



Technical note

Detection of decreases in the amplitude fluctuation of pulse photoplethysmography signal as indication of obstructive sleep apnea syndrome in children

Eduardo Gil ^{a,*}, José María Vergara ^b, Pablo Laguna ^a

^a *Communications Technology Group (GTC), Aragón Institute of Engineering Research (I3A), CIBER-BBN, University of Zaragoza, María de Luna 1, 50018 Zaragoza, Spain*

^b *Sleep Department, Miguel Servet Children Hospital, CIBER-BBN, Zaragoza, Spain*

Received 15 May 2007; received in revised form 5 December 2007; accepted 6 December 2007

Available online 20 February 2008

Abstract

In this paper, a methodology for using pulse photoplethysmography (PPG) signal to automatically detect sleep apnea is proposed. The hypothesis is that decreases in the amplitude fluctuations of PPG (DAP), are originated by discharges of the sympathetic branch of autonomic nervous system, related to arousals caused by apnea. To test this hypothesis, an automatic system to detect DAP events is proposed.

The detector was evaluated using real signals, and tested on a clinical experiment. The overall data set used in the studies includes the polysomnographic records of 26 children which were further subdivided depending on the evaluation of interest. For real signals, the sensitivity and positive predictive value of the DAP detector were 76% and 73%, respectively. An apnea detector has been developed to analyze the relationship between apneas and DAP, indicating that DAP events increase by about 15% when an apnea occurs compared to when apneas do not occur. A clinical study evaluating the diagnostic power of DAP in sleep apnea in children was carried out. The DAP per hour ratio r_{DAP} was statistically significant ($p = 0.033$) in classifying children as either normal $r_{\text{DAP}} = 13.5 \pm 6.35$ (mean \pm S.D.) or pathologic $r_{\text{DAP}} = 21.1 \pm 8.93$.

These results indicate a correlation between apneic events and DAP events, which suggests that DAP events could provide relevant information in sleep studies. Therefore, PPG signals might be useful in the diagnosis of OSAS.

© 2007 Elsevier Ltd. All rights reserved.

Keywords: Obstructive sleep apnea; Pulse photoplethysmography signal; Children

1. Introduction

Obstructive sleep apnea syndrome (OSAS) is characterised by repetitive episodes of upper airway obstruction during sleep, involving periods of breathing cessation [1,2]. The prevalence of OSAS is estimated as 4% in adult men, 2% in adult women, and 2–3% in children, most of whom are undiagnosed and untreated [3]. The resulting sleep fragmentation [4] and blood gas modifications causes malfunctions of sleep-related restorative processes, and induce chemical and structural injuries in the cells of the central nervous system. Not only does that cause daytime sleepiness, but it can also, in turn, lead to systemic hypertension [5] and an increase in the likelihood of

cardiovascular diseases. Childhood is a critical time for acquiring core academic and social skills, and repeated failures related to sleep fragmentation at critical stages of development can fundamentally influence a child's motivation and behavior [6–8]. Currently, the preferred treatment is adenotonsillectomy for most children [9]. The gold standard diagnostic test for OSAS is overnight polysomnography (PSG), which is very involved and so alternatives will be very welcome.

Wall arteries are covered by muscles that contract or relax, which produces arterial constriction or dilatation. That process is regulated by several mechanisms, such as the vegetative system, which determines vascular muscle tone. The dominant system (i.e., sympathetic or parasympathetic) causes blood vessels to contract (vasoconstriction) or dilate (vasodilatation). Several studies suggest that when apnea occurs, sympathetic activity increases. Hypoxia plays a key role in that relationship [10,11]. The increase in sympathetic activity is associated with

* Corresponding author. Tel.: +34 976762360.

E-mail address: edugilh@unizar.es (E. Gil).

vasoconstriction and, possibly, is related to transient arousal [12–16]. Vasoconstriction is reflected in the pulse photoplethysmography (PPG) signal by decreases in the signal amplitude fluctuation [17,18]. Therefore, the hypothesis to be tested in this work is that detection of episodes of PPG attenuation might be useful in indirectly quantifying apneas during sleep. There are already studies about the diagnosis of OSAS based on the detection of vasoconstriction using peripheral arterial tonometry [19–21], which is a similar physiologic signal. The relationship between autonomic nervous system and PPG has also been studied in [18,22].

PPG, which was developed by Hertzman [23], is a simple and useful method for measuring the pulsatile component of the heartbeat and evaluating peripheral circulation. The present study aims to evaluate the usefulness of PPG as a means of diagnosing OSAS. For that we developed a decrease in the amplitude fluctuations of PPG (DAP) detector and made a clinical study to evaluate the correlation between DAP and apneas so to show the usefulness of DAP to diagnose OSAS. To study the relationship between apneas and episodes of DAP, different episodes detectors based on respiratory flow and oxygen saturation (apnea detector), and PPG signals (DAP detector) have been developed.

2. Methods

A scheme of the complete study is presented in Fig. 1. The different sensors and clinical devices are shown in conjunction with the block diagram of the developed signal processing. This processing tool was developed on a PC workstation under MATLAB[®] platform. The complete PSG data, acquired using standard procedures, were used to derive the reference clinical diagnosis. The automatic study is restricted to PPG, oxygen saturation SaO₂ and air flow signals.

2.1. Data sets

2.1.1. Real respiratory data set from adults containing apneic events

A real PSG data set from adults was selected from the ECG-Apnea Data Base available on Physionet, [24], which contains 70 records, each of which includes a continuous digitized ECG signal, a set of apnea annotations (derived by experts on the basis of simultaneously recorded respiration and related signals), and a set of machine-generated QRS annotations. From those records, we selected eight recordings that had four additional signals (chest and abdominal respiratory effort signals obtained using inductance plethysmography, oronasal airflow measured using nasal thermistors, and SaO₂, oxygen saturation). This data set is used to evaluate the respiratory flow reduction stage of the apnea detector.

2.1.2. Real PSG data set from children

A real PSG data set from 26 children was acquired in Miguel Servet Children's Hospital, Zaragoza, Spain, according to the standard methods defined by American Thoracic Society [25], using a commercial digital polygraph (EGP800, Bitmed) and

recording six EEG channels, two electro-oculogram channels, a chin electromyogram channel, an ECG channel, air flow (ornasal thermocoupler), and respiratory plethysmography. PPG and arterial oxygen saturation were recorded continuously by pulse oximetry (COSMO ETCO₂/SpO₂ Monitor Novamatrix, Medical Systems), see Fig. 1. All the signals were stored at a sampling rate of $f_s = 100$ Hz.

The PSG data were gathered from children suspected of having OSAS, and were scored manually following standard procedures [26,25] used to discriminate children suffering from OSAS from those who are not. The procedures and protocols used in this study were approved by the Ethics Committee of the Miguel Servet Children's Hospital of Zaragoza.

Three different subsets of the data set were selected for different substudies according to criteria in Table 1.

2.2. Decreases in the amplitude of PPG (DAP) detector

The first step in this study was the detection of DAP events based on the PPG signal, $x_p(n)$. The DAP detector is intended to detect DAP events based on the envelope of $x_p(n)$. The proposed detector includes PPG pre-processing, an artifact detector, an envelope estimation stage, and a decision rule to identify vasoconstriction reflected on a DAP episode, see Fig. 1(b).

2.2.1. Pre-processing

The mean PPG cardiac cycle length, T , is estimated automatically from the PPG signal, $x_p(n)$, and is used by the detector as a time reference unit. The cardiac cycle is estimated using a zero-crossing detector applied to $x_p(n)$ after being corrected for the mean. The mean is removed by a moving average filter and the resulting signal is denoted by $x_{pDC}(n)$.

2.2.2. PPG artifact detector

An artifact detector based on Hjorth parameters [27–29] was implemented. The principle behind the detector is that when the signal differs largely from an oscillatory signal, it is very likely an artifact, see Fig. 2. One efficient and robust procedure to determine up to what degree the signal is oscillatory comes from the EEG domain, where the Hjorth parameter \mathcal{H}_1 has been proposed as an estimation of the central frequency of a signal and \mathcal{H}_2 as half of the bandwidth.

Hjorth parameters are defined from the i th-order spectral moments \bar{w}_i

$$\bar{w}_i = \int_{-\pi}^{\pi} w^i S_{x_{pDC}}(e^{j\omega}) d\omega, \quad (1)$$

where $S_{x_{pDC}}(e^{j\omega})$ is the power spectrum of $x_{pDC}(n)$, as

$$\mathcal{H}_1(n) = \sqrt{\frac{\bar{w}_2(n)}{\bar{w}_0(n)}} \quad \text{and} \quad \mathcal{H}_2(n) = \sqrt{\frac{\bar{w}_4(n)}{\bar{w}_2(n)} - \frac{\bar{w}_2(n)}{\bar{w}_0(n)}} \quad (2)$$

which can be estimated using the temporal expressions of the moments, made as a function of time n , using a shifting

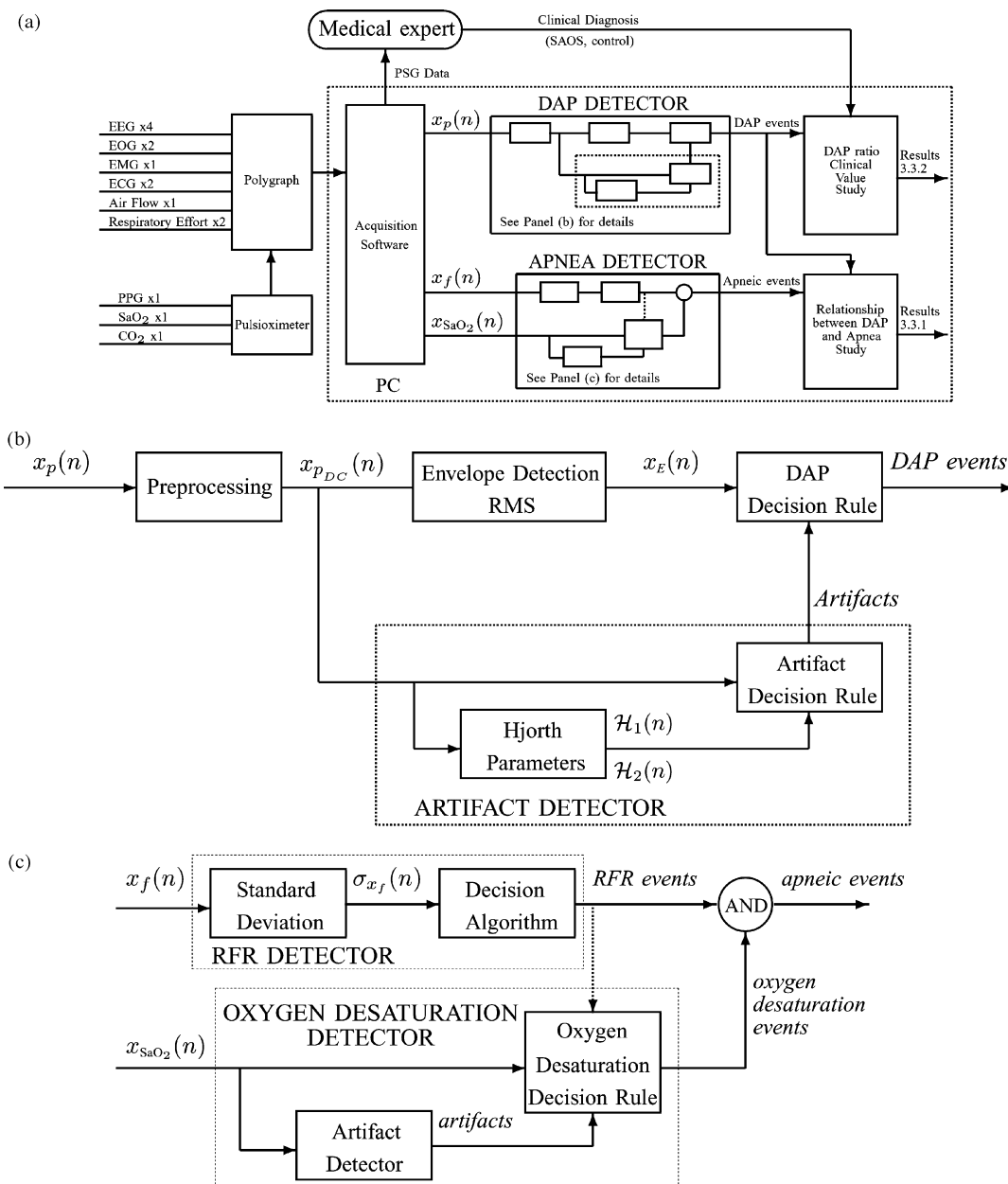


Fig. 1. (a) Scheme of the complete study, $x_p(n)$ is the PPG signal, $x_f(n)$ is the air flow signal and $x_{SaO_2}(n)$ is the oxygen saturation signal. Panel (b) shows the DAP detector diagram; (c) shows apnea detector diagram. Dashed line gives information to the oxygen desaturation detector just to operate when a RFR event appears.

overlapped window of P samples.

$$\hat{w}_i(n) \approx \frac{2\pi}{P} \sum_{k=n-(P-1)}^n \left(x_{pDC}^{(i/2)}(k) \right)^2, \quad i = 0, 2, 4 \quad (3)$$

where $x_{pDC}^{(i/2)}(n)$ is the $i/2$ derivative of $x_{pDC}(n)$, in this case implemented as successive first-order differences on the $x_{pDC}^{(i/2-1)}(n)$ signal.

PPG is an oscillatory signal that shows a marked cyclical pattern synchronized with heart rate, see Fig. 2(a and b). When artifacts are present this property is lost, (c and d). Two thresholds for $\mathcal{H}_1(n)$ series, η_1^l and η_1^u , have been defined.

When the PPG main frequency differs clearly from heart rate frequency, $\mathcal{H}_1(n) \leq \eta_1^l$ or $\mathcal{H}_1(n) \geq \eta_1^u$, the sample n is considered as artifact, see (e). One threshold for $\mathcal{H}_2(n)$ series, η_2 , has been defined. When PPG does not have a oscillatory pattern, it also presents a wider spectrum, $\mathcal{H}_2(n) \geq \eta_2$, and the sample n is also considered as artifact, see (f).

2.2.3. Envelope estimation

The objective is to obtain an envelope signal, $x_E(n)$, to be compared to a threshold in the subsequent decision rule, see below. The method implemented is based on the root mean square (RMS) series.

Table 1
Characteristic of the data subsets

	Data set		
	Data set I	Data set II	Data set III
Studies in which the data set is used	DAP detector evaluation	Relationship between DAP and apneas	DAP ratio clinical value r_{DAP}
#	9	13	22
Age (mean \pm S.D.) (years)	3.88 ± 1.92	4.85 ± 2.53	4.52 ± 1.77
Sex (boys/girls)	5/4	8/5	15/7
Mean length (h)	7.30	7.34	7.37
Clinical diagnosis (OSAS/doubt/control)	(5/3/1)	(5/1/7)	(11/0/11)
Exclusion criteria	Lack of DAP events manually annotations	Respiratory flow signals of unacceptable quality	Doubtful clinical diagnosis

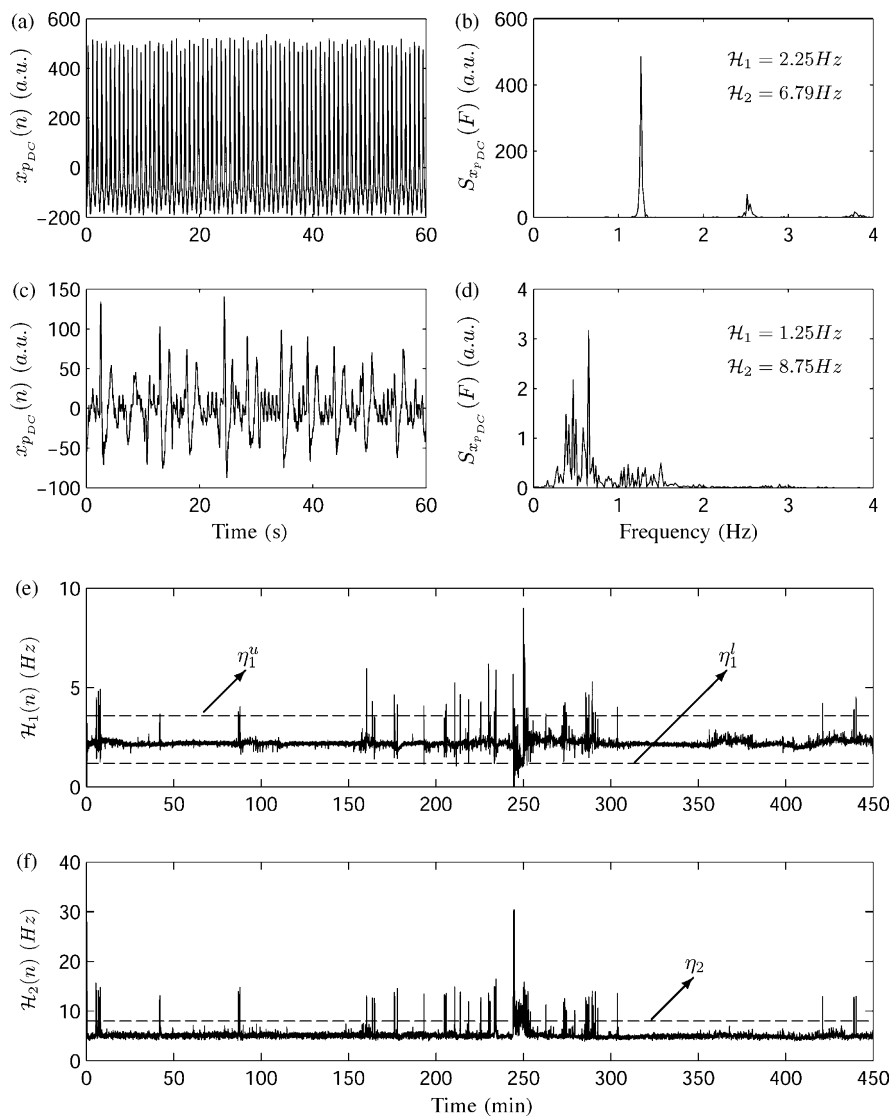


Fig. 2. PPG signal, $x_{pDC}(n)$, without artifact (a) and its power spectral density (b). Example of artifacted $x_{pDC}(n)$ is in (c) with its power spectral density in (d). Running estimation of Hjorth parameters, $\mathcal{H}_1(n)$ in (e) and $\mathcal{H}_2(n)$ in (f), from a real signal (solid line) and their rejection thresholds η (dashed line).

$x_E(n)$ was estimated in an N_p -length running window.

$$x_E(n) = \sqrt{\frac{1}{N_p} \sum_{k=n-(N_p-1)}^n x_{pDC}^2(k)} \quad (4)$$

According to [19], vasoconstriction periods last between 3 and 30 s. The larger the N_p value, the higher the low-pass filtering and, then, the transitions at $x_E(n)$ become attenuated; therefore, a value of N_p (equivalent to two cardiac cycles) is used, which roughly permits the tracking of attenuation changes greater than three beats. This decision rises the risk of an increase in short-length false positives, caused by high signal variability, and several DAP events, rather than a single event, can be interpreted as being different when the signal amplitude is near the threshold of the decision rule. To account for this, a minimum duration of events and a minimum distance between events is imposed. In that way, short-length false positives are suppressed and detections close in time are grouped together.

2.2.4. DAP decision rule

The last stage of the detector is a decision rule based on an adaptive threshold, which is adapted when neither DAP event nor artifacts are present. The decision rule considers a DAP event when $x_E(n)$ is lower than the established threshold, $x_E(n) < \zeta(n)$, for at least a minimum duration, $2T$, and n does not belong to an artifact.

$$\zeta(n) = \begin{cases} \frac{U_p}{100L_p} \sum_{k=n-(L_p-1)-T_{L_p,n}}^n x_E(k) & n \in \{n_a\}_\zeta \\ \zeta(n-1) & n \in \{n_c\}_\zeta \end{cases} \quad (5)$$

where $\{n_a\}_\zeta$ is the sample set that fulfills the criterion of eligibility for threshold adapting and $\{n_c\}_\zeta$ is the sample set that does not fulfill the criterion, $T_{L_p,n}$ is the number of samples $\in \{n_c\}_\zeta$ inside the interval $[n - (L_p - 1) - T_{L_p,n}, n]$, so that L_p is always the number of samples in $\{n_a\}_\zeta$ set from the interval.

The threshold is calculated as the U_p percent of the mean of $x_E(n)$ calculated using the L_p pass samples belonging to $\{n_a\}_\zeta$.

The set of samples ineligible for threshold adapting, $n \in \{n_c\}_\zeta$, so keeping constant $\zeta(n)$, are those accomplishing any of the following conditions:

- When a DAP event is detected, accomplished when $x_E(n) < \zeta(n-1)$.
- When the artifact detector identifies $x_{pDC}(n)$ as an artifact, see in Section 2.2.2.
- When an abrupt change in $x_E(n)$ occurs, as when $x_E(n)$ amplitude starts to fall because of an onset of a DAP event, the threshold remains constant. The abrupt changes are controlled by the derivative of $x_E(n)$, and a change is considered abrupt when

$$|x_E(n) - x_E(n-1)| > \frac{5}{f_s} A_E \quad (6)$$

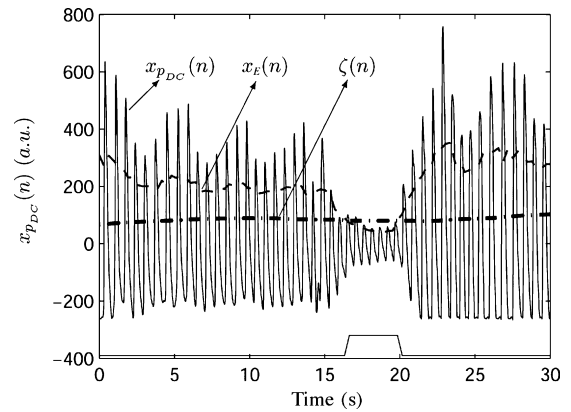


Fig. 3. Example of a DAP event detection. $x_{pDC}(n)$ (solid line), $x_E(n)$ (dashed line) and $\zeta(n)$ (dash-dotted line). $U_p = 45\%$, $L_p = 30 f_s T$.

where A_E is half of the oscillation amplitude range of $x_{pDC}(n)$ at the beginning of the recording.

Fig. 3 illustrates the detector functioning on a real DAP event.

2.2.5. DAP detector evaluation

The DAP detector was evaluated on real signals. The optimum sensitivity (S) and positive predictive values (+PV) were obtained using annotated signals, data set I, see Table 1.

S and +PV were calculated using gross averages by comparing DAP-detected events with the record annotations. The number of true positives (N_{TP}), false positives (N_{FP}), and false negatives (N_{FN}) were estimated by comparing detected and annotated event's onsets using different parameters configurations.

Decreases greater than 60% in the amplitude of PPG fluctuations were scored manually by an individual who was blind to PSG and the design of the detector. These annotations constitute the DAP reference for the detector evaluation.

The DAP detector was also evaluated using simulated signals in a previous work, [30].

2.3. Apnea detector

To study the relationship between apneas and DAP events, we need an apneic events detector based on respiratory signals. The entry signals of the apnea detector are the air flow signal, $x_f(n)$, which is measured using an oronasal thermocoupler, and the oxygen saturation signal, $x_{SaO_2}(n)$. The apnea detector (Fig. 1(c)) is formed by two subdetectors which later conforms their outputs. The first is a respiratory flow reduction (RFR) detector applied on the $x_f(n)$ signal to locate breathing cessation, and the second is a oxygen desaturation detector applied on the $x_{SaO_2}(n)$ signal to corroborate when a RFR detection can be consider as apneic.

We have constrained ourselves to well-evidenced apneas, and that is why only apneas accompanied with oxygen desaturation were analyzed. Apnea and hypopnea were not differentiated. An apneic event was considered to have occurred when a period of RFR lasting 5 s or longer is

associated with an oxygen desaturation $x_{\text{SaO}_2}(n)$ (drop $> 3\%$).

2.3.1. RFR detector

The objective of the first stage of the detector is to obtain an adequate signal, $\sigma_{x_f}(n)$, to be compare with a threshold, see below. The standard deviation $\sigma_{x_f}(n)$ is obtained from $x_f(n)$ using a N_f samples length running window.

The second stage of the detector is a decision rule based on an adaptive threshold, which is very similar to that shown in Section 2.2. A RFR event is identified by the decision rule when $\sigma_{x_f}(n)$ is lower than the established threshold at that moment, $\sigma_{x_f}(n) < \varphi(n)$.

$$\varphi(n) = \begin{cases} \frac{U_f}{100L_f} \sum_{k=n-(L_f-1)-T_{L_f,n}}^n \sigma_{x_f}(k) & n \in \{n_a\}_\varphi \\ \varphi(n-1) & n \in \{n_c\}_\varphi \end{cases} \quad (7)$$

where $\{n_a\}_\varphi$ is the sample set that fulfills the criterion of eligibility for threshold adapting, $\{n_c\}_\varphi$ is the sample set that does not fulfill this criterion, and $T_{L_f,n}$ is the number of

$$\beta = \begin{cases} \frac{\text{Mo}[x_{\text{SaO}_2}(n)]}{\text{Mo}[x_{\text{SaO}_2}(n)] + \text{Mo}^-[x_{\text{SaO}_2}(n)]} & \begin{cases} p(\text{Mo}[x_{\text{SaO}_2}(n)]) \geq 0.3 \\ p(\text{Mo}[x_{\text{SaO}_2}(n)]) + p(\text{Mo}^-[x_{\text{SaO}_2}(n)]) \geq 0.3 \\ |\text{Mo}[x_{\text{SaO}_2}(n)] - \text{Mo}^-[x_{\text{SaO}_2}(n)]| < 1.7\% \end{cases} \\ \text{Meaningless} & \text{Otherwise} \end{cases} \quad (11)$$

samples, $\in \{n_c\}_\varphi$ inside the interval $[n - (L_f - 1) - T_{L_f,n}, n]$ such that L_f is always the number of samples in $\{n_a\}_\varphi$ set from the interval. The threshold is calculated as the U_f percent of the mean of $\sigma_{x_f}(n)$ calculated using the L_f pass samples belonging to $\{n_a\}_\varphi$. The set of samples not eligible for threshold adapting, $n \in \{n_c\}_\varphi$, so keeping constant $\varphi(n)$, result from those accomplishing any of the following conditions:

- When a flow cessation event is detected. If the sample n accomplishes that $\sigma_{x_f}(n)$ is lower than the threshold $\varphi(n-1)$.
- When there is an abrupt change in $\sigma_{x_f}(n)$, such that when $\sigma_{x_f}(n)$ amplitude starts to fall because of a flow cessation onset event, the threshold remains constant. The abrupt changes are controlled by the derivative of $\sigma_{x_f}(n)$, and a change is considered abrupt when

$$|\sigma_{x_f}(n) - \sigma_{x_f}(n-1)| > \frac{10}{f_s} A_F \quad (8)$$

where A_F is the mean of the $\sigma_{x_f}(n)$ signal.

Fig. 4(a) illustrates how the detector works and how two flow reduction events are detected in a real flow signal. The RFR decision rule outputs are the onset $n_o^f(k)$ and end $n_e^f(k)$ of flow reduction events k .

2.3.2. Oxygen desaturation detector

The k th RFR event identified by the RFR detector, is a candidate apneic event which will be considered an apneic event if an oxygen desaturation event is associated with it. To identify desaturations the following procedure applies.

First a SaO₂ artifact detector is developed. The equipment provides a zero value in $x_{\text{SaO}_2}(n)$ when the measurement of the pulse oxymeter is invalid. Therefore, an artifact in $x_{\text{SaO}_2}(n)$ is identified when $x_{\text{SaO}_2}(n) < 50\%$.

Then an analysis window $[n_o^w(k), n_e^w(k)]$ is defined for each RFR event k , where $n_o^w(k)$ and $n_e^w(k)$ are the onset and the end samples of the window, respectively. The onset, $n_o^w(k)$, is the beginning of the RFR event $n_o^f(k)$, as determined by the RFR decision rule, and the end, $n_e^w(k)$, is 20 s after the end of the RFR event $n_e^f(k)$, or the onset of the next RFR event $n_o^f(k+1)$ if it occurs within that time.

$$n_o^w(k) = n_o^f(k) \quad (9)$$

$$n_e^w(k) = \min \{n_e^f(k) + 20 f_s, n_o^f(k+1)\} \quad (10)$$

To establish when a desaturation event occurs within the defined window, a baseline reference value β is considered for the $x_{\text{SaO}_2}(n)$ signal, according to the following expression:

where $\text{Mo}[x_{\text{SaO}_2}(n)]$ corresponds to the $x_{\text{SaO}_2}(n)$ signal mode of the entire recording, which is the most frequent value. $\text{Mo}^-[x_{\text{SaO}_2}(n)]$ is the second most frequent value of the signal, and $p(\cdot)$ is the probability density function of $x_{\text{SaO}_2}(n)$, which has a bin resolution of 1 in % value.

When a value for β is determine, the RFR event is considered to have an oxygen desaturation associated with it, and then it is labeled as apneic event, $k \in \{e_a\}$, when the following rule is satisfied:

$$\beta - \min [x_{\text{SaO}_2}(n_o^w(k)), \dots, x_{\text{SaO}_2}(n_e^w(k))] \geq 3\% \quad (12)$$

In situations where a baseline β has no sense to determine desaturations due to a high variability in SaO₂ signal, the following two alternative criteria are used.

- The local maximum and minimum of $x_{\text{SaO}_2}(n)$ signals are calculated using a peak detector. Next, the drop in amplitude between the maximum and the posterior minimum is calculated. If the drop is greater than or equal to 3%, it is concluded that an oxygen desaturation event has occurred. When one of those oxygen desaturation events occurs within the analysis window of a RFR event k , the RFR event is included in the set of apneic events, $k \in \{e_a\}$. An example of the detection of local maximum and minimum of $x_{\text{SaO}_2}(n)$ is shown in Fig. 4(b).

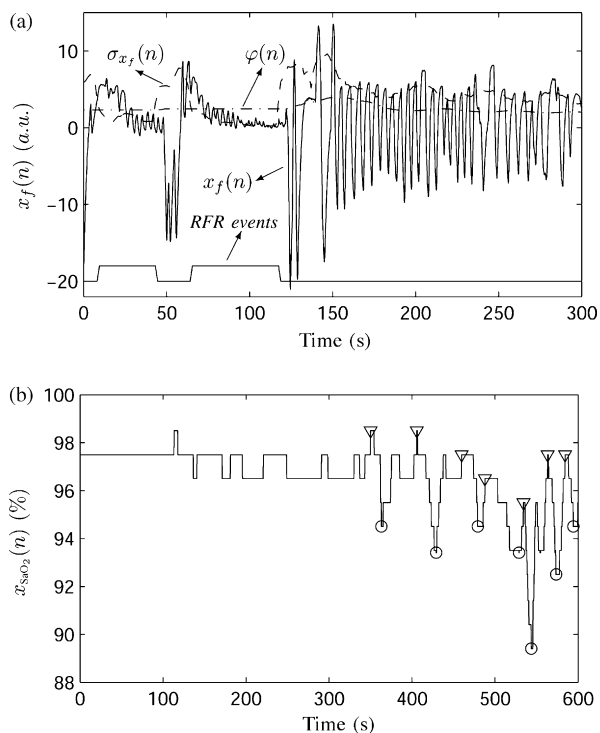


Fig. 4. Example of RFR detector performance. $x_f(n)$ (solid line), $\sigma_{x_f}(n)$ (dashed line) and $\varphi(n)$ (dash-dotted line). $U_f = 40\%$, $N_f = 14f_s$ and $L_f = 30f_s$. In (c), desaturation events. Minimums (circle); maximums (triangle).

(b) If the following rule is accomplished,

$$x_{\text{SaO}_2}(n_o^w(k)) - \min [x_{\text{SaO}_2}(n_o^w(k)), \dots, x_{\text{SaO}_2}(n_e^w(k))] \geq 3\% \quad (13)$$

a RFR event also is considered to have an oxygen desaturation event associated with it, therefore, $k \in \{e_a\}$.

In cases where either criterion (a) or (b) are satisfied, the respiratory flow reduction is considered an apneic event because of the oxygen desaturation event.

2.3.3. Evaluation of the respiratory flow reduction detector

The detection of respiratory flow reduction events was evaluated in terms of sensitivity (S) and positive predictive values (+PV) [31], calculated using the gross averages by comparing detected respiratory flow reduction events with the

record annotations. The number of true positives, false positives, and false negatives were estimated by comparing an event's onset for each of the parameter configurations. The ECG-Apnea Data Base, see Section 2.1.1, was used to evaluate this detector.

The apnea detector is the adding of the oxygen desaturation detector to the RFR detector, as showed in Fig. 1(c) and since no manual annotations are available for oxygen desaturations in $\text{SaO}_2(n)$ the evaluation is restricted to the RFR detector.

2.4. Clinical data analysis

2.4.1. Relationship between DAP and apneas

The relationship between DAP and apneas was analysed to get a more comprehensive knowledge of the clinical significance of DAP events. This relationship was evaluated using PPG, air flow and SaO_2 signals from data set II, see Table 1.

The evaluation process included the following steps:

- The detection of apneic events using the method described in Section 2.3.
- The detection of DAP events using the method described in Section 2.2.
- The exclusion of all detected apnea matching an artifact on $x_{p_{\text{DC}}}(n)$ and the exclusion of all of the detected DAP matching an artifact on $x_f(n)$.
- Only apneic events separated by more than 30 s were included in the analysis. This is done to avoid other adjacent respiratory events influencing the PPG signal under analysis.
- For each of the apneic events, we analyzed the presence of DAP in different pairs of related windows based on four protocols w_1, w_2, w_3 and w_4 , see Fig. 5. In all cases, a window previous to the apnea event and another around the end of the event, including the post-apnea, both of the same duration L , were examined for DAP events. Then we calculated the proportion (%) of apneic events that contained DAP events within the window previous to ($\%_p$) or late in ($\%_l$) the apnea.

Fig. 6 shows an example of the global analysis involving signals and detection results.

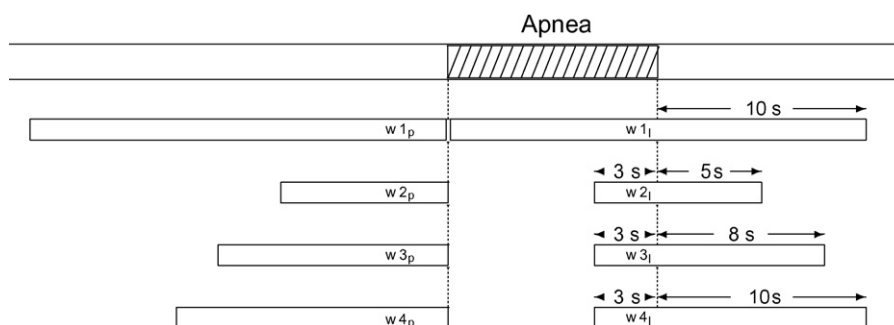


Fig. 5. Windows definition around apnea to analyse the incidence of DAP previous and during or posterior to apnea.

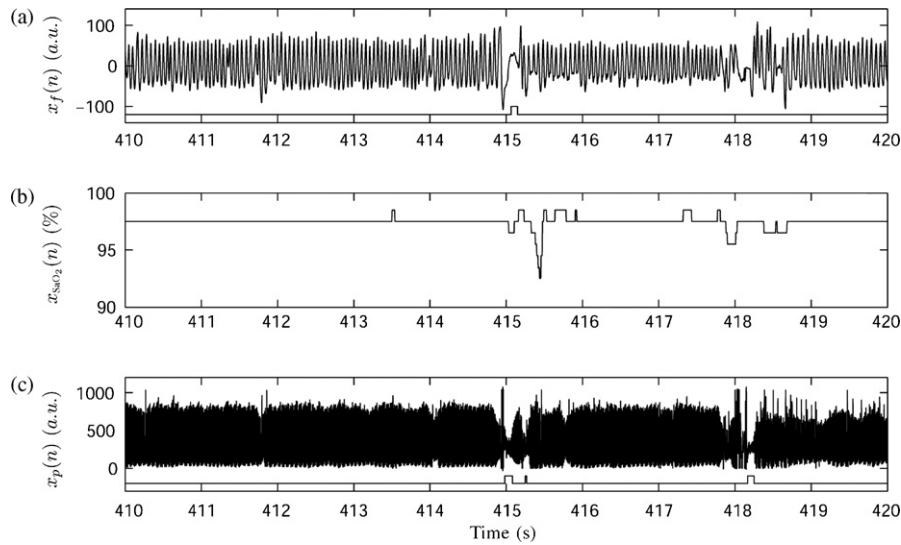


Fig. 6. Example of performance of the total system. $x_f(n)$ in (a), where the marks indicate apnea detections; $x_{SaO_2}(n)$ in (b); $x_p(n)$ in (c), where the marks indicate DAP detection.

2.4.2. DAP ratio clinical value

This study constitute the first phase in validating the use of DAP events as a means of diagnosing OSAS in children. The PPG signals from data set III were used. Once the best parameters configuration for the DAP detector is known, based on Section 2.2.5, the number of DAP events per hour ratio r_{DAP} was calculated. The data were computed as mean \pm S.D. of r_{DAP} . To compare groups, we used the Levene test for equality of variances and Student's t -test for differences between means. Tests that had a p -value < 0.05 were considered statistically significant.

3. Results

3.1. Evaluation of the DAP detector

To determine the optimum detector parameters, a diverse set of parameter configurations were examined using the real data set I and the procedures described in Section 2.2.5. At the artifacts detector stage, window length P of 5 s ($P = 5 f_s$) was used when estimating the Hjorth parameters, Eq. (3). The window value N_p for envelope estimation was set to two cardiac cycles, $N_p = 2 f_s T$, as indicated in Section 2.2.3.

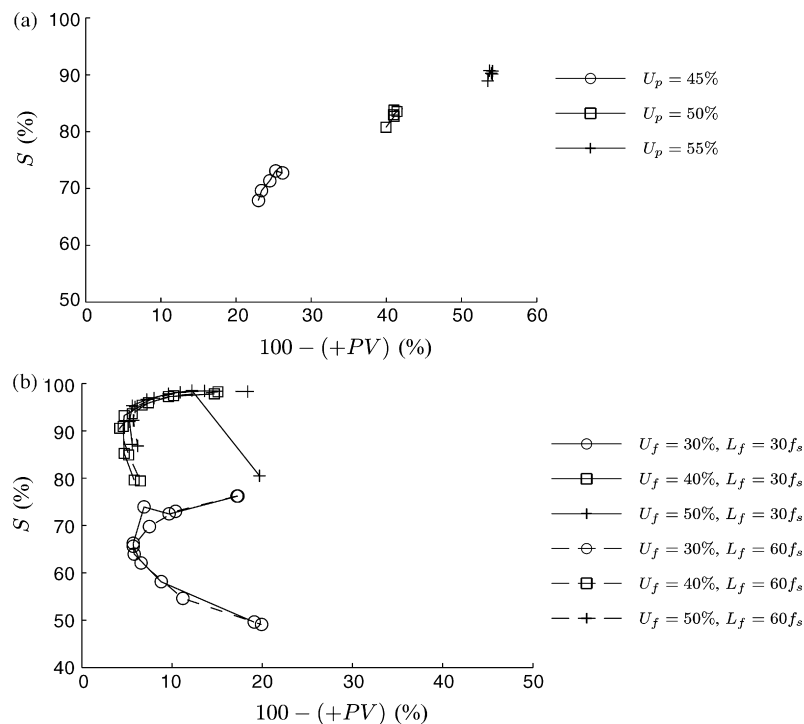


Fig. 7. Curves for different detectors evaluations. In (a), S against $100 - (+PV)$ for DAP detector evaluation with parameter L_p varying in the curve. Panel (b) shows S against $100 - (+PV)$ for apnea detector evaluation with N_f varying in the curves.

DAP detector for 60 different parameter configurations were tested. The results are shown in Fig. 7 (a). Values of $S = 73\%$ and $+PV = 75\%$ are obtained for $U_p = 45\%$, $L_p = 30 f_s T$, which are taken as the working parameters in the subsequent clinical data analysis.

3.2. Evaluation of the respiratory flow reduction detector

For the evaluation of the RFR detector, we used the ECG-Apnea Data Base, see Section 2.1.1, where 2180 RFR events were annotated, within 42 different configurations of the parameter variables set N_f , U_f and L_f . Fig. 7(b) shows the results. $S = 95.3\%$ and $+PV = 94.4\%$, which were obtained using $U_f = 50\%$, $N_f = 14 f_s$, and $L_f = 30 f_s$, where selected as the optimum results.

3.3. Clinical data results

3.3.1. Relationship between DAP and apneas

The detectors parameter configurations were selected as follows:

- *Apneic events detector.* $U_f = 40\%$, $L_f = 30 f_s$, $N_f = 5 f_s$. Those parameter values differ from the optimum values established in Section 3.2 because they were optimized using the respiratory flow data from adults. Several studies have demonstrated that children with OSAS can present fewer and generally shorter episodes of complete obstruction, but prolonged periods of partial upper airway obstruction [25,32]. For that reason, N_f is taken shorter on the children records.
- *DAP events detector.* As in Section 3.1.

In the data set II, 433 RFR events were detected which were reduced to 207 apneas because not all of the RFR were considered apneic and only apneas separated by more than 30 s were considered. The results that bear on the relationship between DAP and apneic events for each analysis window are shown in Table 2. The proportions $\%_p$ and $\%l$ indicate how many of the apneic events had a DAP event within their previous or late windows.

3.3.2. DAP ratio clinical value

To determine the validity of the r_{DAP} index as a means of discriminating between control and pathologic subjects, we used the data set III and the detector parameters established in Section 3.1. For patients with OSAS, mean r_{DAP} was $21.13 \pm$

8.93 and for patients without OSAS, mean r_{DAP} was 13.49 ± 6.35 ($p = 0.033$).

4. Discussion

A DAP detector and an apnea detector were presented and evaluated. At this stage the objective was to determine the optimum values of detector parameters in terms of maximizing S and $+PV$. When used with real signals, the operating points reached for the DAP detector were $S = 73\%$ and $+PV = 75\%$. A method based on Hilbert transform was also tested for the envelope detection stage [30]. Since both (RMS and Hilbert) envelope detection strategies produced only a marginal difference in performance, and given that the computational cost is lower for RMS than for Hilbert, RMS was taken as the working method. Values of $S = 95.3\%$ and $+PV = 94.4\%$ were obtained for respiratory flow reduction, RFR, detection. These values were considered acceptable according to the clinical routine, and so, the parameters corresponding to those values of S and $+PV$ were selected for the subsequent studies.

We investigated the effects of an apnea on the PPG signal. Gross averages in the analysis were used so all of the apneic events have the same incidence, and no distinction was made between patients. As expected, almost all of the apneic events belonged to pathologic subjects (93%), therefore the pathologic records had higher incidence in this study. The DAP events that took place in the window previous to the apnea events do not have a known apnea-related/sleep-related physiological connection; therefore, this can be used as a reference beyond which an increased DAP ratio in the window later in the apnea can be associated with additional sympathetic activity or arousals generated by apneas. The DAP event in the control window might be caused by baseline arousal or arousal generated by other reasons.

The best results in terms of the ability to discriminate between DAP events in the window previous to the apnea and the window after the apnea was obtained using the window configuration w_3 , see Fig. 5 and Table 2, with a 15% increase in DAP which suggests that the increase in sympathetic activity is produced just in the interval between 3 s before the end of the apnea and 8 s after the end of it.

An increase in the value of the U_p parameter of the DAP detector results in an increase in the number of detected DAP events, but also in greater discrimination between DAP events in the window previous to and those in the window later in an apnea, see Table 2. That might imply that many of the deeper DAP events are not associated with apnea; or even, they could be missed PPG artifacts.

Table 2
Relationship between DAP and apnea results

U_p (%)	# DAP	Analysis windows w1				Analysis windows w2				Analysis windows w3				Analysis windows w4			
		# previous	%p	# later	%l	# previous	%p	# later	%l	# previous	%p	# later	%l	# previous	%p	# later	%l
40	1980	60	29	66	32	29	14	26	13	34	16	48	23	60	29	66	32
50	4063	91	44	98	47	52	25	47	23	58	28	75	36	91	44	98	47
60	6406	114	55	128	62	67	32	75	36	78	38	109	53	114	55	128	62
70	9697	146	71	153	74	78	38	99	48	98	47	129	62	146	71	153	74

Several DAP events occurred within the analysis window previous to apnea which shows that not all of the DAP events were associated with an apnea. Since we are restricting to deep apneas ($U_f = 40\%$ and oxygen desaturation), some of those DAP events that took place in the window previous to the apnea might be related to a previous subthreshold apnea that was not or could not be detected. In addition, there were apneic events that were not associated with DAP events, which is why the agreement between DAP and apnea is always lower than 100%, see Table 2%₀₁. These results corroborate that not all of the DAP events are associated with an apnea event. These events may be related to arousals not associated with apnea. So there is a need for alternative criteria for discriminating between DAP events associated with apnea and those without that association. According to [33], variability in heart rate might be an interesting alternative as has been investigated [19,34].

The results of our DAP ratio clinical value study indicate that the discriminant index ratio of DAP events per hour, r_{DAP} , was able to classify children as either control or pathologic. The ratio in the pathological group was significantly higher 21.13 ± 8.93 compared with 13.49 ± 6.35 in the control group ($p = 0.033$). The still high values (13.49) of r_{DAP} within the control group of children again suggest the presence of DAP events not related to apneas.

The results of our clinical data analysis have demonstrated an association between apneic events and DAP events or DAP event ratio, which indicates that DAP events provide important information in sleep research and PPG signal might be useful in the diagnosis of OSAS. More research is needed in this area. Although the PPG signal contains information relevant for apneas detection, it is essential to determine whether this method is an improvement over existing methods. The use of peripheral arterial tonometry signal may improve further these results due to the increased range of decreases in the amplitude fluctuations of this signal compared with PPG, as a result of introducing an external compensatory pressure [19].

5. Conclusion

In conclusion, DAP events can be automatically detected on the PPG signal with high sensitivity/specificity performance 73/75. Apneic events increased the ratio of DAP in the PPG signal, and this ratio r_{DAP} was able to classify children as either control or OSAS within a statistically significant probability. DAP are more often present in the post-apnea period than in previous to apnea period (15% higher incidence). PPG signal apart from being clinically useful for OSAS diagnosis has the advantage of being less complicated and better suited for ambulatory monitoring than alternative methods. Nevertheless, extended studies are needed to corroborate the potential of PPG signal in diagnosing sleep disorders.

Acknowledgements

This study was supported by Ministerio de Ciencia y Tecnología and FEDER under Project TEC2004-05263-C02-

02, in part by the Diputación General de Aragón (DGA), Spain, and through Grupos Consolidados GTC ref:T30.

References

- [1] C. Guilleminault, A. Tilkian, W.C. Dement, The sleep apnea syndromes, *Annu. Rev. Med.* 27 (1976) 465–484.
- [2] American Academy of Sleep Medicine Task Force, Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research, *Sleep* 22 (5) (1999) 667–689.
- [3] T. Young, M. Palta, J. Dempsey, J. Skatrud, S. Weber, S. Badr, The occurrence of sleep-disordered breathing among middle-aged adults, *N. Engl. J. Med.* 328 (1993) 1230–1235.
- [4] R.J. Kimoff, Sleep fragmentation in obstructive sleep apnea, *Sleep* 19 (9) (1996) 61–66.
- [5] F.J. Nieto, T.B. Young, B.K. Lind, E. Shahar, J.M. Samet, S. Redline, R.B. D'Agostino, A.B. Newman, M.D. Lebowitz, T.G. Pickering, Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study, *JAMA* 283 (2000) 1829–1836.
- [6] D.W. Beebe, D. Gozal, Obstructive sleep apnea and prefrontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits, *J. Sleep Res.* 11 (2002) 1–16.
- [7] D.J. Gottlieb, R.M. Vezina, C. Chase, S.M. Lesko, T.C. Heeren, D.E. Weese-Mayer, S.H. Auerbach, M.J. Corwin, Symptoms of sleep-disordered breathing in 5-year-old children are associated with sleepiness and problem behaviors, *Pediatrics* 112 (2003) 870–877.
- [8] R.D. Chervin, K.H. Archbold, J.E. Dillon, P. Panahi, K.J. Pituch, R.E. Dahl, C. Guilleminault, Inattention, hyperactivity, and symptoms of sleep-disordered breathing, *Pediatrics* 109 (2002) 449–456.
- [9] American Academy of Pediatrics, Clinical practice guideline: diagnosis and management of childhood obstructive sleep apnea syndrome, *Pediatrics* 109 (2002) 704–712.
- [10] J.C. Hardy, K. Gray, S. Whisler, U. Leuenberger, Sympathetic and blood pressure responses to voluntary apnea are augmented by hypoxemia, *J. Appl. Physiol.* 77 (1994) 2360–2365.
- [11] U. Leuenberger, E. Jacob, L. Sweer, N. Waravdekar, C. Zwillich, L. Sinoway, Surges of muscle sympathetic nerve activity during obstructive apnea are linked to hypoxemia, *J. Appl. Physiol.* 79 (1995) 581–588.
- [12] H. Schneider, C.D. Schaub, C.A. Chen, K.A. Andreoni, A.R. Schwartz, P.L. Smith, J.L. Robotham, C.P. O'donnell, Neural and local effects of hypoxia on cardiovascular responses to obstructive apnea, *J. Appl. Physiol.* 88 (2000) 1093–1102.
- [13] U.A. Leuenberger, J.C. Hardy, M.D. Herr, K.S. Gray, L.I. Sinoway, Hypoxia augments apnea-induced peripheral vasoconstriction in humans, *J. Appl. Physiol.* 90 (2001) 1516–1522.
- [14] A. Anand, S. Reimsburg-Sailor, S.H. Launois, J.W. Weiss, Peripheral vascular resistance increases after termination of obstructive apneas, *J. Appl. Physiol.* 91 (2001) 2359–2365.
- [15] V.K. Somers, M.E. Dyken, M.P. Clary, F.M. Abboud, Sympathetic neural mechanisms in obstructive sleep apnea, *J. Clin. Invest.* 96 (1995) 1897–1904.
- [16] V.A. Imadojemu, K. Gleeson, K.S. Gray, L.I. Sinoway, U.A. Leuenberger, Obstructive apnea during sleep is associated with peripheral vasoconstriction, *Am. J. Respir. Crit. Care Med.* 165 (2002) 61–66.
- [17] Y. Mendelson, Pulse oximetry: theory and applications for noninvasive monitoring, *Clin. Chem.* 38 (9) (1992) 1601–1607.
- [18] M. Nitzan, A. Babchenko, B. Khanokh, D. Landau, The variability of the photoplethysmographic signal—a potential method for the evaluation of the autonomic nervous system, *Physiol. Meas.* 19 (1998) 93–102.
- [19] R.P. Schnall, A. Shlitner, J. Sheffy, R. Kedar, P. Lavie, Periodic, profound peripheral vasoconstriction—a new marker of obstructive sleep apnea, *Sleep* 22 (7) (1999) 939–946.
- [20] A. Bar, G. Pillar, I. Dvir, J. Sheffy, R.P. Snall, P. Lavie, Evaluation of a portable device based on peripheral arterial tone for unattended home sleep studies, *Chest* 123 (2003) 695–703.

- [21] C.P. O'Donnell, L. Allan, P. Atkinson, A.R. Schwartz, The effect of upper airway obstruction and arousal on peripheral arterial tonometry in obstructive sleep apnea, *Am. J. Respir. Crit. Care Med.* 166 (2002) 965–971.
- [22] M. Nitzan, A. Babchenko, I. Faib, E. Davidson, Assessment of changes in arterial compliance by photoplethysmography, in: *Proceedings of the IEEE Convention of the Electrical and Electronic Engineers, Israel*, 2000, pp. 351–354.
- [23] A. Hertzman, The blood supply of various skin areas as estimated by the photo-electric plethysmograph, *Am. J. Physiol.* 124 (1938) 328–340.
- [24] A.L. Goldberger, L.A.N. Amaral, L. Glass, J.M. Hausdorff, P.C. Ivanov, R.G. Mark, J.E. Mietus, G.B. Moody, C.-K. Peng, H.E. Stanley, PhysioBank, PhysioToolkit, and PhysioNet: components of a new research resource for complex physiologic signals, *Circulation* 101 (23) (2000 (June 13)) e215–e220, *circulation Electronic Pages*: <http://circ.ahajournals.org/cgi/content/full/101/23/e215>.
- [25] American Thoracic Society, Standards and indications for cardiopulmonary sleep studies in children, *Am. J. Respir. Crit. Care Med.* 153 (1996) 866–878.
- [26] A. Rechtschaffen, A. Kales, *A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects*, Public Health Service, US Government, UCLA.
- [27] B. Hjorth, EEG analysis based on time domain properties, *Electroencephal. Clin. Neurophysiol.* (1970) 306–310.
- [28] B. Hjorth, The physical significance of time domain descriptors in EEG analysis, *Electroencephal. Clin. Neurophysiol.* 34 (1973) 321–325.
- [29] L. Sörnmo, P. Laguna, *Bioelectrical Signal Processing in Cardiac and Neurological Applications*, Academic Press, Elsevier, 2005, ISBN: 0-12-437552-9.
- [30] E. Gil, V. Monasterio, J.M. Vergara, P. Laguna, Pulse photoplethysmography amplitude decrease detector for sleep apnea evaluation in children, in: *Proceedings of the 27th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 2005.
- [31] E. Gil, J.M. Vergara, P. Laguna, Study of the relationship between pulse photoplethysmography amplitude decrease events and sleep apnea in children, in: *Proceedings of the 28th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 2006, pp. 3887–3890.
- [32] C.L. Marcus, Sleep-disordered breathing in children, *Am. J. Respir. Crit. Care Med.* 164 (2001) 16–30.
- [33] C. Guilleminault, R. Winkle, S. Connolly, K. Melvin, A. Tilkian, Cyclical variation of the heart rate in sleep apnoea syndrome: mechanisms, and usefulness of 24 h electrocardiography as a screening technique, *Lancet* 323 (1984) 126–131.
- [34] E. Gil, M.O. Mendez, O. Villantieri, J. Mateo, J.M. Vergara, A.M. Bianchi, P. Laguna, Heart rate variability during pulse photoplethysmography decreased amplitude fluctuations and its correlation with apneic episodes, *Comput. Cardiol.* (2006) 165–168.