EVALUATION OF RESPIRATORY SLEEP EVENTS USING CHILDHOOD PULSE TRANSIT TIME

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ABSTRACT
Pulse transit time (PTT) is a non-invasive measure and has shown potential to estimate breathing effort variations in response to involuntarily changes of the upper airway in adults during sleep. The objectives of this study were to assess the capability of PTT to classify respiratory sleep events as either central or obstructive in nature and its sensitivity to detect both apnoeas and hypopnoeas. 291 respiratory events occurred in 24 routine overnight polysomnographic (PSG) studies performed on children (19 male and 5 female, mean age 6.7 years). PTT measurements were evaluated against the corresponding PSG results pre-scored by 2 blinded observers. Obstructive events showed a mean change of 5.35% (p<0.05), with ±11.54ms standard deviation (SD) and maximal change of 12.94% (p<0.05) from baseline PTT value during tidal breathing. Central events showed a mean 1.42% (p>0.05) change, with ±3.00ms SD and maximal change of 1.98% (p>0.05). PTT was able to categorise central and obstructive respiratory events accordingly, including hypopnoeas. Hence, PTT shows promises to differentiate respiratory events accordingly in absence of motion artefacts and can be a useful tool in a simplified ambulatory screening system for children for sleep-disordered breathing investigation.

KEY WORDS
Measurement and instrumentation, pulse transit time, obstructive sleep apnoea, and sleep-disordered breathing

1. Introduction
Obstructive sleep apnoea-hypopnoea syndrome (OSAHS) in children is characterised by recurring episodic upper airway obstructions and may be associated with hypoxemia and hypercarbia [1]. Through the different interactions of these respiratory stimuli, children with SDB may exhibit transient respiratory arousals in response to a narrowed or collapsed upper airway in order to restore their ventilation [2]. The effects of OSAHS can range from mild irritation to physiological and psychological deficits including hypertension, IQ loss or even death [1], [3]. Early detection of these respiratory events then becomes important to minimise the possible long-term neurobehavioral deficits. In addition, the accurate classification of these events as either central or obstructive in nature can be critical to determine the appropriate treatment for the child [4] as the treatment for both can be quite different [5].

Pulse transit time (PTT) has shown its potential ability to estimate breathing effort changes and arousals in response to involuntarily changes in the upper airway [3-5]. PTT is the time taken for the arterial pulse pressure wave to travel from the left ventricle to a periphery. The principle determinant of this pressure wave is the changes in blood pressure (BP) which is in turn affected by the degree of stiffness of the arterial wall [3-5]. In OSAHS events, respiration can be terminated by events of an obstructive nature that can lead to a marked transient increase in BP [1]. These abrupt changes are caused by the pleural pressure swings initiated in response to involuntarily obstructions in the upper airway [3]. During such episodes, BP rises with an increase in stiffness of the arterial wall [5]. Conversely, events of central respiratory nature are denoted by lesser variations in respiratory efforts [4] with reduction or possible termination of the entire ventilation process. Argod et al [4] and Pitson et al [6] in their studies have demonstrated the inverse and significant correlation of PTT with BP and esophageal pressure measure respectively.

Based on these findings, changes in PTT can reflect changes in respiratory efforts. Furthermore, no known studies were performed to assess PTT capabilities to differentiate respiratory events in children during sleep. Hence, the objectives of this study were (1) to determine the possible use of PTT to detect changes in respiratory efforts, (2) assess the capability of PTT to differentiate obstructive from central apnoeas and (3) its ability to detect obstructive and central hypopnoeas.

2. Materials and Methods
2.1. Polysomnography (PSG)
Routine overnight PSG was performed in the sleep laboratory with monitoring that included electroencephalography (electrodes C3-A2 and O2-A1), left and
right electrooculogram (LE-A2 and RE-A1), oronasal airflow tracing via pressure transducer, AC-coupled respiratory inductance plethysmograph (RIP) recording of chest and abdominal movement (Respirace Calibrator System, Ambulatory Monitoring Inc, Ardsley, USA), infrared photoplethysmography (PPG), heart rate (HR) calculation and oxygen saturation (SaO2) by pulse oximetry (Novametrix Medical Systems Inc, Wallingford, USA). The studies were continuously observed by experienced PSG personnel and all readings were recorded by a commercial computerised PSG system (Uniquant system, LaMont Medical Inc, Wisconsin, USA). An episode of obstructive apnoea was defined as a complete cessation of airflow with the presence of chest or/and abdominal wall movement. An obstructive hypopnoea has similar characteristics except that airflow was reduced by at least 50% from its baseline [1], [4]. To simplify the categorising process, both were classified as obstructive event (OE) in this study. Central hypopnoea events were defined as a reduction of 50% or more in airflow proportional to the decrease in respiratory drive [4]. While for central apnoea, it was the complete cessation in both airflow and respiratory drive. Similarly, they were regarded as central event (CE). Mixed apnoeas or hypopnoeas were classified as OE to simplify the comparison process in this study.

2.2. PTT Measurements
A stand-alone PTT system using a microcontroller to continuously acquire physiologic data from a single-lead electrocardiography (ECG) machine (S&W Medico, Teknik, Denmark) and PPG signals derived from the PSG oximetry was developed. This system has an accuracy of 1ms. The ECG signal was sampled at 1ms interval and a slope detection algorithm was used to determine the initial upstroke of the R-wave. A differentiator in firmware then detected the peak and a timer was initiated at this point. The PPG signal was also sampled at 1ms sampling period and a moving threshold detector was used to minimise baseline instability. The corresponding 25% of peak-to-peak amplitude was derived as suggested by Katz et al [1] and Smith et al [5] in their similar studies to mark the arrival of the pulse wave at the periphery. At this point, the timer was terminated and its count was stored as the PTT value. This system then outputs an analogue voltage signal to the PSG system so as to allow comparison of PTT with all other measured parameters.

2.3. Subjects and Experimental Protocol
This study included 24 child subjects (19 male and 5 female). Their mean age with their standard deviations (SD) were 6.7 ± 3.9years (range 1-14years). Their mean height and weight with their SD were 115.4 ± 29.4cm and 30.0 ± 22.1kg respectively. They were scheduled to undergo routine overnight PSG studies. Prior to the studies, their parent and they were given the study purposes and procedures verbally. Institutional ethical approval and informed consent were obtained for these studies. The accuracy of PTT measurements was verified against the corresponding readings of both the RIP and oronasal airflow measurement. The RIP method usually detects increased respiration efforts through the desynchronization of chest and abdominal movements [7], while airflow measurement is determined by changes in the respiration pressure at the nares.

2.4. Data Analysis
PTT is a non-continuous respiratory effort measure since it is only available with each heartbeat [5], [6]. Therefore, PTT examination needs to be based over several consecutive breaths to quantify any respiratory effort events. In order to classify these events, the average PTT measurement for the duration of the event was computed. This is then compared against the baseline PTT history value during tidal breathing prior to the event. Furthermore, the maximal decrease in PTT was registered for all of these events. Only events that fulfilled the following criteria were considered in this study: (1) Respiratory events that were pre-scored by 2 blinded observers, (2) must last for more than 10 PTT readings and (3) no apparent motion artefacts can be observed. The latter criterion was achieved by monitoring the baseline stability of PPG signals. The two exclusion criteria in this study were the age of the child and children with coexisting cardiac diseases. For the former, the method which respiratory events were categorised with PSG scorings may be inadequate for newborns. Particularly, the contribution of the chest to tidal breathing may be limited in newborns due to its shape, high compliance and deformability. Studies have shown that by 1 year of age this contribution is similar to that of the adolescent [8]. In order to minimise complications with results, newborns (<12 months) were excluded in this study. For the latter, cardiac diseases may affect the isometric contraction time of the left ventricle and there was limited information about the PTT behaviour in these pathological states [5].

Statistical analysis was performed using SPSS version 10 for Microsoft Windows (SPSS, North Chicago, Illinois, USA). Differences between respiratory events of CE and OE at baseline tidal breathing were assessed by using the Student’s t-test for paired variants. Two-way analysis of variance was also used to test for differences between CE and OE from baseline. The mean, SD, mean % decrease and maximal % decrease in PTT in each event were also calculated. A value of p<0.05 was considered significant in this study and all data are expressed as mean ± SD.

3. Results
From the 291 respiratory events, the mean PTT change (%), ± SD range (ms), maximal PTT decrease (%) and p value are shown in Table 1 accordingly. There were distinctive differences between events of tidal breathing, OE and CE. During OE, this exhibits a wider PTT variation (p<0.05) and CE displays negligible variation in its nominal values (p>0.05) during its occurrence. These
comparisons were made in respect to its prior tidal breathing baseline history. Variations in PTT can be observed even during normal respiration as they reflected the respiratory drive of the child during sleep.

Figure 1: 3-year-old male with central events with no airflow, rib cage nor abdominal movement. PTT has lesser variations when compared to tidal breathing. (SCA and ECA denotes start and end of central apnoea)

In CE, PTT variations became less prominent with a general reduction in respiratory drive as shown in Figure 1. The rib cage and abdominal component of the RIP in this example showed a cessation of breathing efforts as well as the termination of airflow. Without the ongoing breathing efforts, the nominal PTT variations due to the mechanical respiration drive diminished. The SaO₂ value of the subject deteriorated with the progression of the prolonged CE. On the other hand, OE exhibited greater PTT decreases and wider variations as compared against their baseline tidal breathing (p<0.05). In Figure 2, it can be seen that the consequent of OE is notable PTT decrease. A total of 157 respiratory events were rejected on the basis of motion artefacts in this study. However, it is common to have arousals that followed the termination of OE [9] and these arousals can fashion artefacts on non-invasive measurements, like PTT.

<table>
<thead>
<tr>
<th>Events</th>
<th>n</th>
<th>Δ (%)</th>
<th>SD (ms)</th>
<th>Max Δ (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal</td>
<td>291</td>
<td>-</td>
<td>6.87</td>
<td>3.69</td>
<td>-</td>
</tr>
<tr>
<td>OE</td>
<td>69</td>
<td>5.35</td>
<td>11.54</td>
<td>12.94</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CE</td>
<td>222</td>
<td>1.42</td>
<td>3.00</td>
<td>1.98</td>
<td>&gt;0.05</td>
</tr>
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</table>

Table 1: Results of respiratory events

4. Discussions and Conclusions

From this study, it can be seen that PTT measurement can be used as a simple supportive technique in assessing respiratory effort changes in children during sleep because it has shown its ability to differentiate respiratory events accordingly. PTT fluctuations have shown their correlations with abnormal changes in respiratory efforts detected by both RIP and oronasal airflow. During normal sleep, it can also be observed that there are marginal PTT fluctuations and this is depended on their BP fluctuations during tidal breathing. Trinder et al [10] reported that these breath based BP changes may be due to the mechanical effects of changing intrathoracic pressure and lung volume, thereby affecting the cardiac preload and afterload. Furthermore, they suggested that oscillations of venous return and cardiac output caused by periodic rises and falls in ventilation as well as pleural pressure during tidal breathing may also lead to BP fluctuations. From the results obtained, the marginal PTT fluctuations observed during tidal breathing signified the ability of PTT to monitor even small changes in respiratory efforts.

In normal sleep architecture, alterations in BP and HR can be affected by sleep stage and primarily determined by changes in autonomic circulatory control [11]. There is a progressive reduction in sympathetic activity through the reductions in HR and BP during the deepening of NREM sleep stages while increasing during REM [12]. On the contrary for individuals with OSAHS, there were abnormal variations in the circulatory system and this was largely determined by the duration and severity of their SDB symptoms [13]. Previous studies have established that BP and HR can influence each other though they may not be solely dependent on one another [14]. Monitoring either of these cardiovascular parameters can help identify the occurrence of any abnormality in the circulatory system during sleep. Using its dependence on BP and HR,
observing PTT value over a period of time can detect changes in sympathetic activity during sleep in children.

It was established that BP fluctuation was more pronounced during tidal breathing [10] hence, changes in PTT were then primarily correlated with BP fluctuations rather than HR changes. From this study, it can be seen that PTT measurement has the required sensitivity to detect such fluctuations. PTT not only has the ability to monitor changes in respiratory efforts, but also shows the potential to differentiate CE from OE. Moreover, PTT is sensitive enough to distinguish central from obstructive hypopnoeas. It has been established by other studies that there is an inverse correlation between changes in BP and PTT values [1]. Based on these studies, a parallel relationship of PTT variations with changes in respiratory efforts can be drawn. It can be observed that PTT can discriminate respiratory events during sleep accordingly. It may therefore be useful as part of a non-invasive simplified screening method for children in respiratory sleep studies. Classification of respiratory events during sleep is clinically important for both future pathological studies and their distinct treatment [5]. As there can be differences in BP and vascular compliance in children, their corresponding transit time can vary [15]. Hence, PTT value may only be useful when it was observed over a period of time on an individual basis. Furthermore, PTT may not reflect true variations of respiratory efforts in subjects with coexisting cardiac diseases. These diseases can affect the isometric contraction time that cause false changes in PTT measurement [5]. More importantly, the major limitation of PTT is motion artefacts caused by either movement from the chest wall affecting ECG signals or at the periphery interfering with the PPG signals. These may cause a shift in PTT baseline and may be incorrectly regarded as the occurrence of arousals or changes in respiratory drive [4].

Identifying SDB in children is an important process. However, this cannot be done unless adequate techniques are available. PTT has shown potential to be one of the important elements for such purposes. It is relatively easy to implement and non-invasive. In this study, PTT shows not only the ability to detect changes in respiratory efforts, but also able to differentiate central from obstructive apnoeas in the absence of motion artefacts. Furthermore, PTT has showed its sensitivity to monitor marginal BP fluctuations during tidal breathing. Identifying hypopnoeic events accordingly when they occurred in children during sleep is also possible using PTT technique. Hence, it can form as part of a simplified SDB screening package to address the number of children referred for respiratory sleep studies.

References:

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