

Pulse Rate Variability in Children with Disordered Breathing during Different Sleep Stages

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Abstract

Heart Rate Variability (HRV), the variation of time intervals between heartbeats, is an indirect and noninvasive method for monitoring the autonomic activities that control heart rate. Traditionally, HRV is measured from the electrocardiogram. In this study, we estimated HRV from the photoplethysmogram (PPG), called pulse rate variability (PRV) and investigated the effects of sleep disordered breathing (SDB) and different sleep stages on it. We recorded the overnight PPG signals from 160 children using the Phone Oximeter, an oximeter connected to a mobile phone, simultaneously with the other signals within standard polysomnography. We analysed the mean pulse-to-pulse intervals, the power of low (LF) and high frequency (HF) bands of PRV and also the ratio of LF power to HF power (LF/HF) in the children with SDB during non-rapid eye movement (non-REM) and rapid eye movement (REM) sleep. The results showed that the normalized LF increased in children with SDB (from 0.26 ± 0.12 to 0.29 ± 0.13 during non-REM sleep and from 0.37 ± 0.12 to 0.40 ± 0.15 during REM sleep), the LF/HF ratio increased in children with SDB (from 0.67 ± 0.55 to 1.05 ± 1.00 in non-REM sleep and from 1.46 ± 2.20 to 1.74 ± 1.38 in REM) and the HF components decreased in children with SDB (from 0.61 ± 0.16 to 0.55 ± 0.17 in non-REM sleep and from 0.47 ± 0.14 to 0.43 ± 0.16 in REM sleep). The results may confirm the pronounced sympathetic and the diminished parasympathetic activity in children with SDB. This study indicates that PRV obtained from the PPG reflects the autonomic regulation of heart rate in disordered breathing during different sleep stages.

1. Introduction

Heart rate variability (HRV) is defined as the variation in the time interval between consecutive heartbeats. It is

an indirect indicator used to evaluate the interaction between the autonomic nervous system and the cardiovascular system. It is also used to monitor the balance between the sympathetic and parasympathetic activities that control the heart rate. In spectral analysis of HRV usually three frequency bands are of interest: very low (< 0.04 Hz, VLF), low ($0.04 - 0.15$ Hz, LF) and high frequency band ($0.15 - 0.4$ Hz, HF). The physiological interpretation of the components in these bands is debatable. The low frequency components of HRV may indicate the sympathetic activity and the high frequency components may reflect the parasympathetic activity. The ratio of LF power to HF power is an index of sympathetic/parasympathetic balance [1]. Traditionally, HRV is obtained from the electrocardiogram. Some previous studies have shown the feasibility and accuracy of extracting the variation of heart rate from photoplethysmogram (PPG) [2], [3] and [4].

Pulse oximeter photoplethysmography (PPG) is a non-invasive and low-cost measurement technique for detecting blood volume in body tissues (e.g. fingertip or earlobe). The pulsatile feature of the PPG waveform is synchronized with the heart rate. It means that each pulse wave of PPG arises from blood volume changes in arterial tissues due to each heartbeat [5]. Pulse rate variability (PRV) is defined as the variation between pulse-to-pulse time intervals of the PPG signal.

Sleep disordered breathing (SDB) includes a large group of breathing irregularities during sleep (i.e., pauses in breathing or abnormalities of the quantity of ventilation). Obstructive sleep apnea/hypopnea syndrome (OSAHS), the most prevalent type of SDB, is characterized by periodic interruption of breathing during sleep and is generally caused by a partial or complete collapse in muscles of the upper airway [6]. Central sleep apnea whose occurrence is far less common than OSAHS is characterized as reduced respiratory effort during sleep [6]. The severity of sleep apnea syndrome is defined by the frequency

of apnea/hypopnea events per hour or the apnea/hypopnea index (AHI). Untreated SDB disturbs normal respiration, oxygenation and sleep quality. SDB is as common in children, as in adults and results in daytime sleepiness, fatigue, poor school performance, inattention, hyperactivity, and other behavioural disturbances [7].

A wide range of studies have suggested that apnea, hypopnea and arousals cause changes in the normal variation of heart rate during sleep. These studies have shown that the LF components of HRV and also the LF/HF ratio are more pronounced in subjects with SDB while HF components of HRV are reduced during SDB [8]. These studies suggest that the sympathetic activity increases during sleep and even wakefulness in patients with SDB while the parasympathetic activity decreases.

Additionally, autonomic activity changes during different sleep stages. In non-random eye movement (non-REM) sympathetic activity decreases compared to wakefulness. In random eye movement (REM), sleep sympathetic activity is similar to wakefulness but is higher compared to non-REM sleep [9].

In this study, we investigated the effects of SDB and also the effects of different sleep stages on heart rate. Considering the information that the PPG signal provides about heart rate and also the simplicity of using pulse oximeter, we have estimated the variation of heart rate from the PPG signal instead of using ECG. The PPG signals were recorded in a sleep laboratory using a Phone Oximeter, an oximeter sensor connected to a mobile phone [10], simultaneously with other signals recorded during standard polysomnography.

2. Materials and methods

2.1. Database

This study was approved by the University of British Columbia Clinic Research Ethics Board. Following informed consent, 160 children referred to the British Columbia Children’s Hospital for overnight PSG were recruited. The sleep studies of 18 subjects were excluded from study due to inadequate length of sleep or absence of a PPG signal. Polysomnography recording included the electroencephalogram, left and right electrooculogram, leg movements, body positions, thoracic and abdominal wall movement (from respiratory inductive plethysmography), oro-nasal airflow (from nasal pressure), arterial oxygen saturation SpO₂, PPG and electrocardiogram lead I and II. In addition, the PPG (62.5 Hz), HR (1 Hz), and SpO₂ (1 Hz) were recorded using the Phone Oximeter simultaneously. Using results of PSG and the diagnostic report of the paediatric respiratory specialist, subjects were divided into two groups: children with AHI ≥ 5 (SDB group) and children with AHI < 5 (Non-SDB group) (Table 1).

2.2. Pulse rate analysis

The PPG signal recorded by the Phone Oximeter was used for estimating the pulse rate variability (PRV). The baseline was removed by a forward-backward second order Butterworth high-pass filter with a cut off frequency of 0.5 Hz. Then a Savitzky-Golay FIR filter (order 3, frame size 11 samples) was applied for the purpose of smoothing the PPG signal. A signal quality index, obtained by an adaptive version of the algorithm developed by Karlen et al [10] was used for automatic rejection of artifacts. After that, the PPG signal was divided into one-minute segments with a 50% overlap between adjacent segments. In each segment, the temporal location of each pulse peak was detected as the maximum of the PPG signal within the pulse wave. Each pulse time series was converted to a pulse-to-pulse interval series or tachogram. The pulse-to-pulse intervals with the lengths less than 0.33 and more than 1.5 seconds were deleted from the time series. PRV was obtained by using a cubic interpolation of tachogram sampled evenly at 4 Hz.

The power spectral density (PSD) of PRV was calculated through a parametric PSD based on an autoregressive model, with 1024 points and order 7.

For analysing PRV, the time and frequency domain parameters widely used for analysing HRV, were calculated according to the standard definitions of these parameters [1]. In the time domain, for each segment of PP interval series, the mean PP intervals, the standard deviation of all PP intervals (SDPP) and the root mean square of the difference of successive PP intervals (RMSSD) were calculated. The normalized powers of LF and HF bands, and the LF to HF power ratio (LF/HF) were determined in the frequency domain. All annotated periods of NREM and REM sleep were separately analysed.

Table 1. Demographic metrics and AHI index of studied database expressed as mean \pm standard deviation

	Total (n = 145)	Non-SDB (n = 89)	SDB (n = 56)
Age (years)	9.1 \pm 4.2	9.3 \pm 4.0	8.7 \pm 4.5
BMI (kg/m ²)	20.00 \pm 6.40	17.41 \pm 6.43	23.00 \pm 8.22
AHI	8.40 \pm 15.0	1.40 \pm 1.20	19.77 \pm 19.68

3. Results

3.1. Effects of sleep disordered breathing on pulse rate variability

During both non-REM and REM sleep (Table 2 and Table 3), the mean PP intervals appeared shorter for the children with SDB compared to the children without SDB. The

difference between the sample means is 0.06 during non-REM sleep and 0.05 during REM sleep with 95% confidence interval from 0 to 0.1. For SDPP and RMSSD, no significant difference was found between children with and without SDB.

Normalized LF increased in the children with SDB during both non-REM and REM sleep. The difference between sample mean normalized LF in the children without and with SDB is -0.03 with confidence interval from -0.07 to 0.01.

During both non-REM and REM sleep, normalized HF was lower in the group of children with SDB relative to the children without SDB. In non-REM sleep the difference between sample mean normalized HF in the children without SDB and with is 0.06 with 95% confidence interval from 0.00 to 0.12. During REM sleep the difference of means is 0.04 with 95% confidence interval from 0.00 to 0.10.

The LF/HF ratio was found to be higher in the group of children with SDB during both periods of non-REM and REM sleep. In non-REM sleep the difference between sample mean LF/HF ratio in the children without SDB and with is -0.38 with 95% confidence interval from -0.66 to -0.10. During REM sleep the difference of means is -0.27 with 95% confidence interval from -0.70 to 0.43.

Table 2. Descriptive results for the parameters obtained from PRV for two groups of subjects with and without SDB in non-REM sleep.

	non-SDB	SDB	diff. of means	%95 CIs(low,high)	P
mean					
PP intervals	0.81±0.15	0.75±0.15	0.06	0.00,0.11	0.01
SDPP	0.07±0.05	0.07±0.03	0.00	-0.02,0.17	0.16
RMSSD	0.08±0.10	0.07±0.04	0.01	-0.04,0.02	0.34
normalized LF	0.26±0.12	0.29±0.13	-0.03	-0.07,0.01	0.05
normalized HF	0.61±0.16	0.55±0.17	0.06	0.00,0.12	0.03
LF/HF	0.67±0.55	1.05±1.00	-0.38	-0.66,-0.10	0.05

3.2. Effects of sleep stages on pulse rate variability

For both groups of children with and without SDB, when the sleep progressed from the non-REM to REM, the normalized LF power and LF/HF ratio increased while the normalized HF parameter was found to be lower (Figure 1 and 2).

Table 3. Descriptive results for the parameters obtained from PRV for two groups of subjects with and without SDB in REM sleep.

	non-SDB	SDB	diff. of means	%95 CIs(low,high)	P
mean					
PP intervals	0.76±0.15	0.71±0.15	0.05	0.00,0.10	0.01
SDPP	0.06±0.05	0.06±0.03	0.00	-0.02,0.20	0.16
RMSSD	0.07±0.11	0.06±0.04	0.01	-0.02,0.04	0.34
normalized LF	0.37±0.12	0.40±0.15	-0.03	-0.09,0.01	0.09
normalized HF	0.47±0.14	0.43±0.16	0.04	0.00,0.10	0.02
LF/HF	1.46±2.20	1.74±1.38	-0.27	-0.7,0.43	0.05

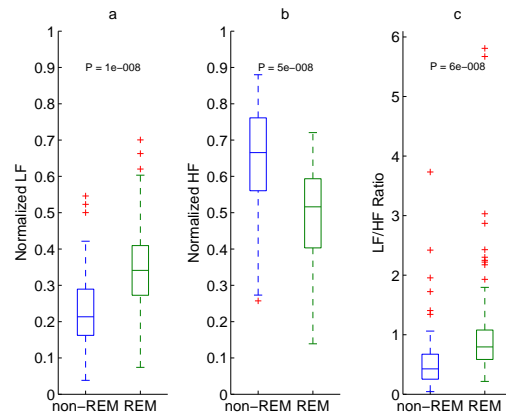


Figure 1. The boxplot shows (a) normalised LF, (b) normalised HF and (c) LF/HF ratio in non-REM and REM sleep in children without SDB. Lower quartile, median, and upper quartile values were displayed as bottom, middle and top horizontal line of the boxes. Whiskers were used to represent the most extreme values within 1.5 times the interquartile range from the quartile. Outliers (data with values beyond the ends of the whiskers) were displayed as crosses.

4. Discussion and conclusions

In this study, we recorded the PPG signal using the Phone Oximeter with other signals recorded during overnight polysomnography. The PPG signal was used to estimate the variation of heart rate (pulse rate variability (PRV)) in children with and without disordered breathing during REM and non-REM sleep.

During both REM and non-REM sleep, the mean of PP intervals appeared shorter for children with SDB in respect to children with control breathing. It shows higher heart rate in children with SDB which may indicate higher sym-

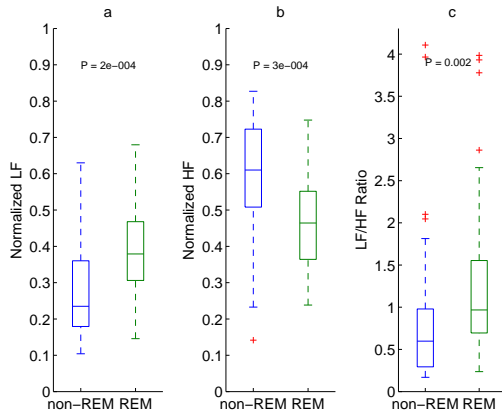


Figure 2. The boxplot shows (a) normalised LF, (b) normalised HF and (c) LF/HF ratio in non-REM and REM sleep in children without SDB.

pathetic activity. It is also possible that the arousals which almost accompanied the apnea events contributed to the increased heart rate. Khandoker *et al.* [3] who investigated PRV during sleep apnea also reported significant higher heart rate. For SDPP and RMSSD, no significant difference was found between children with and without SDB.

In spectral analysing, during both REM and non-REM, the low frequency components of PRV (0.04 - 0.15 Hz) and the LF/HF ratio were higher in children with SDB compared to the children without disordered breathing. In children with SDB, the high frequency components of PRV (0.15 - 0.4 Hz) diminished during both non-REM and REM sleep. We replicate the results of a study conducted by Penzel *et al.* for analysing HRV in sleep and sleep apnea [11]. These results may indicate the higher sympathetic and lower parasympathetic activity in children with SDB during both REM and non-REM.

In both groups of children with and without SDB, when the sleep progressed from non-REM to REM sleep, the power of low frequency band and the LF/HF ratio increased while the power of high frequency band decreased. It may confirm the increase of sympathetic activity and the decrease of parasympathetic activity during REM sleep in both groups of children.

This study investigated the changes of PRV in disordered breathing during different sleep stages. Our findings obtained from PRV replicate the existing results of previous studies conducted to analysis HRV in SDB [11]. It confirms the feasibility of using PRV in monitoring the autonomic regulation of heart rate in SDB during different sleep stages. One subject that remains to be explored is

identifying the children with SDB and also classifying the different sleep stages based on analysing PRV.

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