# Sleep Architecture and Respiratory Disturbances in Children with Obstructive Sleep Apnea

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**Little is known regarding sleep architecture in children with the obstructive sleep apnea syndrome (OSAS). We hypothesized that sleep architecture was normal, and that apnea increased over the course of the night, in children with OSAS. We analyzed polysomnographic studies from 20 children with OSAS and 10 control subjects. Sleep architecture was similar between the groups. Of obstructive apneas 55% occurred during rapid eye movement (REM) sleep. The apnea index, apnea duration, and degree of desaturation were greater during REM than non-REM sleep. OSAS data from the first and third periods of the night (periods A and C) were compared. Both the overall and the REM apnea index increased between periods A and C (11 to 25/h, $p < 0.02$; and 24 to 51/h, $p < 0.01$, respectively). There was no difference in $Sa_{O_2}$ over time. Spontaneous arousals, but not respiratory-related arousals, were more frequent during non-REM than REM sleep; these did not change from periods A to C. We conclude that children with OSAS have normal sleep stage distribution. OSAS is predominantly a REM phenomenon in children. Obstructive apnea worsens over the course of the night, independent of the changing amounts of REM sleep. We speculate that this increase in apnea severity may be secondary to upper airway muscle fatigue, changes in upper airway neuromotor control, or changes in REM density.**

The obstructive sleep apnea syndrome (OSAS) in children is a disorder of breathing during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction that disrupts normal ventilation during sleep and normal sleep patterns (1). Childhood OSAS is not simply adult OSAS in little people, and adult definitions and criteria are not applicable to children (1, 2). Adults with OSAS frequently have fragmented sleep. In contrast, children with OSAS often do not have cortical arousals in response to obstructive apneas (3), and may therefore have preservation of their sleep architecture. However, few systematic studies of sleep architecture have been performed in children with OSAS, and the effects of different sleep stages on sleep-disordered breathing have not been described in detail. Worsening of respiratory parameters through the night has been described in obstructive sleep apnea in adults (4), but data are not available for children. This information may shed some light on the understanding of the disease pathophysiology and mechanisms involved in the termination of apnea events in children. We hypothesized that because children with OSAS do not have frequent cortical arousals, sleep architecture would not differ between children with OSAS and control subjects. Further, based on our clinical observations, we hypothesized that obstructive apneas would worsen over the course of the night, with increases in apnea density and apnea-related desaturation.

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## METHODS

### Study Group

We retrospectively analyzed overnight polysomnographic studies from otherwise healthy children aged 2–12 yr, performed between June 1996 and March 1997. The first 20 consecutive subjects with an apnea index greater than 10 were selected. Subjects had no medical conditions apart from suspected OSAS secondary to adenotonsillar hypertrophy, based on history, and were referred for a sleep study to rule out obstructive sleep apnea. All patients with suspected gastroesophageal reflux (i.e., studies with pH probes) were excluded. Patients with a history of prior treatment of OSAS (including tonsillectomy and adenoidectomy, or continuous positive airway pressure [CPAP] therapy) referred for reevaluation were also excluded from this study. Patients were compared to age-matched, asymptomatic, nonsnoring control subjects who had been previously recruited from the community as control subjects for other studies (5–7).

### Polysomnography

Standard polysomnography consisted of electroencephalogram (C3/A2, C4/A1, O1/A2), electromyogram (submental and tibial), electrooculogram (right/left), $Sa_{O_2}$ (Nellcor N-1000, Van Nuys, CA), oximeter pulse waveform, end-tidal carbon dioxide tension (Nellcor N-1000), oronasal airflow (thermistor), thoracic and abdominal wall motion (piezoelectric bands), electrocardiography, and a body position sensor. Studies were performed on a computerized system (Alice 3; Healthdyne, Marietta, GA). Subjects were also recorded on videotape, using an infrared video camera, and were continuously observed by a polysomnography technician. Patients arrived in the laboratory at 8:00 P.M., and studies were terminated at 5:00 A.M.

Sleep studies were interpreted according to standard pediatric criteria (1). The apnea index was defined as the number of obstructive and mixed apneas, of at least two respiratory cycles duration, per hour of total sleep time (1, 8). Hypopneas were defined as a qualitative reduction in thermistor airflow $\geq 50\%$, associated with desaturation $\geq 4\%$. However, as the definition of hypopneas has not been standardized in children (1) (nor, indeed, in adults [9]), hypopneas were not analyzed in detail. For assessment of arterial oxygen saturation, the $Sa_{O_2}$ nadir and mean $Sa_{O_2}$ were determined. $Sa_{O_2}$ measurements associated with a poor pulse waveform were discounted. An $Sa_{O_2}$ nadir $< 92\%$ was considered abnormal (8). The mean and peak end-tidal $P_{CO_2}$ ($P_{ET_{CO_2}}$) were determined. $P_{ET_{CO_2}}$ measurements associated with a poor waveform were discounted. Hypoventilation was assessed by measuring the percentage of total sleep time with $P_{ET_{CO_2}} \geq 50$ mm Hg (10). Sleep architecture was scored in 30 s epochs according to the criteria outlined by Rechtschaffen and Kales (11). Because there is no consensus on definitions for pediatric arousals, arousals were defined according to the standard American Sleep Disorders Association criteria (12). They were classified as respiratory-related (occurring immediately after an apnea or hypopnea), technician-induced (related to external disturbances) or spontaneous (not associated with any of the above). The arousal index was calculated as the number of arousals per hour of total sleep time.

### Data Analysis

All data were analyzed by a single investigator to ensure consistency, and all polysomnograms were scored by a single experienced sleep

technologist and subsequently reviewed by the principal investigator. The total sleep time was divided into equal thirds (periods A, B, and C) and data were compared between periods A and C, as well as between rapid eye movement (REM) and non-REM (NREM) sleep, and between stage 1, stage 2, and slow wave sleep (SWS). Six subjects did not have any REM sleep during period A; their data were excluded from REM-related analyses. For the analysis of desaturation episodes ($\Delta Sa_{O_2}$), the pre- and postapnea $Sa_{O_2}$ was calculated. The pre value was taken at the start of each obstructive event and the post value was the lowest value attained within 6 s of the end of the event, due to the time delay of the oximeter. Analysis of changes in end-tidal $P_{CO_2}$ in the breaths immediately following apneas was not possible, due to variations in waveform quality in the first few nonobstructed breaths.

Comparison between study and control subjects was performed using the two-tailed, unpaired *t* test. For nonparametric data, statistical analysis was performed using the Wilcoxon signed rank test. Data that were normally distributed are shown as mean ± standard deviation; skewed data are shown as median and interquartile range. A p value $< 0.05$ was considered significant.

## RESULTS

### Study Group

A total of 418 sleep studies were performed during the 9-mo period, of which 36% were excluded because they were special studies (e.g., CPAP or pH studies), and 26% were excluded because the patients had congenital syndromes or chronic disease. Of the remaining 38% of studies, 74% demonstrated apnea indices of 0–4/h, 7% 5–9/h, and 19% ⩾ 10/h. The first 20 studies from the latter group were chosen for analysis, and compared with the studies of 10 age-matched controls. All patients with OSAS presented with chief complaints of snoring and difficulty breathing at night. Four of the subjects with OSAS were obese (body mass index > 95th percentile for age) (13). Subject characteristics are shown in Table 1.

### Sleep Architecture in OSAS Compared to Control Subjects

The percentage of total sleep time spent in various sleep stages did not differ significantly between patients with OSAS and control subjects (Table 1). However, children with OSAS did have significantly more arousals from sleep than control subjects.

**TABLE 1**

**POPULATION CHARACTERISTICS AND POLYSOMNOGRAPHIC RESULTS***

| | OSAS | Controls |
|---|---|---|
| n | 20 | 10 |
| Age, yr | 5 ± 3 | 6 ± 2 |
| Male, n (%) | 13 (65) | 3 (30) |
| Body mass index, kg/m$^2$ | 19.2 ± 8.3 | 16.6 ± 2.0 |
| Total recording time, min | 449 ± 32 | 473 ± 65 |
| Total sleep time, min | 386 ± 31 | 390 ± 46 |
| Sleep efficiency, % | 86 ± 6 | 84 ± 13 |
| Arousal index, n/h | 11 ± 4† | 5 ± 2 |
| Stage 1, %TST | 4 ± 2 | 5 ± 3 |
| Stage 2, %TST | 48 ± 9 | 51 ± 9 |
| Slow wave sleep, %TST | 26 ± 8 | 26 ± 8 |
| Rapid eye movement sleep, %TST | 22 ± 6 | 19 ± 6 |
| REM cycles, n | 5 ± 2 | 4 ± 1 |
| Apnea index, n/h TST | 22.8 ± 8.7† | 0.0 ± 0.1 |
| $Sa_{O_2}$ nadir, % | 74 ± 15† | 95 ± 1 |
| Peak $P_{ET_{CO_2}}$, mm Hg | 55 ± 7† | 46 ± 3 |
| Duration of hypoventilation ($P_{ET_{CO_2}}$ ⩾ 50 mm Hg), %TST | 11 ± 17‡ | 0 ± 0 |

*Definition of abbreviations*: OSAS = obstructive sleep apnea syndrome; $P_{ET_{CO_2}}$ = end-tidal $P_{CO_2}$; REM = rapid eye movement; TST = total sleep time.

* All data displayed as mean ± SD unless otherwise specified.

† $p < 0.001$.

‡ $p < 0.005$.

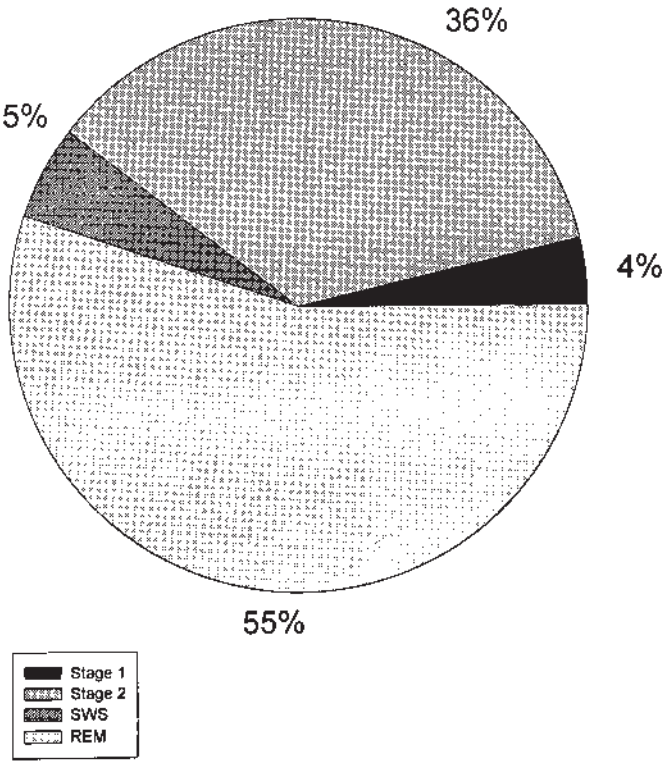


***Figure 1.*** The percentage of obstructive apneas occurring in the different sleep stages are shown. SWS, slow wave sleep; REM, rapid eye movement sleep.

### Sleep State and Obstructive Apneas

In patients with OSAS, the majority (55%) of all obstructive apnea events occurred during REM sleep, though REM accounted for only 22% of total sleep time (Figure 1). The overall apnea index was significantly higher during REM compared with NREM sleep: 56 (38,68 [median, interquartile range])

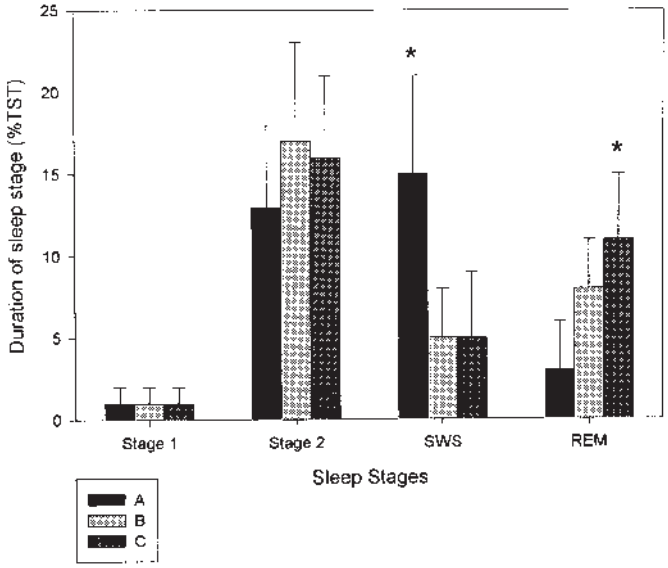


***Figure 2.*** The changes in sleep architecture over the course of the night are shown. Period A, first third of the night; period B, middle third; period C, last third. TST, total sleep time; SWS, slow wave sleep; REM, rapid eye movement sleep. *$p < 0.001$ for A versus C.

**TABLE 2**

**CHANGES IN GAS EXCHANGE OVER THE COURSE OF THE NIGHT***

| | Period A | Period C |
|---|---|---|
| Mean $Sa_{O_2}$, % | 97 (96,98) | 97 (95,98) |
| $Sa_{O_2}$ nadir, % | 86 (75,90) | 81 (70,86) |
| Duration $Sa_{O_2} < 92\%$, % TST | 2 (0,5) | 3 (1,16) |
| Mean $P_{ET_{CO_2}}$, mm Hg | 42 (40,45) | 42 (38,44) |
| Peak $P_{ET_{CO_2}}$, mm Hg | 52 (49,54) | 53 (49,58) |
| Duration $P_{ET_{CO_2}} \geq 50$ mm Hg, % TST | 1 (0,6) | 1 (0,4) |

*Definition of abbreviations*: $P_{ET_{CO_2}}$ = end-tidal $P_{CO_2}$; TST = total sleep time.

* All data displayed as median (interquartile range). There were no significant differences between groups.

versus 9 (6,16)/h, $p < 0.001$). Obstructive apneas were rare during SWS. Sleep state specific apnea indices were 22 (5,43)/h sleep for stage 1, 11 (7,23)/h for stage 2, 2 (0,5)/h for SWS, and 56 (38,68)/h for REM sleep. As with complete apneas, hypopneas were also more common during REM than NREM sleep ($p < 0.02$).

The median obstructive apnea duration (MAD) was higher in REM than NREM sleep (12 [10,14] versus 10 [9,11] s, $p < 0.005$). There was a tendency for the MAD to be highest in REM and lowest in SWS, but this did not reach significance (stage 1, 9 [8,10] s; stage 2, 10 [8,12] s; SWS, 9 [7,10] s; and REM, 12 [10,14] s).

Spontaneous arousals, but not respiratory-related arousals, were more frequent during NREM than REM sleep (spontaneous arousals: 3 [2,4] versus 1 [0,2]/h, $p < 0.002$; respiratory arousals: 1 [1,4] versus 3 [1,6]/h, NS).

The preapnea $Sa_{O_2}$ was slightly lower during REM than NREM sleep (96 [95,98] versus 97 [96,98]%, $p < 0.001$). The $\Delta Sa_{O_2}$ following apneas was significantly lower during REM than NREM sleep (4 [2,7] versus 1 [0,3]%, $p < 0.001$).

### Progression of Sleep and Apnea Characteristics Through the Night

The amount of REM sleep as a percentage of total sleep time (TST) increased from period A to C ($p < 0.001$), whereas the amount of SWS decreased from period A to C ($p < 0.001$) (Figure 2). Six subjects had no REM sleep during period A; these subjects were excluded from REM-related analyses. The amount of stage 1 and 2 sleep did not change significantly between the first and last thirds of the night.

There were no significant differences in the patients' sleep position between the first and last thirds of the night, although there was a tendency for patients to spend less time on their side and more time supine during the first third of the night than the last third [60 (37,83)% of time on the side, 43 (21,70)% supine, and 24 (16,31)% prone during period A versus 81 (63,100)%, 24 (7,62)%, and 22 (17,31%), respectively, for period C]. Gas exchange values for the first third of the night compared with the last third are shown in Table 2. There were no significant differences in the degree of desaturation or hypoventilation between the two time periods.

There was a cumulative total of 615 obstructive apneas during period A and 1169 obstructive apneas during period C. Therefore, a total of 1784 events were analyzed. Patients had a median of 24 (14,37) obstructive apneas during period A, compared with 54 (45,77) during period C. Thus, the apnea index increased between periods A and C, from 11 (6,17) to 25 (21,36) ($p < 0.02$). This was due primarily to an increase in the REM apnea index (Table 3, Figure 3). In comparison, the apnea index in NREM sleep did not change significantly through the night (Table 3). Between the first and last thirds of the night, there was a tendency for an increase in the MAD (Table 3, $p = 0.06$). There was little change in the REM MAD (Table 3, $p = 0.93$).

There were no significant changes in the total, NREM, or REM spontaneous arousal indices from period A to C (Table 3). There were no significant changes in the total or NREM respiratory arousal indices from A to C. However, the REM respiratory arousal index increased from period A to period C ($p < 0.01$), concomitant with the increase in the REM apnea index. There were no differences in the degree of desaturation following apneas ($\Delta Sa_{O_2}$) for either REM sleep, NREM sleep, or total sleep between periods A and C (Table 3).

## DISCUSSION

This study evaluated sleep architecture, the effects of sleep state, and changes in sleep and apnea characteristics over the course of the night, in children with obstructive sleep apnea. Children with OSAS tend to have fewer obstructive apneas than adults, but nevertheless have significant gas exchange abnormalities (1, 14); thus, the patients in this study all had severe OSAS by pediatric standards. We found that the children with OSAS had relatively normal sleep architecture, in contrast to adults with OSAS (15). In the children, OSAS was very much an REM-related disease, with obstructive apneas occurring more frequently, for a longer duration, and with more desaturation during REM than NREM sleep. The number of obstructive apneas increased over the course of the night, independent of changes in REM time.

### Sleep Architecture

Few data are available in the literature regarding sleep architecture in children with OSAS. The sleep architecture in our group of children with OSAS did not differ from control subjects, and was comparable to previously published data on

**TABLE 3**

**CHANGES IN REM VERSUS NREM SLEEP OVER THE COURSE OF THE NIGHT***

| | Period A | | | Period C | | |
|---|---|---|---|---|---|---|
| | Total | REM | NREM | Total | REM | NREM |
| Duration, min | 130 (114,137) | 9 (0,18) | 115 (105,124) | 129 (122,136) | 44 (36,54) | 82 (69,98) |
| Apnea index, n/h | 11 (6,17) | 24 (7,56) | 9 (4,17) | 25† (21,36) | 51‡ (46,71) | 10 (3,17) |
| Mean apnea duration, s | 9.2 (7,12) | 8.0 (8,14) | 10.4 (8,12) | 11.3 (9,14) | 11.5 (9,14) | 10.2 (8,13) |
| $\Delta Sa_{O_2}$, % | 3 (0,4) | 4 (2,6) | 1 (0,3) | 2 (1,4) | 4 (1,8) | 2 (0,3) |
| Spontaneous arousal index (n/h) | 3 (1,3) | 0 (0,0) | 3 (1,3) | 2 (1,3) | 0 (0,1) | 3 (1,3) |
| Respiratory arousal index n/h | 1 (1,2) | 0 (0,0) | 1 (0,2) | 2 (0,4) | 2 (1,7)‡ | 1 (0,1) |

*Definition of abbreviations*: NREM = non-rapid eye movement; REM = rapid eye movement.

* All data displayed as median (interquartile range).

† $p < 0.02$ for period A versus period C.

‡ $p < 0.01$ for period A (REM) versus period C (REM).

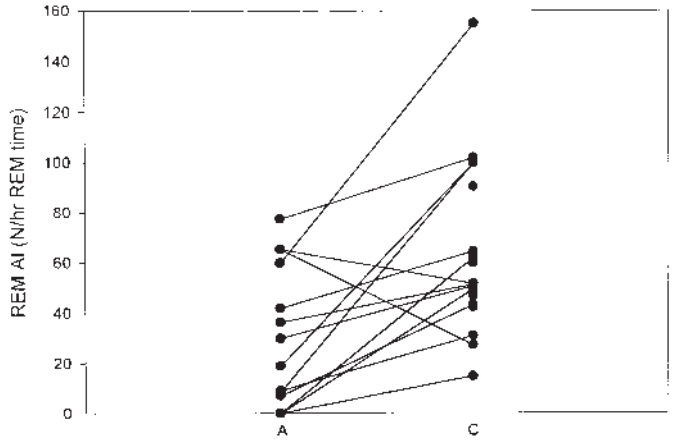


***Figure 3.*** Individual changes in the rapid eye movement obstructive apnea index (REM AI), from the first third (A) to the last third (C) of the night are shown. The REM AI increased significantly over the course of the night ($p < 0.01$). Note that six patients did not have any REM sleep during period A.

normal children (16). This is consistent with previous studies showing no change in sleep architecture following surgical treatment of childhood OSAS (7, 17). Although the current study was limited to children with severe OSAS, the results would presumably apply to children with lesser degrees of upper airway obstruction as well. These findings in children are in contrast to adults with OSAS, who often have decreased slow wave and REM sleep (4, 15, 18). These findings also differ from previous reports on infants with OSAS, who have decreased REM time (19). The reason for these differences between the age groups is unclear. The difference between children and adults may be related to the decreased frequency of cortical arousals in response to obstructive apnea in children (3), thereby resulting in less sleep fragmentation. Although the children with OSAS had a higher arousal index than control subjects, their arousal index was considerably lower than their apnea index. However, as infants have even higher arousal thresholds to apnea than older children (3), the reason for the difference between infants and older children is unclear. Another possible explanation for our findings may be that children with OSAS have subtle changes in sleep architecture that cannot be detected by standard EEG techniques, but may need more sophisticated types of analysis, such as EEG spectral analysis (20).

### OSAS and REM Sleep

We found that the majority of respiratory events occurred during REM sleep. This confirms a previous report by Morielli and coworkers (21). In the current study, 55% of all obstructive apneas occurred during REM sleep, although REM sleep occurred for only 22% of total sleep time. In comparison, slow wave sleep appeared to be protective, with only 5% of obstructive apneas occurring during slow wave sleep, despite the fact that slow wave sleep was more abundant than REM sleep. This finding is in contrast to reports in adults, in whom obstruction occurs more commonly during NREM than REM sleep (4). There are a number of reasons why REM sleep predisposes to obstructive apnea in children, including muscular hypotonia, decreased ventilatory responses to hypoxia and hypercapnia (5), and an increased arousal threshold in response to apnea (22). As with adults, the apneas were longer during REM than NREM sleep (4, 18, 23), and were associated with more profound desaturation.

The finding that obstructive apnea is much worse during REM than NREM sleep demonstrates the importance of sleep architecture monitoring and, most importantly, ensuring adequate REM duration during polysomnography, in order to avoid underestimation of the severity of OSAS in children.

### Progression of Sleep and Apnea Characteristics during the Night

The proportion of time spent in REM sleep increased from the first to the last third of the night, together with an increase in the apnea index. This progression of apnea frequency through the night was not just a result of the increasing REM duration, as the corresponding REM apnea index also showed a significant increase. Neither was it due to a change in body position. There was a tendency for the apnea duration to increase, but this did not reach significance. These findings in children are different from adults with OSAS, in whom the apnea index does not increase over the course of the night (except, perhaps, in the most severe patients [4]), whereas the apnea duration does increase (4, 18, 24, 25). Many children with OSAS have persistent, partial upper airway obstruction associated with hypercapnia, rather than discrete apneas (1). Therefore, we evaluated not only the changes in the number of apneas, but also the changes in gas exchange over the course of the night. There was no significant change in $P_{CO_2}$. As in studies of adults, we found no change in the degree of desaturation over the course of the night (4, 24, 25). There was no change in the frequency of arousals.

The above findings confirmed our suspicion that there is a worsening of respiratory parameters in children with OSAS through the night. As suggested by Charbonneau and coworkers (4), changes in the apnea index could be a reflection of abnormalities leading to apnea initiation, and changes in apnea duration a reflection of factors leading to apnea termination. We could thus interpret our findings as a demonstration of progression through the night primarily of the factors initiating apnea. There are a number of potential causes for the progression of OSAS over the course of the night. One cause may be ventilatory muscle fatigue. However, previous studies in adults with OSAS have found no evidence of diaphragmatic fatigue during sleep (26, 27). Of note, however, these studies were limited to NREM sleep. Further, no studies have evaluated the upper airway muscles for fatigue over time. Therefore, it is possible that muscle fatigue may contribute to the worsening of apnea over the night in our patients. It is also possible that upper airway neuromotor control changes over the course of the night. Increasing upper airway edema during the night may contribute to increased obstruction. Another potential cause is a change in the arousal threshold to upper airway occlusion, which could be caused by habituation to recurrent obstruction during the night, or be secondary to sleep fragmentation (28). This is unlikely, as the pediatric patients did not show a change in the number of spontaneous or respiratory arousals over the course of the night. Furthermore, many of the apneas were not terminated by cortical arousals. Nonetheless, a possible role for subcortical (autonomic) arousals cannot be excluded (29). Finally, as OSAS in children is such an REM-related disease, it is possible that the worsening of apnea over the night is due to changes in the quality of REM sleep itself, such as ventilatory instability related to increases in phasic REM (30). Further studies are necessary to delineate the pathophysiology of apnea progression over the course of the night in children.

### Study Limitations

A limitation of this study was the premature termination of our polysomnographic studies at approximately 5:00 A.M., after achieving at least 6 h of sleep. This could theoretically result in missing the last portion of a normal sleep pattern, including further REM periods. Thus, assuming further progression of the apnea severity, our study may actually be underestimating the progression of OSAS. It would be interesting to repeat this study prospectively, with extension of the sleep period to coincide with normal sleep patterns (i.e., until spontaneous awakening in the morning) to see if apnea events would worsen further, or if there would be a significant change in apnea duration over the course of the night.

In this study, we chose to use the standard American Sleep Disorders Association criteria for defining arousals (12). These criteria include a duration of arousal $\geq$ 3 s, in addition to other criteria. Over the years, different criteria for arousals have been used for both children and adults, and it has been difficult to determine which definitions are the most important pathophysiologically. We elected to use the American Sleep Disorders Association criteria as theses criteria are standardized, have better interscorer reliability than shorter arousals (12, 31), and enable comparisons to be made with the existing literature. However, it is possible that scoring shorter apneas would have yielded different results.

This study only evaluated children with relatively large numbers of apneas, in order to have sufficient events to analyze statistically. Thus, it is possible that these results do not apply to children with mild OSAS.

### Clinical Implications

In summary, this study has demonstrated that childhood obstructive sleep apnea is predominantly an REM-related disease, that progresses over the course of the night. The important clinical implications of these findings are the limitation of daytime nap studies (32), as well as split-night studies, in the evaluation of OSAS in children, as these could seriously underestimate the severity of the condition.

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