Respiratory timing and variability during sleep in children with sleep-disordered breathing

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1School of Electrical and Electronic Engineering, University of Adelaide, Adelaide, Australia; 2School of Psychology, Social Work and Social Policy, University of South Australia, Adelaide, Australia; 3Department of Respiratory and Sleep Medicine, Women’s and Children’s Hospital, Adelaide, Australia; 4Childrens Research Centre, School of Pediatrics and Reproductive Health, University of Adelaide, Adelaide, Australia; and 5School of Medical Sciences, University of Adelaide, Adelaide, Australia

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Immanuel SA, Pamula Y, Kohler M, Martin J, Kennedy D, Kabir MM, Saint DA, Baumert M. Respiratory timing and variability during sleep in children with sleep-disordered breathing. J Appl Physiol 113: 1635–1642, 2012. First published September 27, 2012; doi:10.1152/japplphysiol.00756.2012.—Sleep-disordered breathing (SDB) in children is assessed by quantification of hypopnea and apnea events. Little is known, however, about respiratory timing and breath-to-breath variability during sleep. The aim of this study was to investigate respiratory parameters across sleep stages in children with SDB before and after treatment compared with healthy children. Overnight polysomnography (PSG) was conducted in 40 children with SDB prior to and 6 mo following adenotonsillectomy. For comparison, a control group of 40 healthy sex- and age-matched children underwent two PSGs at equivalent time points but without intervention. The following variables were measured breath by breath during obstruction-free periods in stage 2 nonrapid eye movement (NREM), stage 4 NREM, and REM sleep: inspiratory time (Ti), expiratory time (Te), total time (Ttotal), inspiratory duty cycle (DC = Ti/Ttotal), respiratory frequency (fR), and SD of the parameters Ti, Te, fR, and DC. Variability in waveform morphology was also computed using the residue of respiratory patterns. The severity of SDB was relatively mild in the study cohort (obstructive apnea hypopnea index: baseline, 5.1 ± 9.4 vs. 0.1 ± 0.2, P < 0.001; follow-up, 0.3 ± 0.3 vs. 0.8 ± 1.0, P < 0.01). Compared with healthy controls, children with SDB showed significantly longer Ti and Te and a lower fR at the baseline study. These differences were not significant after adenotonsillectomy. Sleep stages were associated with significant differences in all of the respiratory measures in both groups of children. In conclusion, children with relatively mild SDB showed prolonged inspiration and expiration indicative of chronic narrowing of the upper airway. Treatment of SDB normalizes respiratory timing. Documentation of these parameters may aid in both understanding and management of children with SDB.

sleep apnea; upper-airway resistance; adenotonsillectomy; sleep stages; respiratory-inductive plethysmography

DURING WAKEFULNESS, THE CONTROL OF BREATHING IS A MULTIFACETED process involving a complex network of neurons in the brainstem responding to stimuli from chemoreceptors, mechanoreceptors, and higher cortical inputs. Sleep significantly modifies breathing behavior, particularly with respect to central respiratory control, respiratory muscle activity, and respiratory mechanics (28). Furthermore, the modulating effects of sleep on breathing differ markedly between the two major sleep states: nonrapid eye movement (NREM) sleep and REM sleep. The observed changes in breathing during sleep are a reflection of changes in metabolic demand, direct postural effects on breathing mechanics, as well as the state of the brain (34, 39). In adults, the volume, rate, and pattern of breathing are also influenced by age, gender, and body mass index (BMI) (30-33). In healthy adults, sleep is associated with an attenuated responsiveness to chemical and mechanical stimuli, resulting in a reduction in tidal volume and minute ventilation. In addition, sleep results in increased upper-airway resistance and a reduction in functional residual capacity and in REM sleep, tonic inhibition of skeletal muscles (12, 28). Analysis of tidal volume, minute ventilation, and inspiratory flow rate during sleep in healthy adults has shown that the greatest ventilatory reduction occurs during REM sleep, which is associated with a fall in inspiratory drive (6). Ventilatory changes during sleep have also been investigated in adolescents (43), where minute ventilation, inspiratory timing, and respiratory frequency (fR) were shown to differ significantly between NREM and REM sleep. This study also demonstrated high variability in respiratory parameters, decreased intercostal muscle activity, and diminished ribcage contribution to breathing during REM sleep. Comparably, little is known about ventilation during sleep in younger children. Carskadon et al. (5) observed gender and sleep-stage effects on breathing rate and its regularity in healthy children. Sleep stage has also been found to influence interbreath variability in children undergoing polysomnography (PSG) for suspected sleep apnea (7).

In addition to the normal physiological changes seen in breathing during sleep, abnormal ventilatory responses, including changes in inspiratory-expiratory timing, breathing rate, and increased respiratory muscular activity, can be caused by respiratory disorders (42, 44). Obstructive sleep apnea syndrome is a disorder characterized by repeated partial or complete upper-airway obstruction (UAO), causing a reduction or cessation of airflow resulting in hypoxemia, hypercapnia, and sleep fragmentation (20). In adults, this causes excessive daytime sleepiness and cardiovascular disease (4, 18, 29). Sleep-disordered breathing (SDB) is characterized by repeated episodes of apnea, disrupting normal respiratory patterns (27). In particular, increased pharyngeal resistance due to narrowing of the upper airway requires greater respiratory effort to maintain airflow, and this may alter both respiratory timing and respiratory variability. The etiology of childhood SDB is different

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than that of adults (8, 22), and hence, the impact of SDB on respiratory behavior may also be different in children.

This study therefore analyzed a range of breathing parameters in children with SDB and in healthy controls during periods of sleep free of apnoea and hypopneas. The specific aims of this study were to 1) compare measures of respiratory timing and variability as derived from respiratory impedance plethysmography (RIP) between children with SDB and healthy controls, 2) investigate the effects of sleep stage on these respiratory parameters, and 3) evaluate the effect of surgical treatment (adenotonsillectomy) for SDB on the parameters. We hypothesized that 1) breathing patterns in children with SDB would differ from controls even during apneic-free periods of breathing, 2) ventilatory parameters would be influenced by sleep stage, and 3) in children with SDB, surgical treatment by adenotonsillectomy would normalize breathing parameters.

METHODS

Participants in this study were 40 children with SDB, aged 3–12 yr awaiting adenotonsillectomy for suspected UAO and a matched group of 40 healthy controls. Both groups of children underwent overnight PSG to evaluate sleep and breathing parameters. Children with SDB had two PSGs before and after surgical intervention (adenotonsillectomy), whereas control children had two PSGs at the same time points. More details on the study protocol are published elsewhere (15).

Subjects. This study was approved by the Women’s and Children’s Health Network Human Research Ethics Committee (South Australia), with parental consent and child assent obtained from all participants. Overnight PSG was conducted in children with SDB while awaiting adenotonsillectomy and again at 6 mo following surgery using a repeated measures design. Nonsnoring control children matched for age and gender also underwent PSG at the same time points. Children with SDB were those with a history of frequent snoring and were scheduled for surgery as diagnosed by an experienced pediatric otorhinolaryngologist at the Women’s and Children’s Hospital (Australia). All children were between 3 and 12.9 yr of age at baseline. Children were excluded if they had undergone previous ear, nose, throat, or craniofacial surgery; had a medical condition (other than UAO) associated with hypoxia or sleep fragmentation; or were taking medication known to affect sleep or cardiorespiratory physiology. The same exclusion criteria were applied to controls, with the additional requirement that they did not snore on more than two nights/wk as confirmed by parental report.

Overnight PSG. Overnight PSG was conducted for all children if they were well on the scheduled night and free of sedation, sleep deprivation, or any recent illness, including respiratory infection. Overnight, PSG began close to each child’s usual bedtime, and a parent was present throughout the procedure. The S-Series Sleepwatch System (Compumedics, Australia) was used to continuously record: EEG (C3-A2 and C4-A1), left and right electrooculogram (EOG), heart rate by ECG, submental and diaphragmatic electromyogram (EMG) with skin-surface electrodes, leg movements by piezoelectric motion detection, oronasal airflow by thermistor and nasal airflows using calibrated respiratory-inductive plethysmography, arterial oxygen saturation (SpO2) by pulse oximetry (Nellcor N-595, Covidien, Ireland; with a 3-s averaging time), and transcutaneous carbon dioxide, using a heated (43°C) transcutaneous electrode (TINA, Radiometer Pacific, Australia). Each child was monitored continuously overnight via an infrared camera and by a pediatric sleep technician who also documented observations of sleep behavior including the presence or absence of snoring. A repeat sleep study was performed overnight after withdrawal of all medications, with a parent present throughout the procedure. The S-Series Sleepwatch System (Compumedics, Australia) was used to continuously record: EEG (C3-A2 and C4-A1), left and right electrooculogram (EOG), heart rate by ECG, submental and diaphragmatic electromyogram (EMG) with skin-surface electrodes, leg movements by piezoelectric motion detection, oronasal airflow by thermistor and nasal airflow using uncalibrated respiratory-inductive plethysmography, arterial oxygen saturation (SpO2) by pulse oximetry (Nellcor N-595, Covidien, Ireland; with a 3-s averaging time), and transcutaneous carbon dioxide, using a heated (43°C) transcutaneous electrode (TINA, Radiometer Pacific, Australia). Each child was monitored continuously overnight via an infrared camera and by a pediatric sleep technician who also documented observations of sleep behavior including the presence or absence of snoring. A repeat sleep study was performed overnight after withdrawal of all medications, with a parent present throughout the procedure. The S-Series Sleepwatch System (Compumedics, Australia) was used to continuously record: EEG (C3-A2 and C4-A1), left and right electrooculogram (EOG), heart rate by ECG, submental and diaphragmatic electromyogram (EMG) with skin-surface electrodes, leg movements by piezoelectric motion detection, oronasal airflow by thermistor and nasal airflow using uncalibrated respiratory-inductive plethysmography, arterial oxygen saturation (SpO2) by pulse oximetry (Nellcor N-595, Covidien, Ireland; with a 3-s averaging time), and transcutaneous carbon dioxide, using a heated (43°C) transcutaneous electrode (TINA, Radiometer Pacific, Australia). Each child was monitored continuously overnight via an infrared camera and by a pediatric sleep technician who also documented observations of sleep behavior including the presence or absence of snoring. A repeat sleep study was performed overnight after withdrawal of all medications, with a parent present throughout the procedure. The S-Series Sleepwatch System (Compumedics, Australia) was used to continuously record: EEG (C3-A2 and C4-A1), left and right electrooculogram (EOG), heart rate by ECG, submental and diaphragmatic electromyogram (EMG) with skin-surface electrodes, leg movements by piezoelectric motion detection, oronasal airflow by thermistor and nasal airflow using uncalibrated respiratory-inductive plethysmography, arterial oxygen saturation (SpO2) by pulse oximetry (Nellcor N-595, Covidien, Ireland; with a 3-s averaging time), and transcutaneous carbon dioxide, using a heated (43°C) transcutaneous electrode (TINA, Radiometer Pacific, Australia). Each child was monitored continuously overnight via an infrared camera and by a pediatric sleep technician who also documented observations of sleep behavior including the presence or absence of snoring. A repeat sleep study was performed overnight after withdrawal of all medications, with a parent present throughout the procedure.

Sleep stages were scored visually in 30-s epochs according to the standardized EEG, EOG, and EMG criteria of Rechtschaffen and Kales (23). PSG polysomnography; SDB, sleep-disordered breathing; BMI, body mass index; TST, total sleep time; REM, rapid eye movement; WASO, wake after sleep onset time; PLMI, periodic limb-movement index; SAI, spontaneous arousal index; RAI, respiratory arousal index; SpO2, oxygen saturation; OAHI, obstructive apnea-hypopnea index. *P < 0.005; **P < 0.01; ***P < 0.05; ****P < 0.001, upper airway obstruction vs. control. aAnalysis using transformed values. Data are mean ± SD.
Table 2. Numbers of 3-min sleep segments that met the inclusion criteria for respiratory analysis

<table>
<thead>
<tr>
<th>Sleep Stage</th>
<th>Control</th>
<th>SDB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>2</td>
<td>970 (24.2 ± 9.0)</td>
</tr>
<tr>
<td>REM</td>
<td>4</td>
<td>1,043 (26.0 ± 6.5)</td>
</tr>
<tr>
<td>Follow-up</td>
<td>2</td>
<td>1,032 (28.6 ± 9.3)</td>
</tr>
<tr>
<td>REM</td>
<td>4</td>
<td>869 (24.1 ± 6.8)</td>
</tr>
<tr>
<td>REM</td>
<td>3</td>
<td>316 (9.0 ± 4.9)</td>
</tr>
</tbody>
</table>

Data in parentheses represent mean ± SD of the number of segments in each group.

Kales (46). Movement time (>50% of an epoch obscured by movement artifact) was scored as a separate category and was not included in either sleep or wake time. Respiratory variables were scored according to standard guidelines recommended for pediatric sleep studies (20). The total number of obstructive apneas, mixed apneas, and obstructive hypopneas divided by the total sleep time and expressed as the number of events/h of sleep yielded the obstructive apnea/hypopnea index (OAHI). The SpO2 desaturation index represents the number of ≥3% O2 desaturations/h of sleep. The BMI z-scores were calculated using the height and weight of the children measured on the night of PSG, along with established growth charts corrected for age and gender (31).

Respiratory timing and frequency analysis. Respiratory data, digitized at 25 Hz, were extracted from the thoracic and abdominal RIP channels of the standard PSG using the programming library libRASCH (37). Custom-written computer software was developed under the MATLAB signal processing toolbox. Data were low-pass filtered at 0.5 Hz using a Butterworth forward and reverse digital filter. The offset of the signals was removed before processing. The thoracic and abdominal RIP signals were extracted over 3 min of consecutive stage 2 NREM sleep, stage 4 NREM sleep, and REM sleep. Stage 3 NREM sleep was excluded from analysis due to the potential overlap with stage 2 NREM sleep in transitional epochs.

Three-minute segments, which met the following inclusion criteria, were retained for further analysis: absence of body movements, absence of any abnormal cardiorespiratory events (e.g., apnea), absence of any signal artifact as identified by the scoring technician, and no change in sleep stage within the 3-min segment. From each nonoverlapping, 3-min period that satisfied the above criteria, inspiratory and expiratory onsets were determined from the thoracic signal by identifying the peaks and valleys using the first-order derivative. These points were further used to compute breath-by-breath measures of inspiratory time (Ti), expiratory time (Te), and duty cycle [DC = Ti/total time (T_total)], i.e., the fraction of the respiratory cycle time spent in inspiration and the fR. The mean values of Ti, Te, DC, and fR and their SDs, SD_Ti, SD_Te, SD_DC, and SD_fR, were also computed for each 3-min epoch.

In addition to the SDs, which are time point-based variability measures, the residuum was calculated as an estimate of the pattern-based variability. Over each 3-min period, the inspiratory and expiratory curves of all breaths were superimposed and averaged to obtain an average inspiratory curve and an average expiratory curve. The inspiratory and expiratory breaths used for averaging were then subtracted from their respective average curves to obtain residual measures for inspiration (Res_Ins) and expiration (Res_Exp), which then quantified the degree of respiratory variability.

Statistical analysis. The breath-by-breath parameters were averaged for each individual within respective sleep stages so that each child contributed equally to the group mean. Data were analyzed using the statistical software SPSS version 18 and the GraphPad Prism version 5.01 for Windows. Normality of data distribution was tested using the Kolmogorov-Smirnov tests. Student’s t-test and one-way ANOVA were used to compare demographic data and PSG results between groups. Differences in respiratory parameters between the control and SDB group, as well as among different sleep stages, were analyzed using two-way ANOVA for repeated measures. Post hoc analysis between groups was performed using Student’s unpaired t-test (two-tailed) and corrected for multiple comparisons by the Holm-Bonferroni method. Within each group, post hoc comparison of respiratory parameters among sleep stages was carried out using Tukey’s multiple comparison tests. Associations with age and BMI were determined using Pearson correlation analysis, and association with OAHI was determined using Spearman’s correlation coefficient.

RESULTS

Subject characteristics and PSG results. As reported previously (2), baseline PSG confirmed the presence of respiratory abnormalities in the children with SDB who had a significantly higher OAHI, elevated respiratory arousals, increased frequency of SpO2 desaturations, and a significantly lower mean SpO2 nadir compared with controls. There were no significant differences between groups with respect to sleep architecture (Table 1).

PSG data for respiratory analysis were available for 36 of the 40 initial controls and 32 of the 40 children with SDB who came back for the follow-up study. Following adenotonsillectomy, there was a marked reduction in OAHI, SpO2 desaturation frequency, and respiratory arousal rate in the SDB group, but they still had significantly greater OAHI, SpO2 desaturation frequency, and SaO2 nadir compared with controls (Table 1). The time between adenotonsillectomy and follow-up PSG ranged between 14 and 44 wk, allowing sufficient time for recovery from surgery. Repeat PSG on controls were done at similar time points.

The number of 3-min epochs in each sleep stage, which met the inclusion criteria for respiratory analysis at baseline and follow-up PSG across both groups, is summarized in Table 2.

Table 3. Inspiratory duty cycle and variability measures during stages 2 and 4 and REM sleep in control and SDB children during baseline PSG

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>SDB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stage 2</td>
<td>Stage 4</td>
</tr>
<tr>
<td>DC</td>
<td>0.48 ± 0</td>
<td>0.49 ± 0</td>
</tr>
<tr>
<td>SD_Ti (ms)</td>
<td>37.2 ± 27</td>
<td>7.85 ± 6.1</td>
</tr>
<tr>
<td>SD_Te (ms)</td>
<td>15.3 ± 15.6</td>
<td>10.2 ± 6.7</td>
</tr>
<tr>
<td>SD_DC</td>
<td>0.01 ± 0</td>
<td>0.002 ± 0</td>
</tr>
<tr>
<td>SD_fR (bpm)</td>
<td>1.5 ± 0.7</td>
<td>1.4 ± 0.8</td>
</tr>
</tbody>
</table>

DC, duty cycle; SD_Ti, SD of inspiratory time; SD_Te, SD of expiratory time; SD_fR, SD of respiratory frequency. *P < 0.001. Data are mean ± SD.
Effect of UAO on respiratory parameters. The respiratory parameters during stages 2 and 4 and REM sleep for both controls and SDB children during the baseline study are shown in Table 3. It was found that Ti, Te, and fR exhibited significant group differences. Ti was significantly longer in the SDB group across all sleep stages compared with controls (stage 2: 1.73 ± 0.2 vs. 1.63 ± 0.2; P < 0.05; stage 4: 1.7 ± 0.2 vs. 1.6 ± 0.2; P < 0.05; REM: 1.58 ± 0.2 vs. 1.44 ± 0.1, P < 0.01; Fig. 1). In addition, Te was significantly longer in children with SDB than in controls during NREM sleep stages 2 and 4 (stage 2: 2.0 ± 0.3 vs. 1.79 ± 0.4, P < 0.01; stage 4: 1.85 ± 0.3 vs. 1.66 ± 0.23, P < 0.01) but not during REM sleep (1.99 ± 0.3 vs. 1.92 ± 0.4, P > 0.05; Fig. 1). There was also a significant sleep-stage-by-group effect for Te at the baseline study (F = 4.04, P > 0.05; Table 3). The prolonged Ti and Te were reflected by a significantly lower fR in the SDB group in all three sleep stages (stage 2: 16.2 ± 1.7 vs. 17.7 ± 2.3, P < 0.01; stage 4: 17.1 ± 2.07 vs. 18.6 ± 2.4, P < 0.01; REM: 17.0 ± 2.09 vs. 18.1 ± 2.5, P < 0.05; Fig. 1). SD measures were not significantly different between the SDB children and controls. The respiratory pattern was evaluated for regularity during the inspiratory and expiratory portions of each breath using the measures Res_Ins and Res_Exp. These residual measures were also not significantly different between the two groups. Representative plots of inspiratory and expiratory curves over a selected 3-min period of stage 2 sleep with the average curves superimposed are shown in Fig. 2.

Effect of sleep stages on respiratory parameters. All respiratory parameters exhibited highly significant sleep-stage effects during the baseline PSG (Table 3). A within-group repeated measures ANOVA followed by multiple comparisons uncovered the following sleep-stage effects within the control and SDB group: significantly shorter Ti (Fig. 1) and DC in REM sleep compared with stages 2 and 4 NREM sleep; significantly shorter Te in stage 4 sleep compared with stage 2 and REM sleep. The SD measures SD_Ti, SD_Te, and SD_DC also exhibited significant sleep-stage effects, and a within-group repeated measures ANOVA showed that all three measures were significantly higher in REM sleep compared with stages 2 and 4 NREM sleep in both groups of children (Table 3). Also, Res_Ins and Res_Exp in both the control and SDB group were significantly different among sleep stages. Respiratory variability was highest in REM sleep and lowest in stage 4 NREM sleep (Table 3 and Fig. 3).

Effect of treatment on respiratory parameters. The differences in Ti, Te, and fR between the control and SDB groups at the baseline study were no longer significant after the SDB children underwent adenotonsillectomy (Table 4). Within each group, the sleep-stage effects on respiratory parameters were found to be consistent with the baseline results.

Effect of age, BMI, gender, and SDB markers on respiratory parameters. Correlation analysis between age and BMI and respiratory measures were assessed at the P = 0.01 level. Age exhibited a significant negative relationship with DC in stage 2 and REM sleep (stage 2: r = −0.42, P < 0.01; REM: r = −0.31, P < 0.01). None of the other respiratory parameters were found to significantly correlate with age in any of the sleep stages. In this relatively nonobese cohort of children, no correlation was observed between BMI and respiratory parameters. Also, the respiratory parameters were not significantly different between male and female children. A subgroup cor-

![Fig. 1. Comparison of mean (±SD) inspiratory time (Ti; top), expiratory time (Te; middle), and respiratory frequency (fR; bottom) at baseline polysomnography (PSG) between control and sleep-disordered breathing (SDB) groups with respect to sleep stage (*P < 0.05; **P < 0.01). ss2, sleep stage 2 nonrapid eye movement (NREM); ss4, sleep stage 4 NREM; REM, rapid eye movement.](http://japl.physiology.org/)

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relation analysis was performed among clinical PSG-derived markers of SDB, such as OAHI, respiratory arousal index (RAI), SpO2 nadir, and the respiratory parameters measured in SDB children. A moderate negative correlation was observed between fR and RAI in stage 2 NREM sleep ($r = -0.42$, $P < 0.01$).

**DISCUSSION**

To the best of our knowledge, this is the first study to report changes in respiratory timing in children with SDB. The main findings from this study are: 1) inspiratory and expiratory timing were significantly longer and breathing rate significantly lower in children with SDB compared with controls in all sleep stages considered for analysis; 2) no significant differences in respiratory timing and variability were observed between the two groups after the children with SDB underwent adenotonsillectomy; 3) within each group, respiratory timing and variability measures showed significant sleep-stage effects with REM sleep exhibiting the highest breath-to-breath variability; and 4) the sleep-stage effects on respiratory parameters showed the same pattern in the follow-up study for both groups of children.

**Influence of SDB on respiratory parameters.** Our study showed a prolongation in Ti in children with relatively mild SDB compared with controls in all sleep stages during periods free of apneas and hypopneas. A probable explanation for this prolongation in Ti is that adenotonsillar hypertrophy leads to upper-airway narrowing because of increased tissue mass. In a collapsible airway, flow is independent of driving pressure but is dependent on transmural pressure, which with increased tissue mass leads to smaller airway diameter, and this in turn is the most important parameter in determining airway resistance, which cannot be overcome readily with increased driving pressure; i.e., Ti will therefore be prolonged to try to maintain minute ventilation. Prolonged Ti could be due to the additional, prolonged effort required by the inspiratory muscles even during apneic-free periods (9). A prolonged Ti has been shown to occur in adults as a compensatory response to increased inspiratory-resistive loading (IRL) (45). A fall in tidal volume and minute ventilation with induced IRL has been observed in healthy children (26). Also, decreased airflow with an increase in Ti, DC, and fR has been observed in children (11) and in adults (36) during short periods of experimentally induced flow limitation compared with their baseline values. However, it is to be noted that these were interventional approaches as opposed to our analysis, which is a case-control study comparing respiratory timing between healthy children and children with relatively mild SDB during tidal-breathing sleep periods free of apnea/hypopnea events. In regard to expiratory timing, children with SDB had a significantly longer Te in stages 2 and 4 NREM sleep. Although REM sleep showed a similar trend of longer Te in SDB, this was not statistically significant.
Our data are the first to demonstrate expiratory flow limitation in children. Expiratory flow limitation has been reported previously in adult heavy snorers (40), and it was argued that muscle relaxation resulted in airway narrowing in both inspiration and expiration. A further study (47) in healthy, snoring adults has confirmed expiratory pharyngeal airway obstruction during sleep. This author proposed a multiple element model in which the upstream supraglottic/retroglossal segment decreases in size, and the retropalatal segment remains with a relatively constant cross-sectional area during expiration—the latter being the common site for inspiratory flow limitation. The predominant site of expiratory obstruction in otherwise healthy children with SDB is not known. Upper-airway closure during sleep could occur at the end of expiration or at the onset of inspiration (1, 35). Therefore, the expiratory cycle, though a passive process, could still involve an additional effort in overcoming flow limitation. However, increased tissue mass (i.e., increased tonsillar and adenoidal mass) is the most likely cause for the supraglottic decrease in cross-sectional airway diameter during expiration. Thus in children with SDB, a sleep-induced increase in supraglottic airway resistance, due to increased tissue mass and muscle relaxation, which is also likely to occur during expiration, resulting in an overall increase in internal-resistive loading, might account for the prolonged expiration.

None of the respiratory variability measures exhibited group differences nor did they correlate with the SDB indices. Children with SDB appeared to exhibit the same level of respiratory regularity compared with controls in each sleep stage. This might be due to comparable elastic or flow-resistive properties of the lungs per se between the groups. Kowallik et al. (16) analyzed variability in nonapneic breath intervals using nasal flow signals in adults with obstructive sleep apnea (OSA), where an increased variability compared with controls was observed in all sleep stages. They also reported significant correlation between degree of respiratory variability and the severity of OSA. This is, however, in contrast to our results, where an increased variability compared with controls was observed in all sleep stages. They also reported significant correlation between degree of respiratory variability and the severity of OSA. This is, however, in contrast to our results, and possible reasons for this discrepancy could be the younger age group used in our study, differences in the severity of SDB, and possible reasons for this discrepancy could be the younger age group used in our study, differences in the severity of SDB, or differences in pattern of obstruction and upper-airway response between children and adults with SDB (23, 25).

**Influence of sleep stages on respiratory parameters.** Our results showed that Ti was shorter in REM sleep compared with stages 2 and 4 NREM sleep. This finding corroborates what has been shown previously in adolescents (43). The

Table 4. Respiratory timing and variability measures during stages 2 and 4 and REM sleep in control and SDB children during follow-up PSG

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>SDB</th>
<th>F value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stage 2</td>
<td>Stage 4</td>
<td>REM</td>
</tr>
<tr>
<td>Ti (s)</td>
<td>1.65 ± 0.2</td>
<td>1.59 ± 0.2</td>
<td>1.46 ± 0.2</td>
</tr>
<tr>
<td>Te (s)</td>
<td>1.85 ± 0.3</td>
<td>1.67 ± 0.2</td>
<td>1.92 ± 0.3</td>
</tr>
<tr>
<td>DC</td>
<td>0.47 ± 0.0</td>
<td>0.4 ± 0.0</td>
<td>0.43 ± 0.0</td>
</tr>
<tr>
<td>IR (beats/min)</td>
<td>17.4 ± 2.2</td>
<td>18.6 ± 2.4</td>
<td>17.9 ± 2.3</td>
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<tr>
<td>SD_Ti (ms)</td>
<td>7.3 ± 3.7</td>
<td>7.7 ± 3.9</td>
<td>39.9 ± 34.6</td>
</tr>
<tr>
<td>SD_Te (ms)</td>
<td>11.2 ± 5.2</td>
<td>10.9 ± 5.4</td>
<td>69.8 ± 50.3</td>
</tr>
<tr>
<td>SD_DC</td>
<td>0.002 ± 0</td>
<td>0.002 ± 0</td>
<td>0.01 ± 0</td>
</tr>
<tr>
<td>SD_IR (beats/min)</td>
<td>1.8 ± 0.6</td>
<td>1.5 ± 0.8</td>
<td>2.0 ± 0.7</td>
</tr>
<tr>
<td>Res_Ins (µV)</td>
<td>152.9 ± 39</td>
<td>134.2 ± 34</td>
<td>250 ± 55.6</td>
</tr>
<tr>
<td>Res_Exp (µV)</td>
<td>236.2 ± 47</td>
<td>192.9 ± 47</td>
<td>374 ± 59</td>
</tr>
</tbody>
</table>

Res_Ins, residual measures for inspiration; Res_Exp, residual measures for expiration. *P < 0.001. Data are mean ± SD.
longer Ti in NREM sleep could be attributed to a higher inspiratory load. Inspiratory and expiratory airflow resistance is distinctly different between wakefulness and sleep and also varies among stages of sleep (6, 10, 14, 17, 19). It has been shown in adults that these airflow resistances are higher during NREM than REM sleep and that inspiratory resistance is higher than the expiratory resistance (12). A possible manifestation of this elevated inspiratory resistance during NREM sleep is the prolongation of Ti. A similar impact on the expiratory part of the breathing cycle is quite plausible. Inter-costal muscle activity has been shown to increase during NREM, followed by a substantial fall in REM sleep (43). This increased effort might be to overcome the elevated airflow resistance. Our findings on fR are comparable with those reported by Carskadon et al. (5), where a higher fR was observed in children during stage 4 sleep.

**Effect of age and respiratory arousal.** A weak negative relationship between age and DC in stage 2 and REM sleep was observed. Changes in DC are a compensatory response to altered upper-airway-resistive loads during sleep (13). A decrease in DC with an increase in age might be indicative of a reduced loading effect in the older children, although the underlying cause for this cannot be determined from this study. On correlating respiratory parameters with clinical PSG-derived markers of SDB, only a moderate negative correlation was observed between fR and RAI in the SDB group, suggesting that clinically used PSG markers provide an incomplete picture of SDB.

**Effect of adenotonsillectomy.** Following adenotonsillectomy in children with SDB, clinical parameters of obstruction (SpO2 nadir and desaturation index and OAHI) were reduced significantly but still statistically elevated significantly in the SDB group compared with controls during the follow-up PSG. In contrast, adenotonsillectomy has normalized the prolonged inspiratory and expiratory periods and the reduced breathing rate, presumably by reducing upper-airway resistance, thereby improving the efficiency of respiratory mechanics during unobstructed breathing. The residual SDB events following surgery do not appear to be consistent with generally impaired breathing. Marcus et al. (24) have demonstrated an impaired upper-airway dynamic response to negative pressure and hypocapnia and a trend toward normalization of the response after adenotonsillectomy in children with OSA. This is in support of our findings, suggesting that the structural load of the tonsils and adenoids might have caused the upper-airway muscles to work at a disadvantage, and this improved postoperatively with unloading of the upper airway.

**Limitations.** Inductive plethysmography is a widely used, nonobtrusive technique to monitor respiration. However, the RIP signals used in our current study were uncalibrated and hence, lack information on the tidal volume. Consequently, we were unable to analyze volume-based parameters such as minute ventilation and mean inspiratory flow rate. However, timing components, such as Ti, Te, Ttotal, and fR, should be independent of the mode of acquisition. Indeed, validation studies using uncalibrated RIP signals compared with a face-mask pneumotachograph demonstrated highly reliable measures of DC and ratio of time-to-peak tidal expiratory flow to Te (21, 41). This study did not consider circadian influences on the parameters measured, as the time of night during which sleep is investigated is thought to influence cardiorespiratory physiology (38). Also, it is unclear whether the observed differences in respiratory timing are restricted to the resistive loading effects of the upper airway or whether there are broader influences originating from the central neuronal processes controlling reflex reactions, response to metabolic demands, and respiratory on-off switching mechanisms.

**Conclusion.** Children with relatively mild SDB had significantly prolonged inspiration and expiration and slower respiratory rates than the controls during sleep periods free of apneas and hypopneas. This may be attributed to chronic narrowing of the upper airway, increasing airway resistance, and demanding greater inspiratory and expiratory effort. Treatment of SDB with adenotonsillectomy appears to have reduced upper-airway resistance, as evidenced by normalized breathing effort and breathing rate. Documentation of these parameters related to respiratory flow limitation/obstruction may aid in both understanding and management of children with SDB.

**REFERENCES**