Effect of positional changes of anatomic structures on upper airway dilating muscle shortening during electro- and chemostimulation

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Oliven, A., and M. Odeh. Effect of positional changes of anatomic structures on upper airway dilating muscle shortening during electro- and chemostimulation. J Appl Physiol 101: 745–751, 2006. First published May 4, 2006; doi:10.1152/japplphysiol.01462.2005.—Positional changes of anatomic structures surrounding the upper airway are known to affect pharyngeal mechanics and collapsibility. We hypothesized that these alterations also affect the ability of the upper airway dilator muscles to enlarge the pharynx by altering their ability to shorten when activated. Using sonomicrometry, we evaluated in seven anesthetized dogs the effects of changes in tracheal and head position on the length of the genioglossus (GG) and the geniohyoid (GH) and the effects of these positional changes on the magnitude of shortening of the two muscles in response to electro- (ES) and chemostimulation (CS). Caudal traction of the trachea lengthened the GG and GH in all dogs, whereas cranial displacement of the trachea and flexion of the head to a vertical position shortened the muscles. Compared with the magnitude of ES-induced shortening in the neutral position, ES-induced shortening of the GG was 144.7 ± 14.6, 49.3 ± 4.3, and 33.5 ± 11.6% during caudal and cranial displacement of the trachea and during head flexion, respectively. Similar effects of the positional changes were found for the GH, as well as for both muscles during respiratory stimulation with PCO2 of 90 Torr at the end of CO2 rebreathing. Although inspiratory muscle shortening during CS reached only one-quarter to one-third of the magnitude observed during ES. We conclude that positional alterations of anatomic structures in the neck have a dramatic effect on the magnitude of shortening of the activated GG and GH, which may reduce substantially their ability to protect pharyngeal patency.

sonomicrometry; genioglossus; geniohyoid; sleep apnea; pharynx; electrical stimulation; respiratory stimulation

THE PHARYNGEAL AIRWAY FUNCTIONS mechanically as a self-supporting, soft-walled collapsible tube, whose collapsibility depends on wall characteristics and forces that impinge on the airway. Although many anatomic abnormalities have been implicated in the pathogenesis of pharyngeal collapse in patients with obstructive sleep apnea (OSA), the role of changing functional factors is obvious, because apneas occur only during sleep. Decrease in upper airway dilator muscle (UADM) tone is believed to be the prime functional mechanism leading to pharyngeal occlusion during sleep, as these muscles counteract the forces that promote pharyngeal collapse (4, 17).

In addition to UADM activity, however, other functional mechanisms, primarily transient mechanical alterations, appear to affect pharyngeal patency. Although phasic inspiratory electrical activity of the UADM parallels the phasic changes in resistance of the isolated canine upper airway occurring over the respiratory cycle, denervation of the UADM had only a minor effect on these changes, which ceased only after transection of all structures connecting the pharynx to the chest (25, 26). These and later observations lead to recognition of the effects on pharyngeal resistance and collapsibility of forces arising in the chest, assumed to originate primarily from displacement of lung and trachea during breathing and/or changes in the functional residual capacity (6, 7). In experimental animal preparations, caudal traction of the trachea (Tca) has been shown to stabilize the pharynx, with the opposite effect observed during cranial displacement (18, 24). Similarly, changes in head (including mandibular) position have a large effect on pharyngeal patency and collapsibility (12). Both increased pharyngeal wall tension and lower surrounding pressure were proposed as potential causes for these changes (8, 18).

Positional and mechanical alterations may also affect the UADM and their ability to shorten, and, therefore, to enlarge the pharyngeal lumen and/or prevent its collapse. We have previously noticed that the mechanical effects of UADM contraction are affected by head position (12). Brennich et al. (3) have shown that relatively small decreases in intrapharyngeal pressure have a major effect on genioglossus (GG) inspiratory shortening. Therefore, the present study was undertaken to assess the effect of positional changes on the UADM length and ability to shorten. Specifically, we measured length changes of two UADMs, the GG and the geniohyoid (GH), using sonomicrometry, and evaluated the effect of structural alterations (changes in tracheal and head position) on the resting length and on the magnitude of active shortening of these muscles, both during electrical stimulation (ES) and during chemostimulation (CS).

METHODS

Seven mongrel dogs, weighting 18–34 kg, were anesthetized with phenobarbital (30 mg/kg initially, followed by supplemental doses of 5 mg as needed, to maintain stable anesthesia). The dogs were kept in the animal facilities of the Technion Faculty of Medicine for at least 2 wk before the studies and were found to be healthy. The studies were approved by the Institutional Animal Care and Use Committee. The dogs were studied in the supine position, with the head secured at ~30° from the horizontal (baseline position), and the tip of the tongue and the lower jaw were secured to the upper jaw with tape. Temperature and blood pressure were monitored and maintained constant.

A midline ventral incision was made in the neck, and the trachea was transected and both ends were cannulated with short endotracheal tubes. A pneumotachograph was connected to the distal tracheal tube to measure ventilation when animals were breathing spontaneously. The proximal tracheal tube was mounted on a bracket that glided
along a rod, which secured the trachea in its original position but enabled proximal and distal displacement in the longitudinal direction.

Changes in muscle length during positional changes and muscle contraction were measured with a sonomicrometer (Triton Technology, San Diego, CA). Paired piezoelectric transducers were implanted 10–15 mm apart, the distal one ~15 mm from the mandible, in the body of contralateral GG and GH, along the orientation of the muscle fibers. They were held in place with purse-string sutures placed in the muscle fascia and connected to the sonomicrometer. With this technique, the distance between the transducer pair is continuously sampled (1,537 Hz), providing a continuous assessment of muscle length.

Pairs of Teflon-coated, stainless steel electrodes (0.007 in.) with bare ends were inserted into the GG and GH, close to the mandible. These electrodes, connected to an electrical stimulator (Dynex III, Medtronic, Minneapolis, MN), were used for electrical activation of the muscles during the ES studies. The GG electrodes were also used, after amplification, band-pass filtering (50–1,000 Hz), rectification, and integration, for EMG measurement to assess the magnitude of this muscle activation during CS.

Two modes of stimulation were used to activate the dilator muscles studied: selective simultaneous bilateral ES of the GG and GH was applied using 2- to 3-s trains of 50-Hz stimulation with 0.2-ms pulse duration. The intensity used was the one that produced maximal muscle shortening. During these studies, the dogs were mechanically ventilated sufficiently to abolish spontaneous respiratory activity. Generalized increases in ventilation and UADM activity were achieved by progressive CS, obtained by CO2 rebreathing. During these studies, the dogs breathed spontaneously, with ventilation, GG-EMG, end-tidal CO2, and piezoelectric length of the two muscles continuously sampled.

Three positional alterations were evaluated: caudal traction of the proximal tracheal stump, which elongates the pharynx; cranial displacement of the trachea, which has the opposite effect; and head flexion to 90° from the horizontal.

Study protocol. After preparation, the dogs were mechanically ventilated to abolish spontaneous respiration. The resting length of the muscles was determined piezoelectrically in the baseline position, i.e., with the dogs head at 30° from the horizontal and the proximal tracheal stump secured in its original position. This was followed by measurement of the magnitude of muscles contraction during ES. Thereafter, both the effect of positional changes on muscle length and the magnitude of ES-induced muscle shortening in each of the three positions were measured. Each measurement was repeated two to three times. In the second part of each study, mechanical ventilation was stopped, and after animals resumed steady-state spontaneous breathing, progressive hyperoxic hypercapnia was produced by having the animals rebreathe a mixture of 7% CO2 and 93% O2. Positional changes (i.e., tracheal displacement and head flexion) were repeated at end-tidal Pco2 of 90 Torr.

In five dogs, resistance to airflow of the isolated upper airway was also measured. A pneumotachograph was connected in series between the cranial tracheal tube and a negative pressure source, to measure airflow in the inspiratory direction through the isolated upper airway. Pharyngeal pressure above the vocal cords was measured with a catheter inserted rostrally through the cranial tracheal tube. Resistance was measured at the end of the study, to prevent changes in intraluminal pressure, known to alter muscle shortening (3). Flow was set at a level without flow limitation. With the dogs’ head and trachea in the baseline position, flow and supralaryngeal pressure were measured before and during ES, and again at Pco2 of 90 Torr, at the end of a second CO2 rebreathing run.

All data were recorded on a Graphtec WR 7700 writer. Changes in muscles length were measured in millimeters, on the basis of pretest in vitro calibration and in vivo resting length measurements. Muscle length and length changes during positional alterations, before and during the two modes of muscle activation, were calculated as percentage of resting length in the baseline position. Data are presented as means ± SE. A two-tailed, paired t-test was used to assess statistical significance of changes.

RESULTS

Tracings of the piezoelectric signals from the GG of one of the dogs are shown in Fig. 1. Caudal traction of the upper tracheal stump lengthened the GG (and GH) in all dogs, whereas cranial displacement and flexion of the head to a vertical position shortened the muscles. ES and activation during inspiration at high levels of Pco2 always lengthened the muscles. The magnitude of shortening during ES was much larger than during CS and depended on the precontractile muscle length.

The mean effects of positional changes and ES on the length of the GG and GH are shown in Fig. 2. Tca (5.1 ± 0.5 cm) resulted in lengthening of the GG to 121.4 ± 7.4 and 124.9 ± 4.3% of baseline length, respectively. Cranial displacement of the trachea (3.7 ± 0.3 cm) shortened the GG to 69.3 ± 6.5 and GH to 84.7 ± 6.7%, respectively. Head flexion resulted in the GG to 69.3 ± 6.5 and GH to 84.7 ± 6.7%, respectively. Head flexion shortened the GG and GH to 69.3 ± 6.5 and 57.7 ± 6.7%, respectively (P < 0.01 for all changes).

![Fig. 1. Representative tracings from 1 of the dogs, showing the effects of positional changes and stimulation on the length of the genioglossus. The distance between the piezoelectric crystals, in the passive, baseline position, was 15 mm. ES, electrical stimulation; CS, chemostimulation (Pco2 = 90 Torr); BL, baseline position; Tca, caudal traction of the trachea; Tcr, cranial displacement of the trachea; Hf, head flexion.](http://jap.physiology.org/DownloadedFrom/10.1152/jappl.00578.2005)
The changes in muscle length in response to ES were affected substantially by the positional changes. In the baseline position, the GG and GH shortened during ES-induced contraction by 31.6 ± 6.1 and 20.3 ± 1.3%, respectively (Fig. 2). The magnitude of shortening increased significantly to 44.9 ± 6.9 and 30.1 ± 1.5%, respectively, during caudal displacement of the trachea (P < 0.05 and P < 0.01 for the comparison of the response to ES to that observed in the baseline position, for the two muscles, respectively). Cranial displacement of the trachea decreased the response to ES to 17.0 ± 4.9 and 13.6 ± 2.6%, respectively (P < 0.01 and P < 0.05 compared with the magnitude of shortening in the baseline position). During head flexion the magnitude of shortening was only 7.0 ± 1.6 and 7.3 ± 1.7%, respectively (P < 0.001 compared with shortening in the baseline position).

CO2 rebreathing resulted in progressive and intensive stimulation of ventilation, increasing breathing rate and minute ventilation from 26.0 ± 6.0 breaths/min and 4.7 ± 0.9 l/min at PCO2 = 50 Torr to 54.6 ± 6.8 breaths/min and 17.6 ± 2.3 l/min at PCO2 = 90 Torr. These changes were associated with progressive increase in peak GG-EMG. No increase in tonic EMG activity was observed in any of the dogs. In all dogs, phasic shortening of both muscles was observed during inspiration, without tonic shortening. Figure 3 depicts mean changes of GG-EMG, tidal volume, and sonomicrographic activity of the tongue protrusors at the baseline position, observed during CO2 rebreathing. Although no phasic EMG activity was present during room air breathing, such respiratory activity was recorded in all dogs at Pco2 of 50 Torr (33.4 ± 12.5% of the magnitude observed at Pco2 of 90 Torr). On the other hand, phasic shortening of the GG and GH could be recognized only at higher levels of hypercapnia (58.6 ± 2.2 and 60.3 ± 4.3 Torr for GG and GH, respectively).

Figure 4 depicts the effects of positional changes on inspiratory muscle shortening during intense CS (Pco2 = 90 Torr), compared with the shortening obtained with ES. It can be seen that muscle length changes induced by this level of Pco2 were substantially smaller than those observed during ES of the muscles. At Pco2 of 90 Torr, the mean inspiratory shortening of the GH, both at the neutral position and other conditions, reached only one-third or less of the shortening observed during ES. The comparable shortening of the GG was even less (P < 0.01 for all comparisons between ES and CS). However, positional changes affected the relative magnitude of muscle shortening similarly, independently of the mode of stimulation.
When inspiratory shortening of the GG and GH in the baseline position, at \( P_{CO_2} = 90 \) Torr, was used as the index for comparison of changes during CS (i.e., considered to represent 100%), the magnitude of shortening was very close to the ES-induced shortening, calculated as percentage of the magnitude of ES-induced shortening in the baseline position (Table 1). As for ES-induced shortening, the magnitude of CS-induced shortening of both the GG and GH was significantly larger during caudal tracheal displacement and smaller during cranial displacement and head flexion than in the baseline position.

Figure 5 depicts the relationships between the magnitude of GG and GH shortening during ES (solid symbols) and CS (open symbols). Both muscles shortened similarly down to \( \sim 70\% \) of their baseline length. Therefore, in the mean, shortening was similar for GG and GH during CS. Larger degrees of shortening (produced mainly by ES during caudal tracheal traction) were obtained for the GG only.

Resistance to airflow through the isolated upper airway, measured in the baseline position, decreased from \( 42.2 \pm 9.0 \) to \( 10.6 \pm 1.5 \) cmH\( _2 \)O\( \cdot \)l\( ^{-1} \)\( \cdot \)s during ES of the GG and GH, and to \( 11.4 \pm 1.2 \) cmH\( _2 \)O\( \cdot \)l\( ^{-1} \)\( \cdot \)s at \( P_{CO_2} \) of 90 Torr (\( P < 0.05 \) for both).

**DISCUSSION**

The main findings of this work are the following. First, tracheal and head position had a large effect on the resting length of the UADM studied, associated with large changes in their length response to ES and CS. Second, intensive CS resulted in substantially smaller magnitude of shortening of the two UADMs compared with ES, independently of head and tracheal position. Nevertheless, the intense CS used in the present study resulted in a similar decrease in upper airway resistance as ES of the GG and GH.

Pharyngeal patency depends on a large number of factors that affect intra- and extraluminal pressure and pharyngeal wall characteristics. Positional changes and UADM contraction can alter, directly or indirectly, both pressures and wall tension. The present work focuses on the specific effect of positional changes on UADM active shortening. Previous studies have shown that widening of the pharynx is proportional to GH shortening (27–29). Therefore, alterations of UADM shortening capacity will have a direct effect on their ability to defend pharyngeal patency. The positional changes employed in the present study were chosen by considering the most important anatomic degrees of freedom of the muscles insertion points, i.e., the physiological conditions that move the insertion points of this UADM, for example the geniohyoid. The positional changes chosen encompass the physiological range of movements of the insertion points of this muscle. Hf shifts the mandibular (M) insertion point caudally and closer to the pharynx (Ph). Caudal (Tca) and cranial (Tcr) tracheal displacements shift the pharyngeal insertion point (i.e., the hyoid bone) closer to or away from the mandible.

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**Table 1. Relative length changes of the GG and GH during positional changes, ES, and CS (\( P_{CO_2} = 90 \) Torr)**

<table>
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<tr>
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<th>BL</th>
<th>Tca</th>
<th>Tcr</th>
<th>Hf</th>
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<tr>
<td><strong>Genioglossus</strong></td>
<td></td>
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<tr>
<td>ES: stimulation-induced shortening</td>
<td>100</td>
<td>144.7±14.6*</td>
<td>49.3±4.3†</td>
<td>33.5±11.6†</td>
</tr>
<tr>
<td>CS: inspiratory shortening</td>
<td>100</td>
<td>148.1±17.4†</td>
<td>44.3±9.6†</td>
<td>32.7±6.0†</td>
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<tr>
<td><strong>Geniohyoid</strong></td>
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<tr>
<td>ES: stimulation-induced shortening</td>
<td>100</td>
<td>158.7±14.5†</td>
<td>62.1±11.5*</td>
<td>31.6±7.6†</td>
</tr>
<tr>
<td>CS: inspiratory shortening</td>
<td>100</td>
<td>127.7±7.0†</td>
<td>38.6±10.3†</td>
<td>26.7±9.6†</td>
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</table>

Data (mean ± SE) are presented as percent of muscle length measured in the baseline position (BL). Tca, caudal traction of the trachea; Tcr, cranial displacement of the trachea; Hf, head flexion; ES, electrical stimulation; CS, chemostimulation (\( P_{CO_2} \) 90 Torr). *\( P < 0.05 \), †\( P < 0.01 \), for the comparison with the magnitude of shortening observed with the same mode of stimulation at the neutral position. Differences between ES and CS are not significant, except for geniohyoid at the Tca position (\( P = 0.048 \)).
The magnitude of in situ active shortening of a muscle during physiological or electrical stimulation depends, in addition to the intensity of stimulation, on multiple interacting forces (Fig. 7). For the UADM, they were grouped into forces that oppose shortening, termed “afterload,” and those that produce the tension applied to the muscle and define its precontractile length, termed “preload” (3). The afterload includes passive (viscoelastic) tissue forces, concomitant activation of antagonists (like tongue retractors), and negative intraluminal pharyngeal pressure (in the presence of inspiratory flow). The preload determines the force produced by the muscle for a given stimulation intensity, defined by the muscles’ length-tension relationships, as acting below or above the muscles’ optimal length ($L_o$) produces lower tension. In other words, the preload relates to forces acting on the passive muscle, before contraction, whereas afterload includes all external forces acting on the muscle during contraction and shortening. Assuming that UADM are in the vicinity of $L_o$ when in the baseline position, positional changes that alter muscle length will also affect active force production, with passive shortening reducing force more than stretching of the muscle, because the latter is associated with increased passive tension. However, the magnitude of active shortening at any given stimulation intensity depends only partially on the length-tension relationships of the muscle and is the result of a complex interaction between pre- and afterload. The increased magnitude of shortening during Tca, for example, does not necessarily indicate that Tca brought the muscles closer to their $L_o$ and can be explained by reduction in afterload. Under physiological conditions, tracheal displacement, head flexion, and other anatomic alterations that affect UADM length, change also perimuscular structures, and therefore affect both the pre- and the afterload of the UADM.

Whereas positional alterations were expected to affect UADM function, our findings indicate that the effect of these alterations on the magnitude of shortening during both modes of stimulation is considerable. For example, the magnitude of shortening during ES of the GG was 0.90 ± 0.61 mm during head flexion, compared with 6.03 ± 3.05 mm during distal displacement of the trachea. During sleep or anesthesia, combined positional alterations, due to relaxation of neck and other skeletal muscles that are not activated by respiratory stimulation, may have even larger effects on the UADM. It is conceivable, therefore, that physiological changes in the position of the UADM may be sufficient to substantially reduce their ability to maintain pharyngeal patency, even when maximally activated.

Moreover, UADMs are not expected to be maximally activated during sleep or anesthesia. In the present study, we induced extreme CS, but the magnitude of UADM shortening obtained reached only one-third or less of that observed during ES. The magnitude of CS-induced shortening was similar to that previously reported for anesthetized cats (28, 29). Obviously, the length response to respiratory stimulation is complex, and the smaller magnitude of shortening does not necessarily indicate a proportionally lower degree of activation. Forces arising from the chest, as well as coactivation of tongue retractors (5) and other muscles that participate in respiration, are likely to affect the magnitude of the inspiratory shortening of the UADM. Previous studies have demonstrated even inspiratory elongation of the sternohyoid (28, 29) or the GG (3) under certain circumstances, despite substantial increases in their EMG activity, owing to concomitant activation of antagonists or negative inspiratory intrapharyngeal pressures. However, this phenomenon was not encountered in our study. Moreover, the effects of the positional alterations of the trachea and the head on muscle length were equal at rest and at the end of CO2 rebreathing. Similarly, the effect of the positional alterations on UADM shortening during CS was, proportionally, similar to that observed during ES (Table 1). In addition, with ES, GG shortened more than GH (Fig. 4), probably because of the lower afterload on this muscle, compared with the GH that insert into the hyoid bone. A similar trend should have been observed during CS, if increasing afterload during respiratory stimulation prevented muscle shortening. All these considerations suggest that changes associated with respiratory stimulation had no substantial effect on UADM pre- and afterload and that, during anesthesia, even intense respiratory stimulation causes only partial UADM shortening. Actually, under the experimental conditions, we were unable to detect any muscle shortening at PCO2 levels below 60 Torr in most dogs, despite the presence and progressive increases in EMG activity during CO2 rebreathing (Fig. 3). Independently of the causes for the limited shortening-response to CS, our findings indicate that the effects of positional changes on UADM shortening are not compensated and remain relevant during respiratory stimulation.

On the other hand, the results of upper airway resistance measurements indicate that the mechanisms that improve pharyngeal patency during CS include important parameters in...
addition to GG and GH shortening, because the decrease in resistance was similar with both modes of these muscles' activation, despite the large differences in the magnitude of shortening they produced. Despite the above-mentioned considerations, it remains possible that concomitant activation of other peripharyngeal muscles during CS both reduced GG and GH shortening and participated in the reduction in pharyngeal resistance. More likely, this finding adds to previous observations that reported relatively little effect of UADM on pharyngeal flow mechanics in anesthetized or decerebrated animals and challenged the causative linkage drawn between UADM electromyographic activity and concomitantly observed mechanical effects. Denervation of the UADM failed to affect the magnitude of pharyngeal widening during inspiration (25, 26), and bilateral transection of the hypoglossus nerves had a negligible effect on pharyngeal collapsibility in eunepic dogs (13) or on the mechanical response to hypercapnia of the feline pharynx (19). These results could be explained by relatively low activation of the tongue muscles in the animal models used, but also by mechanically disadvantageous position of the UADM, similar to the ones studied in the present study. On the other hand, these studies clearly indicated the presence of dilatory forces not related to GG and GH activation, and their nature as well as their response to positional alterations remain to be elucidated. ES of striated muscles provides an important tool to assess their mechanical effect and has been largely employed for the study of UADM function. As in the present study, ES-induced contraction of UADM has been shown to improve pharyngeal flow mechanics both in animals (1, 2, 9, 11, 21) and humans (10, 14, 15, 20, 22). These findings led to repeated attempts to stimulate the GG in OSA patients for therapeutic purpose (10, 13). With recent improvements in ES techniques (23), questions concerning the pathophysiology and role of the tongue muscles in maintaining pharyngeal patency also gained clinical significance and relevance. Our findings indicate that ES of the GG and GH reduces pharyngeal resistance similar to intense CS. On the other hand, positional alterations may decrease the effectiveness of GG contraction considerably. Such alterations may explain, in part, the relatively modest mechanical effects of ES of the GG in patients with OSA during sleep and anesthesia (16, 23).

Head flexion as well as cranial displacement of the trachea that models positional changes occurring during lung deflation have been shown to alter pharyngeal pressure-flow relationships and increase collapsibility in animals and humans (7, 6, 24). These observations were explained by changes in pharyngeal wall tension and surrounding pressure (8, 18). Our present findings demonstrate that these positional changes also alter the response of the UADM to both ES and CS, thereby reducing considerably their ability to compensate for the anatomic manipulations.

GRANTS
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REFERENCES


