Reduced genioglossal activity with upper airway anesthesia in awake patients with OSA

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Fogel, Robert B., Atul Malhotra, Steven A. Shea, Jill K. Edwards, and David P. White. Reduced genioglossal activity with upper airway anesthesia in awake patients with OSA. J Appl Physiol 88: 1346–1354, 2000.—We examined whether topical upper airway anesthesia leads to a reduction in genioglossal (GG) electromyogram (EMG) in patients with obstructive sleep apnea (OSA). Airway mechanics were also evaluated. In 13 patients with OSA, we monitored GG EMG during tidal breathing and during the application of pulses of negative airway pressure (−10 to −12 cm H2O). Airflow resistance and airway collapsibility were determined. All measurements were performed with and without topical anesthesia (lidocaine). Anesthesia led to a significant fall in the peak GG EMG response to negative pressure from 36.1 ± 4.7 to 24.8 ± 5.3% (SE) of maximum (P < 0.01). This was associated with a fall in phasic and tonic EMG during tidal breathing (phasic from 24.4 ± 4.1 to 16.4 ± 3.4% of maximum and tonic from 10.9 ± 1.6 to 8.0 ± 1.3% of maximum, P < 0.01). A significant rise in pharyngeal airflow resistance was also observed. Our results demonstrate that topical receptor mechanisms in the nasopharynx importantly influence dilator muscle activity and are likely important in driving the augmented dilator muscle activity seen in the apnea patient.

upper airway dilator muscles; genioglossal muscle; pharyngeal muscles; neuromuscular adaptation; electromyogram; obstructive sleep apnea

THERE IS SUBSTANTIAL EVIDENCE in animals and humans that the activity of the upper airway dilator muscles plays an important role in maintaining airway patency during breathing (28). Many of the pharyngeal dilator muscles are known to demonstrate inspiratory phasic activity, the timing of which often precedes diaphragmatic activity, thus “preparing” the pharyngeal airway for the development of negative pressure during inspiration. It has been shown in patients with obstructive sleep apnea (OSA) during wakefulness that there is augmented activity of the genioglossal (GG) muscle as well as other pharyngeal muscles compared with healthy subjects without sleep apnea (20). This activity is thought to represent a neuromuscular compensatory mechanism for an anatomically small and more collapsible pharyngeal airway. This augmented upper airway dilator muscle activity is lost at sleep onset and is associated with pharyngeal collapse (19).

The activity of the pharyngeal dilator muscles is influenced by numerous variables, including blood gases (arterial PO2 and PCO2), sleep-wake state, gender-specific hormones, blood pressure, temperature, lung inflation, and intrapharyngeal negative pressure (9, 10, 13, 14, 19, 23–25). The relative role that each plays in the augmented basal level of muscle activity in patients with OSA has not been established. It is well known that the application of negative pressure to the pharyngeal airway in animals and humans leads to a substantial increase in the activity of the GG muscle as well as other upper airway muscles (9, 16, 29). The time course of this response (maximal response within 200 ms) suggests that it is a neural reflex. It has also been shown that the GG muscle response to negative pressure can be substantially reduced or abolished by the combination of nasopharyngeal anesthesia and superior laryngeal nerve blockade, suggesting that mucosal receptors in these areas mediate the afferent limb of this reflex (9, 16). However, a role for muscle spindles in this reflex has not been ruled out. It has been proposed that this negative pressure reflex is the principal stimulus to the neuromuscular compensation observed in apnea patients.

In the majority of human studies in which this reflex has been assessed, fairly large negative pressures (−10 to −25 cm H2O) have been applied to the airway to activate it (9, 10, 29). Whether the relatively small changes in pressure that occur in the pharynx during tidal breathing in normal subjects and apnea patients can activate this reflex, leading to increased muscle activity, is unclear. However, it seems likely that topical receptor mechanisms, responsive to local conditions (negative pressure, airflow resistance, airway deformation, or muscle stretch) on a breath-by-breath basis, exist and are responsive to changes in airway mechanics. Such local reflex mechanisms may play a role in neuromuscular compensation for individual variability in airway size and shape, mucosal blood flow, and tissue characteristics, all of which are likely to play a role in determining an individual’s susceptibility to upper airway collapse.

It has previously been demonstrated that dense upper airway anesthesia leads to increased airflow...
resistance during sleep in healthy subjects and a prolongation of apnea in patients with OSA (3, 7). We recently demonstrated in normal subjects that dense upper airway anesthesia leads to a significant fall in basal GG muscle activation [peak phasic and tonic GG electromyogram (EMG)] accompanied by a trend toward rising pharyngeal airflow resistance and airway collapsibility (30). Thus, in normal subjects, topical receptor mechanisms located in the upper airway importantly modulate upper airway dilator muscle activity, even during normal tidal breathing. However, it remains unknown whether these mechanisms are also important in driving the augmented dilator muscle activity in the apnea patient during wakefulness. To address this question, we determined the influence of topical naso- and oropharyngeal anesthesia on basal GG activity and the muscle response to negative pressure and pharyngeal airway mechanics in awake patients with OSA. We hypothesized that such anesthesia would substantially reduce the negative pressure reflex, which would be associated with diminished GG muscle activity during tidal breathing, leading to increased airflow resistance and airway collapsibility.

**METHODS**

Thirteen patients (10 men and 3 women) with moderate-to-severe OSA syndrome (apnea-hypopnea index ≥25/h of sleep) were studied. The participants were recruited from patients referred to the sleep laboratory of the Brigham and Women's Hospital. None had serious medical problems or were on medications likely to affect upper airway muscle function. A history and an upper airway examination were performed to ensure that the patients were without known nasal or upper airway disease, including nasal polyps, septal deviation, or chronic nasal congestion. None had undergone surgical therapy for sleep apnea. Premenopausal women were studied during the follicular phase of the menstrual cycle (between days 5 and 11, with day 1 being the 1st day of menses). Informed consent was obtained from each patient; the protocol had the prior approval of the Human Subjects Committee of the Brigham and Women's Hospital.

Instrumentation and techniques for the study were as follows. Breathing was monitored with a nasal continuous positive airway pressure (CPAP) mask (Healthdyne Technologies, Marietta, GA) connected to a two-way valve partitioning inspiration and expiration. Inspiratory flow was determined with a pneumotachograph (Fleisch, Lausanne, Switzerland) and a differential pressure transducer (Validyne, Northridge, CA). This instrument was calibrated with a rotameter, and the inspiratory flow signal was integrated to produce tidal volume (Grass 7P10 integrator). Expiratory mask leaks were the inspiratory flow signal was integrated to produce tidal

**CA**. This instrument was calibrated with a rotameter, and the differential pressure signal was referenced to the atmosphere (just external to the nares) was determined with a standard water manometer. These three signals, plus flow, were simultaneously used in a rigid cylinder before insertion with use of a standard water manometer. These three signals, plus flow, were demonstrated to be without amplitude or phase lags at up to 2 Hz.

Negative airway pressure stimuli were generated using a partially evacuated 50-liter canister and a solenoid valve, as described previously (9). The canister was pressurized to between −60 and −80 cmH₂O, and negative pressure could be applied to the upper airway at a predetermined point in early inspiration by triggering the solenoid valve at a preset inspiratory flow threshold. Each negative pressure application had a rapid onset and offset for a total duration of <0.5 s. Each negative pressure application generated 8 to −14 cmH₂O pressure at the choanae, with a goal of −10 to −12 cmH₂O. An index of airway collapsibility was assessed during negative pressure application, as previously described (29). This collapsibility index was taken as the pressure difference between the choanae and the epiglottis during negative pressure application (29). If the pharyngeal airway were a completely rigid tube, there would be no pressure drop between these two points during negative pressure application. However, if the airway were completely collapsible, none of the pressure applied at the choanae would be transmitted to the epiglottis. All levels of collapsibility between these extremes should be quantifiable.

Nasopharyngeal anesthesia was accomplished with nebulized 4% lidocaine hydrochloride applied to both nasal passages until a cotton-tipped swab could be inserted with minimal detection. The oropharynx was next anesthetized, with a goal of achieving loss of the gag reflex, as well as effective laryngeal anesthesia, as manifested by the subjective sensation of difficulty swallowing. All studies performed under anesthesia were completed within 30 min because of the short duration of action of lidocaine.

Experimental protocol. Each subject reported to the laboratory during the day, having been without food for ≥4 h. After

-25 gauge needle, which was quickly removed, leaving the wire in place. The two electrodes were inserted on opposite sides of the muscle, each just lateral to the frenulum and close to the GG muscle insertion onto the mandible, as previously described (20). Each electrode was referenced to a common ground (placed on the forehead) to yield a bipolar recording. The raw EMG was amplified, band-pass filtered (between 30 and 1,000 Hz), rectified, and electronically integrated on a moving-time-average (MTA) basis with a time constant of 100 ms (CWE, Ardmore, PA). The GG EMG was quantified as a percentage of the maximal signal for the muscle established during three maneuvers: swallowing, maximal negative inspiratory force against an occluded airway, and maximal tongue protrusion against the front teeth (20, 24). The highest single EMG value was considered to be 100%, and electrical zero was defined as 0% activity.

Pressures were monitored in the nasal mask and in the airway at the level of the choanae and the epiglottis. One nostril was decongested (oxymetazoline hydrochloride) and anesthetized (lidocaine hydrochloride), and two pressure-tipped catheters (model MPC-500, Millar, Houston, TX) were inserted through this nostril to determine choanal and epiglottic pressures. One was located at the choanae by advancement through the nostril until it impacted the posterior nasopharyngeal wall. It was then extruded 0.5 cm and taped to the nose to ensure stability. The second catheter tip was located at the level of the epiglottis by visual inspection through the mouth. It also was taped to the nose. Mask pressure (just external to the nares) was determined with a differential transducer (Validyne) referenced to the atmosphere. All three pressure signals were calibrated simultaneously in a rigid cylinder before insertion with use of a standard water manometer. These three signals, plus flow, were demonstrated to be without amplitude or phase lags at up to 2 Hz.

Any data collected during episodes of drowsiness were discarded. During drowsiness, the patients were instructed to keep their eyes wide open throughout the study. The GG EMG was recorded using two stainless steel Teflon-coated 30-gauge wire electrodes. Each was inserted 15–20 mm into the body of the GG muscle with the use of a
informed consent was obtained, the pressure catheters, EMG
wires, and nasal CPAP mask were attached, and the subject
lay in the supine posture. Each subject was studied under two
temporary conditions: in the baseline state and after nasopharyngeal
anesthesia. The order of the studies was arbitrarily assigned.
If the subject was studied in the anesthetized condition first,
1 h was allowed to pass between the collection of this data set
and the collection of basal data.

The subject was initially monitored during tidal breathing
for ~15 min and then during repeated trials of negative
pressure application until ~40 negative pressure applications
had been collected under each experimental condition.

Data recording and analysis. All signals [GG EMG (raw
and MTA), airway pressure (mask, choanal, and epiglottic),
inspiratory flow, and tidal volume] were recorded on a 16-
channel polygraph (model 78, Grass Instruments, Quincy,
MA). Certain signals (GG EMG MTA, airway pressures, and
inspiratory flow) were also recorded onto a computer by use of
signal-averaging software (SIG-AVG, Cambridge Electronic
Design, Cambridge, UK). During the basal breathing condi-
tion, all signals were digitized at 200 Hz. The computer
triggered off inspiratory flow, storing data for 0.5 s before and
3.5 s after the initiation of inspiration. The computer gener-
ally sampled every third or fourth breath, and sampling was
continued until ≥50 breaths had been collected. All breaths
were subsequently signal averaged, yielding a single cali-
brated waveform of each variable for subsequent data analy-

During negative pressure application, all signals were
digitized at 1,000 Hz, and signal averaging was performed
with the waveform centered around the start of the negative
pressure application as detected on the choanal pressure
signal. The onset of negative pressure at the choanae was
considered time 0. The latency of the GG EMG response was
measured as the interval from time 0 until a rapid rise in the
GG EMG signal was detected. The peak GG EMG response
and its latency were also determined from the signal-
averaged waveform of many breaths. The GG EMG response
to negative pressure was quantified as the increase in GG
EMG from time 0 to its maximum during the negative
pressure stimulus. This increase in GG EMG was determined
(within each condition in each subject) in several ways: 1) as
the peak GG EMG value obtained (in percentage of maximum
units), 2) as the change in EMG from time 0 to the peak value
(in percentage of maximum units), and 3) as percent change
from baseline (time 0). The percent change was calculated
using the following formula: [(peak GG EMG — baseline GG
EMG)/baseline GG EMG] × 100 (20, 29). This allowed for
valid comparisons between the anesthetized and unanesthe-
tized states.

To ensure that topical anesthesia did not lead to a reduc-
tion in central respiratory drive (which might then alter
upper airway muscle activity), we measured ventilatory
variables on a breath-by-breath basis during 1 min of basal
respiration before and during anesthesia. These included
peak inspiratory flow, tidal volume, inspiratory time, and
minute ventilation. The number of swallows in the first 3 min
of basal breathing were counted as well.

Statistical analysis. All statistical analyses were per-
formed with commercially available software (Statview ver-

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Base</th>
<th>Anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>45.82 ± 11.36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height, cm</td>
<td>171.45 ± 9.52</td>
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</tr>
<tr>
<td>Weight, kg</td>
<td>116.77 ± 20.85</td>
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<td></td>
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<tr>
<td>Body mass index, kg/m²</td>
<td>40.40 ± 10.38</td>
<td></td>
<td></td>
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<tr>
<td>Apnea-hypopnea index, no./h sleep</td>
<td>66.93 ± 31.72</td>
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</table>

Values are means ± SE.

RESULTS

A total of 13 patients (10 men and 3 women) com-
pleted the protocol. The characteristics of the patients
are listed in Table 1. The patients were fairly represen-
tative of those with moderate-to-severe OSA, in that
they were middle-aged and moderately obese. EMG
data sets were acquired in all 13 patients. Data sets for
analysis of airflow resistance and airway collapsibility
were acquired in 11 patients; in 2 patients, difficulties
with equipment made it impossible to obtain adequate
pressure measurements. Table 2 summarizes the mea-
sured ventilatory parameters before and during upper
airway anesthesia. Although there were not significant
differences in peak flow, inspiratory time, minute venti-
lation, or the number of swallows that occurred during
the anesthetized state, there was a significant increase
in tidal volume after anesthesia (0.65 ± 0.18 vs. 0.79 ±
0.28 liter).

Negative pressure reflex. Table 3 summarizes the
results of the effects of anesthesia on the GG reflex
response to negative pressure. This is also demon-
strated in Fig. 1 for the 11 patients in whom all
necessary signals were obtained. Table 3 shows a
significant reduction in the GG negative pressure reflex
after upper airway anesthesia. This is demonstrated by
the reduction in peak EMG response to negative pres-
sure from 36.08 ± 6.25 to 24.78 ± 5.32% of maximum
(P < 0.01). Anesthesia also led to an attenuation in the
absolute increase in GG EMG in response to negative
pressure (12.65 ± 3.35 vs. 6.62 ± 1.99% of maximum,
P < 0.01) and the percent change in GG EMG during

Table 2. Ventilatory parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No Anesthesia</th>
<th>Anesthesia</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak flow, l/s</td>
<td>0.67 ± 0.05</td>
<td>0.64 ± 0.06</td>
<td>NS</td>
</tr>
<tr>
<td>Tidal volume, ml</td>
<td>647 ± 184</td>
<td>789 ± 283</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Minute ventilation, l/min</td>
<td>10.75 ± 2.9</td>
<td>12.25 ± 3.7</td>
<td>NS</td>
</tr>
<tr>
<td>Inspiratory time, s</td>
<td>1.82 ± 0.98</td>
<td>1.72 ± 0.56</td>
<td>NS</td>
</tr>
<tr>
<td>No. of swallows in 3 min</td>
<td>1.77 ± 1.8</td>
<td>1.85 ± 1.51</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are means ± SE. NS, not significant.
negative pressure (95.84 ± 23.38 vs. 41.47 ± 10.80% of maximum, \( P < 0.01 \)). There was no significant difference in the latency to peak GG EMG, in the peak choanal pressure used to stimulate the reflex, or in the timing of the onset of negative pressure between the anesthetized and unanesthetized conditions.

Basal GG EMG. Upper airway anesthesia led to a significant reduction in inspiratory phasic and expiratory tonic muscle activity (Table 4). The peak phasic GG EMG declined from 24.41 ± 4.08 to 16.38 ± 3.36% of maximum (\( P < 0.01 \)), whereas the tonic expiratory EMG decreased from 10.94 ± 1.57 to 7.99 ± 1.34% of maximum (\( P < 0.01 \)). A representative example of the signal-averaged results from one patient during normal respiration before and after anesthesia is shown in Fig. 2. As shown in Fig. 2, although inspiratory phasic activation of the GG muscle is still present in the anesthetized state, it is markedly reduced. For the group, the decrease in inspiratory phasic basal GG EMG after anesthesia was significantly correlated with the decrease in peak GG EMG response to negative pressure (\( r = 0.73, P = 0.01 \); Fig. 3).

Airway mechanics. The indexes of airway mechanics derived during basal breathing (resistance) and during negative pressure application (collapsibility) are shown in Table 5. Airway collapsibility was slightly increased after upper airway anesthesia, although this difference did not reach statistical significance (4.90 vs. 6.22 cmH\(_2\)O, \( P = 0.08 \)). After airway anesthesia, significant increases in pharyngeal and supraglottic resistance were seen. When measured at peak inspiratory flow, there was a significant increase in pharyngeal resistance from 3.70 to 4.53 cmH\(_2\)O·l\(^{-1}\)·s \( (P < 0.05) \). When measured at 0.2 l/s, pharyngeal resistance (from 2.18 to 4.72 cmH\(_2\)O·l\(^{-1}\)·s; \( P = 0.02 \)) and supraglottic resistance (from 3.05 to 6.13 cmH\(_2\)O·l\(^{-1}\)·s; \( P = 0.02 \)) increased (Fig. 4). There was no change in nasal resistance with upper airway anesthesia. We were unable to demonstrate any significant correlation between the change in basal muscle activation and increasing airflow resistance. However, a trend was seen between the change in peak phasic GG EMG and the change in pharyngeal airflow resistance (\( r = -0.57, P = 0.09 \)).

**DISCUSSION**

Our results indicate that pharyngeal anesthesia leads to a decrement in the responsiveness of the GG muscle to pulses of negative airway pressure in awake patients.

### Table 3. GG response to negative pressure

<table>
<thead>
<tr>
<th></th>
<th>No Anesthesia</th>
<th>Anesthesia</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal GG EMG, % of max</td>
<td>23.43 ± 4.72</td>
<td>18.16 ± 4.04</td>
<td>0.07</td>
</tr>
<tr>
<td>Peak response, % of max</td>
<td>36.08 ± 6.25</td>
<td>24.78 ± 5.32</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>( \Delta ) EMG, % of max</td>
<td>12.65 ± 3.35</td>
<td>6.62 ± 1.99</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>% Reflex increase</td>
<td>95.84 ± 23.38</td>
<td>41.47 ± 10.80</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Latency to response, ms</td>
<td>44.00 ± 9.59</td>
<td>47.31 ± 10.16</td>
<td>NS</td>
</tr>
<tr>
<td>Peak choanal negative pressure, cmH(_2)O</td>
<td>11.63 ± 0.43</td>
<td>11.62 ± 0.40</td>
<td>NS</td>
</tr>
<tr>
<td>Latency to negative pressure onset, ms</td>
<td>189 ± 41</td>
<td>171 ± 37</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are means ± SE. GG, genioglossus muscle; EMG, electromyogram; max, maximum; \( \Delta \), change.

### Table 4. Basal GG EMG

<table>
<thead>
<tr>
<th></th>
<th>No Anesthesia</th>
<th>Anesthesia</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expiratory tonic GG EMG, % of max</td>
<td>10.94 ± 1.57</td>
<td>7.99 ± 1.34</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Inspiratory phasic GG EMG, % of max</td>
<td>24.41 ± 4.08</td>
<td>16.38 ± 3.36</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Phasic EMG, % of max</td>
<td>13.40 ± 2.90</td>
<td>8.38 ± 2.27</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Values are means ± SE.

Fig. 1. Signal-averaged results from all subjects demonstrating genioglossal (GG) electromyogram (EMG) response to negative pressure application before (A) and during (B) topical anesthesia. P choanal, pressure at choanae; P epiglottic, pressure at epiglottis; max, maximum. Note marked reduction in peak GG EMG response to negative pressure with anesthesia. Pharyngeal airway also became more collapsible (pressure difference between choanae and epiglottis, arrow) after anesthesia.
with OSA, as has been previously demonstrated in normal subjects (9). Associated with this decrease in the negative pressure reflex was a significant reduction in peak phasic and tonic GG EMG after anesthesia and an increase in pharyngeal airflow resistance. A trend toward increasing airway collapsibility during negative pressure was also seen ($P = 0.08$). In addition, the decrease in peak GG EMG response to negative pressure after topical anesthesia was correlated with the decrease in peak phasic GG EMG during basal breathing. These results strongly suggest that local mucosal receptors in the upper airway importantly influence GG activity in patients with OSA. From these results, however, we cannot definitively conclude that the decrement in muscle activity is a direct product of the reduced reflex responsiveness.

A great deal of prior work in humans and animals indicates that the application of negative pressure to the upper airway leads to a reflex increase in dilator muscle activity (10, 15, 16, 29). Multiple upper airway muscles have been studied in humans, and the results have been quite consistent (10, 29). However, several problems exist with these studies if the results are to apply to the physiological situation in the OSA patient. First, in the majority of these studies, relatively large negative pressure pulses were utilized (−7 to −25 cmH$_2$O). These pressures are much larger than those generated during normal breathing, even in the apnea patient. Second, the majority of these studies looked at

| Table 5. Airflow resistance and collapsibility |
|-----------------|-----------------|-----|
|                 | NoAnesthesia    | Anesthesia |
| Peak flow       |                 |       |
| Nasal           | 1.56 ± 0.31     | 1.92 ± 0.50 | 0.4 |
| Pharyngeal      | 3.70 ± 0.73     | 4.53 ± 0.95 | <0.05 |
| Supraglottic    | 5.27 ± 0.86     | 6.43 ± 1.23 | 0.13 |
| 0.2 l/s         |                 |       |
| Nasal           | 0.876 ± 0.243   | 1.38 ± 0.481 | 0.13 |
| Pharyngeal      | 2.18 ± 0.48     | 4.72 ± 1.29 | 0.02 |
| Supraglottic    | 3.05 ± 0.58     | 6.13 ± 1.60 | 0.02 |
| Collapsibility, cmH$_2$O | 4.90 ± 0.66 | 6.22 ± 0.51 | 0.08 |

Values are means ± SE.
normal individuals rather than patients with OSA. Although it is believed that patients with sleep apnea have augmented upper airway dilator activity during wakefulness, some data suggest that the negative pressure reflex in these patients is impaired and improves with treatment of apnea (21). As a result, the role of negative pressure in driving the augmented upper airway muscle activation during basal breathing in patients with OSA remains unclear.

Despite these limitations, there is an increasingly large body of experimental data that supports the concept that local airway events are important in determining basal muscle activity. First, it has been well established from human and animal data that the upper airway is rich in receptors that respond to changes in airflow, temperature, and pressure (2, 4, 6, 17, 26). Thus the mechanism to respond to the local environment is clearly present. Second, DeWeese and Sullivan (7) demonstrated a significant increase in pharyngeal resistance during quiet wakefulness and an even larger increase (~60%) during non-rapid-eye-movement (NREM) sleep in normal humans after topical anesthesia of the pharynx and glottis. No obstructive events or flow limitation occurred in this study. Second, DeWeese and Sullivan (7) demonstrated a significant increase in pharyngeal resistance during quiet wakefulness and an even larger increase (~60%) during non-rapid-eye-movement (NREM) sleep in normal humans after topical anesthesia of the pharynx and glottis. No obstructive events or flow limitation occurred in this study. Third, we and others previously reported a decrement in pharyngeal dilator muscle activity in patients with sleep apnea after the application of nasal CPAP (20). This decrement in basal GG EMG is likely due to the effects of positive pressure on upper airway mechanoreceptors, although it is possible that the decrement may have been due to a CPAP-induced increase in static lung volume, which has previously been shown to decrease dilator muscle activity (27). Fourth, preliminary data from our laboratory have shown that, in patients with tracheostomies for OSA, GG EMG is substantially higher when the patients breathed through the upper airway than when they breathed through the tracheostomy, again suggesting an important role for local mechanisms. Additional preliminary data from our laboratory suggest that when subjects are passively ventilated using an iron lung (negative pressure ventilation), the phasic activation of the GG muscle is strongly correlated with negative pressure changes in the pharynx (1). Finally, we recently showed that in normal subjects the application of topical anesthesia is associated with a decrease in basal GG activity during wakefulness, along with a trend toward rising airflow resistance (30). However, as stated, a direct assessment of local influences on pharyngeal muscle activity during eupneic breathing in awake apnea patients has not previously been reported.

We speculated that if the response to relatively small swings in negative pressure were in part driving the neuromuscular compensation in the apnea patient, this would likely be reduced by topical anesthesia in much the same way that the negative pressure reflex is decreased (9, 16). Thus we set out to inhibit the negative pressure reflex and assess the impact on basal muscle activation and pharyngeal airflow mechanics. We were able to demonstrate that a moderate reduction in the negative pressure reflex was associated with a significant reduction in basal muscle activity. The peak reflex activity diminished by ~50%, whereas peak phasic GG EMG during tidal breathing was reduced by ~33% (approaching levels seen in normal subjects) (30). We believe that these results indicate that topical receptor mechanisms are responsible for ~30% of GG activity during tidal respiration, and likely quite a bit more, inasmuch as we almost certainly did not achieve complete local anesthesia with our technique. Inasmuch as there was a significant correlation between the decrement in peak reflex activation of the GG muscle after anesthesia and the reduction in peak phasic GG activity during normal breathing, it is tempting to speculate that negative pressure or the negative pressure reflex is driving this local modulation. However, such conclusions cannot be definitively drawn from these data.

From this study we are unable to identify the locations or the type of receptors involved in responding to local airway events and modulating dilator muscle function. The fact that topical anesthesia led to a significant decrease in muscle activation makes it likely that the involved receptors are superficial (mu-
Thus muscle spindle receptors are unlikely to be mediating the response seen in this study but could still have a important additional role in modulating local airway muscle activity. Some have speculated that a mucosal mechanoreceptor, located in the larynx (where they have clearly been demonstrated) or in the pharynx, might be involved, and there are strong data in animals and humans supporting the concept that the superior laryngeal nerve mediates the afferent limb of the negative pressure reflex (11, 26). Nasal receptors, innervated by the trigeminal nerve, may also play a role (9). Our diffuse anesthesia protocol does not allow us to further localize these sensory mechanisms. In addition, it seems quite possible that multiple types of receptors are involved, with some integration of this information occurring in the brain stem, leading ultimately to modulation of muscle activity.

The functional importance of these local receptor mechanisms is quite clear, inasmuch as we were able to demonstrate a statistically significant increase in pharyngeal airflow resistance associated with the fall in GG activation after anesthesia. This suggests that the airway is able to respond to local events and that, by decreasing sensory input with topical anesthesia, muscle activity fell and airway patency deteriorated. These results are similar to those of DeWeese and Sullivan (7) in normal subjects. Although it is possible that anesthesia could lead directly to an increase in secretions and thus directly increase resistance in the upper airway, it seems likely that the largest effect would be seen in the nose, and there was no increase in nasal resistance after anesthesia.

In comparing our results on the effects of local anesthesia in apnea patients with those in normal subjects, several points should be noted. During quiet tidal breathing the GG EMG response was not significantly greater in the apnea patients than in normal controls (percentage of maximum, \( P > 0.05 \)), which differs from our previous data (20). This was likely due to the fact that we changed EMG amplification systems between the two studies, with the earlier system producing a considerably higher percentage of maximum GG EMG than the present one for unclear reasons (30). As previously demonstrated, pharyngeal airflow resistance (at peak flow and 0.2 l/s) was significantly higher in the apnea patients before and during anesthesia (\( P < 0.01 \)). Somewhat surprisingly, the percent reduction in GG EMG during tidal respiration after anesthesia, although it was greater in the apnea patients, was not significantly greater (−33 vs. −19%, \( P = 0.22 \) compared with data from Ref. 30). One could argue that these airway receptor mechanisms should be of greater importance in the apnea patient with an anatomically small airway, serving to promote neuromuscular compensation during wakefulness (20). This may explain why we were able to demonstrate a significant increase in airflow resistance after anesthesia in apnea patients, whereas only a trend toward increasing resistance was seen in normal controls (30). It could be argued that the pharyngeal airway should collapse completely if this reflex were adequately attenuated, as occurs during sleep in these individuals. However, the reflex was not completely abolished, and one would expect volitional muscle activation to occur if upper airway patency was seriously threatened during wakefulness. The apnea patient may recruit additional mechanisms to activate dilator muscles should airway patency be compromised during wakefulness. This could have diminished the observed decrement in muscle activity observed after anesthesia in these patients.

The role of the negative pressure reflex and local receptor mechanisms in maintaining airway patency during sleep has been difficult to elucidate. We and others have shown that there is a substantial decrement in the negative pressure reflex in normal subjects during stable NREM sleep, as well as a marked reduction in muscle activation in the apnea patient at sleep onset (19, 29). However, the influence of sleep on the reflex in apnea patients has not been studied. We believe that loss of this reflex in apnea patients at sleep onset leads to the decrement in muscle activity and subsequent airway closure that is seen in these individuals. However, some data are available to suggest that the upper airway may still be responsive to local events during sleep. DeWeese and Sullivan (7) showed in normal subjects a substantial increase in transpharyngeal resistance during NREM sleep after upper airway anesthesia. In addition, McNicholas and colleagues (18) showed an increase in upper airway obstruction and the development of apneic events in snorers during sleep after topical oropharyngeal anesthesia. These data suggest that some ability of the airway to respond to local events is likely maintained during sleep and can be diminished with anesthesia. Although it is possible that this is due to maintenance of responsiveness to negative pressure during sleep, this may also represent local responsiveness to chemical stimulation of the upper airway, inasmuch as receptors responsive to CO₂ have been clearly demonstrated in the larynx and lead to increased activity of the GG muscle (5, 22, 26). In addition, recent data from Berry et al. (3) showed that, in subjects with OSA, airway anesthesia decreased the response of the GG muscle to ventilatory effort (measured as esophageal pressure swings) during apnea. These data suggest that the negative pressure reflex (which present data suggest to be markedly diminished during sleep) is not the only important local modulator of muscle activity; or this reflex is better maintained during sleep than previous work has suggested. More investigation into this area is clearly needed.

In interpreting the results of this study, several potential technical limitations must be kept in mind. First, it is highly unlikely that all topical receptors were anesthetized with our protocol. With very invasive, dense anesthesia, Horner et al. (9) were able to nearly completely abolish the reflex response to −25 cmH₂O in normal subjects. With our protocol, the negative pressure reflex was reduced to about −50% of control values but was clearly still present. Thus it is likely that our results, if anything, underestimate the degree...
to which this reflex, in particular, and topical receptors, in general, participate in driving upper airway muscle activity in apnea. Second, although we attempted to complete all studies within 30 min after anesthesia, it is certainly possible that some of the anesthetic effect was dissipating toward the end of the study. However, if anything, this would again tend to diminish the strength of our findings and cause us to underestimate the importance of local mechanisms. Third, it could be argued that direct absorption of lidocaine into the muscle or the bloodstream led to the reduced muscle activity observed, rather than anesthetizing local receptors. However, our subjects had no difficulty with volitional activation of the upper airway muscles during anesthesia, and several previous studies have reported no change in muscle function after topical lidocaine (7, 16). In addition, the amount of lidocaine administered was ~200 mg, much of which was expectedly absorbed. As a result, circulating levels of lidocaine were likely to be much below those previously reported to affect neuromuscular function (12). We cannot rule out the possibility that the lidocaine led to a change in central neural activation and the pattern of respiration. We did see a significant increase in tidal volume and a slight increase (not significant) in minute ventilation after anesthesia. However, this increase in respiratory drive would, if anything, be expected to increase GG muscle activity rather than decrease it, as was found. From Table 2, it can also be seen that the tidal volume and minute ventilation are high in these patients compared with normal subjects during quiet respiration. We believe that this is likely due to a number of factors, including the patients' obesity (and thus high resting metabolic rate), the increased dead space of the nasal mask system employed, and the invasive nature of the protocol. We cannot completely rule out the possibility that the development of relative hypocapnia with increased minute ventilation may have led to a decrease in GG activity during anesthesia but believe this to be extremely unlikely, inasmuch as minute ventilation did not increase significantly. Thus we believe that the results reported in this study have stemmed from the topical blockade of mucosal afferent receptor mechanisms. In addition, during this study we evaluated the effect of topical anesthesia on the function of only one upper airway muscle and attempted to extend those results to the entire pharyngeal airway. It is certainly possible that other pharyngeal muscles would behave differently from the GG muscle, inasmuch as we have demonstrated that the effect of sleep for the tensor palatini is different from that for the GG muscle. Finally, our methods for defining muscle activity (percentage of maximum) could be faulted because of such factors as variable needle electrode placement and subject effort. However, inasmuch as this study was designed not to compare muscle activity or pharyngeal mechanics between one patient or one group and another but, rather, to assess the influence of topical anesthesia, we believe our methodology to be adequate to support our conclusions.

In conclusion, we believe that our results strongly support the notion that local receptor mechanisms are present in the upper airway and importantly influence the augmented pharyngeal dilator muscle activity in the awake apnea patient. These mechanisms likely allow for precise neuromuscular adaptation to the local environment and are able to respond to changes in multiple variables, including airway size, airway shape, and compliance characteristics. How this information is processed and integrated by the central nervous system remains poorly understood, as does the effect of sleep on these mechanisms.

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