Detection of Cortical Arousals in Children Using Frontal EEG Leads in Addition to Conventional Central Leads

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Study Objective: This study was designed to assess the efficacy of using Fz as an additional electrode in screening arousals during polysomnography in children.

Methods: Polysomnograms from 24 children were randomly selected from a sleep-study database of children from different diagnostic categories. Of the children whose polysomnograms selected, 5 were normal, 5 had severe obstructive sleep apnea syndrome, 5 had mild obstructive sleep apnea syndrome, 5 had snoring, and 4 had periodic limb movement disorder. American Academy of Sleep Medicine criteria for arousal were applied to Fz only, C3/C4 only, or both electrode sites combined.

Results: C3/C4 electrode sites picked up 96.33% of arousals in the polysomnograms of children, compared with 87.46% arousals identified at Fz. An additional 3.3% of arousals were identified at Fz that were not detected at C3/C4. The average median number of arousals per subject, accompanied by the interquartile range, was 29 (19.2-39.7) at C3/C4 and 27.5 (19.2-33.7) at Fz, reflecting a significant difference between the two (p = .005). The use of both electrodes sites resulted in the detection of the highest number of arousals per subject, with a median of 29 (20.2-40.7).

Conclusion: Unlike findings recently reported in adults, our study detected a higher number of arousals from central electrodes rather than frontal, with the maximum number of arousals obtained using a combination of frontal and central electrodes. A possible explanation for differences in the optimal location for detection of arousals between adults and children is discussed.

Keywords: Cortical arousals, central arousals, frontal arousals, children, polysomnogram (PSG)

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Revised guidelines for scoring arousals on polysomnograms (PSGs) were published by the American Sleep Disorders Association in 1992, and a modification of this system for children is also presently in use.1,2 Electroencephalographic (EEG) arousal is typically defined as an abrupt shift in background frequency (including alpha waves or higher frequencies, but not spindles) lasting 3 seconds or longer and preceded by at least 10 seconds of sleep.1 Conventionally, arousals in PSGs have been scored using central (C3/C4) electrodes. Recently, O’Malley et al1 demonstrated that the addition of frontal EEG leads, especially Fz, significantly improved the detection of EEG arousals associated with obstructive respiratory events by 24% in adults.

The present study was designed to investigate whether conventional central electrodes (C3/C4) are sufficient for detecting cortical arousals during PSGs in children or if there is improved efficacy with the addition of a frontal lead (Fz).

Disclosure Statement
This was not an industry supported study. Drs. Kothare, Kaleyias, Grant, Darbari, Ajagbe, and Cepelowicz-Rajter have indicated no financial conflicts of interest.

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METHODS

Subjects and Data Collection

Conventional PSGs utilize central leads (C3/C4) and occipital leads (O1/O2), referenced to the ear lobes according to the International 10-20 system of electrode placement. In our study, conventional PSGs were supplemented with a frontal lead (Fz) to further analyze arousal activity, cross-referenced to linked ears. Following Institutional Review Board approval, PSGs of 24 children (mean age 8 years, age range 5-10 years; equal number of boys and girls) selected randomly from different diagnostic groups in our sleep-study database, were retrospectively analyzed. None of the children included in this study were on psychoactive medications. Selected subjects were divided into 5 groups based on their polysomnographic diagnosis. There were 5 children with normal PSGs, 5 with severe obstructive sleep apnea syndrome (OSAS) [apnea-hypopnea index ≥ 10/hour], 5 with mild OSAS [apnea-hypopnea index < 5/hour], 5 with snoring (without apnea or hypopnea), and 4 with periodic limb movement disorder (leg movements lasting 0.5-5 seconds in duration, in clusters of 4 or more, interspersed with interleg movements from 10-90 seconds and > 5/hour). None of the subjects had skull defects, hydrocephalus, or any known structural brain abnormality at the time of their sleep study. All PSGs were performed using simultaneous pressure transducer and thermistor for nasal flow, piezoelectric chest and abdominal belts, and end-tidal CO2 monitoring. In addition, each PSG included pulse oximetry, snore microphone, 2 leg
channels, chin electromyogram, and simultaneous video monitoring.

Data Analysis

EEG arousals occurring during non-rapid eye movement sleep were scored by 3 physicians (board certified or board eligible in sleep medicine). During the scoring process, the physicians were blinded to the diagnoses and the electrode sites, and all data was scored from 1 channel at a time. The physicians initially scored all arousals from the central C3/C4 channel in the absence of the Fz channel, then rescored arousals independently on the Fz channel in the absence of the C3/C4 channel. Arousals were defined as an abrupt shift in frequency (excluding delta waves and spindles) lasting more than 3 seconds and preceded by at least 10 seconds of sleep.1 Arousals from the central, frontal, and a combination of central and frontal electrode sites were analyzed using linked-ear references.

The precipitating events contributing to arousals were scored by physicians (FD, OA, and JC) blinded to the diagnoses and EEG channels, and these events were then correlated with the EEG arousals. Snoring was categorized into primary snoring and upper airway resistance syndrome.4 Arousal events were subsequently identified as either spontaneous arousals or awakenings (not associated with any identifiable cause), arousals occurring due to primary snoring (not accompanied by oxygen desaturations or changes in airflow), upper-airway resistance syndrome (accompanied by oxygen desaturation of ≥ 4%), and cyclical arousals without apnea or hypopnea, apnea (cessation of airflow for 2 respiratory cycles), hypopnea (decrease in amplitude of airflow signal by ≥ 50% lasting for 2 respiratory cycles and accompanied by oxygen desaturation of > 4%), or leg movements. Hence, there were 6 types of arousal events recorded in the 24 subjects from the 5 diagnostic groups. The examiners did not attempt to score arousals occurring in rapid eye movement sleep due to the confounding effect of differentiating and analyzing chin electromyogram data along with EEG arousals.

The average number of arousals per subject is expressed as a median value accompanied by the interquartile percentiles (25th-75th percentile). Analyses included Wilcoxon sign rank nonparametric test for nonnormally distributed variables for comparison of differences in the total number of arousals or awakenings at different electrode sites (C3/C4, Fz, and a combination of C3/C4 or Fz), as well as differences in the number of arousals associated with different precipitating events and differences detected across diagnostic groups. Due to the high number of comparisons performed across the 3 electrode-site groups, a Bonferroni correction was applied. An adjusted probability value less than 0.007 was used to detect significant differences in arousals associated with different precipitating events, and an adjusted p value of less than .01 was used to detect significant differences across diagnostic groups. The differences in the number of arousals detected at the central and frontal electrodes are presented in the Tables. All statistical analyses were performed with the SPSS statistical software package (SPSS for Windows, Inc., Chicago, IL).

RESULTS

A total of 747 arousals were detected at the combined (C3/C4 or Fz) electrode sites in our current sample of 24 children. Of these, 723 (96.7%) arousals were identified at C3/C4, and 659 (87.5%) arousals were detected at Fz electrode. Of the total sample of 747 arousals, only 3.3% (24) were detected at Fz and not at C3/C4. Arousals detected at Fz but missed at C3/C4 included 5 of 238 (2.1%) events associated with spontaneous arousal, 8 of 158 (5%) primary snoring, 4 of 179 (2.2%) upper-airway resistance syndrome, and 7 of 134 (5%) hypopnea events.

The average median number of arousals (25th-75th percentiles) per subject detected at C3/C4 was 29 (19.2-39.7), which is significantly higher (p = .005) than the average of 27.5 (19.2-33.7) detected at Fz. Results from the Wilcoxon signed rank tests indicated that the use of a combination of central and frontal electrode sites was a superior method of detecting arousals than either the central or frontal only electrodes (p = .005 and p = .0001, respectively). Even though the median value of 29 (20.2-40.7) per subject was similar between the combined and central sites, a review of the differences between these 2 revealed a tie in 58% of the cases, with an increase in the magnitude of the differences in

![Table 1](image-url)

Table 1—Arousals per Subject at Electrode Site by Precipitating Events

<table>
<thead>
<tr>
<th>Events</th>
<th>No.</th>
<th>Combined</th>
<th>Central</th>
<th>Frontal</th>
<th>Difference</th>
<th>Ties</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Positive</td>
<td></td>
<td>Central vs Frontal</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>29</td>
<td>29</td>
<td>27.5</td>
<td>(20.2-40.7)</td>
<td></td>
<td>.005</td>
</tr>
<tr>
<td>Related to</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(19.2-39.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SP</td>
<td>23</td>
<td>7 (2-19)</td>
<td>7 (2-18)</td>
<td>7 (2-16)</td>
<td>10</td>
<td>1</td>
<td>.034</td>
</tr>
<tr>
<td>PS</td>
<td>18</td>
<td>5.5</td>
<td>5.5</td>
<td>4.5</td>
<td>6</td>
<td>3</td>
<td>.5</td>
</tr>
<tr>
<td>UARS</td>
<td>21</td>
<td>5 (3-13.5)</td>
<td>5 (3-13.5)</td>
<td>4 (3-8.5)</td>
<td>11</td>
<td>1</td>
<td>.004</td>
</tr>
<tr>
<td>LMs</td>
<td>6</td>
<td>2 (1-16.2)</td>
<td>2 (1-16.2)</td>
<td>1.5 (1-15.2)</td>
<td>3</td>
<td>0</td>
<td>.08</td>
</tr>
<tr>
<td>HY</td>
<td>8</td>
<td>11.5</td>
<td>11.5</td>
<td>9.2</td>
<td>4</td>
<td>1</td>
<td>.09</td>
</tr>
<tr>
<td>AP</td>
<td>6</td>
<td>3 (1-5.2)</td>
<td>3 (1-5.2)</td>
<td>2 (0.7-5.2)</td>
<td>3</td>
<td>0</td>
<td>.08</td>
</tr>
</tbody>
</table>

Data are presented as median (25th, 75th percentiles) unless otherwise indicated. The Bonferroni adjusted p value (Wilcoxon rank sum test) = .007. Combined refers to C3/C4 either/or Fz electrode; Central or C, C3/C4 electrode; Frontal or F, Fz electrode; Difference, the difference in the median number of arousals between C3/C4 vs Fz electrodes; SP, spontaneous arousal; PS, primary snoring; UARS, upper airway resistance syndrome; LMs, leg movements; HY, hypopnea; AP, apnea.
Arousals can be subclassified into cortical and/or subcortical arousals, which act as a protective reflex against life-threatening hypoxemia; however, in children, most apneas do not terminate with arousals. Arousal events in adults terminate with arousals during sleep in our study of young children. The maximum number of total arousals was detected using a combination of central and frontal electrode sites during PSGs to identify the presence of arousals occurring as a result of different events during sleep in a population of young children between the ages of 5 to 10 years. We found that conventional central leads detected the vast majority of the arousals (96.3%), whereas the frontal leads detected a smaller number (only 87.4%) of the total arousals recorded at both sites. In our population of children, an additional 3.3% of arousals were detected only at frontal and not central leads, and these events were primarily associated with snoring, which is far below the 24% increase in arousals resulting from obstructive respiratory events that have recently been identified in adults. Not unexpectedly, the maximum number of total arousals was detected using a combination of frontal and central electrodes. Therefore, unlike the response pattern in adults, arousals during sleep in our study of young children were maximally detected in the central regions. This general response pattern was consistent across all types of precipitating events.

We hypothesize that the localization difference in cortical arousals between young children and adults may be the result of maturational effects upon underlying neurologic structures involved in these processes. This is based on age-related results obtained from a larger body of scientific data from neurophysiologists, cognitive neuroscientists, and neuropsychologists.

Within the electrophysiologic domain, studies have identified age-related differences in the temporal emergence and spatial localization of various sleep-related events. The detection of arousals on surface EEG electrodes is of particular interest in the field of sleep medicine, as it provides valuable information regarding sleep architecture and vigilance states. The use of different electrode configurations can significantly affect the detection of arousals, as demonstrated in our study.

### DISCUSSION

Sleep is interrupted in children and adults by arousals that can be spontaneous, related to external environmental events, or related to physical factors such as snoring, apneas, hypopneas, and leg movements. Apneic events in adults terminate with arousals, which act as a protective reflex against life-threatening hypoxemia; however, in children, most apneas do not terminate with arousals. This may, in part, be explained by the fact that the central nervous system pathways mature later than peripheral pathways. In children, the mechanism of apnea termination is dominated by peripheral rather than central reflex responses, and neuromuscular drive increases sufficiently to overcome upper airway closure without involving a behavioral, EEG-detectable response. Accordingly, in our study, we investigated the occurrence of arousals resulting from a variety of etiologies, including, but not limited to, respiratory causes.

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### Table 2—Arousals per Subject at Electrode Site by Diagnostic Group

<table>
<thead>
<tr>
<th>Events</th>
<th>No.</th>
<th>Combined</th>
<th>Central</th>
<th>Frontal</th>
<th>Positive (C&gt;F)</th>
<th>Negative (C&lt;F)</th>
<th>Ties (C=F)</th>
<th>Central vs Frontal</th>
<th>Combined vs Central</th>
<th>Combined vs Frontal</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>5</td>
<td>22 (14.5-26.5)</td>
<td>20 (14-26)</td>
<td>21 (12.5-25)</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>.28</td>
<td>.1</td>
<td>.1</td>
<td></td>
</tr>
<tr>
<td>SN</td>
<td>5</td>
<td>28 (22-41)</td>
<td>24 (21-40.5)</td>
<td>28 (17.5-38.5)</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>.58</td>
<td>.1</td>
<td>.1</td>
<td></td>
</tr>
<tr>
<td>PLMS</td>
<td>4</td>
<td>25.5 (9-42)</td>
<td>25 (9-41.7)</td>
<td>23.5 (8-39)</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>.07</td>
<td>.3</td>
<td>.063</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>5</td>
<td>34 (31.5-65.5)</td>
<td>34 (31.5-63)</td>
<td>33 (27-53)</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>.042</td>
<td>.3</td>
<td>.043</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>4</td>
<td>40 (18-41.5)</td>
<td>39 (15.5-40.5)</td>
<td>31 (15-38)</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>.19</td>
<td>.18</td>
<td>.07</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as median (25th, 75th percentiles) unless otherwise indicated. The Bonferroni adjusted p value (Wilcoxon rank sum test) = .01. Combined refers to C3/C4 and Fz electrode; Frontal or F, Fz electrode; Difference, the difference in the median number of arousals between C3/C4 vs Fz electrodes; SN, snoring; PLMS, periodic limb movements of sleep; OSAS, obstructive sleep apnea syndrome.

O’Malley et al. demonstrated that, in adults, the addition of frontal EEG channels yields a significant increase in respiratory-related arousal information by approximately 24%, suggesting that a conventional montage using only C3/C4 electrode sites may significantly underestimate the total number of cortical arousals in adults.

In the present study, we investigated the use of central, frontal, and a combination of central and frontal electrode sites during PSGs to identify the presence of arousals occurring as a result of different events during sleep in a population of young children between the ages of 5 to 10 years. We found that conventional central leads detected the vast majority of the arousals (96.3%), whereas the frontal leads detected a smaller number (only 87.4%) of the total arousals recorded at both sites. In our population of children, an additional 3.3% of arousals were detected only at frontal and not central leads, and these events were primarily associated with snoring, which is far below the 24% increase in arousals resulting from obstructive respiratory events that have recently been identified in adults. Not unexpectedly, the maximum number of total arousals was detected using a combination of frontal and central electrodes. Therefore, unlike the response pattern in adults, arousals during sleep in our study of young children were maximally detected in the central regions. This general response pattern was consistent across all types of precipitating events.

We hypothesize that the localization difference in cortical arousals between young children and adults may be the result of maturational effects upon underlying neurologic structures involved in these processes. This is based on age-related results obtained from a larger body of scientific data from neurophysiologists, cognitive neuroscientists, and neuropsychologists.

Within the electrophysiologic domain, studies have identified age-related differences in the temporal emergence and spatial localization of various sleep-related events. The detection of arousals on surface EEG electrodes is of particular interest in the field of sleep medicine, as it provides valuable information regarding sleep architecture and vigilance states. The use of different electrode configurations can significantly affect the detection of arousals, as demonstrated in our study.

In analyzing the 6 different types of events that preceded arousals on the PSGs for all of the children in the study, C3/C4 was more sensitive than Fz in detecting upper-airway resistance syndrome-related arousals (p = .004). The p values did not reach statistical significance in the other groups. Differences between the median number of arousals detected at the central and frontal electrode sites are presented in Table 1.

Across various diagnostic groups, the detection rate of total arousals showed a trend toward higher detection at central leads, as compared with frontal leads, only for severe OSAS (p = .04) but not for the other diagnostic groups (Table 2). Differences between the median number of arousals detected at the central and frontal electrode sites are presented in Table 1.

Thirty-three percent of the observed periodic leg movements, 28% of the snoring events, and 23% of the apnea and hypopnea episodes did not lead to detectable arousals at either the frontal or central electrode sites.
location of cortical electrophysiologic components, such as the N100 wave form generated during event-related potential studies.\textsuperscript{10,11} The amplitude and location of the N100 waveform are impacted by stimulus type and factors such as task demands.\textsuperscript{12} However, unlike other cortical waveform components that are detected even in infancy during auditory event-related potentials studies, the N100 is not present in very young children, and, when first detected in children aged 6 to 8 years, it has maximum amplitudes at posterior/parietal sites. The N100 component changes as children grow older and is not consistently detected in an adult-like frontal/anterior scalp location until 10 to 12 years of age, suggesting a significant maturational effect in neurons eliciting the component.\textsuperscript{13,14} This developmentally related evoked-potential response pattern is similar to the apparent age-related differences in cortical localization of arousals between children and adults.

Similarly, there is a significant progression in the development of cognitive executive function skills and working memory capacity between the ages of 9 and 18 years that have been found to correlate with increased neuronal activity in the dorsolateral frontal and parietal regions.\textsuperscript{13,14} In addition, continued myelination and maturation of cortical and subcortical pathways and structures have been clearly documented, predominantly within the prefrontal and frontal regions, throughout adolescence and young adulthood.\textsuperscript{15,16}

In conclusion, our study demonstrates that arousals occurring during sleep in young preteen children are most often detected during PSGs at central sites or a combination of central and frontal leads, but significantly fewer arousals are detected only at frontal leads in children. This contrasts with recent findings of studies in adults that have shown a prevalence of arousals at frontal sites. As such, professionals evaluating sleep studies (PSGs) across the developmental age span will need to be aware that there appears to be a neurologically based maturational effect impacting the location at which electrophysiologic cortical arousals are detected in sleep, and the conventional use of central leads or a combination of central and frontal leads appears to be strongly recommended in working with young preteen children. Further studies are indicated to determine the optimum rate of detection of arousals in older school-age children and adolescents.

REFERENCES