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Original Article

Sleep Apnea Detection from Single-Lead ECG Using Features Based on ECG-Derived Respiration (EDR) Signals

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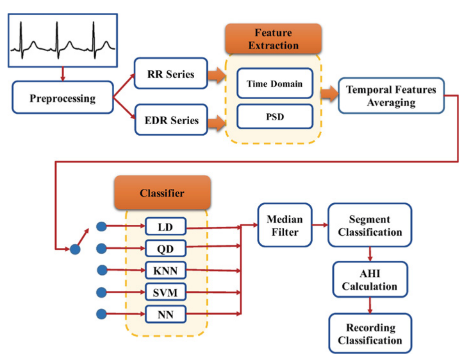
Highlights

- Two new algorithms for extracting ECG-derived respiration (EDR) using single-lead ECG.
- Comparing EDRs to other state-of-the-art EDR in terms of similarity to a reference respiration signal.
- Extraction features from EDRs to be used in an automatic sleep apnea detection algorithm.
- Improving automatic ECG-based sleep apnea detection accuracy.

Graphical abstract



Abstract

Background and objective: One of the important applications of non-invasive respiration monitoring using ECG signal is the detection of obstructive sleep apnea (OSA). ECG-derived respiratory (EDR) signals, contribute to useful information about apnea occurrence. In this paper, two EDR extraction methods are proposed, and their application in automatic OSA detection using single-lead ECG is investigated.
Methods: EDR signals are extracted based on new respiration-related features in ECG beats morphology, such as ECG variance (EDR_{Var}) and phase space reconstruction area (EDR_{PSR}). After evaluating the EDRs by comparing them to a reference respiratory signal, they are used in an automatic OSA detection application. Fantasia and Apnea-ECG database from PhysioNet are used for EDRs assessments and OSA detection, respectively. The final performance of our OSA detection is tested on an independent test data which is also compared with results of other techniques in the literature.
Results: The extracted EDRs, EDR_{Var} and EDR_{PSR} show correlations of 72% and 70% with reference respiration, which outperform the other state-of-the-art EDR methods. After feature extraction from EDRs and RR intervals series, the combination of RR and EDR_{PSR} feature sets achieved 100% accuracy in subject-based apnea detection on independent test data, and also minute-based apnea detection is done with accuracy, sensitivity and specificity of 90.9%, 89.6% and 91.8%, which is better than other automatic algorithms in the literature.

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Conclusions: Our OSA detection system using EDRs features yields better independent test results compared with other state-of-the-art automatic apnea detection methods. The results indicate that ECG-based OSA detection system can classify OSA events with high accuracy and suggest a promising, non-invasive and efficient method for apnea detection.

Keywords: Obstructive sleep apnea; ECG; EDR; Classification; Phase space reconstruction

1. Introduction

Sleep-related breathing disorders (SRBDs) are originated from repetitive interruption of respiration which usually produce sleep arousals, hypoxia, or both. There are different syndromes for SRBD: three of them are obstructive sleep apnea (OSA), central sleep apnea (CSA) and mixed apnea with both obstructive and central syndromes [1]. OSA is caused by the collapse of the airway which is a 10-second or larger pause in respiration activity along with continuing ventilatory effort. Obstructive hypopneas also make decreases in ventilation, but not complete cessation of it and cause a fall in oxygen saturation or arousal. OSA is diagnosed when a patient has an apnea-hypopnea index (AHI; number of apneas and hypopneas per hour of sleep) larger than 5 and shows symptoms such as daytime sleepiness. CSA is determined by repeated cessation of respiration during sleep resulting from the loss of ventilatory drive that causes a 10-second or larger pause in ventilation with no respiratory effort [2]. Mixed sleep apnea is the combination of both CSA and OSA events. Among the three different forms of sleep apnea (obstructive, central, or mixed), OSA is the most common [3].

Polysomnography (PSG) test is the traditional OSA detection method which requires an all-night analysis in a clinic environment with medical supervision. PSG as the reference standard for diagnosing OSA is a complex diagnostic sleep test that includes at least electroencephalogram (EEG), electromyogram (EMG), electrooculogram (EOG), electrocardiogram (ECG), breathing/respiratory effort, airflow and oxygen saturation (SaO2) recording. PSG is difficult, time-consuming and, at times, out of reach or even impractical [4]. Hence, a simple screening method, which provides a reliable diagnosis of sleep apnea without referring to PSG is of interest.

Abnormal heart activities or high heart rate variability (HRV) can provide evidence of OSA occurrence [5]. Heart rate (HR) is based on the time between two consecutive R-peaks, known as the RR interval. In addition, ECG recording signals convey respiration information that can be derived from ECG which are called ECG-derived respiration (EDR) [6], and using these indirect extracted respiration information can also be useful in OSA diagnosis. Thus, ECG-based screening systems are promising in noninvasive OSA diagnosis. Few studies have addressed sleep apnea detection from ECG until the PhysioNet/Computers in Cardiology Challenge 2000. PhysioNet and the Coordinators of the 2000 Computers in Cardiology (CinC) Conference jointly organized this competition to prove the efficacy of ECG-based methods for sleep apnea detection using a large and representative set of data [7]. PhysioNet is an online library of biomedical signals and open-source software, and its sponsor is US National Institutes of Health's National Centre for Research Resources [8]. Competitors were invited to two challenges: 1) classifying the recordings in the test set with sleep apnea and the normal recordings, 2) labeling each minute in all 35 test recordings as an apnea or non-apnea minute [7]. Accordingly, the steady stream of research articles were published which indicates that there is a connection between sleep apnea and ECG signal. In those researches either, rule-based or learning algorithms are used for apnea detection.

Respiration activity causes some morphological changes in the ECG signal due to some mechanisms, such as: **i)** changes in volume of the lung during inspiration and expiration cycles that leads to fluctuation in electric impedance of thorax, and **ii)** changes in the heart vector position with respect to ECG electrodes [9]. According to these morphological changes caused by respiration effects on recorded ECG signal, respiratory information or EDR signal can be extracted from ECG using some signal processing techniques.

Most of ECG-based OSA detection algorithms in the literature have used different ECG-derived parameters related to respiration (EDR signals) and HRV signal to extract time domain, frequency domain and other nonlinear features. They have used these features as inputs of the black-box decision making process and classifiers. The top-three algorithms participated in PhysioNet/CinC Challenge 2000 used time and frequency domain features of HRV or EDR signals that could classify all 30 test subjects correctly and were the top-scoring algorithms (up to 89.4% accuracy) in the minute-by-minute apnea detection [10–12]. Apart from the winner that used visual classification procedure [10], the other two participants automatically detected apnea events. In addition, each method used different EDR extraction algorithms based on morphology of ECG beats, because changes in respiration activity affect the ECG morphology [7]. EDR signals are generated by measurements of the T-wave amplitude [10], S-wave amplitude [11] or R amplitude [12]. In another study, a variety of features are extracted from HRV and the EDR signal obtained by sampling the area enclosed by QRS waves (EDR_{Area}), and the performance of classifiers, such as linear and quadratic discriminants were compared [13]. In [14], minute-by-minute apnea detection is provided using features derived from R-peak amplitude series as an EDR sample series (EDR_{Ramp}). Some other studies used wavelet-based features from EDR_{Ramp} or EDR_{Area} and HRV for automatic recognition of patients with OSA [15,16]. Time and frequency domain features were obtained from RR intervals and EDR based on QRS area in [17] and minute-by-minute classification was achieved with an Extreme Learning Machine (ELM). In [18], Permutation Entropy (PE) and cepstrum coefficients of HRV and a set of band powers obtained from the EDR_{Ramp} are the features for minute-by-minute apnea detection. Recently, in [5], the temporal dependency of RR time series and EDR_{Area} signal by a discriminative hidden Markov model is used for recognition of patients with OSA. In another recent research [19], the coefficients of the Hermite expansion QRS complex of the ECG signal along with three features, based on RR intervals, are used for apnea detection. All the methods mentioned above, have used the whole database represented by PhysioNet/CinC Challenge for the evaluation.

This work concentrates on automatic OSA detection using single-lead ECG. Distortion in EDRs (surrogate respiration derived from ECG) and RR intervals (inverse of heart rate) are reported highly related to the occurrence of apnea events. We proposed two new EDR extraction methods and used features extracted from them for automatic OSA detection. First, the performance of EDRs are evaluated in terms of cross-correlation with a reference respiration signal and are compared with two EDRs in the literature. Then, features are extracted from EDRs and RR interval series, and a variety of classifier techniques are used to assess apnea detection. In addition, the efficacy of proposed automatic apnea detection approach is compared with the ones from the literature.

This paper is organized as follows. In Section 2 methods, learning strategy, data and evaluation criteria are described. In Section 3 the experimental results are reported. Section 4 discusses the results, and finally Section 5 concludes the paper.

2. Method

In this section, our developed automatic OSA detection algorithm is described (Fig. 1). In this system, single-lead ECG recordings are divided into 1-minute segments. Since the physiological processes that link changes in the ECG to OSA events are not fully known, we use supervised learning approach. This is one type of machine learning algorithm that uses a transformation of training dataset (features) to classify test dataset into different categories. The aim of this study is to classify each 1-minute ECG segments into apnea or normal segments which is called segment or minute-by-minute classification. After detection of apnea events, the overall AHI, number of apneas per hour in each recording, is estimated in order to discriminate the ECG recording of a subject as an apnea or a normal one. This is called recording or subject-based classification. Features are extracted from a corrected version of EDR and RR series. Two new EDR estimation methods are also introduced and their agreement with reference respiration signal are evaluated before using them as surrogate respiration signals in OSA detection. In this work, RR interval or EDR time series are a sequence of data points indexed in R-peak times, and their estimated signals will be the interpolated version of these time series.

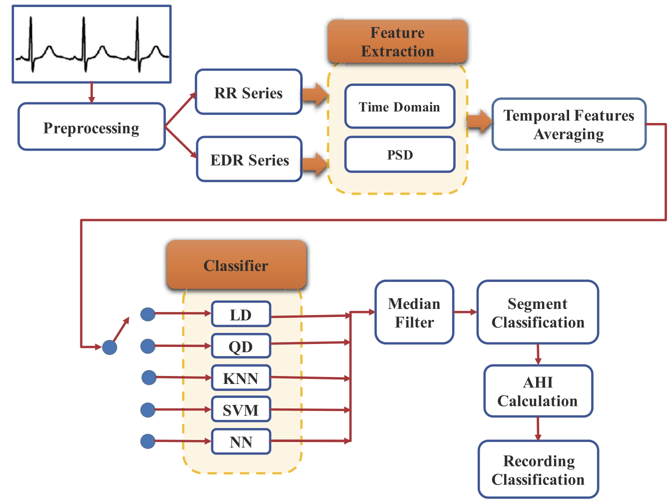

Fig. 1. Schematic representation of automatic OSA detection.

2.1. Preprocessing and RR series extraction

In the preprocessing step, each one minute ECG segment is first filtered in order to remove the 60 Hz supply interference noise, then the median filters approach (described in [20]) is used for removal of ECG baseline wander. Furthermore, all R-peaks are found via the Pan–Tompkins algorithm [21]. RR interval series are generated by calculating interval time between successive R-peak points. RR series need to be corrected because of poor signal quality and errors of R-peak detections algorithm. An automatic preprocessing step, described in [13], is used to correct RR-interval sequence errors due to spurious R-peak detections or missed R-peaks.

2.2. EDR extraction

In this section, our new EDR extraction methods are described. These methods are based on tracking variation patterns in ECG morphology caused by respiration activity.

2.2.1. EDR I

Our first EDR extraction method is based on a statistical feature that is introduced as a respiration-related feature. The variance of ECG signal amplitudes in each inter-beat RR interval is calculated. After variance computation in each interval of two successive R-peaks, EDR series are constructed by assigning variance values to each former R-peaks, and other EDR values in times between each R intervals can be estimated by applying the spline interpolation (Fig. 2). EDR series also need to be corrected. Suspect EDR samples are found by applying a median filter of width five to the sequence. The output provides a robust estimate of the expected value for each EDR, then EDR samples with variations larger than 2 times from output of median filter are replaced by the output of the median filter. We use EDR_{Var} notation for this EDR extraction method.

2.2.2. EDR II

Our second EDR extraction method is based on a phase space reconstruction (PSR) feature. In a time series, such as

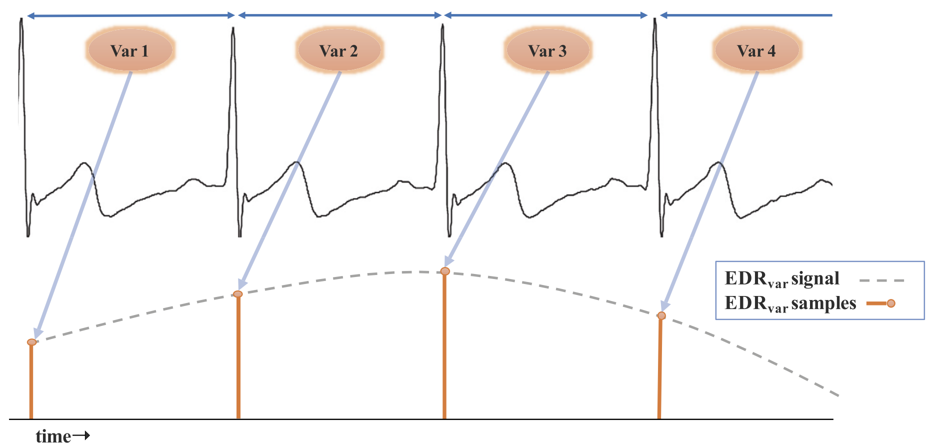

Fig. 2. EDR extraction based on beat-to-beat variance variation induced by respiration activity.

the ECG signal, it is sometimes difficult to search for small changes in patterns in the time series itself, but searching in a higher dimensional transformation of the time series can be helpful. The reconstructed phase space is an example of such transformation [22]. In EDR extraction approach we need to track morphological changes in ECG caused by respiration effects, and this morphological changes can be hidden or small in time domain. Therefore, searching in reconstructed phase space of ECG can be a probable solution for EDR estimation.

In the PSR technique, the original QRS wave and its delayed version are plotted to get the trajectory of the dynamic system. This gives a phase-space loop which can have respiration information. In one study, area under major portrait radius (MPR) curve derived from PSR loop has been introduced as a respiration-related feature for EDR extraction [23]. In this paper, phase space of ECG beats have been reconstructed the same way in [23], but a new feature from PSR is proposed as a respiration-related feature to generate EDR series.

The method to obtain PSR can be briefly described as follows: phase space reconstruction expands a time series $x(t)$, $t = 0...T$ into a series of vectors $\mathbf{x(t)}$, $t = 0...(T - (d_m - 1))\tau$

$$\mathbf{x(t)} = \left[\, x(t)\;\; x(t+\tau)\;\; \cdots\;\; x(t+(d_m-1)\tau) \,\right] \tag{1}$$

where $\mathbf{x(t)}$ is one point of the trajectory in the phase space at time t, τ is a constant time delay between the points of the time series, and d_m is the embedding dimension. Plotting $\mathbf{x(t)}$ in multiple dimensions depicts the phase space loop of the time series. Different choices of τ and d_m make different reconstructed trajectories. Here we use a two-dimensional phase space diagram ($d_m = 2$) to reconstruct the phase space of the windowed QRS complex, and the time delay is set to 8 ms which is close to the best choice τ established for ECG signals [24]. To capture the windowed QRS complexes for reconstruction of phase space, 40 ms before and 40 ms after each R-peak are selected. Although a fixed window around R peaks does not lead to capture the whole QRS complex duration, we used this fixed window since there is no need to exact segmentation of QRS complexes. The reason is that respiration cycle length (reciprocal of respiration rate) is larger than cardiac cycle (reciprocal of heart rate). Then changes in window samples around R peaks can reliably reflect changes in respiration effects on ECG. Therefore, we can ignore QRS duration variation during all ECG beats, since it does not affect the overall results.

An example of QRS transformation to a two-dimensional PSR plot can be seen in Fig. 3. This figure shows many consecutive QRS waves affected by respiration activity and corresponding PSR of QRS waves. We hypothesize that respiration activity can change the area of the polygon specified by QRS phase space trajectory; therefore, the area of windowed QRS phase space trajectory is introduced as a respiration-related feature to construct EDR series at the R-peak times. Estimation of EDR signal from EDR series is done similar to the first EDR by spline interpolation. The suspected samples of this EDR are also corrected similarly to EDR_{Var} correction. We use EDR_{PSR} notation for this EDR extraction method.

For comparison, one of the well known EDR extraction method in the literature that also has been used in apnea detection studies, area of QRS complex (EDR_{Area}), is implemented. This EDR signal is derived by computation of the area enclosed by consecutive QRS waves [13,17,15,16,5]. In addition, the EDR proposed by [23] (EDR_{MPR}) is also implemented to compare with our PSR-based EDR.

2.3. Feature extraction

After generating RR and EDR time series for 1-minute ECG segments, a set of features that could be possibly useful in apnea event classification are extracted. This set of features are described by a feature vector that represents information derived from each 1-minute segment. 50 and 35 features are extracted from RR and each EDR series, respectively. The following features extracted from RR intervals are the most effective set of RR-based features for apnea detection [25–27,13,28,5]. The RR and EDR features are as follows:

- average and standard deviation of RR-interval series;
- RR-interval series correlation calculation and using the first five correlation coefficients;
- the number of two neighboring RR-interval points that the first RR-interval point is 50 ms or more, larger than the second RR-interval point (variant 1);

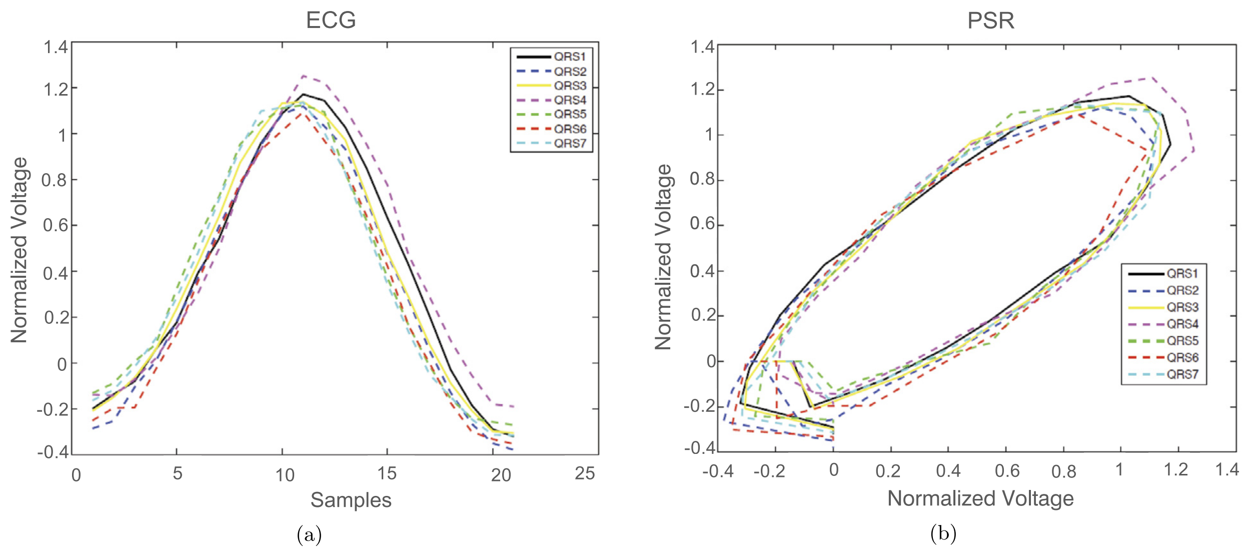

Fig. 3. (a) Consecutive QRS waves, (b) QRS waves phase space reconstruction.

- the number of two neighboring RR-intervals points that the second RR-interval point is 50 ms or more, larger than the first RR-interval point (variant 2);
- two above variant 1 and variant 2 divided by the total number of RR-interval points define another two features;
- the standard deviation of the differences between neighboring RR-intervals points;
- the square root of the average of the squares of differences between RR-intervals points;
- the Allan factor $A(T)$ evaluated at a time scale T of 5, 10, 15, 20, and 25 s in which $A(T) = E\{[N_{i+1}(T) - N_i(T)]^2\}/2E\{N_{i+1}(T)\}$, $N_i(T)$ is the number of detected QRS points that are in a window of length T stretching from iT to $(i+1)T$ and E is the expectation operator [29];
- power spectral density (PSD) of the RR-intervals [30]; 256-point FFT is taken and after averaging four neighboring frequency bins, first 32 features are used;
- mean EDR amplitude series;
- standard deviation of the EDR amplitude series;
- the PSD of the EDR signal; 256-point FFT is taken and after averaging four neighboring frequency bins, first 32 features are used;
- average of the standard deviations of EDR quartiles.

The PSD-based features from RR intervals and EDR series are extracted in the same manner as [13].

2.4. Classification

In this study, different classifiers are used. Classification tackles the problem of assigning an unknown input feature vector to one of a predefined and learned set of classes [31]. Five different classifiers, Linear and Quadratic Discriminant (LD and QD) models, K-Nearest Neighbors classifiers (k-NN), Support Vector Machine (SVM), and Artificial Neural Network (ANN), are used to assess the performance of the proposed sleep apnea detection method. The basic rule of the k-NN algorithm is assigning the input vector to the class that the most of the k nearest samples in the training set belong to. If data are assumed to be distributed as a multivariate Gaussian, linear discriminant function classifier divides the feature space by hyperplanes, so it would be a proper model when the problem is linearly separable. For non-linearly separable problems, a quadratic discrimination model might be useful. SVM is a linear classifier in high dimensional spaces and can also be applicable in the non-linear problems using kernel SVM. ANN is a non-linear statistical tool to find complex relationships between inputs and outputs samples by adapting to the data using a training phase [31]. In the current study, ANN is implemented by two-layer feed-forward with the log-sigmoid transfer function (logsig) for hidden layers and linear transfer function for the output layer. The number of neurons in the hidden layer has been tested to achieve a good performance. Training the network is done by minimizing the mean squared error (MSE) using scaled conjugate gradient algorithm, and the percentage of training and validation data during training phase are set to 70% and 30%. Performance of the k-NN classifier with euclidian distance is tested for different k, and the best results are reported. SVM algorithm is also implemented with different kernels that the best results belong to SVM with linear kernel, that is why only these results are reported. We have used Statistics Toolbox and Neural Network Toolbox of Matlab for implementation of the algorithms.

Apnea segments are observed to be concentrated in time rather than randomly distributed, and there is some dependency in the apnea times [5,13]. Using this temporal information about distribution of apnea occurrence can help improving the performance of the classifiers. In the current study, we average input feature vectors of adjacent segments before feeding to classifiers (similar to one of boosting classification performance techniques in [13]) and then apply a median filter to the output predictions of the classifiers. The optimum number of feature vectors to be averaged and the median filter length are found by assessing the performance of LD classifier using the

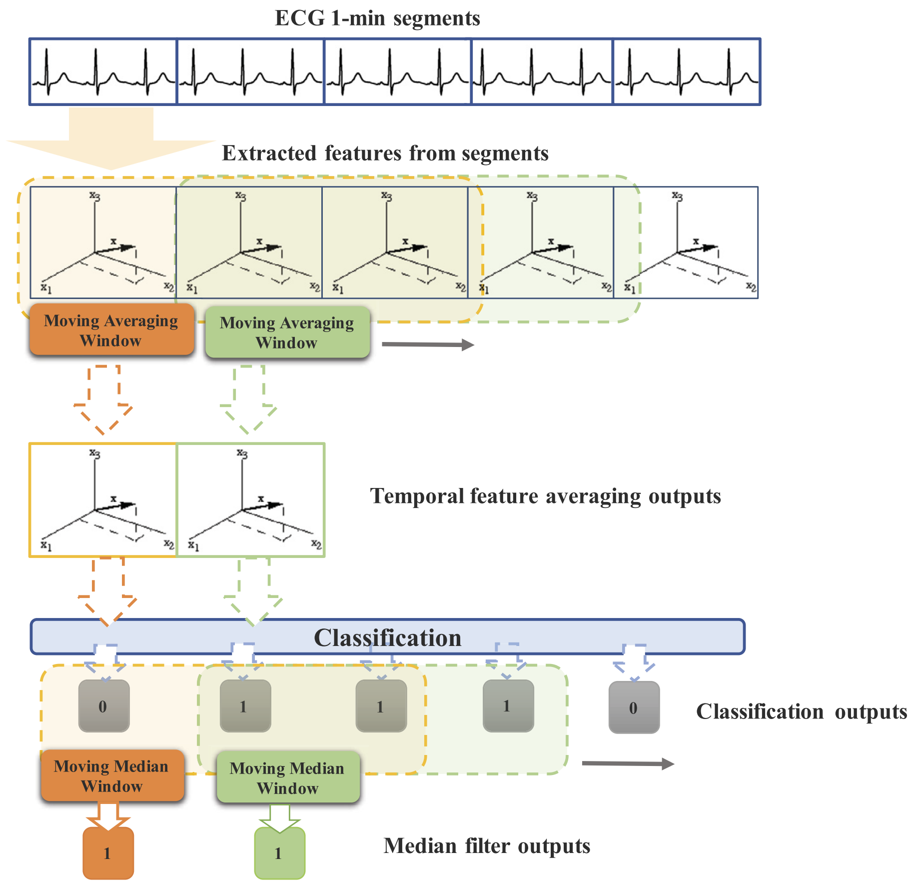

Fig. 4. Apnea detection improving via averaging the feature vectors of adjacent segments and median filter.

cross-validation on training dataset. The median filter applied to the classification outputs can correct some classification errors (Fig. 4). For further improving the results, feature reduction using PCA and LDA and feature selection using sequential forward and sequential backward selection algorithms have also been tested, but since no improvement has been made, their results are not reported.

2.5. Data

For evaluation of this study, two databases, one for EDR extraction and one for OSA detection evaluation are used. The performance of our EDR extraction methods is assessed by Fantasia database. Fantasia database is freely available at Physionet [8], containing 20 simultaneously lead II ECG recording as well as respiration signal (sampling rate of 250 Hz) from both young (21–34 years) and old (68–85) healthy subjects. The respiration signal is thought to be impedance pneumography (IP) signal that is widely used to monitor respiration [32]. During the measurements, all subjects were in resting state, breathing spontaneously, and watching the movie Fantasia (Disney, 1940) to maintain wakefulness. From each subject, ten 12-seconds segments (in total 2 minutes) with no observation of perceivable artifacts in signals are selected manually. To assess the performance of OSA detection algorithm, the Apnea-ECG dataset generated for PhysioNet/CinC Challenge 2000 [8,33] is used. Apnea-ECG includes 70 single-lead (lead II) ECG recordings of varying lengths between 7 hours to 10 hours. ECG signals are sampled at the rate of 100 Hz and contain minute-by-minute apnea annotation (labeled by experts using PSG test). In addition to minute-based apnea labels, each recording is classified into to three classes “apnea”, “borderline”, and “normal” based on AHI calculation for each recording. Recordings labeled as “apnea”, “borderline” and “normal” have $AHI > 10$, $5 < AHI < 10$ and $AHI < 5$, respectively. Withheld-set and released-set recordings belong to 8 subjects and 9 subjects, respectively.

The database is divided into two sets, each containing 35 recordings. The first set (released-set) is used as a training set for the learning process of classification algorithms. The second set (withheld-set) is used as a test set for an independent assessment of classification methods. Both released-set (training data) and withheld-set (test data) contain 20 “apnea”, 5 “borderline”, and 10 “normal” recordings with overall 17045 and 17268 1-minute segments for each set.

2.6. Evaluation of performance

The performances of our EDR extraction algorithms are assessed by comparing the EDR signals to a respiratory signal. The similarity between extracted EDRs and reference respiration signal is evaluated by means of the normalized cross-correlation coefficient (c) [20]. This criterion is determined as the largest cross-correlation value over a lag range of one sec-

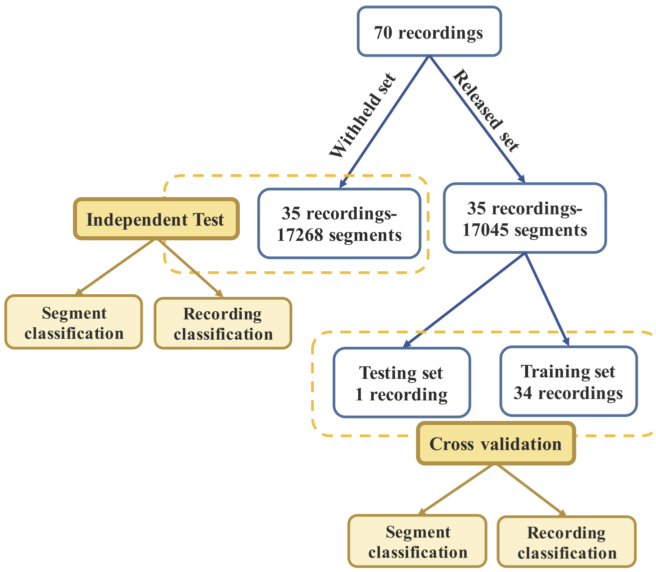

Fig. 5. Dataset devision for released-set cross-validation and withheld-set independent test.

ond to allow for possible phase delays between EDR and reference respiration signal. Results of EDR extraction for each subject are measured by average c, because ten 12-second ECG segments are processed in each subject. The cross-correlation coefficient between two signals (EDR signal, $r(k)$; respiration signal, $y(k)$) is defined as follows:

$$c(n) = \frac{\frac{1}{N-1}\sum_{k=1}^{N-n}(r(k)-\overline{r(k)})(y(k+n)-\overline{y(k+n)})}{\sqrt{\frac{1}{(N-1)^2}\sum_{k=1}^{N}(r(k)-\overline{r(k)})^2\sum_{k=1}^{N}(y(k)-\overline{y(k)})^2}} \tag{2}$$

To assess the significant difference between EDR techniques, the Friedman's test with Tukey honesty significant difference criterion is applied, where $p < 0.05$ is considered as statistically significant.

The apnea detection algorithm provides two outputs: segments classification and recording classification. Segment or minute-by-minute classification is evaluated in two ways (Fig. 5):

- released-set (training data) cross-validation (CV); CV with 35 folds while each fold is the data from one recording.
- withheld-set independent test; training the classifiers with the whole released-set data and test them with the whole withheld-set as the final evaluation.

After predicting all segments labels, AHI is calculated for each recording to provide recording classification. Classifying 30 non-borderline recordings in the withheld-set was the first challenge in PhysioNet/CinC competition to assess distinguishing between normal subjects and subjects with clinically significant apnea using only ECG recordings. The second challenge was classifying 17268 1-minute ECG segments in withheld-set as an independent test. The performance of minute-based apnea

Table 1
Normalized cross-correlation coefficient between the reference respiration signal and EDRs for 40 subjects.

EDR	EDR_{Var}	EDR_{PSR}	EDR_{MPR}	EDR_{Area}
Mean	0.723	0.703	0.55	0.611
Median	0.73	0.72	0.56	0.624
Std	0.1	0.12	0.12	0.13

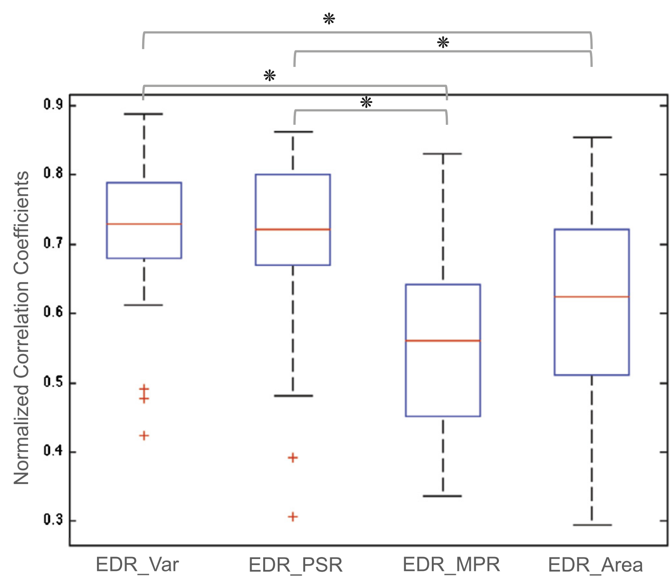

Fig. 6. Comparison of EDR signals using box plot representation of cross-correlation coefficients for all 40 subjects (significant differences ($p < 0.05$) between EDRs are indicated by $*$).

detection is evaluated by accuracy (Acc), sensitivity (Sen) and specificity (Spe):

$$Acc = \frac{TP+TN}{TP+TN+FP+FN} \tag{3}$$

$$Sen = \frac{TP}{TP+FN} \tag{4}$$

$$Spe = \frac{TN}{TN+FP} \tag{5}$$

where TP is true positive, FP is false positive, TN is true negative and FN is false negative.

3. Results

In this section, the results of EDR extraction algorithms and their effectiveness in apnea detection are reported.

3.1. EDR extraction

The performance of the proposed EDR techniques, EDR_{PSR}, EDR_{Var} and other state-of-the-art single-lead EDR algorithms such as EDR_{Area} and EDR_{MPR} are evaluated. Table 1 shows the performance of the EDRs extraction techniques in term of average, median and std (standard deviation) of the cross-correlation coefficient (c) on 40 subjects. Fig. 6 represents the box plot of c calculated between each EDR and the respiration signal for 40 subjects. The statistical test results for

Table 2
LD classification accuracy by CV on training data for different numbers of features vectors to be averaged and median filter lengths.

Accuracy		Number of features to be averaged (N)									
		1	2	3	4	5	6	7	8	9	10
Median filter length (L)	3	0.828	0.828	0.837	0.839	0.841	0.842	0.842	0.842	0.841	0.839
	4	0.680	0.761	0.790	0.803	0.810	0.815	0.818	0.820	0.820	0.819
	5	0.850	0.855	0.851	0.847	0.846	0.847	0.847	0.845	0.843	0.841
	6	0.804	0.824	0.822	0.823	0.827	0.829	0.832	0.831	0.830	0.828
	7	0.856	0.858	0.856	0.851	0.850	0.849	0.849	0.846	0.845	0.842
	8	0.822	0.833	0.835	0.831	0.834	0.834	0.835	0.833	0.832	0.830
	9	0.857	0.861	0.859	0.858	0.854	0.853	0.851	0.849	0.846	0.844
	10	0.829	0.840	0.841	0.842	0.838	0.838	0.838	0.836	0.834	0.832
	11	0.859	0.861	0.858	0.859	0.857	0.854	0.853	0.850	0.848	0.844
	12	0.835	0.843	0.843	0.844	0.843	0.840	0.840	0.838	0.835	0.833
	15	0.858	0.860	0.858	0.858	0.858	0.857	0.855	0.851	0.848	0.845

Table 3
LD classification sensitivity by cross-validation on training data for different numbers of features vectors to be averaged and median filter lengths.

sensitivity		Number of features to be averaged (N)									
		1	2	3	4	5	6	7	8	9	10
Median filter length (L)	3	0.718	0.718	0.718	0.714	0.712	0.711	0.708	0.707	0.704	0.700
	4	0.564	0.631	0.657	0.664	0.669	0.671	0.675	0.677	0.675	0.673
	5	0.739	0.730	0.724	0.716	0.712	0.712	0.708	0.708	0.704	0.701
	6	0.673	0.686	0.680	0.681	0.685	0.686	0.686	0.687	0.683	0.683
	7	0.741	0.730	0.728	0.721	0.716	0.713	0.710	0.707	0.703	0.701
	8	0.689	0.692	0.696	0.690	0.693	0.690	0.689	0.687	0.684	0.682
	9	0.740	0.733	0.728	0.725	0.719	0.717	0.714	0.710	0.704	0.701
	10	0.697	0.699	0.699	0.701	0.695	0.697	0.694	0.691	0.686	0.682
	11	0.741	0.731	0.726	0.726	0.723	0.720	0.714	0.710	0.704	0.699
	12	0.703	0.700	0.700	0.702	0.700	0.697	0.692	0.690	0.683	0.682
	15	0.734	0.721	0.718	0.714	0.716	0.712	0.706	0.705	0.698	0.696

analyzing the difference between each two EDR is shown by $*$ if there is a significant difference ($p < 0.05$) between EDRs.

It can be seen in Table 1 and Fig. 6 that the best EDR, based on the similarity of time pattern to the reference respiration signal, is EDR_{Var} which also performs slightly better than EDR_{PSR}. Both proposed EDRs are statistically significantly better than EDR_{Area} and EDR_{MPR}.

3.2. Apnea detection

First, the results of segment classification are reported, then recording classification is evaluated. As mentioned before, the optimum number of features vectors to be averaged before classification, and the median filter length need to be found. We use LD classifier results over the training set using cross-validation. Table 2 and Table 3 show LD classification accuracy and sensitivity for different choices of number of features vectors temporally averaged and median filter length. The features are extracted from RR intervals and EDR_{PSR}.

According to Table 2 and Table 3, accuracy and sensitivity are quite larger when two features extracted from two adjacent segments are averaged and median filter length is set to 11. From now, these two parameters are set and would not be changed for other classification or other feature sets, since we do not want them to be dependent on classifier type or feature sets.

Results of cross-validation on training data using LD, QD, k-NN (N = 5 and 10), ANN classifier (with two hidden layers each containing 4 neurons, learning rate 0.3 and 5000 iterations, with notation $NN[4,4], 5000, 0.3)$ and different feature sets are reported in Table 4. The EDR_{MPR} is not assessed for apnea detection due to its poor results in EDR extraction evaluation according to Table 1. The best results are achieved from ANN classification using features extracted from both RR se-

Table 4
Cross-validation on training data using different classifiers and feature sets.

Classifier	LD			QD			K-NN (K=5)			K-NN (K=10)			ANN		
Features	ACC	Sen	Spe	ACC	Sen	Spe	ACC	Sen	Spe	ACC	Sen	Spe	ACC	Sen	Spe
RR	0.835	0.688	0.923	0.438	0.991	0.107	0.829	0.738	0.883	0.829	0.734	0.885	0.814	0.653	0.903
EDR_{Area}	0.789	0.549	0.931	0.795	0.726	0.835	0.790	0.695	0.845	0.791	0.660	0.868	0.799	0.656	0.885
EDR_{Var}	0.812	0.621	0.921	0.821	0.792	0.834	0.796	0.730	0.828	0.797	0.711	0.841	0.839	0.757	0.884
EDR_{PSR}	0.836	0.686	0.922	0.824	0.866	0.796	0.800	0.800	0.795	0.810	0.797	0.812	0.848	0.773	0.890
RR+ EDR_{Area}	0.861	0.731	0.938	0.442	0.995	0.110	0.824	0.726	0.881	0.818	0.686	0.895	0.870	0.811	0.904
RR+ EDR_{Var}	0.887	0.804	0.935	0.467	0.994	0.151	0.838	0.771	0.876	0.835	0.740	0.889	0.891	0.829	0.926
RR+ EDR_{PSR}	0.892	0.816	0.935	0.476	0.994	0.166	0.851	0.819	0.867	0.851	0.798	0.880	0.896	0.854	0.919
RR+ EDR_{Area}+ EDR_{Var} + EDR_{PSR}	0.893	0.822	0.935	0.371	1	0	0.825	0.726	0.882	0.807	0.652	0.896	0.865	0.83	0.894

Table 5
Results of classifiers on withheld-set as an independent test.

Classifier	LD			KNN (K=5)			KNN (K=10)			SVM			ANN		
Features	ACC	Sen	Spe	ACC	Sen	Spe	ACC	Sen	Spe	ACC	Sen	Spe	ACC	Sen	Spe
RR+EDR_{Area}	0.864	0.803	0.921	0.860	0.862	0.878	0.859	0.828	0.897	0.847	0.776	0.911	0.864	0.845	0.876
RR+EDR_{Var}	0.886	0.86	0.922	0.882	0.913	0.883	0.881	0.902	0.888	0.866	0.806	0.923	0.903	0.881	0.916
RR+EDR_{PSR}	0.895	0.86	0.937	0.885	0.92	0.884	0.886	0.912	0.891	0.871	0.805	0.933	0.909	0.896	0.918

ries and EDR_{PSR} with accuracy, sensitivity, and specificity of 0.89, 0.85 and 0.91, respectively. All of the results from SVM classifier are not reported, but it is expected using RR and EDR_{PSR} features yields better results after comparing all classifiers results in Table 4; therefore, SVM classifier is only tested using RR series and EDR_{PSR}. SVM classification using cross-validation on training data resulted in accuracy of 0.86, sensitivity of 0.78 and specificity of 0.90 which is still not better than LD classifier. It is noticeable that QD classifier with the lowest classification results was not successful in apnea detection. Hence, for the next evaluations, its results are not reported. It can be seen that the best results of ANN classifier are achieved by features from RR and EDR_{PSR} (acc = 0.896, sen = 0.854, spe = 0.919). ANN classifier with higher iteration, $(NN[4,4], 10000, 0.3)$, is only tested using RR series and EDR_{PSR} which resulted in accuracy of 0.893, sensitivity of 0.846 and specificity of 0.919. In case of ANN number of layers, we tested limited number of layers to achieve acceptable results using cross-validation on training data, and we selected the optimal one $(NN[4,4], 5000, 0.3)$.

Table 5 represents the results of LD, SVM, k-NN (K = 5, 10) and ANN classification on withheld-set as an independent evaluation. The LD classifier with RR and EDR_{PSR} features yields the best results (acc = 0.89, sen = 0.86 and spe = 0.93) among the others (SVM and k-NN) on test data. ANN (NN[4, 4], 5000, 0.3) classification of withheld-set data using features from RR series and EDR_{PSR} resulted in accuracy of 0.909, sensitivity of 0.896 and specificity of 0.918. It is worth noting that the classifier performance of the participants in PhysioNet/CinC competition were evaluated based on only accuracy of apnea detection in the withheld-set data.

As mentioned before, after segment classification of recordings, AHI can be calculated. Then recording classification can be done by determining a threshold to separate the 30 "normal" and "apnea" recordings. Fig. 7a and Fig. 7b show the AHI derived from segment classification of LD and ANN using RR series and EDR_{PSR} features for 35 subjects of training data. Threshold shown by a dashed line is set to $AHI = 5.5$. As it can be seen, the "normal" and "apnea" subjects are separable using a threshold set on AHI. Furthermore, Figs. 8a, 8b and 8c show the AHI derived from segment classification of LD, k-NN (k = 5) and ANN using RR series and EDR_{PSR} features for 35 subjects of test data as an independent evaluation of recording classification. Threshold shown by a dashed line is also set to $AHI = 5.5$. As it can be seen, the "normal" and "apnea" subjects are not separable in LD classifier with 100% accuracy in spite of its good results on segment classification (LD classifiers have diagnosed one of normal subject as an apnea subject), but

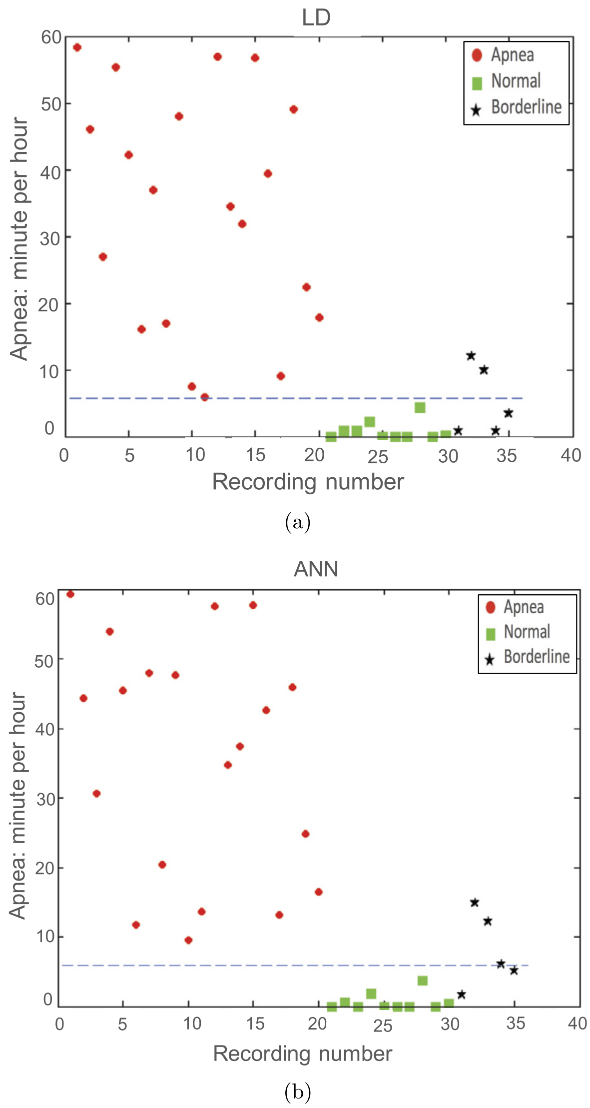

Fig. 7. AHI calculated for 35 subjects in training data from segment classification of: (a) LD, (b) ANN.

ANN and k-NN (k = 5) classifiers can classify all 30 "normal" and "apnea" subjects in test set correctly.

4. Discussion

In this study, our aim is to assess automatic OSA detection using RR interval series and EDR signal. In the case of EDRs evaluation, according to Table 1 and Fig. 6, our two proposed EDR extraction algorithms, EDR_{PSR} and EDR_{Var}, outperform the other methods in the literature, EDR_{Area} and EDR_{MPR}. Although both proposed EDRs are comparable to each other, since no statistical difference was observed in their corresponding cross-correlation coefficients, EDR_{Var} performs slightly better than EDR_{PSR}. In [23], the reliability of proposed EDR_{MPR} method has been tested by coherence analysis of frequency spectrum on a different database than our used database. In [23], a high coherence in frequency domain for EDR_{MPR} is reported while this evaluation cannot be linked

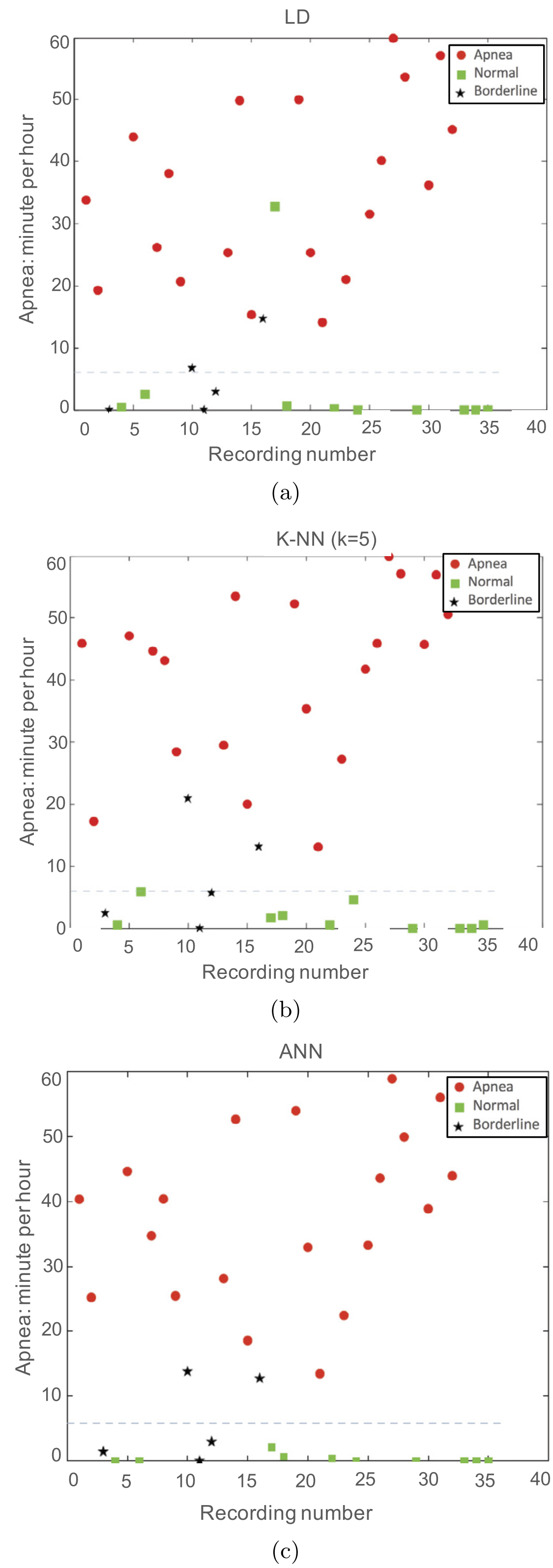

Fig. 8. AHI calculated for 35 subjects in test data from segment classification of: (a) LD, (b) k-NN, (c) ANN.

to a high consistency between a long segment of EDR and respiration signal in time domain, because EDR and reference signal could be uncorrelated in time domain while extracted respiratory rate can be similar. For this reason, the results of EDR_{MPR} implemented in this study are poor in time domain evaluation. Besides, the database recorded in [23] is limited due to the small number of subjects (8 subjects). That is why the results of EDR_{MPR} implemented here are not consistent with [23].

EDRs are expected to represent respiration activity information. For this reason, evaluating their effectiveness in OSA detection can be another way to assess their performance. In order to evaluate the performance of the EDR algorithms, inspiration and expiration time patterns of EDR can be compared to recorded respiratory signal as what we have done in this paper by c measure. The respiratory frequency estimated from the EDR can also be compared to that one estimated from a simultaneously recorded respiratory signal (reference signal). The first evaluation method is more challenging, because EDR and reference signal could be different in time domain while the extracted respiratory rate is similar.

In the case of OSA detection, features are extracted from all three EDRs and RR intervals, and different classifiers and effectiveness of all feature sets are compared. The optimum number of features vectors to be averaged (N) and median filter length (L) for improving OSA detection are found using LD classifier. Since LD classifier has shown quite acceptable performance in apnea detection using CV on training data, we decided to use its results on training data while sweeping parameters of N and L. Due to Table 2 and Table 3, we choose the proper L and N, L = 11 and N = 2. Table 4 compares the different classifiers and features sets. The percentage of apnea segments in both train and test dataset is 37%, then it is expected that an effective classifier achieves accuracy above 63%. With this in mind, QD classifier shows poor performance for features extracted from RR series. The reason can be due to the distribution of features of RR series that are linear rather than non-linear separable. The QD results on RR series may seem to be inconsistent with regularized QD results using automatically generated QRS times series in [13]. The optimal regularization parameter defined in [13] made the class-conditional covariance matrices (for QD) to be close to common covariance matrix (covariance matrix defined for LD classifier). Therefore in that work, regularized QD performance would be close to LD. Also, the RR series of training data in some evaluations in [13] are manually corrected while here all the corrections of training series were done automatically. By comparing EDRs ability for apnea detection in QD classifier, it can be seen that apnea detection results using features set from EDR_{PSR} and EDR_{Var} are comparable to each other and both are better than using EDR_{Area}. Considering LD classifier in Table 4, results of features extraction from RR series and EDR_{PSR} are comparable to each other and both are better than the other two EDRs, suggesting that EDR_{PSR} have apnea detection information as much as RR series. Therefore, using RR series and EDR_{PSR} performed better than the other combination of features. Furthermore, as it could be expected, using all the feature sets improved the results, but not significantly, at the cost of dimension increasing. Both k-NN classifiers have resulted in a similar way regarding different feature sets. RR series and EDR_{PSR} for k-NN classifiers are the best combinations of features compared to other combinations. In general, LD classifier with its optimum feature sets achieved acceptable results in apnea detection, and the combinations of EDR_{PSR} and RR can be the potential proper feature sets to detect apnea events in test data. Also, feature sets RR and EDR_{PSR} are the best combination for ANN classifier. Evaluating the EDRs in terms of apnea detection, it can be seen that EDR_{PSR} have performed better than EDR_{Var}, and EDR_{Var} performed better than EDR_{Area} which is consistent with LD classification improvement process with feature sets.

After using withheld-set as an independent evaluation in Table 5, the effectiveness of EDRs in apnea detection is once again proved. Similar to classifiers results on training data, features from EDR_{PSR} yield better classification than EDR_{Var}, and EDR_{Var} performed better than EDR_{Area} on the independent test set which is the main assessments of apnea detection algorithms in PhysioNet/CinC competition. The best results on test dataset are acc = 0.909, sen = 0.896, spe = 0.918, by ANN (NN[4, 4], 5000, 0.3) using RR and EDR_{PSR} feature sets.

According to Fig. 8 and Fig. 7 all the 30 non-borderline subjects in training data and test data can be separated from each other using a threshold on AHI estimated by ANN, which means a 100% accuracy in recording classification. We consider ANN as our optimum classifier in apnea detection approach. Some studies have focused only on this subject-based diagnosis to be used in OSA screening methods as an evaluation of apnea detection which does not seem to be very challenging if segment classification is done with high accuracy, but in this work both recording and segment classification are used as an evaluation of apnea detection algorithm.

These results can be compared to other stat-of-the-art apnea detection algorithms which are applied on the Apnea-ECG database. Table 6 compares our results by ANN classifier with the best results of apnea detection algorithms reported in the literature such as algorithms proposed in [10,12,11,13–19] and [5]. There are some other researches focused on apnea detection from ECG, but their evaluations are not based on the whole Apnea-ECG database, and we can not compare our results with them because they used a different database or used only a part of Apnea-ECG database. Classifiers performance on the test data as the main assessments of the competition are only based on accuracy (accuracy of segment classification and accuracy of recording classification), and sensitivity and specificity criteria were not considered for competition participant ranking. That is why some of the performance of the algorithms in Table 6 are only reported by accuracy.

According to Table 6, the best results on training data belong to De Chazal [13] work in which the classification procedure is not automatic, and apnea detection is done visually. Putting visual (De Chazal et al. [13], Reymond et al. [10] and McNames et al. [11]) rather than automatic methods aside, it can be seen that there is only one automatic method (De Chazal et al. [13]) whose results are better than our approach using CV on training data, but considering independent test on withheld-set, our automatic approach have reached the highest accuracy (91%) among the other automatic methods. In addition, accuracy of recording classification in our automatic approach is 100% and is similar to some of the other automatic methods (De Chazal

Table 6
Apnea detection performance comparison on the whole Apnea-ECG database.

Algorithm	Method	Recording classification	Train cross-validation			Independent test		
			Acc (%)	Sen (%)	Spe (%)	Acc (%)	Sen (%)	Spe (%)
Reymond (2000) [10]	Auto	29/30	–	–	–	81	–	–
Reymond (2000) [10]	Visual	30/30	–	–	–	92.3	–	–
De Chazal (2000) [12]	Auto	29/30	88.2	84.1	90	88.9	–	–
McNames (2000) [11]	Visual	30/30	–	–	–	92.6	–	–
De Chazal (2003) [13]	Visual	30/30	92.5	91.4	93.1	90.6	–	–
De Chazal (2003) [13]	Auto	30/30	91.2	88.5	92.9	90.5	–	–
O'Brien (2007) [14]	Auto	–	88.2	77.6	85.1	–	–	–
Khandoker (2009) [15]	Auto	30/30	–	–	–	–	–	–
Yildiz (2011) [16]	Auto	30/30	–	–	–	–	–	–
Sadr (2014) [17]	Auto	–	–	–	–	87.7	81.3	91.7
Garcia (2015) [18]	Auto	–	–	–	–	84.6	75.1	95.5
Sharma (2016) [19][a]	Auto	–	–	–	–	83.8	79.5	88.4
Song (2016) [5]	Auto	29/30	–	–	–	86.2	82.6	88.4
Our approach	Auto	30/30	89.6	85.4	91.9	90.9	89.6	91.8

[a] 16854 segments from released-set and 15873 segments from withheld-set are used for evaluation while the overall numbers of segments in released and withheld-set are 17045 and 17268, respectively.

et al. [13], Khandoker et al. [15], Yildiz et al. [16]) in the Table 6. According to recording classification results, it seems that single-lead ECG-based apnea detection could be used for OSA screening application with similar reliability to PSG tests with multi biological signal recordings.

The proposed approach of OSA detection is based on estimating new EDRs. The extracted features in this study are derived from both RR series and EDRs. The results show that both RR and EDR series convey information related to OSA occurrence. The accuracy improvement process in withheld-set classification shows that EDR_{PSR} and EDR_{Var} take priority than EDR_{Area} in apnea detection, and that proves the significance of choosing proper EDR signal in apnea detection applications. These results are also consistent with the first evaluation of EDRs in terms of cross-correlation, suggesting that respiration information in EDR_{PSR} and EDR_{Var} are more significant than information in EDR_{Area}. Selecting the features that provide an important contribution in distinguishing two classes can be one of the ways to improve the results which is left for future work.

5. Conclusion

In this study, we proposed an automatic algorithm for OSA detection from a single-lead ECG recording. We hypothesized that choosing a proper EDR can improve the accuracy of OSA detection, that is why we introduced two new EDR extraction methods, EDR_{PSR} and EDR_{Var}. After evaluating them in terms of time pattern similarity to a reference respiration signal (using cross-correlation coefficients) and comparing them to other EDR methods, EDR_{Area} and EDR_{MPR}, we used them in apnea detection. The cross-correlation coefficients between proposed EDRs and reference respiration signal are statistically higher than EDR_{Area} and EDR_{MPR}. Furthermore, the accuracy of apnea detection in independent test data using EDR_{PSR} and also EDR_{Var} shows that these EDRs are more effective than EDR_{Area}. In comparison with other work, our ANN classifier using features from RR and EDR_{PSR} yields the best performance on independent test data in terms of accuracy, sensitivity, and specificity of segment classification. Besides, the subject or recording classification is done 100% accurate with our OSA detection algorithm. This study indicates that OSA can be monitored using single-lead ECG with satisfactory accuracy, and that makes a portable OSA monitoring system feasible since the results are comparable to PSG tests with multi biological signal recordings.

Conflict of interest statement

No conflict of interest.

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