DIFFERENTIATING RESPONSES TO OBSTRUCTIVE SLEEP APNOEA USING PULSE TRANSIT TIME

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ABSTRACT
Conventional overnight polysomnography (PSG) used to determine the respiratory behaviour during sleep can be a complex and expensive procedure. Pulse transit time analysis (PTT) has shown potential to detect obstructive apnoeic and hypopnoeic events in adults. This study was undertaken to determine the potential of PTT to differentiate responses to upper airway obstruction. 103 obstructive respiratory events occurred in PSG studies performed on 11 children (10 male and 1 female, mean age 7.5 years). PTT measurements were evaluated against the corresponding PSG results pre-scored by 2 blinded observers. Broadly, there were 2 types of responses. They can be either short period of rapid PTT decreases (Type 1) or prolonged but gradual PTT decreases (Type 2). Type 1 obstructive events showed a mean change of 51.77% (p<0.05), with ±8.48ms standard deviation (SD) (p<0.05) and maximal change of 54.80% (p<0.05) from baseline PTT value during tidal breathing. Type 2 events showed a mean 12.01% (p<0.05) change, with ±5.28ms SD (p<0.05) and maximal change of 13.32% (p<0.05). PTT was able to categorise different responses during obstructive respiratory events. The results attained here can suggest that PTT can have greater potentials for use in childhood respiratory sleep studies.

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

1. Introduction
The obstructive sleep apnoea syndrome (OSAS) in children is characterised by episodic upper airway obstruction that may be associated with hypoxemia, hypercarbia, and arousal. The prevalence of OSAS can be common for children that can affect about 2% of the pediatric population [1]. Current gold standard for its diagnosis is nocturnal polysomnography (PSG) but this procedure is unable to cope with the number of children referred for OSAS investigation. The effects of airway obstruction during sleep in children can range from mild irritation to documented IQ loss [2].

Studies conducted on the association between apnoeas and chemoreception reveals discordant results with some OSAS individuals having blunted ventilatory response to chemical stimulation while others having an increased responsiveness to hypercapnia [3]. In general, the sensory systems react to changes in the external or internal environment promptly and with finely tuned responses. An appropriate ventilatory response must occur with sufficient strength and within an optimal time interval. A response which is not appropriate may destabilise the system resulting in inadequate compensation [3]. Chemoreceptor dysfunction can be described both in terms of response strength and reaction time [4] can be an important contributing factor to the aetiology of apnoea [3]. If children with obstructive apnoeas have weak or delayed chemoreceptor responses, this can be evidence for a dominant role played by central respiratory control mechanisms in the pathogenesis of apnoea. However, if chemoreceptor responses are intact, this can indicate that factors other than the central respiratory drives are important in triggering apnoea. The approach of describing chemoreception in terms of strength and response time has been validated by others [4-5].

Pulse Transit Time (PTT) has shown the potential to estimate the degree of breathing effort in adults in response to involuntary physiological changes in the upper airway. PTT is a non-invasive and indirect measure of blood pressure changes associated with obstructive breathing [6]. PTT is the time difference between the origins of a pulse wave in the left ventricle to its detection at a periphery. This technique is usually measured as the time delay between the R-wave on the electrocardiogram (ECG) and its subsequent arrival at the selected periphery. The principal speed determinant by which these waves propagate is the compliance of the arterial wall. This compliance in turn, is highly dependent on the instantaneous blood pressure (BP) [7]. As the BP increases, this affects the geometric and mechanical properties of the arterial wall thus, leading to an increase in its stiffness. This can occur when there is an abrupt BP changes during pulsus paradoxus generated by high pleural pressure swings encountered during OSAS. During such occurrences, these pulse waves propagate faster and thereby decreasing the duration of PTT
measurement [6-7]. Based on these findings, this study was undertaken with the following objectives: (1) to determine the use of PTT to detect the occurrences of obstructive respiratory events (OE) and (2) to determine any differences in ventilatory responses.

2. Materials and Methods

2.1. Polysomnography
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 plethysmography (RIP) recording of chest and abdominal movement (Respitrace 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.

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 signal derived from the PSG oximeter was developed. This system has an accuracy of 1ms for all measurements taken. 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 Smith et al [6] in their similar studies to mark the arrival of the pulse wave at the peripheral. 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.

2.3. Subjects and Experimental Protocol
This study included 11 child subjects (10 male and 1 female). Their mean age with their standard deviation (SD) was 7.5 ± 3.8years (range 1-14years). Their mean height and weight with their SD were 122.4 ± 24.4cm and 33.0 ± 25.9kg respectively. They were scheduled to undergo routine overnight PSG studies. Prior to the studies, all subjects and their parent 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. Children with coexisting cardiac diseases may affect the accuracy of PTT measurement [6]. Hence, these children were excluded from this study.

2.4. Data Analysis
PTT is a non-continuous respiratory effort measure since it is only available with each heartbeat [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 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 two 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. It can be observed that deviations of PTT during OE from its nominal baseline were broadly two types. They were either a short period that consisted of rapid PTT decreases (Type 1) or prolonged but gradual PTT decreases (Type 2). Type 1 OE was defined as having no more than three PTT measurements exhibiting more than 30% decrease from its tidal breathing PTT baseline. All other valid OE in this study was regarded as Type 2. Statistical analysis was performed using SPSS version 10 for Microsoft Windows (SPSS, North Chicago, Illinois, USA). Differences between respiratory events of obstructive nature at baseline tidal breathing were assessed by using the Student’s t-test for paired variates. 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.

3. Results
From the 103 obstructive 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 and OE. Variations in PTT can be observed even during normal respiration as they reflected the respiratory drive of the child during sleep. Broadly, there were two distinctive responses when OE occurred in the subjects of this study. They were further categorised into Type 1 and Type 2 as shown in Table 1 to analyse their individual characteristics. Generally, Type 1 exhibited greater PTT decreases as compared to their Type 2 counterparts. Both types of OE were significantly different (p<0.05) against their baseline tidal breathing.
In Figure 1, it can be observed that there was a short period of rapid PTT decreases. This may signify a notable increased negative intrathoracic pressure generated to overcome the obstruction. While in Figure 2, there were gradual PTT fluctuations over a period after the occurrence of the OE. Subjects with Type 2 OE had milder and prolonged cardiovascular responses to that event. Regardless of the type of OE, PTT deviations were much greater than those during tidal breathing.

### 4. Discussions and Conclusions

In this investigation of OE, the train of PTT displayed distinctive characteristics from tidal breathing during its occurrence. However, the mechanisms of upper airway collapsibility during OE were not well understood. Schwartz et al. [8] suggested that alterations in pharyngeal structure or disturbances in neuromuscular control were the most likely causes for such airway collapse. The intrinsic properties of pharyngeal structure depended on the wall compliance, airway configuration and surface adhesive forces. These also determined its functional characteristics during sleep. They affected not only the ability of the upper airway to withstand the effects of the negative intrathoracic pressures that occurred on inspiration, but also the ease to which patency was re-established following an OE [2]. During the occurrence of OE, the hemodynamic effects similar to the Valsalva and Muller manoeuvre can occur [9-10]. In which, the Valsalva manoeuvre increased the end-expiratory pleural pressures marginally and Muller manoeuvre decreased the end-inspiratory pleural pressures considerably [10]. Breitenbucher et al. [9] also suggested that these changes in the intrathoracic pressure led to changes in transmural vascular pressure, thus affecting the BP. Moreover, the structure of the upper airway can determine the extent to which negative intrathoracic pressures were generated. A collapse in a longer and narrower upper airway was expected to generate a stronger negative intrathoracic pressure than a similar collapse in those with a shorter and wider pharynx [11].

During an OE, both hypoxemia and hypercapnia acting through chemoreflexes escalated sympathetic activity with subsequent increases in the stiffness of arterial wall as well as HR [12-13]. With an increasing inspiratory effort to ventilate the airway, a progressive increase in the inspiratory afterload to the left ventricle can occur and thus impairing its subsequent emptying during expiration [14]. This may also lead to an increase in right ventricular preload to produce substantial inspiratory increased in right ventricular end-diastolic pressure. These inspiratory swings in intrathoracic pressure that occurred with OE may contribute to the decreased cardiac output during these events [15]. Variations in the ventricular filling time and stroke volumes of the heart may be caused by the progressive increase in the size of the heart throughout the occurrence of OE [14]. Garpestad et al. [16] reported that this decrease in stroke volume occurred not only from the onset of the obstructive apnoeic event, but also there was a further decrease immediately after the termination of the event. On the contrary, with the resumption of breathing after these events, these resulted in an increase in venous return and consequently increased cardiac output [12].
These revived inspiratory efforts may increase the vascular pressure around the vessels [14] and causing a severely vasoconstricted peripheral vasculature resulting in surges in BP [13]. Hence, the exact physiological responses to the onset of OE greatly depended on cardiovascular stability of individual.

From the results, it can be seen that there were two kinds of PTT response to an OE. While the consequences of these obstructions have been investigated, however, their pathophysiology was yet to be well-defined [12]. It was not clear at this point, the exact factors that influenced these two responses to the obstruction. This can be attributed to the structure of the upper airway and pharyngeal neuromuscular control that determined the nature of their response [8]. In this study, it was discovered that Type 2 OE subjects generally had hypotonic upper airway structure while Type 1 subjects had normal pharyngeal muscle tone. This can be the main distinction that determined the two types of response. Due to their hypotonic pharyngeal muscle, Type 2 subjects cannot generate the same degree of negative intrathoracic pressure during an OE like their Type 1 counterparts. This may be reflected as a prolonged and smaller PTT drops as compared to the response of Type 1 subjects.

From the obtained results, it can also be seen that Type 2 subjects needed extended period to recover from the occurrence of an OE. While for Type 1 subjects, only one or two of their breaths were affected. It is acknowledged that the numbers of OE in the present studies are limited and may not represent the distinct ventilatory responses of the general child population during an OE. It is then recognised that this study be conducted with a larger sample of children. The mechanism underlying the degree of obstructed sleep breathing can vary. This depended on the nature and location of the obstruction as well as the variability in the upper airway control function [2]. It is hoped that the findings presented here can provide a framework to which future respiratory studies using PTT as an adjunct measure. From these data, they can supplement the existing knowledge in childhood PTT in respiratory sleep studies. PTT shows not only the ability to detect changes in respiratory efforts, but also able to differentiate ventilatory responses during an OE in the absence of motion artefacts. Furthermore, PTT has showed its sensitivity to monitor marginal BP fluctuations during tidal breathing. The findings attained here can demonstrate that PTT is still to realise its full potential in childhood respiratory sleep studies.

References:


