Upper airway pressure-flow relationships and pharyngeal constrictor EMG activity during prolonged expiration in awake goats

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O’Halloran KD, Bisgard GE. Upper airway pressure-flow relationships and pharyngeal constrictor EMG activity during prolonged expiration in awake goats. J Appl Physiol 105: 100–108, 2008. First published May 1, 2008; doi:10.1152/japplphysiol.00810.2007.—We undertook the present investigation to establish whether narrowing/closure of the upper airway occurs during spontaneous and provoked respiratory rhythm disturbances and whether pharyngeal constrictor muscle recruitment occurs coincident with upper airway occlusion during prolonged expiratory periods. Upper airway pressure-flow relationships and middle pharyngeal constrictor (mPC) EMG activities were recorded in 11 adult female goats during spontaneous and provoked prolongations in expiratory time (Te). A total of 213 spontaneous prolongations of expiration were recorded. Additionally, 169 prolonged expiratory events preceded by an augmented breath were included in the analyses. In separate trials on different days, Te was prolonged by systemic administration of dopamine, by raising the inspired fraction of O2 from 0.10 to 1.00 during poikilocapnic conditions or by systemic administration of clonidine. Continuous tonic activation of the mPC EMG was observed during each prolonged Te period regardless of the duration or initiating cause. However, significant increases in subglottic tracheal pressure, with expiratory airflow braking indicative of upper airway narrowing or closure, was only observed during spontaneous events without a preceding augmented breath and during clonidine-induced events. Tonic mPC activation proved an unreliable indicator of airway occlusion. Furthermore, mPC muscle activation alone is not sufficient to induce pharyngeal occlusion during prolonged expiration. Our data suggest that airway closure is not a common occurrence during provoked respiratory disturbances in awake goats. We propose that airway closure, when present during prolonged Te, is more likely dependent on activation of laryngeal adductor muscles with glottic braking independent of pharyngeal narrowing.

Clonidine; obstructive sleep apnea; upper airway patency

THE HUMAN PHARYNX LACKS BONY and cartilaginous support and is vulnerable to collapse. This vulnerability arises especially during inspiration when a subatmospheric pressure is generated in the upper airway lumen due to activation of the diaphragm and accessory inspiratory pump muscles. Over 20 muscles participate in the regulation of upper airway patency during respiratory- and non-respiratory-related functions. Reflex activation of the pharyngeal dilator muscles protects airway patency on a breath-by-breath basis and may be especially important in reestablishing airflow following occlusion of the highly compliant pharyngeal segment (33). Repetitive collapse of the upper airway exclusively during sleep, associated with arterial oxygen desaturations, is the hallmark of the obstructive sleep apnea syndrome (OSAS) (38). OSAS is associated with significant cardiovascular, metabolic, and neurocognitive dysfunctions and is emerging as a serious and likely underestimated public health problem. Multiple factors contribute to the pathogenesis of OSAS, but sleep-related decrements in upper airway muscle activity in individuals with congenital or acquired abnormal airway anatomy is a key component of the disorder (38). It is also recognized, however, that respiratory rhythm disturbances with prolonged expiration or central apnea may predispose to airway occlusion. Narrowing or occlusion of the upper airway during prolonged expiration may lead to the occurrence of obstructive apneas and the establishment of a mixed apnea phenotype in patients. Thus an understanding of upper airway mechanics during prolonged expiration and central apnea may expand our understanding of potential mechanisms involved in the pathogenesis of OSAS in humans.

Central α2-adrenergic pathways are important modulators of respiratory motor output, including cranial motor drive to the adductor and adductor muscles of the upper airway (10–12, 24, 27, 30). Our laboratory has shown that α2-adrenergic receptor stimulation causes profound disturbances in respiratory pattern in the goat that include periods of prolonged expiration (10–12, 24, 25, 27–30). Dysrhythmic breathing induced by the α2-adrenergic agonist clonidine is associated with continuous tonic activation of expiratory-related drive in laryngeal (11, 12, 24, 27, 30) and pharyngeal (24, 27) motoneurons, leading to active airway closure during central apnea (24, 27). Our results are in general agreement with studies demonstrating tonic activation of laryngeal and pharyngeal adductor muscles during provoked or spontaneous central apneas in animals (3–5, 9, 14–16, 18, 22, 31, 32, 34, 37) and humans (13, 17). These observations have led to suggestions that central apneas are an active process with continuous tonic activation of expiratory-related drive in motoneurons supplying pharyngeal muscles. Although the mechanical consequences of pharyngeal constrictor muscle recruitment during prolonged expiratory periods is not entirely clear, it is speculated that such changes may result in airway narrowing or complete closure. This hypothesis is supported by the observation that pharyngeal narrowing was observed endoscopically during provoked central apneas in normal human subjects (1) and in goats (4, 5, 24). Furthermore, complete pharyngeal occlusion occurs during spontaneous central apneas in preterm infants (35) and in patients with the central sleep apnea syndrome (1). Others, however, have reported no increase in pharyngeal constrictor activation during spontaneous apneas in humans (8), suggesting that pharyngeal occlusion is vulnerable to collapse. This vulnerability arises especially during inspiration when a subatmospheric pressure is generated in the upper airway lumen due to activation of the diaphragm and accessory inspiratory pump muscles. Over 20 muscles participate in the regulation of upper airway patency during respiratory- and non-respiratory-related functions. Reflex activation of the pharyngeal dilator muscles protects airway patency on a breath-by-breath basis and may be especially important in reestablishing airflow following occlusion of the highly compliant pharyngeal segment (33). Repetitive collapse of the upper airway exclusively during sleep, associated with arterial oxygen desaturations, is the hallmark of the obstructive sleep apnea syndrome (OSAS) (38). OSAS is associated with significant cardiovascular, metabolic, and neurocognitive dysfunctions and is emerging as a serious and likely underestimated public health problem. Multiple factors contribute to the pathogenesis of OSAS, but sleep-related decrements in upper airway muscle activity in individuals with congenital or acquired abnormal airway anatomy is a key component of the disorder (38). It is also recognized, however, that respiratory rhythm disturbances with prolonged expiration or central apnea may predispose to airway occlusion. Narrowing or occlusion of the upper airway during prolonged expiration may lead to the occurrence of obstructive apneas and the establishment of a mixed apnea phenotype in patients. Thus an understanding of upper airway mechanics during prolonged expiration and central apnea may expand our understanding of potential mechanisms involved in the pathogenesis of OSAS in humans.

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occlusion during central apnea is a passive phenomenon. Taken together, the results of these studies suggest that airway occlusion (active or passive) is a common feature of prolonged expiratory periods independent of the initiating cause.

Few studies, however, have examined upper airway pressure-flow relationships during spontaneous and induced respiratory rhythm disturbances. To date, most studies have inferred changes in upper airway mechanics on the basis of alterations in upper airway nerve or muscle activities and/or visual observation of the airway by endoscopy. In a previous study, our laboratory reported pharyngeal constrictor electromyogram (EMG) activation coincident with airway closure during clonidine-induced central apnea (27), leading us to speculate that active pharyngeal narrowing contributes to clonidine-induced airway closure in the goat. However, in addition, we observed that prolonged expiratory periods occurring immediately after spontaneous augmented breaths in awake goats were associated with continuous tonic activation of the middle pharyngeal constrictor (mPC) muscle without evidence of expiratory airflow braking or upper airway closure. This suggests that active narrowing/closure of the pharynx may not be a common occurrence during prolonged expiration, at least in goats, and that mPC activation alone may not be sufficient to induce complete airway closure. In light of these studies, and because of the clinical relevance, we wished to further characterize upper airway mechanics following spontaneous, hypocapnia-induced, and pharmacologically induced respiratory disturbances in the goat and compare these with clonidine-induced respiratory disturbances that are known to cause airway closure (27).

We undertook the present investigation to establish whether closure of the upper airway is a common feature during prolonged expiration in adult goats during wakefulness. Additionally, we sought to determine whether mPC muscle activation correlated with evidence of upper airway occlusion during prolonged expiration.

MATERIALS AND METHODS

Animals. Studies were conducted on 11 adult female goats (47–81 kg body mass) of mixed breed. The surgical and experimental protocols were approved by the Animal Care Committee of the University of Wisconsin-Madison.

Surgical preparation. Using aseptic techniques, under general anesthesia (induction with 15–20 mg/kg intravenous thiopental sodium for intubation, and maintenance with 1–5% halothane-40% nitrous oxide-oxygen), each goat was prepared with a unilateral common carotid artery translocation to a subcutaneous position to facilitate the insertion of an arterial catheter at a later time. During a second surgical procedure, at least 2 wk later, EMG wire electrodes were inserted into the mPC muscle using established techniques (24, 25, 27).

Briefly, bipolar Teflon-insulated stainless steel EMG wire electrodes (no. AS 637, Cooner Wire, Chatsworth, CA) were implanted unilaterally in the MPC. The electrodes were sewn in place under direct visualization and fixed securely with a knot. A single lead sewn subcutaneously served as a common reference electrode. The EMG leads were sutured to nearby fascia to relieve any strain on the electrodes, tunneled subcutaneously, and exteriorized through the skin in the neck to facilitate access for recording on experimental days. When not in use, the leads were protected in elastic bandage wraps that were changed regularly. All goats received intramuscular antibiotic (Penicillin G) for 3 days postoperatively to control infection.

After surgical procedures, during a minimum 2-wk recovery period, each goat was trained to stand quietly in a stanchion while wearing a tight-fitting face mask. The day before each study, an arterial catheter was inserted into the elevated carotid artery for anaerobic collection of blood samples for blood-gas analysis and for arterial blood pressure measurement. A catheter was also placed in an external jugular vein for intravenous drug administration where appropriate (see Protocol). All catheters were flushed with heparinized saline and closed until the day of the experiment.

Measurements. Ventilatory data were collected while the goats were wearing a tight-fitting facemask equipped with a low-resistance, one-way breathing valve (model 2700, Hans Rudolph, Kansas City, MO). Inspired gases were delivered to the goat via flexible tubing (3-cm ID). Expired gases were collected in a spirometer (120 liters) from which steady-state expired minute ventilation could be measured during the experiment. Inspired and expired flows were measured using separate pneumotachometers connected to suitably calibrated pressure transducers (models DP45 and MP45, Validyne, Northridge, CA). Subglottic tracheal pressure (Prt) was measured from a 1.3-gauge needle inserted into the trachea 4–6 cm caudal to the larynx. Baseline ventilation and mPC EMG activity were unaffected by this procedure (~30 min recovery after needle insertion was allowed before experimental protocols began). Mask pressure was measured from a port in the face mask. Prt and mask pressure were measured with pressure transducers (models DP45 and MP45, Validyne) calibrated daily with a water manometer. Systemic blood pressure was measured with a pressure transducer (Spectramed) that was calibrated daily with a mercury manometer.

EMG signals were amplified (model 1700, A-M Systems, Everett, WA), filtered (band-pass 0.01–10.0 kHz), passed through an analog-to-digital converter, and sampled at 500 Hz using the WINDAQ data acquisition system (DATAQ Instruments, Akron, OH). All signals were stored on a computer for later analysis. Arterial blood samples were analyzed for arterial pH, PCO₂, and PO₂ using a blood-gas analyzer (model ABL 500, Radiometer Copenhagen, Denmark). A thermistor probe in the rectum was used for measurement of body temperature for blood-gas temperature correction.

Protocol. Each goat was studied on several separate occasions at least 1 wk apart. The animals remained standing throughout the entire experimental periods. After the goat assumed a comfortable standing position, the animal was loosely restrained with the head and neck in a normal resting position. Only ventilatory and EMG data collected in this position were included in the analyses in an attempt to minimize changes in EMG activity that may have been related to postural changes. On each study day, ventilatory and EMG data were collected under baseline control conditions for 2–3 h with the goat breathing room air. Spontaneous expiratory prolongations, including those that were preceded by augmented breaths (postsigh expirations), were included in the analyses.

Table 1. Subglottic pressures and pharyngeal constrictor muscle activity during spontaneous and provoked expiratory prolongations

<table>
<thead>
<tr>
<th>Protocol</th>
<th>n</th>
<th>Ti, s</th>
<th>Pmean, cmH₂O</th>
<th>mPC, AU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>213</td>
<td>6.26±1.08*</td>
<td>3.14±0.25*</td>
<td>810±202*</td>
</tr>
<tr>
<td>Postsigh Events</td>
<td>169</td>
<td>5.59±1.07*</td>
<td>1.32±0.12</td>
<td>353±99</td>
</tr>
<tr>
<td>Control</td>
<td>207</td>
<td>2.07±0.20</td>
<td>1.10±0.06</td>
<td>352±115</td>
</tr>
<tr>
<td>Postsigh Events</td>
<td>169</td>
<td>4.61±0.98*</td>
<td>0.73±0.12</td>
<td>501±124*</td>
</tr>
<tr>
<td>Control</td>
<td>169</td>
<td>1.69±0.07</td>
<td>1.25±0.04</td>
<td>285±115</td>
</tr>
<tr>
<td>Postsigh Events</td>
<td>17</td>
<td>4.22±0.47*</td>
<td>0.98±0.17</td>
<td>711±102*</td>
</tr>
<tr>
<td>Control</td>
<td>199</td>
<td>0.99±0.16</td>
<td>1.10±0.08</td>
<td>355±105</td>
</tr>
<tr>
<td>Postsigh Events</td>
<td>55</td>
<td>6.22±1.57*</td>
<td>5.48±0.47*</td>
<td>611±162*</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of trials conducted in 11 female goats; Ti, expiratory duration; Pmean, mean expiratory subglottic tracheal pressure; mPC, middle pharyngeal constrictor EMG activity in arbitrary units (AU). *Significant difference from control, P < 0.05 (Student’s paired t-test).
recorded during this time. Respiratory events concomitant with swallowing [identified from animal behavior and short maximal activity burst(s) in the EMG trace] were excluded from the analyses. Following this recording period, prolonged expirations were induced by systemic administration of dopamine (10–50 μg/kg); by a modified Dejours Test in which animals were exposed to poikilocapnic hypoxia (arterial Po2 ~40 Torr) for 30 min and expiratory prolongations were induced at the end of hypoxic trials by raising the inspired fraction of O2 from ~0.10 to 1.00 for 30–60 s under poikilocapnic conditions (hypocapnic-induced prolonged expirations); or by systemic administration of clonidine wherein dysrhythmic breathing episodes, including multiple episodes of prolonged expiratory periods, were induced by the α2-adrenergic receptor agonist clonidine administered in cumulative doses (1–2 μg/kg; 5–8 μg/kg total cumulative dose) every 5–10 min consistent with previous studies from our laboratory (24, 27). The experimental protocols were completed in all animals.

Drugs. All drugs were prepared on the day of each experiment. Doses of all drugs were calculated on the basis of salt weight. Dopamine HCl and clonidine HCl (Sigma Chemical, St. Louis, MO) were dissolved in sterile saline (0.9% NaCl) to obtain stock solutions that were further diluted in saline for intravenous administration.

Data and statistical analysis. mPC EMG signals were full-wave rectified and moving-time averaged (100-ms time constant) to quantify the mean electrical activity in arbitrary units, which was derived by dividing the area under the moving average trace by EMG burst duration during a phasic discharge. Mean and peak subglottic Prt and

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**Fig. 1.** Representative recordings of inspiratory and expiratory flows, subglottic tracheal and mask pressures, and middle pharyngeal constrictor “raw” (MPC) and moving average (MPCMA) activity in 2 awake goats (A and B). Note, during spontaneous central apneas, evidence of tonic MPC activation and positive subglottic tracheal pressure with expiratory airflow braking, indicative of airway narrowing. Time bars represent 3 s.
mPC EMG activity were analyzed during the prolonged expiratory duration of spontaneous or provoked events and were compared with data obtained during expiration in the five consecutive control breaths immediately preceding the interventions. All values are presented as means ± SE. Statistical analysis was evaluated by Student’s paired t-test. Statistical significance was taken at \( P < 0.05 \).

**RESULTS**

**Spontaneous events.** A total of 213 spontaneous expiratory prolongations of variable duration were recorded. mPC EMG activity was significantly elevated during the prolonged expiratory duration (TE) of spontaneous events (Table 1). Tonic activation of the mPC persisted throughout the duration of prolonged TE intervals independent of the duration of the events (Fig. 1). Associated with mPC EMG recruitment, mean and peak expiratory subglottic Ptr was significantly increased (Table 1). Positive subglottic Ptr was maintained throughout the prolonged TE of spontaneous events in all animals and was sufficient to retard or prevent expiratory flow until end expiration, indicating complete airway closure (Fig. 1).

**Postsigh events.** A total of 169 postsigh expiratory prolongations of variable duration were recorded. Augmented breaths were characterized by their typical biphasic inspiratory trajectory and prolonged inspiratory duration. Tonic activation of the mPC EMG was observed during the significantly prolonged expiratory phase of augmented breaths (Fig. 2). However, mean electrical activity of the mPC was not significantly different from control activity (Table 1). Mean expiratory subglottic Ptr was not significantly different during postsigh

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**Fig. 2.** Representative recordings of inspiratory and expiratory flows, subglottic tracheal and mask pressures, and MPC and MPC\textsubscript{MA} activity in 2 awake goats (A and B). Note evidence of tonic MPC activation during prolonged expiration following augmented breaths but no evidence of positive subglottic pressure during expiration or airflow braking. Time bars represent 3 s.
expiratory epochs compared with control breaths, and there was no evidence of expiratory airflow braking or airway closure.

**Dopamine-induced events.** Dopamine administration (10–50 μg/kg) resulted in dose-dependent ventilatory depression and variable periods of prolonged Te. A total of 96 dopamine trials were included in the analyses (Table 1). Tonic activation of the mPC EMG at a level equal to or greater than that observed during control breaths (Fig. 3) persisted throughout the dopamine-induced prolonged expiratory periods. On average, mPC EMG activity was significantly greater than activity in control breaths (Table 1). However, mean and peak expiratory subglottic Ptr during dopamine-induced events were not significantly different from control breaths, and there was no evidence of expiratory airflow braking or airway closure.

**Hypocapnia-induced events.** A total of 17 trials of poikilocapnic hypoxia were performed (Table 2). Switching the inspired gas mixture from hypoxia (~10% O2) to hyperoxia (100% O2) for 30–60 s resulted in hypocapnic-induced prolongations of Te of variable duration. mPC EMG activity was significantly elevated during the prolonged Te of hypocapnia-induced events (Table 1). Tonic activation of the mPC persisted throughout the duration of prolonged Te intervals inde-

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**FIG. 3.** Representative recordings of inspiratory and expiratory flows, subglottic tracheal and mask pressures, and MPC and MPCMA activity in 2 awake goats (A and B). Note evidence of tonic MPC activation during prolonged expiration following intravenous dopamine injection (50 μg/kg, at arrows) but no evidence of positive subglottic pressure during expiration or airflow braking. Time bars represent 3 s.
Table 2. Arterial pH and blood-gas values under baseline conditions, during poikilocapnic hypoxia, and following systemic administration of clonidine in 11 awake goats

<table>
<thead>
<tr>
<th>Condition</th>
<th>pHa</th>
<th>PaCO₂ (Torr)</th>
<th>PaO₂ (Torr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>7.41±0.01</td>
<td>39.2±1.4</td>
<td>96.0±2.8</td>
</tr>
<tr>
<td>Prehypoxia</td>
<td>7.42±0.01</td>
<td>39.1±1.6</td>
<td>97.1±2.1</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>7.48±0.02*</td>
<td>32.8±1.9*</td>
<td>42.8±1.7*</td>
</tr>
<tr>
<td>Preclonidine</td>
<td>7.40±0.01</td>
<td>38.0±1.3</td>
<td>93.3±2.9</td>
</tr>
<tr>
<td>Clonidine</td>
<td>7.37±0.01*</td>
<td>45.8±1.7*</td>
<td>83.6±2.7*</td>
</tr>
</tbody>
</table>

Values are means ± SE. pHa, arterial pH; PaCO₂, arterial partial pressure of carbon dioxide; PaO₂, arterial partial pressure of oxygen. *Significant difference from corresponding control value, \( P < 0.05 \) (Student’s paired \( t \)-test).

**Fig. 4.** Representative recordings of inspiratory and expiratory flows, subglottic tracheal and mask pressures, and MPC and MPCₐ activity in an awake goat. A and B are components of a continuous record. The inspired fraction of O₂ was raised from ~0.10 to 1.00 for the period indicated between the arrows. Note evidence of MPC recruitment during prolonged expiratory durations but no evidence of positive subglottic pressure during expiration or airflow braking. Time bar represents 3 s.

Consistent with previous studies from our laboratory (24, 26–28, 30), clonidine induced a highly dysrhythmic pattern of breathing in all animals that was characterized by alternating episodes of tachypnea and slow irregular breathing patterns, including prolonged and variable \( T_E \) intervals. Dysrhythmic ventilatory patterns induced by clonidine were accompanied by significant increases in mPC and peak expiratory subglottic PTR during hypocapnic-induced events were not significantly different from control breaths and there was no evidence of expiratory airflow braking or airway closure.
EMG activity (Table 1). Tonic activation of the mPC persisted throughout the duration of clonidine-induced disturbances in respiratory rhythm (Fig. 5). In all animals, positive subglottic Prt was maintained throughout the clonidine-induced prolonged Te events sufficient to delay expiratory flow until end-expiration, indicating complete closure of the upper airway during clonidine-induced events.

DISCUSSION

The main finding of this study is that airway narrowing/closure is not a common occurrence during prolonged expiration in goats during wakefulness despite mPC muscle activation. Continuous tonic activation of the mPC EMG was routinely observed during prolonged Te, regardless of the intervention or duration of expiration. However, pressure-flow measurements in the upper airway clearly demonstrated that airway narrowing/closure only occurred during spontaneous Te prolongations and clonidine-induced events. Postsigh, dopamine-induced, and hypocapnic-induced respiratory disturbances showed no evidence of early expiratory airflow braking or delayed expiratory flow despite mPC EMG activation.

Tonic activation of pharyngeal constrictor muscles has been observed previously during provoked (3–5, 18, 24, 25, 27, 37) and spontaneous (34) central apneas. These observations have led to suggestions that central apneas are an active process with continuous tonic activation of expiratory-related drive in motoneurons supplying pharyngeal muscles. The significance of these changes is that airway narrowing/occlusion during exp-

Fig. 5. Representative recordings of inspiratory and expiratory flows, subglottic tracheal and mask pressures, and MPC and MPCMA activity in an awake goat. A: recordings made during control conditions. B: recordings in the same animal following intravenous clonidine administration (5 μg/kg, total cumulative dose). Note evidence of tonic MPC activation during prolonged expiration and complete retardation of expiratory flow until late expiration coincident with elevated subglottic pressure, indicative of complete airway closure throughout expiration. Time bars represent 3 s.
tended expiration may predispose to pharyngeal obstruction with adverse effects for pulmonary ventilation on the resumption of respiratory efforts. Thus sleep-related breathing instabilities may predispose to the development of mixed apneas.

Our laboratory has previously demonstrated that the respiratory-related activity of the mPC in the awake goat is similar to that of the thyroarytenoid muscle (25). The pharyngeal constrictor muscles are innervated by the pharyngeal branch of the vagus and are typically active throughout expiration. In the goat, mPC muscle activity shows phasic expiratory-related activity in normoxia and a decline in activity with increased respiratory drive during hypoxia and hypercapnia (5, 25). Consistent with our laboratory’s previous study, mPC activity was lower in hypoxia compared with normoxia in this study (see Table 1). The mechanical effects of pharyngeal constrictor muscle activation depend on airway cross-sectional area and additionally appear to show considerable species differences. Kuna and colleagues (17–21) have suggested that the pharyngeal constrictor muscles in decerebrate cat and humans may act in concert with other classic pharyngeal dilators to stiffen/stabilize the pharyngeal airway, an effect, like that of the tongue retractor muscles in the rat (2), that is dependent on airway volume (20). Our observations suggest that the mPC in goat - similar to the laryngeal adductors - may help brake expiratory airflow and control expiratory timing and end-expiratory lung volume (25). Consistent with this view is the finding of Feroah and colleagues (6), who report a reduction in thyropharyngeus muscle activity in response to isolated upper airway negative pressure in the goat, whereas neural drive to the pharyngeal constrictor muscles of the rat is reflexively increased in response to subatmospheric pressure in the upper airway (36). Our observation of mPC EMG activation coincident with airway closure during clonidine-induced central apnea (27) led us to speculate that active pharyngeal narrowing contributes to clonidine-induced airway closure in the goat. This prompted us to examine mPC muscle behavior in response to a variety of interventions in this study. Our results indicate that mPC activation is not commonly accompanied by occlusion of the upper airway (as evidenced by pressure-flow relationships), and thus pharyngeal constrictor muscle activation does not correlate with reductions in upper airway caliber and is a poor indicator of mechanical events occurring in the upper airway during respiratory disturbances. Furthermore it appears that upper airway occlusion is not a common feature during prolonged expiration in the awake goat.

We suggest that active airway closure observed during spontaneous and clonidine-induced events is more likely dependent on laryngeal adductor muscle recruitment and glottic closure. Previous studies have unequivocally shown that induced central apneas activate laryngeal adductor muscles in animals (3, 10, 14, 16, 22, 24, 27, 31, 32) and sleeping adult humans (17). Furthermore, our laboratory has shown that clonidine-induced apneas clearly produce reciprocal modulation of laryngeal adductor and abductor muscles: tonic activation of thyroarytenoid muscle with complete inhibition of posterior cricoarytenoid muscle activity for the duration of the central apnea (24). This latter finding is entirely consistent with observations during provoked central apneas in awake lambs (14, 16, 32) and during hypocapnic-induced apneas in humans in non-rapid eye movement sleep (17). Thus we suggest that the balance of forces exerted by opposing dilator and constrictor muscles may be especially important in determining airway caliber during prolonged expiration. Reciprocal modulation of airway abductor and adductor muscle activities may be necessary for complete airway occlusion.

There are significant limitations to our study that warrant discussion. In this study, we measured subglottic Ptr to ensure that we would have evidence (or not) of airway occlusion during our manipulations independent of the site (laryngeal or pharyngeal) of occlusion. This method however, cannot distinguish between laryngeal and pharyngeal obstruction and can detect only complete occlusion or severe narrowing starting at early expiration before exhalation. Obstruction could be present in some of our trials at the end-expiratory pause after the intraluminal pressure declined. With our study design, we cannot determine whether the pharynx was occluded at end expiration. Additional measurements of pharyngeal pressure would have allowed us to better define and characterize airway mechanics during spontaneous and provoked events. Additionally, we did not measure diaphragm EMG activity to confirm that respiratory disturbances were central events. However, our laboratory has previously documented that clonidine-induced dysrhythmic events are of a central origin (24). We also acknowledge that prolonged central apneas may result in airway occlusion and that the extended expiratory events in this study may represent events distinct from central apnea. It should also be noted that we cannot exclude the possibility that the same experimental manipulations could have different mechanical consequences in sleeping goats and that events in the goat (awake or sleeping) may be different from other species, including humans.

In conclusion, results from this study are not supportive of the hypothesis that active pharyngeal narrowing contributes to complete airway closure during prolonged expiration. Airway narrowing/closure is not a common occurrence during extended expiration in goats during wakefulness despite mPC muscle activation. We suggest that airway closure, when observed during prolonged expiration, is likely dependent on the recruitment of laryngeal adductor muscles with consequent glottic braking (independent of pharyngeal narrowing) and/or reciprocal inhibition of upper airway dilator muscle activity (passive collapse). We propose that regulation of glottic aperture appears to be the key determinant of airway patency during respiratory rhythm disturbances and that pharyngeal narrowing, when observed, is likely a passive phenomenon related to the withdrawal of tonic abductor muscle activity.

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GRANTS

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REFERENCES


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