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Validation of a quantitative method to measure neural respiratory drive in children during sleep

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ABSTRACT

Aims: Quantitatively measure and validate analysis of neural respiratory drive (NRD) using a commercial polysomnography system in children during sleep.
Method: Surface electromyogram of the diaphragm (sEMGdi) recorded from primary snoring children were analysed. A subset was re-analysed to assess intra- and inter-investigator reproducibility. Effects of different band pass filter settings (20–100 Hz vs 10–1000 Hz) on sEMGdi amplitude were evaluated.
Results: Mean sEMGdi from 45 children aged 4.38 years (median; IQR 3.00–7.96) was 5.05 μV (SD 2.73). The sEMGdi had a high intra-subject intraclass correlation coefficient (ICC) of 0.88. sEMGdi analysis was reproducible with high ICC between occasions (0.99; 95% CI 0.98–0.99) and between investigators (0.98; 95% CI 0.97–0.99). There was also a high ICC (0.99, 95% CI 0.96–1.00) between the sEMGdi measured using different band-pass filter settings. Age and BMI were negative predictors of sEMGdi ($p < 0.0001$ and $p = 0.0004$ respectively).
Conclusion: NRD in children during sleep as assessed by sEMGdi can be quantified in a reliable and reproducible fashion.

1. Introduction

Assessment of neural respiratory drive (or respiratory effort) is an increasingly important aspect of evaluating sleep disordered breathing (SDB). Obstructive sleep apnea (OSA) is characterised by the persistence of respiratory effort during partial and/or complete upper airway obstruction (American Thoracic Society, 1996). Therefore, monitoring respiratory effort is essential in routine polysomnography to differentiate between an obstructive or central respiratory event (Berry et al., 2013). The recognition that partial airway obstruction can cause repeated respiratory effort related arousals (RERA) and significant daytime symptoms in the absence of apnea in upper airway resistance syndrome (UARS) further highlights the need for respiratory effort monitoring during sleep (Guilleminault et al., 1996, 1993). Esophageal pressure (Pes) is the current gold standard for quantitative measurement of respiratory effort in sleep, reflecting changes in intrathoracic pressure resulting from respiratory muscle contraction (Berry et al., 2013). However, its invasive nature and potential to disrupt sleep quality (Chervin and Aldrich, 1997) and distort pharyngeal dynamics (Woodson and Wooten, 1992) means Pes monitoring remains mainly a research tool, particularly in children. Instead, non-invasive technique such as dual thoracoabdominal respiratory inductance plethysmography (RIP) bands are preferable. When RIP bands are calibrated, quantitative measurements of tidal volume can be estimated based on the change in the entire cross-sectional area enclosed by the thoracic and abdominal bands (Carry et al., 1997). However, displacement of the RIP bands and changes in body position during sleep can alter calibration and the estimated volume, limiting its use as a quantitative marker of respiratory effort (Tobin et al., 1983; Whyte et al., 1991).

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Electromyography (EMG) of the diaphragm and other respiratory muscles is another method of detecting respiratory effort (Berry et al., 2013). When muscles such as the diaphragm contract, the electrical activity of multiple motor units summate to form a crescendo-decrescendo pattern which can be recorded indirectly using surface (transcutaneous) electrodes overlying the chest wall. The magnitude of the respiratory muscle EMG represents the neural respiratory drive (NRD) to that muscle, i.e. the balance between the load placed on the respiratory system and the muscle's force generating capacity (Ratnovsky et al., 2008). Compared to evaluating respiratory effort by changes resulting from respiratory muscle contraction such as Pes and lung volume, respiratory muscle EMG is a more direct assessment of NRD. Good correlations between the surface EMGdi and Pes magnitude for adults with OSA have been found (Stoohs et al., 2005). Further, the use of transcutaneous surface electrodes to record costal diaphragm EMG (sEMGdi) is non-invasive and well tolerated by neonates and children (Maarsingh et al., 2000; Prechtl et al., 1977).

Diaphragm and intercostal EMG currently are used as an adjunct to RIP bands as a qualitative sensor to differentiate between obstructive and central respiratory events in sleep studies (Berry et al., 2016). If sEMGdi recorded using a commercial sleep study software and setup is quantifiable, sEMGdi potentially can be used as a non-invasive surrogate for esophageal pressure measurements. However standard EMG filter settings recommended for routine polysomnography have a narrower range of filter settings (10–100 Hz) to those recommended for quantitative analysis of muscle EMG (10–1000 Hz) (ATS/ERS Committee, 2002; Berry et al., 2013), leading to potential loss of data in the high frequency range. The aim for this study was to investigate whether sEMGdi recorded using routine sleep study software and settings could be quantitatively analysed in a reproducible manner as a marker of NRD.

2. Methods

Sleep studies conducted in healthy children <18 years of age without any chronic medical comorbidities, including asthma or cardiac conditions, at Sydney Children's Hospital's (SCH) Sleep Laboratory during a 12-month period were retrospectively reviewed. Only children whose sleep studies were reported as 'normal' without a diagnosis of OSA (defined as an obstructive apnea hypopnea index (OAHI) ≥1/h) (Marcus et al., 1992; Uliel et al., 2004) were included in this study. This included non-snoring children who had routine sleep studies prior to a multiple sleep latency test (MSLT). Sleep studies with poor quality RIP band signals where assessment of breathing movement was not possible, and/or poor quality sEMGdi signals where phasic EMG could not be visualised were excluded.

Full polysomnography (PSG) was performed in all included children using Profusion Sleep® software (Compumedics, Melbourne, Australia). Sleep stages were identified by electroencephalography (C3/A2, C4/A1, O1/A2, and O2/A1), electrooculography, and submental EMG. In accordance with American Academy of Sleep Medicine's (AASM) guidelines (Berry et al., 2013), sleep was staged as light sleep (stage N1 and N2), deep sleep (stage N3), and rapid eye movement (REM) sleep. Electrocardiogram (ECG) was monitored from precordial leads. Oxygen saturation (SpO_2) was measured by oximeters (Masimo RadicalSET, Irvine, California) and airflow was detected by nasal prongs attached to a flow sensor and oronasal thermistor. Concurrent infrared video recording was used to record sounds and to visually monitor sleep. Uncalibrated RIP bands (Compumedics, Melbourne, Australia) placed around the chest and abdomen were used to detect chest wall and abdominal movements.

Sleep and respiratory events were scored according to standard terminology by pediatric sleep physicians (Berry et al., 2013, 2012). Obstructive apneas were defined as the persistence of respiratory effort (based on movement of the chest and abdomen on RIP bands and/or phasic bursts of sEMGdi) associated with the absence of airflow detection by either the nasal flow sensor and/or oronasal thermistor for at least two breaths. A hypopnea was scored when the peak airflow signal excursions dropped by ≥30% of pre-event baseline for at least two breaths accompanied by either ≥3% oxygen desaturation or an arousal.

2.1. Surface (chest wall) diaphragm EMG recording set up and analysis

To record sEMGdi, the active electrode (3 M Red dot®, USA) was placed on the chest in the right mid-clavicular line at the 8th intercostal space and the reference electrode below the active electrode on the rib at the costal margin. The two electrodes were set <2 cm apart without touching. The electrode cables were shielded to minimise line frequency interference. The settings on the configuration panel of Profusion Sleep® for recording sEMGdi were based on the recommended settings from the AASM manual (Berry et al., 2013; Penzel et al., 2007). EMG data were recorded with a sampling rate of 256 Hz and a range of 2 mV. The EMG signals were then amplified and band-pass filtered in the range of 22–100 Hz with a notch filter of 50 Hz set to minimise powerline artefacts.

Each participant's sleep study was reviewed using Profusion Sleep® software. Two excerpts of 10 consecutive tidal breaths with clear stable phasic respiratory effort (evident in both the sEMGdi and the thoracic and abdominal RIP band channels) with the child sleeping in one position without gross body movement artefact were selected from each of the three different sleep stages (light sleep (N1 and 2), deep sleep (N3), and REM sleep). A total of 6 excerpts (60 breaths) from each child were then exported to Spike2® (Cambridge Electronic Design, Cambridge, England) data acquisition and analysis system as European Data Format (EDF) files for offline manual waveform analysis. As demonstrated in Fig. 1a, the sEMGdi signal was phasic and coincided with inspiration as confirmed by the fluctuation in the thoracic RIP band signal to ensure the EMG signal captured originated from the diaphragm and not abdominal muscles. Diaphragm EMG signal contaminated by ECG QRS complex artefact was removed using a custom script (gated EMG). The gated EMG signal was converted to root-mean-square (RMS) with a time constant of 50 ms (Fig. 1a). This resulted in a RMS-sEMGdi signal almost free of ECG signal, although artefacts from P and T waves from the ECG may be seen (Fig. 1b). The peak and trough RMS-sEMGdi signals for every individual breath were manually identified. The difference between the two were used to determine the absolute amplitude of the RMS-sEMGdi signal per breath.

2.2. Data collection and analysis

Age, gender, height, weight, body mass index (BMI) centiles measured on the day of sleep study were recorded for each child. Mean RMS-sEMGdi per breath (referred throughout as sEMGdi) was calculated from the 60 breaths analysed for each child, and reported in μV.

For surface recordings of respiratory muscle activity, a band width of 10–1000 Hz was used customarily as the amplifier filter setting (ATS/ERS Committee, 2002). sEMGdi analysed using standard sleep study filter setting (22–100 Hz) was compared to routine respiratory muscle EMG band-pass filter setting (10–1000 Hz) by analysing 12 sleep study excerpts prospectively recorded on Profusion Sleep® using a sampling frequency of 2000 Hz, amplified and exported using a band-pass filter of 22–100 Hz then 10–1000 Hz.