

Study of the relationship between Pulse Photoplethysmography amplitude decrease events and sleep apneas in children

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Abstract—In this work, a method to analyse the effects of an apnea on the pulse photoplethysmography signal (PPG) is proposed. Therefore, an apnea detector based on respiratory signals has been developed and a decrease in amplitude of PPG (DAP) detector developed in a previous study was used. The apnea detector was tested using real signals. S and $+PV$ of the detector were 95.3% and 94.4%, respectively. For each of the apneic events, we analyzed the presence of DAP in a window previous to the apnea event and another during/after the apnea. An increase of about 15% in DAP events in the window during/after the apnea with respect to the previous to apnea window is produced. These results show an association between apneic events and DAP events, which indicates that DAP events provide useful information in sleep research and PPG signals might be useful in the diagnosis of OSAS.

I. INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterised by repetitive episodes of upper airway obstruction during sleep, involving periods of breathing cessation [1]. The resulting sleep fragmentation 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, in turn, lead to systemic hypertension 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.

The gold standard diagnostic test for OSAS is overnight polysomnography (PSG). Generally, PSG includes monitoring of the patient's airflow through the nose and mouth, as well as the measurement of blood pressure, electrocardiographic activity, blood oxygen levels, brain wave patterns, eye movement, and the movement of respiratory muscles and limbs. A number of alternatives to PSG have been proposed because of the cost and requirement for technical expertise.

One alternative to PSG is pulse photoplethysmography signal (PPG). PPG, which was developed by Hertzman [3], is a simple and useful method for measuring the pulsatile component of the heartbeat and evaluating peripheral circulation.

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The signal is obtained through non-invasive pulse oximetry systems and is based on blood light absorption.

The autonomic nervous system (ANS) regulates bodily activities that are beyond conscious control. Actually, the ANS consists of two subsystems that operate in opposite directions; the sympathetic nervous system is the dominant system when physical activity is called for, and the parasympathetic nervous system dominates during relaxation. Both of the subsystems innervate the same organs and act to maintain a proper balance in the internal organ environment. 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 or dilate.

Several studies suggest that when apnea occurs, sympathetic activity increases. Hypoxia plays a key role in that relationship. The increase in sympathetic activity is associated with vasoconstriction and, possibly, is related to transient arousal [4], [5]. Vasoconstriction is reflected in the PPG signal by a decrease in the fluctuation of the signal amplitude [8]. Therefore, the automatic detection of periods of PPG attenuation might be useful in indirectly quantifying apneas during sleep [6]. There are studies of the diagnosis of OSAS based on the detection of vasoconstriction using peripheral arterial tonometry [7], which is a similar physiologic signal. The relationship between ANS and PPG has been the subject of some studies [8].

The main objective of this study is to assess the potential value of PPG signals in diagnosing OSAS. To that end, the relationship between apneas and DAP is analyzed and described. The expectation of a relationship is based on the hypothesis that DAP events are caused by vasoconstrictions produced by an increase in sympathetic activity and they reflect an arousal that is probably related to an apneic event.

II. MATERIALS

The following data sets were used to evaluate the proposed detector and to evaluate the use of PPG signals in clinical diagnoses.

A. PSG Data set from children

This subset included the records of 13 children (8 boys, 5 girls) whose mean age was 4.85 ± 2.53 (mean \pm S.D.) years. The PSG registers were acquired in Miguel Servet Children's Hospital, Zaragoza, Spain, using a digital polygraph (EGP800, Bitmed) recording six EEG channels, two

electro-oculogram channels, a chin electromyogram channel, an ECG channel, air flow (oronasal thermocoupler), and respiratory plethysmography, with transducers placed around the chest and abdomen. PPG and arterial oxygen saturation were recorded continuously by pulse oximetry (COSMO ETCO2/SpO2 Monitor Novamatrix, Medical Systems). All of the signals were stored at a sampling rate of 100 Hz. The PSG data were gathered from children suspected of having OSAS, and were scored manually following standard procedures used to discriminate children suffering from OSAS from those who are not.

B. Respiratory data set from adults

A real PSG data set from adults was acquired from the ECG-Apnea Data Base of Physionet, [9], 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 oxygen saturation, SaO_2).

III. METHODS

To study the relationship between apneas and DAP, we need detectors that identify DAP events based on PPG signal, $x_p(n)$, and apneic events based on respiratory signals. The DAP detector was developed in a previous study [6]. The apnea detector identifies apneic events based on periods of respiratory flow reduction (RFR), which are considered apneas when they are matched with an oxygen desaturation. 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, $x_{SaO_2}(n)$.

A. Apnea detector

In this work only apneas accompanied with oxygen desaturation were analyzed. Apnea and hipoapnea were not differentiated. An apneic event was considered to have occurred when respiratory flow $x_f(n)$ was reduced and an oxygen desaturation $x_{SaO_2}(n)$ with a drop bigger than 3% was associated with it and lasted by 5 s or longer.

This detector is composed of four stages. The first two stages are designed to identify RFR events. Firstly, a running standard deviation series, $\sigma_{x_f}(n)$, of the respiratory flow signal, $x_f(n)$, is calculated using a sliding window. Subsequently, RFR events are detected using a threshold based decision rule. The third stage identifies artifacts in the oxygen saturation signal $x_{SaO_2}(n)$. The last stage identifies which of the respiratory events are associated with a decrease in the oxygen saturation signal that is not an artifact, see Fig. 1. The details of each stage are as follows:

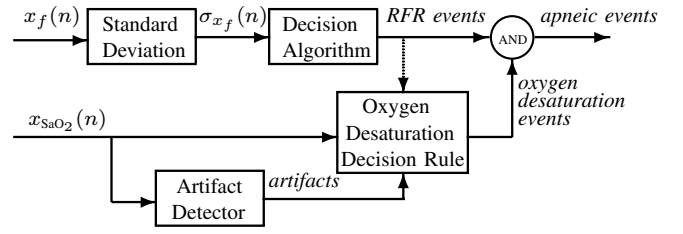


Fig. 1. Apnea detector diagram. Dashed line gives info to the oxygen desaturation detector just to operate when a RFR event appears.

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

$$\sigma_{x_f}(n) = \sqrt{\frac{1}{N_f - 1} \sum_{k=n-(N_f-1)}^n (x_f(k) - \overline{x_{fN_f}}(n))^2} \quad (1)$$

Where $\overline{x_{fN_f}}(n)$ is the mean of $x_f(n)$ within the interval $[n - (N_f - 1), n]$.

2) *RFR decision rule*: The second stage of the detector is a decision rule based on an adaptive threshold. A RFR event is identified by the decision rule when $\sigma_{x_f}(n)$ is lower than the established threshold, $\varphi(n)$, at that moment, $\sigma_{x_f}(n) < \varphi(n)$.

$$\varphi(n) = \begin{cases} \frac{U_f}{100L_f} \sum_{k=n-(L_f-1)-T_{L_f,n}}^n \sigma_{x_f}(k) & n \in \{n_a\} \\ \varphi(n-1) & n \in \{n_c\} \end{cases} \quad (2)$$

Where $\{n_a\}$ is the sample set that fulfills the criterion of eligibility for threshold updating, $\{n_c\}$ is the sample set that does not fulfill this criterion, and $T_{L_f,n}$ is the number of samples, $n \in \{n_c\}$ inside the interval $[n - (L_f - 1) - T_{L_f,n}, n]$ such that L_f is always the number of samples in $\{n_a\}$ set from the interval. The threshold is calculated as the U_f percent of the mean of the L_f pass samples in $\{n_a\}$. The set of samples not eligible for threshold updating can result from 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 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

$$|\sigma_{x_f}(n) - \sigma_{x_f}(n-1)| > \frac{10}{f_s} A_f \quad (3)$$

Where A_f is the mean of the $\sigma_{x_f}(n)$ signal.

When one of those two criteria are accomplished, $n \in \{n_c\}$.

The RFR decision rule outputs are the onset $n_o^f(k)$ and end $n_e^f(k)$ of each k th flow reduction events.

3) *SaO₂ artifact detector*: 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 $x_{\text{SaO}_2}(n) < 50\%$.

4) *Oxygen desaturation decision rule*: The k th RFR event identified by the first two stages of the detector, is a candidate apneic event. The respiratory event is considered an apneic event if an oxygen desaturation event is associated with it.

Firstly, an analysis window $[n_o^w(k), n_e^w(k)]$ is defined for each RFR event k . 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 seconds after the end of the RFR event $n_e^f(k)$, or the beginning of the next RFR event $n_o^f(k+1)$ if it begins within that time.

$$n_o^w(k) = n_o^f(k) \quad (4)$$

$$n_e^w(k) = \min \{n_e^f(k) + 20, n_o^f(k+1)\} \quad (5)$$

To establish when a desaturation event occurs within the defined window, a baseline β is considered to the $x_{\text{SaO}_2}(n)$ signal. The value of β corresponds to:

- The oxygen saturation signal mode, $Mo[x_{\text{SaO}_2}(n)]$. If the probability density function of $x_{\text{SaO}_2}(n)$, $p(\cdot)$, of the mode value is bigger than 0.3.

$$p(Mo[x_{\text{SaO}_2}(n)]) \geq 0.3 \quad (6)$$

- The mean between $Mo[x_{\text{SaO}_2}(n)]$ and the second most frequent value of the signal, $Mo^- [x_{\text{SaO}_2}(n)]$. If the addition of the probability of these two values in the signal is bigger than 0.3, and the difference between them is less than 1.7%.

$$p(Mo[x_{\text{SaO}_2}(n)]) + p(Mo^- [x_{\text{SaO}_2}(n)]) \geq 0.3 \quad (7)$$

$$|Mo[x_{\text{SaO}_2}(n)] - Mo^- [x_{\text{SaO}_2}(n)]| < 1.7\% \quad (8)$$

- Otherwise is not defined.

When a value for β is defined, the RFR event has an oxygen desaturation associated with it, and it is considered an apneic event, $k \in \{e_a\}$, when the following rule is satisfied:

$$\beta - \min [x_{\text{SaO}_2}(n_o^w(k)), \dots, x_{\text{SaO}_2}(n_e^w(k))] \geq 3\% \quad (9)$$

In situations where β is not defined, the following two alternative criteria are used.

- a) 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, $k \in \{e_a\}$.
- b) If the following rule is accomplished,

$$x_{\text{SaO}_2}(n_o^w(k)) - \min [x_{\text{SaO}_2}(n_o^w(k)), \dots, x_{\text{SaO}_2}(n_e^w(k))] \geq 3\% \quad (10)$$

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

IV. PERFORMANCE MEASURES

To obtain the optimum parameters for a balance between sensibility (S) and positive predictive values (+PV), the detector were evaluated using annotated signals. Next, the clinical relationship between DAP and apneic events were analysed.

A. Evaluation of the apnea detector

Only the detection of respiratory flow reduction events, were evaluated. The sensibility (S) and positive predictive values (+PV) were calculated using the gross averages by comparing detected respiratory flow reduction events with the manual 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.

B. Relationship between DAP and apneas

The evaluation process of the relationship between DAP and apneas included:

- The detection of apneic events using the method described in III-A.
- The detection of DAP events using the method described in [6]. This detection was carried out using a threshold based rule as in III-A.2, now with a % threshold denoted by U_p . Different values for U_p which establishes the level of decrease in the amplitude fluctuations of PPG to be considered as DAP were used. An increase in the value of the U_p parameter is associated with an increase in the number of DAP events detected.
- The exclusion of all apnea detected that matched an artifact on $x_p(n)$ and the exclusion of all of the DAP detected that matched an artifact on $x_f(n)$.
- Only apneic events separated by more than 30 s were included in the analysis.
- For each of the apneic events, we analyzed the presence of DAP in two different windows of eight seconds length, a window previous to the apnea event and another whose onset is three seconds before the apnea end. We calculated the proportion (%) of apneic events that contained DAP events within the window previous to ($\%_p$) or late in ($\%_l$) the apnea.

Fig. 2 shows an example signal of the global system.

V. RESULTS

A. Evaluation of apnea detector

The apnea detector was tested with 42 parameter configurations for each record. The parameter variables were N_f , U_f and L_f . Fig. 3 shows the results of all of the records included in the analysis. The optimum results were $S = 95.3\%$ and $+PV = 94.4\%$, which were obtained using $U_f = 50\%$, $N_f = 14f_s$, and $L_f = 30f_s$.

B. Relationship between DAP and apneas

The parameter configurations of the apnea detector were as follows: $U_f = 40\%$, $L_f = 30f_s$, $N_f = 5f_s$. Those parameter values differ from the optimum values established in V-A because they were optimized using the respiratory

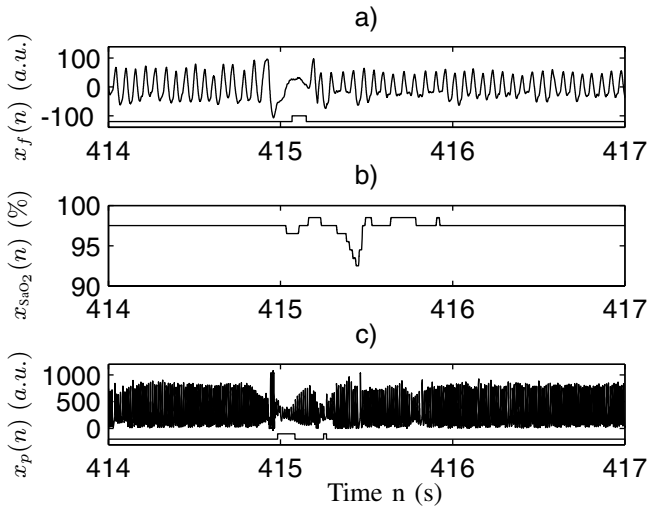


Fig. 2. Example of performance of the total system. $x_f(n)$ in (a), where the marks indicate apnea detections; $x_{SaO_2}(n)$ in (b); $x_p(n)$ in (c), where the marks indicate DAP detection.

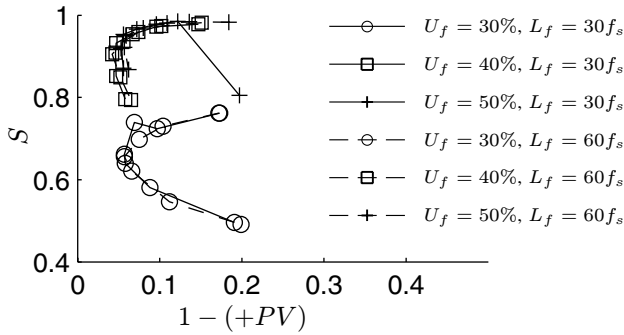


Fig. 3. ROC curves for Apnea detector evaluation.

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 [10]. For that reason, N_f is shorter based on the records from children.

Among all of the signals, 433 RFR events were detected, and the number of apneas in the analysis was 207 because not all of the RFR were considered apneic and only apneas separated by more than 30 s were used.

The results that bear on the relationship between DAP and apneic events are shown in Table I. The proportions $\%_p$ and $\%_l$ indicate how many of the apneic events has a DAP event within their windows.

TABLE I
RELATIONSHIP APNEA DAP RESULTS

U_p	# DAP events	Analysis windows			
		# prev.	$\%_p$	# later	$\%_l$
40%	1980	34	16%	48	23%
50%	4063	58	28%	75	36%
60%	6406	78	38%	109	53%
70%	9697	98	47%	129	62%

VI. DISCUSSIONS AND CONCLUSIONS

In our research, we are investigating the effects of an apnea on the PPG signal. An apnea detector is developed based on the flow signal which has reach a S and $+PV$ of 95.3% and 94.4%, respectively.

The DAP events that took place in the window previous to the apnea events do not have a known 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.

Not all of the DAP events were associated with an apnea event; thus, several DAP events occurred within the analysis window previous to apnea. These events may be related to arousals not associated with apnea. There is a need for alternative criteria for discriminating between DAP events associated with apnea and those without that association. According to [11], variability in heart rate might be an interesting alternative worth investigating, Schnall et al. [7].

Although a broader study using more cases is needed, the results of our study indicate that an increase of about 15% in DAP events in the window following the apnea with respect to DAP events in the previous to apnea window is produced.

These results have demonstrated an association between apneic events and DAP events, which indicates that DAP events provide important information in sleep research and PPG signals might be useful in the diagnosis of OSAS.

REFERENCES

- [1] American Academy of Sleep Medicine Task Force, "Sleep-related breathing disorders in adults: Recommendations for syndrome definition and measurement techniques in clinical research," *Sleep*, vol. 22, no. 5, 1999.
- [2] R. J. Kimoff, "Sleep fragmentation in obstructive sleep apnea," *Sleep*, vol. 19, no. 9, 1996.
- [3] A. Hertzman, "The blood supply of various skin areas as estimated by the photo-electric plethysmograph," *Am. J. Physiol.*, vol. 124, pp. 328–340, 1938.
- [4] U. A. Leuenberger, J. C. Hardy, M. D. Herr, K. S. Gray, and L. I. Sinoway, "Hypoxia augments apnea-induced peripheral vasoconstriction in humans," *J. Appl. Physiol.*, vol. 90, pp. 1516–1522, 2001.
- [5] V. K. Somers, M. E. Dyken, M. P. Clary, and F. M. Abboud, "Sympathetic neural mechanisms in obstructive sleep apnea," *J. Clin. Invest.*, vol. 96, pp. 1897–1904, 1995.
- [6] E. Gil, V. Monasterio, J. M. Vergara, and P. Laguna, "Pulse photoplethysmography amplitude decrease detector for sleep apnea evaluation in children," *Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 2005.
- [7] R. P. Schnall, A. Shlitter, J. Sheffy, R. Kedar, and P. Lavie, "Periodic, profound peripheral vasoconstriction—a new marker of obstructive sleep apnea," *Sleep*, vol. 22, no. 7, 1999.
- [8] M. Nitzan, A. Babchenko, B. Khanokh, and D. Landau, "The variability of the photoplethysmographic signal—a potential method for the evaluation of the autonomic nervous system," *Physiol. Meas.*, vol. 19, pp. 93–102, 1998.
- [9] T. Penzel, G. Moody, R. Mark, A. Goldberger, and J. Peter, "The apnea-ecg database," *Computers in Cardiology*, 2000, <http://www.physionet.org/physiobank/database/apnea-ecg/>.
- [10] American Thoracic Society, "Standards and indications for cardiopulmonary sleep studies in children," *Am. J. Respir. Crit. Care Med.*, vol. 153, pp. 866–878, 1996.
- [11] C. Guilleminault, R. Winkle, S. Connolly, K. Melvin, and A. Tilkian, "Cyclical variation of the heart rate in sleep apnoea syndrome: Mechanisms, and usefulness of 24 h electrocardiography as a screening technique," *The Lancet*, vol. 323, pp. 126–131, 1984.