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Journal of Applied Physiology 95:2030-2038, 2003. First published Aug 1, 2003;
doi:10.1152/japplphysiol.00293.2003

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Sleep-disordered breathing, pharyngeal size and soft tissue anatomy in children

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Submitted 20 March 2003; accepted in final form 28 July 2003

Fregosi, R. F., S. F. Quan, K. L. Kaemingk, W. J. Morgan, J. L. Goodwin, R. Cabrera, and A. Gmitro. Sleep-disordered breathing, pharyngeal size, and soft tissue anatomy in children. *J Appl Physiol* 95: 2030–2038, 2003. First published August 1, 2003; 10.1152/japphysiol.00293.2003.—We tested the hypothesis that pharyngeal geometry and soft tissue dimensions correlate with the severity of sleep-disordered breathing. Magnetic resonance images of the pharynx were obtained in 18 awake children, 7–12 yr of age, with obstructive apnea-hypopnea index (OAH) values ranging from 1.81 to 24.2 events/h. Subjects were divided into low-OAH ($n = 9$) and high-OAH ($n = 9$) groups [2.8 ± 0.7 and 13.5 ± 4.9 (SD) $P < 0.001$]. The OAH correlated positively with the size of the tonsils ($r^2 = 0.42$, $P = 0.024$) and soft palate ($r^2 = 0.33$, $P = 0.049$) and inversely with the volume of the oropharynx ($r^2 = 0.42$, $P = 0.038$). The narrowest point in the pharyngeal airway was smaller in the high- compared with the low-OAH group (4.4 ± 1.2 vs. 6.0 ± 1.3 mm; $P = 0.024$), and this point was in the retropalatal airway in all but two subjects. The airway cross-sectional area (CSA)-airway length relation showed that the high-OAH group had a narrower retropalatal airway than the low-OAH group, particularly in the retropalatal region where the soft palate, adenoids, and tonsils overlap ($P = 0.001$). The “retropalatal air space,” which we defined as the ratio of the retropalatal airway CSA to the CSA of the soft palate, correlated inversely with the OAH ($r^2 = 0.49$, $P = 0.001$). We conclude that 7- to 12-yr-old children with a narrow retropalatal air space have significantly more apneas and hypopneas during sleep compared with children with relatively unobstructed retropalatal airways.

apnea; hypopnea; magnetic resonance imaging; upper airway; obstructive apnea hypopnea index

THE PREVALENCE OF SLEEP-DISORDERED breathing (SDB) in children is ~2% (16). Emerging evidence suggests that, unlike adults, some children with SDB exhibit hyperactivity instead of daytime sleepiness, and they may have poor school performance and/or cognitive abnormalities (10, 13). Given the estimated prevalence of SDB in children and its potential clinical impact, a better understanding of the mechanisms underlying its development is important.

Both anatomic and neuromuscular control mechanisms appear to contribute to SDB in adults (27), and

recent studies suggest that this is also true in children (16, 17). However, the relationships among pharyngeal geometry and soft tissue anatomy and the severity of SDB in children are complex and remain incompletely defined. A recent study evaluating pharyngeal geometry and soft tissue anatomy with magnetic resonance (MR) imaging (MRI) in a group of young children (4–5 yr old) found that children with SDB had smaller pharyngeal airways and enlarged tonsils, soft palates, and adenoids but no differences in craniofacial bony anatomy compared with controls (5). The subjects studied by Arens et al. (5) had a mean age of 4.8 yr. Although the ratio of pharyngeal soft tissue size to craniofacial dimensions does not change significantly over the first 11 yr (3), subtle abnormalities in craniofacial dimensions, the size of pharyngeal soft tissues, or the ratio of soft tissue structures to craniofacial dimensions may exist in children with SDB. Thus it is important to study the relation between pharyngeal airway size and soft tissue anatomy and the severity of SDB during development.

Another factor that could confound the interpretation of previous studies is the use of sedation to obtain MRI studies in young children. Because barbiturates depress the activity of upper airway muscles much more than the activity of the diaphragm in both human (8) and animal subjects (12), the pharynx of a sedated individual is susceptible to narrowing, because the flaccid pharyngeal muscles may not adequately counterbalance the inspiratory collapsing pressures produced by the diaphragm. This mechanism may lead to overestimation of the degree of airway narrowing on MRI.

Accordingly, our major goal was to obtain upper airway MR images from a group of children, aged 7–12 yr, with sleep-related respiratory disturbances of varying severity so that we could test the hypothesis that pharyngeal geometry and/or soft tissue dimensions correlates with the severity of SDB. To avoid the potentially confounding influences of sedation, MR images were obtained in awake, nonsedated children.

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METHODS

Subjects. All methods used to recruit subjects and to collect the present data set were approved both by the University of Arizona Human Subjects Committee and the Tucson Unified School District Research Committee. In all cases, we obtained written, informed consent from the parents and assent from the children. Eighteen children aged 7–12 yr participated in the present experiments. The subjects were drawn from a pool of Hispanic and Caucasian children participating in the Tucson Children's Assessment Of Apnea Study (TuCASA), as described in detail previously (9, 10). In an earlier study (unpublished observations), we examined the chemoreceptor responses of 50 children from a sample of ~240 children who previously had an unattended home polysomnogram performed. We chose these 50 subjects by randomly selecting children with RDI values of >5 or <5. We recruited the first 25 subjects in each of the two RDI ranges who responded to our request. For the present study, we selected a subset of these 50 children by randomly choosing 10 subjects with RDI values of <5 and 10 subjects with values of >5. All 20 of the randomly selected subjects agreed to participate, although one subject from each group failed to show up for their scheduled experiment, leaving us with a final sample of 18 subjects (Table 1). It is important to point out that our subject group is representative of the group as a whole with regard to age and anthropometric distribution, although by design we excluded subjects that had RDI values between 5 and 10. Also note that we corrected the BMI values for age, sex, and ethnicity (21), and we report the resulting body mass index (BMI) percentile values in Table 1. Of the 18 subjects selected for study, 4 snored, and 3 of those 4 also had witnessed apnea. Four other subjects had excessive daytime sleepiness, and two of those also snored. All subjects with symptoms were in the high-obstructive apnea-hypopnea (OAH) group.

Polysomnography. Subjects underwent unattended home polysomnography (9) using the Compumedics PS-2 system (Abbottford, Victoria, Australia). The following signals were obtained: C₃/A₂ and C₄/A₁ electroencephalogram, right and left electrooculogram, a bipolar submental electromyogram,

thoracic and abdominal displacement (inductive plethysmography bands), airflow (nasal-oral thermocouple), nasal pressure, electrocardiogram (single bipolar lead), snoring (microphone attached to a vest), body position (Hg gauge sensor), pulse oximetry (Nonin, Plymouth, MN), and ambient light (sensor attached to the vest to detect lights on or off). With the use of Compumedics W-Series Replay (version 2.0, release 22), sleep stages were scored according to standard criteria (19). The respiratory disturbance index (RDI) was defined as the number of respiratory events (apneas and hypopneas) per hour of the total sleep time irrespective of any associated oxygen desaturation or arousal. Polysomnograms with <4 h of scorable oximetry were classified as failed studies and were repeated if the participant consented.

Although the oximeter pulse waveform was not recorded during acquisition of the polysomnography data, the Compumedics data-acquisition software contains artifact-rejection algorithms. These are noted in the computer-assisted scoring. In addition, because the records were hand scored by the technician, the oximetry signal was inspected for evidence of artifact. Desaturation artifact induced by motion is generally easily recognizable and was excluded if it occurred. Apneas were scored if the peak-to-trough amplitude of the airflow signal using the thermistor decreased below at least 25% of the amplitude of "baseline" breathing and if this change lasted for >6 s or two breath cycles. Central apneas were scored if both airflow and thoracoabdominal effort were absent. However, central events that occurred after movement were not included. Obstructive apneas were identified if the airflow signal decreased to below 25% of the "baseline amplitude," but with continued thoracoabdominal effort. Hypopneas were scored if the magnitude of any ventilation signal decreased below ~70% of the baseline amplitude. Although the polysomnographic montage included monitoring of nasal pressure, we elected not to use this parameter to identify SDB events because experience with this technique in children is quite limited. In addition, some children were unable to tolerate wearing the nasal cannula so that scorable data were not available for all of the subjects.

Table 1. Subject characteristics

OAH Group	Age, yr	Sex	Height, cm	BMI	BMI Percentile	Total sleep time, h	Minimum SaO ₂ , %	RDI	OAH
High	11	M	147.3	16.6	80	8.17	90	10.2	7.10
High	12	F	167.6	25.30	92	7.78	83	30.4	24.16
High	8	M	134.6	18.90	80	6.95	92	10.4	12.37
High	11	M	144.8	17.00	31	8.75	90	12.8	9.83
High	10	M	139.7	19.20	80	8.5	87	19.3	16.47
High	9	M	144.8	23.80	95	7.43	84	14.7	10.77
High	8	F	137.2	16.40	80	8.83	87	14.4	12.00
High	10	M	144.8	16.00	22	7.85	90	15.6	13.50
High	10	M	149.9	18.10	65	8.92	87	15.8	15.36
Low	9	F	132.1	16.30	71	8.83	91	3.2	1.81
Low	11	M	142.2	20.00	85	9.47	89	3.2	3.06
Low	9	F	134.6	13.40	5	10.1	90	4.9	3.37
Low	10	M	129.5	19.50	65	8.93	85	4.2	3.92
Low	9	M	147.3	16.50	59	5.23	91	2.7	2.49
Low	9	M	134.6	17.40	62	7.3	89	3.7	2.74
Low	9	F	134.6	13.60	5	7.15	90	4.5	3.50
Low	9	M	142.2	27.60	95	9.03	89	2.4	2.21
Low	7	M	124.5	17.90	86	7.8	85	2.5	2.75
Mean ± SD	9.5 ± 1.2		140.7 ± 9.6	18.5 ± 3.7	64 ± 29	8.2 ± 1.1	88.3 ± 2.6	9.7 ± 7.7	8.2 ± 6.4

M, male; F, female; SaO₂, arterial O₂ saturation; BMI, body mass index; RDI, respiratory disturbance index (see text); Total sleep time, sleep time obtained during unattended polysomnography test; OAH, obstructive apnea-hypopnea index. Minimum SaO₂ was that obtained during rapid eye movement sleep, as computed from pulse oximetry during unattended home polysomnography.

The RDI that we routinely compute includes central apneas as well as obstructive apneas and hypopneas (9, 10). On the basis of the clinical and physiological uncertainty of central apneas in children (16), we subtracted central events from the RDI to derive the OAH1. In our subjects, this index represents primarily hypopneas, because only 13 of the subjects showed frank obstructive events during their sleep study. The number of frank obstructive events ranged from 0.1 to 0.8 per hour, except for one subject who averaged 7 obstructions per hour.

Airway imaging. Participants were studied between 9:00 AM and 2:00 PM, and they arrived at the MRI facility ~1 h before the time of their scheduled experiment. Subjects were studied in the supine position in the bore of a General Electric 0.5-T MRI instrument and were imaged with the use of a standard head coil. The instrument error is ± 0.5 mm, or 0.5% when calibrated with a 100-mm phantom. After subjects were positioned in the machine, scout images were obtained to confirm and adjust positioning so that the entire pharynx was clearly visible. Axial images were obtained from just above the orbital cavity to just below the larynx. Sagittal images were obtained from the midline to the ears bilaterally. To highlight the air spaces, longitudinal relaxation time (T1)-weighted axial and sagittal spin-echo images [repetition time (TR) = 500 ms; echo time (TE) = 11 ms] were obtained in two separate series. To highlight the pharyngeal soft tissues, we then ran a third sequence consisting of transverse relaxation time (T2)-weighted sagittal fast spin-echo images (TR = 3,500 ms; effective TE = 85 ms, and excitation train length = 8). Data and image matrices were 256×256 , the slice thickness was 4 mm with a 1-mm skip, and the field of view was 22 cm in all three sequences. A bandwidth of ± 10.7 kHz and two averages (2 NEX) were used in all three sequences. Each imaging sequence required ~4 min to complete, and because the children were not sedated they were instructed to remain perfectly still until the scan was completed. Children could view the investigators through a mirror, and could communicate via headphones and a microphone. The children were allowed a few minutes to move their arms and legs in between each of the three scans. Preliminary studies indicated that the time required to complete these three scans was the maximum tolerable given the age of the children and the rigid requirements for subject compliance.

Image analysis. Image analysis was performed on an IBM personal computer using SCION image software (formerly NIH Image), which allows manual tracing of regions and structures of interest. This software computes the minimal and maximal pixel values of 16-bit images and uses the result to linearly scale the data to 8 bits. Because air-filled spaces are black on MRI, we used a threshold method to differentiate the oropharyngeal airway from surrounding tissue, as previously described (6). From a representative sample of axial images, we obtained the minimum, the maximum, and the SD of the pixel values from regions of the black space at the outer boundary of the image. The SD of the black space was used as an estimate of noise in the image (6). The average threshold value plus one SD served as the threshold value for differentiating true black space (airway) from surrounding tissue. Bony and soft tissues were analyzed by using standard radiologic landmarks.

T1-weighted axial slices were used to measure the cross-sectional area (CSA) of the tonsils at their widest point, the pharyngeal fat pad CSA, and the intermandibular distance. Midline T1-weighted sagittal slices were used to obtain the CSA of nasopharynx. T2-weighted sagittal images were used to obtain the CSA of the soft palate and adenoids. We ob-

tained the volume of the oropharynx by measuring the CSA of each relevant axial slice and multiplying the CSA by the slice thickness to obtain a volume for each slice. The volume measures of each sequential slice in a given region were then summed to obtain the regional volume. Each axial slice was separated by a 1-mm "skip," and we cannot measure the CSA of the skipped regions. Therefore, our estimates of regional volumes will be slightly underestimated. However, because the 1-mm skip was constant in all imaging sequences and in all subjects, the omission of these small skipped slices will not influence relative differences in the volume of the airway or the volume of pharyngeal structures. The volume of the adenoids was obtained by the same method using adjacent, T2-weighted sagittal slices.

Boundaries defining the oropharynx included the tongue or soft palate anteriorly, the pharyngeal constrictor muscle posteriorly, and the pharyngeal tonsils laterally. A horizontal line extending from the junction of the hard and soft palate to the posterior wall of the pharynx defined the rostral limit of the oropharynx, and the tip of the epiglottis defined the caudal margin (Ref. 18, and see Fig. 1). Nasopharyngeal CSA was estimated from a midline sagittal slice, and defined as the entire airspace rostral to the horizontal line extending from the junction of the hard and soft palate to the posterior pharyngeal wall (Fig. 1). The retropalatal airway was defined as that part of the oropharynx bounded rostrally by a horizontal line extending from the junction of the hard and soft palate to the posterior pharyngeal wall, anteriorly by the body of the soft palate, posteriorly by the posterior pharyngeal wall, and caudally by the tip of the soft palate (i.e., between the top and middle horizontal lines in Fig. 1). Two different individuals who were trained to use the imaging software analyzed the images. It was not possible to obtain measurements of every variable in every subject because in some cases the boundaries of structures of interest could not be clearly defined. This was generally the result of image blurring caused by movement artifact in the nonsedated subjects.

Data analysis. We first divided the subjects into two groups, one with high (>7) and one with low (<4) OAH1 values (Tables 1 and 2). We used ANOVA (Sigma Stat 3.0) followed by the Student-Neuman-Keuls post hoc procedure to determine which variables were significantly different between the two groups, with a post hoc P value of <0.05 considered significant. If a given variable showed a significant group difference, we then examined the relation between that variable and the OAH1 (dependent variable) by using linear regression analysis. This allowed us to test the hypothesis that a given variable correlated with the severity of SDB. We used a simple linear regression model followed by ANOVA (Sigma Stat 3.0), with significance defined as a P value of <0.05 . We also computed the "retropalatal air space," which we defined as the ratio of the CSA of the retropalatal airway to the CSA of the soft palate, by using midline sagittal images for analysis. This index provides a simple estimate of the size of the retropalatal airway relative to the size of the adjacent soft palate; values below 1.0 indicate that the CSA of the soft palate is larger than the CSA of the retropalatal airway.

RESULTS

Pharyngeal geometry and soft tissue dimensions in high- and low-OAH1 groups. Table 1 gives anthropometric and relevant polysomnography data for all 18 subjects. The subjects with the nine highest and nine lowest OAH1 values were placed into two groups (Table

Fig. 1. Airway imaging. A: representative longitudinal T1-weighted mid-sagittal image showing the landmarks used to define the nasopharyngeal, retropalatal, and oropharyngeal airways (horizontal white lines, from top to bottom). B: longitudinal T1-weighted axial slice through the center of the oropharynx (+), showing how the lateral and anteroposterior diameter of each axial slice was determined.

2). There were no group differences among age, BMI, and the sleep time and minimum arterial O_2 saturation obtained during home polysomnography. We also conducted correlation analyses between each of the variables that we measured and the BMI percentile and failed to find any significant relationships, suggesting that the BMI percentile alone cannot explain variability in the OAH, pharyngeal airway dimensions, or soft tissue anatomy. The high-OAH group was significantly taller than the low-OAH group. However, of all pharyngeal variables measured, only the CSA of the soft palate correlated significantly with height ($r^2 = 0.46$, $P = 0.016$, see DISCUSSION). The OAH and RDI values of the two groups were well separated and significantly different (Table 2). Intermandibular distance averaged 72.5 ± 3.2 mm in the low-OAH group and 73.0 ± 3.4 mm in the high-OAH group ($P =$ not significant).

The CSAs of the tonsils and soft palate were significantly larger in the high- compared with the low-OAH group (Table 3, Fig. 2). Although there was a trend toward a larger adenoid volume and pharyngeal fat pad CSA in the high-OAH group, the differences were not significant (Table 3). The correlation between the OAH and the CSA of the soft palate and tonsils is shown in Fig. 3. Both tonsil and soft palate CSA cor-

related significantly with the OAH, accounting for 44 and 39% of the variability in the OAH, respectively. As shown in Table 3, significant differences between the high- and low-OAH groups were found for the sum of tonsil and soft palate CSA ($P < 0.001$), tonsil plus adenoid CSA ($P = 0.016$), and the sum of tonsil, adenoid, and soft palate CSA ($P = 0.005$). Correlation analyses of these combined soft tissue masses with the OAH revealed significance for the sum of the tonsil and soft palate CSA vs. the OAH ($r^2 = 0.50$, $P = 0.011$) but not for the tonsil plus adenoid CSA or for the tonsil plus adenoid plus soft palate CSA. However, we did not have all soft tissue masses in all subjects, resulting in a diminution of our sample size for the latter two measures by seven and six subjects, respectively; this weakened our statistical power (see DISCUSSION).

We used multiple linear regression analysis to predict the percentage of the variance in the OAH that could be predicted by knowledge of the size of soft tissue structures. We included in our analysis soft palate, tonsils, adenoids, and fat pad areas, although we were able to use a maximum of three variables in the model, given the available sample size. The CSA of the tonsils and soft palate could explain 74.3% of the variance in OAH, but addition of fat pad area and/or adenoid area reduced the predictive power.

Analysis of pharyngeal airway dimensions did not reveal differences in the CSA of the retropalatal or nasopharyngeal air spaces (Table 4) but did show that the volume of the oropharynx was smaller in the high-compared with the low-OAH group ($P < 0.001$). We also found a significant correlation between the OAH and the oropharyngeal volume (Fig. 4A). This led us to examine other oropharyngeal dimensions, including the oropharyngeal length, the smallest anteroposterior (AP) and lateral diameters, and the elliptical ratio (lateral diameter/AP diameter). We found no group differences for any of these variables. We also determined the smallest oropharyngeal diameter, whether it was in the lateral or AP plane, in each subject. This analysis did show that the narrowest diameter mea-

Table 2. Anthropometric and sleep variables from subjects in high- and low-OAH groups.

	High-OAH Group	Low-OAH Group	P Value, High vs. Low
Age, yr	9.9 $\pm$ 1.4	9.1 $\pm$ 1.0	0.19
Height, cm	145.6 $\pm$ 9.6	135.7 $\pm$ 7.1	<0.001
Weight, kg	36.82 $\pm$ 11.4	32.2 $\pm$ 12.3	0.42
BMI	19.03 $\pm$ 3.3	17.8 $\pm$ 4.5	0.693
BMI percentile	69.4 $\pm$ 26	59.2 $\pm$ 33	0.47
Total sleep time, h	8.1 $\pm$ 0.68	8.2 $\pm$ 1.5	0.62
Minimum SO_2 , %	87.8 $\pm$ 3.0	88.8 $\pm$ 2.3	0.97
RDI	15.9 $\pm$ 6.1	3.5 $\pm$ 0.9	<0.001
OAH	13.5 $\pm$ 4.9	2.8 $\pm$ 0.7	<0.001

Values are means $\pm$ SD.

Table 3. Comparison of pharyngeal soft tissue dimensions in high- and low-OAHI groups

	High-OAHI Group	Low-OAHI Group	P Value, High vs. Low
Tonsil CSA, mm ²	617.1 ± 76.8 (n = 6)	435.7 ± 118.6 (n = 6)	0.03
Soft palate CSA, mm ²	321.6 ± 59.7 (n = 9)	225.5 ± 40.4 (n = 9)	0.009
Adenoid CSA, mm ²	322 ± 91 (n = 8)	292 ± 77 (n = 9)	0.25
Soft palate + tonsil CSA, mm ²	939 ± 128.5 (n = 6)	637.5 ± 129.6 (n = 6)	<0.001
Soft palate + adenoid CSA, mm ²	644 ± 86 (n = 8)	517.4 ± 88.9 (n = 9)	0.148
Tonsil + adenoid CSA, mm ²	921.4 ± 135 (n = 6)	739 ± 145 (n = 6)	0.016
Tonsil + soft palate + adenoid CSA, mm ²	1,146.3 ± 288.8 (n = 6)	941.3 ± 161.7 (n = 6)	0.005
Pharyngeal fat pad cross-sectional area, mm ²	176.0 ± 59.1 (n = 7)	151.6 ± 39.8 (n = 7)	0.383
Adenoid volume, mm ³	7,300 ± 2400 (n = 8)	5,600 ± 1,800 (n = 9)	0.109

Values are averages ± SD; n, no. of subjects. CSA, cross-sectional area.

sured at any point in the oropharynx of children with high OAHI values was significantly smaller than that measured in the group with lower OAHI values (Table 4; $P = 0.024$). We also found a significant correlation between this variable and the OAHI (Fig. 4B). The narrowest point in the pharynx was located in the retropalatal airway in all but two subjects.

Airway CSA-length relation. To determine the narrowest segment of the pharynx, we examined the relation between the CSA of each axial slice of the airway, extending from 8 mm above the hard palate to the tip

of the epiglottis (see *inset* in Fig. 5). We then constructed a CSA-length relation for each group, as shown in Fig. 5. The airway was significantly narrower in the region where the soft palate, adenoids, and tonsils are maximally overlapped in both high- and low-OAHI groups ($P < 0.001$ for both). In addition, the area-length curves of the low- and high-OAHI groups were significantly different (2-way ANOVA, $P = 0.034$). We then divided the CSA of the retropalatal airway by the CSA of the soft palate and defined this ratio as the retropalatal air space, which is an estimate of the

Fig. 2. Magnetic resonance images of the upper airway in two 11-yr-old male subjects with relatively high (*left*) and low (*right*) obstructive apnea-hypopnea index (OAHI) values. *Top*: axial images at the point of maximal pharyngeal tonsil cross-sectional area (CSA). *Bottom*: midline sagittal images. Pharyngeal tonsils (*top*, axial images), and soft palate and adenoids (*bottom*, sagittal images) are shaded for ease of differentiation. Note the enlarged tonsils, soft palate, and adenoids in the child with the higher OAHI, as well as the much narrower pharyngeal air space, particularly where the adenoids and soft palate overlap.

Fig. 3. Line plots showing the relation between tonsil area and the OAH I (A) and soft palate area and the OAH I (B). Both correlations were statistically significant, with the *P* value of 0.024 for tonsil area and 0.049 for soft palate area.

fraction of the retropalatal airway cross section that is occupied by the soft palate. We then used linear regression to examine the relation between the retropalatal air space ratio and the OAH I, as shown in Fig. 6. The correlation was statistically significant ($r^2 = 0.49$, $P = 0.001$), indicating that subjects with narrow retropalatal air spaces tend to have higher OAH I values.

DISCUSSION

Summary and conclusions. Our main findings are that the severity of SDB correlates significantly with the oropharyngeal volume and the size of the tonsils

Fig. 4. Line plots showing the relation between oropharyngeal (OP) volume and the OAH I (A) and the smallest OP diameter measured either in the lateral or anteroposterior plane (B). Both correlations were statistically significant ($P = 0.038$ for both).

and soft palate in a population of male and female children 7–12 yr of age; the pharynx of children with high OAH I values is significantly narrower where the adenoids, tonsils, and soft palate overlap; and the OAH I is inversely and significantly related to the size of the retropalatal air space.

Critique of methods. On the basis of the clinical uncertainty of central apneas in children (16), we subtracted central events from the RDI to derive an “obstructive apnea-hypopnea index,” or OAH I. In our subjects, this index represents primarily hypopneas, because only seven of the subjects showed frank obstructive events during their sleep study. We ac-

Table 4. Pharyngeal airway dimensions in high- and low-OAH I groups

	High-OAH I Group	Low-OAH I Group	<i>P</i> Value, High vs. Low
Retropalatal CSA, mm ²	146.4 ± 32.1 (<i>n</i> = 9)	213.1 ± 61.8 (<i>n</i> = 9)	0.82
Nasopharyngeal CSA, mm ²	219 ± 0.88 (<i>n</i> = 9)	301 ± 1.0 (<i>n</i> = 9)	0.10
Oropharyngeal volume, mm ³	3,100 ± 490 (<i>n</i> = 9)	4,300 ± 1,400 (<i>n</i> = 9)	<0.001
Oropharyngeal length, mm	28.3 ± 4.5 (<i>n</i> = 9)	26.6 ± 5.1 (<i>n</i> = 9)	0.46
Smallest oropharyngeal AP diameter, mm	5.1 ± 2.5 (<i>n</i> = 9)	6.9 ± 2.2 (<i>n</i> = 8)	0.29
Smallest oropharyngeal lateral diameter, mm	5.7 ± 3.2 (<i>n</i> = 9)	6.9 ± 2.6 (<i>n</i> = 8)	0.24
Elliptical ratio of oropharynx (lateral diameter/AP diameter)	1.1 ± 0.7 (<i>n</i> = 9)	0.67 ± 0.6 (<i>n</i> = 9)	0.93
Smallest oropharyngeal dimension in any plane, mm	4.4 ± 1.2 (<i>n</i> = 9)	6.0 ± 1.3 (<i>n</i> = 8)	0.024

Values are averages ± SD; *n*, no. of subjects. AP, anteroposterior.

Fig. 5. Average airway CSA-airway length relation in high-OAHI (dashed line) and low-OAHI (solid line) groups. AD, adenoid; SP, soft palate; TON, tonsils. *Inset*, the extent of the pharynx from which 4-mm axial slices were taken in each subject; the scale extends from 0 to 32 mm. Because some subjects had relatively short pharyngeal airways, the number of subjects fell from 18 to 14 at 28 mm and to 4 at 32 mm (discussed in RESULTS). We had data from all 18 subjects for the airway regions of greatest interest (over the range 5–20 mm; see *inset*). In both groups, the airway was significantly narrower at lengths ranging from 10 to 16 mm ($P < 0.001$), and the curves for the 2 groups were also significantly different ($P = 0.034$).

knowledge that our definition of hypopnea did not incorporate an arousal or desaturation criteria. Although such criteria have been recommended (1), more recent reviews have noted that there is no standard definition of hypopnea in children (2, 22). Recently, our laboratory has demonstrated that, using our present definition, there is an association between RDI and several clinical outcomes in children (11). We also wish to emphasize that the definition of hypopnea employed in this study was used to describe a spectrum of SDB ranging from none or mild to severe and not to implicate a specific value as constituting disease. Thus the precise definition utilized is not important if it provides a relatively consistent description of SDB severity. To demonstrate that this is true in the present study, we have performed a correlation matrix using the hypopnea definition employed in our study and others that required an oxygen desaturation event of 2–4%. These indexes were highly intercorrelated with $r = 0.82$ – 0.95 , indicating that the use of a different event definition would only change the absolute values of the OAHI and would not alter any assessment of relative disease severity in these children.

We did not have a true control group composed of children with a total absence of respiratory disturbances during sleep. Nevertheless, our decision to classify children with an OAHI was not arbitrary. Data from TuCASA indicate that children with a RDI of ≥ 5 have a higher prevalence of learning problems and excessive daytime sleepiness (10) as well as an impairment in learning on neurocognitive testing (13). Furthermore, there is little available information on the prevalence of hypopneas in children (16), although our

average OAHI value for the high-OAHI group (13.5) is slightly higher than that reported by Arens et al. (5) in 4-yr-old children with obstructive sleep apnea (OSA). Our low-OAHI group had an average of 2.8 events per hour, which was markedly and significantly lower than the high-OAHI group. Moreover, our subjects had a wide range of OAHI values, and the major goal of the study was to determine the relation between the severity of OSA and pharyngeal airway anatomy.

We chose not to sedate the subjects for the imaging protocol because of the more profound depression by sedatives of upper airway compared with respiratory pumping muscles in human (8) and animal (12) models. However, the imaging sequences that we used required up to 4 min to complete, and if the child happened to move during this time some or all of the image would be blurred by the motion artifact, reducing the image quality significantly. We spent considerable time explaining the importance of staying still to the children, and we gave them opportunities to move their arms and legs in between each of the imaging sequences. Nevertheless, we do not have anatomic data for every variable in each subject because of motion artifact, and this reduced our sample size and statistical power for some of the measurements (see METHODS). We were willing to accept the smaller sample size for some variables as a trade-off for obtaining data in nonsedated subjects, and we believe that the resulting data set is fairly representative of the target population.

Pharyngeal soft tissue anatomy. We found significant correlations between the OAHI and the size of the soft palate. We also demonstrated that the soft palate relative to the size of the retropalatal airway (the retropalatal air space) is significantly larger in subjects with high OAHI values, leading to a rather strong and statistically significant correlation between the OAHI and the retropalatal air space. Arens et al. (5) also found a significantly larger soft palate CSA in a group of younger children (average age ~ 4 yr) with SDB compared with normal control subjects. The large soft palate in the high-OAHI subjects is consistent with

Fig. 6. Line plot showing the relation between the retropalatal air space (ratio of the CSA of the retropalatal airway to the SP CSA), as a function of the OAHI. The correlation was statistically significant ($P < 0.001$).

recent studies in adults with OSA. Thus Malhotra et al. (15) showed that men had significantly larger soft palates than age- and BMI-matched women, and Ciscar et al. (7) also showed that adults with SDB had significantly larger soft palates than disease-free adults. It is of interest that our high-OAHI group was also taller than the low-OAHI group and that of all measured variables the soft palate CSA was the only one that correlated significantly with height. Perhaps rapid growth in general is associated with relatively rapid growth of the soft palate relative to growth of the retropalatal airway. Our measurements of the retropalatal air space and its strong inverse correlation with the OAHI are consistent with this hypothesis.

We also found a significant correlation between the OAHI and the size of the tonsils but not the adenoids. Although we did show a significant difference in combined tonsil and adenoid CSA in the high- and low-OAHI groups, the relation between tonsil plus adenoid CSA and the OAHI was not statistically significant. Arens et al. (5) also measured the difference in combined tonsil plus adenoid volume in their 4-yr-old patients and their age-matched control subjects and found that this value correlated significantly with the apnea-hypopnea index (AHI) ($r^2 = 0.26$). Both tonsils and adenoids grow very rapidly between age 4 and 8 yr, with slower growth of craniofacial bony structures (16). As a result, the tonsils and adenoids are large relative to the upper airway, resulting in a narrowed pharynx. The subjects in the study of Arens et al. were at an age where large tonsils and adenoids are expected, so it is remarkable that the subjects with sleep apnea had even larger tonsils and adenoids than the age-matched control subjects (5). This observation underscores the profound importance of pharyngeal soft tissue structures as one of the underlying causes of SDB in children. However, the pharyngeal soft tissue mass that has the most dominant effect on pharyngeal obstruction and the severity of the underlying pathology may change with age.

We also failed to show a significant correlation between the OAHI and the size of the parapharyngeal fat pad. Arens et al. (5) also failed to show a larger fat pad volume in the SDB group compared with the control group. Thus fatty deposits in the pharyngeal walls do not appear to be a significant problem in most children with SDB, although the size of the pharyngeal fat pad certainly contributes to airway obstruction in adults (7, 23–25). The present results extend the work of Arens et al. (5) by demonstrating that the severity of sleep-disordered breathing correlates significantly with the size of the tonsils and soft palate, and that this is true across an age spectrum where the size of pharyngeal soft tissues relative to pharyngeal volume normally declines.

Pharyngeal geometry. The oropharyngeal volume of our high-OAHI subjects was 39% smaller than the volume measured in the low-OAHI group. In addition, oropharyngeal volume correlated significantly with the OAHI. Arens et al. (5) found the pharynx to be 40% smaller in the children with SDB, a difference that is in

substantial agreement with the present observations. However, they did not find a significant correlation between airway volume and the AHI in their subjects. It is possible that their inclusion of central events in the computation of the AHI weakened the relationship between this index and the pharyngeal anatomy because central apneic events are very common in children with no pharyngeal abnormalities or sleep-related breathing disturbances (16).

We also measured the narrowest AP and lateral diameter of axial airway slices in all subjects, as well as the ratio of the lateral to AP diameter (the elliptical ratio, an index of airway shape), but found no differences in any of these variables between the high- and low-OAHI subjects. However, we did find that the narrowest airway dimension, measured in either the AP or lateral plane, was significantly smaller in the high- compared with the low-OAHI subjects. We are unaware of similar information in children, and the data on airway shape in adults with OSA are equivocal. Some studies show that the airway is more elliptical in OSA subjects compared with control subjects, with the long axis oriented in the AP plane (14, 20). In contrast, a more recent study failed to show differences in the AP or lateral dimensions of the pharynx between OSA subjects and controls, and the study also suggested that these dimensions may differ depending on whether the subjects are studied while awake or asleep and on whether the measurements are made during inspiration or expiration (7). The present results in awake children show that the oropharyngeal airway of children with high OAHI values tends to be narrower than that observed in low-OAHI subjects, but the relative narrowing in the AP and lateral dimensions appears to be more uniform in children compared with adults.

Pharyngeal airway CSA-length relation. We found that the high-OAHI group had a significantly narrower pharynx in the region where the soft palate, adenoids, and tonsils overlap. This region is within the classically defined oropharynx [e.g., *Gray's Anatomy* (26)] but is often termed the velopharynx, the retropalatal airway, or the transpalatal airway, among other names (18). We have chosen to term this region the retropalatal airway because it corresponds to that segment of the oropharynx located immediately posterior to the soft palate. This appears to be the most common site of obstruction in adults with OSA (18).

The average CSA-length curves for the two groups were significantly different by ANOVA, which is consistent with our observation of different airway volumes in the two groups (i.e., the area under the CSA-length curve is equivalent to airway volume). These observations are in agreement with a more recent study by Arens et al. (4), wherein an advanced imaging technique known as fuzzy connectedness was used. This method allows estimation of the position of the airway centerline. This in turn allows better precision in aligning each axial slice orthogonal to the airway centerline. Although we did not have access to this technology, our results are virtually identical to theirs

[please compare our Fig. 5 with Figs. 1 and 2 in Arens et al. (4)], except that the adenoids and tonsils occupied a much larger fraction of the pharynx in the subjects of Arens et al.

In conclusion, the OAH in children aged 7–12 yr correlates positively with the size of their tonsils and soft palate and inversely with the volume of their oropharynx. We also found that the retropalatal air space is inversely correlated with the OAH, due mainly to abnormally large soft palates relative to the size of the retropalatal airway.

The authors thank Elena Antonio, Cortnie Cherry, Jason Quan, Dan Stoker, Veronica Tapia, and Jesse Winer for technical assistance.

DISCLOSURES

This work was supported by National Heart, Lung, and Blood Institute Grants HL-62373 and HL-51056 and by a grant from the Max and Victoria Dreyfus Foundation.

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