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Scoring arousals in the home environment

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Abstract

Arousals from sleep and consequent sleep disruption may be a causal link between sleep-disordered breathing and its sequellae in children. Quantification of arousals therefore makes an important contribution to the overall assessment of the sleep of a child with suspected obstructive sleep apnea (OSA) or other sleep disorders. Arousals are classically defined by changes in the electroencephalographic (EEG) channels, but most arousals in children involve body movement in addition to EEG changes. Several methods of quantifying arousals without the use of EEG have been proposed, with the aim of simplifying testing in children with suspected OSA so that it can be safely and efficiently performed in the child's home. The following paper gives a background to the assessment of arousals from sleep in children, and describes methods for detecting arousals and their potential application to recordings performed in a child's home.

Keywords: Arousal; Child; Sleep; Polysomnography; Apnea; Ambulatory monitoring

1. Arousal from sleep

1.1. Neurophysiology

The transition from sleep to wakefulness is characterized by abrupt changes in electroencephalographic (EEG) and skeletal muscle activity [1]. The neuroanatomic basis of this response lies in the brainstem reticular activating system (RAS). The RAS receives input from sensory systems, and has projections via the thalamus, hypothalamus, subthalamus, and basal forebrain to the cortex. It also influences activity of spinal motor neurons via the caudal pontine reticular formation.

The moments just after awakening from sleep are associated with profound changes in many aspects of autonomic functioning, particularly stimulatory effects on respiration and sympathetic activity, and a reduction in vagal activity. This leads to transient elevations in ventilation, heart rate, and blood pressure that are in excess of the stable awake state [2,3] suggesting that arousal from sleep is not just a return to the awake state, but is associated with a state of 'hyperarousal.'

1.2. Definitions

Arousal from sleep may take the form of a change in EEG rhythm to one characteristic of the awake state (often termed desynchronization), an increase in muscle activity visible on electromyography (EMG), and/or a visible behavioral awakening. For the purposes of polysomnography, arousals in adults are often defined according to the American Sleep Disorders Association (ASDA) criteria [4]. The essentials of the standard ASDA criteria require (1) that the subject is asleep, (2) that a minimum of 10 s of sleep must intervene before a second arousal is scored, (3) an abrupt shift in EEG frequency to theta, alpha, and/or frequencies greater than 16 Hz of 3 s or more in duration, (4) an increase in submental EMG in rapid eye movement (REM) sleep. Inter-observer agreement for arousals using this definition is only moderate [5], and is likely to be even worse for events of shorter duration, despite the possible physiologic significance of these shorter events [4].

Some arousals from sleep occur seemingly 'spontaneously', usually associated with the end of a sleep cycle and a change in body position [6]. Few studies have described the rate of spontaneous arousals in healthy infants and children. Cortical (EEG) arousals have been reported to occur in healthy infants an average of 16 times per hour in non-REM (NREM) sleep and 31 per hour in REM sleep, plus frequent brief startles that do not proceed to full cortical arousal [7]. Scholle and Zwacka described a median (interquartile range) of 9.0 (4.1) EEG-arousals per hour of sleep in 20 normal children with a median age of 7.5 years [8]. This is similar to the finding of McNamara et al. [9], who described a mean (SD) spontaneous arousal frequency of 6.8 (1.8) per hour in quiet sleep and 7.1 (0.9) per hour in active

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sleep in 15 children who were being evaluated for obstructive sleep apnea (OSA) but had normal polysomnography (mean age 4.6, SD 1.1 years). Normal adolescents arouse approximately three to five times per hour of sleep, rising slightly to five to six times per hour in young adults [10]. This frequency rises with increasing age in adulthood [11,12].

2. Arousal in obstructive sleep apnea

2.1. Mechanisms and age factors

In adults with OSA, arousal from sleep commonly follows episodes of upper airway obstruction [11]. Arousal is induced by a variety of factors including hypoxia, hypercapnia, stimulation of upper airway mechano- and sensory receptors, and increasing ventilatory effort [13–15]. In children, the likelihood of arousal from sleep in response to airway occlusion depends significantly on age, with infants being less likely to arouse in response to upper airway obstruction than older children [16,17]. Outside the first year of life, however, arousal becomes an increasingly frequent response to episodes of upper airway obstruction [8,9,18]. Children with OSA have more arousals from sleep than normal children, but return to a normal arousal frequency following treatment [8,19].

It has been demonstrated in animal models that exposure to repeated airway occlusion leads to a delay in arousal response to subsequent occlusions, with a consequent worsening in desaturation, and augmentation of negative pleural pressure swings and changes in blood pressure [20,21]. Infants habituate to tactile stimuli during sleep, with progressively diminishing arousal response [22]. While this diminution in response to stimuli during sleep may be beneficial in terms of sleep quality, it has potentially adverse effects on the response to life-threatening airway compromise.

2.2. Consequences of frequent arousals

Arousals associated with sleep-related breathing disorders are particularly important, both as a mechanism of recovery from respiratory events during sleep, and as one of the key mediators of the morbidity of these disorders. Independent of the effects of recurrent hypoxemia, the surges in heart rate and blood pressure seen with arousal terminating an obstructive apnea have been implicated in the cardiovascular morbidity of OSA, such as hypertension and myocardial infarction [23]. Frequent arousals from a non-respiratory cause in an experimental setting have also been demonstrated to lead to excessive daytime sleepiness and reduced psychomotor functioning [12,24,25].

Indeed, full cortical arousal is not required to produce daytime sleepiness and impairment of mood. Martin et al. showed that repeated arousal stimuli is sufficient to lead to elevations in heart rate or blood pressure without visible EEG arousals or a reduction in total sleep time leading to a reduction in slow wave sleep, increased daytime sleepiness, and impaired mood [26]. Fragmentation of sleep by arousals leads types and levels of impairment similar to those caused by sleep deprivation [27].

The consequences of frequent arousal from sleep have been less well studied in children than in adults. OSA in children is associated with arterial and pulmonary hypertension, failure to thrive, behavioral problems, and neurocognitive deficits [28–32]. However, the relative contributions to this morbidity of recurrent hypoxemia versus frequent arousals have not been well defined. Young adults have been demonstrated to be more sensitive to sleep disruption than older adults, in terms of effects on psychomotor performance [12], but experimental sleep disruption has not been performed in children. It has been postulated that growth impairment in children with OSA may be due in part to reduced growth hormone secretion due to sleep disruption, and growth hormone secretion has been demonstrated to be impaired in children with OSA [33]. However, the association between growth failure, impairments in growth hormone secretion, OSA, and arousals is not clear.

2.3. Arousals in pediatric OSA

Children with OSA have more arousals from sleep than normal children [19], but the macrostructure of sleep is usually preserved [8,34–36]. Microdisruption of sleep may be present however, and arousal may occur following a respiratory event not associated with significant hypoxia or hypercapnia [9,18].

The role of arousals in the termination of respiratory events in children is not entirely clear. Three groups of investigators have studied this association. Mograss at al. used a definition that included arousals of greater than 1 s to increase the sensitivity of detecting an arousal following a respiratory event [18]. They found that movement arousals terminated nearly all obstructive apneas and hypopneas in children (mean age 5.2 years, SD 2.7 years). McNamara et al. challenged this finding, showing that for children (mean age 4.7 years), only 39.3% of respiratory events in quiet sleep and 37.8% of events in active sleep resulted in arousal [9]. Scholle and Zwacka showed an increase in arousal frequency in children with OSA that returned to normal after treatment, but could not detect a direct correlation between the apnea/hypopnea index and the arousal index [8]. These different conclusions probably stem from differences in definition of both arousals and respiratory events, and differences in the population under study. For example, McNamara et al. [9] included central apneas longer than 5 s, whereas Mograss et al. [18] only included central apneas longer than 10 s or shorter apneas if associated with desaturation. More research is needed to clarify the role of arousal in the recovery from respiratory events in children.

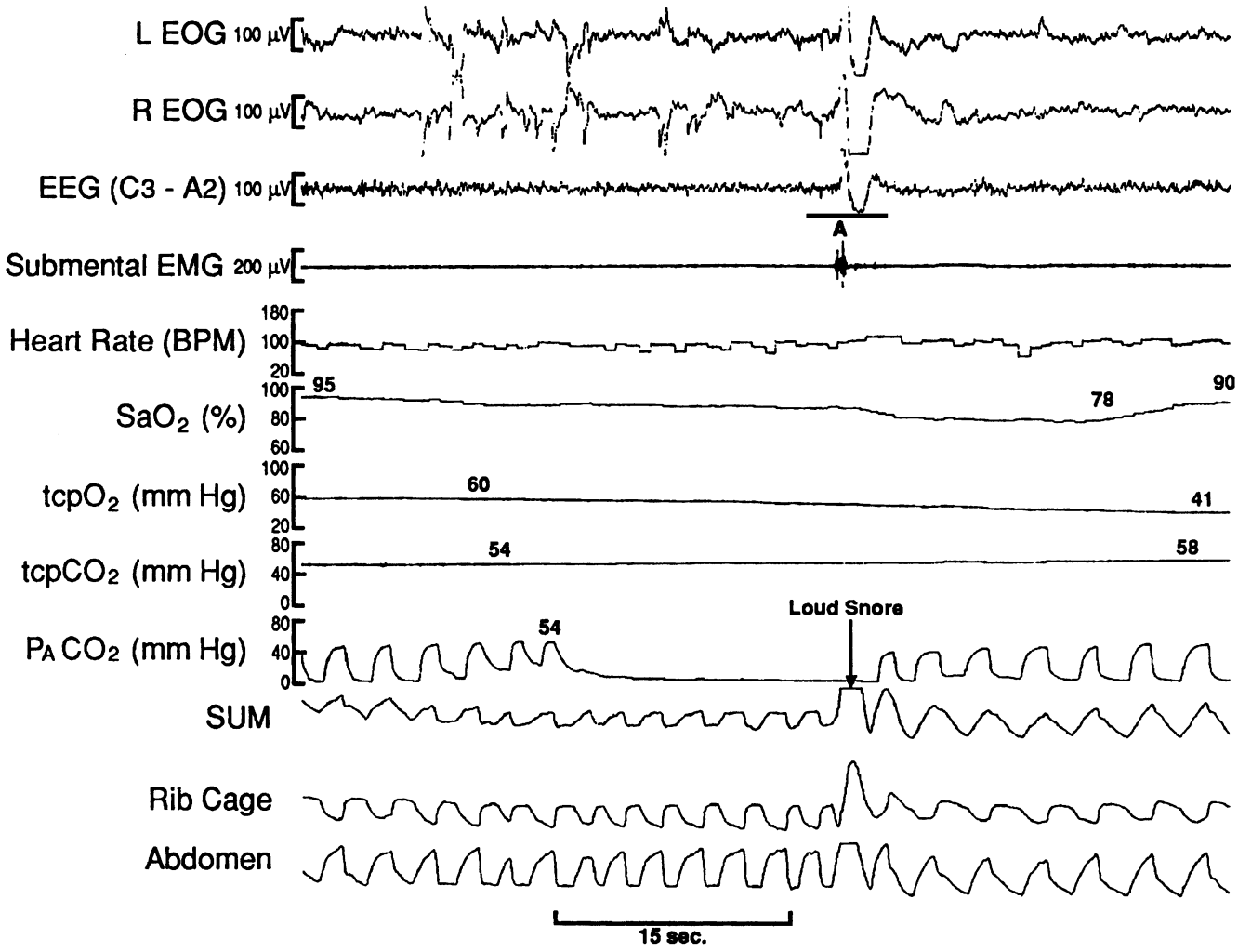

Fig. 1. Example of recordings from a PSG of a child with OSA, showing an obstructive apnea followed by a brief arousal ('A'; duration indicated by line). The arousal is accompanied by a change to a fast frequency rhythm and then a large distortion related to artifact on the EEG recording. Note also an increase in submental EMG activity, a rise in heart rate, and distortion of the respiratory traces secondary to movement.

3. Detecting arousals in the home setting

A polysomnogram (PSG) performed in a sleep laboratory provides a detailed assessment of respiration during sleep and its potential consequences such as frequent arousals and fragmentation of sleep. However, PSG is a complicated and expensive test, requiring a high staff-to-patient ratio, and is not widely available. Also, spending a night in the sleep laboratory is disruptive for families and monitoring may interfere with normal sleep [37]. For these reasons, less labor-intensive methods of assessing both breathing and sleep disturbance have been sought, particularly methods that can be carried out in a child's home. One of the key difficulties with this type of testing lies in quantifying microdisruption of sleep due to upper airway obstruction without EEG recordings. Several investigators have evaluated non-EEG methods of quantifying arousals in children, and these are outlined below.

3.1. Cardiorespiratory sleep studies

Three studies to date have demonstrated that in children, cortical (EEG) arousals are usually associated with movement. Mograss et al. [18] found that nearly all respiratory events were associated with a movement arousal, and that 83% of movement arousals detected by PSG could be detected using only a cardiorespiratory montage (heart rate, SaO_2, pulse waveform, respiratory movements by respiratory inductance plethysmography, and EKG). Fig. 1 shows an example of an EEG arousal following a respiratory event; note the changes on cardiorespiratory channels consistent with a movement arousal. The movement arousal index determined from the cardiorespiratory montage averaged 83.6% of that from PSG (Fig. 2) [18]. This slight underestimation may be explained by the fact that the cardiorespiratory montage alone misses small numbers of arousals that are only seen on the EEG or EMG channels, more

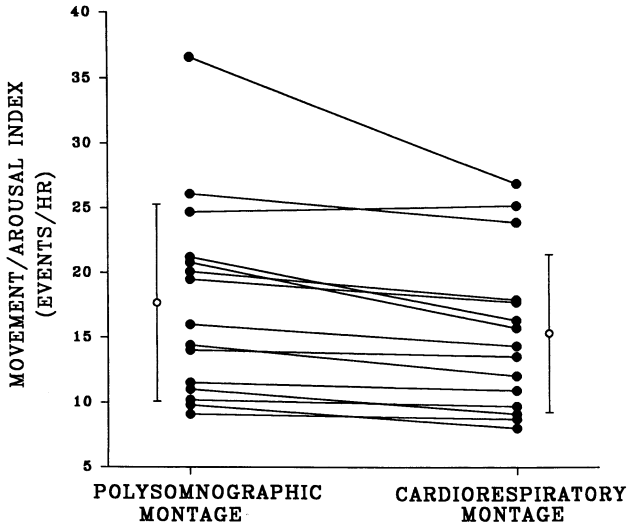

Fig. 2. Movement arousals as calculated from a full polysomnographic montage and a cardiorespiratory montage in 15 children with OSA. The mean (SD) movement arousal index was slightly lower using the cardiorespiratory montage (15.3 ± 6.1 events/h) than using the full polysomnographic montage (17.8 ± 7.6 events/h). Overall, 82.9 ± 7.6 SD% of movement arousals were detected using only the cardiorespiratory montage ([18]).

subtle movements, and multiple arousals separated by brief (10–15 s) periods of sleep (the latter often grouped into one arousal using the cardiorespiratory montage). Scholle and Zwacka found a similar number of EEG and movement arousals (Fig. 3) and that 73% of EEG arousals were combined with body movement as defined by activation of tibialis anterior EMG, although they did not analyze specifically what proportion of EEG arousals would have been identified without the EEG/EOG/EMG channels [8]. Jacob et al. performed polysomnography in the laboratory and a cardiorespiratory sleep study at home in 21 children aged 2–12 years referred for possible OSAs and found no significant difference in the respiratory and spontaneous movement arousal indices determined by the two studies [37]. Thus, cardiorespiratory sleep studies performed in the home can provide a reliable assessment of arousal frequency.

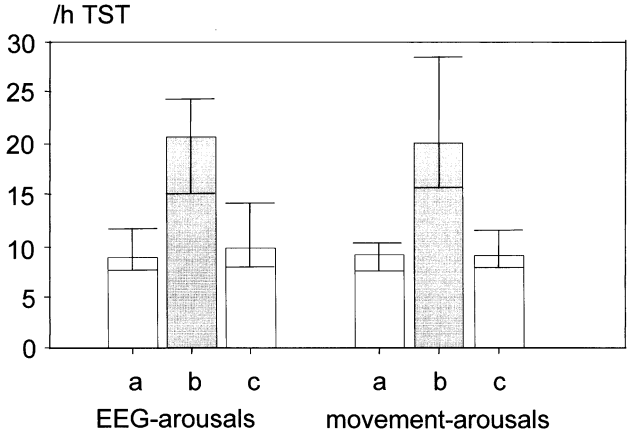

Fig. 3. The number of EEG- (cortical-) arousals and movement arousals in 20 controls (a), and 20 children with OSA before (b) and after (c) treatment with adenotonsillectomy, continuous positive airway pressure or nasal bilevel ventilation. Adapted from Ref. [8].

3.2. Video recordings

Continuous video recording during the night permits discrimination of sleep versus wakefulness, but not sleep state, in infants [38] and older children [39]. In order to try to quantify movement arousals using video recordings, Stradling et al. investigated the use of automatic detection of movement during sleep using photodiodes attached to a video monitor screen to detect changes in light intensity [19]. This method demonstrated an increase in time spent moving during sleep in eight children with OSA compared to eight controls, and a reduction in movement time after adenotonsillectomy. No comparison was made between detection of movement arousals by this method and polysomnography-defined arousals, and 12-s epochs were used, making comparison with arousal indices determined by PSG impossible. Another report from the same center using the same methodology in 61 children with OSA and 31 controls also demonstrated increased movement time in children with OSA and with a decrease to the same level as control children after T and A [40].

3.3. Audio recordings

The analysis of sound during sleep has not been widely studied in children. Potsic reported a good agreement between sleep sonography (breathing sounds) and PSG findings for detection of apnea in children with OSA, but sonography was not able to differentiate central from obstructive apneas [41]. Evaluation of the proportion of respiratory events associated with arousal, or the quantification of non-respiratory arousals was not assessed.

3.4. Measurements of movement during sleep

Various devices have been investigated for quantifying movement during sleep, including accelerometers, EMG and artifact on the pulse waveform channel of an oximeter.

The use of motion-sensitive recording devices such as accelerometers (actigraphy) makes long-term recordings of an individual's movement patterns possible. The sensor is worn on the body, frequently, around a limb. Movements are quantified in various ways, usually averaging activity over a specified time period such as 1 min. These devices are able to provide fairly reliable estimates of sleep duration [42,43], although they tend to overestimate sleep, as lack of movement is interpreted as sleep. As people with OSA have been noted to be more restless during sleep than normal people, actigraphy provides an attractive possibility for the non-invasive quantification of movement arousals

during sleep. In adults, studies have yielded conflicting results with regard to the ability of actigraphy to reliably differentiate those with OSA from normals [44–46]. Differences in actigraphy technology and methods of quantifying respiratory events may be part of the explanation for this discrepancy. In children with suspected OSA, Suratt et al. have reported only a weak correlation between actigraphic indices and AHI, with too much variability to reliably detect OSA in individual subjects [47].

The ability of actigraphy to quantify arousals depends on two main factors: its sensitivity for small movements and its ability to detect movements of short duration. Averaging movement over 1 min intervals as is commonly practiced will clearly miss short arousals; however, as averaging time decreases, memory capacity fills more quickly, decreasing total recording time. Even given ideal detection of short movements, actigraphy cannot differentiate between movement arousals related to respiratory events and spontaneous movement arousals or those from another cause such as periodic limb movements. In the future, this technology may have applications for home use in monitoring the effects of treatment in patients with sleep disorders that lead to increased movement during sleep.

EMG may be used to detect muscle activity during movement. Abdominal muscle EMG activity is frequently seen during sleep in children with OSA, but rarely in age-matched controls [48]. Peaks in abdominal EMG have also been demonstrated to correspond with arousal following apnea, in both REM and NREM sleep [49]. While the recording of limb EMG is part of standard laboratory PSG [50], very low amplitude biopotentials are recorded and the practical issues in achieving good recordings probably preclude the widespread use of EMG recordings in the home.

3.5. Pulse transit time

Pulse transit time (PTT) measures the time taken for the pulse pressure wave to travel from the heart to the periphery, usually recorded as the time from the electrocardiographic R wave to detection of the corresponding pulse wave at the finger using a photoplethysmograph. The PTT is inversely correlated with blood pressure and reflects beat-to-beat changes in blood pressure. It has been demonstrated to mirror the fluctuations in pleural and blood pressure that occur during respiration against a partly occluded upper airway. Rapid dips in PTT are also seen after respiratory events as a result of the surge in blood pressure that occurs with an arousal [51–54].

Pitson et al. examined the correlation between conventional indices of sleep disruption (EEG-defined arousals, the apnealhypopnea index and the oxygen desaturation index) and two autonomic indices (heart rate and blood pressure rises defined by PTT) [55]. Blood pressure rises were highly correlated with SaO_2 dips ($r = 0.71$) and EEG microarousals ($r = 0.65$). Thus, PTT looks promising as a non-invasive method of detecting increased respiratory effort and arousal in adults with OSA, both in the laboratory [55] and in the home environment [56].

Investigation of the use of this technique in children has recently been presented in abstract form. Pagani et al. found a relationship between the change in PTT during a single inspiratory effort (ΔPTT) and the degree of applied inspiratory resistance in awake children [57]. Delavie et al. reported an increase in the number of detected arousals when PTT was added to analysis of other signals (ASDA criteria) [58]. Further investigation of this technique is required to determine the reliability of PTT in detecting arousals in children, and the clinical significance of the arousals that are detected.

3.6. Heart rate variability

Acute rises in heart rate are often seen in conjunction with arousals following respiratory events in adults [55]. Mograss et al. described a rise in heart rate in 74% of movement arousals following respiratory events in children [18]. Pitson et al. reported an association between arousal frequency and acute rises in heart rate in adults [55], but this technique has not been evaluated in children.

Evaluation of beat-to-beat changes in heart rate over the night has been proposed as a non-invasive method of detecting children with OSA. Baharav et al. evaluated this method in ten children with OSA and ten controls [59]. They found a greater low frequency power in the OSA group, consistent with increased sympathetic activity during the night in children with OSA. The principal difficulty with this method is that periods containing artifact have to be removed prior to analysis (comprising 60% of the test time in the paper by Baharav et al.). Thus longer movement arousals are likely to be removed prior to analysis, and shorter arousals will also not be detected as this fast Fourier transform method analysed time intervals of 256 s each.

4. Summary and conclusions

Arousals from sleep are potentially an important link between sleep-disordered breathing and its consequences in children. As access to PSG is limited, methods of quantifying and characterizing these arousals in the home setting have been sought. Using a definition based on movement artifact on respiratory channels in conjunction with an increase in heart rate and movement on video recordings detects the majority of arousals secondary to respiratory events in children [18]. The use of movement detectors such as accelerometers and evaluation of PTT also show promise in providing reliable quantification of arousals from sleep in the home. However, further assessment of these and other devices is needed before they can be recommended for the quantification and characterization of arousals from sleep in childhood.

5. Future research directions

- Establish normative data for the frequency of arousals from sleep, with emphasis on the effects of age and state.
- Investigate the presence of a link between arousal from sleep and the sequelae of OSA in childhood. In particular, researchers should focus on the potential link between frequency of arousals of any cause and neurocognitive sequelae such as learning and behavioral problems.
- Clarify the effect of age on the frequency of arousal as a mechanism of apnea termination.
- Further evaluate practical methods of quantifying arousals and awakenings without using EEG, so that reliable portable diagnostic systems can be developed for use in children in the home environment.

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