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Classification of Cheyne Stokes Breathing and Obstructive Sleep Apnea Using ECG

Sanjee R. Suhas*, Sridhar Vijendra*, John R.Burk**, Edgar A. Lucas**, Khosrow Behbehani*
*Joint Biomedical Engineering Program, University of Texas at Arlington and University of Texas Southwestern Medical Center at Dallas,** Sleep Consultants Inc., Fort Worth, Texas.

Abstract—**High cost of diagnostic studies to detect sleep disordered breathing and lack of availability of certified sleep laboratories in all inhabited areas make investigation of alternative methods of detecting sleep disordered breathing attractive. This study aimed to explore the possibility of discerning obstructive sleep apnea (OSA) from Cheyne- Stokes respiration (CSR) using overnight electrocardiography (ECG). Polysomnographic and ECG signals were acquired from the 13 OSA and 7 CSR volunteer subjects. Two signals: R-Wave Attenuation (RWA) and Heart Rate Variability (HRV) series were derived from the ECG. Using frequency domain analysis, various frequency bands in the power spectrum of RWA and HRV signals were identified that showed sensitivity to OSA and CSR events. A three-stage algorithm was developed to detect and differentiate OSA events from CSR events using RWA and HRV analysis. To test the algorithm, the ECG data was divided into fifteen minute epochs for analysis. Seventy two epochs containing OSA and 72 with CSR events were selected. 48 OSA clips and 48 CSR clips were randomly selected to form the training set. The remaining 24 clips in each category formed the test set.**
This method produced an average sensitivity of 95.83% and specificity of 79.16% in the training set and sensitivity of 87.5% and a specificity of 75% in the test set.

Keywords—**Cheyne Stokes Breathing, Obstructive Sleep Apnea, ECG, Heart Rate Variability, R Wave Attenuation, Sleep Disordered Breathing**

I. INTRODUCTION

Sleep-Disordered Breathing (SDB) is a general term applicable to a wide variety of sleep-related breathing disorders of diverse pathophysiology that is usually associated with recurrent episodes of apnea or hypopnea during sleep [8]. Apnea is defined as the complete cessation of breathing for 10 seconds or more whereas hypopnea is a term used to identify events of shallow breathing that result in oxygen desaturation. The American Academy of Sleep Medicine Task Force divides sleep-related breathing disorders in adults into four categories [13]. The first, the Obstructive Sleep Apnea-Hypopnea Syndrome is characterized by intermittent total collapse of the upper airway during sleep. This manifests as a reduction in (hypopnea) or complete cessation (apnea) of airflow despite ongoing inspiratory efforts. The Central Sleep Apnea-Hypopnea Syndrome (CSAHS) is marked by a decreased output to the muscles of inspiration from the respiratory control center in the central nervous system. The Cheyne-Stokes Breathing Syndrome is characterized by a cyclical fluctuation in breathing with periods of central apneas or hypopneas alternating with periods of hyperpnea and is seen in patients with cardiac dysfunction usually in association with Congestive Heart Failure (CHF). Mortality appears to be increased in patients with CSR compared to control subjects with a similar degree of left ventricular dysfunction. The last category is the Sleep Hypoventilation Syndrome (SVHS), characterized by an abnormal increase in $PaCO_2$ during sleep, which results in severe hypoxemia [8].

CSA and CSR are characterized by reduced or absent respiratory effort whereas there is maintained or increased respiratory effort during OSA. CSR and OSA may coexist and often patients with OSA may have a crescendo-decrescendo pattern to their breathing, as seen in CSR [8].

Prevalence, Pathophysiology and Treatment: OSA is estimated to occur in 1 out of every 20 adults. In children, it is said to have a minimum prevalence of 2 to 3% and prevalence as high as 10 to 20% in habitually snoring children [14]. It is estimated that nearly 5 million Americans suffer from CHF [7]. CSR is a form of SDB seen in approximately 40% of the CHF patients with a left ventricular ejection fraction of < 40%. CSR is not specific to CHF and is also seen in patients with neurological disorders and in the healthy subjects at high altitudes [6].

CSR in patients with CHF is attributed to decreased ejection fraction and ventilatory instability due to circulatory delay [9, 11]. OSA is characterized by upper airway occlusion during sleep. It is caused by the collapse of a narrow, highly compliant pharynx and leads to the development of a negative intra-thoracic pressure and hypoxia. The negative intra-thoracic pressure increases the left ventricular afterload leading to reduced stroke volume and cardiac output. Systemic blood pressure (BP) falls as a result of reduced stroke volume and cardiac output. At the same time, prolonged hypoxia causes gasping and subsequent arousal from sleep and muscle sympathetic nerve activity (MSNA) and systemic BP peak after the onset of breathing [8].

Studies indicate reduction in CSR when patients are treated for CHF. A short term non-randomized study reports 50% reduction in CSR with captopril administration over a four week period. Similar, cases reported reduction of CSR following cardiac valve surgery and cardiac transplantation, but conversion of CSR to OSA has also been reported following cardiac transplantation [15].

OSA is commonly treated with CPAP, wherein constant pressure is delivered to keep the airway open. Surgical procedures like Uvulopalatopharyngoplasty, Laser-assisted Uvulopalatoplasty and Tracheostomy are also available.

Nocturnal Polysomnography (NPSG) is the current standard method available for diagnosis of sleep disordered breathing. This method is rather expensive and hence cannot

be afforded by all [12]. Also, there is a limited number of sleep laboratories in the country, creating often a long waiting period for tests. These drawbacks form the motivation for developing methods of detecting sleep apnea using ECG morphology and Heart Rate Variability (HRV). The proposed method uses R Wave Attenuation (RWA) and HRV to differentiate epochs of CSR and OSA. Previous studies have established that RWA contains sufficient breathing information to provide reliable diagnostic information on sleep disordered breathing.

II. METHODOLOGY

NPSG was performed on the samples of OSA and CSR subjects. Thirteen volunteer OSA subjects were recruited from the patients who had previously undergone NPSG and already diagnosed to have OSA. Seven volunteer subjects previously having CSR were also recruited. Proper institution review board approval for human subject testing was obtained. The mean, standard deviation and range of age, apnea-hypopnea index (AHI) and body mass index (BMI) for the subjects are shown in Table I.

NPSG was performed on all the subjects at an accredited sleep lab. Nine ECG leads (I, II, III and six pericardial leads) and airflow were also acquired. Other standard polysomnography signals such as electroencephalography, electromyography, and electrooculography were also collected. A certified sleep specialist blind to the objectives of this study scored all the records to identify different sleep stages and SDB events. The NPSG data collected from 7 CSR patients was visually examined and the epochs containing the Cheyne Stokes respiration were identified. These identified epochs were then verified by the certified sleep technician to contain CSR. The identified epochs were then divided into fifteen minute clips in such a way that each clip had CSR either for the entire fifteen minutes or during some part of the clip. Seventy two (72) such clips were selected and these formed the set of CSR clips. Similarly, the NPSG scoring of the 13 OSA subjects were examined and 72 clips were selected so that they contained OSA events in them. These form the set of OSA clips. Each of these clips contained signals from all the nine ECG leads, sampled at 1 KHz.

ECG preprocessing: A thorough investigation of the recorded ECG leads showed that Lead V4 was most sensitive to the presence of CSR [9]. The Lead V4 ECG signal in each of the clips was passed through a high pass FIR filter with 200 terms and cut off frequency 0.8 Hz. Bidirectional filtering was performed to nullify the phase shift produced by the filter [3]. The ECG was then normalized by its range and detrended by subtracting its mean to get a zero mean signal. The R Peaks in the filtered ECG are detected by using an algorithm, proposed by *Benitez et al* [4]. The R-peak detection algorithm was previously tested on the MIT-BIH Arrhythmia database. The results from 10 half-hour records from the database produced a mean detection error of 1.14% (max: 4.5%, min: 0%) [1]. The detected R peaks were subsequently manually verified and corrected if required.

R Wave Attenuation (RWA) Signal: The RWA was derived by extracting the amplitudes of the detected R peaks. This signal contained one sample every heart beat and since there is variation in the instantaneous heart rate, these samples were not equally spaced. This signal was evenly resampled at 10 Hz using cubic spline interpolation. The 1024 point power spectrum of RWA was computed by using the Welch's averaged periodogram method with an overlap of 50%. Hanning window which was detrended by its mean was used for this purpose. Vijendra et. al., identified the frequency band 0 – 0.1 Hz, the power over which is sensitive to OSA for ECG Lead I [1]. Visual inspection of the power spectral densities revealed that the power over two frequency bands 0.1-0.5 Hz and 0.15-0.2 Hz were different for OSA and CSR clips. The discriminant RA_R was computed by trapezoidal integration of its power spectrum over the band 0.1-0.5 Hz. The RWA trend was normalized by its maximum value and the power spectrum of the resulting signal is computed. The discriminant RA_{TN} was computed by trapezoidal integration of this power spectrum over the band 0.15-0.2 Hz.

Heart Rate Variability (HRV): The time difference between the consecutive R peaks forms HRV series. This signal is resampled at 1.2 Hz using cubic spline interpolation to get 1080 points. This series is then truncated to 1024 points. The signal is normalized by its maximum value and 1024 point power spectrum of RR interval series was computed by using the Welch's periodogram method with an overlap of 50%. A hanning window was used for this purpose. The power of the HRV within the band 0.01 to 0.4 Hz was computed by trapezoidal integration of its power spectrum over this band. For convenience, the power in this band is called $HR_{TN.}$ The frequency bands 0.019 to 0.071 Hz and 0.019 to 0.036 Hz has been identified by *Hilton et al* to be sensitive to obstructive sleep apnea [2].

TABLE I
Subject Demographic Information

	Parameter	Mean	SD	Range
OSA Subjects (7 Males, 6 Females)	Age, years (n=13)	49	8.8	37-69
	BMI, kg m -2 (n=13)	31.2	6.5	21.9-43.5
	AHI, h-1 (n=13)	28.6	22.7	4-70
CSR Subjects (6 Males, 1 Female)	Age, years (n=7)	69	7.2	56-78
	BMI, kg m -2 (n=7)	31.6	5.2	25.4 – 41.5
	AHI, h-1 (n=7)	71.6	43.4	29 - 158

Detection Scheme: The three discriminants are combined as shown in Fig 1. The definitions of the discriminants used in the detection scheme are shown in Table II. The detection scheme consists of 3 stages. The first stage and second stage involves classification of clips based on discriminants derived from RWA. The clips classified as OSA are

subjected to third stage of screening which is based on HRV.

TABLE II
Discriminants used in Figure 1

RA_R	Integral of RWA power spectrum over 0.1 to 0.5 Hz (RWA time sequence is not normalized)
RA_{TN}	Integral of RWA power spectrum over 0.15 to 0.2 Hz (RWA time sequence is normalized)
HR_{TN}	0.01 to 0.4 Hz Integral of normalized HRV Power Spectrum over 0.01 to 0.4 Hz.

Sensitivity and Specificity: The sensitivity is defined as the percentage of CSR clips identified correctly and specificity is defined as the percentage of OSA clips identified correctly. They are calculated as follows

$$Sensitivity = \frac{C_c}{C_c + C_f}$$

C_c : No. of CSR Clips identified correctly
C_f : No. of CSR Clips falsely identified as OSA

$$Specificity = \frac{N_c}{N_c + N_f}$$

N_c: No. of OSA Clips identified correctly
N_f: No. of OSA Clips falsely identified as CSR

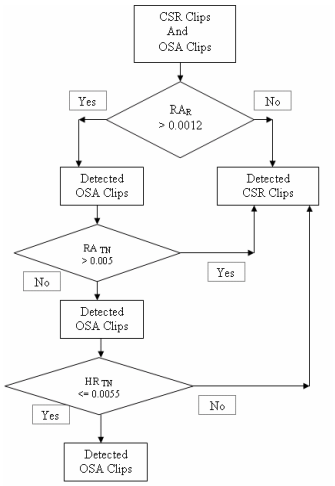

Fig 1: The Detection Scheme which combines parameters HR_{TN} and RA_R RA_{TN}.

Detection Scheme Performance Evaluation: The 72 OSA and 72 CSR clips were randomly divided into the training and test clips with a ratio of 2/3 for training and 1/3 for testing. After establishing, the necessary thresholds for the detection scheme (Fig. 1), the sensitivity and specificity of the detection scheme for the training and test clips were computed.

III. RESULTS

The Figures 2, 3 and 4 show the scatter plots of RA_R RA_{TN} and HR_{TN} respectively for training set. It can be seen from Figure 2 that the values of RA_R are, on the average, greater for OSA clips than those for CSR clips. Also, the values of RA_{TN} are greater for CSR clips than those for OSA clips as seen from Figure 3. Figure 4 suggests that the values of HR_{TN} are lower for OSA clips in comparison with those for CSR clips. Table III shows the detection rates when each of the discriminants defined in Table II is used alone.

Table IV shows the sensitivity and specificity obtained when the combination of these three parameters are used (Figure 1). From Table III and Table IV, it can be seen that the detection accuracy can be increased significantly by using HRV parameters with those of RWA.

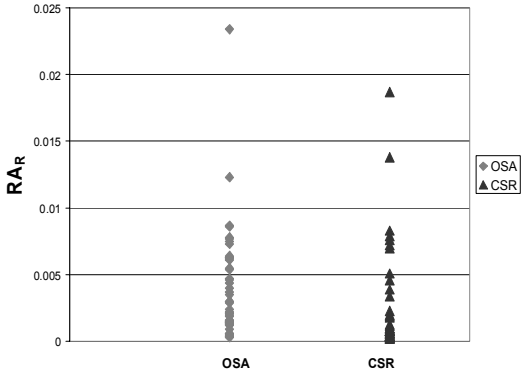

Figure 2: Scatter Plot of discriminant RA_R for the OSA and CSR Clips for Training Set

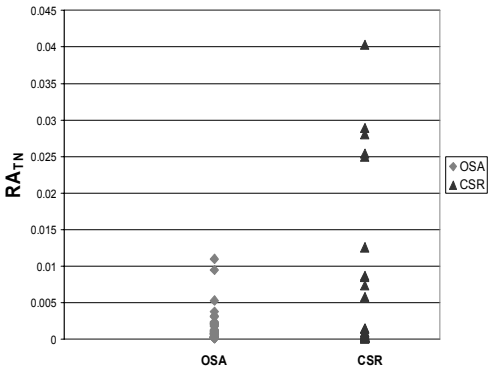

Figure 3: Scatter Plot of discriminant RA_{RTN} for the OSA and CSR Clips for Training Set

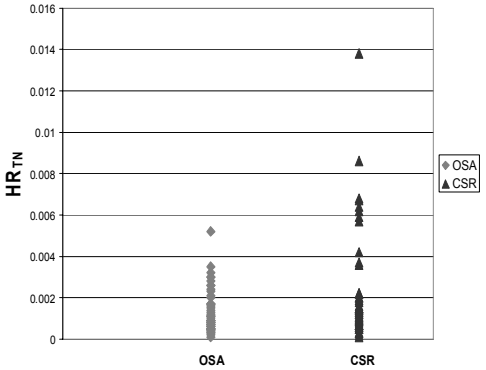

Figure 4: Scatter Plot of discriminant HR_{TN} for the OSA and CSR Clips for the Training Set

TABLE III
Detection Rates when parameters were used individually

RA_R		
	Training Set	Test Set
Sensitivity	66.66 %	54.16 %
Specificity	85.41 %	83.33 %
RA_{TN}		
	Training Set	Test Set
Sensitivity	20.8 %	25 %
Specificity	93.75 %	91.66 %
HRV_{TN}		
	Training Set	Test Set
Sensitivity	16.66 %	4.16 %
Specificity	100 %	100 %

TABLE IV
Detection Rates for detection scheme shown in Fig. 1

	Training Set	Test Set
SENSITIVITY	95.83%	87.5
SPECIFICITY	79.16%	75%
Threshold for RA_R		1.2E-03
Threshold for RA_{TN}		5E-03
Threshold for H_R		5.5E-03

IV. DISCUSSION

Results reveal that by combining RA_{TN}, and RA_R with HRV_{TN} as shown in Figure 1, the sensitivity can be increased. Table IV shows that the sensitivity and specificity for the training and the test set are nearly same. Hence the algorithm performs equally well on the clips which are not used for training.

The level of sensitivity and specificity obtained in this study suggests that the proposed detection scheme holds promise for larger investigation and eventual adaptation in the clinical applications. There several improvements that can be considered for increasing the detection rate of the proposed scheme. They are as follows.

A phenomenon that affects the sensitivity and specificity of the algorithm is that the alterations in RWA and the HRV series due to respiratory events occur both prior and post a CSR and OSA events. Hence, if a CSR or OSA event occurs at the beginning or near the end of a data clip, the variations associated with that event in the RWA will not be fully reflected. Future studies need to include a a sliding window to center the events in the data clip, whenever possible. . Also, in some of the clips, the CSR event only lasted for a fraction of the clip duration. It is suspected that the duration of CSR in a clip may also affect the detection accuracy.

Another factor which affects the detection accuracy is that CSR and OSA can co-exist. The CSR clips used in this study have OSA events. This might cause the CSR clip with lot of OSA events to be classified as OSA clip. The reduced specificity of the proposed method can be attributed to this.

In the present study, the discriminants were combined heuristically. More systematic methods like fuzzy logic and neural networks may prove to be useful in increasing the detection rates.

V. CONCLUSION

The RWA is sensitive to changes during CSR and can be used as a reliable diagnostic marker. The HRV is also sensitive, but RWA is more reliable. The detection accuracy can be increased by combination of different parameters from these RWA and HRV trends.

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