cerebral diseases, unlike the data employed in (Pincus, 1991; Richman, 2000) where both chaotic and random signals were used, or in (Rajendra, 2012; El-Kishky, 2012) where only signals of epileptic seizures were considered. Moreover, the length of the segments of abnormal transients here considered is shorter than the length recommended in (Pincus, 1991), which is at least of 1000 samples to calculate ApEn. Nonetheless, the range of values $0.15 \leq r \leq 0.2$ shows to be optimum to

calculate the entropy via the ApEn and SampEn algorithms for the cases here considered. Moreover, the standard deviation of the results obtained with SampEn tend to diminish from r = 0.15. In order to obtain a stronger support for the partial conclusions drawn here, it is necessary to analyze a larger database with recordings from patients with the considered neurological disorders.

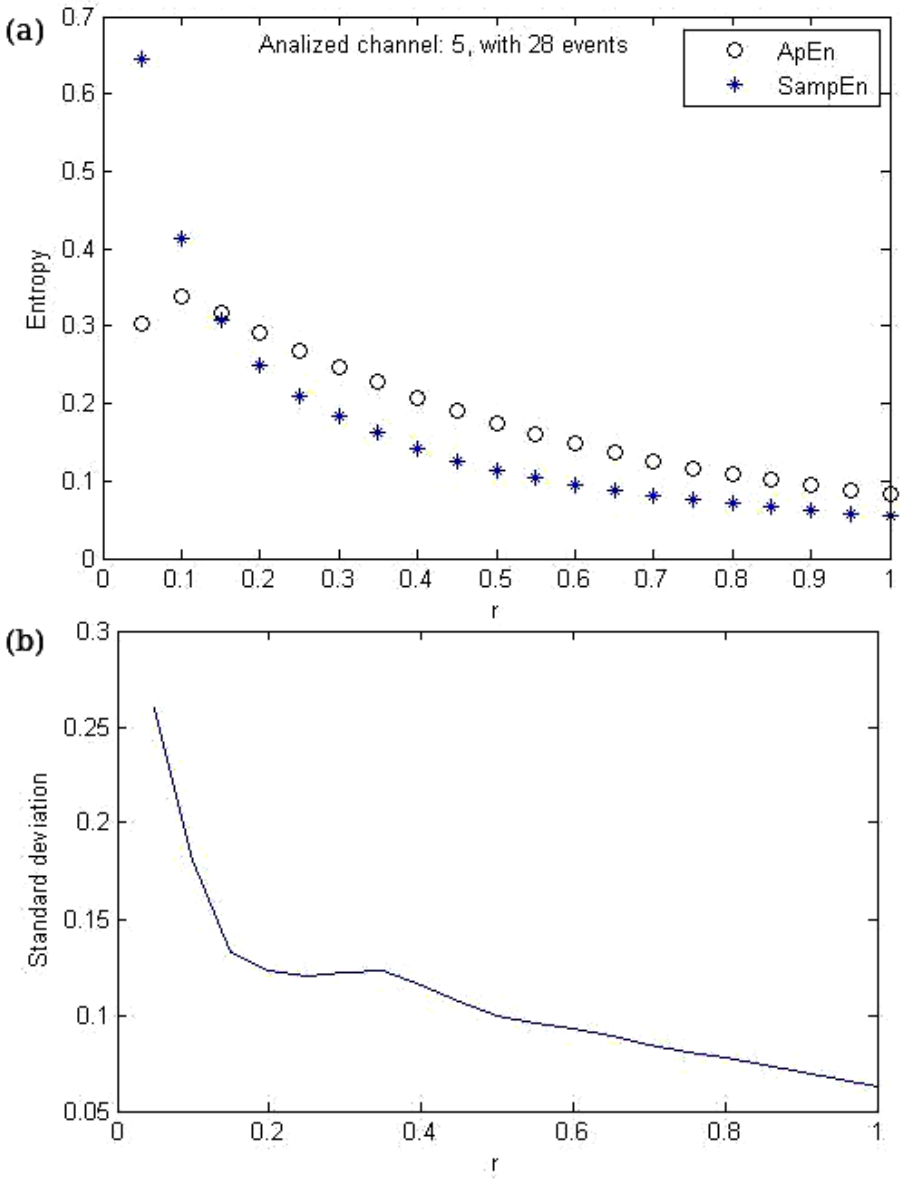

Figure 5: ApEn and SampEn obtained from EEG transients of a patient diagnosed with CD

Finally, unlike the results of (Castiglioni, 2008; Restrepo, 2014) where $ApEn_{max}$ and r_{max} were introduced, respectively, the results of entropy found in this work, show certain uniformity from r = 0.15. Hence, in order to classify abnormal transients, we can take values about r = 0.15 as reliable for the tolerance parameter, in segments with a relatively small duration. Due to the small number of samples (about 400 samples), there is an

additional advantage of reducing the computation time for characterizing transients.

7. Conclusions

In this work it was considered a methodology to determine an appropriate value of the parameter r for the estimation of entropy of abnormal EEG transients on the basis of non-linear analyses, considering that the abnormal transients are events occurring suddenly in natural conditions without external elements that provoke them. With the implementation of the proposed methodology to obtain an optimum parameter of tolerance r to accurately estimate the entropy of abnormal EEG transients, and the results obtained from the analysis of six EEG recordings having different neurological disorders, it was observed that it is possible to obtain an accurate estimation of entropy in abnormal EEG transients. The parameter r is a tool to extract enough information of either an event or a set of similar events, which allows to characterize them when the entropy is estimated.

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