Respiratory-related pharyngeal constrictor muscle activity in decerebrate cats

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Kuna, Samuel T., and Christi R. Vanoye. Respiratory-related pharyngeal constrictor muscle activity in decerebrate cats. J. Appl. Physiol. 83(5): 1588–1594, 1997.—Respiratory-related activity of the hyopharyngeus (middle pharyngeal constrictor) and thyropharyngeus (inferior pharyngeal constrictor) muscles was determined in decerebrate, tracheotomized adult cats and compared with the electromyographic activity of the thyroarytenoid, a vocal cord adductor. During quiet breathing, the hyopharyngeus and usually the thyroarytenoid exhibited phasic activity during expiration and tonic activity throughout the respiratory cycle. Respiratory-related thyropharyngeus activity was absent under these conditions. Progressive hyperoxic hypercapnia and progressive isocapnic hypoxia increased phasic expiratory activity in both pharyngeal constrictor (PC) muscles but tended to suppress thyroarytenoid activity. Passively induced hypocapnia and the central apnea that followed the cessation of the mechanical hyperventilation were associated with tonic activation of the hyopharyngeus and thyroarytenoid but no recruitment in thyropharyngeus activity. The expiratory phase of a sigh and progressive pneumothorax were associated with an increase in phasic thyroarytenoid activity but no change in phasic PC activity. The results indicate that a variety of stimuli modulate respiratory-related PC activity, suggesting that the PC muscles may have a role in the regulation of upper airway patency during respiration.

The superior, middle, and inferior pharyngeal constrictors (PCs) are saillike muscles that help form the lateral and posterior walls of the pharyngeal airway. They arise from the dorsal midline pharyngeal aponeurosis and attach to various anterior structures in the ventral wall of the pharyngeal airway. In animals, the middle PC is termed the hyopharyngeus (HP) and consists of the chondropharyngeus and keratopharyngeus muscles. The inferior PC is termed the thyropharyngeus (TP). The pharyngeal branch of the vagus nerve supplies motor output to the PC muscles in cats (4, 6, 21, 24).

The PC muscles are activated after the oral phase of swallowing and are believed to promote pharyngeal airway closure. Respiratory-related PC activity is of interest because previous investigators have speculated that PC muscle activation may promote pharyngeal airway closure during sleep in patients with obstructive sleep apnea (25). Previous investigators have examined the respiratory-related activity of the PC muscles in cats. Sherrey and Megirian (24) performed whole nerve recordings in anesthetized, spontaneously breathing cats and found expiratory activity in the nerve branches innervating the TP and HP. More recently, Grélot et al. (6) recorded the discharge of motor axons supplying the PC muscles in decerebrate, paralyzed, artificially ventilated cats. Most units fired only in expiration and exhibited a steady, a decreasing, or a late augmenting discharge pattern. Inspiratory units with a steady, late augmenting, or tonic discharge pattern were also present. From electromyogram (EMG) studies in anesthetized cats, it has been found that 1) the HP and TP exhibit phasic activity in expiration and tonic activity throughout the respiratory cycle during quiet breathing, 2) phasic HP activity increases under hypercapnic conditions (5% inspired CO₂), and 3) passively induced hypocapnia is associated with the emergence of tonic PC activity (21, 23). Murakami and Kirchner (21) report that the chondropharyngeus and keratopharyngeus portions of the HP have the same activation patterns. These previous studies are largely qualitative and report the response to only one level of hypercapnia.

The purpose of the present study was to extend this previous work by providing a quantitative analysis of respiratory-related PC activity in response to a variety of respiratory-related stimuli, including progressive changes in chemical drive and lung volume. Respiratory-related activity of the TP and HP was determined in decerebrate cats during 1) quiet breathing, 2) spontaneous sighs, 3) progressive hyperoxic hypercapnia, 4) progressive isocapnic hypoxia, 5) passively induced hyperventilation, and 6) decreased lung volume. The EMG responses of the PC muscles under these conditions were compared with those of the thyroarytenoid muscle, a vocal cord adductor that helps brake expiratory airflow. The results indicate that a variety of stimuli modulate respiratory-related PC activity, suggesting that the PC muscles help regulate pharyngeal airway patency during respiration.

METHODS

Acute experiments were performed in 21 adult cats of either sex weighing 3.0–4.0 kg. The protocol was approved by the Animal Care Committee of The University of Texas Medical Branch at Galveston. Anesthesia was induced with halothane. The animals were intubated, and the anesthetic was continued until completion of all surgery. Arterial blood pressure was monitored with a cannula attached to a pressure transducer (Statham) in the femoral artery. A cannula in the femoral vein was used to infuse medications and fluids. Mean blood pressure remained above 100 mmHg in all animals. Temperature of the animals was controlled at 37°C with a servo-controlled heating pad (Yellow Springs Instruments). After administration of 3 mg iv dexamethasone to help control brain edema, an intercellular decerebration was performed by using the technique of Kirsten and St. J ohn.
A tracheotomy was performed through a midline ventral neck incision, and cannulas were placed in the rostral and caudal trachea. The animals breathed through the caudal tracheotomy tube throughout the recordings. A pneumotachograph (Fleisch) attached to a differential pressure transducer (Statham) was connected to the tracheotomy tube. The resulting flow signal was integrated over time to obtain tidal volume. Volume was calibrated with a 50-ml syringe. A sidearm in the tracheotomy tube was used to continuously sample gas for the measurement of end-tidal CO2 (Datex) and O2 (Amtek). Paired 38-gauge hooked-wire electrodes (Belden) were implanted under direct vision into the chondropharyngeous part of the HP (n = 21), TP (n = 5), and transversus abdominis (n = 10) muscles. The chondropharyngeous part of the HP was chosen because it is the larger part of the HP and is easily exposed (21). TP recordings were only obtained in the last several experiments. There were no technical problems associated with recording this EMG. Electrodes were also implanted into the thyroarytenoid muscle (n = 15) through the cricothyroid membrane. Correct position of the latter electrodes was confirmed on autopsy. The EMG signals were amplified, filtered (Grass, Tektronics), and displayed on an oscilloscope. All data were recorded on polygraph (Gould) and magnetic tape (Neurocorder).

Recordings were obtained under the following conditions: quiet breathing, spontaneous sighs, progressive hyperoxic hypercapnia, progressive isocapnic hypoxia, passively induced hypoxia, and progressively induced pneumothorax. At least 10 min separated each intervention, during which all signals returned to their baseline state. Normally the animals breathed room air supplemented with O2. Progressive hyperoxic hypercapnia was induced by connecting the tracheotomy tube to a 1-liter reservoir bag containing 7% CO2-balance O2. The rebreath was continued until the end-tidal CO2 reached 9%. Progressive isocapnic hypoxia was induced by altering the levels of inspired O2 and CO2 as the animals breathed through a T tube attached to the pneumotachograph. Each level of O2 was maintained for a minimum of 3 min. The minimum level of end-tidal O2 tested was 5%. The effect of passively induced hypoxia on EMG activity was determined by hyperventilating the animals with the mechanical ventilator (Harvard Apparatus). During the hypocapnic state, abrupt cessation of mechanical ventilation induced a central apnea, i.e., a cessation of tracheal airflow for at least 5 s. Only trials resulting in a central apnea were considered for analysis.

At the end of the experiments, an 8-Fr tube was inserted through the thoracic wall into the pleural space. A unilateral pneumothorax was induced by injecting 20-ml aliquots of air into the thoracic cavity every minute to a maximum volume of 100 ml. TP and transversus abdominis EMGs were not recorded during the pneumothorax trials. Posterior cricoarytenoid (PCA) EMG activity was recorded in three cats. Hooked wires were implanted into the PCA by gently rotating the larynx and inserting the electrodes dorsal to the cricoide cartilage. Correct placement of the PCA electrodes was confirmed on autopsy. Also during the progressively induced pneumothorax trials, a constant airflow (37°C, saturated) was passed in the expiratory direction through the rostral tracheal cannula and subglottic pressure (Statham) was recorded from a sidearm in the cannula.

Data analysis. The data were digitized offline at 500 Hz (R.C Electronics) and analyzed by using computer software (Run Technologies). The EMG signals were processed with a 100-ms time constant to obtain moving averages, which were used to quantify EMG activity in arbitrary units. Peak height of the moving average during a phasic discharge was defined as the distance between electrical zero and peak activity. Tonic activity was the minimum height of the moving average from electrical zero during the respiratory cycle and included any noise in the recording system. Phasic activity was the difference between peak height and tonic activity. In many cases, phasic PC activation began in the latter part of inspiration. This preactivation was quantified as the time from onset of phasic activity to the start of expiratory flow and was expressed in seconds and as a percentage of inspiratory time.

Under hyperoxic conditions, EMG activity was determined for five consecutive breaths at normocapnia and at 7.5, 8, 8.5, and 9% end-tidal O2. Under isocapnic conditions, EMG activity was determined for five consecutive breaths during hyperoxia and at least three different levels of hypoxia. PC EMG activity during progressive hypercapnia and progressive hypoxia was expressed as a percentage of maximum peak activity during the respective rebreathes. In those muscles with phasic activity under control conditions, phasic EMG activity was also expressed as a percentage of control. During the passive hypoxic hyperventilation trials, EMG activity was determined for five consecutive breaths just before the start and end of mechanical ventilation. During progressively induced pneumothorax, EMG activity was determined for five consecutive breaths during control and at the end of each minute at each pneumothorax volume. The decrement in lung volume resulting from the air injections was not determined. However, the similar size of the animals makes it likely that the decrement in lung volume at given pneumothorax volumes was similar among the animals. Three sighs were analyzed in each animal. PC and thyroarytenoid activities during inspiration and expiration were determined for the reason before and associated with the sigh.

Mean values at given levels of hypercapnia and pneumothorax volumes were compared with their respective controls by using a one-way repeated-measures analysis of variance. A similar analysis could not be performed for the hypoxia trials because the same levels of end-tidal O2 were not attained in each animal. Comparisons were made among 1) isocapnic hyperoxia and the lowest level of end-tidal O2 (5.1 ± 0.4%), 2) data during the inspiratory and expiratory phases of a sigh and their respective controls on the preceding breath, and 3) peak activity during quiet breathing and just before the cessation of mechanical hyperventilation. On the basis of normality testing, these data were compared by either paired t-test or signed-rank test. In results, the lowest level of hypoxia is referred to as 5% end-tidal O2. Comparisons with P < 0.05 were considered statistically significant.

RESULTS

Quiet breathing. During quiet breathing under normocapnia conditions, the HP exhibited respiratory-related activity in all cats (Fig. 1). Phasic HP activation began at the end of inspiration and maintained a relatively constant level of discharge throughout expiration. Tonic activation was present throughout the respiratory cycle. In contrast, the TP and transversus abdominis did not exhibit respiratory-related activity under these conditions. The thyroarytenoid exhibited phasic expiratory activity in 12 of 15 cats. In 2 of the 12 cats, respiratory-related thyroarytenoid activity was intermittent.

Progressive hyperoxic hypercapnia and progressive isocapnic hypoxia. Minute ventilation at 9% end-tidal CO2 was 463 ± 166% of control. The effect of progressive hyperoxic hypercapnia on PC activity in individual
cats is shown in Figs. 1 and 2. For the group as a whole, progressive hypercapnia was associated with progressive recruitment of phasic expiratory activity of the two PC muscles but no change in tonic activity (Fig. 3). Phasic HP activity at 8.0, 8.5, and 9.0% end-tidal CO₂ was significantly increased from that at normocapnia. Phasic HP activity at 9.0% end-tidal CO₂ was 264 ± 124% of its normocapnic value. Phasic TP activity appeared soon after the onset of hypercapnia and tended to increase with progressive hypercapnia.

Phasic TP and HP activity usually had a plateau-like discharge pattern throughout expiration at moderate hypercapnic levels and an augmenting or plateau-like discharge pattern throughout expiration at the highest levels of hypercapnia. Onset of phasic activity often began in late inspiration, and, in some instances, a biphasic discharge pattern was present. Preactivation of the HP was 0.16 ± 0.07 s or 26 ± 13% of inspiratory time during quiet breathing and 0.18 ± 0.04 s or 34 ± 6% of inspiratory time at 9% end-tidal CO₂. TP preactivation was 0.14 ± 0.02 s or 25 ± 5% of inspiratory time at 9% end-tidal CO₂ and showed no significant difference over the hypercapnic range.

Minute ventilation at 5% end-tidal O₂ was 390 ± 204% of its hyperoxic value. Compared with progressive hyperoxic hypercapnia, progressive isocapnic hypoxia was associated with a relatively small increase in phasic expiratory HP and TP activation. Phasic HP activity was significantly increased at 5% end-tidal O₂ (149 ± 26% of control). There was no change in PC tonic activity during progressive hypoxia.

In general, phasic thyroarytenoid activity either decreased or was not recruited under hypercapnic and hypoxic conditions. However, phasic thyroarytenoid activity increased at the highest end-tidal CO₂ levels in three cats and increased at the lowest end-tidal O₂ levels in three cats. Two of the three cats were common to both conditions. For the group as a whole, the
changes in phasic thyroarytenoid activity were not significant. Phasic thyroarytenoid activity was $94 \pm 11.7\%$ of control at 9% end-tidal CO$_2$ and $139 \pm 59\%$ of control at 5% end-tidal O$_2$. Phasic expiratory transversus abdominis activity appeared under hypercapnic and hypoxic conditions and increased with increasing chemical drive (Fig. 1).

Passively induced hypocapnia. During passive hyperventilation, the end-tidal CO$_2$ was $4.9 \pm 0.7\%$ during quiet breathing before the onset of mechanical ventilation and $3.0 \pm 0.5\%$ just before cessation of mechanical ventilation. During passive hyperventilation, the HP became tonically active at a level less than or equal to its peak activity during spontaneous breathing just before the onset of passive hyperventilation (Fig. 4). Peak HP activity just before the cessation of passive hyperventilation was $77 \pm 24\%$ of peak activity during the control period. Cessation of passive hyperventilation resulted in a central apnea. Tonic activation of the HP never increased during the apnea and in some instances decreased in the latter part of the apnea. Phasic HP activation resumed with the onset of spontaneous respiration. In some cases, phasic activity of the HP continued throughout the hyperventilation and apneic periods, despite the absence of respiratory efforts as evidenced by absence of flow during the apnea.

Like the HP, the thyroarytenoid became tonically active during mechanical hyperventilation. In contrast to the HP, thyroarytenoid activity progressively increased during the passive hyperventilation. Peak thyroarytenoid activity just before the cessation of hyperventilation was $564 \pm 852\%$ of peak activity during spontaneous breathing. There was no recruitment of TP or transversus abdominis activity during the passive hyperventilation or ensuing central apnea.

Sighs. Sighs were most commonly observed under hypoxic conditions and during the progressive pneumothorax trials. The EMG discharge patterns during sighs appeared to be independent of the underlying condition. Figure 5 shows the PC discharge pattern during a sigh. The inspiratory portion of the sigh was associated with a significant decrease in tonic HP activity ($84 \pm 22\%$ of control) but no change in thyroarytenoid activity ($99 \pm 5\%$ of control). The expiratory portion of the sigh was associated with a significant increase in thyroarytenoid activity ($779 \pm 947\%$ of control) but no change in HP activity ($120 \pm 16\%$ of control). Transversus abdominis activity during the expiratory portion of the sigh was not significantly different from control ($170 \pm 54\%$ of control). Sighs were present in only three of the five cats with TP EMG recordings, and the results were inconsistent.
Progressively induced pneumothorax. Progressively induced unilateral pneumothorax was associated with the appearance of a rapid shallow breathing pattern. Minute ventilation at 100-ml pneumothorax volume was $114 \pm 26\%$ of control. As shown for one cat in Fig. 6 and for the group in Fig. 7, progressive pneumothorax was not associated with a change in HP activity. Phasic HP activity at 100 ml pneumothorax volume was $91 \pm 14\%$ of control. In contrast, progressive pneumothorax was associated with a significant increase in phasic thyroarytenoid activity. At 100-ml pneumothorax volume, phasic thyroarytenoid activity was $858 \pm 655\%$ of control. Manual chest wall compression was also associated with an increase in phasic thyroarytenoid activity but no change in PC activity.

**DISCUSSION**

Our results in decerebrate cats are in general agreement with the findings of previous investigators (4, 6, 21, 23, 24). Our results indicate that a variety of respiratory stimuli modulate middle and inferior PC muscle activity. During quiet breathing, the HP (middle PC) routinely exhibited phasic expiratory activity and tonic activation throughout the respiratory cycle. Respiratory-related TP (inferior PC) activity was absent during quiet breathing. Previous investigators have reported an increase in phasic expiratory PC muscle activity with increased chemical drive (21, 23). However, Sherrey and Megirian (23) only tested the HP response to one level of hypercapnia (5% inhaled CO$_2$), and the chemical stimulus used by Murakami and Kirchner (21) is not detailed. The present results show that progressive hyperoxic hypercapnia is associated with progressive recruitment of phasic expiratory activity in both PC muscles. Similar responses were seen during progressive isocapnic hypoxia. In agreement with previous investigators, phasic PC activity when present began in late inspiration. In general, the phasic activation had a plateau-like discharge pattern throughout expiration at normocapnia but a progressively increasing ramp-like pattern under hypercapnic conditions.

It is important to note that technical limitations associated with hooked-wire EMG recordings may have influenced the results. For the same muscle activation, distortion of the muscle by its own contraction or that of neighboring muscles can alter the ohmic resistance between the recording electrodes, modifying the EMG...
signal. This is of particular concern for a region so mechanically complex as the upper airway. Electroneu- 
gramos of the nerve supplying motor output to the PC 
muscles would circumvent this potential problem but 
were not obtained in this study.

The results reported in this study and in previous 
studies in cats contrast with those reporting PC activ-
ity in other animal species. Basmajian and Dutta (2) 
detected no respiratory-related PC activity in conscious 
or anesthetized adult rabbits. In contrast, Kawasaki et 
al. (10, 11) reported that PC muscles in anesthetized 
dogs exhibit phasic activity on expiration and, in some 
cases, on inspiration. Although not presented in the 
results, phasic PC activation on inspiration was only 
apparent in our experiments during induced cough.

Comparison of the present results with those of 
previous studies in normal adult humans reveals both 
similarities and differences (2, 8, 19, 20, 22). During 
quiet breathing in normal adult humans, the superior, 
middle, and inferior PC muscles rarely exhibit respira-
tory-related activity during wakefulness and are elec-
trically silent during non-rapid-eye-movement (NREM) 
sleep. When present, phasic activation occurs in expira-
tion. The results of Sauerland et al. (22) that the 
superior PC in normal adult humans usually exhibits 
phasic expiratory activity during wakefulness and sleep 
is not supported by more recent studies (19, 20). The 
results of Sauerland et al. during wakefulness may be 
explained by their subjects being instructed to “breathe 
deeply (even forcefully) to emphasize EMG activity 
related to respiration.” As in decerebrate cats, progres-
sive hypercapnia and progressive hypoxia in adult 
humans are associated with a recruitment and progres-
sive increase in phasic expiratory PC activity (19, 20).

In decerebrate cats, passive hypoxic hyperventila-
tion is associated with tonic activation of the HP but no 
TP recruitment. In contrast, passive hypoxic hyper-
vентilation during NREM sleep in adult humans is not 
associated with PC muscle activation (19).

The mechanical effect of the PC muscles on pharyn-
geal airway function is unknown (1). Of particular 

interest is the increased PC activation during expira-
tion under hypercapnic and hypoxic conditions. Why 
would constrictor muscles surrounding a potentially 
collapsible portion of the airway be activated when the 
organism is attempting to increase minute ventilation? 
Sherrey and Megirian (24) speculated that PC activa-
tion under hypercapnic conditions may help reduce 
anatomic dead space. Murakami and Kirchner (21) 
speculated that PC activation functions to “lift” the 
hyoid bone and thyroid cartilage rostrally after their 
descent in the preceding inspiration. Grelot et al. (6) 
speculated that respiratory-related PC activation may 
stiffen and dilate the pharyngeal airway.

Both the PC muscles and the laryngeal adductor 
muscles exhibit phasic activation on expiration. This 
similarity has led to the speculation that the respira-
tory-related function of the PC muscles is similar to that 
of the laryngeal adductors, i.e., to brake expiratory air-
flow, thus helping to control the time of expiration and 
expiratory lung volume (1). However, hypoxia and 
hypercapnia increased PC activity but tended to sup-
press TA activity. Stimuli associated with a decrease in 
lung volume (progressive pneumothorax, chest wall 
compression) were associated with an increase in thyro-
arytenoid activity but no change in PC activity. Sherrey 
and Megirian (24) reported that deflating the lungs 
over one respiratory cycle by aspirating 20–30 ml of air 
from the lungs at end expiration was associated with a 
virtual elimination of TP activity. However, this state-
ment is not supported by the actual recordings, which 
show a decrease in tonic activity without a change in 
phasic expiratory activity (Fig. 1 in Ref. 24). The 
marked differences between PC and thyroarytenoid 
responses to respiratory stimuli provide circumstantial 
evidence suggesting that the PC muscles and vocal cord 
adductors have different mechanical effects on upper 
airway function. This difference is not surprising given 
the very different anatomy of the two respective airway 
segments. Whereas the larynx is a valvelike structure, 
the pharyngeal segment is a potentially collapsible 
tube.

Unlike known pharyngeal dilator muscles such as 
the genioglossus, which have phasic inspiratory activ-
ity, phasic PC activity is predominantly expiratory. 
Except for this difference, the response of the PC 
muscles to respiratory-related stimuli is much more 
similar to that of the pharyngeal dilators than to the 
laryngeal adductors. A progressive increase in phasic 
genioglossus activity is consistently observed with pro-
gressive hyperoxic hypercapnia or isocapnic hypoxia. 
The similar recruitment in phasic PC activity with 
increased chemical drive suggests that the PC muscles 
may be functioning in a manner similar to or in concert 
with other pharyngeal dilators to stiffen and enlarge 
the pharyngeal airway. Supporting this speculation are 
the observations that the superior PC has an activation 
pattern similar to that of a pharyngeal dilator during 
NREM sleep in patients with obstructive sleep apnea (7, 17).

In summary, our EMG findings in decerebrate cats 
show marked differences in the respiratory-related
activation of the PC and thyroarytenoid muscles. Progressive hypercapnia and progressive hypoxia increased phasic PC activity but tended to suppress phasic thyroarytenoid activity. The expiratory phase of a sigh was associated with an increase in phasic thyroarytenoid activity but no change in phasic PC activity. Progressive pneumothorax was associated with an increase in phasic thyroarytenoid activity but no change in PC activity. The results strongly suggest that the PC muscles, unlike the vocal cord adductors, do not brake expiratory airflow. On the basis of our EMG findings in decerebrate cats and humans, we hypothesize that the PC muscles may constrict or dilate the pharyngeal airway dependent on airway size. This functional duality would not be unique to the PC muscles. Though internal intercostal muscles generally promote exhalation, their contraction at very low lung volumes facilitates inspiration (5). Although the evidence is circumstantial, this hypothesis regarding the mechanical effects of PC muscle activation would reconcile the seemingly contradictory activation of these muscles during swallowing and respiration.

REFERENCES