

# Discrimination of sleep apnea related decreases in the amplitude fluctuations of PPG signal in children by HRV analysis

Eduardo Gil, Martín Mendez, José María Vergara, Sergio Cerutti, *Fellow Member, IEEE*,  
Anna Maria Bianchi, *Member, IEEE*, and Pablo Laguna, *Senior Member, IEEE*

**Abstract**—In this paper, an analysis of HRV during decreases in the amplitude fluctuations of PPG (DAP) events for OSAS screening is presented. 268 selected signal segments around the DAP event were extracted and classified in 5 groups depending on  $\text{SaO}_2$  and respiratory behavior. Four windows around each DAP are defined and temporal evolution of time-frequency HRV parameters were analyzed for OSAS screening. Results show a significant increase in sympathetic activity during DAP events which is higher in cases associated with apnea.

DAP events were classified as apneic or non apneic using a linear discriminant analysis from the HRV indexes. The ratio of DAP events per hour  $r_{\text{DAP}}$  and the ratio of apneic DAP events per hour  $r_{\text{DAP}}^a$  were computed. Results show an accuracy of 79% for  $r_{\text{DAP}}^a$  (12% increase with respect to  $r_{\text{DAP}}$ ) a sensitivity of 87.5% and a specificity of 71.4% when classifying 1-hour polysomnographic excerpts. As for clinical subject classification, an accuracy of 80% (improvement of 6.7%), a sensitivity of 87.5% and a specificity of 71.4% are reached. These results suggest that the combination of DAP and HRV could be an improved alternative for sleep apnea screening from PPG with the added benefit of its low cost and simplicity.

**Index Terms**—Sleep apnea, children, heart rate variability, pulse photoplethysmography, time-frequency, decreases in the amplitude fluctuations of PPG.

## I. INTRODUCTION

**O**BSTRUCTIVE Sleep Apnea Syndrome (OSAS) is one of the most common sleep pathologies with high prevalence among the general population, with levels reaching values as high as 4% for men, 2% for women and 3% for children [1]. Generally, sleep apnea goes undiagnosed, since painful symptoms do not appear and patients do not seek medical aid. The most common sleep apnea indicators are

daytime sleepiness, irritability, tiredness, low concentration and impaired learning [2]. Those factors generally have more serious consequences such as social problems and job and traffic accidents. In addition, OSAS produces hyperactivity and reduced capability to perform mental tasks during childhood [3]. Severe OSAS generates diurnal hypertension and many other potentially fatal cardiovascular effects [4], [5].

OSAS consists in an interruption of the airflow to the lungs produced by an upper airways occlusion. This is accompanied by a decrease of blood oxygen over time and mechanical respiratory efforts that are intensified in order to reopen upper airways. If these efforts are not sufficient and the hypercapnia level is dangerous, an arousal is generated to reactivate all the peripheral systems and respiration is restored. This episode may recur hundreds of times in a single night, with serious health implications [6].

Polysomnography (PSG) is the gold standard procedure for sleep apnea diagnosis. PSG consists in an overnight recording of different electrophysiological signals. The most common signals recorded are electroencephalogram, electromyogram, electrooculogram, electrocardiogram, airflow and oxygen saturation. The acquisition and analysis of those signals requires human experience and specialized equipment. The latter requirements and the reduced number of sleep centers makes sleep diagnosis a very expensive procedure. In addition, sleep diagnosis produces a psychological impact in case of child patients [7]–[9].

In the last decade, application of different techniques for home sleep apnea monitoring has been extensively developed [10]. These techniques range from the most sophisticated technology, such as video recording, to simple measures such as Photoplethysmography signal (PPG). PPG waveform and its relation with physiological systems have been widely studied for clinical physiological monitoring, vascular evaluation and autonomic behavior. PPG is an easily acquired measurement and provides a measure of the tissue blood volume, which is related to arterial vasoconstriction or vasodilatation generated by the autonomic nervous system (ANS) and modulated by the heart cycle. Indeed, PPG envelope amplitude decreases as a consequence of vessel constriction generated by the activation of the sympathetic nervous system. Amplitude reduction in PPG occurs when an apnea event takes place due to sympathovagal balance changes [11], [12].

On the other hand, another electro-physiological signal very broadly studied for apnea diagnosis is heart rate variability

E. Gil and P. Laguna are with the *Communications Technology Group*, Aragón Institute of Engineering Research (I3A), University of Zaragoza and the CIBER de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN). María de Luna 1, 50018 Zaragoza, Spain (e-mail: {edugilh,laguna}@unizar.es). M. Mendez, S. Cerutti and A.M. Bianchi are with the *Department of Biomedical Engineering*, Politecnico di Milano, Italy (e-mail: martin.mendez@biomed.polimi.it, {sergio.cerutti,annamaria.bianchi}@polimi.it). J.M. Vergara is with the *Sleep Department*, Miguel Servet Children Hospital, Zaragoza, and CIBER de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN) Spain (e-mail: vergeur@comz.org). This work was partially supported by: Ministerio de Ciencia y Tecnología, FEDER under Project TEC2007-68076-C02-02/TCM; Heart Cycle project FP7-216695 of the European Community; and Diputación General de Aragón (DGA), Spain, through Grupos Consolidados GTC ref:T30.

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(HRV). HRV represents fluctuations in the heart rate related to ANS control. HRV exhibits frequency components from 0 to 0.5 Hz, which could be associated to the autonomic nervous system branches. The frequency components between 0.15 and 0.5 Hz represent the vagal tone, frequencies in this band are known as high frequency components (HF). Frequencies from 0.04 to 0.15 Hz manifest the activation of both parasympathetic and sympathetic nervous system and these are labeled low frequency components (LF). Finally, frequencies between 0.0033 and 0.04 give information of the slow processes such as thermoregulation. Since the relative participation of parasympathetic and sympathetic nervous in the low frequency component is uncertain, the ratio between HF and LF is defined as the sympatho-vagal balance [13].

Detection of sleep apnea from PPG [14] and HRV [15]–[18] have been explored independently in the literature. Decrements in the amplitude fluctuations of PPG (DAP) events are markers of sympathetic discharge, because sympathetic activity increases produce vasoconstriction which is reflected in the PPG signal by decreases in the signal amplitude fluctuation [19], [20]. When apnea occurs, sympathetic activity increases [11], [12], therefore DAP events could indirectly quantify apneas during sleep. However, other physiological events such as movements and deep inspiratory gasp produce sympathetic activation and consequently decrements in PPG envelope amplitude [21], which are unrelated to apnea. As respiration modulates HR, a HRV analysis could be useful in distinguish whether DAP events are related to apnea or to other different events. So, the apnea identification by applying detection of decrements in the amplitude fluctuations of PPG (DAP) as reference point and further spectral parameters analysis of the HRV around this point could offer an integrative procedure which represents an alternative solution to define apnea episodes and obtain more specific apnea screening.

The aim of this study is to analyze the sympatho-vagal balance during DAPs related and not related to airflow reductions, oxygen desaturations and no apnea episodes in normal and pathologic children. The dynamics of the sympatho-vagal balance is obtained by the analysis of spectral parameters of the HRV applying a Time-Frequency representation called Smooth Pseudo Wigner-Ville Distribution. Furthermore, comparison between apnea screening using only PPG and the combination of PPG and HRV is carried out. Section II introduces materials and methods. Section III presents the results which are discussed in section IV. Finally section V shows the conclusions.

## II. MATERIALS AND METHODS

### A. Data

One complete night polysomnography recordings from 21 children were used in this study. Age of the children ranges around  $4.47 \pm 2.04$  years. Children were referred to the Miguel Servet Children's Hospital in Zaragoza for suspected sleep-disordered breathing. EEG with electrode positions C3, C4, O1 and O2, chin electromyogram, ECG with leads I and II, eye movements, airflow and chest and abdominal respiratory efforts were recorded by a digital polygraph (BITMED

EGP800), according to the standard procedure defined by the American Thoracic Society [22]. PPG and arterial oxygen saturation ( $\text{SaO}_2$ ) were measured continuously using a pulse oximeter (COSMO ETCO2/SpO2 Monitor Novamatrix, Medical Systems). Signals were stored with a sample rate of 100 Hz, only ECG signals were sampled at 500 Hz. OSAS evaluation from PSG data were scored by clinical experts using the standard procedures and criteria [1]. Ten children were diagnosed with OSAS and eleven were diagnosed as normal.

### B. Decreases in the amplitude fluctuation of PPG (DAP) detection

During sleep, apnea or arousal events increase sympathetic tone generating arterial vasoconstriction. Transient sympathetic activations are reflected as DAP [19], [23]. In order to identify DAP events, we applied a detection algorithm based on detecting the envelope reduction of the PPG [14]. A summary of the algorithm steps is presented next. PPG signal ( $x_p(n)$ ) is detrended ( $x_{p_{DC}}(n)$ ) by removing the mean value obtained with a moving average filter. Artifacts were detected in  $x_{p_{DC}}(n)$  by an algorithm based on Hjorth parameters and the artifacted signal segments were rejected. The envelope  $x_e(n)$  of  $x_{p_{DC}}(n)$  is obtained at the artifact free signal segments by:

$$x_e(n) = \sqrt{\frac{1}{N_p} \sum_{k=n-(N_p-1)}^n x_{p_{DC}}^2(k)} \quad (1)$$

Where  $N_p$  is the number of samples in two cardiac cycles. This was selected according to the results in Gil et. al. [14]. A DAP event is identified at time  $n$  when  $x_e(n)$  is lower than a pre-defined adaptive threshold and this situation has a minimum duration. This adaptive threshold is updated when neither DAP event nor artifacts are present and is calculated as a percentage of the mean of the last  $L_p$  non artifacted samples of the envelope  $x_e(n)$ .

### C. DAP clustering criteria related to apnea signs

Medical diagnosis consisted in classifying the available records in the database in two groups: normal or pathologic. DAP events for each recording were detected with the procedure described in section II-B and [14] at the PPG signal. Segments from ECG, PPG,  $\text{SaO}_2$ , air flow and abdominal effort centered at the DAP event onset and lasting 5 minutes were extracted, and from here denoted as DAP events. From these events, those who had clear signatures were taken to obtain five different groups with uniform patterns based on the gold standard criterion for defining sleep apneas [1]. DAP event is classified into: Group 1 ( $G_1$ ) when  $\text{SaO}_2$  decreases by at least 3% and there is not a clear reduction in airflow signal. Group 2 ( $G_2$ ) when airflow decreases by at least 50% with respect to the baseline for a minimum duration of 5 seconds. Group 3 ( $G_3$ ) when airflow reduces by more than 50% from base line and is accompanied by a reduction in  $\text{SaO}_2$  of at least 3%. Group 4 ( $G_4$ ) when DAP event correlated neither to airflow reduction nor  $\text{SaO}_2$  decrement. Finally, Group 5 ( $G_5$ ) when DAP events are related neither to apneas nor to  $\text{SaO}_2$

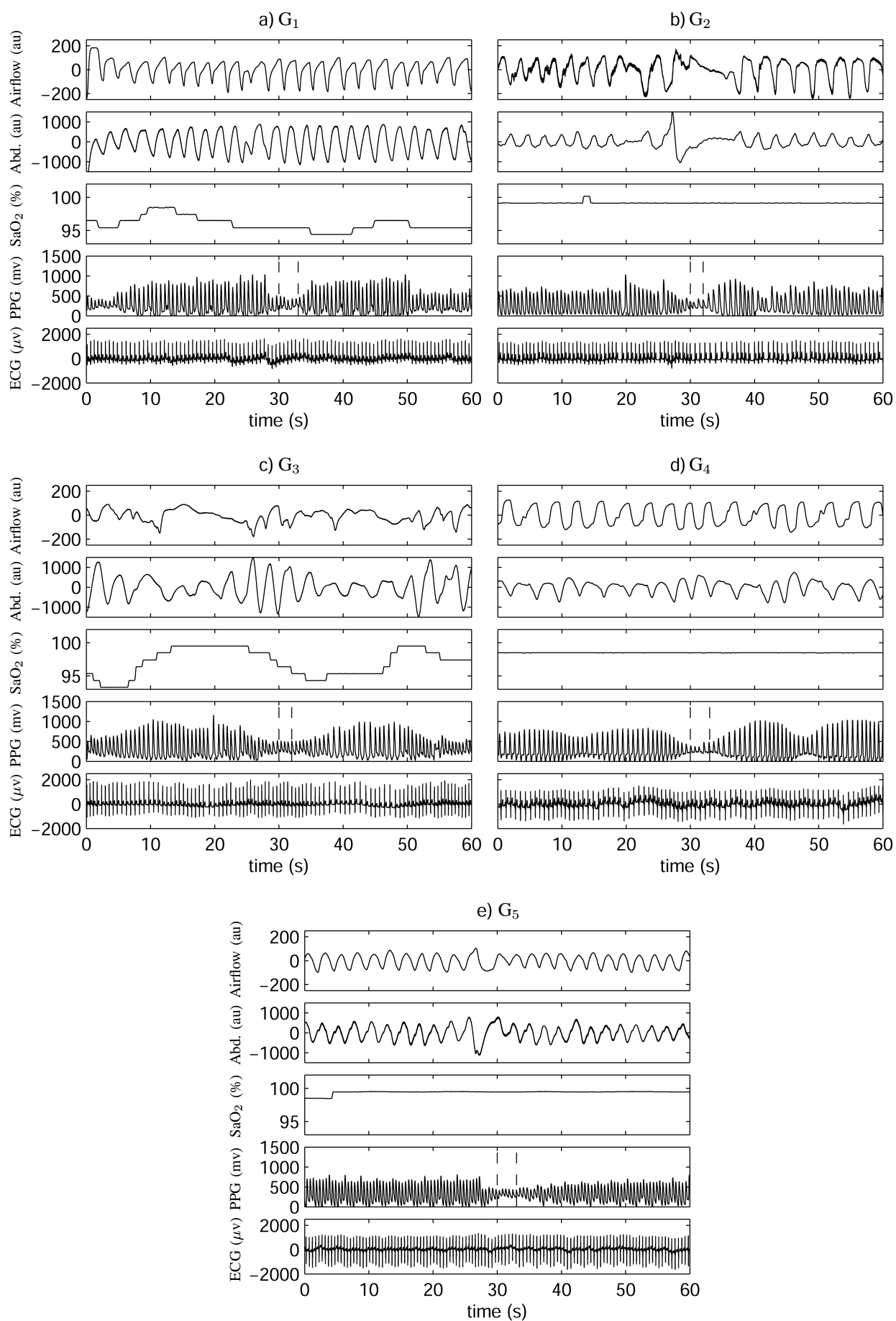


Fig. 1. DAP events examples. The DAP event onset and end (as given by the detector) are marked with dashed lines.

TABLE I  
NUMBER OF DAP EVENTS IN EACH GROUP

Clinical Diagnosis	DAP group					Total
	G <sub>1</sub>	G <sub>2</sub>	G <sub>3</sub>	G <sub>4</sub>	G <sub>5</sub>	
Normal	4	32	5	76	31	148
OSAS	44	21	33	11	11	120
Total	48	53	38	87	42	268

decrements but a change in respiration occurs. Figure 1 shows typical examples of airflow, abdominal efforts, SaO<sub>2</sub>, PPG and ECG for the different groups. G<sub>1</sub>, G<sub>2</sub> and G<sub>3</sub> can be merged in a single group named G<sub>a</sub> (apneic group) as well as G<sub>4</sub> and G<sub>5</sub> can also be regrouped in a single set, G<sub>n</sub> (non apneic group). A total of 268 DAP events were extracted. Table I shows a summary of the DAP events in each group.

Notice that G<sub>2</sub> group has a comparable number of events belonging to subjects clinically classified as normal or OSAS, while more could have been expected for OSAS. The reason could be that oxygen desaturation is a leading parameter for clinical diagnosis, so these G<sub>2</sub> events, which do not have a strong impact on SaO<sub>2</sub>, do not necessarily lead to OSAS label explaining this apparent inconsistency.

#### D. HRV analysis

Inverse interval function  $d_{\text{IFF}}(t_j)$  [24] denoting the heart rate time series were extracted from the ECG segments by an automatic QRS detector [25] providing the  $t_j$  beat location for every  $j$ th beat.  $d_{\text{IFF}}(t_j)$  series were re-sampled at 2 Hz by cubic spline interpolation. Resulting time series, were detrended by subtracting the mean value. Subsequently, analytic signals from each segment were obtained by applying the Hilbert transform to the detrended series. After that, Time-Frequency representation was used to decompose the signals in their different frequencies at each time. Then, the time evolution of the heart rate variability indexes was evaluated: total power, from 0.0033 to 0.5 Hz ( $\mathcal{P}_T$ ); very low frequency power, from 0.0033 to 0.04 Hz ( $\mathcal{P}_{\text{VLF}}$ ); low frequency power, from 0.04 to 0.15 Hz ( $\mathcal{P}_{\text{LF}}$ ); high frequency power, from 0.15 to 0.5 Hz ( $\mathcal{P}_{\text{HF}}$ ); and low to high frequency ratio ( $\mathcal{R}_{\text{LF/HF}}$ ). The representations and the spectral indexes were obtained using the absolute values of the time-frequency distributions.

Time-Frequency analysis presents interesting mathematic features to analyze short time series with high time-frequency resolution. In our study, a good time resolution is required because apneas in children present rapid changes. Therefore, Cohen's class time-frequency distributions were considered. This class obeys the property of time and frequency shift invariant [26]. Cohen's class is defined by the next equation:

$$C_x(t, f) = \int \int \phi(t - t', \tau) x(t' - \frac{\tau}{2}) x(t' + \frac{\tau}{2}) e^{-2\pi f \tau} dt' d\tau \quad (2)$$

Where  $\phi(t - t', \tau)$  is a function labeled kernel and  $x(t)$  is the analytic signal to be analyzed. The kernel properties define the distribution properties. A specific kernel univocally defines a distribution. The kernel is a bi-dimensions filter, the purpose of which is to eliminate noisy energy components generated by the quadratic nature of the distribution. Those

spurious components are known as cross-terms, and disturb the energy signal interpretation in the time-frequency plane. In this study, the kernel used for minimizing the cross-term errors effect was the Smooth Pseudo Wigner-Ville Distribution (SPWVD). This distribution was introduced by Martin W. and Flandrin P. in 1985 [27] and is characterized by independent smoothing functions in time and in frequency, originated by  $\varphi(t)$  and  $\eta(\frac{\tau}{2})\eta^*(-\frac{\tau}{2})$  windows respectively.

$$\phi(t, \tau) = \varphi(t)\eta(\frac{\tau}{2})\eta^*(-\frac{\tau}{2}) \quad (3)$$

The SPWVD parameters were selected in order to allow us to evaluate the spectral components of the heart rate variability with high time and frequency resolution [28], and on the basis of recommendations and experimental results reported in previous studies [29], [30]. For smoothing in time,  $\varphi(t)$ , a Hamming window of 10.5 seconds was selected, whereas for smoothing in frequency,  $\eta(\frac{\tau}{2})$ , a Hamming window of 64.5 seconds was used.

#### E. Statistical Analysis and Classification

1) *Statistical Analysis*: In order to quantify the evolution of autonomic variations when a DAP event is associated or not associated to airflow decrements, SaO<sub>2</sub> reductions or to nothing, four time windows were defined in specific time intervals related to DAP events onset. Figure 2 shows the mean of the  $d_{\text{IFF}}$  sequences when DAP is related or not related to an apneic episode, as well as the windows defined in relation to DAP event. Time 0 s is assigned to DAP onset. The time windows are defined as follows: a) Reference window ( $w_r$ ) is located 15 seconds previous to the DAP event onset with a duration of 5 s. b) DAP episode window ( $w_d$ ) is found two seconds before the DAP onset and lasting 5 s. c) Post DAP event window ( $w_p$ ) located 15 seconds after DAP onset and lasting 5 s. d) Global window ( $w_g$ ) starting at 20 seconds previous to the DAP onset, lasting 40 s and containing the others windows. Mean absolute values in the time windows were computed for  $d_{\text{IFF}}$  sequences,  $\mathcal{P}_{\text{VLF}}$ ,  $\mathcal{P}_{\text{LF}}$ ,  $\mathcal{P}_{\text{HF}}$  and  $\mathcal{R}_{\text{LF/HF}}$  as well as for the normalized versions with respect to the total power  $\mathcal{P}_{\text{VLF}_n}$ ,  $\mathcal{P}_{\text{LF}_n}$  and  $\mathcal{P}_{\text{HF}_n}$ . Kruskal-Wallis non parametric statistic approach was performed in two cases: one, to compare the time variations among windows of HRV parameters, and the other, to compare differences among groups for each parameter and window. Post-hoc analysis was applied to determine which pairs had statistic differences ( $p < 0.05$ ).

2) *Features Sets*: From the grouped groups were extracted a series of features in order to select a set of them that could provide separation between normal (apneic unrelated) and apneic (apneic related) DAP events. The set of features is formed by the mean and the variance within the four different windows ( $w_r$ ,  $w_d$ ,  $w_p$  and  $w_g$ ) referred to the DAP detection of  $d_{\text{IFF}}$ ,  $\mathcal{P}_{\text{LF}_n}$ ,  $\mathcal{P}_{\text{HF}_n}$ ,  $\mathcal{R}_{\text{LF/HF}}$  indexes. In addition, for each index the difference between reference,  $w_r$ , and DAP episode window,  $w_d$ , as well as between  $w_r$  and post DAP event window,  $w_p$ , was computed. In order to reduce the biovariability in  $d_{\text{IFF}}$  temporal indexes, signal were first normalized by subtracting the mean value and dividing by the variance during the

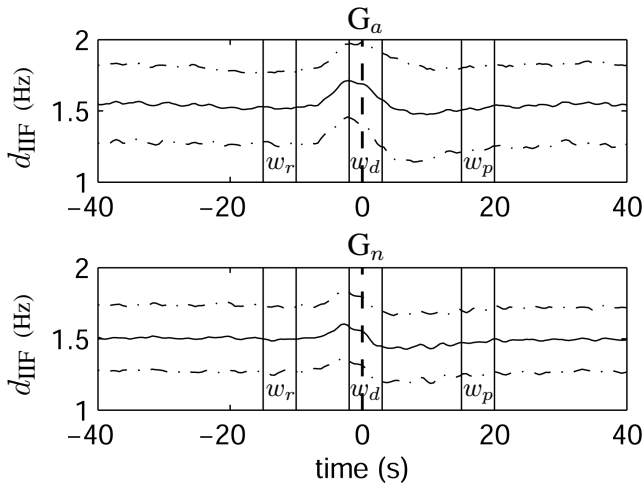


Fig. 2.  $d_{III}$  mean  $\pm$  S.D. for apneic ( $G_a \equiv G_1+G_2+G_3$ ) and non-apneic ( $G_n \equiv G_4+G_5$ ) DAP events. Analysis windows (r reference, d DAP episode, p post DAP event). Dashed line at reference time indicate DAP onset.

complete (5 minutes) DAP event. Spectral indexes normalized with respect to the total power were used. Features are denoted as either  $\overline{X}_n^w$ ,  $\sigma_{X_n^w}$  or  $\Delta \overline{X}_n^{w_1-w_2}$  where the overline and  $\sigma$  denote the mean and variance respectively,  $X$  the main index, with  $X \in \{d_{III}, P_{LF}, P_{HF}, R_{LF/HF}\}$ , the subscript  $n$  the normalized version and the superscript  $w$  the analysis window ( $w_r$  for reference,  $w_d$  for DAP episode,  $w_p$  for post DAP event and  $g$  for global),  $\Delta$  indicate a differential index and in this case  $w_1$  and  $w_2$  denote the two windows involved. A total of 34 features were extracted.

3) *Classifier*: A linear discriminant analysis was used to separate between DAP events related and not related to apnea episodes ( $G_a$  and  $G_n$ ). Let  $\mathbf{y}_i = [y_{1i}, y_{2i}, \dots, y_{di}]$  be a row vector with  $d$  values where each column represents a feature value from  $i$ th DAP. And suppose we wish to assign  $\mathbf{y}_i$  to class  $k$  of the  $c$  possible classes, then the discriminant value  $f_k$  for each class is evaluated from the following equation:

$$f_k = \mu_k \Sigma^{-1} \mathbf{y}_i^T - \frac{1}{2} \mu_k \Sigma^{-1} \mu_k^T + \log(\pi_k) \quad (4)$$

where  $T$  represents the transpose and  $\mu_k$  is the row mean vector obtained from the whole  $N_k$  training vectors belonging to class  $k$ . In order to evaluate  $\mu_k$  let  $N$ , be the total number of  $\mathbf{y}_i$  in the training set, then  $\mu_k$  is obtained by:

$$\mu_k = \frac{1}{N_k} \sum_{i=1}^{N_k} \mathbf{y}_{ik} \quad (5)$$

For an LD classifier  $\Sigma$  represents the pooled covariance and its is evaluated as:

$$\Sigma = \frac{1}{N-c} \sum_{k=1}^c \sum_{i=1}^{N_k} (\mathbf{y}_{ik} - \mu_k)^T (\mathbf{x}_{ik} - \mu_k) \quad (6)$$

$\pi_k$  represent the prior probability that  $\mathbf{y}_i$  belongs to a class  $k$ . A practical way to evaluate  $\pi_k$  is :

$$\pi_k = \frac{N_k}{N} \quad (7)$$

Finally  $\mathbf{y}_i$  is assigned to the class,  $k$  with higher  $f_k$ .

TABLE II  
PSG FRAGMENTS CLASSIFICATION

Clinical diagnosis	# subjects	# fragments	PSG fragments classification		
			# normal	# doubt	# pathologic
Normal	10	46	42	4	0
Pathologic	11	59	28	20	11
Total	21	105	70	24	11

4) *Selection and Transformation of the Features*: Feature selection can be addressed in different ways, it being possible to evaluate it by statistical analysis of features, wrap methods, Principal Component Analysis or Factor Analysis. Wrap methods consist in selecting the features based on the classifier performance by gradually adding one more feature and selecting the combination which provides the highest classification accuracy. The wrap method was used in this work.

#### F. Clinical Study

To evaluate the improvement of adding HRV information for OSAS diagnosis based on PPG, a clinical study was carried out. The available one night PSG recordings described in section II-A were split into 1-hour length fragments. These one hour PSG fragments were labeled as control, doubt or pathologic based on  $\text{SaO}_2$  desaturation in order to later be able to evaluate the classifier accuracy for these fragments. To establish this separation, a baseline level  $\beta$  corresponding to the  $\text{SaO}_2$  signal mode of the entire night recording, was considered [14]. In all recordings  $\beta \geq 97\%$ . Total time intervals with  $\text{SaO}_2$  signal below  $\beta - 3\%$ ,  $t_{\beta-3}$ , was calculated for each fragment. PSG fragments were classified according to the following criteria:

$$\begin{aligned} t_{\beta-3} < 0.9 \text{ minutes} & \quad \text{control} \\ 0.9 \text{ minutes} < t_{\beta-3} < 3 \text{ minutes} & \quad \text{doubt} \\ t_{\beta-3} > 3 \text{ minutes} & \quad \text{pathologic} \end{aligned} \quad (8)$$

This implies a minimum of 5% of the time with evident oxygen desaturation to be considered as pathologic, which corresponds to a severe OSAS criteria in children [31] of 18 apneas/hour having a mean duration of 10 seconds. For control group the threshold corresponds to 5 apneas/hour. Table II shows the classification for these PSG fragments.

Now the objective is to classify these one hour fragments based on the DAP per hour ratio. This classification will be done both just with the DAP coming from the DAP detector in section II-B,  $r_{\text{DAP}}$ , and with those classified as apneic DAP events with the methodology presented in II-E,  $r_{\text{DAP}}^a$ . For training the classifier, DAP events in II-C selected from groups  $G_1$  to  $G_5$ , were used. ROC curves were calculated for both indexes and the optimum thresholds in terms of maximizing sensitivity ( $Se$ ) and specificity ( $Sp$ ), were established. In addition, Wilcoxon non parametric statistical analysis was carried out for both indexes in order to evaluate their discriminant power between groups.

Since we are interested in having a label attached to a patient, we need a rule to determine when a patient with a given number of pathological fragments is considered as

TABLE III

KRUSKAL-WALLIS ANALYSIS RESULTS OF STATISTICAL COMPARISON AMONG GROUPS FOR EACH FEATURE. FIRST ROW IS THE  $p$  VALUE TEST. THE REMAINING ROWS SHOW A NUMBER (OR NUMBERS) INDICATING WHICH GROUP (OR GROUPS) HAS STATISTICAL DIFFERENCES WITH THE GROUP ASSOCIATED TO THE ROW (FIRST ROW ELEMENT).

	$\sigma_{d_{\text{HF}_n}^{w_r}}$	$\sigma_{d_{\text{HF}_n}^{w_d}}$	$\sigma_{d_{\text{HF}_n}^{w_p}}$	$\sigma_{d_{\text{HF}_n}^{w_g}}$	$\bar{d}_{\text{HF}_n}^{w_r}$	$\bar{d}_{\text{HF}_n}^{w_d}$	$\bar{d}_{\text{HF}_n}^{w_p}$	$\bar{d}_{\text{HF}_n}^{w_g}$	$\Delta \bar{d}_{\text{HF}_n}^{w_r-w_d}$	$\Delta \bar{d}_{\text{HF}_n}^{w_r-w_p}$
$p$	0,015	<0,0001	0,085	0,0002	0,194	<0,0001	0,309	0,48	<0,0001	0,435
G <sub>1</sub>	-	-	-	-	-	4	-	-	4	-
G <sub>2</sub>	-	4 5	-	-	-	4	-	-	4	-
G <sub>3</sub>	-	4 5	-	5	-	4	-	-	4	-
G <sub>4</sub>	-	2 3	-	5	-	1 2 3 5	-	-	1 2 3	-
G <sub>5</sub>	-	2 3	-	3 4	-	4	-	-	-	-

	$\bar{\mathcal{P}}_{\text{LF}_n}^{w_r}$	$\bar{\mathcal{P}}_{\text{LF}_n}^{w_d}$	$\bar{\mathcal{P}}_{\text{LF}_n}^{w_p}$	$\bar{\mathcal{P}}_{\text{LF}_n}^{w_g}$	$\Delta \bar{\mathcal{P}}_{\text{LF}_n}^{w_r-w_d}$	$\Delta \bar{\mathcal{P}}_{\text{LF}_n}^{w_r-w_p}$	$\bar{\mathcal{P}}_{\text{HF}_n}^{w_r}$	$\bar{\mathcal{P}}_{\text{HF}_n}^{w_d}$	$\bar{\mathcal{P}}_{\text{HF}_n}^{w_p}$	$\bar{\mathcal{P}}_{\text{HF}_n}^{w_g}$	$\Delta \bar{\mathcal{P}}_{\text{HF}_n}^{w_r-w_d}$	$\Delta \bar{\mathcal{P}}_{\text{HF}_n}^{w_r-w_p}$
$p$	0,0039	0,017	0,0047	0,0006	0,297	0,484	<0,0001	<0,0001	<0,0001	<0,0001	0,032	0,218
G <sub>1</sub>	-	-	-	-	-	-	4	4	4	4	-	-
G <sub>2</sub>	-	-	-	4	-	-	4	4	4 5	4	-	-
G <sub>3</sub>	4	4	4	4	-	-	4	4	4 5	4 5	-	-
G <sub>4</sub>	3	3	3	2 3	-	-	1 2 3 5	1 2 3 5	1 2 3	1 2 3	-	-
G <sub>5</sub>	-	-	-	-	-	-	4	4	2 3	3	-	-

	$\bar{\mathcal{R}}_{\text{LF/HF}}^{w_r}$	$\bar{\mathcal{R}}_{\text{LF/HF}}^{w_d}$	$\bar{\mathcal{R}}_{\text{LF/HF}}^{w_p}$	$\bar{\mathcal{R}}_{\text{LF/HF}}^{w_g}$	$\Delta \bar{\mathcal{R}}_{\text{LF/HF}}^{w_r-w_d}$	$\Delta \bar{\mathcal{R}}_{\text{LF/HF}}^{w_r-w_p}$	$\bar{\mathcal{P}}_{\text{VLF}_n}^{w_r}$	$\bar{\mathcal{P}}_{\text{VLF}_n}^{w_d}$	$\bar{\mathcal{P}}_{\text{VLF}_n}^{w_p}$	$\bar{\mathcal{P}}_{\text{VLF}_n}^{w_g}$	$\Delta \bar{\mathcal{P}}_{\text{VLF}_n}^{w_r-w_d}$	$\Delta \bar{\mathcal{P}}_{\text{VLF}_n}^{w_r-w_p}$
$p$	<0,0001	<0,0001	<0,0001	<0,0001	<0,0001	0,341	0,0007	<0,0001	<0,0001	<0,0001	0,38	0,668
G <sub>1</sub>	4	4	-	4	4	-	4	4	4	4	-	-
G <sub>2</sub>	4	4	4	4	4	-	4	4	4	4	-	-
G <sub>3</sub>	4	4	4 5	4 5	-	-	4	4	4	4	-	-
G <sub>4</sub>	1 2 3 5	1 2 3 5	2 3 5	1 2 3	1 2	-	1 2 3	1 2 3 5	1 2 3	1 2 3	-	-
G <sub>5</sub>	4	4	3 4	3	-	-	-	4	-	-	-	-

a pathologic subject. For that, the percentage of time under pathologic fragments based on  $r_{\text{DAP}}$  and  $r_{\text{DAP}}^a$  was analysed. The threshold for this percentage was selected for maximizing  $Se$  and  $Sp$ . From the total of 21 children, six subject were excluded because only less than 4 hours had ECG and PPG signals of acceptable quality, so 15 registers were included in this study corresponding to 8 OSAS and 7 normal according to clinical diagnosis.

### III. RESULTS

#### A. Statistical Analysis Results

Table III shows Kruskal-Wallis analysis results of statistical comparison among groups for each feature. First row is the  $p$  value test. The remaining rows show a number (or numbers) indicating which group (or groups) has statistical differences with the group defining the row.

Figure 3 shows mean and standard error of  $\bar{d}_{\text{HF}_n}$ ,  $\sigma_{d_{\text{HF}_n}}$  and spectral indexes obtained by smooth pseudo Wigner-Ville distribution. Letters refers to the temporal windows analyzed during DAP (r reference, d DAP episode, p post DAP event). From the top to the bottom, mean heart rate ( $\bar{d}_{\text{HF}_n}$ ), standard deviation heart rate ( $\sigma_{d_{\text{HF}_n}}$ ), low frequency ( $\bar{\mathcal{P}}_{\text{LF}_n}$ ), high frequency ( $\bar{\mathcal{P}}_{\text{HF}_n}$ ) and low to high frequency ratio ( $\bar{\mathcal{R}}_{\text{LF/HF}}$ ) of heart rate. All the spectral parameters were normalized with respect to the total power at each time. \* refers to  $p < 0.05$  between windows  $w_r$  and  $w_d$  and § to  $p < 0.05$  between windows  $w_d$  and  $w_p$ .

The best features to classify between  $G_a$  and  $G_n$  obtained by the wrap method were  $\bar{\mathcal{P}}_{\text{HF}_n}^{w_g}$ ,  $\bar{\mathcal{R}}_{\text{LF/HF}}^{w_g}$ ,  $\sigma_{d_{\text{HF}_n}^{w_d}}$  and  $\Delta \bar{d}_{\text{HF}_n}^{w_r-w_d}$ , having an accuracy of 68.77%, a  $Se = 70.5\%$  and a  $Sp = 68.46\%$ .

TABLE IV  
PSG FRAGMENTS CLASSIFICATION RESULTS

Index	PSG Fragments classification			Subjects classification		
	$S$ (%)	$Sp$ (%)	Accuracy (%)	$S$ (%)	$Sp$ (%)	Accuracy (%)
$r_{\text{DAP}}$	81.8	64.3	66.7	75	71.4	73.3
$r_{\text{DAP}}^a$	72.7	80	79	87.5	71.4	80

#### B. Clinical Study Results

Results regarding PSG fragments and subject classification are shown in Table IV. The inclusion of HRV information improves the PSG fragments classification accuracy in 12.3%, reaching a 79%, and obtaining values of 72.7% and 80% for sensitivity and specificity, respectively. In addition, the Wilcoxon statistic analysis shows a higher discriminant power between pathologic and normal for  $r_{\text{DAP}}^a$  ( $p = 0.0061$ ) than for  $r_{\text{DAP}}$  ( $p = 0.0225$ ). ROC curves in Fig. 4, varying thresholds in  $r_{\text{DAP}}$  and  $r_{\text{DAP}}^a$ , demonstrate the advantage of including HRV information. As for subject classification, the improvement in accuracy is 6.7%, reaching a 80%, and obtaining values of 87.5% and 71.4% for sensitivity and specificity respectively.

### IV. DISCUSSION

Analysis of autonomic control during decreases in the amplitude fluctuation of photoplethysmography signal in children was presented. Table III shows statistical differences among  $G_1$ ,  $G_2$  and  $G_3$  ( $G_a$ ) with respect to  $G_4$  and  $G_5$  ( $G_n$ ) for most of the features, confirming the association made in section II-C based on the apnea physiology. As for time features,  $\Delta \bar{d}_{\text{HF}_n}^{w_r-w_d}$  evidence a higher rise in  $d_{\text{HF}_n}$  for DAP associated with apneic events ( $G_a$ ) than for DAP without apnea connection ( $G_n$ ). Respiration modulates HR, HF being the

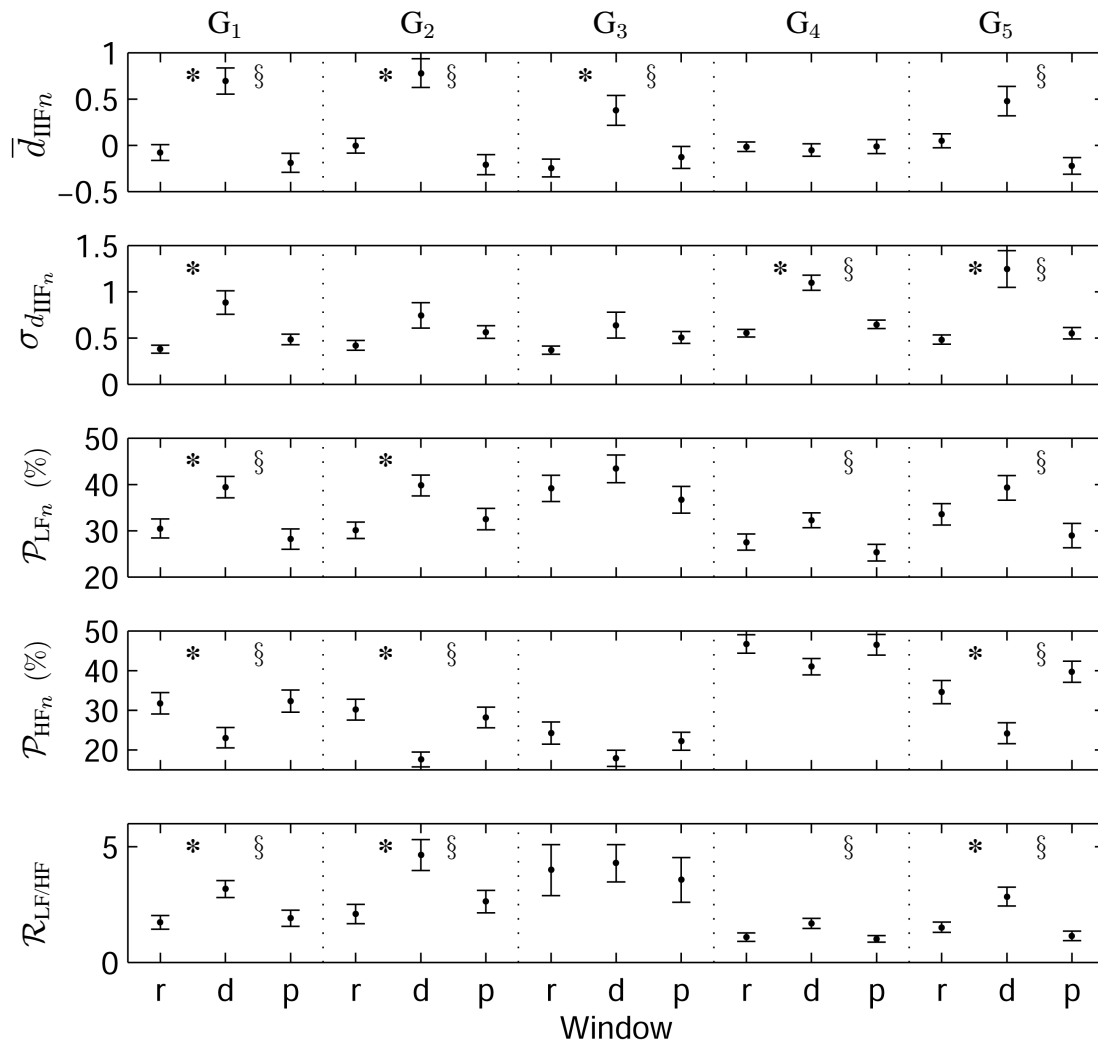


Fig. 3.  $\bar{d}_{III^n} \pm SE$ ;  $\sigma_{d_{III^n}} \pm SE$  and spectral indexes obtained by smooth pseudo Wigner-Ville distribution. Window refers to the temporal windows analyzed during DAP (r reference, d DAP episode, p post DAP event). From the top to the bottom, mean heart rate ( $\bar{d}_{III^n}$ ), standard deviation heart rate ( $\sigma_{d_{III^n}}$ ), low frequency ( $P_{LF^n}$ ), high frequency ( $P_{HF^n}$ ) and low to high frequency ratio ( $R_{LF/HF}$ ) of heart rate. All the spectral parameters were normalized with respect to the total power at each time. \* refers to  $p < 0.05$  between windows  $w_r$  and  $w_d$  and § to  $p < 0.05$  between windows  $w_d$  and  $w_p$ .

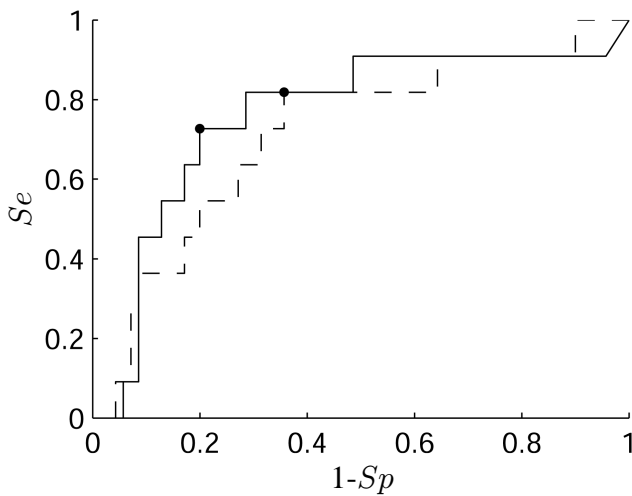


Fig. 4. ROC curves for  $r_{DAP}$  (dashed line) and  $r_{DAP}^a$  (solid line). Bullet dots indicate the points where the global results are presented.

component which mainly reflects the respiratory process. Our hypothesis is that this modulation is different among groups and at the different temporal windows, these differences being the parameters used to distinguish among groups. Results show that differences (higher  $P_{LF^n}$  and lower  $P_{HF^n}$  values) appear in frequency features for all groups with respect to G<sub>4</sub> during all time references ( $w_r$ ,  $w_d$ ,  $w_p$  and  $w_g$ ) indicating a predominance of the sympathetic system during apnea, in agreement with [11], and the fact that different respiratory patterns appear. As  $P_{HF}$  presents higher values in G<sub>4</sub> and important significant statistical differences with G<sub>a</sub>, the feature  $\bar{P}_{HF^n}^{w_g}$  was the first selected by the wrap method for feature selection, section II-E4.

Figure 3 shows increments in the  $d_{III}$  signal during the DAP event window for all groups, except G<sub>4</sub>. Time evolution of frequency features shows similar patterns in all groups, an increase in  $P_{LF^n}$  and  $R_{LF/HF}$  and a decrease in  $P_{HF^n}$  during DAP, indicating an activation of the sympathetic branch of

the ANS followed by a recovery period. However, increments in the  $d_{\text{HF}}$  signal during the DAP event window turn out to be statistically significant with respect to reference and post DAP event window only for groups 1, 2 and 3. This means that changes are better marked for apneic events as indicated  $\Delta \bar{d}_{\text{HF}n}^{w_r - w_d}$  in Table III.  $\mathcal{P}_{\text{LF}n}$  reveals significant increments only during the DAP event window in  $G_1$  and  $G_2$  with respect to reference window and  $G_1$ ,  $G_4$  and  $G_5$  with respect to the post DAP event window. DAP event window shows reduction in the  $\mathcal{P}_{\text{HF}}$  for all groups, however significances are found in  $G_1$ ,  $G_2$  and  $G_5$ .  $\mathcal{R}_{\text{LF/HF}}$  also presents significant differences in those groups, but with an increment in the DAP event window.

Our main findings were: an increase in sympathetic activity occurs during DAP events, in concordance with [19]. When DAP events are not associated to either respiratory events or  $\text{SaO}_2$  decrements, heart rate variability shows just a slight alteration and its spectral power is more shifted to the high frequency component. On the contrary, DAP events associated to apnea produce a stronger variation in heart rate and spectral power is concentrated in the low frequency range. These results suggest that sympathetic activation is deeper in case of association with apnea. The statistical differences between DAP events associated with apnea and those without association indicate that HRV analysis is useful to discriminate between these two groups of events. This has led to better specificity in apnea detection, as corroborated by the clinical study in section III-B.

Photoplethysmography signal carries information related to the cardiovascular function as well as blood gases concentration. This signal presents interesting characteristics that can be used to detect apneic episodes. However, its high sensitivity could produce misdetections and overestimate apneic episodes. Generally, in most of the studies PPG has been directly related with the cardiac function, giving as a result a measure of the Pulse Transit Time (PTT) [32]–[34]. PTT gives a quantitative measure of the time that a pulse wave needs for passing from one arterial to another, and is evaluated as the time interval between the ECG R peak and the start of the corresponding PPG wave. PTT decreases after an apneic event due to a sympathetic activation related to arousal which produces heart rate increment, higher stroke volume and vasoconstriction, which in turn generate pulse wave acceleration [35]. However, some other physiological events such as slow paced breathing [36] and deep inspiratory gasp [37] also induce variation in the PTT that could be mistaken for sympathetic activations. However, this integration loses important information that could be obtained from the heart rate spectral parameters. Heart rate dynamics and spectral parameters offer time and frequency information that discriminates between small cardiovascular variation and more severe ones, as when an apneic episode occurs.

Heart rate control oscillates in a specific range of frequencies. These frequencies characterize autonomic nervous system control, that is activated or inhibited as a result of feedback mechanisms. Under constant conditions such as rest, autonomic control is very regular and RR sequence shows a stationary pattern. This situation allows the application of techniques such as Fourier transform to obtain the spectral

components of the time series. However, under conditions of rapid change such as sit to stand and sleep apnea, autonomic control adapts speedily to satisfy the system requirements, so the RR sequence shows non-stationary behavior. Under such conditions, more sophisticated techniques of signal processing are required to analyze the time evolution of the autonomic control mechanism. Different approaches have been developed to deal with this problem. Time-Frequency [26], Time-Varying [38] and Time-Scale [39] analysis are some of the most powerful tools. In our study, a good time resolution is required because apneas in children present rapid changes. Therefore, Cohen's class time-frequency distributions were considered. For minimizing the cross-term errors effect of these quadratic distributions the Smooth Pseudo Wigner-Ville Distribution was used. The smoothing functions defining the kernel were selected in order to allow us to evaluate the spectral component of heart rate variability with high time and frequency resolution [28].

This methodology could be evolved if the spectral parameters of the heart rate could be extracted from the PPG. In this way, only acquisition of one signal could be enough to analyze sleep apnea episodes. Since PPG signal is a very simple, cheap, and easy to acquire measure, PPG presents great potential for home apnea monitoring, reducing the cost of wearable devices and complex technology for analysis. Processing of PPG signals could be implemented in real time and with a very low computation cost.

Our results fall within the reported interrater reliabilities for sleep scoring [40], where the mean epoch by epoch agreement between five scorers was 73%, and within the inter-observer agreement on apnea-hypopnea index (AHI) using portable monitoring of respiratory parameters [41], where the AHI agreement scored by 8 physicians was 73% measured by intraclass correlation coefficient.

Many studies have been carried out for OSAS screening attempting to reduce PSG cost and complexity. Different techniques have been proposed, oximetry-based screening being one of the most widely suggested for both the adult and pediatric population. Although these methods have high sensitivity, they tend to have very low specificity [42]. In addition, a confounding factor in children is that obstructive events frequently do not lead to significant oxyhemoglobin desaturation. Pulse oximetry in children has the same limitation as in adults [43]. Brouillette et al [44], in an extensive study involving 349 children, obtained a positive predictive value of 97%, but the negative predictive value was only 53%. Other approaches based on ECG [15] have shown very good results for adults, achieving perfect scores of 100% in accuracy for subjects classification. However, few ECG-based studies are aimed at children, for which physiology is different and important differences in sleep disorders exist [22], [31]. Shouldice et al [45] reported a sensitivity of 85.7% and a specificity of 81.8% in an ECG-based study on children by adapting previous research on adults where information of ECG-derived respiratory signal was included. Cardiorespiratory sleep studies that typically include 2 or more signals have also been considered. These studies have been shown to be sensitive to OSAS, but mostly in adults [46].



Some other alternatives, such as nap studies, clinical history, sonography or videography exist [43].

In summary, in terms of sensitivity and specificity, the results of our proposed method are similar to [45] or better than [3], [43], [44] currently investigated alternatives for OSAS screening in children. However, performance improvement to reach the accuracy of adult methods would be desirable, and extended studies are needed to corroborate the potential of our method in diagnosing sleep disorders in children.

## V. CONCLUSION

In conclusion, our results suggest that an increase in sympathetic activity occurs during DAP events. When DAP events are not associated to either respiratory events or  $\text{SaO}_2$  decrements, heart rate variability shows slight alterations, and its spectral power is more shifted to the high frequency component. On the contrary, DAP events associated to apnea produce strong variation in heart rate and spectral power is concentrated in the low frequency range. These results suggest that sympathetic activation is deeper in case of association with apnea.

The ratio  $r_{\text{DAP}}^a$  present an increase of 12% in accuracy for classifying 1-hour polysomnographic segments with respect to  $r_{\text{DAP}}$ , reaching 79% and obtaining values of 72.7% and 80% for sensitivity and specificity, respectively. As for subject classification, the improvement in accuracy is 6.7%, reaching 80%, obtaining values of 87.5% and 71.4% for sensitivity and specificity respectively. Consequently, HRV analysis improves the utility of PPG signal in sleep disorder diagnosis, so that the combination of DAP and HRV could be an alternative for sleep apnea screening with the added benefit of low cost and simplicity. Nevertheless, extended studies are needed to corroborate the potential of PPG signal in conjunction with HRV analysis in diagnosing sleep disorders.

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**Eduardo Gil** was born in Zaragoza, Spain, in 1978. He received the M.S. degree in telecommunication engineering from the University of Zaragoza (UZ) in 2002. In 2003, he started working towards the Ph.D. degree at the Department of Electronic Engineering and Communications, UZ, with a grant supported by the Spanish government. Since 2006, he is an Assistant Professor in the same department. In 2007, he received the master's degree "Master universitario en Sueño: Fisiología y Medicina" from the University Pablo Olavide of Sevilla, Spain. His main

research activity lies in the field of biomedical signal processing, especially in the analysis of the photoplethysmography signal for obstructive sleep apnea diagnosis.



**Martín Mendez** has an Engineer degree in Electronics from the Tecnológico de Aguascalientes, Mex (2001) and has obtained a MSc degree in Bioengineering in 2003 with a thesis on non parametric and non linear analysis of the Heart Rate Variability during Apnoea Manoeuvres. In 2007, he obtain his PhD at the Department of Bioengineering of the Politecnico di Milano. Nowadays, he works in the analysis and classification of bioelectrical signals during Sleep and on related pathologies (such as Sleep Apnoea) using parametric and non parametric

approaches as well as pattern recognition techniques.



**José María Vergara** was born in Vitoria, Spain, in 1952. He received the M.D. from the University of Zaragoza in 1977. Since 1981 he works as Clinical Neurophysiologist at the Miguel Servet Children's Hospital of Zaragoza. In 1990 he obtained the PhD from the University of Zaragoza. Currently he is also Associated Professor at the same university. His main research interest lies in the field of sleep and q-eeg.



**Sergio Cerutti** Sergio Cerutti, Professor in Biomedical Signal and Data Processing at the Department of Biomedical Engineering of the Politecnico di Milano, Italy. He has been the Chairman of the same Department from 2000 to 2006. His research interests are mainly in the following topics: biomedical signal processing (ECG, blood pressure signal and respiration, cardiovascular variability signals, EEG and evoked potentials), cardiovascular modelling, neurosciences, regulation and standards in medical equipments and devices. Since 1983 he has taught a course at a graduate level on Biomedical Signal Processing at Engineering Faculties (Milano and Roma) as well as at Specialisation Schools of Medical Faculties (Milano and Roma). He has been Elected Member of IEEE-EMBS AdCom (Region 8) in the period 1993-1996. He is actually Fellow Member of IEEE and of EAMBES and Associate Editor of IEEE Trans BME. He is a member of the Steering Committee of the IEEE-EMBS Summer School on Biomedical Signal Processing: he was the local organiser of four Summer Schools held in Siena. He is author of more than 400 international scientific contributions (more than 160 on indexed scientific journals).



**Anna M. Bianchi** received the Laurea degree from the Politecnico di Milano in 1987. In the period 1987-2000 she was research assistant in the Lab. of Biomedical Engineering of the IRCCS S.Raffaele Hospital in Milano, where her scientific and research activity was in connection with the Dep. of Biomedical Engineering of the Polytechnic University. Since 2001 she is Research Assistant in the Department of the Biomedical Engineering of the Politecnico di Milano. She is now Assistant Professor of Fundamentals of Electronic Bioengineering in the Biomedical Engineering School and of Biomedical signal and data processing in the PhD course. Since 2004 she is in the board of the PhD program in Bioengineering. She is author of about 50 peer reviewed international papers, and is the local coordinator of a national MIUR project and an European IP Project in the area of biomedical signal processing. She is member of the IEEE-Engineering in Medicine and Biology Society and is reviewer of many international journals on Biomedical Engineering.



**Pablo Laguna** was born in Jaca (Huesca), Spain in 1962. He received the Physics degree (M.S.) and the Doctor in Physic Science degree (Ph.D.) from the Science Faculty at the University of Zaragoza, Spain, in 1985 and 1990, respectively. The Ph.D. thesis was developed at the Biomedical Engineering Division of the Institute of Cybernetics (U.P.C.-C.S.I.C.) under the direction of Pere Caminal. He is Full Professor of Signal Processing and Communications in the Department of Electrical Engineering at the Engineering School, and a researcher at the Aragón Institute for Engineering Research (I3A), both at University of Zaragoza, Spain. From 1992 to 2005 was Associated professor at same University and From 1987 to 1992 he worked as Assistant professor of Automatic control in the Department of Control Engineering at the Politecnico University of Catalonia (U.P.C.), Spain and as a Researcher at the Biomedical Engineering Division of the Institute of Cybernetics (U.P.C.-C.S.I.C.). His professional research interests are in Signal Processing, in particular applied to Biomedical applications. He is, together with L. Sörnmo, the author of *Bioelectrical Signal Processing in and Neurological Applications* (Elsevier, 2005)