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SOME ASPECTS OF EPILEPSY

Predicting Epilepsy and Deep Learning

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Abstract

Epilepsy is one of the most common nervous diseases, which occurs unconsciously and unpredictably due to the brain transient disorders. In this paper, deep neural networks is used to predict epilepsy attacks thorough simultaneous use of EEG signals and Heart Rate Variability (HRV) analysis on a public database containing 8 patients. Deep neural networks is a type of neural architectures, which has more than one hidden layer and capable of better generalization in comparison with conventional neural networks. In this work, eight features are extracted from HRV signals in time and frequency domains. Also, 22 features are extracted from EEG signals in time, frequency and time-frequency domains. In addition, six features are extracted through trial and error from ECG signals and five features are extracted from EEG signals through deep neural networks. Then they are all given to a Multi-Layer Perceptron (MLP) network for the prediction process. Simulation results reveal that the proposed method can predict the epilepsy attacks with 73.05% average sensitivity and 70.28% specificity.

Introduction

Epilepsy is the most common neurological disorder of children and the third common nervous system disorder among adults, after Alzheimer and stroke [1]. Nowadays, more than 50 million people throughout the world, forming 1% of the global population, suffer from epilepsy [2]. More than 30% of these patients are resistant to the drug. Epilepsy can directly affect the human's quality of life through various issues such as memory disorders, lesions due to the seizures, or potential psychotic disorders which are followed by social isolation [3]. To date, various approaches have been proposed for epilepsy prediction using EEG signals. EEG is the most reliable method to predict the majority of seizures and a number of studies have reported seizure prediction methods based on the EEG. However, people with seizures are often associated with changes in heart rate and respiration rate [4]. A seizure prediction attitude relies on two distinctive approaches [5]. In the first approach, a binary classifier is trained to exploit differences between a preictal and interictal states [5]. The classification can be performed directly on the raw signals or after feature extraction. In the second approach, the analysis is focused on identifying the increasing or decreasing trends in values of examined features. If the values exceed the activation thresholds an alarm is raised to declare an incoming seizure [5]. Here, the time interval before the preictal is considered as the interictal period. It is also medically referred to as the period in which the signal is in the normal mode. To extract the features, a moving window analysis is usually used for dividing the raw EEG or ECG signals into segments of smaller duration. Feature extraction provides dimensionality reduction and more complex, higher order feature spaces which can increase the discriminative power of the classification algorithm used to isolate preictal EEG and ECG segments [5]. Features can be extracted either manually

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or automatically, using deep learning approaches. For EEG, univariate [6] and multivariate [7] features can be extracted in the time and frequency domains. Spectral features [8] such as the spectral power estimation are the most common univariate features. Temporal features include the statistical moments [9], mean [10], variance [11], skewness [12] and kurtosis [7], entropy approximation [13], entropy [14], phase-locking values [15], Hjorth parameters [16], Lyapunov exponent [16] and Principle Component Analysis (PCA) [17]. The frequency domain features are extracted from the Fast Fourier Transform (FFT) [18] and Discrete Wavelet Transform (DWT) [19] [20]. Relative power differences in different frequency bands have shown great potential in detecting preictal and interictal signals [21,22]. Machine learning has revolutionized the seizure prediction field, offering tools to answer the high complexity of EEG signals and evaluate multivariate features to distinguish hidden preictal characteristics [5,23]. Many scientists have suggested deep learning approaches for the prediction of seizures. Mirowski et al. [24] compared the convolutional networks with logistic regression and support vector machines for epileptic seizure prediction from intracranial EEG signals. Daoud and Bayoumi [25] used the Convolutional Neural Network (CNN) and bidirectional recurrent neural network in predicting the seizures by extracting the spatial features from the multichannel raw EEG signals. Their method was based on detecting the preictal and interictal state [25,26]. Hosseini et al. [27] presented a cloud-based brain-computer interface system for the analysis of the big EEG data. They further followed a deep-learning approach in which a stacked AE was trained in two steps for unsupervised feature extraction and classification. Tsiouris et al. [5] introduced the Long Short-Term Memory (LSTM) networks for epileptic seizure prediction using EEG signals, expanding the use of deep learning algorithms with CNN. The LSTM model exploits a wide range of features for classification, including the time and frequency domain features. Sun et al. [23] presented a patient-specific method for extracting the frequency domain and time-series features based on the two-layer CNNs. LSTM networks were introduced for seizure prediction using pre-seizure clips of the EEG dataset, expanding the use of deep learning algorithms with recurrent neural networks [25]. Eberlein et al. [28] used the CNN topology for determination of the appropriate signal features as well as the binary classification of preictal and interictal segments. Usman et al. [29] introduced a deep learning method for the seizure prediction by preprocessing the scalp EEG signals, automated feature extraction using CNN and classification with the support of vector machines. Meisel and Bailey [30] presented a deep learning method to extract the information from complex data on a large epilepsy data set containing multi-day, simultaneous recordings of ECG, ECoG, and EEG. They used the relative performance of their algorithms to compare the preictal information contained in each modality. Rosas-Romero et al. [31] applied CNN to predict the epileptic seizures by analyzing fNIRS signals. Although most of the previous studies recruited simultaneous analysis of the EEG and ECG signals or various deep learning approaches for seizure prediction, there is a lack of literature on such a multi-modal study, applying deep learning method, for predicting the seizures. The main idea of the current study is the simultaneous use of EEG and ECG signals in the prediction of epilepsy using deep learning features along with some manually extracted features. Here, we predicted epileptic seizures by considering both the preictal and interictal states and by extracting some features introduced in the previous studies as well as some unsupervised features obtained using an automated encoder.

Deep neural network

Auto-Encoder

Due to the simplicity of the Auto-Encoders' (AEs) learning process compared with other algorithms in stack encoder networks, AEs are used as main components of the network. This neural network encodes the input data and reduces the input vector dimensions. In deep structures, one AE is used in each layer, which is trained separately [32]. An AE is used as a nonlinear compression method required to encode the input vector X to a representation, so as to regenerate the input. Consequently, X is the output, and the target of the AE is the input of the AE. Figure 1 depicts the structure of an AE, in which X is the input vector, h^1 is the generated hidden code vector and X is the output vector, i.e. the regenerated input. In details, $\mathrm{X} \in [-1,1]_{n_0 \times 1}$ denotes the input of the AE, where n_0 is the input dimension. The AE will encode the input vector X to the generated hidden vector, $\mathrm{h}^1 \in [-1,1]_{n_1 \times 1}$ with n_1 dimension and generated h^1 converts to the input space with lower dimensions. Equation 1 demonstrates the coding procedure and Eq. 2 and 3 show decoding procedures.

$$\mathrm{h}^0 = \mathrm{X} \quad (1)$$

$$\mathrm{h}^1 = \mathrm{tansig}(\mathrm{w}^1\mathrm{x} + \mathrm{b}^1) \quad (2)$$

$$\mathrm{h}^2 = \mathrm{r} = \mathrm{purline}(\mathrm{w}^2\mathrm{h}^1 + \mathrm{b}^2) \quad (3)$$

In the above equations, tansig is a sigmoid function, purline is a linear function, w^k is weighting matrix and b^k is the bias vector of the layer k. Furthermore, r denotes the output vector of the AE.

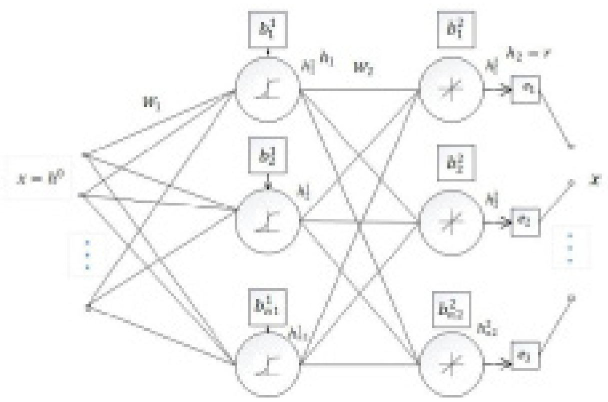

Figure 1: Schematic of the AE.

Since the desired output is the input vector X, the output is compared with the input and error vector will be generated, based on Eq. 4.

$$e = X - h^2 \quad (4)$$

In order to train the AE neural network, the error function is considered as Eq. 5.

$$\mathrm{E} = \frac{1}{2}\mathrm{e}^2 \quad (5)$$

Error back propagation training algorithm

To train the considered network, the descent gradient-based error back propagation method is commonly used. Training algorithm of the weights and bias parameters for each input data is performed according to Eq. 6.

$$\theta_t = \theta_{t-1} - \varepsilon \frac{\partial E_{t-1}}{\partial \theta_{t-1}} \quad (6)$$

Training weights in AE

In unsupervised training process, similar weights are used for the hidden layer and the output layer of the network. Equation 7 holds for the weight matrix denoting the assumption that weights are the same. This assumption prohibits the network from increasing the weights in one of the encoder or decoder layers and decreasing them in the other layer, which deteriorates the network through learning a co-linear function, not able to record nonlinear relationships among the inputs.

$$w^2 = (w^1)^T \tag{7}$$

Stack-Encoder neural network

In this section, a number of encoder networks are arranged together and features are trained with no supervision, based on EEG and ECG data. The AE number k is represented by AE^k. In the first layer, the input of AE^1 is the EEG and ECG signals, segmented with moving windows. In the hidden layer, the input vector h^{k-1} related to AE^{k-1} is fed. For training the stack AE neural network, three-steps are considered. The first step is started by training the AE^1. By incrementing k, corresponding AE^k are trained with no supervision. This is continued toward the regression layer. In the second step, one linear regression layer is located at the end of the last AE, and the last layer is trained through a supervised measure, based on the true predicted epilepsy at one time-step later. In the final step, all parameters of the network are trained by true predicted values, in a supervised manner. A statistical descent gradient method is used for the supervised training purpose, applied in the second and third steps.

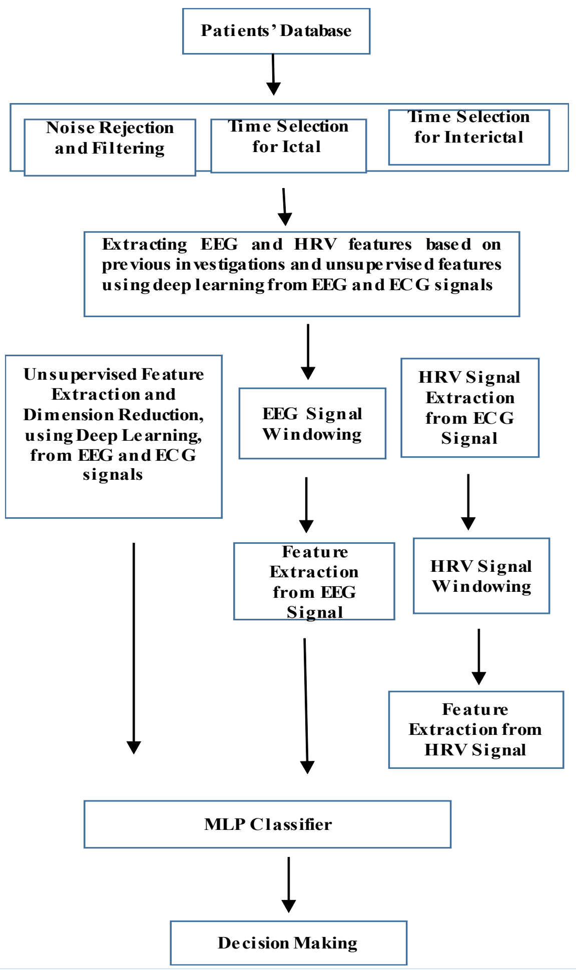

Figure 2: The proposed block diagram of the epilepsy prediction through simultaneous analysis of ECG and EEG signals.

Materials and methods

Participants, EEG and ECG recordings

The study was carried out in accordance with a protocol approved by the Razavi Hospital Ethics committee, Mashhad, Iran. EEG and ECG signals from video monitoring unit of Razavi Hospital were analyzed for the purposes of the current study. Dataset of 8 subjects, including 6 females (16-40 years) and 5 males (10-35 years) were recruited. Twenty-four-hours recordings were performed with a sampling rate of 256 Hz. The EEG data were recorded using 23 electrodes FP1, FP2, F3, F4, C3, C4, P3, P4, F7, F8, T3, T4, T5, T6, O1, O2, T9, T10, TP9, TP10, FZ, PZ placed on the scalp of patients with epilepsy, and 2 channels were used for the ECG recording.

Seizure prediction methodology

We proposed a seizure prediction method that predicts start of preictal state few minutes before the seizure onset. Figure 2 shows the block diagram of the proposed method.

Signal preprocessing

Here, the aim was to eliminate the noise and motion artifacts. Therefore, a band-pass filter was designed with 0.05 and 70 Hz lower and upper cut off frequencies, respectively. Moreover, a Notch filter was used to remove the high frequencies as well as the AC line noise (50 Hz). Regarding the time intervals selection, 10 minutes before the seizure was considered as the preictal and 20 minutes before preictal was considered as the interictal period. Since the biological signals, such as the ECG and EEG are non-stationary, the features must be extracted in time intervals in which the signals can be considered as the stationary signals. The length of the window, in which the signals were considered as stationary, was 2 seconds for the HRV and EEG signals.

HRV signal extraction from ECG signal

ECG signal analysis was performed by extracting the HRV signal. An ECG cycle includes P, QRS and T waves, among which R wave has the highest peak. The distance between two consecutive R peaks is referred to as the R-R interval (RRI) and R-R interval variabilities in the ECG signal is referred to as the HRV. RRI raw data were interpolated and sampled at certain time intervals using spline method. Pan-Tampkin algorithm [33] was used in order to extract the R peak.

Feature extraction from HRV signal

Time domain features

Time domain features which were calculated from the RRI data include [7]:

- Mean: The mean value of the RRI
- SD: Standard deviation of the RRI
- RMSSD: Root mean square of difference of adjacent RRI
- Variance: RR interval variance
- NN50: The number of pairs of adjacent RRIs whose difference was more than 50 ms.

Frequency domain features

Following features were calculated from the HRV signal [7]:

- LF: Low frequency power within 0.04-0.15 Hz representing the sympathetic and parasympathetic activity of the central nervous system.
- HF: High frequency power within 0.15-0.4 Hz representing the parasympathetic activity of the central nervous system.
- LF/HF: Indicating the balance between sympathetic and parasympathetic activity of the central nervous system.

The LF and HF values were normalized to the Total Power (TP) due to the variability of the HRV among the subjects.

Feature extraction from EEG signal

Statistical features

Table 1, presents the statistical features extracted from the EEG signals. Here, X (i) indicates the sample i of the time-series and *n* represents the total number of the samples.

Feature	Mathematical Relationship
Mean	$\bar{X} = \frac{1}{n}\sum_{i=0}^{n} X[i]$
Variance	$\sigma_x^2 = \frac{1}{n}\left(\sum_{i=0}^{n}(X[i] - \bar{X}\right)^2$
Skewness	$\text{Skewness} = \frac{\frac{1}{n}\sum_{i=1}^{n}(X[i] - \bar{X})^3}{\left(\frac{1}{n}\sum_{i=1}^{n}(X[i] - \bar{X})^2\right)^{\frac{3}{2}}}$
Kurtosis	$\text{Kurtosis} = \frac{\frac{1}{n}\sum_{i=1}^{n}(X[i] - \bar{X})^4}{\left(\frac{1}{n}\sum_{i=1}^{n}(X[i] - \bar{X})^2\right)^2}$

Table 1: Statistical features extracted from the EEG signals.

Hjorth Parameters

These parameters specify the dynamics and complexity of the signal. They are calculated according to the Eq. 8 and 9, based on the original signal (x), as well as its first and second derivatives (denoted by x' and x'', respectively). σ Represents the square root of the variance.

$$\text{Mobility} = \frac{\sigma_{x'}}{\sigma_x} \quad (8)$$

$$\text{complexcity} = (\sigma_{x''}/\sigma_{x'})/(\sigma_{x'}/\sigma_x) \quad (9)$$

Decorrelation Time

Decorrelation time is defined as the first time when zero crossing occurs in the autocorrelation sequence of the EEG signal. Zero decorrelation time implies that signal samples have low correlation with each other. In many cases, decorrelation time of a sequence of the white noise is theoretically zero. Before seizure, the power of the signal correlation, for the lowest frequency has a significant decrease which leads to the reduction of the decorrelation time [11].

Energy of the signal

The energy of the continuous-time EEG signal can be calculated according to the Eq. 10, where X (t) denotes the EEG signal.

$$\int_{-\infty}^{+\infty} |X(t)|^2 dt \quad (10)$$

Frequency domain features

The EEG signal power at different frequency bands and the median frequency were calculated as the following:

- Delta frequency band power (δ) measured at 0.1-4 Hz.
- Theta frequency band power (θ) measured at 4-7 Hz.
- Alpha frequency band power (α) measured at 7-14 Hz.
- Beta frequency band power (β) measured at 14-30 Hz.

Median frequency (f_{med}) power calculated according to the Eq. 11:

$$\int_0^{f_{med}} S(w)\,dw = \int_{f_{med}}^{\infty} S(w)\,dw \quad (11)$$

Where S denotes the power spectrum density. The signal power at these frequency bands was calculated by periodogram method.

Time-frequency features

Historically, the Fourier spectrum analysis is a popular method for evaluating the power/frequency distribution. However, it is not applicable for biological signal analysis, such as EEG and ECG, due to its limitation for non-stationary signals. Therefore, DWT analysis was applied in the current study. The energy of the wavelet coefficients were calculated by Daubechies-4 wavelet function with 6 sub-bands.

Feature extraction using stack-Encoder neural network

EEG and ECG raw signals (segmented by two-second windows), were considered as the first AE inputs. For the dimension reduction and features extraction purposes, five consecutive AEs were used. The number of consecutive AEs were selected based on the trial and error. In fact, a two-second window containing 512 samples (i.e. features) was considered as the AE input. Then it was passed over five consecutive AEs. Consequently, 512 feature were reduced to 150, 50, 20, 10 and finally 6 features for the ECG modality and similarly, 512 features were reduced to 150,50,20,10 and finally 5 features for EEG modality. Selecting the number of features in each AE (i.e. outputs of the AE) was based on the trial and error, by considering the error. After passing over a linear layer, the output was obtained. Then, the error back propagation algorithm was applied to the generated outputs to update weights and biases of two ending layers. Time series data of ECG and EEG signals at each time step have a lot of common information. As a result, a new deep hierarchical model was designed to predict the epilepsy time series, through simultaneous use of EEG and ECG signals (Figure 3).

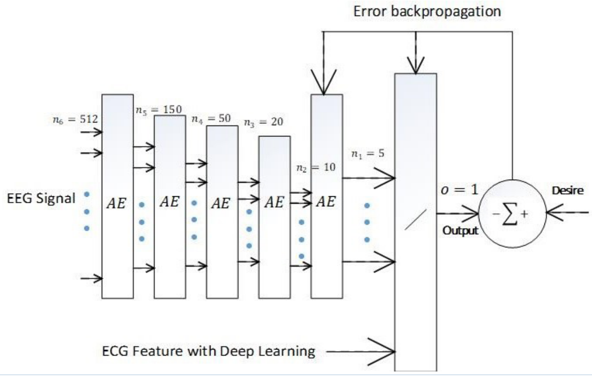

Figure 3: Hierarchical stack AE model.

In this hierarchical model, the dimensions of EEG and ECG signals were simultaneously reduced and corresponding data were compressed and processed. Finally, through trial and error, five and six features were obtained from EEG and ECG signals, respectively. Hence, 11 features were passed over a linear function and the output was generated. After generating the output and calculating the prediction error, weights and biases of layers were updated through the error back propagation algorithm.

Eight temporal and frequency features were extracted from the HRV signal, based on the features noted in previous studies. Moreover, six other features were extracted from the ECG signal through trial and error, by the AE. Hence, 14 features were extracted from HRV and ECG signals for each patient. In addition, 19 features were extracted from the EEG signal based on previous studies and five other features were extracted through trial and error for each EEG channel by the AE. Totally, 24 features were extracted from the EEG signals for each patient. The stack encoder algorithm was employed for the unsupervised learning in time series.

Multilayer perceptron classifier

In this study, MLP was used as a reference to evaluate the proposed model. Two classes were considered; the label of the preictal class was denoted by 0 and that of the interictal class was denoted by 1. The prediction time was considered 10 minutes, which was corresponding to the preictal interval. After windowing and determining suitable labels for each window, some features were extracted.

In the current study, data were divided as follows: 60% of each group of the seizure and normal data was allocated for the training, 20% was allocated for the validation and 20% was allocated for the testing purpose.This categorization was performed in random and there were no common data among the groups. For determining the training stop-time of the algorithm, the validation data were given to the network and obtained outputs were compared with desired outputs. The error of the network was determined by Mean Square Error (MSE) criteria. When the value of the MSE reached less than 0.01, the training phase for validation data was stopped.

For those patients with more than one seizure, the MLP algorithm was evaluated as follows. The first seizure was used as the training data and others were used for testing. In order to validate the proposed algorithm, accuracy, sensitivity, specificity and confusion matrix were used as criterions, which were calculated as Eq. 12-14:

$$\text{Accuracy (Ac)} = \frac{TP + TN}{TP + FN + TN + FP}(\%) \quad (12)$$

$$\text{Sensitivity (Sn)} = \frac{TP}{TP + FN}(\%) \quad (13)$$

$$\text{Specificity (Sp)} = \frac{TN}{TN + FP}(\%) \quad (14)$$

Where TP, TN, FP and FN are true positive, true negative, false positive and false negative values, respectively. These values were computed in MATLAB Software through the confusion matrix.

Results

Table 2, represents the results obtained from feature extraction based on the previous studies and features extracted by using the stack AE.

Table 2: Results of the proposed algorithm for 8 patients.

Fusion (EEG, ECG)			
Patient	Sensitivity (%)	Specificity (%)	Accuracy (%)
1	84.7	76.4	80.5
2	63.12	65.58	64.38
3	64.55	63.125	65.2
4	88.96	86.16	87.66
5	65.7	62	63.85
6	60	74.46	67.23
7	85.65	61	73.32
8	71.7	73.55	72.63
Average	73.05	70.28	71.85

Considering features extracted from the stack AE besides significant features will increase the sensitivity, specificity and accuracy.

Conclusion

Predicting seizure in epileptic patients is of great importance. Numerous attempts have been taken to automatically perform this process and they are continually developing. A key point in such prominent attempts is employing non-invasive methods, which enhance the safety and welfare of the patient. In the current study, time and frequency domain features were extracted from the HRV signals and the time, frequency, and time-frequency features were extracted from the EEG signals. These features are more oscillating in the preictal rather than the interictal mode, which means that the seizure effects are more evident in the preictal mode. All the features were provided to the neural networks to accurately predict epilepsy and distinguish between the interictal and preictal periods.

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