A Robust Sleep Apnea-hypopnea Syndrome Automated Detection Method Based on Fuzzy Entropy Using Single Lead-EEG Signals

Yao Wang
Department of Biomedical Engineering, School of Life Sciences, Tiangong University, Tianjin, 300387
Tianshun Yang
School of Electrical and Electronic Engineering, Tiangong University, Tianjin, 300387
Siyu Ji
School of Electrical and Electronic Engineering, Tiangong University, Tianjin, 300387
Xiaohong Wang
Department of Biomedical Engineering, School of Life Sciences, Tiangong University, Tianjin, 300387
Huiquan Wang
Department of Biomedical Engineering, School of Life Sciences, Tiangong University, Tianjin, 300387
Jinhai Wang
Department of Biomedical Engineering, School of Life Sciences, Tiangong University, Tianjin, 300387
Xiaoyun Zhao (zxydoctor@163.com)
Department of Respiratory and Critical Care Medicine & Sleep Center, Tianjin Chest Hospital, Tianjin, 300222

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A robust sleep apnea-hypopnea syndrome automated detection method based on fuzzy entropy using single lead-EEG signals

Yao Wang [a, b,c], Tianshun Yang[b], Siyu Ji[b], Xiaohong Wang[a], Huiquan Wang[a], Jinhai Wang[a] and Xiaoyun Zhao[d,*]

a. Department of Biomedical Engineering, School of Life Sciences, Tiangong University, Tianjin, 300387, China;
b. School of Electrical and Electronic Engineering, Tiangong University, Tianjin, 300387, China;
c. School of Precision Instruments and Optoelectronics Engineering, Tianjin University, Tianjin, 300072, China;
d. Department of Respiratory and Critical Care Medicine & Sleep Center, Tianjin Chest Hospital, Tianjin, 300222, China;
* Correspondence: zxydoctor@163.com;

Abstract: Sleep apnea-hypopnea syndrome is a relatively common disease, characterized by a repetitive reduction or cessation of respiratory airflow, which seriously affects sleep quality and in the long term, can lead to heart disease, hypertension, diabetes, and stroke. Polysomnography is currently the standard method for diagnosing apnea/hypopnea. However, accurate diagnosis can be difficult due to the complex process of multi-signals acquisition in polysomnography. Instead, this paper presents a novel automated fuzzy entropy-based method for detecting apnea/hypopnea using single-lead electroencephalogram signals. The method consists of four steps: (1) The electroencephalogram signals corresponding to respiratory events are partitioned into five sub-bands according to frequency; (2) Features of fuzzy entropy in each sub-band are extracted; (3) The extracted features are evaluated using statistical methods; (4) The features are classified using a classifier, such as the support vector machine, k-nearest neighbor, and random forest algorithms. In this study, data were obtained from a total of 55 subjects with sleep apnea-hypopnea syndrome from both a public and clinical database. The experimental results indicated that all of the selected metrics, including accuracy, sensitivity, and specificity were close to or above 90% for both publicly available and clinical data. Moreover, this approach is sensitive to all types of sleep apnea/hypopnea, an important aspect that is rarely explicitly discussed in the literature.

Keywords: machine learning; sleep apnea/hypopnea; fuzzy entropy; EEG signals; automated detection

1. Introduction

Sleep apnea-hypopnea syndrome (SAHS) is a common clinical sleep disorder that seriously affects sleep quality [1–3]. Apnea is defined as a complete cessation of respiratory airflow for a duration of more than 10 seconds. Hypopnea refers to a decrease in the intensity of respiratory airflow of more than 50% from the base level, accompanied by a decrease in blood oxygen saturation of more than 4% from the base level or wakefulness [4]. In a sense, apnea is an aggravated form of hypopnea. Apnea can be categorized into three main types according to its pathogenic mechanism: obstructive, central, and mixed [5–6]. Obstructive apnea is most common and typically involves stenosis and obstruction of the upper airway [7]. Central apnea is mainly caused by dysfunction of the respiratory center in the brain [8]. Mixed apnea is a combination of obstructive apnea and central apnea [9]. Both apnea and hypopnea have adverse effects on health and can significantly increase the risk of hypertension, cardiovascular disease, cognitive impairment, and decreased immunity [10–12].

Polysomnography (PSG) is currently the gold standard for detecting SAHS [13–14]. In PSG, various physiological signals are recorded, including an electroencephalogram (EEG), electrocardiogram (ECG), and electromyogram (EMG) signals, as well as respiratory airflow and blood oxygen saturation signals [15–16]. A comprehensive analysis of these physiological parameters is then performed to assess the occurrence and severity of apnea or hypopnea [17]. However, this method has a number of limitations. The multi-lead electrodes used in PSG greatly affects normal sleep [18–19]. Moreover, attaching the body to a variety of medical instruments to perform PSG is not convenient. Hence, many researchers have investigated machine learning methods for detecting SAHS based on single lead-EEG signals, which could greatly reduce the difficulties associated with PSG signal acquisition and analysis [20–24].

Compared with other physiological signals, EEG presents a number of advantages in terms of SAHS detection. Although respiratory airflow, ECG, and other signals cannot be used for patients with irregular breathing or obvious arrhythmias, EEG can accurately assess sleep stages and respiratory states under these conditions [25]. In addition, for patients with central nervous system diseases (epilepsy, Alzheimer's disease, dementia, etc.) or neuromuscular diseases (lateral sclerosis, polio, motor neuron disease, etc.), sleep-related breathing events based on EEG signals can be interpreted with higher sensitivity and specificity [26,27]. Therefore, automated detection of SAHS based on EEG signals has become a research hot spot in recent years [28–32]. Almuhammadi et al. [28] extracted time-domain features of the EEG signal and effectively differentiated between apnea patients and normal people with an accuracy of up to 97%. Similarly, Zhou et al. [29] used detrended fluctuation analysis and a support vector machine (SVM) to detect apnea from the nonlinear features of EEG signals. The average classification accuracy of 95.1%, sensitivity of 93.2%, and specificity of 98.6% were reported. However, these methods were only used to classify apnea patients and not specific apnea events [28,29].

Classifying apnea events is much more difficult, but more clinically meaningful, than simply identifying apnea patients [30]. For instance, the apnea–hypopnea index (AHI) indicates the severity of SAHS, which is reflected by the number of apnea/hypopnea events that occur within a certain period of time. Correspondingly, Saha et al. [31] proposed a sleep apnea event detection method based on EEG signal entropy using the k-nearest neighbor (KNN) algorithm. An accuracy of 87.64% and a sensitivity of 89.02% were achieved. Furthermore, Bhattacharjee et al. [30] proposed an algorithm for detecting apnea/hypopnea events that uses the Rician model to extract features. The method was capable of detecting apnea events with an accuracy of 89.30% and 86.14% based on data from two different public databases using a leave-one-out cross validation scheme. Shahnaz et al. [32] used the band power ratio extracted from EEG signals as time-domain features to detect apnea events. The highest accuracy of 87.03% was achieved using a 10-fold cross-validation scheme and KNN classifier.

Although many methods have been proposed in the literature, most have focused on obstructive apnea/hypopnea, whereas the detection of central and mixed apnea/hypopnea are rarely discussed [23,33–35]. In addition, previously published results are based on public databases, whereas the performance of these methods has not been widely tested with clinical EEG data [28–34]. To address these shortcomings, this paper proposes a fuzzy entropy-based method for SAHS detection. In this study, EEG signals were divided into five sub-bands according to specific rhythms in the EEG signals, and then the fuzzy entropy was calculated as the features in each sub-band. Finally, the features were fed into three different machine learning classifiers to detect apnea/hypopnea versus normal breathing events. The experimental results show that this method can be used to detect all types of apnea/hypopnea. Moreover, the method was further verified with clinical data. This method achieved high accuracy of up to 92.56% and 92.88% for the publicly available and clinical data, respectively.

The remainder of this paper is organized as follows. Section 2 describes the proposed method for automated detection of SAHS and the data used in this work. The performance of the method is analyzed in Section 3 and the experimental results are discussed in Section 4. Finally, the main conclusions of this paper are summarized in Section 5.

2. Methods

2.1 EEG data used in the study

This study used EEG data derived from a both a public database and clinical data. Data of 21 males and 4 females between the ages of 32–51 years (the average age was 50) with BMI in the range of 25.1–42.5 kg/m² (average of 31.6 kg/m²) were obtained from the public database [36]. The AHI range was 1.7–90.9 (average of 24.1) and the PSG records consisted of multiple physiological signals including EEG, electrooculogram (EOG), submental EMG, and ECG signals. The EEG (C3–A2) signals were sampled at 128 Hz. The clinical PSG data was collected in the sleep monitoring laboratory at Tianjin Chest Hospital, Tianjin, China. Data included PSG recordings from 23 males and 7 females aged between 37–78 years (the average age was 56) with BMI in the range of 19.8–39.3 kg/m² (average of 29.2 kg/m²). The range of AHI values were in the range of 8.2–68.9 (average of 40). The EEG (C3–A2) signals were

sampled at 100 Hz. The raw EEG data of apnea and normal respiratory events in the clinical data are illustrated in Fig. 1.

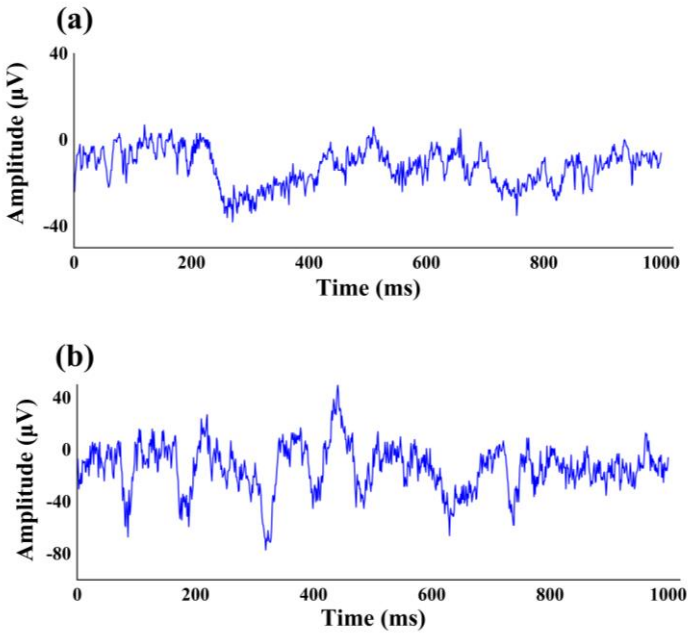

Fig. 1. Original EEG signals of apnea and normal respiratory events. (a) apnea. (b) normal.

The apnea/hypopnea events were annotated and classified into obstructive, central, and mixed by expert clinicians. In this paper, obstructive apnea and obstructive hypopnea were grouped into the same category of obstructive respiratory events. Similarly, central respiratory events consisted of both central apnea and central hypopnea. Mixed respiratory events were comprised of mixed apnea and mixed hypopnea.

2.2 proposed method

First, the raw EEG frames were divided into different frequency sub-bands. Then, the fuzzy entropy-based feature extraction method was applied to each band-limited signal. Statistical analysis was performed to test if the extracted features between the two groups (apnea vs. normal) were different from each other. Finally, the features were classified using three different machine learning models. A detailed description of each step is presented in Fig. 2.

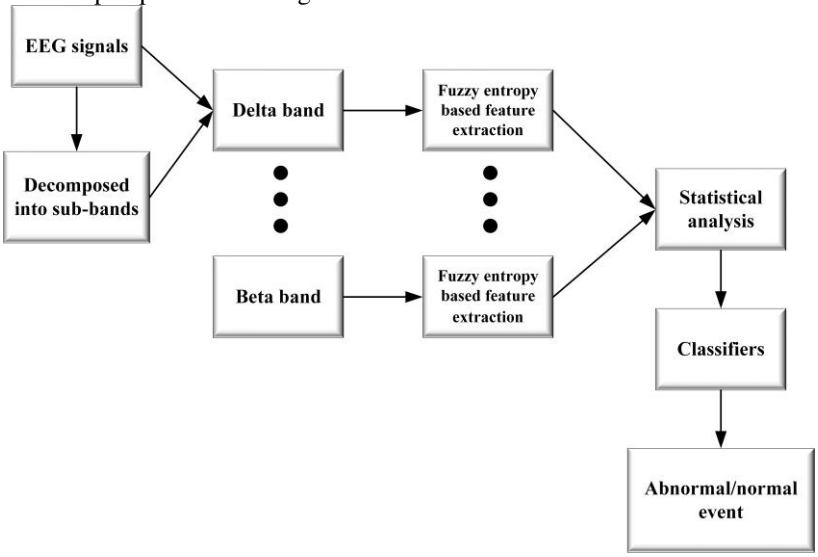

Fig. 2. Block diagram describing the main steps involved in the proposed method.

2.2.1 Data preprocessing.

Brain waves are spontaneous and rhythmic neural electrical activities. Usually, EEG signals can be segmented into finer sub-bands according to frequency. The state of the brain can be reflected by the activity of the different sub-bands. Features extracted from band-limited EEG signals can be used to more accurately capture the variation in EEG signals representing apnea events and normal events. A fourth-order Butterworth filter was chosen to partition the EEG signals into delta (0.25–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), sigma (12–16 Hz), and beta (16–49 Hz) frequency bands [30].

2.2.2 Fuzzy entropy features extraction

Feature extraction is a crucial step in machine learning-based classification methods since features reflect differences between the objects being classified. As a measure of complexity, fuzzy entropy has been widely used for nonlinear physiological signals with satisfactory results [37]. Since EEG signals are nonlinear, unstable, and irregular, fuzzy entropy is proposed to capture subtle changes in EEG signals caused by SAHS [38]. For a given time series consisting of N points $\{u(i):1\le i\le N\}$, fuzzy entropy can be defined as follows [39]:

For $1\le i\le N-m+1$, create a set of m-vectors $X_1^m \ldots X_{N-m+1}^m$ according to the sequence order. Here, X_i^m was defined as

$$X_i^m = \{u(i),u(i+1),\ldots,u(i+m-1)\} - u_0(i), \tag{1}$$

where, $\{u(i),u(i+1),\ldots,u(i+m-1)\}$ denotes m consecutive u values beginning with the *i*th point and $u_0(i)$ was defined as

$$u_0(i) = \frac{1}{m}\sum_{j=0}^{m-1} u(i+j). \tag{2}$$

The distance between vectors X_i^m and X_j^m is defined as the maximum absolute difference between their scalar components d_{ij}^m. Here, d_{ij}^m can be expressed as

$$d_{ij}^m = d\left[X_i^m, X_j^m\right] = \max\left\{\left|u(i+k)-u_0(i)-u(j+k)-u_0(j)\right|\right\} (0\le k\le m-1). \tag{3}$$

For given *n* and r, the similarity degree D_{ij}^m between the vectors X_i^m and X_j^m can be defined using a fuzzy function, as follow:

$$D_{ij}^m = \mu(d_{ij}^m,n,r) = \exp(-\frac{(d_{ij}^m)^n}{r}). \tag{4}$$

Where, n and r are the gradient and width of the exponential function boundary, respectively.

The function $\phi^m(n,r)$ can be defined as

$$\phi^m(n,r) = \frac{1}{N-m}\sum_{i=1}^{N-m}\left(\frac{1}{N-m-1}\sum_{j=1,j\ne i}^{N-m} D_{ij}^m\right). \tag{5}$$

Eqs. (2)-(5) are used to produce m+1 vectors. Then function $\phi^{m+1}(n,r)$ can be defined as

$$\phi^{m+1}(n,r) = \frac{1}{N-m}\sum_{i=1}^{N-m}\left(\frac{1}{N-m-1}\sum_{j=1,j\ne i}^{N-m} D_{ij}^{m+1}\right). \tag{6}$$

Fuzzy entropy can be expressed as

$$fuzzy\ entropy(m,n,r,N) = \ln\phi^m(n,r) - \ln\phi^{m+1}(n,r). \tag{7}$$

For the parameters in fuzzy entropy, we set m=2, n =3 and r=0.0077∗SD. In this study, fuzzy entropy in

each sub-band was calculated. Five features were obtained for each apnea/hypopnea and normal respiratory event. Boxplots for features extracted from each sub-band of EEG signals are shown in Fig. 3. As shown in Fig.3, the fuzzy entropy between normal and apnea/hypopnea respiratory event were different. From delta to alpha band, the fuzzy entropy of apnea was smaller than that of normal respiratory event, whereas the opposite trends were presented in sigma and beta band.

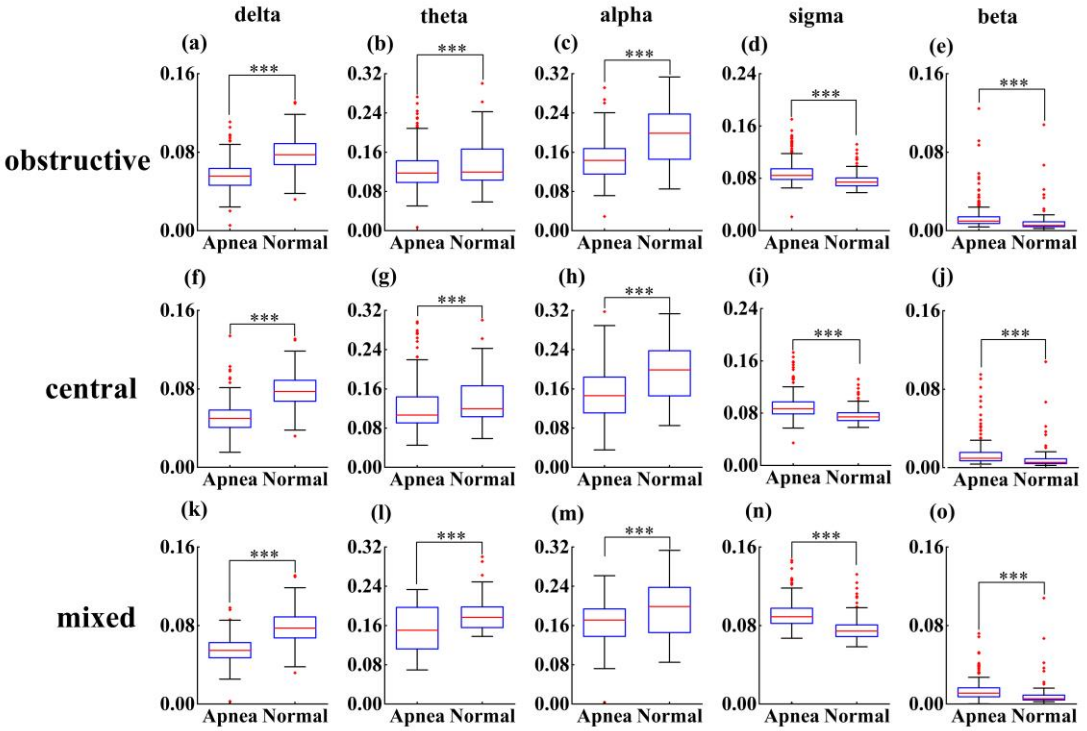

Fig. 3. The boxplots for features extracted from each sub-band of EEG signals in the public database. Each column represents features extracted from different sub-bands of apnea and normal events. Each row represents a different type of apnea. (a) delta band (obstructive), (b) theta band (obstructive), (c) alpha band (obstructive), (d) sigma band (obstructive), (e) beta band (obstructive), (f) delta band (central), (g) theta band (central), (h) alpha band (central), (i) sigma band (central), (j) beta band (central), (k) delta band (mixed), (l) theta band (mixed), (m) alpha band (mixed), (n) sigma band (mixed), (o) beta band (mixed). *** denotes the p-value is lower than 0.001.

2.2.3 Features statistical analysis

The independent sample t-test and Mann-Whitney U test were used to evaluate whether the values of fuzzy entropy between the two groups (apnea vs. normal) are different from each other. The independent sample t-test is suitable for normally distributed data, whereas the Mann-Whitney U test is a nonparametric test that can be applied to data with a non-normal distribution [40]. For both methods, p-values smaller than 0.05 were considered statistically significant. All statistical analyses were carried out using IBM SPSS Statistics 23.

2.2.4 Detection of sleep-apnea hypopnea syndrome using classifiers

The obtained features were randomly segmented into training data and test data. The training data were used to train the machine learning model and the test data were to assess its classification performance. In this work, three machine learning classifiers were used including the KNN, SVM, and RF classifiers. All of the models and algorithms were designed in MATLAB R2013b.

The KNN algorithm can solve classification problems as well as regression problems. Classification is realized by measuring the distance between different eigenvalues. The core idea is that the categories of unlabeled samples can be determined by the properties of their k nearest neighbors. In this work, we set k as 7 and the Mahalanobis distance was adopted as the distance measure.

The SVM is a machine learning classifier also commonly used for solving classification problems. SVM can be used to classify both linear and nonlinear separable samples. In the case of nonlinear separable data, feature vectors in low-dimensional space are converted into features in the high-dimensional feature space using a certain kernel function. In the new feature dimension space, features are easier to separate. In this work, we selected the radial basis function (RBF) as the kernel function of the SVM.

The RF classifier is an integrated classifier composed of multiple decision trees. In the RF, unmarked test samples are sent to each decision tree for classification, then all the trees vote and the class with the most votes is chosen as the final classification class. In this work, the number of decision trees was set to 40.

Various performance metrics were used to evaluate the classification results including accuracy, sensitivity, specificity, precision, and F1-score. The metrics were calculated using the following formulas:

$$Accuracy = \frac{TP + TN}{FP + FN + TP + TN}, \tag{8}$$

$$Sensitivity = \frac{TP}{TP + FN}, \tag{9}$$

$$Specificity = \frac{TN}{TN + FP}, \tag{10}$$

$$Precison = \frac{TP}{TP + FP}, \tag{11}$$

$$F\text{-}score = \frac{2 \times Precision \times Sensitivity}{Precision + Sensitivity}, \tag{12}$$

where true positive (TP) is the number of apnea/hypopnea events detected correctly as apnea/hypopnea events by the classifier, false positive (FP) denotes the number of normal events detected incorrectly as apnea/hypopnea events, true negative (TN) is the number of normal events detected correctly as normal events, and false negative (FN) denotes the number of apnea/hypopnea events detected incorrectly as normal events.

3. Experiment and Results

In the public database, a total of 3299 apnea/hypopnea and 1402 normal respiratory events were obtained from the annotation files. Similarly, a total of 2400 apnea/hypopnea and 800 normal respiratory events were acquired from the clinical database. Details of the respiratory events from both the public data and the clinical data are provided in Table 1. For the clinical database, there were only 800 mixed respiratory events in the 30 PSG recordings. To compare the detection results of three kinds of apnea/hypopnea, the same number of obstructive and central apnea/hypopnea events were used

Table 1. The detailed composition of the respiratory events.

Respiratory events type	obstructive	central	mixed	normal
Public data	1641	1409	249	1402
Clinical data	800	800	800	800

Five groups of hypothesis tests were performed for each type of apnea/hypopnea. In the publicly available data, only features extracted from the delta band in mixed apnea/hypopnea events were normally distributed. For this group, independent sample t-tests were used and the Mann-Whitney U test was selected for the remaining 14 groups. In the clinical data, all features of the 15 groups were not normally distributed and the Mann-Whitney U test was employed. The results show that all p-values

were lower than 0.001, indicating that there is a significant difference between features of the apnea/hypopnea and normal respiratory events.

Multiple indicators were used to objectively assess the classification results. Average values of accuracy, sensitivity, specificity, precision, and F1-score were computed using a 10-fold cross-validation and compared. For the k-fold cross-validation, k independent trials were carried out and the average result was adopted. For the public data, the performance of the KNN, SVM, and RF classifiers is summarized in Table 2. Similarly, Table 3 shows the classification results for the clinical data. The results clearly show that the SVM achieved the highest accuracy (93.19%). Furthermore, for all three types of apnea/hypopnea, values of all five metrics were close to or above 90%.

This paper also assessed the classification performance when the abnormal events are composed of different types of apnea/hypopnea. The results for public and clinical data are outlined in Fig. 4, and show that the proposed method still maintains high accuracy. As shown in Fig. 4, the SVM classifier exhibited the best performance.

Table 2. Classification performances verified in the public data.

Classifiers	SAHS type	Accuracy	Sensitivity	Specificity	Precision	F1-score
KNN	Obs vs Normal	91.45%	92.09%	90.74%	92.10%	92.07%
	Cen vs Normal	92.16%	91.17%	93.07%	92.02%	91.58%
	Mix vs Normal	92.16%	92.14%	92.49%	92.33%	92.09%
SVM	Obs vs Normal	91.92%	94.25%	89.23%	91.13%	92.64%
	Cen vs Normal	92.29%	93.68%	91.07%	90.22%	91.89%
	Mix vs Normal	92.17%	93.88%	90.58%	90.54%	92.06%
RF	Obs vs Normal	91.26%	93.69%	88.48%	90.48%	92.03%
	Cen vs Normal	92.00%	93.01%	91.10%	90.21%	91.57%
	Mix vs Normal	92.56%	93.62%	91.58%	91.68%	92.54%

SAHS is the abbreviation of sleep apnea-hypopnea syndrome. Obs is short for obstructive apnea-hypopnea syndrome. Cen is short for central apnea-hypopnea syndrome. Mix is short for mixed apnea-hypopnea syndrome.

Table 3. Classification performance verified in the clinical data.

Classifiers	SAHS type	Accuracy	Sensitivity	Specificity	Precision	F1-score
KNN	Obs vs Normal	91.25%	92.22%	90.42%	90.66%	91.31%
	Cen vs Normal	88.75%	89.94%	87.75%	87.73%	88.76%
	Mix vs Normal	92.31%	93.31%	91.37%	91.53%	92.37%
SVM	Obs vs Normal	91.69%	92.18%	91.25%	91.37%	91.72%
	Cen vs Normal	88.94%	89.85%	88.09%	88.17%	88.97%
	Mix vs Normal	93.19%	93.27%	93.17%	93.12%	93.15%
RF	Obs vs Normal	91.63%	91.46%	91.76%	91.73%	91.52%
	Cen vs Normal	88.50%	89.84%	87.29%	87.58%	88.60%
	Mix vs Normal	92.88%	93.27%	92.44%	92.54%	92.89%

SAHS is the abbreviation of sleep apnea-hypopnea syndrome. Obs is short for obstructive apnea-hypopnea syndrome. Cen is short for central apnea-hypopnea syndrome. Mix is short for mixed apnea-hypopnea syndrome.

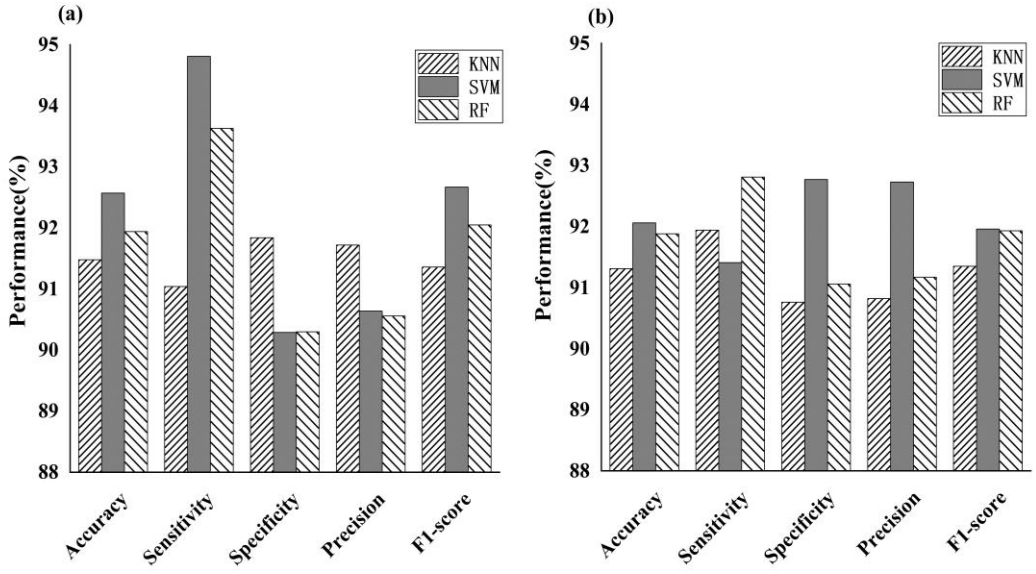

Fig. 4. Classification performances of different classifiers when abnormal data were composed of different types of apnea/hypopnea events. (a) public data. (b) clinical data.

4. Discussions

This research developed an efficient automated fuzzy entropy-based method for detecting SAHS with single-lead EEG signals. Compared to previously published studies, the present work offers three main contributions.

First, to the authors' knowledge, this is the first time that fuzzy entropy has been applied to detect SAHS events from EEG signals. The occurrence of apnea/hypopnea can increase the amount of carbon dioxide in the blood, which can trigger changes in the complexity of the EEG. Due to irregular fluctuations, nonlinearity, and instability of EEG signals, features extracted from the time-domain, frequency-domain, time-frequency domain, and spatial domain signals cannot effectively capture changes in the EEG signals during apnea/hypopnea. As a measure of complexity and a method of nonlinear dynamics, fuzzy entropy introduces the concept of fuzzy set based on sample entropy and approximate entropy, providing a more accurate measurement of changes in the complexity of the EEG signal corresponding to abnormal respiratory events. As shown in the Fig. 3, significant differences in EEG fuzzy entropy between apnea/hypopnea and normal respiratory events were observed in this study, which provide new possibilities for SAHS detection using EEG.

Second, the proposed method can be used to detect of all types of apnea/hypopnea events. Most previously proposed methods for detecting apnea-hypopnea syndrome have focused on obstructive apnea/hypopnea [23,33–35]. Few studies have introduced methods for explicitly detecting central and mixed apnea/hypopnea. Furthermore, due to the different pathogenesis of each kind of apnea/hypopnea, existing methods for detecting SAHS in the clinic may easily miss a diagnosis. The proposed method can detect all types of apnea/hypopnea and maintains high accuracy classification for each type of apnea/hypopnea events and normal respiratory events (Table 2 and 3).

Third, the method was effectively verified with clinical data, demonstrating a certain degree of robustness. One important disadvantage of machine learning is that its models are often sensitive to the data used. To this end, in addition to data from a public database, clinical data were used to verify the effectiveness of the method. The accuracy of this method was higher than 92% for both data sets, which is superior to the existing state of the art [16,22,35,41–42]. To the best of our knowledge, this

investigation is one of only a few studies related to the SAHS detection to use clinical data to verify the method, which demonstrates the reliability of the proposed method.

However, we should like to point out that there is certain limitation in this study. As mentioned in Section 2.1, the apnea and the hypopnea were considered as the same category of abnormal respiratory events because this method is restricted to distinguish between apnea and hypopnea. For that we will further improve the algorithm in future research.

5. Conclusions

The paper presented a novel fuzzy entropy-based method for the automated discrimination of apnea/hypopnea events from normal respiratory events. The EEG signal is first divided into sub-bands according to frequency, the fuzzy entropy features are extracted from the sub-band signals as inputs to the machine learning classifiers to classify apnea/hypopnea and normal respiratory events. The results show that the method yields an average accuracy of approximately 90% for all kinds of apnea/hypopnea based on both public and clinical data. Therefore, it is a reliable EEG-based method for detecting apnea/hypopnea.

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Competing interests

The authors declare no conflict of interest.

Ethics approval and consent to participate.

This study was approved by the Ethics Committee of Tianjin Chest Hospital and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent.

Informed consent was obtained from all individual participants included in the study.

Figures

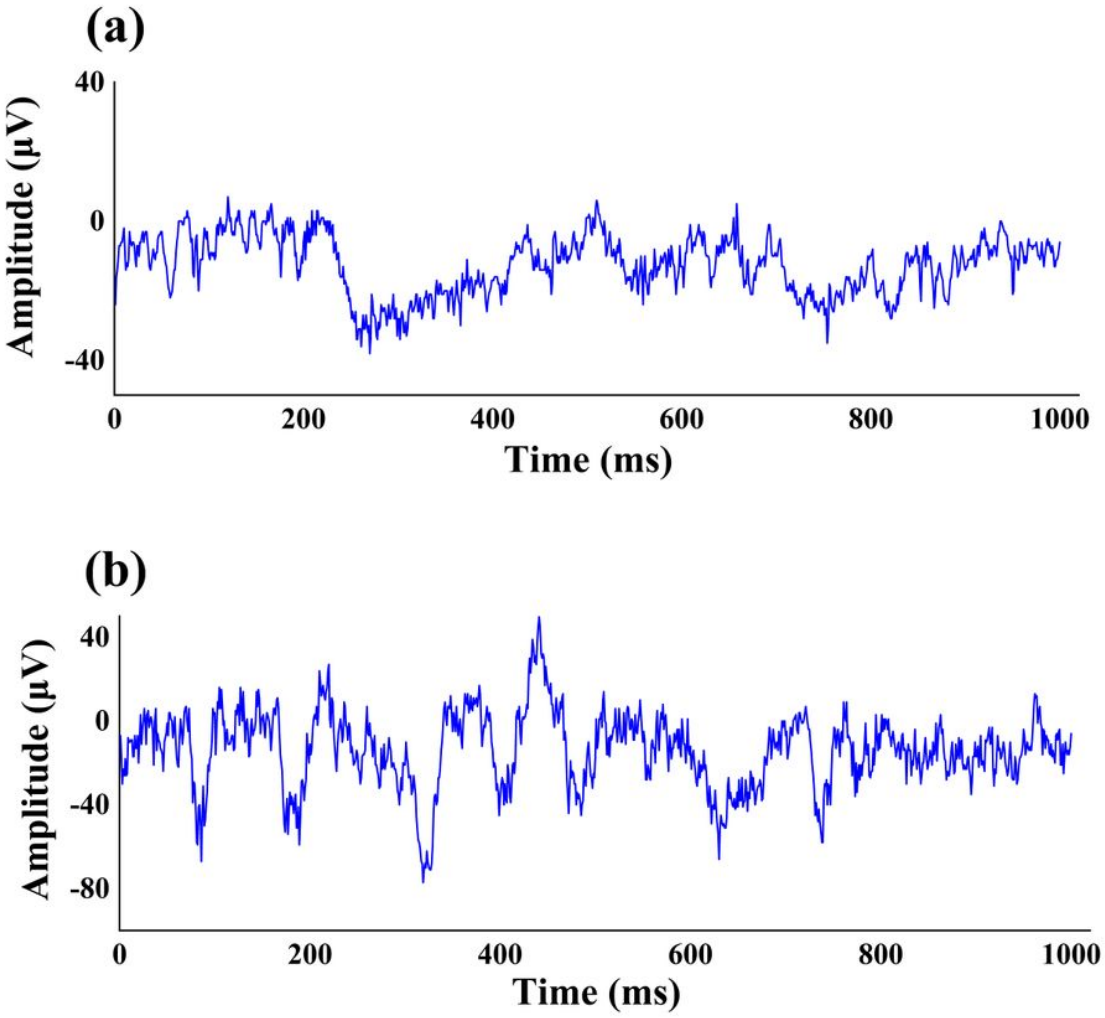

Figure 1

Original EEG signals of apnea and normal respiratory events. (a) apnea. (b) normal.

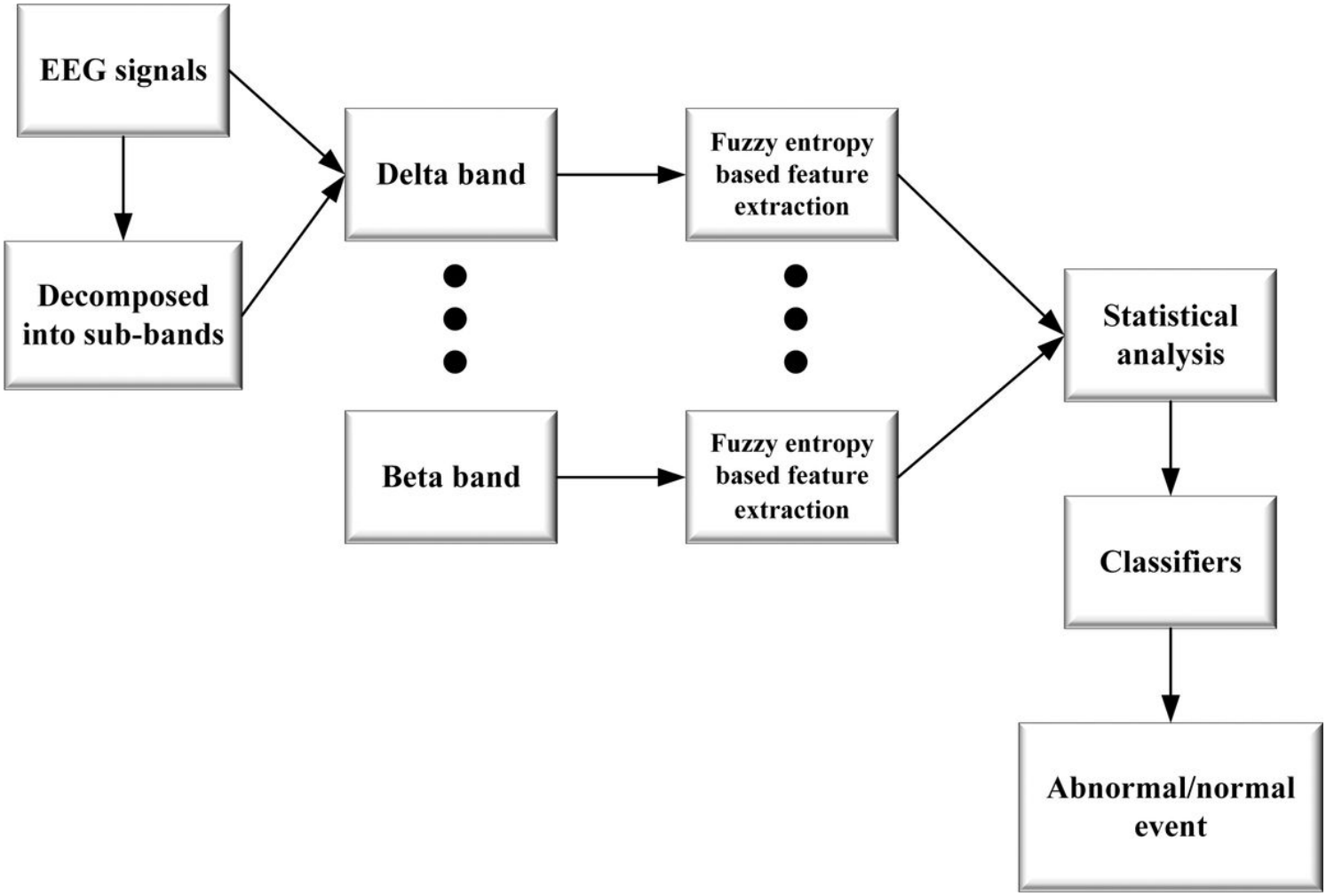

Figure 2

Block diagram describing the main steps involved in the proposed method.

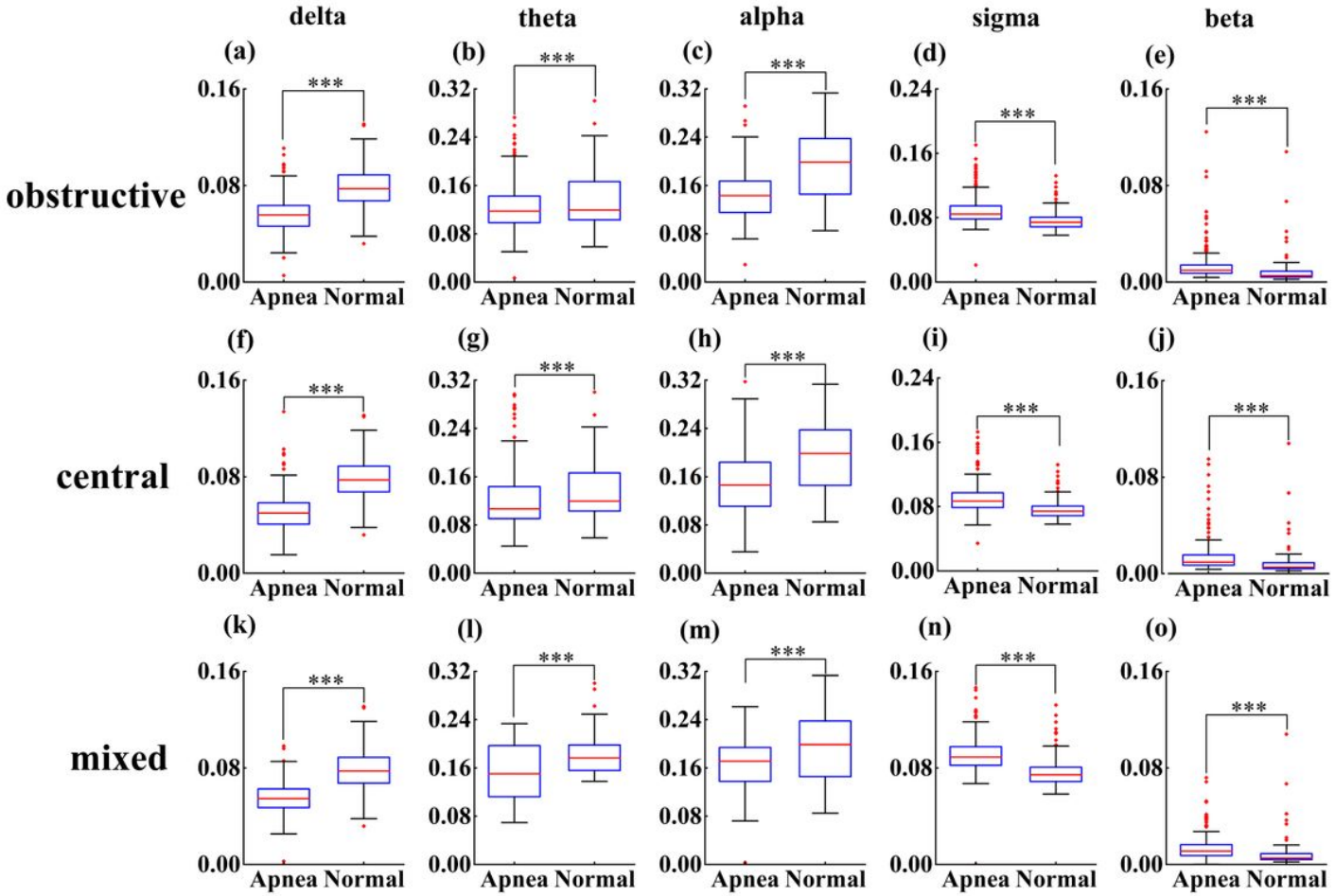

Figure 3

The boxplots for features extracted from each sub-band of EEG signals in the public database. Each column represents features extracted from different sub-bands of apnea and normal events. Each row represents a different type of apnea. (a) delta band (obstructive), (b) theta band (obstructive), (c) alpha band (obstructive), (d) sigma band (obstructive), (e) beta band (obstructive), (f) delta band (central), (g) theta band (central), (h) alpha band (central), (i) sigma band (central), (j) beta band (central), (k) delta band (mixed), (l) theta band (mixed), (m) alpha band (mixed), (n) sigma band (mixed), (o) beta band (mixed). *** denotes the p-value is lower than 0.001.

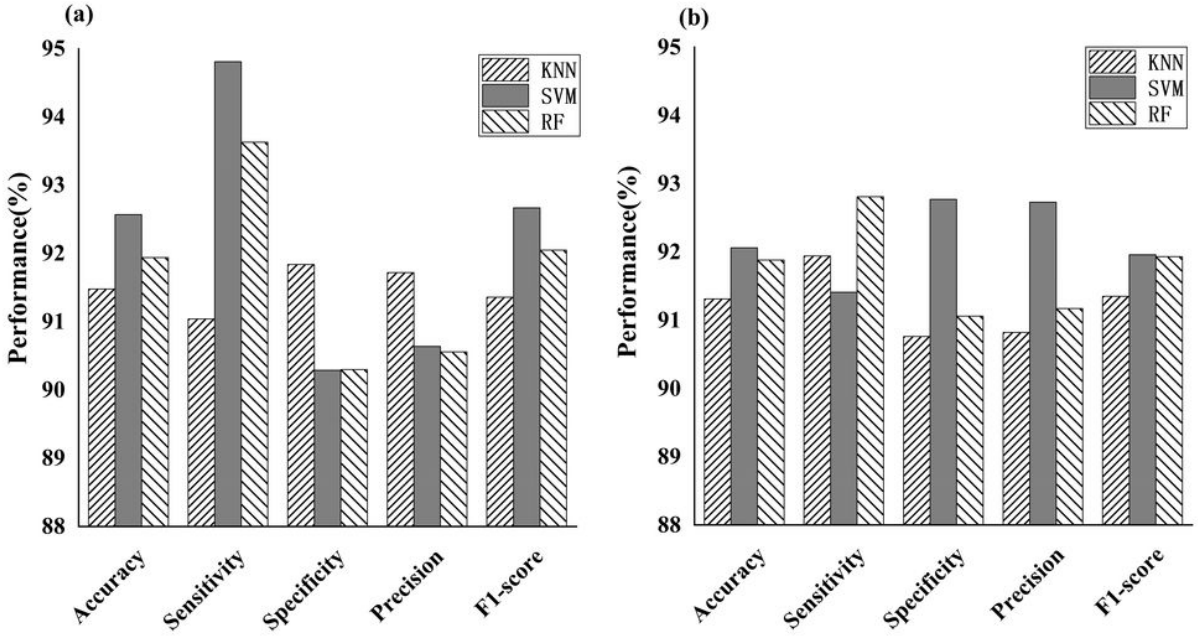

Figure 4

Classification performances of different classifiers when abnormal data were composed of different types of apnea/hypopnea events. (a) public data. (b) clinical data.