Obstructive Sleep Apnea Syndrome analysis in children by Decreases in the Amplitude Fluctuations of Pulse Photoplethysmography: role of recording duration and Heart Rate Variability.

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***Abstract*— Heart rate variability (HRV) during Decreases in the Amplitude fluctuations of Pulse Photopletysmography signal events (DAP) is studied. The DAP duration and the time span of the polysomnography (PSG) recording under study are also considered for identification of Obstructive Sleep Apnea events in children. Oxygen desaturation is used as reference. The study involves recordings of 21 children.**

Periods of time associated with a drop in SaO_2 of 3% from baseline during at least 5% of the time were labeled as pathologic. DAP events were detected using an automatic detector, HRV signal processing using the Smooth Pseudo Wigner-Ville Distribution was carried out in order to obtain several time and frequency HRV indexes. T-test was used to analyze differences between groups. The results show discrimination power between groups that increases as the duration of the time period under analysis, becomes shorter, and so more tune to the apneic episodes. Also HRV increase the discrimination power helping in discriminating DAP event non related to apnea.

I. INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a breathing disorder characterised by brief periods of breathing cessation during sleep, with recurrent arousals being required to reestablish upper airway patency [1]. The prevalence of OSAS is estimated as 2% to 3% in children, most of whom are undiagnosed and untreated. The associated consequences include sleep fragmentation, associated with malfunctioning of sleep-related restorative processes, blood gas modifications which induce chemical and structural injuries in the cells of the central nervous system and it may lead to adverse cardiovascular consequences such as myocardial infarction and hypertension [2]. Repeated failures related to sleep fragmentation at critical stages of development like childhood can fundamentally influence a child's motivation and behavior.

Polysomnography (PSG) is the most commonly used diagnostic sleep procedure, but some alternatives to this technique have been proposed because of the cost and requirement for technical expertise. One alternative to PSG is pulse photopletismography signal (PPG) which is a simple and useful method for measuring the pulsatile component of the heartbeat and evaluating peripheral circulation.

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 [3]. Vasoconstriction is reflected in the PPG signal by a decrease in the fluctuation of the signal amplitude [4], [5]. Therefore, the automatic detection of decreases in the amplitude fluctuations of PPG (DAP) 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 physiological signal. The relationship between autonomic nervous system (ANS) and PPG has been the subject of some studies [5], [8].

Nevertheless, not all of the DAP events are associated with an apnea event [9]. These events may be related to arousals not associated with apnea. Some studies [7], [10] include HRV as an alternative criteria for discriminating between DAP events associated with apnea and those without that association, according to [11].

The main objective of this study is to assess the potential value of DAP events together with HRV in diagnosing OSAS. To that end, different DAP events duration and HRV parameters have been analyzed for diverse time span of the PSG recording under study.

II. DATA

This study includes the records of 21 children (11 boys, 10 girls) whose mean age was 4.47 ± 2.04 ($mean \pm S.D.$) years. The PSG registers were acquired in Miguel Servet Children's Hospital, Zaragoza, Spain, according to the standard methods defined by American Thoracic Society [12], using a commercial digital polygraph (EGP800, Bitmed) and recording six EEG channels, two electro-oculogram channels, a chin electromyogram channel, two ECG channels, air flow (oronasal thermocoupler), and respiratory plethysmography, with transducers placed around the chest and abdomen. PPG and arterial oxygen saturation (SaO_2) were recorded continuously by pulse oximetry (COSMO ETCO2/SpO2 Monitor Novametrix, Medical Systems). All of the signals were stored at a sampling rate of 100 Hz, except ECG channels whose sampling rate was 500 Hz. Only PPG, SaO_2 and ECG signals were used in the automatic analysis. The PSG data were scored manually following standard procedures used

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TABLE I
FRAGMENTS CLASSIFICATION

PSG Fragments	# control	# pathologic	# doubt	# total
$\mathcal{D}_{15}$	365	74	58	497
$\mathcal{D}_{30}$	159	41	31	231
$\mathcal{D}_{60}$	78	23	21	122
$\mathcal{D}_{120}$	41	13	9	63
$\mathcal{D}_{180}$	27	10	7	44
$\mathcal{D}_{240}$	22	7	6	35
$\mathcal{D}_{all}$	12	3	6	21

to discriminate children suffering from OSAS (10 children) from those who are not (11 children).

III. METHODS

A. Classification of different time-span of the PSG recording.

Complete night PSG recordings were split into segments $\mathcal{D}_L$ corresponding to length $L = 15, 30, 60, 120, 180, 240$ minutes. This fragments and the complete night were classified as control, doubt or pathologic based on SaO_2 desaturation. To establish this classification, a baseline level β, corresponding to the SaO_2 signal mode of the entire night, is considered. In all recordings $\beta \geq 97\%$ and the probability of its value was higher than 0.3 from a bin resolution of 1%. The total time intervals that SaO_2 signal is below $\beta - 3\%$, $t_{\beta-3}$, was calculated for each fragment in $\mathcal{D}_L$. PSG fragments were classified according to

$$\begin{array}{cc} t_{\beta-3}/L < 0.015 & control \\ 0.015 < t_{\beta-3}/L < 0.05 & doubt \\ t_{\beta-3}/L > 0.05 & pathologic \end{array} \quad (1)$$

This imply a minimum of 5% of the time with evident oxygen desaturation to be consider as pathologic, which corresponds to a severe OSAS criteria of 20 apneas/hour having a mean duration of 10 seconds. For control group the threshold corresponds to 5 apneas/hour. This classification is the reference used here to assess the utility of DAP and HRV for OSAS evaluation in children. Table I shows the classification for the different PSG time-span fragments.

B. DAP events detection

PPG signal was analyzed using the method described in [6] for DAP detection. This detector is based on a preprocessor stage which suppress the mean, an envelope detection using root mean square technique and a decision rule based on an adaptive threshold. The detector also includes an artifact detector stage based on Hjorth parameters, see figure 1.

C. HRV analysis

A HRV signal processing analysis was carried out in order to obtain several time and frequency indexes to study their value for discriminate between apneic and non-apneic DAP events.

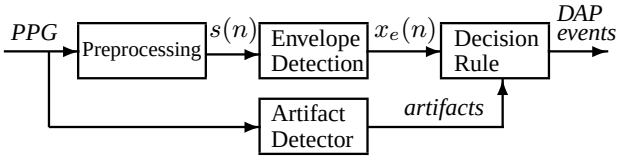


Fig. 1. DAP Detector diagram.

Previous to QRS detection, we implemented a preprocessing. Nonlinear filtering technique was used for removal of the powerline interference [13]. A wavelet-based ECG delineator [14] was used for QRS detection. After that, a ECG signal spline interpolation around each QRS detection was carried out to increase resolution in time of the fiducial point up to an equivalent sampling rate of 2000 Hz. An anomalous beat exclusion rule [15] was applied in order to determine normal beats which were used for the interval tachogram generation used in HRV. To analyze the spectral parameters of the HRV in a time-frequency plane we used the Smooth Pseudo Wigner-Ville Distribution $S_x(t, f)$, since this heart rhythm signal is clearly non stationary. This distribution is characterized by an independent smoothing, in time and frequency, originated by $\gamma(t)$ and $\eta(\frac{\tau}{2})\ \eta^*(-\frac{\tau}{2})$ windows respectively and is defined as:

$$S_x(t,f) = \int\int \varphi(t-t',\tau) x(t'+\frac{\tau}{2}) x^*(t'-\frac{\tau}{2}) e^{-j2\pi f\tau} dt' d\tau \quad (2)$$

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

LF and HF indexes are computed as the power in the LF (0.004-0.15 Hz) and HF (0.15-0.5 Hz) bands respectively.

D. Statistical analysis

To be sure that HRV measures are robust, only DAP events containing a mean of 0.8 normal beats per second within the previous to DAP minute and within the subsequent minute in the ECG signal were considered.

The number of DAP events per hour ratio r was obtained for each analysis segment D_L. From those detected DAP, it was excluded the ones which do not satisfy some restrictions based on DAP events duration and HRV parameters.

DAP onset was considered as the time reference for HRV analysis. According to [10], two windows, five seconds duration each, were defined for each DAP event in order to determine changes in ANS: a control window starting at 10 seconds previous to DAP (W_c) and another window starting at 2 seconds after the DAP detection onset (W_d), see Fig. 2.

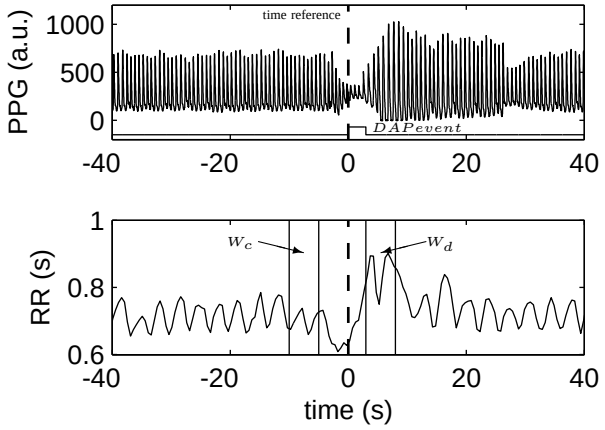


Fig. 2. Analysis windows for determining HRV changes with respect to DAP onset (top).

TABLE II
HRV CONDITIONS

Condition to accept a DAP	Associate index
$\overline{RR}_d/\overline{RR}_c > 1.1$	r^{RR}_{10}
$\overline{RR}_d/\overline{RR}_c > 1.2$	r^{RR}_{20}
$\overline{RR}_d/\overline{RR}_c > 1.3$	r^{RR}_{30}
$\overline{RR}_d/\overline{RR}_c > 1.4$	r^{RR}_{40}
$\overline{RR}_d/\overline{RR}_c > 1.5$	r^{RR}_{50}
$(LF/HF)_d/(LF/HF)_c > 1.1$	r^{LH}_{10}
$(LF/HF)_d/(LF/HF)_c > 1.2$	r^{LH}_{20}
$(LF/HF)_d/(LF/HF)_c > 1.3$	r^{LH}_{30}
$(LF/HF)_d/(LF/HF)_c > 1.4$	r^{LH}_{40}
$(LF/HF)_d/(LF/HF)_c > 1.5$	r^{LH}_{50}
No restriction	r

Mean RR ($\overline{RR}$) and mean low to high frequency ratio (LF/HF) were calculated for each analysis window by averaging $S_x(t,f)$ in the time span of each window, and then computing the LF and HF indexes, finally the ratios between this indexes in W_d and W_c were considered as exclusion criteria of the DAP event. Only DAP that fulfills the HRV conditions showed in Table II were considered in the corresponding DAP per hour ratio r calculation. $r^{\mathrm{RR}}_{\mathrm{x}}$ meaning ratio satisfying RR criteria of $x\%$ and $r^{\mathrm{LH}}_{\mathrm{x}}$ meaning ratio satisfying low to high frequency criteria of $x\%$.

Depending on DAP events duration 5 different situations were considered by restricting to DAP event fulfilling some length restrictions: DAP events of any length (G_{all}), shorter than 4 seconds (G_{-4}), shorter than 2 seconds (G_{-2}), larger than 2 seconds (G_{+2}) and larger than 4 seconds (G_{+4}).

A statistical analysis based on Student's t test was used to compare between groups (control, pathologic) for each DAP per hour ratio index r (Table II). p values < 0.05 were considered statistically significant.

IV. RESULTS

The total number of DAP events included in the analysis after applying the exclusion criteria in III-D were 3031.

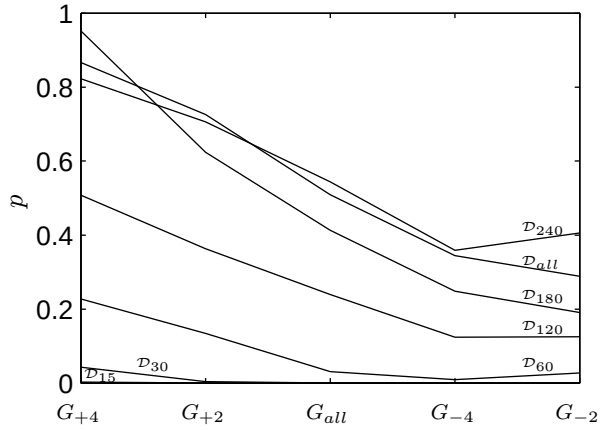
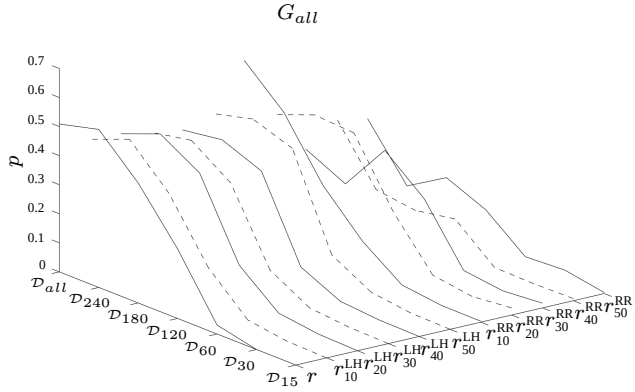


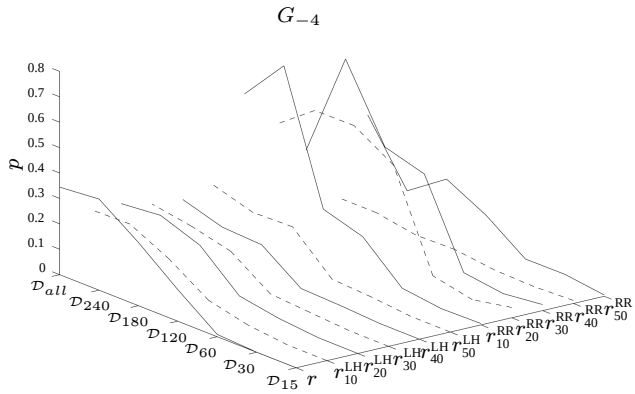
Fig. 3. p values for r ratio depending on the DAP events duration for the different time span of the PSG recording.

Figure 3 shows the p values for r ratio depending on the DAP events duration for the different time span of the PSG recording defined in the study.

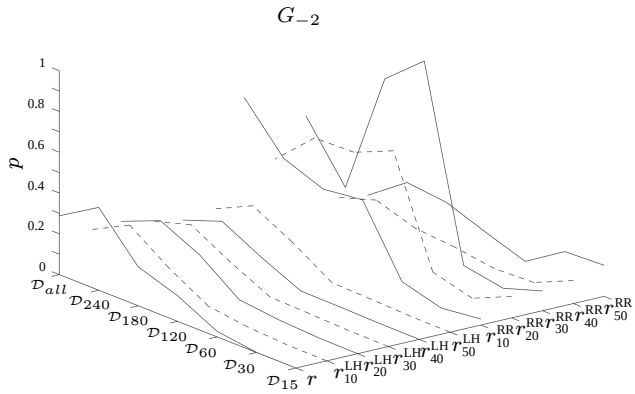
In all cases the highest p values are obtained for DAP durations larger than 2 seconds (G_{+2}) and larger than 4 seconds (G_{+4}), so these restrictions to DAP durations are not considered in the subsequent analysis for HRV.



(a) p values for the different r ratios for any DAP events duration



(b) p values for the different r ratios for DAP events shorter than 4 seconds



(c) p values for the different r ratios for DAP events shorter than 2 seconds

Fig. 4. p values for the different r ratios depending on the increases of HRV parameters for the different time span of the PSG recording.

TABLE III

RESULTS FOR EACH PSG TIME-SPAN ANALYSED

PSG Duration	DAP duration	$p(r)$	p(best index)
$\mathcal{D}_{15}$	G_{-4}	r: 0.000004	r_{10}^{LH}: 0.000001
$\mathcal{D}_{30}$	G_{all}	r: 0.000183	r: 0.000183
$\mathcal{D}_{60}$	G_{-2}	r: 0.027570	r_{40}^{LH}: 0.005756
$\mathcal{D}_{120}$	G_{-2}	r: 0.088331	r_{40}^{LH}: 0.007869
$\mathcal{D}_{180}$	G_{-4}	r: 0.248608	r_{40}^{RR}: 0.024846
$\mathcal{D}_{240}$	G_{-4}	r: 0.358634	r_{40}^{RR}: 0.051962
$\mathcal{D}_{all}$	G_{-2}	r: 0.288491	r_{50}^{RR}: 0.037334

Figure 4 shows the p values for the different r ratios defined in Table II depending on the increases of HRV parameters for the different time span of the PSG recording and for any DAP events duration 4(a), DAP events shorter than 4 seconds 4(b) and shorter than 2 seconds 4(c).

Table III shows the best index for discriminating between groups, indicating DAP events duration, and the associated p value for each of the PSG time-span analysed.

V. DISCUSSION AND CONCLUSIONS

In our research, we have investigated the value of DAP events in conjunction with HRV for OSAS analysis in children. To that end, a clinical study have been developed for diverse time span of the PSG recordings. Fragments of PSG where classified, based on SaO_2 desaturation, for reference.

Our results related to DAP events duration showed better discrimination between groups for shorter DAP events. This result is concordant with the previous study [9]. That might imply that many of the larger DAP events are not associated with apnea; or even, they could be missed PPG artifacts.

The best result for discrimination between groups corresponds to the r_{10}^{LH} index restricted to DAP duration $G_{-4}$and applied to 15 minutes PSG fragments, resulting in a p value of 0.000001.

Results showed in Fig. 3 and in Fig. 4 indicate that discrimination power between groups increases as the PSG time-span under analysis becomes shorter, and so more tune to the apneic episodes. In general, for pathologic patients, larger PSG time-span comprise both oxygen desaturation periods related to apneas and normal periods without sleep problems making more difficult their classification.

HRV increase the differentiation power in some cases, mainly when large PSG time-span is considered, then helping in discriminating DAP event non related to the apneic event. This improvement by including HRV analysis is more relevant for indexes depending on LF/HF restriction, r^{LH} than for those depending on RR restriction, r^{RR} for shorter PSG time-span. On the other hand r^{RR} get better results when PPG fragments are larger.

The described method was compared just to oximetry which is not sufficiently accurate or validated to recommend for use in OSAS diagnosis according to ASDA criteria. Nevertheless most of the pathologic fragments corresponds to children suffering from OSAS according to clinical diagnosis (93% for $\mathcal{D}_{15}$, 98% for $\mathcal{D}_{30}$, 100% for $\mathcal{D}_{60}$, $\mathcal{D}_{120}$, $\mathcal{D}_{180}$, $\mathcal{D}_{240}$ and $\mathcal{D}_{all}$) so the results could be extrapolated from oxygen desaturation events to pathological events, at least within each record.

In conclusion the number of DAP events per hour ratio is able to classify PSG fragments of children as related to SaO_2 desaturation or normal breathing within a high statistically significant probability ($p = 0.000001$). This discrimination between groups is better for shorter PSG time-span and the inclusion of HRV analysis improve the results, mainly when large PSG time-span is considered which corresponds to the situation of more difficult discrimination. The results evidence a clear link between oxygen desaturation and DAP events presence.

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