The Influence of Lung Volume on Pharyngeal Mechanics, Collapsibility, and Genioglossus Muscle Activation during Sleep

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Study Objectives: Previous studies in both awake and sleeping humans have demonstrated that lung-volume changes substantially affect upper-airway size and pharyngeal resistance and, thus, may influence pharyngeal patency. We sought to systematically investigate the isolated effects of lung-volume changes on pharyngeal collapsibility and mechanics and genioglossus muscle activation during stable non-rapid eye movement sleep. We hypothesized that lower lung volumes would lead to increased pharyngeal collapsibility, airflow resistance, and, in compensation, augmented genioglossus muscle activation.

Design: Nineteen normal individuals (age, 30.4 ± 0.5 years; body mass index,: 24.5 ± 0.4 kg/m2) were studied during stable non-rapid eye movement sleep in a rigid head-out shell equipped with a variable positive/negative pressure attachment for manipulations of extrathoracic pressure and, thus, lung volume.

Setting: Sleep physiology laboratory

Participants: Normal healthy volunteers

Interventions: N/A

Measurements and Results: We measured change in end-expiratory lung volume (EELV)(magnetometers), genioglossus electromyogram (GGEMG) (intramuscular electrodes), pharyngeal pressure, and collapsibility of the pharynx in response to a brief pulse of negative pressure (-8 to -15 cm H20) under the following conditions: (1) baseline, (2) increased EELV (+1 liter), and (3) decreased EELV (-0.6 liter). Reduced lung volumes led to increased inspiratory airflow resistance (7.54 ± 2.80 cm H20·L-1·s-1 vs 4.53 ± 1.05 cm H20·L-1·s-1, mean ± SEM, P = 0.02) and increased genioglossus muscle activation (GGEMG peak 14.6% ± 1.5% of maximum vs 8.6% ± 1.5% of maximum, maximumP = 0.001) compared to baseline. The pharynx was also more collapsible at low lung volumes (4.3 ± 0.5 cm H20 vs 5.4 ± 0.6 cm H20, P = 0.04).

Conclusions: We conclude that upper-airway muscles respond to changes in lung volumes but not adequately to prevent increased collapsibility. These results suggest that lung volume has an important influence on pharyngeal patency during non-rapid eye movement sleep in normal individuals.

Key Words: Lung volume, genioglossus, pharyngeal collapse

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INTRODUCTION

DEFINING THE MECHANISMS CONTROLLING PHARYNGEAL PATENCY DURING SLEEP IS IMPORTANT IF WE ARE TO UNDERSTAND THE PATHOPHYSIOLOGY OF OBSTRUCTIVE SLEEP APNEA (OSA), A DISORDER THAT IS CHARACTERIZED BY RECURRENT PHARYNGEAL COLLAPSE DURING SLEEP. This disorder is common and associated with important morbidity.[1-9] Substantial investigation has been directed at determining the factors modulating upper-airway patency. This work has demonstrated the importance of the interaction between upper-airway anatomy and the activation of pharyngeal dilator muscles in the pathophysiology of OSA. Stimuli that modulate pharyngeal muscle activation include intrapharyngeal negative pressure, PO_2, PCO_2, inspired air temperature, sleep-wake transitions, blood pressure, gender-specific hormones, and lung volumes.[10-22] In addition, an association between upper-airway caliber and volitional changes in thoracic gas volume has been described for both normal subjects and OSA patients during wakefulness.[23-25] Similarly, others have observed that passive lung-volume changes have important effects on pharyngeal resistance during wakefulness.[26,27] Reduced lung volume leads to increased pharyngeal resistance and airflow limitation. Thus changes in lung volume may influence airway size or mechanics and, hence, collapsibility of the pharyngeal airway during wakefulness. However, the influence of lung-volume changes on upper-airway mechanics and collapsibility during non-rapid eye movement (NREM) sleep is less clear. Begle et al previously reported reduced pharyngeal resistance with passive lung inflation during NREM sleep and, in 2 subjects, observed decreased peak genioglossus electromyogram (EMG) (GGEMG) activation.[14] Previous work from the same laboratory demonstrated that inspiratory muscle (diaphragm) EMG activity increased with lung hyperinflation during sleep.[28] Collectively these studies suggest an independent influence of lung volume on the upper airway that may importantly modulate pharyngeal muscle activation and patency or collapsibility in normal individuals. This may occur primarily through structural linkages with the thorax. At higher lung volumes, caudal displacement of the trachea may result in a stiffening of the pharyngeal airway. At low lung volumes, loss of this tension may contribute to pharyngeal collapse. However, no previous studies have systematically assessed the influence of lung volume (both increases and decreases) on pharyngeal mechanics and collapsibility and genioglossus activation in normal individuals during NREM sleep. We, therefore, hypothesized that lower lung volumes during sleep would lead to increased pharyngeal collapsibility and airflow resistance and, in response, augmented genioglossus muscle activation. Conversely, high lung volumes would lead to reduced pharyngeal collapsibility, airflow resistance, and genioglossus muscle activation.

METHODS

Subjects

We studied 19 normal individuals (16 men, 3 women) with no historical evidence of a medical problem or a sleep disorder. The protocol was

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approved by the Human Subjects Committee at Brigham and Women's Hospital. All subjects provided informed written consent prior to participation in the study. Women were studied during the follicular phase of their menstrual cycle (days 7-11 from the onset of menses).[11]

Instrumentation, Measurements, and Analysis

To assess the function of a representative upper-airway dilator muscle, the activity of the GGEMG was measured using 2 stainless-steel, Teflon-coated, wire electrodes inserted intramuscularly.[29] Each needle was inserted into the floor of the mouth at a location 3 to 5 mm on either side of the frenulum and 15 to 20 mm into the body of the genioglossus muscle near its insertion in the mandible. After insertion, the needles were extracted, leaving the intramuscular wires in place. The wires were referred to a ground electrode on the forehead. The EMG signal was amplified, band-pass filtered, (Grass Model 7P122G, Grass-Telefactor, West Warwick, RI, filter settings 50 Hz-5 kHz), rectified, and moving time averaged with a time constant of 100 milliseconds (MA-821-4 CWE, Inc, Ardmore, Penn). Peak inspiratory phasic and tonic expiratory values are reported as a percentage of maximum (as determined by swallow, maximum inspiratory force, and tongue protrusion).[29]

Airway pressures were recorded at the level of the choanae and in the hypoglossal airspace at the level of the epiglottis (Millar MPC-500 pressure catheter, Houston Tex). Before insertion of the catheters, 1 nostril was decongested with 0.05% oxymetazoline hydrochloride (Afrin) and anesthetized with 1 mL of 4% lidocaine hydrochloride topical spray. The epiglottic catheter was then inserted until visible through the mouth. It was then advanced 2 to 3 cm below the back of the tongue. The choanal catheter was advanced until it reached the posterior wall of the nasal cavity and was then pulled back 0.5 cm. After placement, both catheters were taped to the nose to ensure stability. Subjects breathed through a nasal mask (Respironics, Murraysville, Penn) with airflow being measured by a pneumotachograph (Fleisch #2, Lausanne, Switzerland) and pressure transducer (Validyne MP-45, Northridge, Calif). End-tidal carbon dioxide ($PETCO_2$) was sampled at the mask using a calibrated infrared carbon-dioxide analyzer. (BCI, Inc., Waukesha, Wisc). During these studies, the mouth was gently taped closed to eliminate mouth breathing.

To assess airway collapsibility, brief (<0.5 seconds) negative pressure pulses (-8 to -15 cm H_20 at the choanae) were applied during early inspiration.[30] The fall in pressure between the choanae and the epiglottis was quantified for each individual at each lung volume as an index of airway collapsibility, as previously described.[30] This was accomplished by subtracting the peak epiglottic from the peak choanal pressure via a signal-averaged breath for each individual, under each condition (described below).[31] We also measured genioglossus muscle responsiveness to these brief negative pressure pulses as the difference between baseline and peak activation (percentage of maximum units [% maximum units]) during the pulse.[30]

Lung volumes were manipulated with the subject lying supine in a head-out rigid shell (Porta-Lung, Denver, Colo) adapted with a vacuum/blower attachment (ShopVac, Williamsport, Penn) that increased or decreased extrathoracic pressure to produce low and high lung volumes, respectively. Changes in end expiratory lung volume (EELV) were measured with thoracic and abdominal magnetometers (Basil, Switzerland), calibrated with both 800-mL Spirobags (AMI, Ardsley, NY) and tidal volumes obtained with a pneumotachograph. Changes in EELV were determined using a standardized formula previously validated against the Konno-Mead least squares method.[32,33] Briefly, average values for changing anterior-posterior diameter (in centimeters) of the chest wall and abdomen were determined for each subject (from magnetometer recordings) during quiet breathing through a pneumotachograph, while in the supine position for 3 minutes. In addition, magnetometer recordings were obtained during 3 breaths from an 800-mL Spirobag. The change in chest wall and abdominal anterior-posterior diameter was averaged over 12 breaths and combined with the pneumotachograph data. Average change in anterior-posterior diameter values was then entered into the following equation describing the relationship between tidal volume and chest/abdominal wall excursion: $VT = X (4RC + AB)$. Tidal volume (VT) is determined using X, a coefficient determined by the calibration procedure (described above) for a given individual, and RC/AB, which represents the mean change in rib cage and abdominal wall excursion during respiration in centimeters. All calibration maneuvers were performed with subjects instrumented, lying supine, in the rigid shell. Neck position was stabilized by a nylon collar and plastic guard attached to the rigid shell, which prevented neck motion while positive and negative pressure was developed in the lung.

Wakefulness and sleep stages were determined using a standard electroencephalography, chin EMG, and electrooculogram montage. Sleep was scored according to standardized criteria.[34] If the patient awoke during any portion of the protocol, the study procedures were terminated and repeated once stable NREM sleep was again achieved. If a polysomnographic awakening or behavioral awakening occurred, that entire data file was eliminated and repeated once

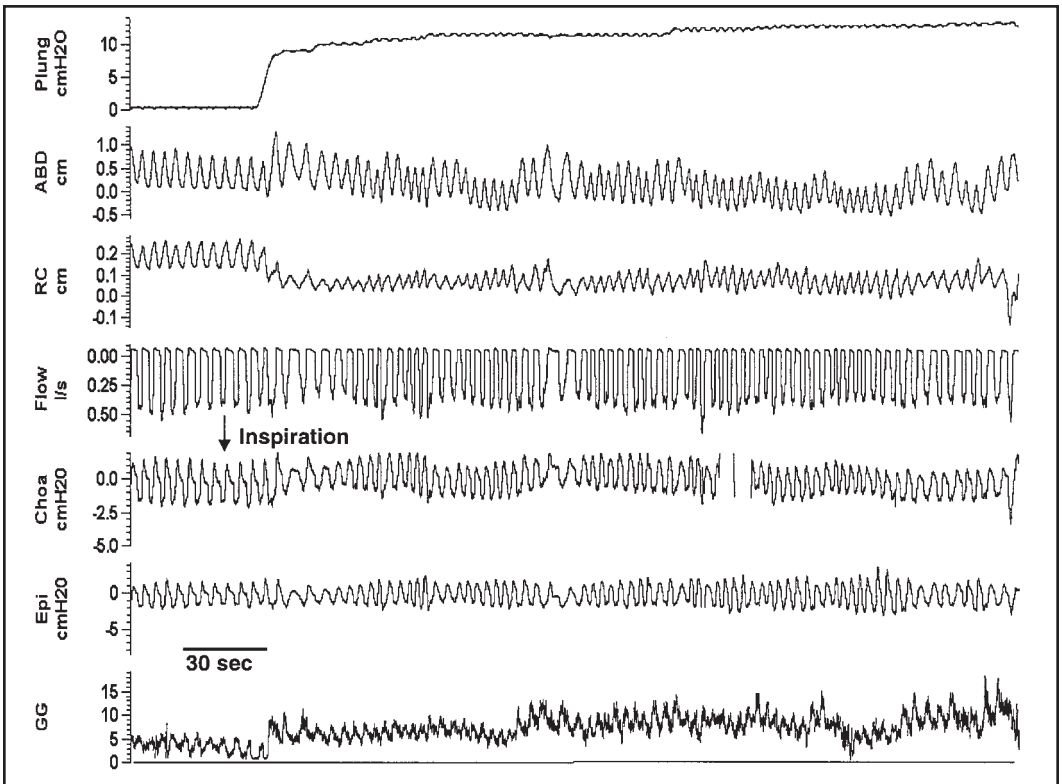

Figure 1—Raw data from 1 subject presented as a representative example of the decreasing anterior-posterior diameter of the rib cage and abdomen (cm) during the application of positive extrathoracic pressure lowering end expiratory lung volume. Note the rise in genioglossus electromyogram (GGEMG) activation as lung volumes are lowered. GG indicates genioglossus muscle activation, (% maximum units); Flow, airflow (L/min), inspiration is downward direction (arrow); RC/ABD, ribcage and abdomen magnetometer signal (cm); $PETCO_2$, end-tidal carbon-dioxide pressure (mmHg); Plung, extrathoracic pressure measured within the head-out plastic shell; Pcho, choanal pressure (cm H_20); Pepi, epiglottic pressure (cm H_20).

stable NREM sleep was again achieved. If 2 or more American Sleep Disorders Association-defined arousals were observed in a recording, the protocol was discontinued and again restarted during stable NREM sleep. We cannot rule out the possibility that non-American Sleep Disorders Association arousals were present in some patients and may have contributed to the variability in our resistance measurements. However, more-subtle measures of arousal such as heart-rate patterns were not analyzed in this study.

Protocol

After the subject achieved stable NREM sleep (Stages 2, 3, 4) in the supine position while in the rigid shell, the aforementioned signals were recorded under the conditions described below. The order of conditions was randomized.

Basal Breathing

All signals were recorded under baseline conditions for 3 minutes. Next, with the EELV at the baseline sleeping level, 20 to 40 brief negative pressure pulses (-8 to -15 cm H_20) were applied to the airway while measures of collapsibility were recorded

Increased EELV

The sleeping level of EELV was increased by approximately 1 liter with the application of continuous negative extrathoracic pressure (-8 to -20 cm H_20). After achieving a stable increased EELV, all signals were recorded for 3 minutes. Next, with the EELV increased by 1 liter, 20 to 40 brief negative pressure pulses (-8 to -15 cm H_20) were again applied.

Decreased EELV

The EELV was decreased by 600 mL from basal sleeping condition by applying continuous positive extrathoracic pressure (8 to 20 cm H_2O). After achieving a steady-state decreased EELV, all signals were recorded for 3 minutes. Next, with the EELV decreased by 600 mL, 20 to 40 negative pressure pulses (-8 to -15 cm H_20) were again applied to the upper airway.

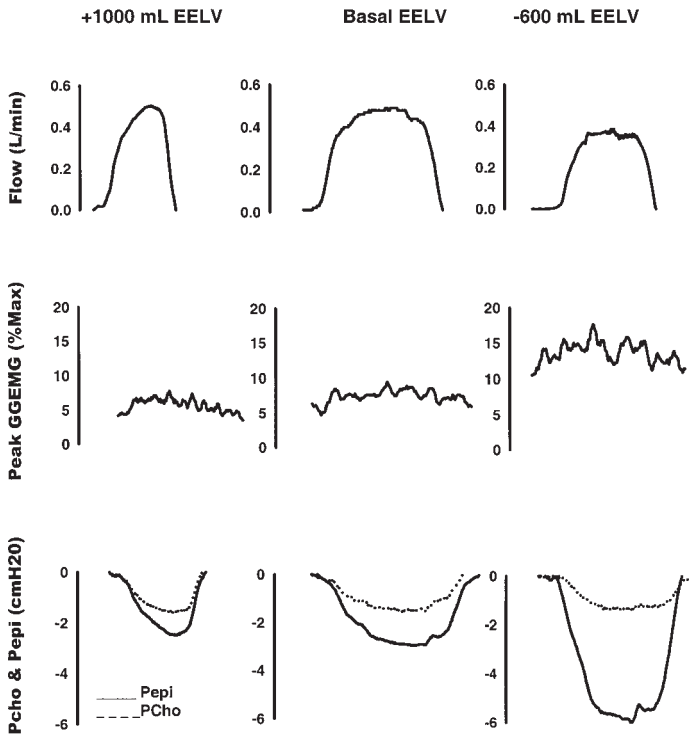

Figure 2—Data from a single individual presented as a single breath at different lung volumes. Note the influence of changing end-expiratory lung volume (EELV) on flow, peak phasic genioglossus activation (GGEMG), and pharyngeal pressures (Pcho, choanal, and Pepi, epiglottic, pressure).

Data Analysis

Signals were recorded on a 16-channel polygraph (Grass model 78, Grass-Telefactor, West Warwick, RI). The GGEMG (moving time-average signal), $PETCO_2$, airflow, airway pressures, and change in baseline end-expiratory magnetometer signal (ie, EELV) were also recorded on computer and analyzed using signal processing software (Spike 2, CED Ltd. Cambridge, UK). Signal-averaged buffer breaths were generated for analysis of GGEMG and pharyngeal resistance for each condition by aligning all consecutive breaths (from a 3-minute stable recording) to the onset of inspiratory flow. For the collapsibility analysis, 20 to 40 consecutive negative pressure pulses were signal averaged for each individual at each different lung volume and analyzed as a single signal set aligned to the beginning of the negative pressure pulse. The GGEMG response to the negative pressure pulse was also determined from these signal-averaged data. Pharyngeal resistance (choanae to epiglottis) was calculated at peak flow. The EELV change was determined by the decrease or increase in baseline magnetometer signal (expressed in centimeters) as measured at end-expiration during application of extrathoracic pressure. The absolute change in lung volume was then obtained by entering the change in baseline positions of ribcage/abdomen signal into the equation described above. Change in EELV was determined for the high and low lung-volume conditions for each subject. For each measurement, individual and group means (± SEM) were determined. A repeated-measures analysis of variance (ANOVA) was used to compare mean values for measurements between conditions, followed by a student-Newman Keuls posthoc test for normally distributed data or ANOVA on ranks for nonnormally distributed data. An α level of 0.05 was considered significant (Sigma Stat software version 2.03, SPSS Corp., Chicago, Ill). Previous experiments from this laboratory have suggested that the proposed sample size should be adequate to determine any differences in pharyngeal collapsibility and pharyngeal mechanics across different lung volumes.

RESULTS

Twelve patients (9 men, 3 women) completed the entire protocol (mean age in years, 30.4 ± 4.2; body mass index, 24.5 ± 1.2 kg/m^2) with 7 additional individuals (mean age in years, 30.2 ± 0.6; body mass index, 24.7 ± 0.3 kg/m^2) being studied only under basal and increased EELV conditions.

Mechanics

Lung volumes were increased 971 ± 30 mL by applying 13.1 ± 1.0 cm H_20 of negative extrathoracic pressure, while lung volume was decreased 582 ± 40 mL with the application of 11.7 ± 0.7 cm H_20 positive extrathoracic pressure. Figure 1 presents raw data from 1 individual during manipulation of EELV and shows the change in the baseline anterior-posterior distance measured at the chest/abdomen as lung volume decreased. Figure 2 presents 1 steady-state breath under each of the 3 lung-volume conditions (augmented EELV, baseline, and reduced EELV). The change in pharyngeal resistance (airway pressures) that occured with lung-volume manipulations is notable. Pharyngeal resistance increased at low lung volumes for the group when compared with baseline values (7.5 ± 2.8 cm $H_20 \cdot L^{-1} \cdot s^{-1}$ vs 4.5 ± 1.0 cm $H_20 \cdot L^{-1} \cdot s^{-1}$, P = 0.02) and showed a downward trend at high lung volumes (3.2 ± 0.7 cm $H_20 \cdot L^{-1} \cdot s^{-1}$ vs 4.5 ± 1.0 cm $H_20 \cdot L^{-1} \cdot s^{-1}$, P = 0.31).

Genioglossal EMG

Figures 1 and 2 demonstrate the rise in GGEMG with falling lung volume. Figure 3 (A and B) shows the individual data and means for both

peak phasic and tonic GGEMG activation. As can be seen (Figure 3), decreased EELV led to increases in GGEMG compared to baseline (peak phasic, 14.90% ± 1.53% of maximum units vs 8.56% ± 1.50% of maximum units, P <0.001; tonic, 9.87% ± 1.04% of maximum units vs 5.58% ± 1.50% of maximum units, P <0.001). The GGEMG tended to decrease at high lung volumes (peak phasic, 7.16% ± 1.56% of maximum units vs 8.56% ± 1.50% of maximum units, P = 0.15; tonic, 4.34% ± 0.90% of maximum units vs 5.58% ± 1.50% of maximum units, P = 0.12) although these differences did not reach statistical significance. The $PETCO_2$ did not change when lung volume was reduced (42.2 ± 2.3 mmHg vs 42.3 ± 2.2 mm Hg, P = 0.22) but was elevated compared with baseline (43.4 ± 0.6 mm Hg vs 42.2 ± 2.3 mmHg, P = 0.003) at increased lung volume. Genioglossus muscle responsiveness (% of maximum) to brief negative pressure pulses was not statistically different at high or low lung volumes compared to baseline values (baseline lung volume: 1.11% ± 0.33 % of maximum units; increased lung volume: 2.32% ± 0.56% of maximum units; decreased lung volume: 3.46% ± 1.53% of maximum units, P = 0.07). In addition, these values are comparable to the reduced responsiveness of the genioglossus previously observed during sleep by Wheatley et al.[30] They observed a change in genioglossus moving time-averaged EMG from basal to peak levels during NREM sleep of 2.7% ± 1.2% of maximum units.

Collapsibility

Pharyngeal collapsibility was affected by changing lung volume. Figure 4 illustrates the individual and group mean results for the changes in collapsibility at different lung volumes. Data for the group show that the pharynx was more collapsible at reduced EELV during NREM sleep (4.3 ± 0.5 cm H_20 vs 5.4 ± 0.6 cm H_20, P = 0.04), while at high lung volumes, the pharynx tended to be less collapsible (3.5 ± 0.6 cm H_20 vs 4.3 ± 0.5 cm H_20, P = 0.21).

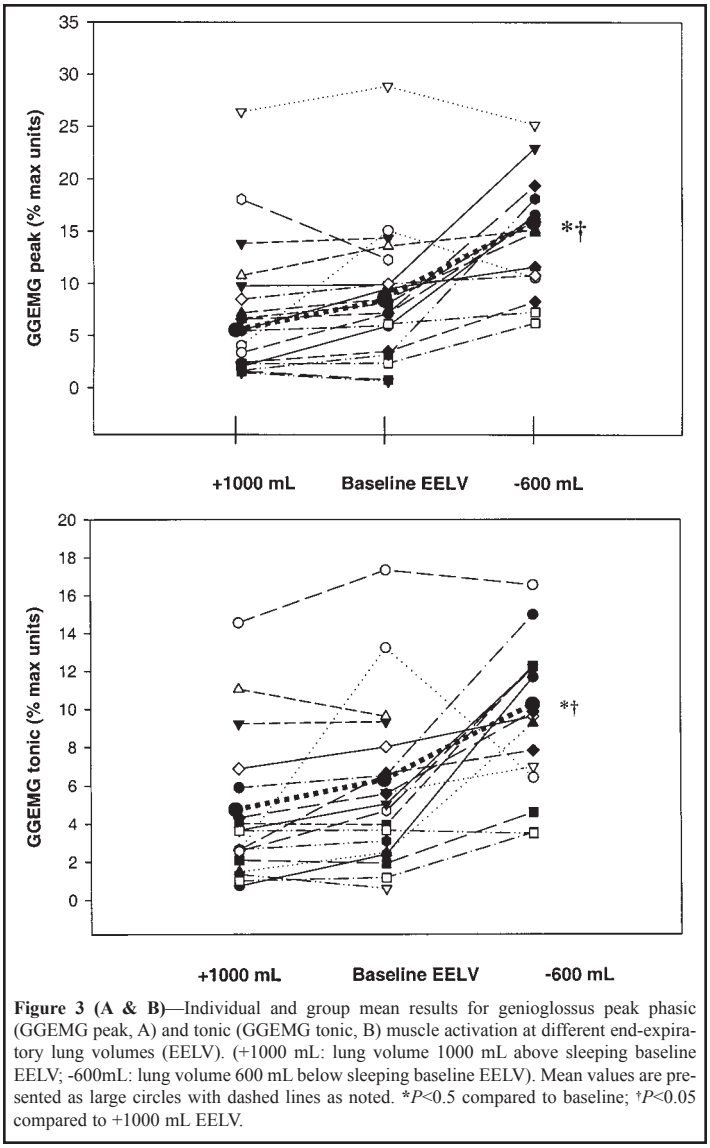

Figure 3 (A & B)—Individual and group mean results for genioglossus peak phasic (GGEMG peak, A) and tonic (GGEMG tonic, B) muscle activation at different end-expiratory lung volumes (EELV). (+1000 mL: lung volume 1000 mL above sleeping baseline EELV; -600mL: lung volume 600 mL below sleeping baseline EELV). Mean values are presented as large circles with dashed lines as noted. *P<0.5 compared to baseline; †P<0.05 compared to +1000 mL EELV.

DISCUSSION

The results of this study indicate that in normal individuals, during NREM sleep, passive changes in lung volume influence upper-airway mechanics, collapsibility, and genioglossus muscle activation. Low lung volumes are associated with increased airflow resistance and collapsibility despite increased genioglossal muscle activity.

Pharyngeal Collapsibility

These observations suggest that a lung-volume dependence of upper-airway collapsibility exists during NREM sleep when the EELV is passively manipulated. The etiology of this change in pharyngeal collapsibility is not entirely clear. However, 4 mechanisms are plausible. First, altering lung volumes may lead to anatomic changes in the airway, such that a decreased EELV leads to a smaller and thus more collapsible pharyngeal airway. Previous reports have noted that upper-airway size is smallest when lung volumes are volitionally reduced to residual volume or passively lowered with positive extrathoracic pressure during wakefulness.[23,27] This may be important given that the smaller airway size in OSA patients[35] has been associated with greater pharyngeal collapsibility compared to controls. Second, altering lung volumes may change surface tension in the airway, which could accentuate or attenuate pharyngeal collapsibility. Thus the increased pharyngeal resistance we observed, coupled with a reduced airway size at low lung volume, would lead to increased surface tension favoring airway collapse.[36] Third, altered activation of the pharyngeal dilator muscle by changes in EELV may affect pharyngeal collapsibility. We observed that, at low lung volumes, peak genioglossus muscle activation increased. However, pharyngeal collapsibility also increased with similar but opposite results occurring with increased lung volumes. Thus genioglossus activation certainly did not contribute to the increased collapsibility observed at low lung volumes, although it did not completely compensate for it either. Fourth, tethering forces between the upper airway and the thoracic cage may lead to changes in pharyngeal collapsibility.[37-40] Van de Graaff observed in mongrel dogs that airway resistance could be decreased, despite denervation of the upper airway muscles, by increasing traction on the trachea. The pharyngeal airway segment lengthens with caudal displace-

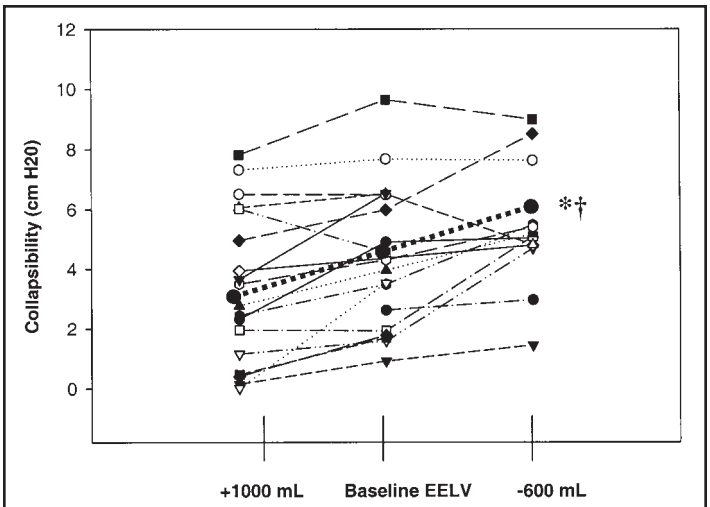

Figure 4—Individual and group mean results for the pharyngeal collapsibility measured at different end-expiratory lung volumes (EELV). (+1000 mL: lung volume 1000 mL above sleeping baseline EELV; -600 mL: lung volume 600 mL below sleeping baseline EELV). Mean values are presented as large circles with dashed lines as noted. *P<0.5 compared to baseline; †P<0.05 compared to +1000 mL EELV.

ment, thereby stiffening the airway. Similarly, we propose that when lung volumes are passively augmented in sleeping humans, the upper airway is unfolded and stretched, making it less compliant and thus less collapsible.

Pharyngeal Resistance

Upper-airway resistance measured at peak flow was increased during the low lung-volume condition in this study. Aronson et al have reported[41] that, with passive hyperinflation during wakefulness (2.24 L above resting EELV), upper-airway resistance was reduced 67.8% compared to control. At low lung volumes (0.86 L below resting EELV), pharyngeal resistance increased by 172% compared to controls. We observed similar findings during stable supine NREM sleep, yet of smaller magnitude, while lung volume was manipulated. Upper-airway resistance commonly is increased at sleep onset and further increases with advancing stages of sleep.[42-44] The explanation for this rise in pharyngeal resistance has been attributed to a loss of tonic upper-airway muscle activation or changes in airway compliance, surface adhesive forces, and possibly vascular perfusion. The results from this study suggest that decreasing lung volume is associated with increased pharyngeal resistance, although the mechanism of this association remains unclear. Thus, falling lung volume may contribute to the increment in upper-airway resistance noted in normal subjects. We did note substantial variability in upper-airway resistance among subjects, suggesting that individual responsiveness to changing EELV may be quite different. This is supported by the previous findings of Wiegand and colleagues who reported substantial variability in the response to external loads applied to the upper airway.[45] Whether this relates to differences in pharyngeal anatomy, muscle activation, tissue compliance, or yet-to-be-defined variables is unclear at this time.

Genioglossus Muscle Activation

Changing EELV led to alterations in both peak and tonic genioglossus activation. The stimulus to the increase in GGEMG cannot be established from these studies, although several possibilities were considered. First, the absence of vagal lung-inflation feedback induced by restriction of the chest at low lung volumes may contribute to the increased peak GGEMG that we observed. Thus, by limiting maximal chest-wall expansion with positive extrathoracic pressure, we may have removed the vagally mediated reflexes that generally inhibit upper-airway muscle activity. Hence at low lung volumes, the GGEMG was substantially augmented compared to baseline. Second, by lowering lung volumes and thus altering chest-wall mechanics, we may have increased respiratory drive and, hence, output from the central respiratory-pattern generator to the genioglossus. Third, our group and others have previously observed that, during wakefulness, negative pharyngeal (epiglottic) pressure is important for genioglossus muscle activation (GGEMG),[30] but during NREM sleep, combinations of chemical and mechanical input are necessary to activate this muscle.[22,46] In the present study, pharyngeal resistance increased at low lung volumes and tended to decrease at high lung volumes, although, as noted above, there was wide variability in individual measures. Negative epiglottic pressure was higher in the low lung-volume condition and lower in the high lung-volume condition but correlated poorly with absolute values or changes in peak phasic GGEMG. Thus we cannot directly attribute changes in muscle activity to changes in epiglottic pressure. In addition, no significant change in $PETCO_2$ was noted in the low lung-volume condition and thus cannot explain the increased GGEMG we observed. Finally, the influence of lung volume on the magnitude of the genioglossus response to negative pressure pulses was examined. No significant difference was noted across lung volumes, although the low lung-volume condition was associated with the greatest genioglossus muscle responsiveness to negative pressure. This degree of muscle responsiveness to a negative pressure stimulus is similar to the substantially reduced levels observed previously in sleeping individuals compared to the responsiveness awake.[30]

The potential clinical relevance of the increase in GGEMG observed during the low lung-volume condition deserves comment. We observed nearly a doubling of baseline genioglossus muscle activity in response to passively reduced EELV. Despite this, increased resistance and collapsibility of the pharyngeal airway was observed at low lung volumes. This suggests that genioglossus muscle activation has little effect on pharyngeal patency or collapsibility. However, if the GGEMG were not activated, it is likely that pharyngeal collapsibility and resistance might have increased further. The ability to recruit muscle units during sleep, although incomplete to prevent pharyngeal collapse in this model, may be an important factor in preventing further upper-airway collapse after sleep onset in some individuals.

The increase in tonic GGEMG activity deserves comment as well. This activity has been shown to be augmented in OSA patients compared to controls.[29] In addition, Orem et al[47] and Tangel et al[48] have observed a larger attenuation in tonic neural or muscle activation during NREM sleep when compared to phasic activity. However, our data would suggest that this tonic component of muscle activation can respond during sleep to changes in lung volume, although, as for phasic activity, the mechanism driving the increased activation remains unclear.

The relevance of these data to the lung-volume changes that normally occur during sleep also deserves comment. Hudgel et al[49] reported that functional residual capacity declines by 280 mL from sleep onset to stable NREM sleep. On the other hand, Ballard et al observed functional residual capacity to decrease by 440 mL during NREM sleep (2.95 ± 0.13 L vs 2.51 ± 0.14 L).[15] These decrements in lung volume likely contribute to the rise in resistance commonly seen during sleep.[50] The passive lung-volume changes induced in this study were of greater magnitude than the normal situation. However, we attempted not to emulate the normal physiologic changes in EELV at sleep onset, but rather to test the hypothesis that lung-volume changes could have an important effect on pharyngeal mechanics and collapsibility. We observed that the airway was more collapsible following a slightly greater decrease in lung volume (582 ± 40 mL). Although no data in this study were collected in OSA patients, we speculate that similar falls in lung volume may have a greater affect in these patients due to their already compromised airway. Alternatively, due to obesity, they may have greater falls in lung volume.

Several limitations to this study should be noted. First, we did not directly measure lung volume but only changes in EELV. Thus, the absolute lung volumes may have been different between subjects. However, in each subject, we measured pressure-induced lung-volume change from baseline during stable NREM sleep. Thus each subject served as his or her own control, which improves the validity of the observations. In addition, at the end of each condition, we remeasured the change in EELV and found no substantial differences from the beginning of the condition. Second, all of our subjects slept in the supine position, which favors collapse of the pharyngeal airway and thus may have accentuated the lung-volume effect on airway mechanics and genioglossus muscle activation. However, we wanted to test for maximal effects and, thus, used this posture. Third, our measure of pharyngeal collapsibility using negative pressure pulses applied to the upper airway is an indirect measure. However, it has been used in previous studies and although it does not duplicate the intrathoracic pressure that arises within the thorax due to descent of the diaphragm (ie, the pressure is generally greater), collapsibility results using this method do correlate well with other approaches.[51] Finally, altered pressure surrounding the neck generated during changes in extrathoracic pressure may have influenced our outcomes. However, we believe this effect to be negligible for several reasons. First, during previous experiences with iron-lung ventilation, a similar tight seal was used at the neck and during mechanical inspiration (negative extrathoracic pressure), and we observed increased not decreased pharyngeal resistance. Thus negative pressure surrounding the neck in that situation clearly did not dilate the pharyngeal airway. Second, in most individuals, the neck seal was below the larynx. Thus pressures generated this low on the neck are unlikely to affect resistance in the posterior airspace. Finally, a form-fitting piece of Plexiglas was

firmly attached to the Porta-Lung, which separated the nylon webbing from the subject's chin. This apparatus reduced both rostral or caudal movement of the nylon webbing and bowing of the webbing into the subject's chin. Thus, we reduced the effect of head extension and flexion, which has been previously shown by Wasiko et al to alter pharyngeal mechanics and genioglossus muscle activation.[52] Thus we believe direct affects at the neck to be minimal.

In conclusion, we observed that passive lung-volume changes influence pharyngeal patency during NREM sleep in normal individuals. The upper-airway muscles responded to changes in lung volume but did not do so adequately to prevent increased collapsibility. We speculate that during NREM sleep, decrements in lung volume may contribute to increased pharyngeal resistance and collapse. We further speculate that these changes in lung volume may contribute to the pathophysiology of OSA.

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