Peripheral Arterial Tonometry Events and Electroencephalographic Arousals in Children

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Study Objectives: Peripheral arterial tonometry (PAT) is a sensitive measure of moment-to-moment changes in sympathetic activity and reliably identifies arousals in adult subjects. We investigated whether PAT events during sleep are associated with visually recognizable electroencephalographic arousals in healthy children and in children with sleep-disordered breathing.

Design: Prospective cohort.

Setting: Pediatric Sleep Research Laboratory.

Participants: Twenty children with obstructive sleep apnea syndrome, 20 children with mild sleep-disordered breathing, and 20 control children with a mean age of 7.6 ± 2.6 years (range: 5.7-16.5 years); 53% of children were boys.

Interventions and Measurements: Polysomnographic evaluation in the sleep laboratory with concomitant recording of PAT. PAT events were defined as attenuations from immediately preceding baseline of 20% to 50% (PAT20) and > 50% (PAT50) for at least 5 seconds and the indexes calculated per hour of sleep time that included good-quality PAT signals. Total PAT index (the sum of PAT20 index and PAT50 index) was also calculated.

Results: Total PAT index correlated with total arousal index and spontaneous arousal index (r = 0.55, P < .0001, r = 0.64, P < .001, respectively), especially in the group with obstructive sleep apnea syndrome (r = 0.71, P < .0001). The sensitivity and specificity of PAT for identifying electroencephalographic arousals were 95% and 35%, respectively. The PAT device identified pathologic arousals indexes (> 16 per hour) (area under the curve 0.79, P = .002). Thirty-five percent of respiratory events (eg, obstructive apnea or hypopnea) were associated with a visual electroencephalographic arousal, compared to 92% being associated with PAT attenuation events.

Conclusions: Arousals in sleeping children are associated with increased sympathetic discharge, as evidenced by attenuations in PAT signal. However, a significant proportion of PAT attenuations were not accompanied by visual electroencephalographic arousals. Thus, the importance of these autonomic arousals has yet to be explored in association with morbidity related to sleep-disordered breathing and, therefore, PAT technology cannot be recommended as an alternative tool for measuring arousals in children. Nevertheless, these data further support the contention that adult criteria for the measurement for arousals may not be adequate in children.

Key Words: Peripheral arterial tonometry; sleep-disordered breathing; arousal; autonomic function

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INTRODUCTION

SLEEP-DISORDERED BREATHING (SDB) IS A FREQUENT CONDITION THAT AFFECTS BOTH CHILDREN AND ADULTS AND IS ASSOCIATED WITH DISRUPTION OF ALVEOLAR VENTILATION, HYPOXEMIA, AND SLEEP FRAGMENTATION. Sleep fragmentation in healthy adults, ie, the presence of multiple respiratory-related arousals during sleep, correlates with neurobehavioral performance decrements the following day. In contrast, despite the presence of substantial neurocognitive morbidity, it is assumed that sleep architecture is preserved in children with SDB, possibly because criteria for arousal are based on those defined for adults. However, changes in spectral power have been observed during obstructive events in children without obvious electroencephalogram (EEG) arousal, suggesting that current techniques for assessment of arousal may not be sensitive enough in children, and therefore fail to detect sleep fragmentation in the pediatric population.

Arousals during sleep are associated with increases in sympathetic activity in normal adults. Therefore, measurement of sympathetic activity changes using noninvasive approaches, eg, heart-rate variability or pulse transit time, may provide a practical method for arousal detection. A recently developed technique allowing for noninvasive moment-to-moment measurement of sympathetic tone is peripheral arterial tonometry (PAT). PAT employs finger plethysmography such that changes in sympathetic activity, which elicit robust changes in peripheral vascular cutaneous perfusion, are detected on a beat-to-beat basis. In adults, PAT-signal attenuations with concomitant changes in heart rate correlate with respiratory disturbances as well as with EEG arousals. Thus, we hypothesized that PAT monitoring may provide a sensitive measure of arousals in children.

SUBJECTS AND METHODS

Forty consecutive children being evaluated for potential SDB at Kosair Children’s Hospital Sleep Medicine Center were invited to participate. In addition, healthy children with no reports of sleep disturbance were also recruited from a community survey of sleep habits to act as controls. The study was approved by the University of Louisville Human Research Committee. Parental informed consent and child assent, in the presence of a parent, were obtained. Children were excluded if they had any chronic medical condition, psychiatric diagnoses, or any genetic or craniofacial syndromes.

A standard overnight multichannel polysomnographic evaluation was performed in the sleep laboratory. No drugs were used to induce sleep. Chest and abdominal wall movement were measured by respiratory...
impedance or inductance plethysmography and heart rate, by electrocardiogram; airflow was monitored with a sidestream end-tidal capnograph, which also provided breath-by-breath assessment of end-tidal carbon-dioxide levels (PETCO₂, BCI SC-300, Menonemone Falls, Wisc), and a thermistor. Arterial oxygen saturation (SpO₂) was assessed by pulse oximetry (Nellcor N 100; Nellcor Inc., Hayward, Calif), with simultaneous recording of the pulse waveform. The bilateral electrooculogram, 8 channels of EEG, chin and anterior tibial electromyogram, and analog output from a body-position sensor (Braebon Medical Corporation, NY) were also monitored. All measures were digitized using a commercially available polysomnography system (Remibrand, MedCare Diagnostics, Amsterdam). Tracheal sound was monitored with a microphone sensor (Sleepmate, VA), and a digital time-synchronized video recording was performed.

Sleep architecture was assessed by standard techniques.24 Obstructive apnea was defined as the absence of airflow with continued chest wall and abdominal movement for a duration of at least 2 breaths.25-26 Hypopneas were defined as a decrease in nasal flow of at least 50% with a corresponding decrease in SpO₂ of at least 4%, an arousal, or both.26 The apnea-hypopnea index (AHI) was defined as the number of apneas and hypopneas per hour of total sleep time (TST). Children with an AHI of at least 1 but less than 5 per hour of TST were considered to have mild SDB, while children with AHI of at least 5 per hour of were considered to have obstructive sleep apnea syndrome (OSAS). The mean SpO₂, as measured by pulse oximetry in the presence of a pulse waveform signal void of motion artifact, and the SpO₂ nadir were recorded. Since criteria for arousals have not yet been developed for children, arousals were defined as recommended by the American Sleep Disorders Association Task Force report15 using the 3-second rule, the presence of movement artifact, or both.27 Arousals were divided into 2 main subtypes: spontaneous arousals and respiratory arousals. In addition, technical arousals and arousals associated with periodic leg movements were counted and contributed to the total arousal index. Height and weight were obtained from each child. Body mass index (BMI) was calculated and also expressed as relative BMI (relBMI), which also provided breathing, and 20 control children (10 boys) were studied. Subject characteristics are shown in Table 1. There were no significant differences in sex, relBMI, TST, and TPT between the groups. The mean age in the OSAS group was significantly higher compared to the mild SDB and control groups.

Arousal and PAT characteristics for each group are shown in Table 2. Examples of PAT events and of EEG-related spontaneous and respiratory arousals are shown in Figure 1. Typically, the PAT attenuations observed began within 10 seconds of the onset of visually recognizable EEG arousals. Thirty-five percent of respiratory events (eg, obstructive apnea or hypopnea) were associated with a visual EEG arousal, compared to 92% being associated with PAT-attenuation events.

The sensitivity and specificity of PAT for identifying EEG arousals were 90% and 23% respectively. The inclusion of PAT artifacts (ie, a change in the PAT signal accompanied by a movement) improved the sensitivity and specificity to 95% and 35%, respectively. Subanalysis of the 3 groups (ie, OSAS, mild SDB, and controls) showed similar values of sensitivity and specificity, with sensitivities being 93%, 96%, and 95%, respectively, and specificities being 36%, 35%, and 35%, respectively.

### Table 1—Demographic characteristics of 20 children with obstructive sleep apnea syndrome, 20 children with mild sleep-disordered breathing, and 20 control children.

<table>
<thead>
<tr>
<th></th>
<th>OSAS (n = 20)</th>
<th>Mild SDB (n = 20)</th>
<th>Controls (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (range)</td>
<td>9.6 ± 2.6*†</td>
<td>6.5 ± 0.6</td>
<td>6.7 ± 0.5</td>
</tr>
<tr>
<td>Boys, no. (%)</td>
<td>(5.8-16.5)</td>
<td>(5.7-7.8)</td>
<td>(5.8-7.4)</td>
</tr>
<tr>
<td>Relative body mass index</td>
<td>148.8 ± 64.9</td>
<td>117.4 ± 37.8</td>
<td>111.8 ± 22.6</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD. OSAS refers to obstructive sleep apnea syndrome; SDB, sleep-disordered breathing.

### Table 2—Polysomnographic characteristics of 20 children with obstructive sleep apnea syndrome, 20 children with mild sleep-disordered breathing, and 20 control children.

<table>
<thead>
<tr>
<th></th>
<th>OSAS (n = 20)</th>
<th>Mild SDB (n = 20)</th>
<th>Controls (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TST, h</td>
<td>7.6±0.9</td>
<td>8.0±0.8</td>
<td>7.8±0.6</td>
</tr>
<tr>
<td>TPT, h</td>
<td>5.4±1.3</td>
<td>6.4±1.6</td>
<td>6.3±1.0</td>
</tr>
<tr>
<td>AHI</td>
<td>13.9±7.3***</td>
<td>2.5±1.1§§</td>
<td>0.6±0.3</td>
</tr>
<tr>
<td>SpO₂ nadir, %</td>
<td>80.6±10.7***</td>
<td>87.8±6.6§§</td>
<td>94.2±2.9</td>
</tr>
<tr>
<td>ETCO₂, mmHg</td>
<td>50.0±5.1</td>
<td>48.5±1.9</td>
<td>48.7±3.3</td>
</tr>
<tr>
<td>Total Arousal Index</td>
<td>14.6±6.9*</td>
<td>13.0±5.55</td>
<td>10.2±3.2</td>
</tr>
<tr>
<td>Spontaneous Arousal Index</td>
<td>10.5±5.6</td>
<td>12.5±5.4</td>
<td>9.7±3.1</td>
</tr>
<tr>
<td>Respiratory Arousal Index</td>
<td>4.1±3.9***</td>
<td>0.4±1.5</td>
<td>0.2±0.2</td>
</tr>
<tr>
<td>PAT50 index</td>
<td>19.9±10.3*</td>
<td>15.7±7.9</td>
<td>12.3±6.1</td>
</tr>
<tr>
<td>PAT20 index</td>
<td>11.0±6.1</td>
<td>15.7±7.9</td>
<td>10.7±4.5</td>
</tr>
<tr>
<td>PAT artifact index</td>
<td>8.3±5.0</td>
<td>4.7±3.1</td>
<td>6.7±2.4</td>
</tr>
<tr>
<td>PAT index</td>
<td>39.2±15.4</td>
<td>36.1±12.8§§</td>
<td>29.7±10</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD. OSAS refers to obstructive sleep apnea syndrome; SDB, sleep-disordered breathing; TST, total sleep time; TPT, total sleep time that included good-quality PAT signal; AHI, apnea-hypopnea index; PAT, peripheral arterial tonometry; PAT50, attenuations from immediately preceding baseline in > 50% for at least 5 seconds; PAT20, attenuations from immediately preceding baseline in 20% to 50% for at least 5 seconds.

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Figure 2 shows the ROC curve for total PAT index to identify children with arousal indexes of at least 16 per hour. The area under the curve was 0.79, P = .002. This suggests that using PAT index is significantly better than chance, or than not using it at all, for identifying normal subjects from those with pathologic arousal indexes. Analyses were also conducted separately for PAT50 and PAT20, although neither was found to be superior to the total PAT index (area under the curve was 0.76 and 0.63, respectively, with P = .005 for PAT50 index and P = NS for PAT20 index).

Correlations between PAT index and arousal index for the whole cohort and each subgroup are summarized in Table 3.

**DISCUSSION**

The major findings in this study are that surges in sympathetic activity, as measured by PAT-signal attenuations, correlate with EEG arousals in children, similar to the findings in the adult population. However, PAT is a very sensitive but not very specific tool for identifying EEG arousals in children, based on the currently used American Sleep Disorders Association criteria for arousals. Of interest, respiratory events were associated with PAT attenuations more frequently than with EEG arousals (92% vs 35%, respectively).

Increased sympathetic activation is associated with arousals in adults, and we have now found a correlation between EEG arousals and autonomic surges, as measured by PAT, in children. As shown in Table 3, significant correlations between PAT and arousals were found only for spontaneous arousals and not for respiratory arousals. One possible explanation for such a discrepancy may reside in the fact that we did not employ nasal-pressure measurements in our subjects and relied on thermistry alone for determination of hypopnea and oronasal flow characteristics. Thus, we may have misclassified respiratory-related arousals as spontaneous arousals in a substantial proportion of EEG-related arousal events. This is a clear limitation of the current study, and further studies using a more-sensitive tool for measuring airflow changes may improve the yield of the PAT device in this regard. However, before we assign to the absence of nasal-pressure measurements the sole responsibility for the uniquely large discrepancies between EEG arousals and PAT attenuations during respiratory events, we should consider another possibility: since only 35% of the respiratory events in our study were associated with a visual EEG arousal but 92% were association with PAT attenuations, the lack of correlation between respiratory arousals and PAT attenuations may be due to the fact that, in children, the majority of respiratory events do not elicit EEG arousals.

Sleep fragmentation is known to impair cognitive and psychomotor performance in adults. Although sleep architecture is assumed to be preserved in children with SDB, morbidities associated with sleep fragmentation are present, suggesting that current techniques may not be sensitive...
enough to detect sleep fragmentation in pediatric populations. Our findings further support this concept by showing high sensitivity but low specificity for identifying visual EEG arousals. In other words, 95% of the visual EEG arousals were identified by PAT events, but PAT technology identified a significant number of autonomic arousals that were not accompanied by a change in the EEG. These results provide additional evidence that the current criteria for measuring arousals using adult criteria may be inadequate in children. Indeed, substantial dynamic changes have been shown to occur in EEG spectra during respiratory events in children without any visually recognizable changes in the raw EEG signals. Furthermore, a recent study from our group has shown that PAT events not associated with any EEG changes show marked regional alterations in EEG spectral characteristics, suggesting that PAT events are accompanied by changes in cortical activity that are traditionally considered to represent arousals. Although we did not conduct spectral analyses of the EEG in the present study, it is likely that they would be similar to the findings by Ivanenko and colleagues. The PAT attenuations events in this study were likely associated with substantial changes in EEG spectral characteristics. Taken together, the current study emphasizes the need for further studies that include assessment of outcome (ie, neurobehavioral function) to determine whether autonomic arousals are a more sensitive measure of sleep fragmentation in children.

It is important to stress the point that PAT measurements are not suggested as an alternative tool for the measurement of arousals based on the current findings. But, if autonomic arousals (ie, PAT attenuations) are found to be reliably associated with some of the morbidities of SDB in children, the use of PAT during polysomnographic recordings could provide a noninvasive sensitive marker for autonomic disruption and provide more-objective assessment of outcome predictors in snoring children.

We were unable to find an association between the degree of attenuation (ie, PAT50 or PAT20) and the type of arousal. This observation may reflect dynamic and reciprocal changes in the occurrence of arousals in snoring children as well as underlie homeostatic mechanisms of sleep preservation in the pediatric population. Furthermore, dynamic changes in the independently defined thresholds leading to autonomic (ie, PAT attenuations) and EEG arousals, as elicited by the repeated occurrence of respiratory events in snoring children, may account for the different magnitude of responses across the severity spectrum. In other words, any given respiratory or other arousing stimulus could lead to a PAT50 event in a nonsnoring child but may yield only a PAT20 attenuation in a child with significant SDB. The inability to distinguish between spontaneous and respiratory-related arousals is therefore a significant limitation of the device and precludes the use of PAT in isolation from other physiologic sensors. However, we still find that PAT technology was significantly better than chance in identifying normal children from those with elevated arousal indexes. However, such predictive values were clearly not as reliable in children compared to the adult population.

It could be also argued that the absence of concomitant assessment of the recordings of heart-rate changes and those of PAT attenuations is a potential limitation of the present study, since, in adult subjects, this approach improves arousal detection. While inclusion of heart-rate changes in the criteria for “autonomic arousal” may represent a valid approach in adults, we and others would not endorse such an approach in children, since many respiratory events, including severe hypoxemia in children with SDB, are not accompanied by concomitant heart-rate changes. Based on such considerations, we opted for including PAT changes as being representative of sudden increases in autonomic tone regardless of parallel heart-rate alterations. This does not preclude the possibility, however, that a cut-off value for heart-rate change might be identified in future explorations and may potentially improve the reliability of PAT events in the identification of arousals. Measurement of autonomic-activation events is critically important in children, since such events may be a major contributor for systemic hypertension and left-ventricular abnormalities that are frequently identified in children with OSAS. Indeed, repetitive autonomic stimulation during sleep by abnormal breathing has been implicated in the development of sustained hypertension in adults. Thus, PAT recordings may also provide a useful tool for the study of cardiovascular morbidity associated with repetitive autonomic arousals in children with SDB.

In summary, arousals in sleeping children are associated with increased sympathetic discharge, as evidenced by attenuations in PAT signal. However, a significant proportion of PAT attenuations is not accompanied by visual EEG arousals in the pediatric population. Therefore the implications of these autonomic arousals remain to be explored in association with SDB-related morbidities. Notwithstanding such considerations, our current findings further support the contention that adult criteria for the measurement for arousals may not be adequate in children.

**REFERENCES**