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Patient-specific warning of epileptic seizure upon shapelets features

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ABSTRACT

Epilepsy is an intractable chronic neurological disease attached to extensive attention. Due to the fact that unpredictable seizure attacks result in serious physical injuries, early warning before seizure occurrence can help patients to get timely treatment and intervention. This paper presents a novel patient-specific method to predict epileptic seizures by learning shapelets of scalp electroencephalogram (EEG) signals recorded from different channels. In the proposed method, EEG signals are preprocessed to raise the Signal to Noise Rate (SNR). Multichannel shapelets space is constructed by the learning-near-to-optimal shapelets method. EEG signals are converted to distance matrices by projecting them on the shapelets' space. Bi-LSTM, SVM, CNN, and an ensemble of them are used to classify the feature set. Based on the prediction results then raise alarms. The proposed methodology is applied to the CHB-MIT scalp EEG dataset of 10 cases. The proposed method achieves a sensitivity of 91.33% and a false prediction rate of 0.16 h^{-1} .

1. Introduction

Epilepsy, a neurological brain disorder disease, is one of the most intractable diseases in the world. As one of the chronic neurological disorders which are characterized by recurrent episodes of seizures, more than 1% of the world population has been affected [1]. The risk of premature death is up to three times that of the general population. 20% to 30% seizures cannot be controlled by drugs, so fatal injuries increase the mortality rate [2]. Raising an alarm before a seizure occurrence can help to reduce the risk of serious physical damage caused by unexpected seizures. Electroencephalogram (EEG), the electrical recording of brain activities, is widely applied for epilepsy patients to analyze and help physicians to give treatments. For an epileptic patient, brain activity can generally be divided into four states: preictal state, ictal state, postictal state, and interictal state [3]. The Preictal state is a period before the occurrence of a seizure, the ictal state reflects changes in EEG signals when a seizure takes place, the interictal state is the period between two seizures' onset which does not include signals of the preictal state. Fig. 1 shows these states in a section of the EEG signal.

The objective of the early-warning of seizure is the recognize the state of the preictal from the other states. More specifically, the issue of warning prediction can be considered as a binary classification between the preictal state and the interictal state. Most seizure prediction approaches involve three procedures including signal preprocessing, feature extraction, and classification. Preprocessing can reduce the influences of noises and artifacts, and increases the Signal Noise Ratio (SNR). About noise removal, band-pass filter [4,5], Empirical mode decomposition (EMD) [6], Fourier Transform [7,8] and Wavelet Transform [9,10] were used frequently. The

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Fig. 1. EEG signals in different states, including interictal state, preictal, ictal and postictal state.

selected multiple features in the time domain, frequency domain, and time-frequency domain are used to be the input of classifiers [3]. Tsiouris et al. [11] used various features extracted in the time domain, and frequency domain and some of them are about channels cross-correlation and graph-theoretic features. Moreover, non-linear analysis methods are applied to detect the coupling among harmonics in the signal's spectrum, such as entropy, and approximate entropy [12]. Automated features extracted method on deep learning methods are also used. Convolutional Neural Network (CNN) has been used to extract automated features in many works [13–16]. Cui et al. [17] proposed a bag-of-wave feature extraction method for seizure prediction. Moreover, researchers aimed to seek the perfect threshold values in the time or frequency domain to identify different stages of brain activity, such as analysis of positive zero-crossing intervals [18] and Phase/Amplitude Lock Values [19].

After feature extraction, machine learning and deep learning methods are explored in classification. Machine learning algorithms including Support Vector Machine (SVM) [12,20], K-Nearest Neighbors (KNN) [4,21], Bayesian classifier [21] and Multilayer Perceptron (MLP) [22,8,21] are widely used in classification. Deep learning classifiers including CNN [5,15,16,10] and Long Short-Term Memory (LSTM) [11,14] are used to predict seizures.

The main challenges of seizure prediction classification are to extract the most discriminative features representing preictal state and interictal state greatly and to predict seizures as early as possible. Inspired by the work of Cui et al. [17], the local expressions of EEG signal can also be significant features that are worth to be considered. Therefore, it is essential to focus on patterns of local segment changes of each patient. Shapelets provide a new perspective for feature extraction of EEG signals, and they can fully explore discriminative local changes in EEG signals. Shapelets are maximally discriminative subsequences of time series, which have been applied in time series classification applications. Ye and Keogh [23] firstly introduced shapelets to time series classification, and proposed a brute force algorithm to extract significant shapelets. According to the time and space complexity of the brute force algorithm, a series of acceleration techniques have been proposed, including entropy pruning method [23], similarity computation [24], and sorting shapelets [25]. Rakthanmanon and Keogh [26] proposed a technique to transform high-dimensional time series to low-dimensional data based on Symbolic Aggregate approximation (SAX) representation. Grabocka et al. [27] proposed a new method that can directly learn the near-optimal shape elements. Li et al. [28] proposed ShapeNet which embedded shapelet candidates of different lengths into a unified space for feature selection. Medico et al. [29] embedded shapelets as trainable weights into multi-layer neural networks, and extended shapelets-based classification to multi-dimensional environments.

The highlights of this paper are summarized as follows:

- 1. Shapelets is explored to convert EEG signals to new feature vectors for prediction. The local features of different brain states are extracted.
- 2. Different classifiers and their ensemble use new features to predict patients' brain states, including Bi-LSTM, SVM, and CNN.

The rest of the paper is organized as follows. In Section 2, we briefly describe the materials and proposed method. In Section 3, the experiments results including performance evaluation and visualization and interpretation of shapelets are presented. Section 4 concludes the proposed method.

2. Materials and methodology

CHB-MIT scalp EEG database (http://physionet.org/physiobank/database/chbmit/) collected at the Children's Hospital Boston is an available open database, which consists of continuous long-term scalp EEG recordings of several pediatric patients with intractable seizures [30]. These recordings were collected from 22 children, which contained 5 males (ages 3-22) and 17 females (ages 1.5-19). The sampling rate of the collected EEG signal is 256 Hz with 16 bits resolution. EEG signals of most cases were monitored from 23 channels based on the international 10-20 system of EEG electrode positions and nomenclature.

It is noteworthy that there are significant differences among individuals about the identity of the rhythmic activity structure. Seizures from the same brain region exhibit considerable consistency, and similarity in spatial, spectral, and so on. Not all rhythmic



Fig. 2. Schematic representation of the proposed seizure prediction methodology. Features are extracted from m-s long EEG segments.

activity observed is a reflection of an underlying seizure. Some types of EEG signals for specific patients are normal but for other ones are related to seizures. The heterogeneity of EEG signals makes our prediction method be patient-specific.

2.1. Methodology

The seizure prediction problem can be regarded as a binary classification task between the preictal state and the interictal state. The pipeline of the proposed method consists of preprocessing EEG signals, feature extraction based on shapelet, and classification. The details of the steps are shown in Fig. 2. Firstly, the EEG signals of each case are split into segments of a certain length. Then filter technique is used to select channels based on variance. After turning the signals into segments labeled by different brain activity states, segments labeled by preictal and interictal are used for shapelet learning. Signals are converted to distance matrices. Then, Bi-LSTM, SVM, CNN, and ensemble classifier are used in classification. Each seizure is predicted by the classification model trained on the remaining signals.

2.2. Preprocessing of EEG signals

EEG signals recorded from the scalp are easy to be distorted owing to a large distance between neurons and electrodes. The noise in EEG signal is generated by the power line, inter-electrode, electrocardiogram, and the effect of blinking eyes [5]. For CHB-MIT database, the EEG recordings were contaminated by power line noise. In the proposed method, Butterworth filter is used to remove the power line noise at 50-60 Hz. In addition, the high frequency components are useless for shapelets extraction, so EMD has been applied on the signals. After the filtering, the significant and necessary information is retained for the feature extraction and classification. The flowchart in Fig. 3 depicts the preprocessing of EEG signals.

Selection of patients For the seizure prediction problem, it is more useful to consider leading seizures, which refer to the seizures in that the onset interval between them is more than 30 min [31]. If another seizure occurs within half an hour after a seizure, it will be considered as only one seizure. Therefore, if seizures occur more than twice in an hour, only the first one will be considered. Additionally, patients with more than 10 seizures a day is not necessary to use the seizure prediction method because of their high incidence of epileptic. Thus only a few cases in CHB-MIT dataset can be used to train the model.

Imbalanced data set The number of interictal EEG segments is much more than that of preictal segments, resulting data imbalance problem. To avoid such imbalance, we generate more preictal segments using the overlapping technique by sliding a 10-s window and 5-s overlap along time, and the interictal state has been divided into 10-s length segments without overlapping. Fig. 4 represents the overlapping technique of 10 seconds. The segments generating process of preictal and interictal EEG segments are displayed in Fig. 4(a) and Fig. 4(b) respectively. After sliding windows to capture signal segments, there is a similar number of segments between the preictal and interictal states.



Preprocessing of EEG signals

Fig. 3. Preprocessing of EEG signal.



(a) Preictal state segments extracted by a sliding window with an overlap



(b) Interictal state segments extracted by a sliding window

Fig. 4. Generate segments to solve the imbalance problem by sliding a *m*-s window along the time axis. Upper image (a) shows preictal state segments extracted by a sliding window with an overlap meanwhile lower image (b) shows interictal state segments extracted by a sliding window without overlap.

Channel selection To select the most informative channels and reduce computational complexity, a simple channel selection algorithm is introduced into the system. This channel selection algorithm uses the variance of all channels as a filtering technique. For each patient, the variances of all channels are sorted in descending order, then the top ten channels with the highest variance are selected for the following step.



Fig. 5. Process of multi-channel shapelets extraction.

2.3. Shapelets for feature extraction

Shapelets can be derived from original time series, and can significantly represent different classes. Original shapelets learning algorithms try a lot of candidates to learn optimal shapelets, which is effective but time consuming. Here, the method proposed by Grabocka et al. [27], a technique of learning near-to-optimal shapelets by learning true top-K shapelets by capturing their interaction, without search exhaustively among a pool of candidates extracted from time-series segments, is applied for each patient EEG recordings to learn shapelets of the top 10 selected channels separately.

Assume that EEG signal recordings on *K* channels can be seen as *K* time series. For a patient's EEG signal recorded in channel *k*, the signal segments set is defined as $T_k^{n\times p} = \{t_1^k, t_2^k, \dots, t_n^k\}$, while *n* is the number of 10 seconds long segments, $t_i^k (i = 1, 2, \dots, n)$ is $(t_{i1}^k, t_{i2}^k, \dots, t_{ip}^k)$ where *p* represents the number of ordered amplitude values. According to previous sample rate 256 Hz and sliding window length *m*, *p* is equal to $256 \times m$. Our classification target is $Y = \{0, 1\}$ (preictal state and interictal state). All subsequences of length *L* extracted from $t_i^k (i = 1, 2, \dots, n)$ are defined as $S_{i,k}^L = \{T_{i,l,k}^L, f \text{ or } 1 \le l \le p - L + 1\}$. The distances between *j*-th shapelet of channel *k* and *i*-th signal segments t_i^k are defined as $M_{i,j}^k$, which is the minimum distance among the distances between *j*-th shapelet and the $T_{i,k}^L$ and denoted as in equation (1),

$$M_{i,j}^{k} = \min_{l=1,\dots,p-L+1} \frac{1}{L} ||T_{i,l,k}^{L} - Shapelets_{j,k}^{L})||_{2}^{2}.$$
(1)

The learning model predicting approximate target values \hat{Y}_i is given by the formula from equation (2),

$$\hat{Y}_{i} = W_{0} + \sum_{j=1}^{S} M_{i,j}^{k} W_{j}, \quad \forall i \in 1, \dots, n,$$
(2)

where W is linear weights and W_0 is bias, S is the number of all shapelets. The logistic regression operates by minimizing the logistic loss. The loss function is defined as

$$L(Y, \hat{Y}) = -Y \ln \sigma(\hat{Y}) - (1 - Y) \ln(1 - \sigma(\hat{Y})).$$
(3)

Then the loss function (3) is optimized through shapelets stochastic gradient descent, and shapelets can be updated iteratively. The lengths of shapelets are set to be 32 (125 ms) and 64 (250 ms), and the number of shapelets in each channel is uniformly set as 100. The extraction process is displayed in Fig. 5.

2.4. Classification of the seizure state upon shapelets

After learning the shapelets of different channels, interictal and preictal states are classified on using single classifiers and ensemble classifier respectively. In our proposed method, Bi-LSTM, CNN, and SVM based on the voting of different channels are used as classifiers.









Bi-LSTM The Bi-LSTM network's block consists of two blocks of LSTM, and the functions of them are processing temporal sequences in two opposite directions. The advantage of using Bi-LSTM as a classifier is extracting important temporal features of distance vectors. The network in the proposed model consists of three layers with the number of units set as 256, 128, and 128. To avoid overfitting, we use the dropout regularization technique and set the dropout factor as 50%. The sigmoid function is used in the last layer used for predicting EEG signal segments' labels. Adaptive Moment Estimation (Adam) optimizer is selected for optimization.

SVM Support Vector Machine (SVM) has been widely used as classifier for seizure prediction. Due to the different predicting ability of each channel, based on voting strategy the results of multiple channels are integrated into the final prediction. The architecture is illustrated in Fig. 6.

CNN Convolutional Neural Networks have great advantages in pattern recognition and computer vision. A typical CNN consists of three types of layers, including convolution layer, pooling layer and fully connected layer. The proposed CNN architecture is presented in Fig. 7. The projection of EEG segments on shapelets space are inputs of CNN classifier. The architecture consists of three convolutional layers and three maximum pooling layers. The number of kernels in each convolution layer to be 32 with kernel 2×3 , and the number of maximum pooling layers have size of 2×2 . RELU function is used as activation function. Batch Normalization is used to ovoid overfitting.

3. Results and discussion

3.1. Performance evaluation

Seizure prediction horizon (SPH) and Seizure occurrence period (SOP) are two performance metrics for seizure prediction performance evaluation. SOP is the time duration in which the seizure possibly occurs. SPH is the time duration between seizure alarm and SOP. An effective seizure alarm should be generated after the SPH and within the SOP. Therefore, if an alarm raises at any point within the SOP, it is considered a successful prediction. Otherwise, the alarm is false. Park et al. [32] used SOP of 30 min and SPH of 0 min since they defined preictal data as occurring 30 min before a seizure in training, which means it is deemed a false positive if no seizure happens within 30 min.

To evaluate the performance of proposed patient-specific models, 10 different patient EEG signal records in the CHB-MIT dataset are used to identify the preictal EEG segments. For each patient, the leave-one-out cross-validation approach is used, which means each seizure will be used for testing and the remaining seizures will be used for training. In the experiments, the preictal state is defined as the period 30 min before seizure occurrence and the interictal state is the period before the preictal state. The duration of the interictal state before each seizure must be longer than 30 min. For the proposed method of performance evaluation, the prediction results are mainly evaluated by two metrics, the number of successful predictions (SP), positive sensitivity based on seizure events, and false prediction rate per hour (FPR (h^{-1})). SOP and SPH are set as 30 min and 0 min. The prediction is produced every 10 seconds. Here, the *k*-of-*n* analysis is applied for raising alarms, and *k* and *n* are set as 5 and 6 respectively. Specifically, if more than five positive predictions occur in a minute, it is necessary to generate an alarm.

Table 1
Seizure prediction results for 10 cases in CHB-MIT dataset.

Case	Seizures	Shapelet	Bi-LSTM			SVM			CNN			ENSEMBLE		
		length	SP	Sen (%)	FPR (h ⁻¹)	SP SP	Sen (%)	FPR (h ⁻¹)	SP SP	Sen (%)	FPR (h ⁻¹)	SP SP	Sen Sen	FPR (h ⁻¹)
chb01	7	125 ms	7	100	0.4	5	71.43	0.07	7	100	0.34	7	100	0.22
		250 ms	5	71.43	0.31	5	71.43	0.07	7	100	0.21	6	85.71	0.2
chb05	5	125 ms	4	80	0.39	1	20	0.02	5	100	0.15	4	80	0.1
		250 ms	3	60	0.61	1	20	0.02	5	100	0.14	3	60	0.04
chb07	3	125 ms	3	100	0.07	2	66.66	0.09	3	100	0.42	3	100	0.13
		250 ms	3	100	0.03	2	66.66	0.09	3	100	0.98	3	100	0.12
chb08	5	125 ms	5	100	0.29	5	100	0.13	5	100	0.6	5	100	0.31
		250 ms	5	100	0.44	4	80	0.05	5	100	0.31	5	100	0.34
chb11	3	125 ms	3	100	0.35	2	66.66	0.03	2	66.66	0.56	3	100	0.08
		250 ms	3	100	0.98	2	66.66	0.04	2	66.66	0.5	3	100	0.3
chb19	3	125 ms	3	100	0.11	3	100	0.01	3	100	0.16	3	100	0.1
		250 ms	3	100	0.18	3	100	0.01	3	100	0.63	3	100	0.03
chb20	4	125 ms	4	100	0.32	3	75	0.31	4	100	0.31	4	100	0.28
		250 ms	4	100	0.25	3	75	0.17	4	100	0.21	4	100	0.24
chb21	3	125 ms	3	100	0.19	1	33.33	0.03	2	66.66	0.56	2	66.66	0.14
		250 ms	3	100	0.63	2	66.66	0.09	2	66.66	0.11	3	100	0.18
chb22	3	125 ms	3	100	0.16	2	66.66	0.28	1	33.33	0.48	2	66.66	0.19
		250 ms	3	100	0.31	1	33.33	0.22	2	66.66	0.5	2	66.66	0.23
chb23	3	125 ms	2	66.66	0.23	2	66.67	0.06	2	66.66	0.75	2	100	0.04
		250 ms	3	100	0.39	2	66.66	0.01	3	100	0.33	3	100	0.33
Total	39	125 ms	37	94.67	0.25	26	66.64	0.10	34	83.33	0.43	35	91.33	0.16
		250 ms	35	93.14	0.41	25	64.64	0.08	36	90.00	0.39	35	91.237	0.20

Table 2

Comparison of existing epileptic seizure prediction methods using scalp EEG signals.

Ref	Method		Sen	FPR	SOP	SPH
	Feature Extraction	Classification		(h ⁻¹)	(min)	(min)
Zandi et al. [18]	Zero-crossing Intervals	Threshold	88.34%	0.155	40	2
Myers et al. [19]	PLV, ALV	Threshold	76.80%	0.17	60	0
Truong et al. [31]	CNN	CNN	81.20%	0.16	30	5
Usman et al. [12]	Statistical and	SVM	'M 92.23%		-	-
	Spectral Moments					
Khan et al. [13]	CNN	CNN	87.80%	0.142	-	-
Cui et al. [17]	Bag-of-waves	ELM	88.24%	0.25	50	1
Truong et al. [8]	STFT	CNN	83.89%	-	30	5
Proposed method	Shapelets	Bi-LSTM Ensemble	94.67% 91.33%	0.25 0.16	30	0

3.2. Prediction results

In experiments, as could be seen from Table 1, the proposed patient-specific model can accurately predicate the preictal state of each patient and then raise an effective alarm. Shapelets with lengths of 125 ms or 250 ms are learned by learning algorithm using the segments prepared before in the selected channel.

Most of the seizures can be accurately predicted by Bi-LSTM prediction model, and the average successful prediction rate for patients is 94.67% when extracting shapelets of 125 ms in length, and the average FPR is $0.25 h^{-1}$. When extracting shapelets of 250 ms, the average success rate was 93.14% and FPR is $0.41 h^{-1}$. This indicates that the Bi-LSTM model has more predictive power based on the shapelets of 125 ms. The prediction results showed that epilepsies are effectively predicted in most cases. SVM classifier based on multichannel voting strategy, achieves average sensitivity 66.64% with an average FPR of $0.10 h^{-1}$ when shapelet's length is 125 ms. When shapelet's length is 250 ms, the sensitivity and FPR are 64.64% and $0.08 h^{-1}$. The average successful prediction rate of the SVM multichannel inheritance prediction model is lower. However, the FPR of the model is lower than $0.1 h^{-1}$ in most cases. CNN classifier has the average sensitivity of 83.33% and 90.91% for extracted 125 ms and 250 ms shapelets respectively, and the false prediction rates are 0.43 and 0.39. Compared with the Bi-LSTM model, CNN model has a higher FPR. The prediction sensitivity was excellent in most of the pre- and interictal seizure recognition, but it was poor in chb11, chb21, and chb22. CNN prediction model based on a shapelet of length 250 ms performs better.

The ensemble learning model considers the above models, and the final prediction results are derived based on the voting strategy. From the experimental results, the overall average successful prediction rates of the classifier are 91.33% and 91.24% for different shapelet feature segment lengths, and the false prediction rates were 0.16 h^{-1} and 0.20 h^{-1} respectively. The average successful

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Fig. 8. The alarms raised from positive prediction of chb01, chb05, chb07, chb08, chb19, and chb20. Images (a)-(f) show the visualized displays of seizures warning for cases mentioned above. The blue blocks: interictal states, red blocks: preictal states, dark red blocks: ictal states, green blocks: ictal states. The red vertical dotted line represents alarm of an upcoming seizure.

prediction sensitivity is slightly lower than that of the Bi-LSTM and CNN classification models, but the FPR is reduced. Since the model combines the good performance of individual classifiers, it succeeds in generating effective warnings with lower FPR.

Table 2 compares the performance of the proposed algorithm with the state-of-the-art methods. In these researches, Myers et al. [19] use Phase/Amplitude Lock Values (PLV/ALV) which calculate the difference in phase and amplitude between EEG electrodes local and remote to the epileptic event. PLV/ALVs are used as seizure detection markers to demarcate the seizure event. In most cases, sensitivity and precision reach 100%. Truong et al. [31] proposed a generalized retrospective and patient-specific seizure prediction method. Firstly they applied STFT on 30-second EEG windows to extract the time and frequency domain. CNN is used for both feature extraction and classification to classify preictal and interictal segments. The approach achieved a sensitivity of 81.2% and an FPR of 0.16 on the scalp EEG dataset. Khan et al. [13] learned features and defined a prediction horizon with convolutional filters on wavelet transformation of EEG signal. The prediction result on the test set achieved a sensitivity of 87.8% and an FPR of 0.142. Cui et al. [17] proposed a bag-of-wave feature extraction method for seizure prediction. Local segments are projected to the learned preictal and interictal codebook, then extreme learning machine (ELM) is used to classify the sequence of features. The experiment results on scalp EEG signal achieved a sensitivity of 88.24% and FPR of 0.25.

Fig. 8 shows the alarms generated by positive prediction and 5-6 analysis of chb01, chb05, chb07, chb08, chb19, and chb20. The length of the block represents the duration of the state, and a red vertical dotted line represents an alarm before an upcoming seizure. Most of the alarms are produced in the preictal state, and few alarms are in the interictal state, which means the proposed method is available in seizure prediction. As shown in Fig. 8(a), 8(d), 8(e), and 8(f), the majority of seizure warnings are generated in the preictal state in cases including chb01, chb08, chb19, and chb20. In terms of chb05 and chb07, there are several false alarms raised in the interictal state (see Fig. 8(b) and 8(c)).

Different from feature extraction methods above, the proposed method only uses markedly distinguished patterns of scalp EEG signals called shapelets, then applies different classifiers to predict. The results show that the proposed method is effective.

4. Conclusion

To control epilepsy, seizure prediction is of great practical importance. The challenges in the epilepsy prediction problem include preprocessing of EEG signals, imbalance of classification data, effective feature extraction, and improvement of classification accuracy. In this paper, we propose a seizure prediction method based on the shapelet feature extraction approach by extracting shapelets features in multiple channels, learning shapelets with discriminative validity, and then transforming the original sequences into new minimum distance matrices, applying Bi-LSTM, CNN, SVM and an ensemble classifier of the three models for preictal state prediction. In this paper, experiments are conducted in the CHB-MIT dataset, and each seizure is predicted for each of the selected patients using a LOO cross-validation method. The proposed method is demonstrated to be effective for seizure prediction when compared with previous prediction methods for EEG pattern changes under the evaluation of three predictors. In the future, we will combine shapelets with other features to improve the algorithm's representation and robustness. In order to apply the suggested approach to a wider range of patients, we will additionally explore the typical shapelets of epilepsy patients.

CRediT authorship contribution statement

Yingxiang Li: Data curation, Software, Writing – original draft. **Xuejing Zhao:** Methodology, Project administration, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability statement

The data associated with this study is public available for researcher. Data associated with this study has been deposited at http://physionet.org/physiobank/database/chbmit/.

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