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Original Article

Epileptic seizure prediction based on EEG spikes detection of ictal-preictal states

Itaf Ben Slimen[1,✉], Larbi Boubchir[2], Hassene Seddik[1]

[1]*Centre de Recherche et de Production Research Lab., Ecole Nationale Supérieure des Ingénieurs de Tunis, University of Tunis, Tunis 1008, Tunisia;*
[2]*Laboratoire d'Informatique Avancée de Saint-Denis Research Lab., University of Paris 8, Saint-Denis, Cedex 93526, France.*

Abstract

Epileptic seizures are known for their unpredictable nature. However, recent research provides that the transition to seizure event is not random but the result of evidence accumulations. Therefore, a reliable method capable to detect these indications can predict seizures and improve the life quality of epileptic patients. Seizures periods are generally characterized by epileptiform discharges with different changes including spike rate variation according to the shapes, spikes, and the amplitude. In this study, spike rate is used as the indicator to anticipate seizures in electroencephalogram (EEG) signal. Spikes detection step is used in EEG signal during interictal, preictal, and ictal periods followed by a mean filter to smooth the spike number. The maximum spike rate in interictal periods is used as an indicator to predict seizures. When the spike number in the preictal period exceeds the threshold, an alarm is triggered. Using the CHB-MIT database, the proposed approach has ensured 92% accuracy in seizure prediction for all patients.

Keywords: electroencephalogram, epilepsy, seizure prediction, spikes detection

Introduction

Epilepsy is a neurological disorder disease characterized by sudden and disturbed movements of the body, and can be accompanied by excessive electrical discharges, loss of consciousness, and loss of muscle control[1–2]. In most epileptic patients, seizures can be controlled by anticonvulsant therapy. While for about 25% of epileptic cases, no treatment is available, yet. Hence, a reliable and effective prediction method to anticipate the onset of seizures could improve the quality of life of these patients who are constantly facing the fear of random seizure occurrences.

Prediction of epileptic seizures has been the goal of many researchers since the 1990s. In the last years, researchers have claimed that epileptic seizures were not abrupt, but were manifested a few minutes before the seizure onset. Epileptiform in electroencephalogram (EEG) activity has been categorized by three periods that the ictal period refers to a seizure event; the preictal period is the state immediately before the epileptic seizure, and the interictal period refers the state between seizures (seizure free).

✉Corresponding author: Itaf Ben Slimen, Electric Engineering Department, Centre de Recherche et de Production Research Lab., Ecole Nationale Supérieure des Ingénieurs de Tunis, Street Taha Hussien Montfleury, Tunis 1008, Tunisia. Tel: +216-27-542-572, E-mail: itafslimen@gmail.com.

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Therefore, this study aims to distinguish clearly between the interictal and preictal states and detect them before the onset of seizure symptoms, even a few minutes before, in order to take the precautionary measures and protection necessary for epileptic patients.

Thus far, several algorithms based on EEG signals have been proposed in the literature to predict epileptic seizures, such as linear methods based on frequency domain analysis of EEG signals, and parametric models based on multivariate spectrum estimation[3–4]. Various algorithms based on nonlinear signal theory help deal with changes in EEG signal dynamics during the preictal period, such as correlation density[5], largest Lyapunov exponent[6–7], dynamic similarity index[8–9], and find significant changes in prediction characteristics of EEG signals. Novel methods for predicting seizures based on Kolmogorov's entropy phase synchronization and the combination of medium-phase coherence have been used to detect the transition from the preictal state to the ictal state in the EEG signal[10–11].

Seizures in EEG signal are characterized by waveforms called epileptiform discharges that have a high and manifest degree of spike, and slow-wave complexes[12]. Spike is described as transient signals with a short spike on the EEG ranging from 20 milliseconds to 70 milliseconds with amplitudes greater than 100[13–14]. A variety of automated spike detection methods have been implemented, such as multi-level wavelets[15], neural network[16], and adaptive time-frequency parameterization[17]. Some older studies[18–19] have shown that spike numbers vary significantly a few minutes before epileptic seizures begin. It has been found that the rate of bilateral spike increased significantly in predictive segments before 20 minutes to seizure event[18]. It has also been verified that preictal neuronal activity reflected a distinct and extensive physiological state in focal epilepsy, and that changes in neuronal activity could be detected within a few weeks[19]. A method of forecasting seizures based on the spike rate of the EEG signal has also been proposed, proving the effectiveness of the spike number to predict a seizure period with alarm triggering[20].

The feature extraction of the EEG signals requires segmentation into smaller windows to have similar significant features in order to analyze the EEG signals. The duration of these windows for epilepsy analysis ranged from 5 to 60 seconds. Previous studies used a window analysis in 20 seconds with overlap processes[21] or opted a 5-second window without overlap[22–24]. A short window is considered to ensure a compromise between stationarity hypotheses and the ability to capture specific models.

The first prediction algorithms for epileptic seizures date back to more than 25 years but no standard preictal time has yet been chosen. Various methods have reached different predictive times, such as 2[25], 20[8], 30[21], and 90 minutes[26].

Other algorithms have treated other prediction periods. Some studies used 10, 20, 30, and 40 minutes[24] and did not observe any difference in sensitivity between them. They defined that the means of time prediction is 0.47 minutes. Other studies tested the same four prediction times and concluded an optimal average time is 33.7 minutes[23]. Bandarabadi *et al* treated a statistical measure based on amplitude distribution histogram with different periods from 5 to 180 minutes before the onset occurs[27]. They observe an average time of 44.3 minutes. Moghim *et al* proposed a prediction duration that varies from 0 to 20 minutes before seizure state[28]; where the defined forecast epileptic seizure between 14 and 19 minutes was the most reliable and effective time. Each method uses a different anticipation strategy, so no predictive time can be considered a standard, and it can be noted that the optimal time of the prediction state varies between seizure periods even for the same subject[29].

In this study, we proposed a prediction approach for epileptic seizures based on the spike number of EEG signals. Firstly, on all channels, the number of spikes was detected in interictal, preictal, and ictal periods. The epileptic prediction process is presented in the next section; a soft average filter is chosen and used to smooth the number of spikes between segments of the same period. The value of the maximum number of spikes in the interictal period becomes a threshold used for training data to serve prediction in the preictal period; hence, the alarm will be triggered when the number of spikes exceeds the threshold. Finally, the results and comparative study are presented to evaluate the performance of the proposed approaches.

Materials and methods

EEG international database

The international CHB-MIT database contains scalp EEG data collected at Boston Children's Hospital (CHB) from 23 pediatric patients with 9 to 40 recordings for each epileptic patient. This database was collected for epileptic seizure detection[30]. One hundred and twenty-nine of those records that contain one or more seizures and 535 of the recordings contain no seizure activity. The recordings were sampled at 256 samples per second (256 Hz) with a resolution of 16 bits[31]. Specifically, one hour for each patient selected to present an interictal period (seizure free) used for training data with 720 segments, and 40 minutes selected to be a preictal period with 480. All segment's length is 5 seconds. The seizure period is given in database description but its changes between one signal and another even in the same subject and it was segmented into 5-second windows.

Spike detection

The EEG is a non-stationary signal based on geometric characteristics that can be measured and detected using the shape of the corresponding element. Many reported methods are applied to solve the problem of automated peak detection in EEG signal data. A peak is defined as a local phenomenon, whereas a local peak may not be accepted as a true peak comparing with other peaks in the time series. A data point in a time series is considered as a local peak if : (1) it is a high and local maximum value in a window and it is not necessary that the value must be large or maximum in the time series; (2) not too many points have similar values in the window[32].

In this paper, a formal characterization of a peak in a time series is proposed to detect spike forms in order to predict the epileptic seizures in EEG signal. The proposed algorithm uses a raw time series data and does not require any pretreatment such as smoothing that eliminates some subjective aspects and details that are essential for the prediction process. To highlight the epileptiform in EEG signal, the selected element to extract the spike must be adapted to the geometric characteristics of the EEG signals. This section describes the operating process of the proposed algorithm that begins with searching for all maximum local peaks in a 5-second window. A segment can form a set of candidate peaks. Then each peak in the segment, if it occurs in a period less than 20 milliseconds and over 70 milliseconds and its amplitude should be 100 μV and more, is rejected[13–14]. Surviving peaks that exceed 70 milliseconds are discarded and considered as low frequency waves. The remaining peaks are accepted as spikes. In this work, a spike detection process is based on these studies for the extraction of epileptic spike.

The spikes detection process of EEG signal is represented by the flowchart in ***Fig. 1*** and in the following steps:

1) For all the channels, EEG signal is separated into three periods, which are the interictal period chosen to be 1 hour, preictal and ictal periods, where the preictal time is 40 minutes after seizure onset[23–24]. For each period (interictal, preictal, and ictal), a sliding window is used to obtain segments with duration for 5 seconds to obtain the spike number in each segment.

2) Spikes are detected if the duration ranges from 20 milliseconds to 70 milliseconds and the minimum amplitude 100μV such as the sampling frequency of EEG signals is 256 Hz[13–14,20]. EEG epileptic spikes can be extracted efficiently in the CHBMIT database.

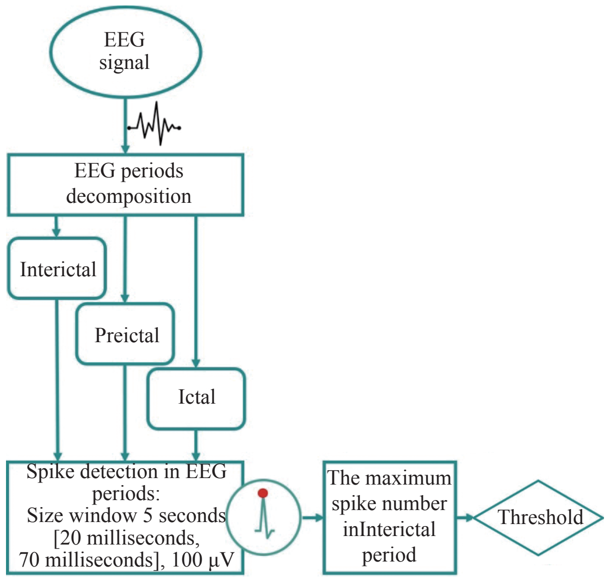

Fig. 1 **Block diagram of EEG spike detection method.**

Fig. 2 presents an example of three EEG signal periods: interictal, preictal, and ictal. One hundred segments in each period are randomly selected from the EEG CHB-MIT database. The length of each segment is 5 seconds. The variation of the spikes number distribution in the EEG periods is well distinguished where the spikes number of ictal segments is the maximum compared to the of the other two periods. The spikes number in preictal period is greater than interictal periods.

Table 1 represents the number of segments, the means of spike number in each period, and the maximum value of spikes/segment are 4, 7, and 11 in interictal, preictal, and ictal period, respectively. The comparison of the three EEG periods shows a significant differentiation according to their spike distributions.

Seizure prediction algorithm

As shown in ***Fig. 2***, the spikes number gradually increases as the seizure approaches and reaches a maximum of seizures. Based on this observation, the rate of peaks was chosen as a tool and as an indicator to predict epileptic seizures. ***Fig. 3*** illustrates the proposed seizure prediction approach. CHB-MIT database (EEG scalp) was used to prove the robustness of the proposed method, and the seizure prediction process based on spikes rate is described in the following algorithm:

1) For all the channels, separate the EEG signal into interictal, preictal, and ictal periods. The preictal time is 40 minutes before the seizure event, and interictal period is chosen randomly from seizure-free recordings with a period of 1 hour.

2) After the extraction of the three period datasets (interictal, preictal, and ictal), a sliding window is

used to separate each period in segment with 5 seconds.

3) Detect the spikes in each segment for all periods then calculate their total number of spikes.

$$N_j(i) = \sum_{k=0}^{k} n(k) \tag{1}$$

j represents the period, i represents the number of segments in j period, and n(k) represents the number of spikes in the i^{th} segment for the j^{th} period in the above, and N_j is the total spike number of j period.

4) Determine the spikes number segments in each period and smooth $N_j(i)$ using the average filter to obtain the new spikes number of i segment relative to its neighbors to equalize the spikes number in a period j. 7 is the length of average filter, and 1 is the moving step.

$$SN(i) = \frac{1}{M} \sum_{a=-\frac{M-1}{2}}^{\frac{M-1}{2}} N_j(i+a) \tag{2}$$

$SN(i)$ is the smoothed spikes number, $N_j(i)$ is the input segment, a is the neighbors of the i^{th} segment, and M represents the length of the smoothing filter who's chosen to be 7.

5) The maximum value of the spikes number for the i^{th} segment in interictal period is the threshold to predict seizure.

$$Thresh = \max[N_{interictal}(i)] \tag{3}$$

For each patient, *Thresh* represents the training data threshold. The alarm is triggered when the spikes value in preictal period exceeds threshold.

6) At least one alarm is triggered in the preictal period (during 40 minutes) in any channel, which may indicate an impending of epileptic seizure will occur in the near future.

The training data represented by 1 hour of interictal, 40 minutes preictal and 5 minutes seizure events were randomly selected from EEG data for each patient, and the test dataset presented by the rest of EEG data to evaluate the performance of the proposed method. Note that the threshold can be different for each patient.

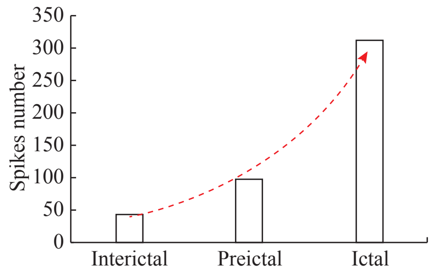

Fig. 2 **Spikes number in 100 EEG segments in each period (interictal, preictal, and ictal).** Each EEG segment's length is 5 seconds. The arrow represents the spike number that increases respectively in interictal, preictal, and ictal periods.

Table 1 **Spikes number in interictal, preictal, and ictal EEG periods**

EEG periods	Segments number	Mean	Maximum spike/segment
Interictal	100	0.43	4
Preictal	100	0.99	7
Ictal	100	3.13	11

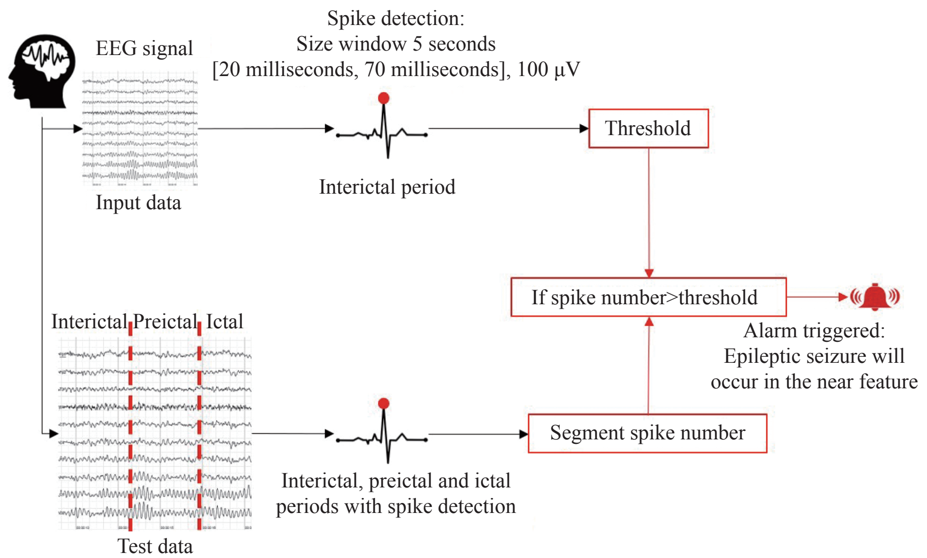

Fig. 3 **Diagram of the proposed seizure prediction method.** The spike number obtained from the interictal period will first be used as a threshold. The segment spike number in the preictal period is then compared to this threshold and the alarm will be triggered when it exceeds it.

Results

Seizure occurrence period (SOP) is defined as the period during which the epileptic seizure is to be expected, while seizure prediction horizon (SPH) is defined as the minimum window of time between the beginning of SOP and any alarm[33]. For a successful prediction, the epileptic seizure must occur during the SOP and not in the SPH. The proposed algorithm was assessed using SOP and SPH.

The EEG CHB-MIT database was used to evaluate the proposed prediction algorithm. The EEG signal is decomposed to segments with 5 seconds in order to detect the spikes of each EEG segment. Then each segment took a new spikes value according to the average of its neighbors to have the rate of spikes compared to all segments in the EEG period. Finally, the number of spikes in each segment was tested according to the threshold obtained in the training data and the alarm is triggered when the SN exceeds the threshold.

Fig. 4 represents three periods (interictal, preictal and ictal) of EEG signal, each period has a duration of 190 seconds, and it is observed the variation of the spike number between periods. Furthermore, the variation of spike number in the three EEG periods is illustrated in ***Fig. 5A–C*** respectively, where the duration in the ictal period is 190 seconds while the interictal and preictal periods are 20 minutes. In this figure, the smoothed spikes number are presented in ***Fig. 5D–F*** respectively to interictal, preictal and ictal. It can be observed from this figure that the spikes increase in the ictal period compared to other periods and are significantly increased suddenly in the preictal period compared to the interictal state.

Fig. 6 shows the level of smoothed spike for EEG signal of a patient: interictal state for 1 hour, preictal state for 40 minutes, seizure event for 190 seconds. The color bars with magenta represent the time of alarm (21 alarms) which are the segments exceeding the threshold presented by horizontal red lines. The smoothed spike rate of this patient shows an obvious increase in the prediction state, with a sharp increase in seizure state compared with reduction in the interictal period. In order to reduce the false alarm in this patient, the first alarm was started before 16 minutes of the ictal period.

The proposed algorithm for seizure prediction makes it possible to give a prediction rate of 92% to the total number of seizures for each patient. The prediction time varies between 1 minute and 23 minutes.

Discussion

Prediction of epileptic seizures and the triggering of an alarm or alert is the goal of different methods to have an effective algorithm to improve the quality of

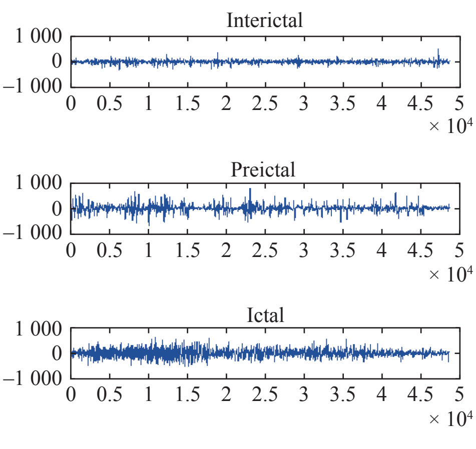

Fig. 4 **An example of three EEG signal with interictal, preictal, and ictal periods.** Each period has duration of 190 seconds.

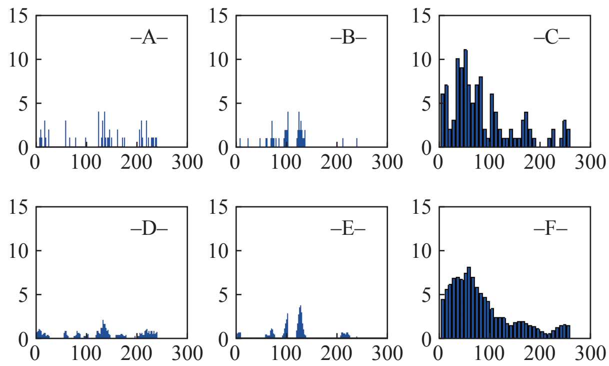

Fig. 5 **Number of spike detection of three EEG periods before and after smoothing.** A, B and C: The segment spike number accumulated to represent the difference between interictal, preictal, ictal, respectively. D, E and F: The smoothed spike number during interictal, preictal, ictal, respectively, where D represents a smoothed number of spikes in A and E represents B where C represented in F.

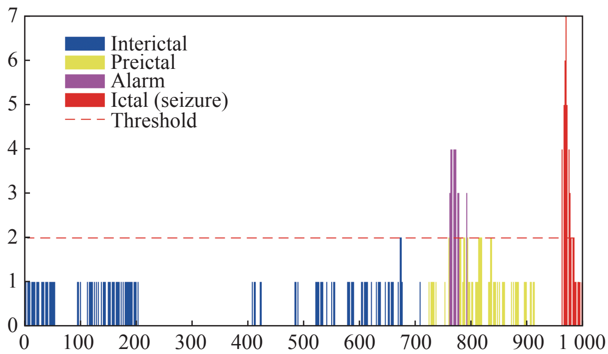

Fig. 6 **Smoothed spike rate in EEG signal for a patient.** Interictal 1 hour (blue), preictal state 40 minutes (yellow), seizure event during 190 seconds (red), the colored bar with magenta is the alarm time (21 alarms) exceeded the threshold that presented with horizontal line.

life of epilepsy patients by eliminating the damage caused by epileptic seizures that can be presented by loss of consciousness. The key point for successful prediction of seizures is to differentiate between preictal state and interictal state. Heretofore, tens of linear and nonlinear methods with univariate measures and multivariate measures have been partially successfully applied to predict epileptic seizure.

Before seizures event, the brain state is stable; there is no epileptiform discharge presented. With the discharge of some neurons that have gone to the abnormal state, the epileptiform, like spike, increases gradually. In ***Table 1***, the statistical analysis of spike rates in different periods of EEG signal (interictal, preictal, and ictal) shows that there is a significant variation between them.

Each prediction method has been realized with a different anticipation strategy. Therefore, it can be concluded that no prediction time can be fixed and considered as a norm. Hence, it is possible to note that the prediction time varies from period to another and from records to another, even for the same subjects. The spike number can vary between different EEG signal periods, so it is necessary to have a specific setting parameter for each patient to make the spike rate threshold stability optimal for all recordings. The performance of the seizure prediction algorithm must be tested and evaluated on clinical cases and can be implemented on an epilepsy prediction device according to simplicity and understandable logic.

Table 2 **Comparative study on recent works conducted on seizure prediction**

Ref.	Database and methodology	Prediction time	Performance
Li SF *et al*[20], 2013	- Freiburg database - Low-pass filter, Morphology filter, Spike rate detection	10 seconds	Sensitivity 75.8%
Zandi *et al*[34], 2013	- Private data - Histogram, Variational GMM, Zero crossing intervals	2 minutes	Sensitivity 88.34%
Zheng *et al*[35], 2014	- Freiburg database - BEMD, Mean phase coherence	20 seconds	Able to detect synchrony changes before the onset
Zhang *et al*[36], 2014	- Freiburg database - Higuchi FD, Bayesian LDA, Kalman filtering	2 minutes	Sensitivity 89.33%
Zhang *et al*[37], 2014	- Private data - Approximate entropy	25 seconds	Accuracy 94.59%
Teixeira *et al*[21], 2014	- EPILEPSIAE database - Auto-regressive modeling, Kruskal-Wallis test, ANN, SVM classifier	15.58 minutes	Sensitivity 73.55, 24.83%
Bandarabadi *et al*[27], 2015	- EPILEPSIAE database - Amplitude distribution histograms, Spectral power features	8 seconds	Able to predict seizures
Bandarabadi *et al*[22], 2015	- EPILEPSIAE database - Relative spectral power features, MRMR feature selection, Amplitude distribution histogram, SVM classifier	5 seconds	Sensitivity 75.8%
Behnam *et al*[38], 2016	- CHB-MIT database - Interpolated histogram feature, Seizure distribution model, Bayesian classifier, Hunting search algorithm, MLP classifier	6.64 seconds	Accuracy 86.56%
Fujiwara *et al*[39], 2016	- Private data - Time, frequency domain features, Multivariate statistical, process control	10 seconds	Sensitivity 91%
Fei *et al*[40], 2017	- Private data, CHB-MIT database - Fractional Fourier transform, Modified LLE features, BPNN classifier	10 seconds	Accuracy 89.67%
Direito *et al*[41], 2017	- EPILEPSIAE database - Auto-regressive modeling predictive error, decorrelation time, statistical moments, energy, SVM classifier	5 seconds	Sensitivity 38.47%
Chu *et al*[42], 2017	- Private data, CHB-MIT database - Spectral feature, Fourier coefficients	20 seconds	Sensitivity 86.67%
Zhang *et al*[43], 2018	- Private data - A mathematical model	10 seconds	Synaptic plasticity has influence on seizure period
Yuan *et al*[44], 2018	- Freiburg database - Wavelet transform, Diffusion distance, Bayesian discriminant analysis	10 seconds	Sensitivity 93.62%
Tsiouris *et al*[45], 2018	- CHB-MIT database - Statistical features, Zero crossings,Wavelet transform, Power spectral, Cross-correlation, Graph theory, LSTM	15 minutes to 20 minutes	Sensitivity 99%
Proposed method	- CHB-MIT database - Spike detection, average filter, threshold from training data. - Alarm triggered	1 minute to 23 minutes	Able to predict seizure period with 92% for true prediction alarm

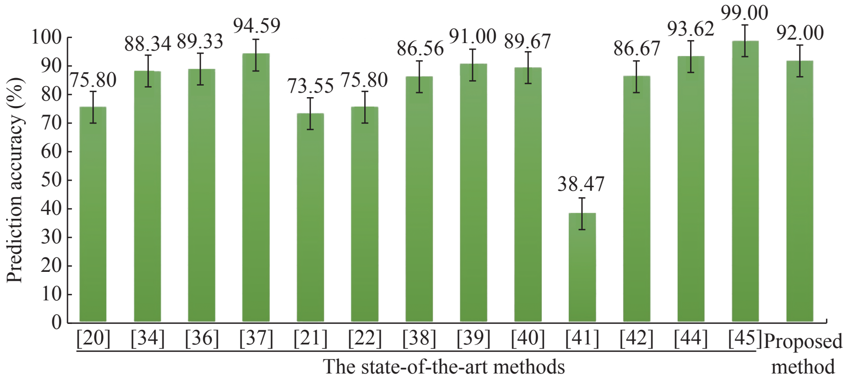

Fig. 7 **Comparison of seizure prediction accuracy rate of the proposed method against the state-of-the-art methods.** Several existing methods have been proposed for the purpose to predict epileptic seizures using CHB-MIT database; where each method is different from other ones according to the approach and strategy proposed. The proposed method achieves a prediction accuracy rate up to 92% of the total number of seizures for each patient, and outperforms the existing methods considered in the comparison.

Table 2 and ***Fig. 7*** present different proposed methods for the purpose to predict epileptic seizures; where each method is different from other methods according to the approach and strategy proposed. Some studies proposed to use epileptiform for seizure prediction with SPH 10 seconds[20]. In the same estimated period, some studies obtained 10 seconds as prediction period; the research were based on Fast Fourier transform and Backpropagation Neural Network classifier, with classification accuracy rate of 89.67%[40], or the Wavelet Transform and Bayesian discriminant analysis was recently used, with classification accuracy rate of 93.62%[44]. The change in the number of epileptiform changes significantly between the periods, which clearly allows anticipating the seizure state.

In this work, an epileptic seizure prediction method is proposed based on the spike rate in the EEG signal. The algorithm detects spikes number in all channels over three EEG periods by applying the local maximum where the time range and amplitude of spike were given. The spike rate is smoothed with an average filter to balance the segments spike distribution in the same EEG periods, where the maximum number of spikes in the interictal period is used as a threshold and as index that there is an impending seizure in the near future. The alarm is triggered when the spike number in an interictal period segment exceeds the threshold. The CHB-MIT database is used to evaluate the algorithm, and it is shown that the spike rate increases with the occurrence of a seizure and reaches a maximum in seizure state. The proposed approach achieves a prediction rate up to 92% for all patients with at least one alarm is triggered at least in one channel. Comparing the epileptic seizure prediction methods such as correlation dimension, phase synchronization and other algorithms, the proposed algorithm allows to obtain a higher precision with a perfect prediction rate. In order to improve the quality of life of epileptic patients, after the validation and according to the simplicity of this algorithm, it is possible to make a portable device for monitoring epileptic seizures.

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