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Increased variability in respiratory parameters heralds obstructive events in children with sleep disordered breathing

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***Abstract*—Sleep disordered breathing (SDB) is characterized by repeated episodes of central or obstructive apneas, disturbing respiratory patterns. The purpose of this study is to quantify respiratory variability associated with apneic/hypopneic events by computing respiratory parameters and thoraco-abdominal asynchrony (TAA) over sleep periods preceding the occurrence of obstructive events in children with SDB. One minute artifact-free epochs of ribcage (RC) and abdominal (AB) signals were extracted from the respiratory inductive plethysmograph (RIP) channel of the PSG prior to the onset of each obstruction. Breath-by-breath values of TAA were computed using a Hilbert transform based technique that measures the phase shift between the RC and AB signals. In addition, the following parameters were computed breath-by-breath from the RC signal: inspiratory time (Ti), expiratory time (Te), total time (Ttot), and the inspiratory duty cycle (DC=Ti/Ttot). Standard deviation of the parameters (SD_TAA, SD_Ti, SD_Te, SD_Ttot, SD_DC) over each 1 min epoch were calculated and averaged over each subject with respect to sleep stage. For comparison, similar measures were computed from within quiet breathing periods of each subject. We found that breaths immediately before apnea/hypopneas were associated with a high degree of variability in respiratory timing and TAA. The proposed variability analysis of RIP signals may be useful for detecting acute epochs of respiratory instability in children with SDB.**

I. Introduction

During quiet tidal breathing, variability in respiratory parameters is reduced and the exertion of ribcage (RC) and abdomen (AB) tend to exhibit a coincident motion, resulting in a high level of synchrony during the respiratory cycle. However the stability of this synchronous movement is influenced by upper airway resistance and respiratory muscle activity, which are distinctly different between wakefulness and sleep [1]. Further, the effects of sleep on breathing differ between the two major sleep states: NREM (non-rapid eye movement) sleep and REM (rapid eye movement) sleep. In addition to these normal physiological changes, abnormal ventilatory responses are caused by sleep related respiratory disorders [2, 3]. Sleep disordered breathing (SDB) is characterised by repetitive partial or complete obstruction of the upper airways, causing a reduction or cessation of airflow resulting in hypoxia, hypercapnia and sleep fragmentation [4]. SDB is estimated to occur in 1-4% of children and is associated with cardiovascular, neurocognitive and behavioural consequences [5].

Polysomnographic sleep studies (PSG) are the gold standard for assessing sleep quality and diagnosing SDB, but they are inconvenient, especially in children, and moreover, expensive, and development of alternate screening methods is desirable. Various sensors and analysis methods have been developed for non-invasive monitoring of respiration [6-8]. Respiratory inductive plethysmography (RIP) is a widely used unobtrusive, non-invasive and well validated technique that captures respiratory excursions of the ribcage and abdomen and this modality was chosen as the signal source in our study. Detecting respiratory cycles from abdominal and thoracic movement signals is feasible, as they typically follow the respiratory cycle faithfully and have a single deflection per respiratory cycle. Our parameters of interest were thoraco-abdominal asynchrony (TAA) and the timing components of breathing.

We hypothesised that increased variability in respiratory timing and thoraco-abdominal coordination may herald upper airway obstructions. To quantify the phase deviation between the RC and AB breathing movements, i.e. the degree of thoraco-abdominal asynchrony (TAA), a simple, robust waveform-independent phase difference estimation method based on Hilbert transform was chosen [9]. In addition, inspiratory and expiratory intervals and respiratory cycle lengths were studied.

II. Methods

A. Phase estimation using Hilbert transform

The Hilbert transform gives the instantaneous amplitude and phase of a signal $x(t)$ via construction of an analytical signal $\zeta(t)$ which is a complex function of time [10] defined as

$$\zeta(t) = x(t) + j\tilde{x}(t) = Ae^{j\phi(t)}, \qquad (1)$$

where $\tilde{x}(t)$ is the Hilbert transform of $x(t)$. The instantaneous amplitude and phase are given by

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$$A(t) = \sqrt{\left(x^2(t) + \tilde{x}^2(t)\right)} \quad (2)$$

$$\phi(t) = \arctan \frac{\tilde{x}(t)}{x(t)} \quad (3)$$

Given two signals $x_1(t)$ and $x_2(t)$, the relative phase between the two signals can be obtained [11] via their Hilbert transforms $\tilde{x}_1(t)$ and $\tilde{x}_2(t)$ as

$$\phi_1(t) - \phi_2(t) = \arctan\left[\frac{x_1(t)\tilde{x}_2(t) - x_2(t)\tilde{x}_1(t)}{x_1(t)x_2(t) + \tilde{x}_1(t)\tilde{x}_2(t)}\right] \quad (4)$$

More details on the evaluation of the above approach for measuring TAA are published elsewhere [9].

B. Subjects

The study comprised of 40 (24 male) children with a history of frequent snoring, awaiting adenotonsillectomy for suspected upper airway obstruction. The age and BMI percentile of the subjects were mean ± SD: 7.5 ± 2.7 yrs and mean ± SD: 65.8 ± 31.9 respectively. This study is a retrospective analysis of a previously published larger study [12-14].

C. Overnight polysomnography

Standard PSG were recorded overnight from each subject using the S-Series® Sleepwatch system (Compumedics, Australia). Respiratory movements of the chest and abdominal wall were recorded using uncalibrated RIP. Each child was monitored continuously overnight via infrared camera and by a pediatric sleep technician, who also documented observations of sleep behavior, including the presence or absence of snoring. More details on the study protocol are published elsewhere [15]. Sleep stages were scored visually in 30 second epochs according to the standardized EEG, EOG and EMG criteria of Rechtschaffen and Kales [16]

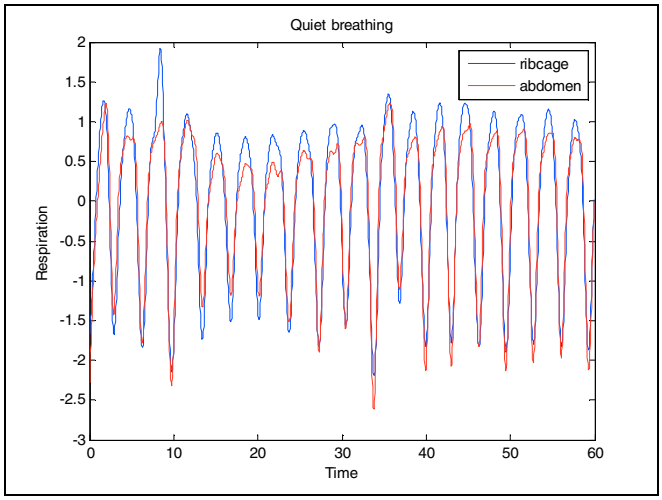

Figure 1. An example segment of a quiet breathing one minute epoch in stage 2 NREM sleep

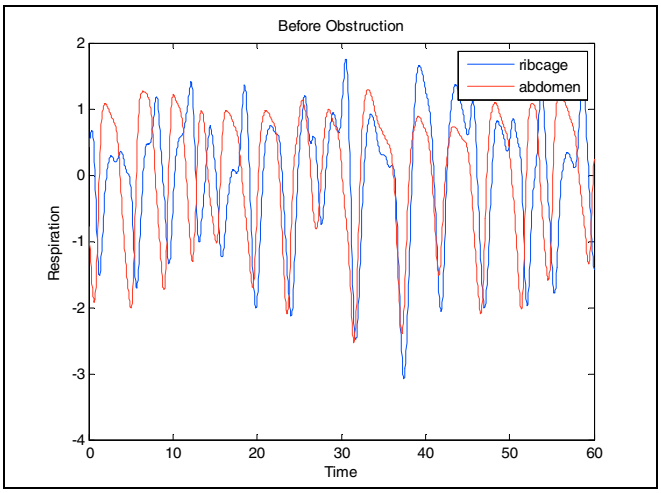

Figure 2. An example segment of a pre-obstruction one minute epoch in stage 2 NREM sleep

D. Respiratory signal processing

Respiratory data from the thoracic and abdominal RIP channels of the standard PSG were digitized at 25 Hz and extracted, using the programming library libRASCH [17]. Custom written computer software was developed, using the MATLAB® signal processing toolbox. Data were low-pass filtered at 1 Hz, using a Butterworth forward and reverse digital filter. The DC offset of the signals was removed before processing. Onset times of obstructive apnea/hypopnea events during stage 2 NREM sleep and REM sleep were extracted from the manual PSG scoring reports of each subject. To exclude the effect of respiratory cortical arousals on the parameters analyzed, only obstructions without respiratory cortical arousals at their termination were included in further analysis.

RC and AB signals of one minute duration were extracted prior to the onset of obstruction as defined by the sleep technician (Pre-Obs) and checked for the presence of respiratory or movement artifacts as scored by the sleep technician. An example segment of a pre-obstruction epoch in stage 2 NREM sleep is shown in Figure 2. Peaks and troughs of the RC breathing signals were detected by finding the local maxima and minima, using a first order derivative based approach. Based on these inspiratory-expiratory time points of the RC signal, the following parameters were computed breath-by-breath: inspiratory time (Ti), expiratory time (Te), total time (Ttot), and inspiratory duty cycle (DC=Ti/Ttot). Breath-by-breath values of TAA were computed using the Hilbert transform approach (eq. (4)). Mean and standard deviation of all the above parameters over the one min pre-obstruction epochs were calculated and averaged over each subject with respect to sleep stage.

For individual-specific comparison with baseline values, the RC and AB signals during quiet stable breathing (QB) were extracted from each subject over one minute of consecutive stage 2 NREM sleep and REM sleep, free of body movements, abnormal cardio-respiratory events (e.g. apnea) and signal artifacts and with no overlapping to pre-obstruction epochs of interest. An example segment is

shown in Figure 1. Mean and standard deviation of breath-by-breath values of all of the above mentioned respiratory parameters were computed from within these quiet tidal breathing epochs and averaged over each subject with respect to sleep stage so that each child contributed equally to the group mean.

G. *Statistical Analysis*

Data were analyzed using the GraphPad Prism version 5.01 for windows (GraphPad Prism Inc.). Student's paired t-test was used to compare quiet breathing and pre-obstruction epochs within each sleep stage. Data are presented as mean ± SD and p values are 2-tailed with statistical significance determined at $\alpha = 0.05$ unless stated otherwise.

III. Results

Demographic and PSG results have been reported previously [13].

A. Thoraco-abdominal asynchrony

The level of TAA before the onset of obstruction was significantly elevated when compared to quiet breathing levels in both stage 2 NREM and REM sleep as shown in Figure 3a.

To further analyze the regularity of thoraco-abdominal coordination prior to the onset of obstructive events, the standard deviation of TAA values obtained from the one min Pre-Obs epochs were compared with those obtained during QB epochs. The variability of TAA was significantly higher in Pre-Obs periods compared to QB in both stage 2 NREM and REM sleep as shown in Figure 3b.

B. Respiratory timing and Duty Cycle

The variability in inspiratory time (SD_Ti), expiratory time (SD_Te), total time (SD_Te) and inspiratory duty cycle (SD_DC) were compared between QB and Pre-Obs epochs in both sleep stages. We observed a significant increase in all variability measures during the one min epochs pre-obstruction compared to QB in both sleep stages. But these differences reached statistical significance only in stage 2 NREM sleep (Figure 3c).

IV. Discussion

The main finding of this study was an increase in TAA and respiratory timing prior to obstructive events.

Inductive plethysmographic signals are routinely recorded during PSG to monitor respiration, detect sleep related breathing disorders and differentiate between central and obstructive apnoeic events based on the presence or absence of respiratory effort. However, quantitative analysis of respiratory variability and ribcage/abdominal coordination during normal and obstructive breathing periods are not rigorously performed, especially in children. Our study aimed to bridge this gap by investigating the ability of RIP signals in detecting respiratory instability prior to clinically relevant respiratory events.

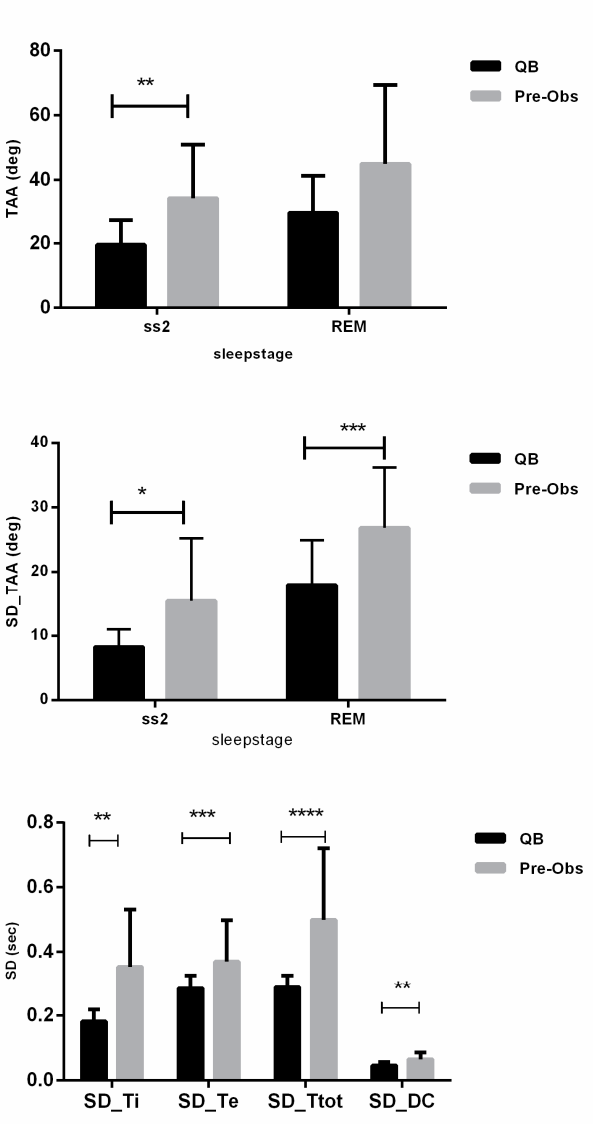

Figure 3. (a) Comparison of mean TAA between QB and Pre-Obs in each sleep stage. (b). Comparison of SD_TAA between QB and Pre-Obs durations in each sleep stage. (c). Comparison of SD_Ti, SD_Te, SD_Ttot and SD_DC between QB and Pre-Obs periods in stage 2 NREM sleep (ss2) (*p<0.05, **p<0.01 ***p<0.005 and ****p<0.001).

Episodes of obstructive apnea/hypopnea as scored by sleep technician were preceded by breathing segments that exhibited significantly higher levels of TAA with an increased degree of variability compared to those during periods of quiet breathing. This might be indicative of an increased work of breathing against the restriction imposed by the narrowing airway that results in a frank apnea or hypopnea. In particular, the increased pharyngeal resistance due to narrowing of the upper airway appears to demand greater respiratory effort to maintain airflow, thus altering both respiratory timing and respiratory variability. It has been shown that an obstructed airway leads to an increased respiratory effort, manifested as asynchronous or paradoxical inward motion of the ribcage [18, 19].

The elevated asynchrony and increased fluctuations in TAA during these Pre-Obs periods are also accompanied by increased variability in inspiratory and expiratory timing, total cycle time and inspiratory duty cycle that are significant in stage 2 NREM sleep. Thus, in addition to increased asynchrony, there is increased variability and fluctuation in the inspiratory and expiratory cycles during pre-obstructive periods, which also indicates increased instability in breathing, predictive of the onset of an airway obstruction. Of clinical significance, our study demonstrates breathing instability that occurs even before an obstruction is scored on the PSG data. One may speculate that periods of respiratory instability may exist that do not lead to a hypopnea/ apnea as defined by clinical scoring guidelines and are therefore not considered in the diagnostic process.

From a monitoring perspective, although PSG is the gold standard method to evaluate sleep quality and diagnose sleep disorders [16], it is expensive and inconvenient especially in infants and young children with sleep related breathing disorders. In this context, the proposed method of evaluating respiratory parameters using non-invasively acquired uncalibrated RIP could assist in developing screening devices for long term monitoring of sleep disordered breathing. More importantly, the findings from this study could potentially be used as features in automated methods for segmentation and scoring of respiratory events [20], in modelling the effects of sleep apnea on the control and mechanics of breathing [21, 22].

V. Conclusion

In summary, this study has demonstrated increased variability in respiratory parameters before the onset of obstructive events in children with SDB. Quantitative assessment of RIP signal may be useful for detecting respiratory disturbances in children with SDB.

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