

Pulse Transit Time Variability versus Heart Rate Variability during Decreases in the Amplitude fluctuations of Photoplethysmography signal.

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Abstract. An analysis of the pulse transit time variability (PTTV) and heart rate variability HRV during decreases in the amplitude fluctuations of photoplethysmography (DAP) events, and their relationship with sleep apnea events is presented. 268 selected DAP events were extracted from complete night polysomnography recordings from 21 children and classified in 5 groups depending on oxygen saturation and respiratory behaviour. PTTV and HRV signal processing using the Smooth Pseudo Wigner-Ville Distribution was carried out. Three windows around each DAP are defined and temporal evolution of HRV and PTTV indexes were studied using Kruskal-Wallis statistic test. Results show a significant increase in LF and decrease in HF during DAP events for both HRV and PTTV, indicating an increase in the sympatho-vagal balance of the autonomic nervous system followed by a recovery period. The increase in sympathetic activity index (LF) for PTTV (85%) is higher than for HRV (33%). However decreases in parasympathetic activity during DAP events produce similar decrements in parasympathetic activity indexes (HF) for PTTV (18%) and HRV (22%). In conclusion, PTTV reflects sympathetic changes more clearly than HRV.

Keywords: Sleep apnea; children; pulse transit time variability; pulse photoplethysmography; time-frequency.

1. Introduction

Spectral analysis of the heart rate variability (HRV) signal has been widely used for evaluating the action of the autonomic nervous system (ANS). Power spectral density of the HRV exhibits oscillations, which are related to the parasympathetic and sympathetic activities [Task Force, 1996]. Wide band of spectral components of the HRV goes from 0.003 to 0.5 Hz, where the range between 0.003 and 0.04 Hz (very low-frequency component, VLF) takes account of long-term regulation mechanisms; the range between 0.04 and 0.15 Hz (low-frequency component, LF) represents both sympathetic and parasympathetic modulation, but an increase in its power is generally associated to a sympathetic activation. However, even nowadays, there is a controversy about the contribution of each autonomic branch to this frequency band. The 0.15-0.5 Hz range (high-frequency component, HF) corresponds to parasympathetic modulation and it is synchronous with respiratory rate. Finally the low to high frequency ratio (LF/HF) is a concise index to evaluate the sympatho-vagal balance controlling heart rate.

On the other hand, pulse photoplethysmography signal (PPG) is a simple and useful method for measuring the pulsatile component of the heartbeat and evaluating peripheral circulation, and is tie related to arterial vasoconstriction or vasodilatation generated by the ANS and modulated by the heart cycle.

PPG has been directly related with the cardiac function, giving as a result a measure of the pulse transit time (PTT) [Foo and Lim, 2006]. PTT gives a quantitative measure of the time that the pulse wave needs for passing from one arterial, typically the aorta, to another, typically in the periphery, and is evaluated as the time interval between the ECG R peak and the corresponding PPG wave.

A sleep apnea event consists in a breathing cessation during sleep. These events lead to oxygen desaturation, and an increase in mechanical respiratory efforts in order to restore breathing. 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. When a sleep apnea occurs sympathetic activity increases as a response to the obstructive event in order to reestablish respiration. The increase in sympathetic activity is associated with vasoconstriction and, possibly, is related to transient arousal [Leuenberger et al., 2001; Somers et al., 1995; Imadojemu et al., 2002]. Vasoconstriction is reflected in PPG by a decrease in the signal amplitude fluctuation [Nitzan et al., 1998]. These decreases in the amplitude fluctuations of PPG (DAP) have shown their utility for sleep apnea detection [Gil et al., 2008]. In addition, 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 [Pitson et al., 1994; Katz et al., 2003].

It's well known that by far the most important part of the ANS for regulating the circulation is the sympathetic nervous system [Guyton and Hall, 2006; Kandel et al., 2000]. Although the parasympathetic nervous system is exceedingly important for many other autonomic functions of the body it plays only a minor role in regulation of the circulation. Its most important circulatory effect is to control heart rate by way of parasympathetic nerve fibers to the sinoatrial node in the vagus nerves. So blood vessels are mainly innervated by sympathetic nerve fibers.

The aim of this study is to compare PTT variability (PTTV) with HRV during DAP events and their relationship with sleep apnea, so to evaluate their potential to improve specificity of DAP as apnea markers. The hypothesis is that, as PTT, which reflects the peripheral circulation, is mainly mediated by sympathetic activity, PTTV reflects sympathetic changes more clearly than HRV.

2. Methodology

2.1. 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 [American Thoracic Society, 1996], using a commercial digital polygraph (EGP800, Bitmed). There were recorded 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 Novamatrix, Medical Systems). All of the signals were stored at a sampling rate of 100 Hz, except ECG channels whose sampling rate was 500 Hz. The PSG data were scored manually following standard procedures used to discriminate children suffering from obstructive sleep apnea syndrome (OSAS) (10 children) from those who are not (11 children).

DAP events for each recording were detected with the procedure described in [Gil et al., 2008] at the PPG signal, $x_{\text{PPG}}(n)$. Segments from ECG, PPG, 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 selected to obtain five different groups with uniform patterns based on the gold standard criterion for defining sleep apneas [American Thoracic Society, 1999]. DAP event is classified into: Group 1 (G_1) when 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 and no reduction in SaO_2 . Group 3 (G_3) when airflow reduces by more than 50% from base line and is accompanied by a reduction in SaO_2 of at least 3%. Group 4 (G_4) when DAP event correlated neither to airflow reduction nor SaO_2 decrement. Finally, Group 5 (G_5) when DAP events are related neither to apneas nor to SaO_2 decrements but a change in respiration occurs. G_1 , G_2 and G_3 can be merged in a single group named G_a (apneic group) as well as G_4 and G_5 can also be regrouped in a single set, G_n (non apneic group). A total of 268 DAP events were extracted. Table 1 shows a summary of the DAP events in each group.

Table 1. Number of DAP events in each group.

Clinical diagnosis	DAP Group					Total
	G_1	G_2	G_3	G_4	G_5	
Normal	4	32	5	76	31	148
OSAS	44	21	33	11	11	120
Total	48	53	38	87	42	268

2.2. Variability analysis

HRV and PTTV were obtained in order to evaluate the ANS. An automatic QRS detector [Martinez et al., 2004] was applied to ECG signal providing the θ_j beat location for every j th beat.

HR. Inverse interval function $d_{\text{IFF}}(\theta_j)$ denoting the heart rate time series were extracted from the ECG segments

$$d_{\text{IFF}}(q_j) = \frac{1}{q_j - q_{j-1}}, \quad (1)$$

and after, the evenly sampled signal $d_{\text{IFF}}(m)$ at 2 Hz was generated using a cubic spline interpolation.

PTT. The following process was applied for obtaining the PTT signal. For every j th beat a PTT value was calculated. First the occurrence time of the pulse wave peak n_{pj} was detected at the PPG signal $x_{\text{PPG}}(n)$

$$n_{pj} = \arg \max_n \left(x_{\text{PPG}}\left(\frac{q_j}{5} + 15\frac{\delta}{\delta}\right), \dots, x_{\text{PPG}}(n), \dots, x_{\text{PPG}}\left(\frac{q_{j+1}}{5} - 15\frac{\delta}{\delta}\right) \right). \quad (2)$$

Then the PPG pulse wave onset n_{oj} was detected

$$n_{mj} = \arg \min_n \left(x_{\text{PPG}}\left(\frac{q_j}{5} - 15\frac{\delta}{\delta}\right), \dots, x_{\text{PPG}}(n), \dots, x_{\text{PPG}}(n_{pj}) \right). \quad (3)$$

$$n_{oj} = \begin{cases} n_{mj} & \text{if } \frac{\|x_{\text{PPG}}(n)\|^2}{\|n\|^2} < 0.03 \\ \arg \min_n \left(\frac{\|x_{\text{PPG}}(n)\|^2}{\|n\|^2} \right) > 0.03 & \text{otherwise} \end{cases} \quad n \in \{n_{mj}, \dots, n_{pj}\} \quad (4)$$

The 0.03 threshold was empirically determined. After that, a spline interpolation for $x_{\text{PPG}}(n)$ within the interval $[n_{oj}, \dots, n_{pj}]$ was carried out to increase resolution in time up to an equivalent sampling rate of 500 Hz, obtaining $x_{\text{PPG}}^i(k)$ signal. Finally the PPG wave reference point k_{rj} was calculated

$$k_{rj} = \arg \min_k \left(x_{\text{PPG}}^i(k) - x_{\text{PPG}}^i(5n_{oj}) + \frac{x_{\text{PPG}}^i(5n_{pj}) - x_{\text{PPG}}^i(5n_{oj})}{2} \right). \quad (5)$$

Then the PTT value for each j th beat, $d_{\text{PTT}}(\theta_j)$ is

$$d_{\text{PTT}}(q_j) = k_{rj} - q_j, \quad (6)$$

PTT values for each beat, $d_{PTT}(\theta_j)$, out of the range [150 ms 400 ms] were considered no valid. Finally, PTT time series was re-sampled at 2 Hz by cubic spline interpolation in order to obtain an evenly sampled signal $d_{PTT}(m)$. Figure 1 shows an example of the process applied to obtain the PTT signal.

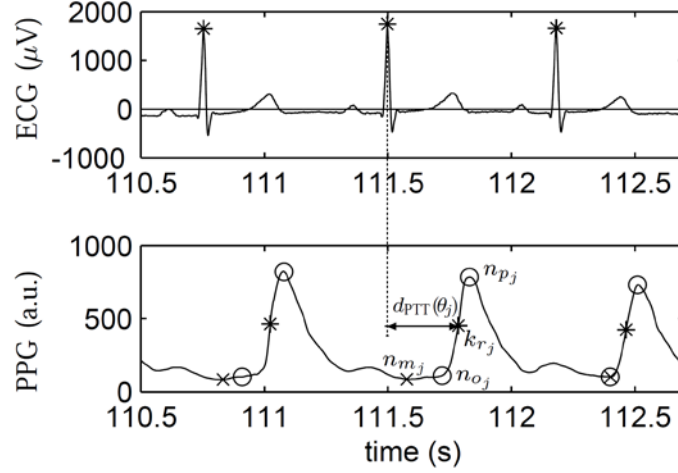


Figure 1. PTT measure example.

Time-frequency transformation. Time-Frequency representation was used to decompose both signals $d_{IF}(m)$ and $d_{PTT}(m)$ in their different frequency contents at each time. Details of time-frequency transformation, where Smooth Pseudo Wigner-ville Distribution was used, are shown in [Gil et al., 2009] and [Mendez et al., 2008]. Then, the time evolution of PTTV and HRV frequency contents were evaluated: total power, from 0.0033 to 0.5 Hz ($P^X_T(m)$); very low frequency power, from 0.0033 to 0.04 Hz ($P^X_{VLF}(m)$); low frequency power, from 0.04 to 0.15 Hz ($P^X_{LF}(m)$); high frequency power, from 0.15 to 0.5 Hz ($P^X_{HF}(m)$); low to high frequency ratio ($R^X_{LF/HF}(m)$); and their normalized versions with respect to the total power $P^X_{VLFn}(m)$, $P^X_{LFn}(m)$ and $P^X_{HFn}(m)$; superscript $X \in \{HRV, PTTV\}$.

2.3. Statistical analysis

In order to quantify the evolution of autonomic variations when a DAP event is associated or not associated to airflow decrements, SaO₂ reductions or to nothing, three time windows were defined in specific time intervals related to DAP events onset. Figure 2 shows the mean±S.D. of $d_{IF}(m)$ and $d_{PTT}(m)$ signals 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) is located 15 seconds after DAP onset and lasting 5 s. Mean absolute values in the time windows were computed for $P^X_{LFn}(m)$, $P^X_{HFn}(m)$ and $R^X_{LF/HF}(m)$, obtaining the indexes $\bar{P}^X_{LFn}(m)$, $\bar{P}^X_{HFn}(m)$ and $\bar{R}^X_{LF/HF}(m)$ for each window $w \in \{w_r, w_d, w_p\}$. Kruskal-Wallis non parametric statistic approach was performed to compare the time variations among windows of HRV and PTTV parameters. Post-hoc analysis was applied to determine which pairs had statistic differences ($p < 0.05$).

3. Results and discussion

Figure 3 shows the results of the Kruskal-Wallis statistical analysis to compare the time variations among windows of HRV and PTTV frequency indexes. Time evolution of frequency indexes shows similar patterns in all groups, an increase in LF and LF/HF and a decrease in HF during DAP for both HRV and PTTV, indicating an increase in the sympatho-vagal balance of the ANS followed by a recovery period.

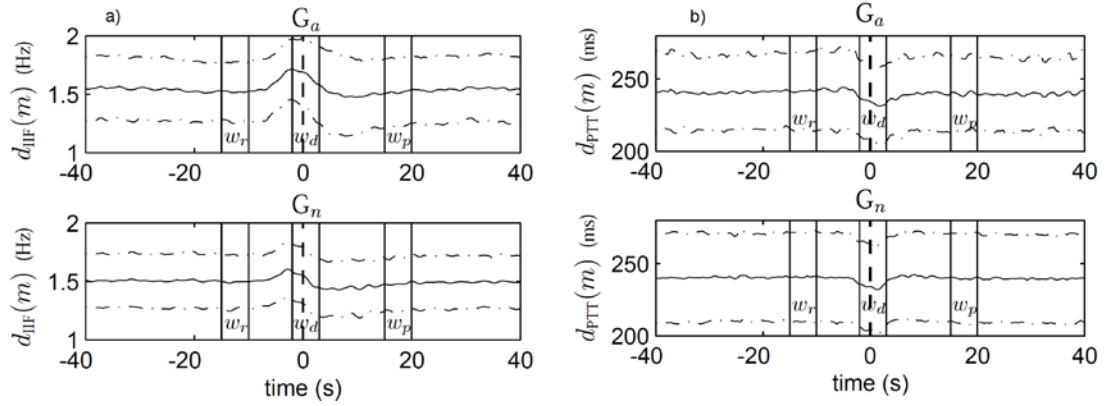


Figure 2. $d_{III}(m)$ mean \pm S.D. in (a) and $d_{PTT}(m)$ mean \pm S.D. in (b) for apneic ($G_a \equiv G_1 + G_2 + G_3$) and non-apneic ($G_n \equiv G_4 + G_5$) DAP events. Analysis windows (w_r reference, w_d DAP episode, w_p post DAP event). Dashed line at reference time indicate DAP onset.

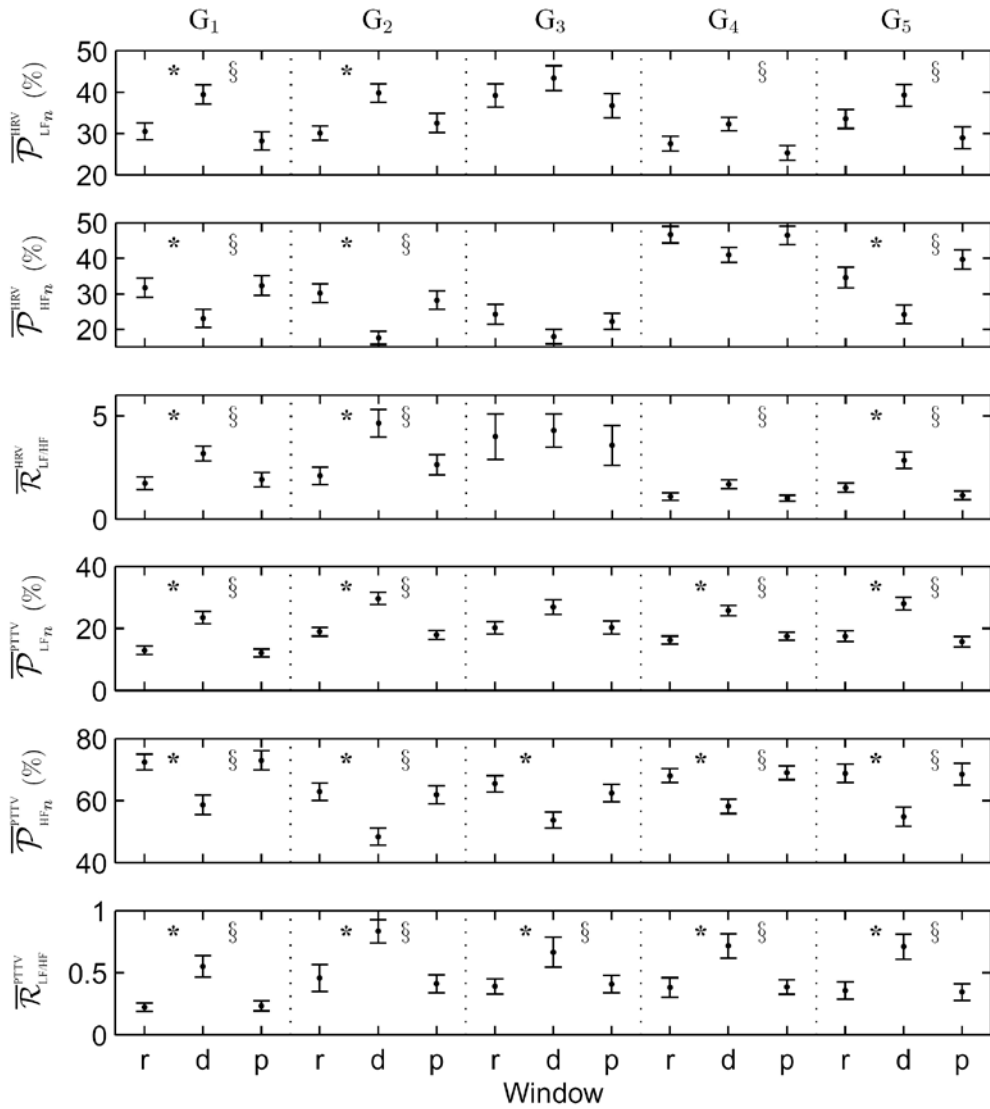


Figure 3. Results of the Kruskal-Wallis statistical analysis to compare the time variations among windows of HRV and PTTV frequency indexes. From the top to the bottom, mean \pm S.E. of $\overline{P}_{LFn}^{HRV}(m)$, $\overline{P}_{HF_n}^{HRV}(m)$, $\overline{R}_{LF/HF}^{HRV}(m)$, $\overline{P}_{LFn}^{PTTV}(m)$, $\overline{P}_{HF_n}^{PTTV}(m)$ and $\overline{R}_{LF/HF}^{PTTV}(m)$ in each window. Window refers to the temporal windows analyzed during DAP (r reference, d DAP episode, p post DAP event). * refers to $p < 0.05$ between windows w_r and w_d and \S to $p < 0.05$ between windows w_d and w_p .

Table 2 shows the mean percentage variation of frequency indexes during DAP events, difference between w_d and w_r for each index is denoted as $\Delta Y^{w_d-w_r}$, where Y means the frequency index. The increase in sympathetic activity index for PTTV, $\overline{P}_{LFn}^{PTTV}$, (85%) is higher than for HRV, \overline{P}_{LFn}^{HRV} , (33%) during DAP, which means that PTTV reflects sympathetic changes more clearly than HRV, confirming our hypothesis. Decreases in parasympathetic activity during DAP events produce similar decrements in parasympathetic activity indexes for PTTV, $\overline{P}_{HF_n}^{PTTV}$, (18%) and HRV, $\overline{P}_{HF_n}^{HRV}$, (22%).

Table 2. Mean percentage variation of frequency indexes during DAP

%	G ₁	G ₂	G ₃	G ₄	G ₅	G _a	G _n	G _T
$\frac{\Delta \overline{P}_{LF_n}^{HRV^{w_d-w_r}}}{\overline{P}_{LF_n}^{HRV^{w_r}}}$	41.7	44.4	18.3	30	25.3	36.4	28.4	32.6
$\frac{\Delta \overline{P}_{HF_n}^{HRV^{w_d-w_r}}}{\overline{P}_{HF_n}^{HRV^{w_r}}}$	-22.7	-37.2	-8.8	-14	-29	-24.5	-18.9	-21.8
$\frac{\Delta \overline{R}_{LE/HE}^{HRV^{w_d-w_r}}}{\overline{R}_{LE/HE}^{HRV^{w_r}}}$	146.3	222.3	81.3	71.7	123.44	157.5	88.6	124.3
$\frac{\Delta \overline{P}_{LF_n}^{PTTV^{w_d-w_r}}}{\overline{P}_{LF_n}^{PTTV^{w_r}}}$	118.8	75.7	55.2	80	97.6	84.4	85.6	85
$\frac{\Delta \overline{P}_{HF_n}^{PTTV^{w_d-w_r}}}{\overline{P}_{HF_n}^{PTTV^{w_r}}}$	-20.1	-20	-17	-14.9	-17.9	-19.2	-15.8	-17.53
$\frac{\Delta \overline{R}_{LE/HE}^{PTTV^{w_d-w_r}}}{\overline{R}_{LE/HE}^{PTTV^{w_r}}}$	203.1	156.5	105.9	134.9	171.5	157.9	146.6	152.3

Frequency indexes derived from HRV were used in a previous study [Gil et al., 2009] for discriminating between DAP events related and not related to apnea episodes (G_a and G_n). $\overline{P}_{HF_n}^{HRV}$ showed the best results because their values are higher in G_n than in G_a. Although a clinical study is necessary preliminary results show that frequency indexes of PTTV are not useful in classifying DAP event as apneic or no apneic because the indexes show similar values for all DAP groups.

4. Conclusions

In conclusion, an analysis of autonomic control derived from PTTV and HRV during decreases in the amplitude fluctuation of photoplethysmography signal in children was presented. When a DAP event occurs, there is an increase in the sympatho-vagal balance. Our results show that frequency indexes derived from PTTV reflects sympathetic changes more clearly than HRV. $\overline{P}_{LF_n}^{HRV}$ mean increase during all DAP events analyzed was 32.6% whereas $\overline{P}_{LF_n}^{PTTV}$ mean increase was 85%. Nevertheless, extended studies are needed to corroborate the potential usefulness of PTTV for evaluating ANS, and their relationship with HRV.

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