Expert Systems With Applications 48 (2016) 42–54

Contents lists available at ScienceDirect

Expert Systems With Applications

journal homepage: www.elsevier.com/locate/eswa

An automatic apnea screening algorithm for children

Sebastián A. Ríos*, Lili Erazo

Business Intelligence Research Center, Department of Industrial Engineering, University of Chile, Av. Republica 701, Santiago, Chile

ARTICLE INFO

MSC:
00-01
99-00

Keywords:
Screening algorithms
Apnea classification
Apnea screening
Ubiquitous health system

ABSTRACT

Sleep Disordered Breathing (SDB) is a group of diseases that affect the normal respiratory function during sleep, from primary snoring to obstructive sleep apnea (OSA) being the most severe. SDB can be detected using a complex and expensive exam called polysomnography. This exam monitors the sleep of a person during the night by measuring 21 different signals from an Electrocardiogram to Nasal Air Flow. Several automatic methods have been developed to detect this disorder in adults, with a very high performance and using only one signal. However, we have not found similar algorithms especially developed for Children. We benchmarked 6 different methods developed for adults. We showed empirically that those models' performance is drastically reduced when used on children (under 15 years old). Afterwards, we present a new approach for screening children with risk of having SDB. Moreover, our algorithm uses less information than a polysomnography and out performs state-of-the-art techniques when used on children. We also showed empirically that no signal alone is a good SDB screening in children. Moreover, we discover that combinations of three signals which are not used in any other previous work are the best for this task in children.

1. Introduction

Several health systems from different countries have agreed on the need of tackling public health by the means of a more preventive, personalized and anticipatory health service. This requires to encouraging patients and caregivers to make them protagonists of their healthcare, assuming responsibility to keep themselves on controlled states without collapsing healthcare centers.

In Chile, we have a severe case of air pollution, which produce episodes where hospitals collapse during autumn and winter. This is why; Health Ministry is developing several programs that aim to treat patients at home. But to do so, we need to know exactly a patient, for example, what is their normal biomedical signals values (mean and standard dev.) or what happens with humidity during winter inside their home or other environmental conditions. Based on specific data and other information from the patients and knowledge extracted from experts we can develop an expert system similar to Echeverría, Jimenez-Molina, and Ríos (2015) that aid patients and caregivers to take better decisions (even from their homes).

This article focuses in the creation of an automatic screening method for Sleep Disordered Breathing (SDB) which are a group of chronic diseases that affect the normal respiration function during the night. These can affect people at any age and are due to different causes: in newborns and young children they are related to congenital defects or premature birth; in older children and adults they may be related to obesity, morphological causes, and hypertension (Goodwin et al., 2003a; 2003b; Levy, Bonsignore, & Eckel, 2009; Rosen, Palermo, Larkin, & Redline, 2002).

The diseases -from least to most severe- considered as SDB are: primary snoring, upper airway resistance, and obstructive sleep apnea (OSA). For example, a newborn with OSA can experience short episodes of apnea, total absence of airflow during night and live a relatively normal life, while a severe OSA may lead to sudden death (Goldstein et al., 2004).

Symptoms of SDB are abnormal day sleepiness, sudden naps during the day (for example, at a red light while driving), general tiredness, fatigue, trouble sleeping, and other related diseases (de la Luz Alonso Álvarez et al., 2008). It has been shown that in children SDBs are closely related to obesity and learning problems (Goodwin et al., 2003a).

The diagnosis of SDB is accomplished through a clinical study called polysomnography (PSG) which collects over 20 different biomedical signals during sleep, including: electrocardiography, electroencephalography, electromyography, plethysmography, oronasal airflow, chest movement, abdominal movement and leg movement among others.

Several automatic methods have been developed in the form of expert systems to detect these disorders in adults, with a very high performance (Álvarez-Estévez & Moret-Bonillo, 2009; De Chazal et al., 2003; Driver et al., 2011; Jarvis & Mitra, 2000; Khandoker, Palaniswami, & Karmakar, 2009). However, we showed empirically

* Corresponding author. Tel.: +56 968353577.
E-mail addresses: srios@dii.uchile.cl, sebastian@rios.tv (S.A. Ríos), lerazo@ing.uchile.cl (L. Erazo).

http://dx.doi.org/10.1016/j.eswa.2015.11.013
0957-4174/

by Erazo and Ríos (2014) that those models' performance is drastically reduced when used in children (under 15 years old).

This time we present a new algorithm able to classify children into two groups: the group at risk of having an SDB, and the group with no risk (or very little risk) of having an SDB. Moreover, our algorithm uses less information than a polysomnography and surpasses state-of-the-art techniques when used on children. This is very important factor since in order to develop a non-invasive solution (to be used at home, for example) we need to reduce the amount of signals used by screening methods.

We showed empirically that no signal alone can be a good OSA predictor in children and also we showed that only three signals: EMG-Chin, EOG and Leg Movement are very good predictors. We need to remark this result, since until today, none of these signals have been used on their own or in combination with other signals for screening in any documented study reviewed in this research.

This work is based on data collected by Pablo E. Brockmann M.D. and his research team in the Sleep Study Center of Clinical Hospital of Catholic University of Chile. This dataset consists in 78 whole night polysomnographies from patients under 15 years old. This is the largest dataset of this characteristics used for OSA screening.

2. Related work

Our main interest is to develop an algorithm that can distinguish between OSA and non-OSA individuals with the least amount of signals from the PSG. In adults, several researchers (Álvarez-Estévez & Moret-Bonillo, 2009; Driver et al., 2011; Flemons et al., 2003) have shown that some signals from PSG have enough predictive power to perform this task. In fact, one-signal screening methods have been successfully tested in adults and children (Roche et al., 2003; Tsai et al., 2013), but those methods still require attending personnel and overnight dedicated systems. Most of them also required a medical evaluation afterwards.

Automated classification methods aim to avoid unnecessary resource consuming screening methods. The most important contribution to this respect was made by the Computers in Cardiology Challenge of 2000. In that work the task was to automatically tag, minute by minute, a single ECG signal as OSA or non-OSA and get to a final diagnosis: OSA or non-OSA for every record (De Chazal et al., 2003; Jarvis & Mitra, 2000; Khandoker et al., 2009; Mendez et al., 2007). Some of these methods reached a precision of 100% in the binary diagnosis and over 85% in minute-by-minute tagging. Unfortunately, none of these studies on automatic classification was performed on children. Besides, most of the algorithms were trained and tested on databases specially designed for this task. In particular, models tested on the Computers in Cardiology 2000 database can not be compared, because this database has been preprocessed to obtain clean, but not realistic data.

This is why we performed a benchmark with real data from 78 children and compared the results among them. This was published by Erazo and Ríos (2014) and a summary of methods tested is shown in Table 1. The best classifiers from all approaches tested were those based on: a Support Vector Machine (SVM), an Artificial Neural Network (ANN). Besides we implemented a Logit classifier to evaluate a simple model, though it is not in the literature. We also selected the three signals that reported best results in the literature, which are: Electrocardiography (ECG or ECGI channel), Air Flow (Patient Airflow channel) and Oxygen Saturation (SpO_2 channel).

Afterwards, we pre-processed ECG, Air Flow and SpO_2 with wavelet transform to extract features. All algorithms were trained with all 14 features generated. Then we trained the models with a cross-validation approach with 70% of the dataset to train the models and 30% to test; and finally, experiments were performed 30 times to generate the final benchmark results computing several measures shown in Section 3.3.

The best performing models were the ANN applied over oronasal Air Flow signals, with $Sensitivity = 84.36\%$. The second best model was the SVM with Air Flow signal that resulted in a $Sensitivity = 75.64\%$. Both classifiers were far from the 90% sensitivity considered as the clinical minimum for a successful classifier. We demonstrated experimentally that state-of-the-art models for OSA screening in adults are not good enough to be used in children.

3. Model construction methodology

After performing our benchmark by Erazo and Ríos (2014), we could not find a good predictor for OSA+ and OSA- in children's data. However, models using Air Flow signal had an outstanding sensitivity, over 80% and regular accuracy (in the Neural Network models). ECG based models, on the other hand showed high specificity, meaning that they have the ability to detect healthy people. This suggests that a combination of these signals may lead to a successful model.

This section describes a novel approach to this task. From a purely mathematical point of view, signal selection is performed in order

Table 1
Automated OSA screening approaches tested in our previous work (Erazo & Ríos, 2014).

Author, Year	Brief description	Results	Comments
Jarvis and Mitra (2000)	Apnea diagnosis based on ECG signal. Features used derived from spectral analysis. Classification based on threshold criteria.	Acc=100%	Tested on Computers in Cardiology 2000 database. 75 records tagged minute-by-minute. All registers corresponding to adults.
De Chazal et al. (2003)	Apnea diagnosis based on ECG signal. Features extracted using black-box methods. Classification methods: linear discriminant, quadratic discriminant.	Acc=100%	Tested on Computers in Cardiology 2000 database. 75 records tagged minute-by-minute. All registers corresponding to adults.
Mendez et al. (2007)	Apnea binary diagnosis based on ECG signal. Features extracted: derived signals (EDR, HRV) coefficients. Classification method: K-Nearest Neighbour.	Acc=85,5%, Sens=83,9%, Spec=88,5%	Tested on Physionet Apnea ECG Database (50 registers) tagged as OSA+ or OSA-.
Álvarez-Estévez and Moret-Bonillo (2009)	A fuzzy reasoning is used to detect apneic events; Air flow signal and Oxygen Saturation signals are used	Sens=87%, Spec=89%	Tested on a 12 patients database (Sleep Heart Health Study), it does not diagnose OSA, it only detects apneic events. All registers corresponding to adults.
Khandoker et al. (2009)	Apnea binary diagnosis (OSA+, OSA-) based on ECG signal. Features extracted: Wavelet Transform coefficients. Classification method: Support Vector Machine.	Acc=100%	Tested on three combined databases: Sleep Research Unit Database, Physionet Apnea ECG Database and Saint Vincent's University Hospital/University College Dublin Sleep Apnea Database. All 125 registers corresponding to adults.
Driver et al. (2011)	Validation of MediByte (portable monitor) as screening method.	Sens=80%, Spec=87%	This monitor requires a clinician to perform the diagnosis.

Table 2
State-of-the-art benchmark results' summary (Erazo & Ríos, 2014).

Method	WT func.	ECG			Air flow			SpO_2		
		Sens [%]	Spec [%]	Acc [%]	Sens [%]	Spec [%]	Acc [%]	Sens [%]	Spec [%]	Acc [%]
SVM	Db1	8,3	82,1	50,0	**75,6**	26,3	54,2	9,7	**82,6**	50,9
	Db9	2,7	**88,2**	51,0	75,4	**28,7**	55,1	**15,0**	79,7	51,6
	Haar	**10,0**	79,7	49,4	70,8	32,7	54,2	13,3	77,2	49,4
	Sym8	5,3	85,1	50,4	75,1	27,0	54,2	12,3	82,1	51,7
NN	Db3	34,3	60,3	49,0	**84,4**	19,0	55,9	30,0	**75,1**	55,5
	Db4	**36,3**	63,9	51,9	80,5	21,7	54,9	19,7	77,7	52,5
	Haar	25,7	**65,9**	48,4	80,3	**26,3**	56,8	38,7	60,0	50,7
	Sym1	28,7	67,7	50,7	80,3	24,3	55,9	**41,0**	63,3	53,6
Logit	Db3	**44,6**	54,5	50,2	18,9	74,6	43,7	44,5	51,4	48,4
	Db4	41,9	53,0	48,2	19,3	**78,9**	44,9	**55,1**	**61,9**	59,0
	Haar	43,6	**58,4**	51,8	**39,3**	58,1	46,3	47,0	55,8	52,1
	Sym7	43,9	51,0	47,9	19,1	75,6	43,4	52,2	57,0	55,0

to construct a minimal signal model able to satisfactorily screen the pediatric population.

3.1. Data understanding

All children included in this study came to the Sleep Center because their parents or doctors had concerns about the quality of their breathing during sleep. Patients' parents had to answer a standard questionnaire in order to evaluate the severity of the potential disorders. Only children considered as a risk population underwent polysomnographic test.

Each patient spent a whole night in the hospital where 20 or 21 different biomedical signals were recorded (approximately 8 h of records),[1] including Electroencephalography (11 channels: EEG F3-A1,EEG C3-A1, EEG P3-A1, EEG O1-A1, EEG F4-A2, EEG C4-A2, EEG P4-A2, EEG O2-A2, EEG A1-A2, EEG Fp1-A1, EEG Fp2-A2), Electrocardiography (ECG or ECGI channel), Electroculography (EOG Right and EOG Left), Electromiography (EMG Chin), Air Flow (Patient Airflow channel) and Oxygen Saturation (SPO2 channel) among others. PSG was collected in Sleep Study Center with an Alice® 5 Diagnostic Sleep System from Respironics (Philips) and transformed using the corresponding software (Alice® Sleepware) to the generally accepted format for biomedical time series: European Data Format (EDF).

Afterwards each test was manually scored by Dr. Pablo E. Brockmann or one of his fellows according to AASM (American Academy of Sleep Medicine) criteria (General, 2005). Apnea, hypopnea, arousals, leg movement, and any other event of interest were reported.

Data corresponds to 78 complete night PSG from 78 different patients of ages from 2 to 16 years old (mean ± SD: 9.7 ± 3.6 years). Sixty-four percent of them are girls.

According to AASM criteria, children are diagnosed with OSA with an Apnea Hypopnea index equal or greater than 1 (General, 2005). Using this specification, 43% of the PSG correspond to children with OSA.

No PSG was excluded because of other diseases presented in patients.

It is important to mention that most studies of OSA screening have small databases, no more than 20 registers. Even though some bigger databases are available, in child data, this is the biggest database documented (as far as this research went).

3.2. Feature extraction

The feature extraction method selection was based on the most referenced one in literature, as explained by Erazo and Ríos (2014). According to this criteria, the Wavelet Transform method was adopted.

Wavelet Transform is used in 1D non–stationary signals to process time series as the ones collected by PSG. It allows for the collecting of frequency information contained in the time series. Also, there is no requirement of the frequency stability, thus it is frequently used for ECG feature extraction.

Several wavelets were tested in order to extract features. Daubechies and Symlet of levels from 1 to 10 were tested, in addition to the Haar function. This means that every signal was processed 21 times under each of these 21 functions of a Wavelet Transform (Daubechies1, Daubechies2, Daubechies3, and so on).

To process the dataset, the Wavelet Toolbox for Matlab was selected. With this objective, EDF's had to be transformed into a compatible Matlab format.

Each signal processed with Wavelet Transform was decomposed to its 14th detail level, obtaining 14 time series for each decomposition function, i.e. 14 time series for ECG processed with the Haar function, 14 time series for ECG processed with Daubechies of level 1 function, and so on.

In order to reduce data and extract features, three features were calculated for each time series, these were: mean, variance and energy; calculated as follows:

$$\text{Mean:} \quad \bar{x} = \frac{1}{N}\sum_{i}^{N} x_i \tag{1}$$

$$\text{Variance:} \quad \sigma^2 = \sum_{i}^{N} (\bar{x} - x_i)^2 \tag{2}$$

$$\text{Energy:} \quad E = \sum_{i}^{N} x_i^2 \tag{3}$$

Coefficients obtained from the preprocessing stage were named $Db1_{mean1}$, $Db1_{var1}$, $Db1_{ene1}$ for the mean, variance and energy of the first detail level for Daubechies1 WT function. The same process was applied for every WT function and to every signal. This way, 21 different databases were generated for every signal –one for each WT function–, each of them containing 42 features: *mean*1, *var*1, *ene*1, *mean*2, *var*2, *ene*2 up to *mean*14, *var*14, *ene*14.

3.3. Evaluation measures

In order to compare models we will compute well known evaluation measures. The main point is to describe the strengths and weaknesses of the models (Fig. 1).

Indicators selected for these tasks are Sensitivity, Specificity and Accuracy (commonly used to assess clinical tests performance); Precision, Recall and F-measure (to assess the classification performance

[1] originally records were almost 9 hours long, but after data cleaning; approximately 8 h remained.

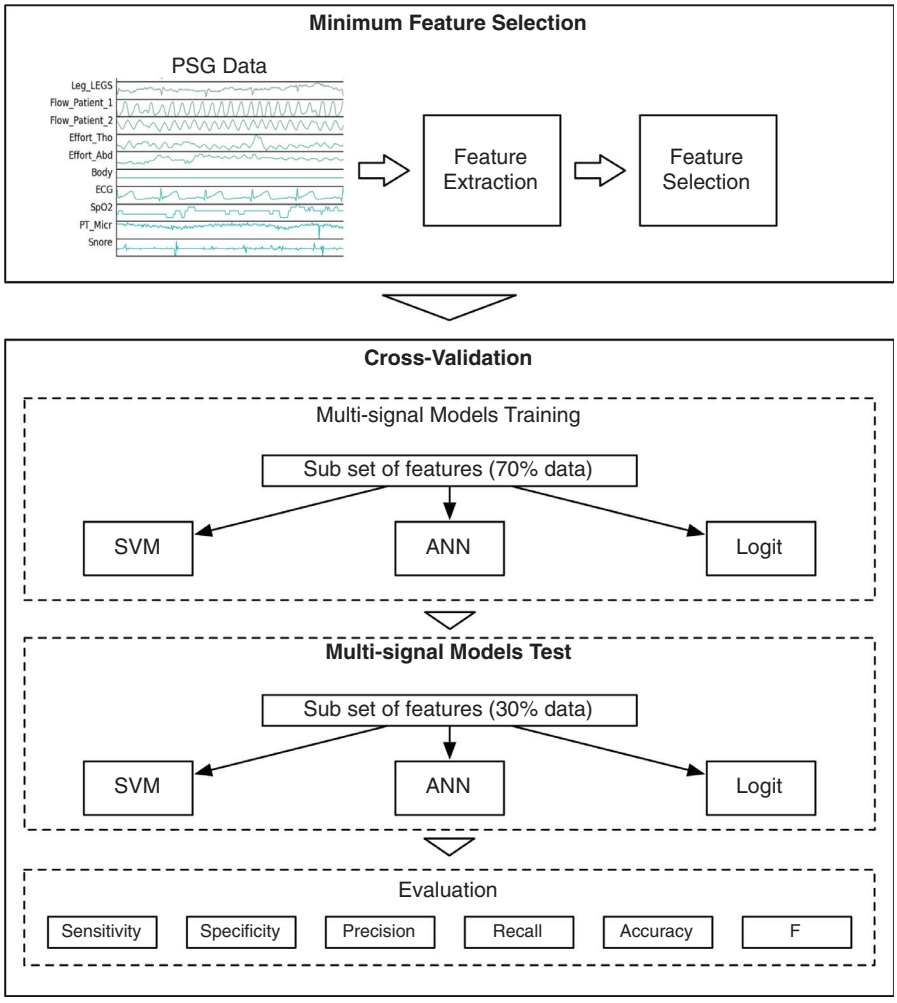

Fig. 1. Summary of Experimental Methodology.

of algorithms). They will be calculated as follows:

$$\text{Recall} = \text{Sensitivity} = \frac{TP}{TP+FN} \tag{4}$$

$$\text{Specificity} = \frac{TN}{TN+FP} \tag{5}$$

$$\text{Accuracy} = \frac{TP+TN}{TP+TN+FP+FN} \tag{6}$$

$$\text{Precision} = \frac{TP}{TP+FP} \tag{7}$$

$$\text{F} = \frac{2*TP}{2*TP+FN+FP} \tag{8}$$

Interpretation of these indicators is based on the ability to detect unhealthy individuals. This is because it is more important to correctly classify sick children as sick than healthy children as healthy.

Sensitivity is the ability to detect unhealthy individuals, Specificity is the ability to detect healthy people, Accuracy is the ability to correctly classify, that is, how many children were correctly classified.

On the other hand, Precision is the proportion of the ill individuals group that are correctly classified. Finally, the F-measure shows how accurate is the model, is in a range of 0 to 1, where 1 is the best model possible.

3.4. ECG feature extraction

To extract relevant features from an ECG signal, it is important to understand how it is analyzed by clinicians.

Fig. 2 shows a sample of an ECG signal corresponding to the A0011823 patient.

A regular ECG wave can be characterized according to some points. As seen in Fig. 3, points P, Q, R, S and T describe a complete pulse of an ECG.

The relevant characteristics for respiratory functions are associated with the QRS complex. This is the name of the area formed by Q, R and S points. Commonly the features are extracted from derived signals from the ECG recording. These signals are: Heart Rate Variability (HRV) and ECG Derived Respiratory Signal (EDR).

HRV corresponds to the time series constructed from R–R intervals; this is the time between successive R points. EDR corresponds to the time series constructed from QRS amplitude. This is the vertical distance between Q and R points.

Before extracting features, all signals had to be normalized to ignore the variance associated with natural variations among different individuals. While a certain heart rate might be normal to a person, it could be considered accelerated for another, so normalization is the standard proceeding when working with biological signals.

Common features extracted from HRV and EDR signal are:

$$\text{Mean:} \quad \bar{x} = \frac{1}{N}\sum_{i}^{N} x_i \tag{9}$$

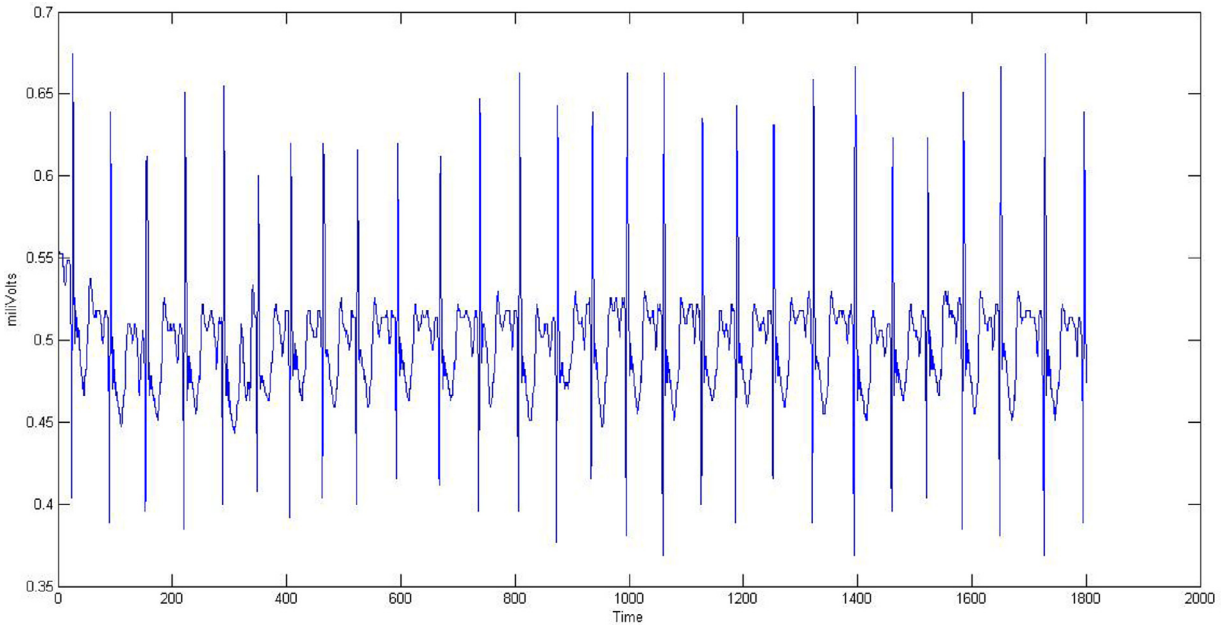

Fig. 2. ECG sample.

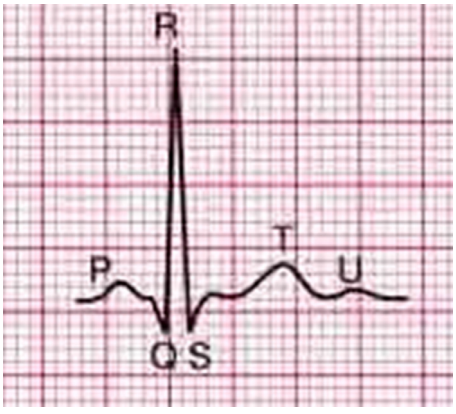

Fig. 3. ECG wave characteristics.

$$\text{Variance:} \qquad \sigma^2 = \frac{1}{N}\sum_{i}^{N}(\bar{x} - x_i)^2 \tag{10}$$

Also, some time domain features were extracted from the HRV signal. In order to do this a new time series had to be constructed, corresponding to the successive differences of the HRV signal. These features were:

$$\text{Root Mean Square of Successive Differences:} = \sqrt{\sum_{i}^{N}(x_i - x_{i-1})^2} \tag{11}$$

$$\text{Standard Deviation of Successive Differences:} = \sqrt{\frac{1}{N}\sum_{i}^{N}(\bar{x} - x_i)^2} \tag{12}$$

With all these transformations the resulting feature set to characterize the ECG signal is: *meanHRV, varHRV, meanEDR, varEDR, RMSSD* and *SDSD*.

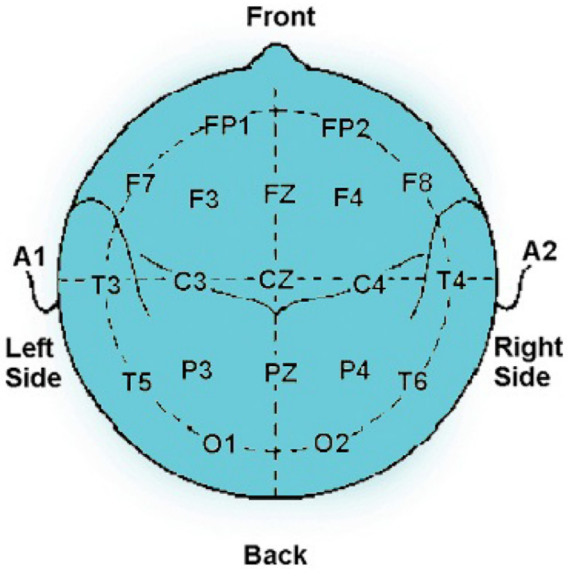

Fig. 4. Electrode positions for an EEG.

3.5. EEG feature extraction

The EEG performed during a PSG has 11 signals as output: $EEGFp1 - A1$, $EEGFp2 - A2$, $EEGA1 - A2$, $EEGF3 - A1$, $EEGF4 - A2$, $EEGC3 - A1$, $EEGC4 - A2$, $EEGP3 - A1$, $EEGP4 - A2$, $EEGO1 - A1$ and $EEGO2 - A2$. Each of them characterized by the position of the electrode in the head, where $A1$ corresponds to the left side, and $A2$ to the right side, as seen in Fig. 4.

Not all patients present every signal. In small children (under 2 years old) not all the electrodes are placed on the head, mainly because they have smaller heads, so 31 of the registers do not contain the signals $EEGA1 - A2$, $EEGFp1 - A1$, $EEGFp2 - A2$, $EEGO1 - A1$ y $EEGO2 - A2$. Although, some techniques propose to process them all together (by adding the signals or applying Principal Components Analysis for example), the selected approach was to process

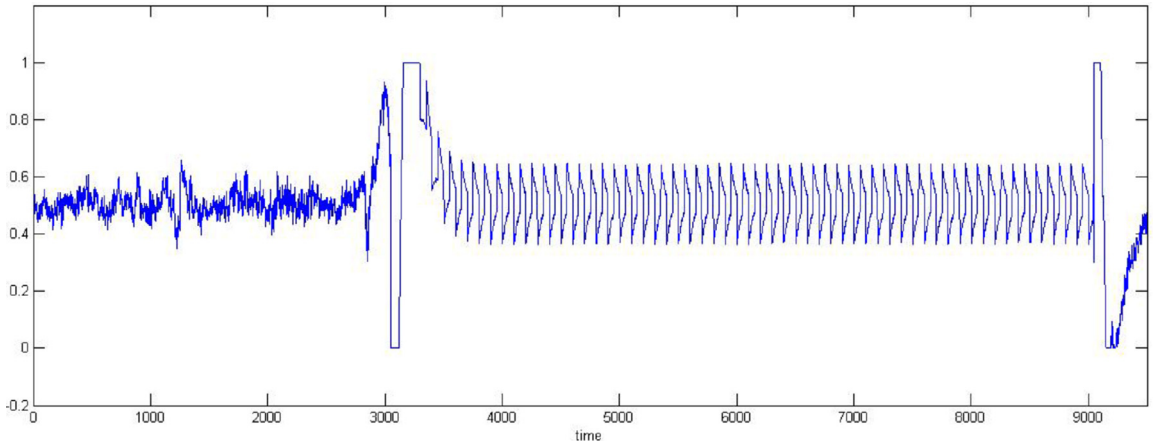

Fig. 5. EEG sample corresponding to patient A0001945.

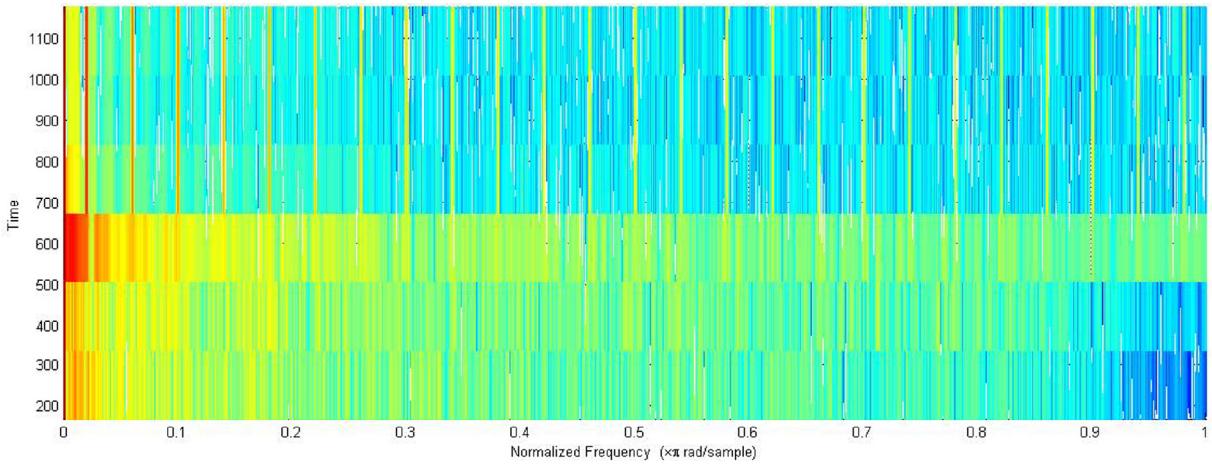

Fig. 6. Spectrogram sample corresponding to patient A0001945.

them separately for two reasons: first, clinicians analyze them separately, and second, if there is a combination that allows for processing them all together it should be reflected in the feature selection stage. This is, if the signals are giving redundant information, the feature selection will detect this effect and eliminate redundancy.

When a PSG is processed, clinicians look into EEG signals to tag time windows according to the sleep stage the patient is in. For example in Fig. 5 is easy to distinguish two stages. So, the main task with these signals is to detect variations in the wave frequencies in order to characterize different stages.

What matters most is to determine how much a wave varies during night, for which a methodology was developed.

First, a spectrogram was constructed. Spectrograms are frequently used to analyze sound waves or pixels. They are a graphic representation of the variety of frequencies in a wave as time varies.

On the *X*-axis a spectrum of frequencies is represented. On the *Y*-axis the time is divided in small windows for analysis, and the color scale shows how strong is the presence of a frequency in a specific time window.

If columns are analyzed independently, the variation of a specific frequency can be observed. Based on this, the features to be extracted characterize the number of times a *big* variation occurs, that is, a change in the sleep stage is suspected.

If smaller time windows are used, smaller changes can be detected, but this effect is not desired, since changes in sleep stages are characterized by big variations, so only eight time windows will be used for the analysis.

In order to do this, an auxiliary time series is defined as the difference of a frequency from one time window to the next. This is performed for every frequency considered in the spectrogram (Fig. 6).

The main idea is to detect significant variations, so the relative differences were calculated as the difference divided by the initial value. With this, a new time series was constructed for each signal. Later, this signal was filtered to make it easier to detect *big* variations.

Fig. 7 shows the processed signal corresponding to the sample in Fig. 5, every frequency analyzed is shown in a different color, the variation in time is represented graphically. This means, peaks represent the big changes indicating a change in the sleep stage is suspected.

Finally, features extracted from each EEG signal correspond to the number of local minimum and the number of local maximum from every frequency filtered signal.

3.6. Abdominal and thoracic effort feature extraction

Abdominal and Thoracic Effort Signals correspond to a band that goes around the abdomen and chest to register a patient's movements while sleeping.

The main idea is to detect peaks of movement, that is, when a patient has a regular respiratory function, no abnormality should appear in the signal. In Fig. 8 for example, an abnormality appears at the end of both signals (time $\sim$ 8500). In order to detect peaks wavelet decomposition was used for its ability to show them in the signal. The methodology implemented to extract features from the signal considers the mean, standard deviation and energy of the signals derived from the decomposition.

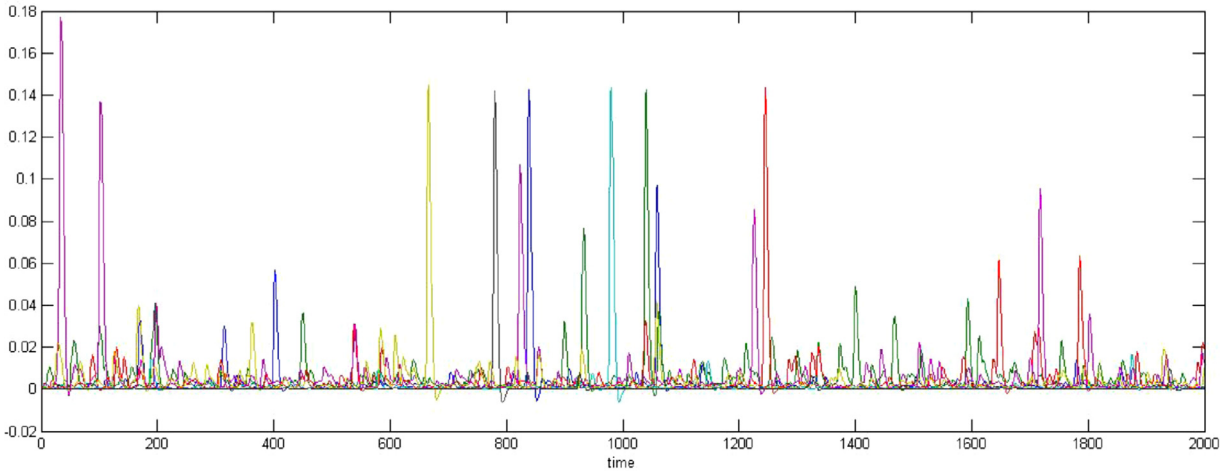

Fig. 7. Processed EEG signal corresponding to patient A0001945.

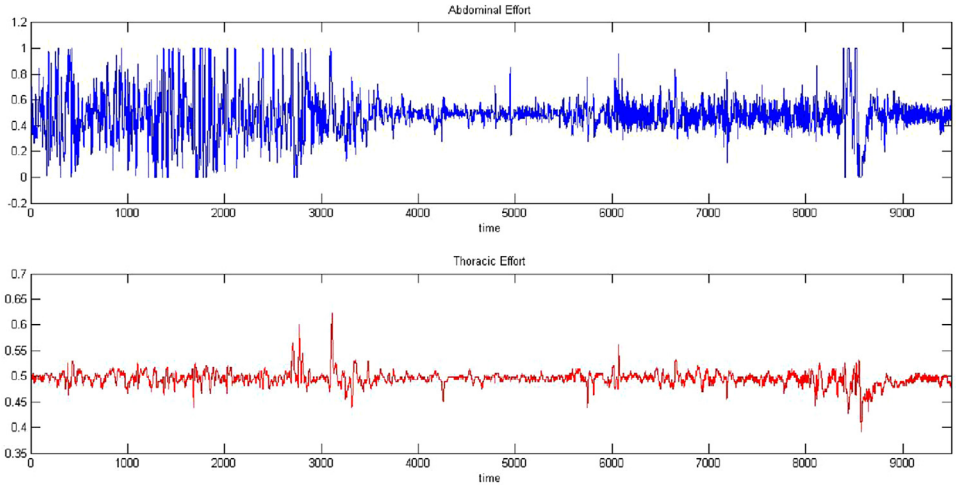

Fig. 8. Abdominal Thoracic Signal (blue) and Abdominal Effort Signal (red) corresponding to patient A0000678. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

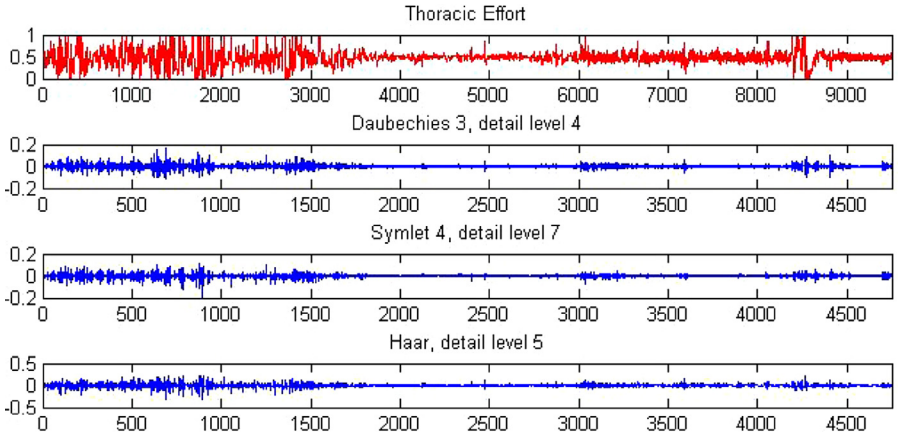

Fig. 9. Different Wavelet Decompositions (blue) for the Thoracic Effort Signal (red) corresponding to patient A0000678. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

As said in the previous section, many families of functions can be used with this decomposition. A visual inspection was done to select the signal that best fits the objectives of this task.

Fig. 9 shows three of the wavelet functions tested. Although all functions seem to detect variations equally, Daubechies 3 had a better performance amplifying small variations, as the one seen at the end of the time window shown in the figure. This is why the function selected to process both signals was Daubechies 3 of level 4.

3.7. Air flow feature extraction

The Air Flow Signal registers the *air movement* through the nose and the mouth. So, to detect the presence of OSA, one must detect

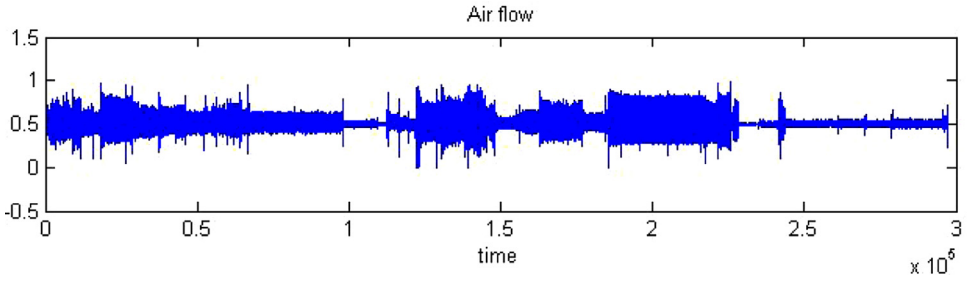

Fig. 10. Air Flow Signal corresponding to patient A0000739.

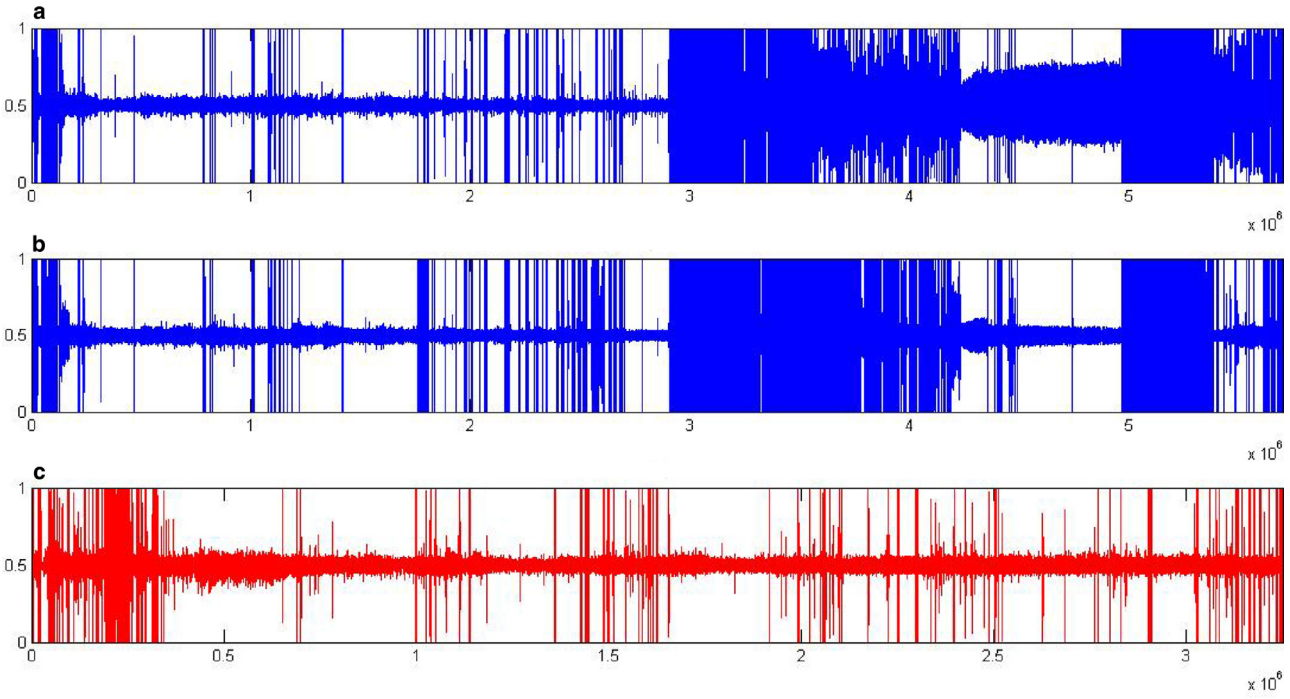

Fig. 11. (a) Leg1 Signal corresponding to patient A0001484. (b) Leg2 Signal corresponding to patient A0001484. (c) Legs Signal corresponding to patient A0011947.

when an abnormal flow occurs, this is, the complete absence of flow or a *big decrease* in it.

Fig. 10 shows a complete night record. The task is to detect the flat areas in the signal.

The same task was approached by Erazo and Ríos (2014) using a Wavelet Transform where the features extracted were used as input for one-signal models. This resulted in high performance models.

Therefore the same strategy was followed and the selected function was Daubechies 3 of level 14.

3.8. Leg movement feature extraction

Of the 78 patients, 36 had only one signal that recorded their leg movement during sleep. Forty-one of them had only one record for each leg, this is two signals per patient to record leg movement. One patient had no record.

As seen on Fig. 11 both legs are highly correlated, so no lost information is suspected in the case of only one record. Yet, both signals were included in the analysis. If the information results are redundant, the Feature Selection Stage should detect it.

The characterization of the signal had to represent the variation of the leg movement to detect abnormal movement or *big movement* episodes.

As before, the Wavelet Transform has the ability to extract these features from the signal.

After testing a variety of functions, Daubechies 8, of level 6 was selected. As in previous cases, mean, variance and energy of every detail level were calculated, obtaining a set of 18 features.

3.9. Body position feature extraction

Body Position signal detects the changes of position of the body, from supine (back facing down) to prone (chest facing down). The main idea is to detect change in positions, as a measure of the movement during the night. The sensor used for this task assigns a number to each position. It is a nominal variable that detects changes in position.

In order to reflect the number of times a patient moves during the night an auxiliary signal was constructed as the successive differences of the signal. Therefore only changes in position would appear as different from zero as seen in Fig. 12. With this, the feature extracted was an index of the number of changes divided by the sleep time.

3.10. Electromyogram feature extraction

The Electromyogram signal (EMG) registers the electrical potential generated by muscle cells, in a PSG in particular is used to register chin movement during sleep. Chin movement is important in the diagnosis of SDB, and OSA, because respiration may occur through

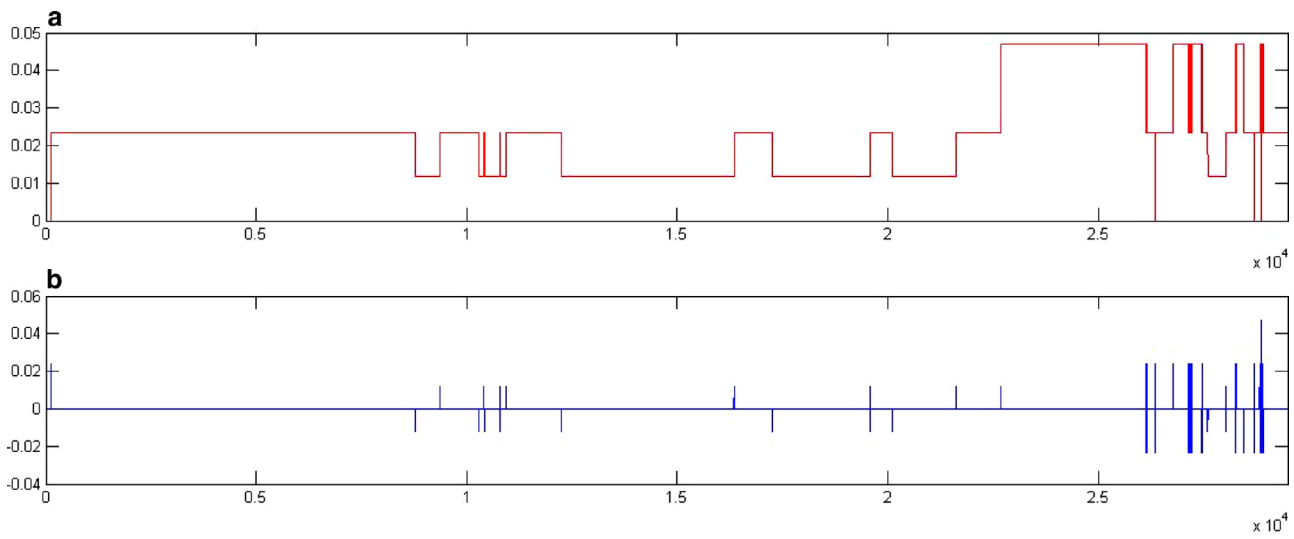

Fig. 12. (a) Body Position Signal corresponding to patient A0001460. (b) Auxiliary signal derived from Body Position Signal for patient A0001460.

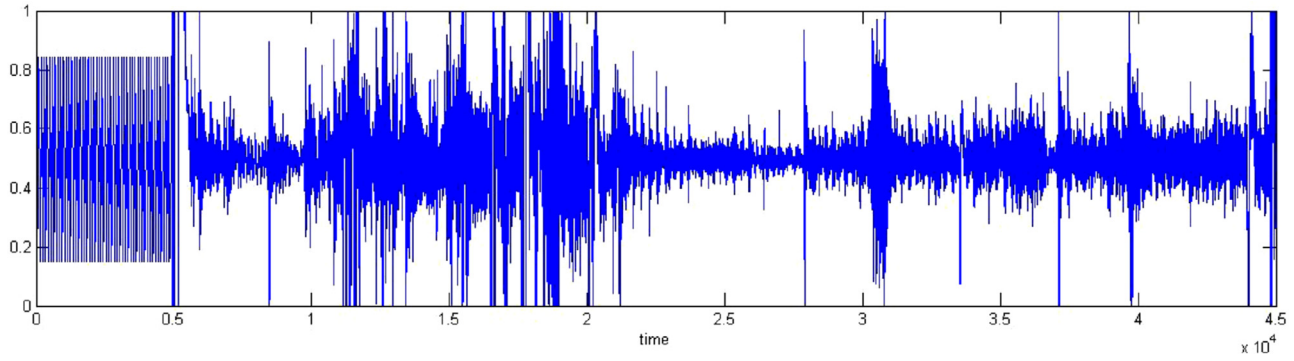

Fig. 13. EMG Chin Signal corresponding to patient A0002197.

nose or mouth, thus chin movement is used as an indicator of mouth movement.

On the other hand, tension in the chin might indicate snoring or another abnormalities during sleep, like bruxism for example.

As other signals that register movement, signal processing was made by a Wavelet Transform. The same selection process was performed, the chosen function was Daubechies 7 of level 8, resulting in 24 features (Fig. 13).

3.11. Electro-oculogram feature extraction

The Electro-oculogram (EOG) registers the movement of the eyes by placing electrodes around them. The result of this exam is one signal for each eye. So, in a complete PSG, two signals correspond to EOG, and they are tagged as EOG Right, and EOG Left for the right eye, and the left eye respectively.

Even though these are separated signals, a high correlation is expected, since eye movements are not independent from each other in most cases.

In Fig. 14 we see the correlation between both left and right eye of patient A0006225. The same correlation is observed in every record from this signal, yet every signal was processed because the feature extraction process should be able to detect these highly correlated features.

In order to be consistent in the treatment of signals, all movement signals were processed with Wavelet Transform. The function used for the EOG feature extraction was Daubechies 7 of level 8.

3.12. Pulse feature extraction

The pulse signal as predictor for OSA prevalence has been used in other studies. As expected, an abnormal pulse rate might be a good indicator of an apnea episode due to the lack of oxygen generated as a consequence.

In particular, Noehren et al. (2010) use four time series derived from the pulse signal:

- APRD: Absolute Pulse Rate Decrease
- APRI: Absolute Pulse Rate Increase
- RPRD: Relative Pulse Rate Decrease
- RPRI: Relative Pulse Rate Increase

For the purpose of this study, only the first two were used.

The pulse signal was normalized to avoid variation among patients (see Fig. 15(a)). Then a Butterworth filter was used to eliminate the noise from the signal and detect easily peaks of local minima and local maxima (see Fig. 15(b)).

The APRD length corresponded to the number of peaks found, and each value was calculated as the difference of a local minimum and the local maximum immediately before (see Fig. 15(d)). The same procedure was applied to construct the APRI (see Fig. 15(c)), calculating the difference between a local maximum and the local minimum immediately before.

After this, the results are two time series. The decision is to extract, from both of them: mean, standard deviation, median, maximum and minimum.

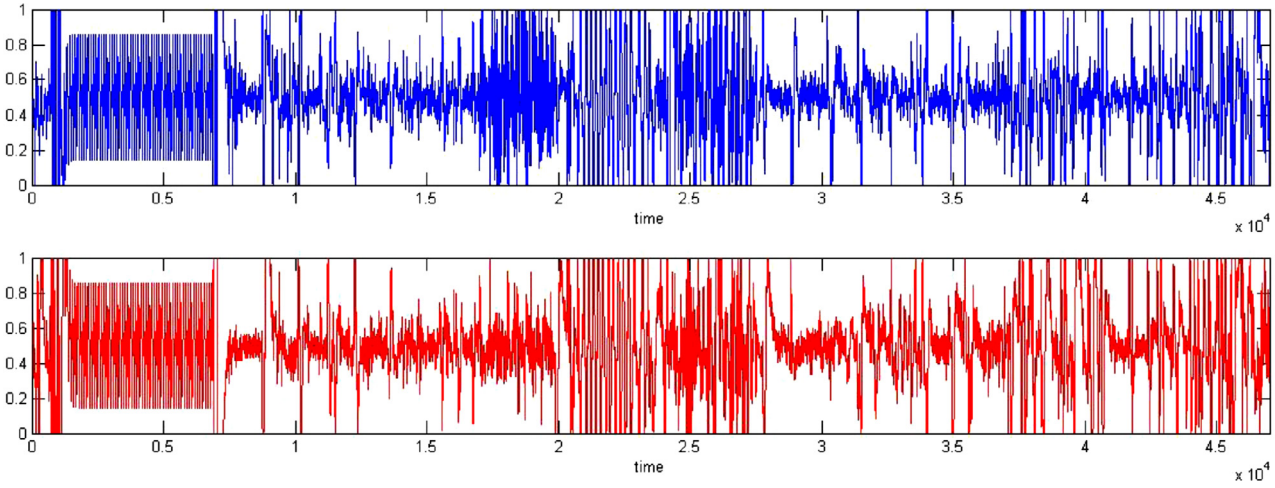

Fig. 14. EOG Sinals of Left (blue) and Right (Red) ayes corresponding to patient A0006225. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

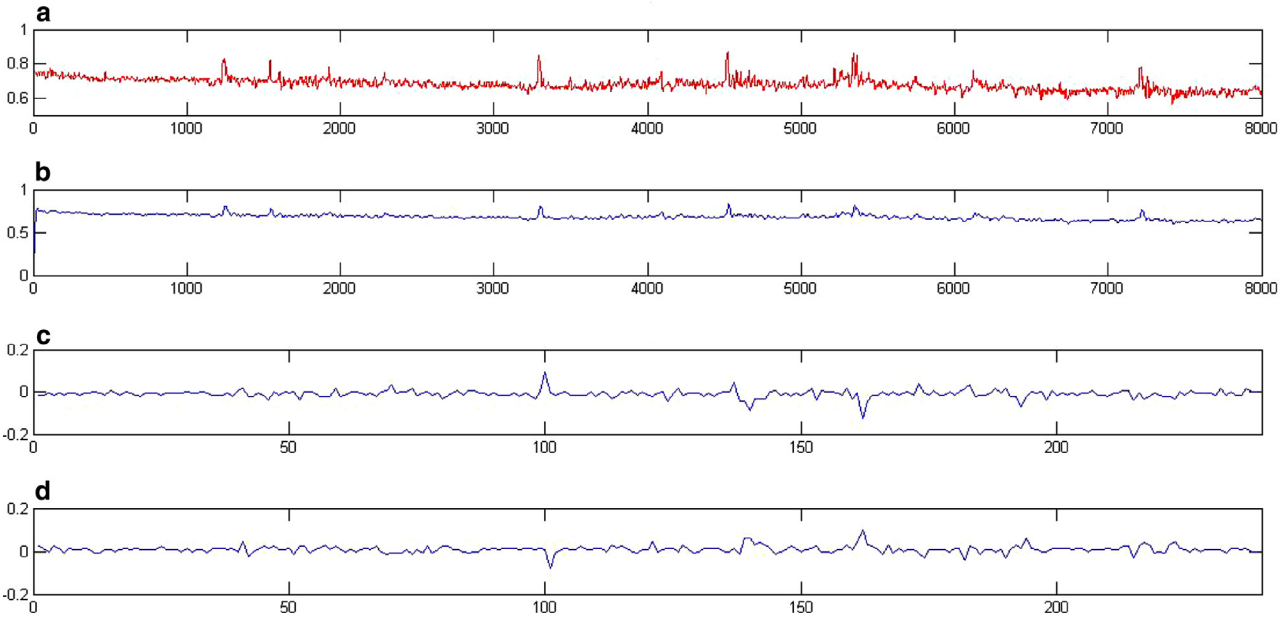

Fig. 15. (a) Pulse signal corresponding to patient A0000294. (b) Filtered pulse signal. (c) Absolute Pulse Rate Increase (APRI) derived from pulse signal. (d) Absolute Pulse Rate Decrease (APRD) derived from pulse signal.

3.13. Snore feature extraction

The snore signal is used to diagnose not only OSA, but other SDB's, like primary snoring. Although very useful for SDB diagnosis, the final classification into OSA+ and OSA- groups can not rely only on this signal.

Snoring is measured by a sensor located on the throat that detects vibration. As snoring is produced by an obstruction of the airway, vibration is produced, and measured this way.

The resulting signal is normalized since the relevant aspects are variations in the signal. As output for the PSG, a signal from 0 to 1 is shown.

The goal when processing this signal was to determine when an abnormal *vibration episode* occurred. The signal provided by the PSG is already normalized, so an abnormal episode was considered when the signal crosses over 0.7 or under 0.3 (blue lines on Fig. 16). This selection was based on preliminary analysis of the signal behavior.

The features extracted correspond to the number of abnormal episodes *up* and abnormal episodes *down*. The resulting feature set was: $Snore_{up}$ and $Snore_{down}$.

3.14. Oxygen saturation feature extraction

PSG also include a sensor that measures the blood's oxygen saturation during the whole night. Usually saturation measures are done periodically. Therefore a PSG is one of the few clinical tests that allows a Saturation Signal.

Evidently this is one of the most important signals to determine a diagnosis, since it is directly related to apnea episodes. A desaturation episode is a clear symptom of an abnormal respiratory function. In particular, it might be the perfect indicator of an apnea episode. Fig. 17 shows a time window of the Oxygen Saturation Signal collected by a PSG from patient A0001183.

Many indicators are used for processing this signal. The most selected and relevant for this study are: DEI (Desaturation Event Index), defined as a saturation signal drop in four or more points (on a scale from 1 to 100); and ODI (Oxygen Desaturation Index), also known as CT90 (Cumulative Time 90). Corresponds to the amount of time the patient has a saturation under 90%. DEI and ODI were selected because of their previous use in continuous positive airway pressure devices (CPAP) tests and previous experiences in

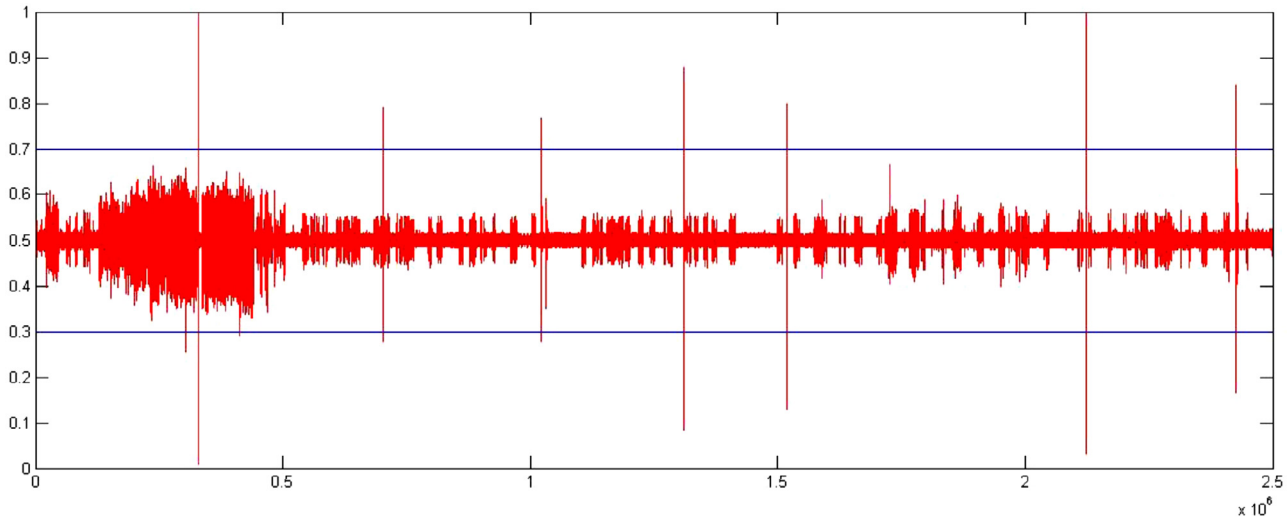

Fig. 16. Snore Signal corresponding to patient A0000884.

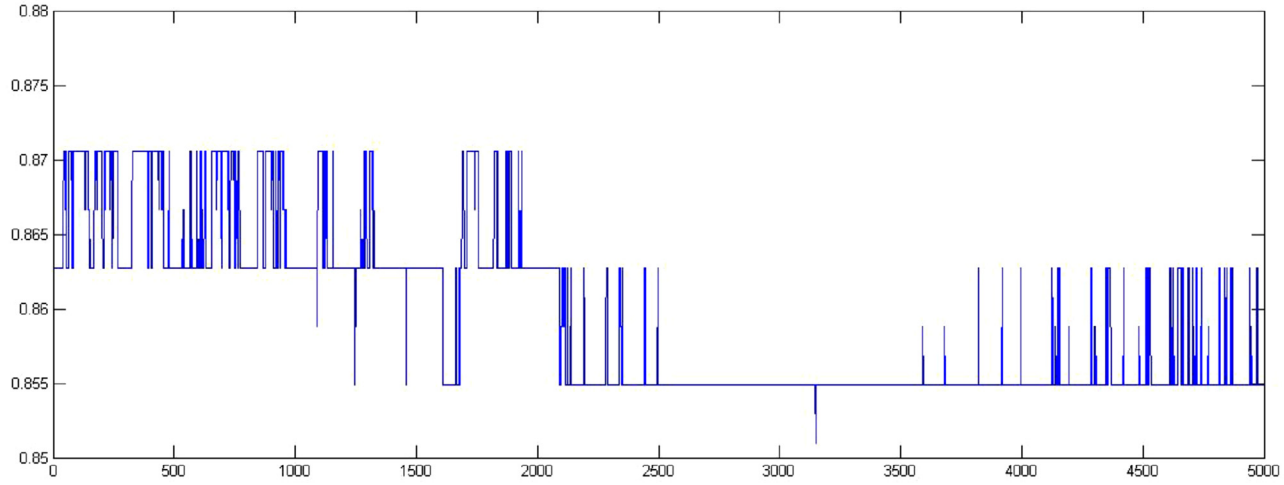

Fig. 17. Oxygen Saturation Signal corresponding to patient A0001183.

diagnosing apnea episodes (Chang, Wu, & Cao, 2012; Chung et al., 2012).

So, as result, the feature set was: *DEI* and *ODI* for each signal.

4. Feature selection

Resulting from the Feature Extraction process, 355 features are used to resume the information collected in a PSG. Table 3 summarizes the features resulting from the previous section.

The hypothesis is that not all the information is needed to perform a high quality screening. If this is true, a less resource-consuming clinical test may be developed to pre-diagnose children with suspected OSA.

The first step to accomplish this is to select features. The selection should imply a reduction in the signals needed to perform a screening.

A filter approach was selected to perform the Feature Selection. This allows the use of the same subset with all three models and allows comparison under the same conditions as shown by Erazo and Ríos (2014).

Embedded methods were discarded due to their dependency on the selected model. Therefore, different models would have ended up with different feature subsets. Wrapper methods were discarded also, because they did not allow for the control of the number of resulting features in the subset.

Before starting the selection, data quality was checked. Features corresponding to the Pulse signal were discarded since only 6 patients had complete Pulse records.

The selection procedure was based on correlation analysis and Principal Component Analysis. The step by step methodology is described as follows:

1. **First.** Principal Component Analysis (PCA) was computed over all the Features included, using Varimax rotation criterion. The main objective was to extract variables that explain most of the variance in order to incorporate as much information as possible in the modeling section.
2. **Second.** The first five components resulting from Factorial Analysis were analyzed, as they explained 89.9% of the variance, and the sixth component added only 2% to the variance explanation.
3. **Third.** Variables eigenvalues were extracted, and only variables with an eigenvalue of 0.05 (5%) or more for the first five principal components were kept.
4. **Fourth.** As mentioned, all features corresponding to selected signals were kept. Resulting from these steps, features corresponding

Table 3
Summary of resulting features from a complete PSG.

Signal	Features extracted	Total
ECG	$mean_{HRV}$, var_{HRV}, $mean_{EDR}$, var_{EDR}, *RMSSD* and *SDSD*.	6
EEG (11)	max_1, max_2, max_3, max_4, max_5, max_6, max_7, min_1, min_2, min_3, min_4, min_5, min_6 and min_7.	154
Abdominal effort	$Db3_{mean1}$, $Db3_{var1}$, $Db3_{ene1}$, $Db3_{mean2}$, $Db3_{var2}$, $Db3_{ene2}$, $Db3_{mean3}$, $Db3_{var3}$, $Db3_{ene3}$, $Db3_{mean4}$, $Db3_{var4}$ y $Db3_{ene4}$.	12
Thoracic effort	$Db3_{mean1}$, $Db3_{var1}$, $Db3_{ene1}$, $Db3_{mean2}$, $Db3_{var2}$, $Db3_{ene2}$, $Db3_{mean3}$, $Db3_{var3}$, $Db3_{ene3}$, $Db3_{mean4}$, $Db3_{var4}$ y $Db3_{ene4}$.	12
Air flow	$Db3_{mean1}$, $Db3_{var1}$, $Db3_{ene1}$, $Db3_{mean2}$, $Db3_{var2}$, $Db3_{ene2}$, $Db3_{mean3}$, $Db3_{var3}$, $Db3_{ene3}$, $Db3_{mean4}$, $Db3_{var4}$, $Db3_{ene4}$, $Db3_{mean5}$, $Db3_{var5}$, $Db3_{ene5}$, $Db3_{mean6}$, $Db3_{var6}$, $Db3_{ene6}$, $Db3_{mean7}$, $Db3_{var7}$, $Db3_{ene7}$, $Db3_{mean8}$, $Db3_{var8}$, $Db3_{ene8}$, $Db3_{mean9}$, $Db3_{var9}$, $Db3_{ene9}$, $Db3_{mean10}$, $Db3_{var10}$, $Db3_{ene10}$, $Db3_{mean11}$, $Db3_{var11}$, $Db3_{ene11}$, $Db3_{mean12}$, $Db3_{var12}$, $Db3_{ene12}$, $Db3_{mean13}$, $Db3_{var13}$, $Db3_{ene13}$, $Db3_{mean14}$, $Db3_{var14}$ and $Db3_{ene14}$.	48
Leg movement (2)	$Db8_{mean1}$, $Db8_{var1}$, $Db8_{ene1}$, $Db8_{mean2}$, $Db8_{var2}$, $Db8_{ene2}$, $Db8_{mean3}$, $Db8_{var3}$, $Db8_{ene3}$, $Db8_{mean4}$, $Db8_{var4}$, $Db8_{ene4}$, $Db8_{mean5}$, $Db8_{var5}$, $Db8_{ene5}$, $Db8_{mean6}$, $Db8_{var6}$ and $Db8_{ene6}$.	36
Body position	CI	1
EMG	$Db7_{mean1}$, $Db7_{var1}$, $Db7_{ene1}$, $Db7_{mean2}$, $Db7_{var2}$, $Db7_{ene2}$, $Db7_{mean3}$, $Db7_{var3}$, $Db7_{ene3}$, $Db7_{mean4}$, $Db7_{var4}$, $Db7_{ene4}$, $Db7_{mean5}$, $Db7_{var5}$, $Db7_{ene5}$, $Db7_{mean6}$, $Db7_{var6}$, $Db7_{ene6}$, $Db7_{mean7}$, $Db7_{var7}$, $Db7_{ene7}$, $Db7_{mean8}$, $Db7_{var8}$ and $Db7_{ene8}$.	24
EOG (2)	$Db7_{mean1}$, $Db7_{var1}$, $Db7_{ene1}$, $Db7_{mean2}$, $Db7_{var2}$, $Db7_{ene2}$, $Db7_{mean3}$, $Db7_{var3}$, $Db7_{ene3}$, $Db7_{mean4}$, $Db7_{var4}$, $Db7_{ene4}$, $Db7_{mean5}$, $Db7_{var5}$, $Db7_{ene5}$, $Db7_{mean6}$, $Db7_{var6}$, $Db7_{ene6}$, $Db7_{mean7}$, $Db7_{var7}$, $Db7_{ene7}$, $Db7_{mean8}$, $Db7_{var8}$ and $Db7_{ene8}$.	48
Pulse	$APRD_{mean}$, $APRD_{std}$, $APRD_{median}$, $APRD_{max}$, $APRD_{min}$, $APRI_{mean}$, $APRI_{std}$, $APRI_{median}$, $APRI_{max}$ and$APRI_{min}$.	10
Snore	$Snore_{up}$ and $Snore_{down}$	2
Oxygen saturation	*DEI* and *ODI*	2
TOTAL		355

Table 4
Summary of selected features.

Signal	Features selected	Total
Leg 1	$Db8_{mean1}$, $Db8_{mean2}$, $Db8_{var2}$, $Db8_{mean3}$, $Db8_{mean4}$, $Db8_{mean5}$, $Db8_{var5}$ and $Db8_{mean6}$.	8
Leg 2	$Db8_{mean3}$, $Db8_{mean4}$, $Db8_{mean5}$ and $Db8_{var5}$.	4
Legs	$Db8_{mean1}$, $Db8_{var1}$, $Db8_{mean2}$, $Db8_{mean3}$, $Db8_{mean4}$ and $Db8_{mean5}$.	6
EOG right	$Db7_{mean1}$, $Db7_{mean2}$, $Db7_{mean3}$, $Db7_{mean4}$, $Db7_{mean5}$, $Db7_{mean6}$, $Db7_{mean7}$ and $Db7_{var7}$.	8
EOG left	$Db7_{mean1}$, $Db7_{var1}$, $Db7_{mean2}$, $Db7_{mean3}$, $Db7_{var3}$, $Db7_{mean4}$, $Db7_{mean5}$, $Db7_{mean6}$, $Db7_{mean7}$, $Db7_{var7}$ and $Db7_{mean8}$.	11
EMG chin	$Db7_{mean1}$, $Db7_{var1}$, $Db7_{mean2}$, $Db7_{mean3}$, $Db7_{mean4}$, $Db7_{mean5}$, $Db7_{mean6}$, $Db7_{mean7}$, $Db7_{var7}$, $Db7_{mean8}$ and $Db7_{var8}$.	11
TOTAL		51

Table 5
SVM performance using the feature subset from PSG.

Model	Sensitivity	Specificity	Accuracy	Precision	Recall	F-measure
SVM	100,00%	100,00%	100,00%	100,00%	100,00%	100,00%

Table 6
NN performance using the feature subset from PSG.

Model	Sensitivity	Specificity	Accuracy	Precision	Recall	F-measure
NN	28,67%	100,00%	28,67%	100,00%	28,67%	39,91%

Table 7
Logit Regression performance using the feature subset from PSG.

Model	Sensitivity	Specificity	Accuracy	Precision	Recall	F-measure
LOGIT	47,30%	100,00%	47,30%	100,00%	47,30%	62,69%

to the following signals formed the preliminary subset: EMG Chin, EOG (Left and Right), Snore and Legs. Preliminary subset had 129 features.

5. **Fifth.** Correlation Matrix was computed over the preliminary subset.
6. **Sixth.** Every pair of signals was analyzed. If a correlation of over 0.6 was found, only one of the pair of signals was kept.
7. **Seventh.** Resulting from these steps, 51 features remain in the subset. This is the definitive Features Subset.

Table 4 shows the resulting subset of features from the Feature Selection process.

5. Classification models

Models used to classify patients into the two groups defined are the same as those used by Erazo and Ríos (2014). These are: Support Vector Machine, Artificial Neural Networks and Logit Regression. Also, the same validation methodology was implemented, as described in Section 3.3.

Thirty different training and testing balanced sets were created and used to train and test every model. Performance metrics were calculated each time.

The resulting performance corresponds to the average of the metrics resulting from every iteration (this is, the result from one training set and one testing set).

6. Results

Tables 5–7 describe the results obtained from each classification model separately.

Support Vector Machines showed an outstanding performance when the minimal signal set are used as input. This result is unexpected because, as far as this research went, no other published research used EMG, EOG and leg movement as input signals. In fact, clinicians use these signals for auxiliary information, and never as the main source of information for diagnosis.

The other models showed poorer performance compared to SVM, but they also showed unexpected Precision results.

7. Discussion

Having as a starting point the previous results presented by Erazo and Ríos (2014), where it is shown that **no signal alone can be a good predictor for OSA in children** when using black-box methods for feature extraction. As a consequence, it can be inferred that a more physiological approach to feature extraction may lead to good quality classification methods.

Evidence in adults and some studies conducted in children showed good-quality screening methods were mainly based on physiological feature extraction methods. Most of these studies also, were based on one-signal only. The few of them that were based on more

than one signal did not show any criterion for the signal selection beyond clinicians criteria.

Always having present the goal of finding the minimum feature set that can effectively screen for OSA. This is why the approach presented here describes a novel method for OSA screening: Signal selection was based only on statistical and optimization criteria.

We discover that three signals: EMG-Chin, EOG and Leg Movement combined are the best predictor for OSA in children. Surprisingly none of these signals have been used on their own or in combination with other signals for screening in any documented study reviewed in this research.

Also, all of this signals are collected with ordinary electrodes, widely available on the market. This fact allows us to think of this algorithm as an actual screening method for future research in developing countries where resources are scarce, and OSA consequences in infant populations are largely overlooked.

Our approach is able to screen OSA with 100% precision was developed using signals collected by polysomnography and the pertinent information needed was reduced using data mining techniques, so only three signals are needed to perform a high quality screening.

Another result of this work, a high quality repository of polysomnographic children data tagged by qualified clinicians is available for further testing and model construction.

It is very important to consider that today is a world wide tendency the development of ubiquitous health (u-health) expert systems that allow the monitoring of patients even at home (Echeverría et al., 2015). Most methods for screening OSA use oxygen saturation and ECG signals (see Table 1); which need very good quality sensors (expensive) in order to obtain good quality measures. This is a barrier to develop a system for use at home or in third world countries. However, the sensors required to measure our approach signals (EMG-Chin, EOG and Leg Movement) are more simple in construction, price and allow to have good quality data for a u-health expert system.

8. Recommendations and future work

For signals like ECG or Air Flow, widely used in screening methods for adults, the results showed no relevance or correlation with the target variable in the feature selection process (see Section 4). Clinicians base their diagnosis on these signals, although they use all the information available from a polysomnography. The intuitive reasoning lead them to think that these signals should appear as relevant in the feature selection. This fact may be evidence that extracted features are not representative enough of the information contained in the signal.

Therefore new approaches to feature extraction should be sought after with more adequate methods for each signal. Some research devote most of the work to performing feature extraction correctly, therefore a comparison of different feature extraction methods is recommended in order to correctly represent signals for the feature selection process.

If this algorithm, or any other, is intended to be implemented as a valid screening method, it must meet minimum requirements. First, is has to be precise. Second, it has to be easier to perform than the gold-standard, less resource consuming and independent of clinician supervision. The proposed method in this research actually meets some of these requirements. But there is a third requirement, not less important: clinicians must trust the screening test in order to actually prescribe it.

As previously mentioned, as far as this research went, no documented work uses any of the resulting signals (EMG Chin, EOG, Leg Movement) alone or combined with others for prediagnosis. This is mainly because these signals are not the main source of information in a regular diagnosis process, so is necessary to check doctor's opinion and their disposition to prescribe this kind of clinical test.

Acknowledgment

This work was financed by CONICYT - IDeA FONDEF programme, project code: CA13i-10300. Also, authors would like to thank the continuous support of "Instituto Sistemas Complejos de Ingeniería" (ICM: P-05-004- F, CONICYT: FBO16).

Last but not least, we would like to thank Dr. Pablo Brockmann and his team at Clinical Hospital from Pontifical Catholic University of Chile and Ivan Videla at Business Intelligence Research Center from University of Chile for his comments on the manuscript.

References

Álvarez-Estévez, D., & Moret-Bonillo, V. (2009). Fuzzy reasoning used to detect apneic events in the sleep apnea-hypopnea syndrome. *Expert Systems with Applications, 36*, 7778–7785.

Chang, L., Wu, J., & Cao, L. (2012). Combination of symptoms and oxygen desaturation index in predicting childhood obstructive sleep apnea . *International journal of pediatric otorhinolaryngology, 77*(3), 365–371.

Chung, F., Liao, P., Elsaid, H., Islam, S., Shapiro, C. M., & Sun, Y. (2012). Oxygen desaturation index from nocturnal oximetry: a sensitive and specific tool to detect sleep-disordered breathing in surgical patients. *Anesthesia & Analgesia, 114*, 993–1000.

De Chazal, P., Heneghan, C., Sheridan, E., Reilly, R., Nolan, P., & O'Malley, M. (2003). Automated processing of the single-lead electrocardiogram for the detection of obstructive sleep apnoea. *IEEE Transactions on Biomedical Engineering, 50*, 686–696.

Driver, H. S., Pereira, E. J., Bjerring, K., Toop, F., Stewart, S. C., Munt, P. W., & Fitzpatrick, M. F. (2011). Validation of the medibyte type 3 portable monitor compared with polysomnography for screening of obstructive sleep apnea. *Canadian Respiratory Journal: Journal of the Canadian Thoracic Society, 18*, 137.

Echeverría, M., Jimenez-Molina, A., & Ríos, S. A. (2015). A semantic framework for continuous u-health services provisioning. *Procedia Computer Science, 60*, 603–612.

Erazo, L., & Ríos, S. A. (2014). A benchmark on automatic obstructive sleep apnea screening algorithms in children. *Procedia Computer Science, 35*, 739–746.

Flemons, W. W., Littner, M. R., Rowley, J. A., Gay, P., Anderson, W. M., Hudgel, D. W., et al. (2003). Home diagnosis of sleep apnea: A systematic review of the literaturean evidence review cosponsored by the american academy of sleep medicine, the american college of chest physicians, and the american thoracic society. *CHEST Journal, 124*, 1543–1579.

General, A. (2005). International classification of sleep disorders, 2nd edn.: Diagnostic and coding manual. westchester, illinois: American academy of sleep medicine, 2005. broughton r. pathological fragmentary myoclonus, intensified sleep starts and hypnagogic foot tremor: three unusual sleep related disorders. *Sleep, 28*, 113–121.

Goldstein, N. A., Pugazhendhi, V., Rao, S. M., Weedon, J., Campbell, T. F., Goldman, A. C., et al. (2004). Clinical assessment of pediatric obstructive sleep apnea. *Pediatrics, 114*, 33–43.

Goodwin, J. L., Babar, S. I., Kaemingk, K. L., Rosen, G. M., Morgan, W. J., Sherrill, D. L., et al. (2003a). Symptoms related to sleep-disordered breathing in white and hispanic children. the tucson childrens assessment of sleep apnea study. *CHEST Journal, 124*, 196–203.

Goodwin, J. L., Kaemingk, K. L., Fregosi, R. F., Rosen, G. M., Morgan, W. J., Sherrill, D. L., et al. (2003b). Clinical outcomes associated with sleep-disordered breathing in caucasian and hispanic children. the tucson childrens assessment of sleep apnea study (tucasa). *Sleep Disordered Breathing, 26*, 587–591.

Jarvis, M., & Mitra, P. (2000). Apnea patients characterized by 0.02 hz peak in the multitaper spectrogram of electrocardiogram signals. In *Computers in cardiology 2000* (pp. 769–772).IEEE.

Khandoker, A. H., Palaniswami, M., & Karmakar, C. K. (2009). Support vector machines for automated recognition of obstructive sleep apnea syndrome from ecg recordings. *Information Technology in Biomedicine, IEEE Transactions on, 13*, 37–48.

Levy, P., Bonsignore, M., & Eckel, J. (2009). Sleep, sleep-disordered breathing and metabolic consequences. *European Respiratory Journal, 34*, 243–260.

de la Luz Alonso Álvarez, M., Santos, J. T., Guevara, J. C., Martínez, M. G., Pascual, L. R., Ba nuelos, J. L. V., et al. (2008). Reliability of home respiratory polygraphy for the diagnosis of sleep apnea-hypopnea syndrome. analysis of costs. *Archivos de Bronconeumología (English Edition), 44*, 22–28.

Mendez, M. O., Ruini, D. D., Villantieri, O. P., Matteucci, M., Penzel, T., Cerutti, S., et al. (2007). Detection of sleep apnea from surface ecg based on features extracted by an autoregressive model. In *Engineering in medicine and biology society, 2007. embs 2007. 29th annual international conference of the ieee* (pp. 6105–6108).IEEE.

Noehren, A., Brockmann, P. E., Urschitz, M. S., Sokollik, C., Schlaud, M., & Poets, C. F. (2010). Detection of respiratory events using pulse rate in children with and without obstructive sleep apnea. *Pediatric pulmonology, 45*, 459–468.

Roche, F., Pichot, V., Sforza, E., Duverney, D., Costes, F., Garet, M., et al. (2003). Predicting sleep apnoea syndrome from heart period: a time-frequency wavelet analysis. *European Respiratory Journal, 22*, 937–942.

Rosen, C. L., Palermo, T. M., Larkin, E. K., & Redline, S. (2002). Health-related quality of life and sleep-disordered breathing in children. *Sleep, 25*, 657–666.

Tsai, C.-M., Kang, C.-H., Su, M.-C., Lin, H.-C., Huang, E.-Y., Chen, C.-C., et al. (2013). Usefulness of desaturation index for the assessment of obstructive sleep apnea syndrome in children. *International journal of pediatric otorhinolaryngology, 77*(8), 1286–1290.