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Control of genioglossus muscle inspiratory activity

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BROUILLETTE, ROBERT T., AND BRADLEY T. THACH. *Control of genioglossus muscle inspiratory activity.* J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 49(5): 801–808, 1980.— Tonic and phasic inspiratory genioglossus (GG) electromyographic activity (EMG) was recorded from 13 anesthetized rabbits during unstimulated breathing. Integrated GG EMG peaked earlier in inspiration and presented a more rounded contour than integrated diaphragmatic (DIA) EMG. Spontaneous augmented deep inspirations (sighs) showed a biphasic pattern in both GG and DIA EMGs. Hyperventilation abolished phasic inspiratory activity in the GG before the DIA, suggesting that the GG has a higher CO_2 apneic point. Hypercapnia increased both EMGs; however, GG EMG increased more, as a percent of base line, than did DIA EMG. Oxygen breathing decreased GG more than DIA EMG; sodium cyanide injection and brief nitrogen breathing increased GG more than DIA EMG; carotid body denervation abolished these responses. Vagotomy abolished the Hering-Breuer inflation-inhibition reflex in both muscles, and tactile, visual, and auditory stimulation increased GG more than DIA EMG. Thus, the GG responses to chemoreceptor input and to nonspecific respiratory stimuli are qualitatively similar but quantitatively different from DIA responses. The relevance to mixed and obstructive apnea is discussed.

tongue; airway obstruction; apnea; pharynx; rabbit; respiratory control; chemoreceptors; pulmonary mechanoreceptors; nonspecific respiratory stimuli; behavioral arousal; electromyography

PHARYNGEAL AIRWAY OBSTRUCTION occurs in various clinical circumstances including anesthetized and sleeping normal adults (3, 22), patients with sleep apnea (14, 16, 21), children with abnormalities of the upper airway (9, 17), and near-miss for sudden infant death syndrome infants (15). Evidence now suggests that the genioglossus (GG) muscles, which pull the tongue forward, function as muscles of inspiration opposing pharyngeal collapse due to negative pressure (4, 21). Thus, phasic inspiratory GG activity maintains a patent pharyngeal airway allowing the diaphragm (DIA) and other inspiratory pressure-generating muscles to draw air into the lungs. Remmers et al. (21) suggested that pharyngeal obstruction occurs when the force of negative pharyngeal pressure exceeds the force of the GG muscles. Direct confirmation of this hypothesis is now available from studies in an animal model (4): after GG paralysis, the pharyngeal airway collapsed when subjected to negative pressure.

Accordingly, the present studies were undertaken to determine the effects of peripheral and central chemoreceptors, pulmonary mechanoreceptors, and nonspecific respiratory stimuli on phasic inspiratory GG activity.

METHODS

Thirteen New Zealand White rabbits, weighing 1.8–5.2 kg, were initially anesthetized with ether and 30 mg/kg intraperitoneal pentobarbital with additional pentobarbital doses as needed. A tracheostomy tube was inserted and tied in the trachea.

Electromyograms (EMGs) were recorded from fine wire electrodes (2) (38 gauge, Isomid, Belden) inserted in one GG muscle and the DIA. GG electrodes were placed near the hyoid bone and halfway between the chin and hyoid bone. Through an abdominal incision, DIA electrodes were inserted approximately 1 cm apart into the left hemidiaphragm. The abdominal incision was then sutured.

Electromyograms were amplified (Grass P15) 100–1,000 times with 30 and 1,000 Hz low- and high-frequency filters. Raw EMGs were rectified and electrically integrated with a RC circuit (Beckman 9852A). The integrator response to a step increase or decrease in input was 90% completed in 250 ms. The integrator bandwidth was 70–1,500 Hz. Using this system, integrated DIA EMG was linearly related to occlusion pressure ($r = 0.98$) as previously reported for a similar integrator (10). This RC circuit therefore approximates (but cannot be considered identical to) the moving time average used by others to electrically estimate the force of muscle contractions (12). Raw and integrated EMGs, tracheal pressure, and end-tidal CO_2 were recorded on a polygraph for later analysis.

Recordings of GG and DIA EMGs were obtained on each animal during unstimulated resting breathing.

Influence of carbon dioxide on phasic inspiratory GG activity. To demonstrate the effect of hypocapnia on GG activity, artificial hyperventilation with air or oxygen was performed 13 times in five animals. Hyperventilation was continued until phasic inspiratory activity in both GG and DIA EMGs was abolished. Hyperventilation was then stopped, and the animal was allowed to resume breathing. Two hyperventilation trials were performed in one animal after carotid body denervation.

To demonstrate the effect of hypercapnia on GG activity, rebreathing was performed 27 times in six animals. The animals rebreathed oxygen from a 1-liter anesthesia

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bag for 1–4 min. In three animals arterial blood gases were obtained before and during rebreathing. End-tidal CO_2 (Beckman LB-2) was measured in three animals. The average amplitudes of the inspiratory increases in GG and DIA integrated EMGs before rebreathing were termed base-line activity (100%). The amplitudes of the integrated EMG inspiratory increases during hypercapnia were expressed as percent of base-line activity and plotted against simultaneous end-tidal or arterial CO_2. This analysis therefore eliminated tonic GG (and DIA) activity from consideration.

Influence of oxygen on phasic inspiratory GG activity. The responses of the GG and DIA EMGs to acute hyperoxia were assessed 20 times in six animals by abruptly changing the inspired gas from air to oxygen. The inspiratory increases in GG and DIA integrated EMGs were measured on the polygraph paper. Base-line values were taken as the average of the five breaths preceding the change to oxygen. Response values were taken as the average of the first five breaths 30 s after the change to oxygen, by which time the GG and DIA responses were complete. Dividing the response values of GG and DIA by the respective base-line values expressed each response as a percent of base-line activity. For each animal, the mean decreases in integrated GG EMG and in integrated DIA EMG were calculated. The group mean decreases in GG and DIA integrated EMGs were compared using the paired *t* test.

The responses of the GG and DIA EMGs to acute hypoxia were assessed by 30 trials in 5 animals of a brief period of nitrogen breathing. The inspired gas was abruptly switched from air or oxygen to nitrogen for 4–33 s; the longer durations of nitrogen breathing followed oxygen breathing. Air-to-nitrogen and oxygen-to-nitrogen experiments were analyzed separately. Base-line values were taken as the average of the three inspirations preceding the change to nitrogen. GG and DIA responses were calculated from the single inspirations showing the largest increase in integrated GG or DIA EMGs, respectively. Augmented breaths were omitted from this analysis. In 16 trials in which the integrated GG EMG went off scale and in 1 trial in which the integrated DIA EMG went off scale, the inspiration preceding the off-scale inspiration was taken as the response value for both GG and DIA.

Sodium cyanide, 0.3–2.0 ml of 100 μg/ml solution, was injected 13 times via a femoral vein catheter into three animals. Control injections of isotonic saline were made in each animal. Results were analyzed as described for the nitrogen breathing experiments.

In one animal the carotid bodies were surgically denervated. Before and after this procedure the following experiments were performed as previously described: *1*) change of the inspired gas mixture from air to oxygen, *2*) brief exposure to nitrogen, and *3*) intravenous injection of sodium cyanide.

Effect of pulmonary mechanoreceptors on phasic inspiratory GG activity. End-expiratory airway occlusion maneuvers were performed in nine animals. Single-breath occlusions were done in all animals and longer (5–20 s) occlusions in four. In these four animals, the effect of occlusion while breathing oxygen was compared to the effect of occlusion while breathing air.

Lung inflation maneuvers were performed in four animals by rapidly applying 18–40 cmH_2O of positive end-expiratory pressure.

Bilateral cervical vagotomies were performed in five animals. Postvagotomy phasic inspiratory GG and DIA integrated EMGs were compared for amplitude and duration to prevagotomy values.

Effects of tactile, auditory, and visual stimulation on phasic inspiratory GG activity. During breathing at rest, 7 animals were stimulated a total of 76 times. A wide variety of stimuli were presented such as shining a flashlight at the eyes, touching a lower extremity, and hitting a metal cabinet to produce a loud noise. For trials in which either GG or DIA EMG increased after a stimulus, the GG and DIA responses were analyzed by the percent base-line activity method.

RESULTS

GG EMG activity during unstimulated breathing. In all 13 animals, phasic inspiratory GG EMG activity was superimposed on tonic or expiratory activity (Fig. 1). In 10 animals, phasic inspiratory GG activity was present

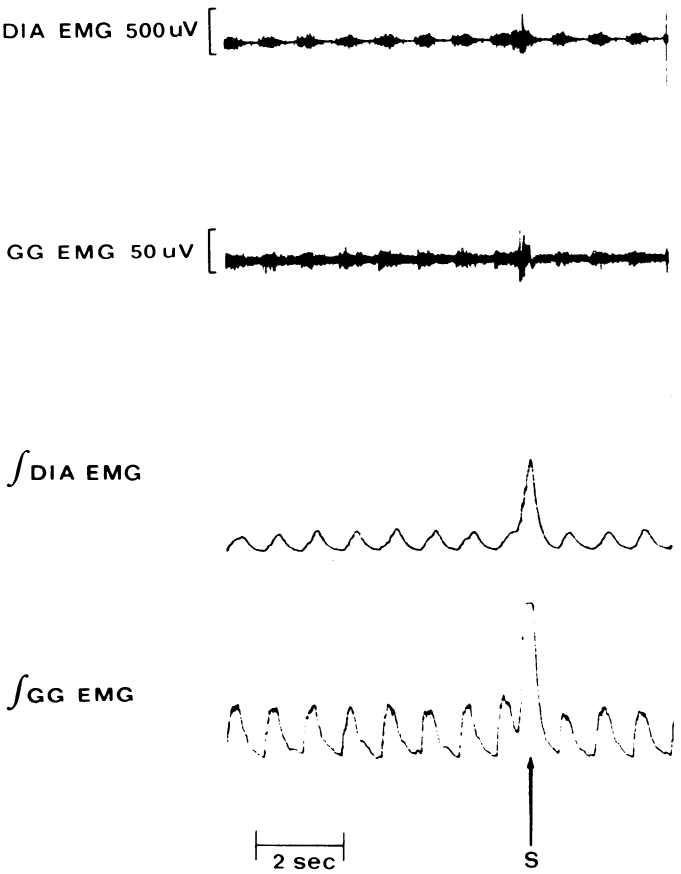

FIG. 1. During spontaneous breathing, phasic inspiratory activity begins simultaneously in genioglossus (GG) and diaphragm (DIA), but peak activity occurs earlier in inspiration for GG rather than DIA. Tonic GG activity is evident in expiration. Augmented breath, or sigh (S), is characterized by increased GG and DIA activity at the end of normal inspiration. Biphasic nature of this augmented inspiration is apparent on both GG and DIA traces. Integrated (∫) GG electromyogram (EMG) goes off scale during second phase of this deep breath. Immediately after the sigh, peak EMG activity is slightly reduced in both GG and DIA.

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throughout the entire experiment; in three animals phasic activity was intermittent.

The intrabreath relation of GG EMG to DIA EMG was similar in all animals (Fig. 1). The inspiratory GG and DIA discharges began almost simultaneously; however, the integrated GG EMG peaked earlier and had a more rounded contour than the integrated DIA EMG. GG EMG often reached peak activity several hundred milliseconds before DIA activity peaked.

In all animals, augmented breaths, or sighs, were characterized by a biphasic GG and DIA EMG pattern with peak GG and DIA activity being greater during the second part of the inspiration. Often the amplitudes of GG and DIA EMGs on the breath after an augmented breath were decreased.

Influence of carbon dioxide on phasic inspiratory GG activity. Artificial hyperventilation with air or oxygen always abolished phasic inspiratory GG and DIA activity (Fig. 2). In each trial, phasic GG was lost before DIA activity. After stopping hyperventilation, phasic inspiratory activity resumed in the DIA before the GG. Results in the carotid body-denervated animal were similar to carotid body-intact animals: GG EMG was abolished before, and returned after, DIA EMG.

During oxygen rebreathing, phasic inspiratory activity in GG and DIA EMGs increased (Fig. 3). Arterial oxygen tensions were uniformly above 300 Torr during rebreathing, thus ensuring that the increased EMG activity could not be due to hypoxic stimulation of peripheral chemoreceptors. In each animal, the increase in GG activity was more marked, as a percentage of base-line activity, than the increase in DIA activity (Fig. 4). Results were similar whether plotted as functions of end-tidal or arterial CO_2.

Effects of oxygen on phasic inspiratory GG activity. Phasic inspiratory activity in both GG and DIA EMGs decreased 5–20 s after switching from air to oxygen breathing (Fig. 5). For each animal, the mean decrease in GG EMG was greater than the decrease in DIA EMG. The group mean decrease in integrated GG EMG was larger than the mean decrease in integrated DIA EMG (Table 1). Phasic inspiratory activity in GG and DIA EMGs increased after the inspired gas mixture was changed from oxygen to air.

In each trial, after changing the inspired gas from air to nitrogen, phasic inspiratory EMG activity increased in both GG and DIA (Fig. 6). For each animal the mean increase in GG activity was greater than in DIA. The group mean increase was larger in the integrated GG EMG than in the DIA (Table 1). In two animals, when the inspired gas mixture was changed from oxygen to nitrogen, integrated GG EMGs increased to 5,360 and 777% of base line, whereas integrated DIA EMGs increased to 152 and 197% of base line.

Both GG and DIA EMGs showed increased phasic inspiratory activity 6–10 s after each cyanide injection (Fig. 7). Spontaneous deep breaths were seen after 6 of 13 injections. The integrated GG EMG increased more than the integrated DIA EMG in each animal. The group mean increase was greater for the GG EMG (Table 1).

In one animal, carotid body denervation abolished the GG and DIA EMG decreases seen when the inspired gas mixture was changed from air to oxygen. After denervation, changing the inspired gas mixture from air to nitrogen did not elicit increases in GG or DIA EMGs; after 35–37 s, EMG amplitudes began to decrease. After denervation, doses of cyanide, which formerly had elicited large increases in GG and DIA EMGs, failed to evoke such increases.

Effects of pulmonary mechanoreceptors on phasic inspiratory GG activity. Before vagotomy, both GG and DIA EMG amplitudes increased on the first inspiration after airway occlusion (Fig. 8*A*). The relative increases in peak integrated EMGs over base-line values appeared similar for both muscles. The durations of the inspiratory bursts in the GG and DIA EMGs were prolonged on the first occluded breath compared to preceding unoccluded breaths. The shape of the integrated GG EMG was generally similar on unoccluded breaths and the first occluded breath; a rapidly augmenting phase was followed by a stable or slowly augmenting phase.

GG and DIA EMGs increased further on subsequent

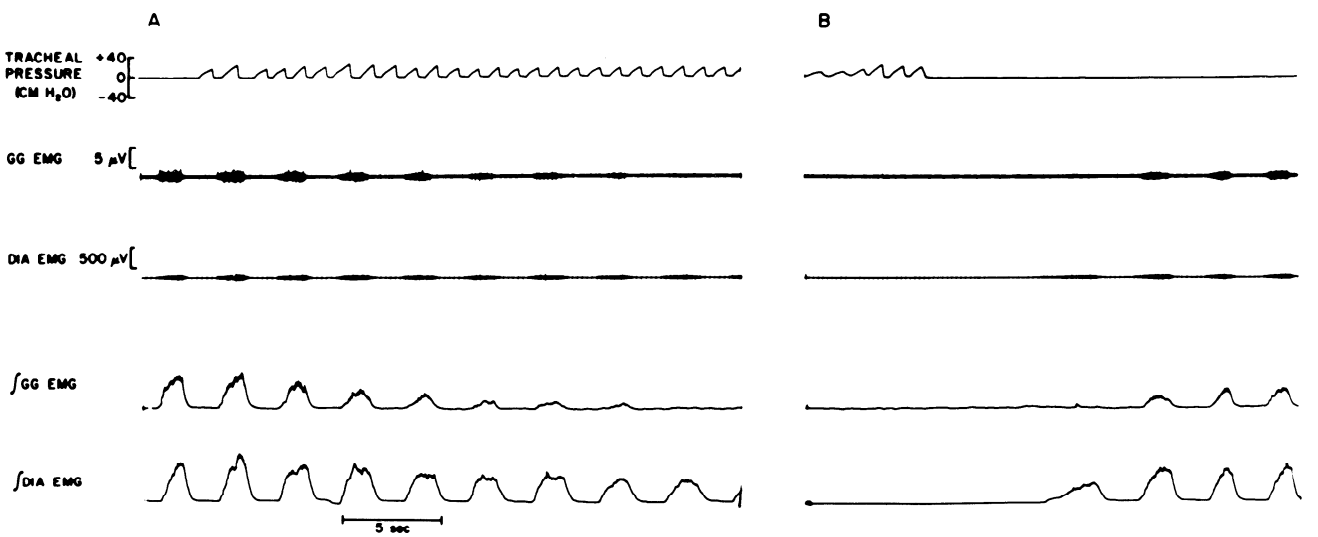

FIG. 2. *A*: during artificial hyperventilation, seen as positive deflections on tracheal pressure trace, GG and DIA EMGs decrease in amplitude. Phasic inspiratory GG activity is lost before DIA activity ceases. With continued hyperventilation, DIA activity stopped (not shown). *B*: 6 s after cessation of artificial hyperventilation, phasic DIA activity returned. Phasic GG activity returned after DIA activity.

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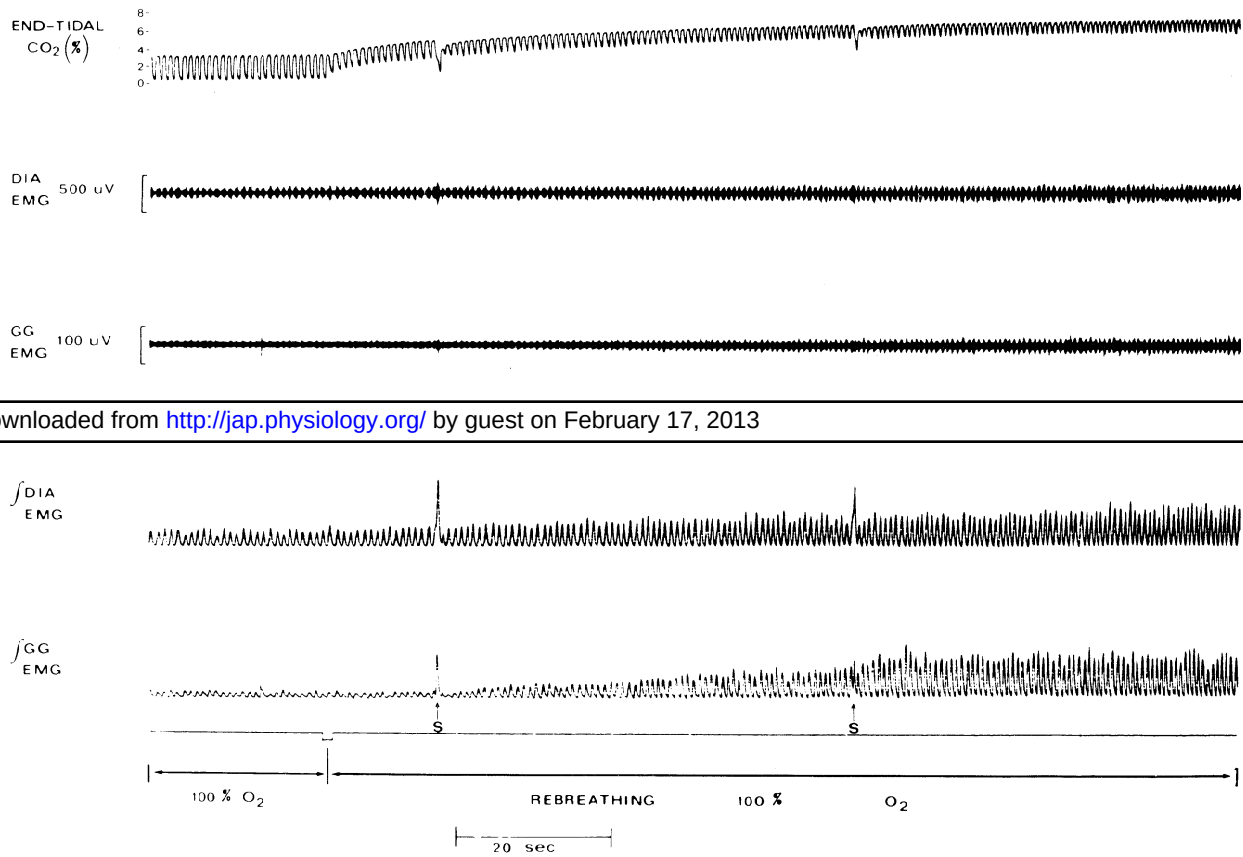

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FIG. 3. O_2 rebreathing experiment in a 5.2-kg rabbit is shown. Before rebreathing, animal is breathing O_2 and has stable phasic inspiratory GG and DIA EMGs. During O_2 rebreathing, phasic inspiratory GG and DIA EMGs increase with elevation of end-tidal CO_2. Two spontaneous sighs (S) are seen during rebreathing. As is apparent on the integrated EMG channels, GG EMG increased more, as a percentage of base-line activity, than DIA EMG, see also Fig. 4.

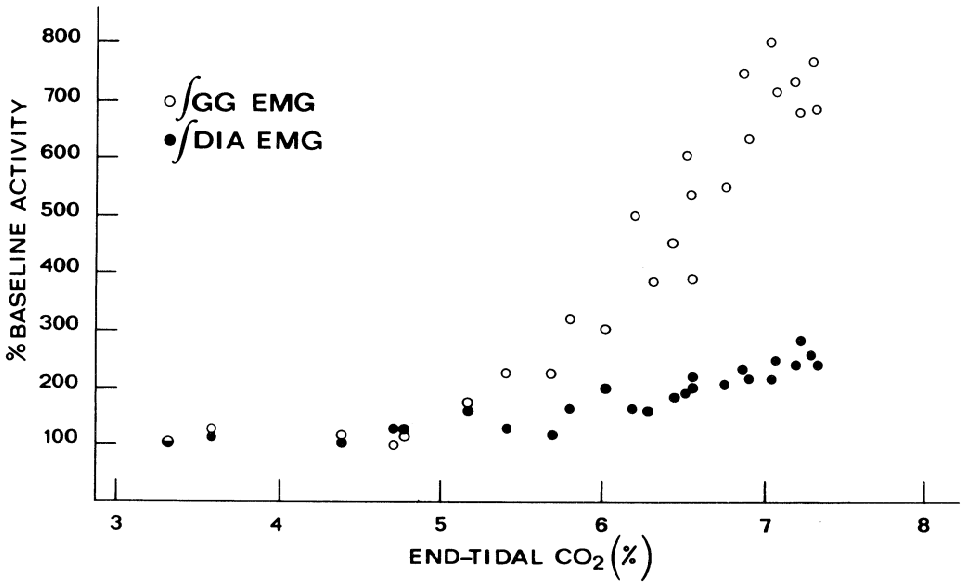

FIG. 4. Increases in GG and DIA EMGs for experiment shown in Fig. 3 are plotted against end-tidal CO_2. Base-line activities were calculated separately for GG and DIA by averaging integrated EMG amplitudes for 16 inspirations prior to starting rebreathing. These base-line values (◒) were taken as 100% and plotted against average end-tidal CO_2 for these breaths. Each point for GG (○) and DIA (●) represents integrated EMG of that breath divided by base-line activity. One breath every 5 s was selected for analysis. Both GG and DIA EMGs increase with increasing end-tidal CO_2; however, increase in GG EMG is greater than increase in DIA EMG.

occluded inspirations; the increase in GG activity was more marked than that of the DIA. When the animal was breathing oxygen prior to the occlusion, the subsequent recruitment of GG and DIA EMGs was attenuated compared to the recruitment seen with occlusions on air.

After vagotomy, GG and DIA EMGs failed to increase on the first occluded breath (Fig. 8*B*). In two of five animals, consistent decreases in DIA EMG on the first occluded inspiration were seen, whereas no such decreases were seen in GG EMG.

Before vagotomy, lung inflation consistently abolished phasic inspiratory GG and DIA activity (Fig. 9*A*); after vagotomy, lung inflation failed to abolish phasic GG and DIA activity (Fig. 9*B*).

Vagotomy increased the amplitudes and prolonged the durations of phasic inspiratory GG and DIA EMG activity. Because tonic GG activity was little changed by vagotomy, this procedure accentuated the phasic inspiratory modulation of GG activity.

Effects of tactile, auditory, and visual stimulation on phasic inspiratory GG activity. Integrated GG EMG amplitudes increased after 35 of 62 stimuli, whereas DIA EMG increased after 21 stimuli (Fig. 10). DIA EMG never increased unless GG EMG increased, whereas GG EMG increased after 14 stimuli when DIA EMG did not increase. The increase in GG EMG was greater, as a percent of base-line activity, than the increase in DIA EMG in all experiments in which a response was seen. In some cases, behavioral arousal, indicated by eye opening and generalized somatic movements, was associated with the increased GG activity after a stimulus. More often, however, increased GG activity was seen without such arousal. Ventilatory rate often increased immediately after a stimulus. The type of stimulus did not appear to affect the response in that each type of stimulus sometimes increased EMG amplitudes and/or increased ventilatory rate.

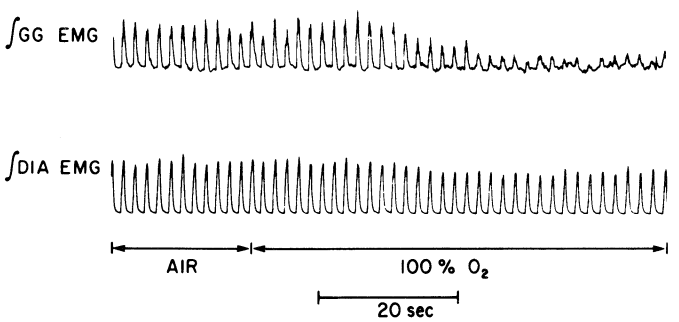

FIG. 5. Typical example of GG and DIA responses after the inspiratory gas mixture is switched from air to O_2. Note stable levels of phasic inspiratory GG and DIA activity during air breathing. Both GG and DIA EMGs decrease after O_2 breathing is begun, but the decrease is more pronounced in GG EMG. Integrated GG EMG decreases to 34% of base-line activity, whereas integrated DIA EMG decreases to 79% of base-line activity.

TABLE 1. *Comparison of integrated GG and DIA EMG responses to O_2 breathing, N_2 breathing, and cyanide infusion*

Expt	Integrated GG EMG	Integrated DIA EMG	*P* Value*	No. of Animals
Change from air to O_2 breathing	35.7 ± 9.5	61.9 ± 7.9	<0.005	5
Change from air to N_2 breathing	352 ± 68	221 ± 38	<0.05	4
NaCN infusion	710 ± 288	203 ± 36	<0.1	3

Values are means ± SD given as a percent of base-line values of the inspiratory increases in integrated electromyograms (EMGs).
* Paired *t* test for a significant difference between the genioglossus (GG) and diaphragmatic (DIA) integrated EMG changes.

DISCUSSION

Long ago it was proposed that GG activity "facilitates the ingress of air into the inspiratory passages" (18). In both adults (21, 22, 25) and infants (28), evidence now suggests that GG contraction prevents airway collapse during unloaded breathing. Although clinical studies have shown that tonic and phasic GG activity changes with sleep state (23) and with alterations of blood gas tensions (14, 15, 21, 25), little is known about the normal control mechanisms and respiratory responses of the GG muscles.

Phasic inspiratory activity and tonic activity with inspiratory modulation have been demonstrated in the posterior cricoarytenoid (PCA) muscles that decrease laryngeal resistance (1, 13, 19). The contours of both the integrated GG EMG and the integrated electroneurogram of the recurrent laryngeal nerve, which innervates the PCA, resemble the contour of inspiratory flow with

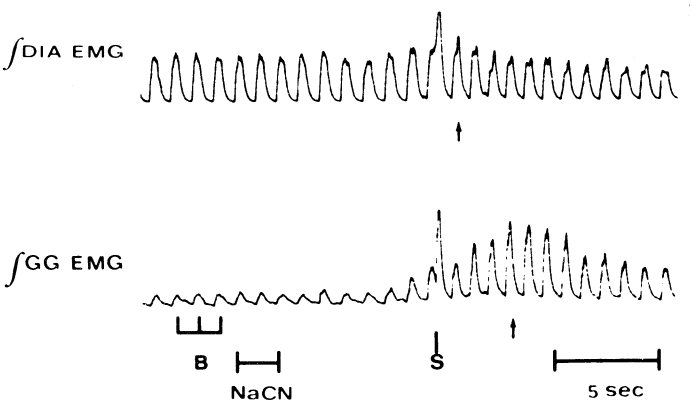

FIG. 7. Results of intravenous injection of 50 μg of sodium cyanide (NaCN) in a 5.0-kg animal. Eight seconds after injection, phasic inspiratory activity increased in GG and DIA EMGs. Inspirations taken as base line (B) activity and as maximal response (↑) are indicated. With this injection integrated GG activity increased to 620% of base line while integrated DIA activity increased to 132%. Augmented breath (S) is seen.

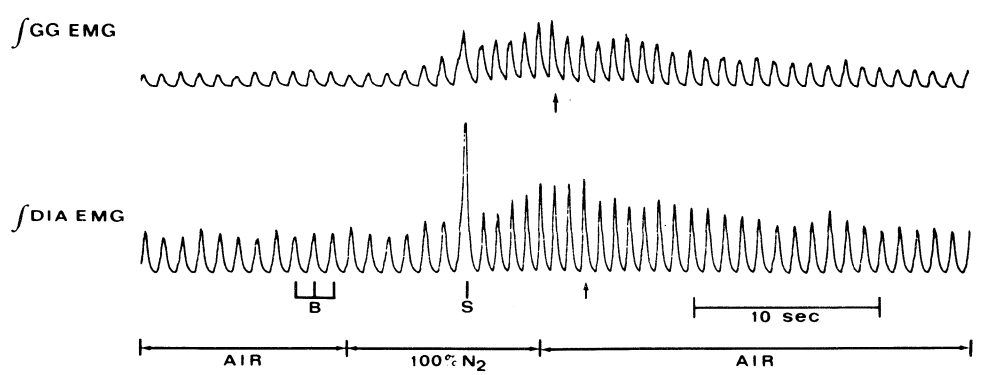

FIG. 6. GG and DIA responses to changing inspired gas mixture from air to N_2 for 10 s. Phasic inspiratory activity increases in GG and DIA EMGs with N_2 breathing. Inspirations taken as base line (B) and as maximal responses (↑) are indicated. For this trial, integrated GG EMG increased to 408% of base line while integrated DIA EMG increased to 230%. Augmented breath, or sigh (S), was not considered for maximal response analysis.

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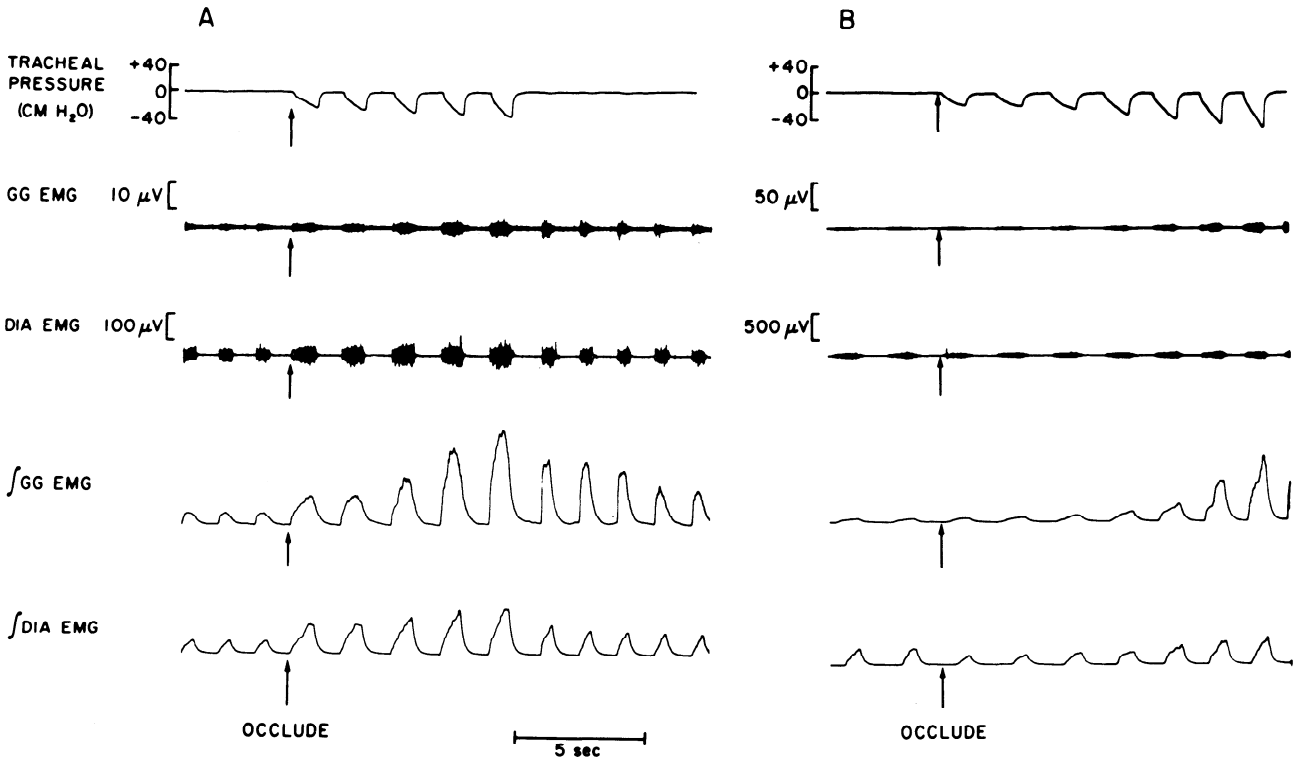

FIG. 8. Effect of airway occlusion maneuver on GG and DIA EMGs. *A*: before vagotomy. On first occluded inspiration (after *arrows*), durations of inspiratory bursts in GG and DIA EMGs are prolonged and integrated EMG amplitudes are increased compared to preceding unoccluded breaths. *B*: after vagotomy. On first occluded inspiration (after *arrows*), GG EMG is unchanged from preceding unoccluded breaths while DIA EMG is decreased. Note decreased gains on raw EMG channels necessitated by increased activity after vagotomy.

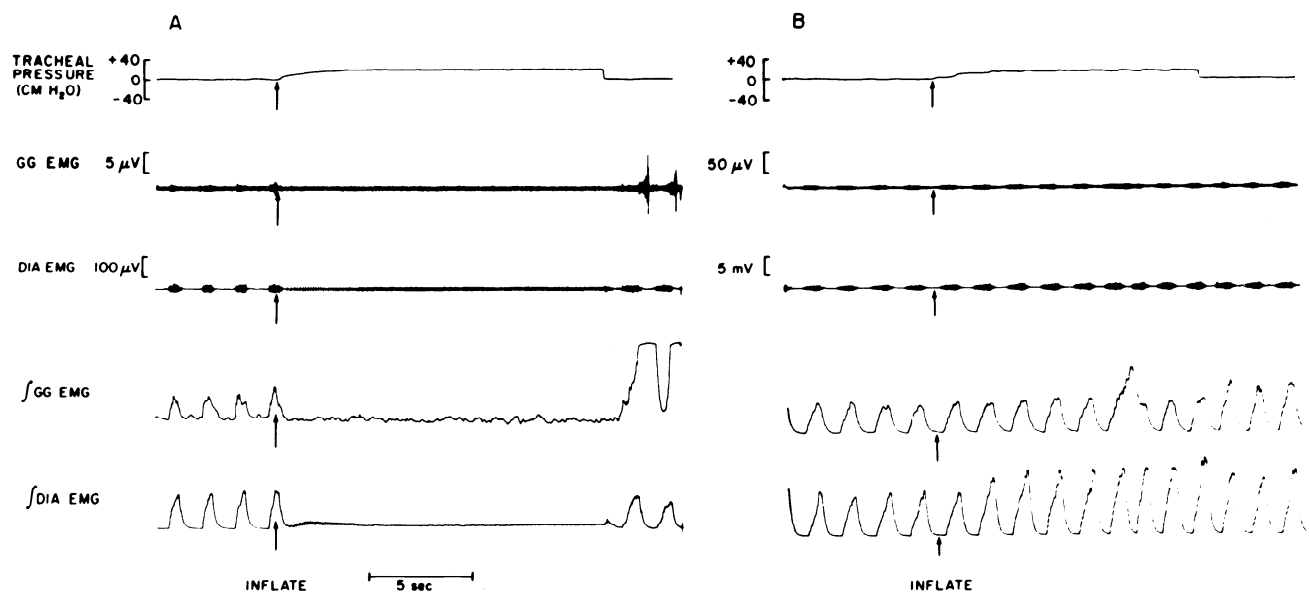

FIG. 9. Effect of lung inflation on GG and DIA EMGs. *A*: before vagotomy. Lung inflation with positive pressure of 20 cmH_2O abolishes phasic inspiratory GG and DIA activity. *B*: after vagotomy. Lung inflation with positive pressure of 20 cmH_2O does not inhibit phasic inspiratory GG or DIA activity. Note reduced EMG gains as in Fig. 8*B*.

peaks early in inspiration followed by a relatively constant level of activity until end inspiration. As Cohen has suggested for the PCA (8), this pattern of GG activation is functionally appropriate for a resistance-lowering inspiratory muscle. Thus, the GG muscles may decrease pharyngeal airfow resistance during inspiration like the PCA muscles that decrease laryngeal airflow resistance.

Similarly, the increased GG activity during the latter part of spontaneous deep breaths may facilitate inspiratory airflow. Here again the pattern of GG activation resembles the pattern of laryngeal abductor activation; Szereda-Przestaszewska et al. (26) observed abrupt decreases in laryngeal resistance during spontaneous deep breaths. The previously reported postsigh tidal volume

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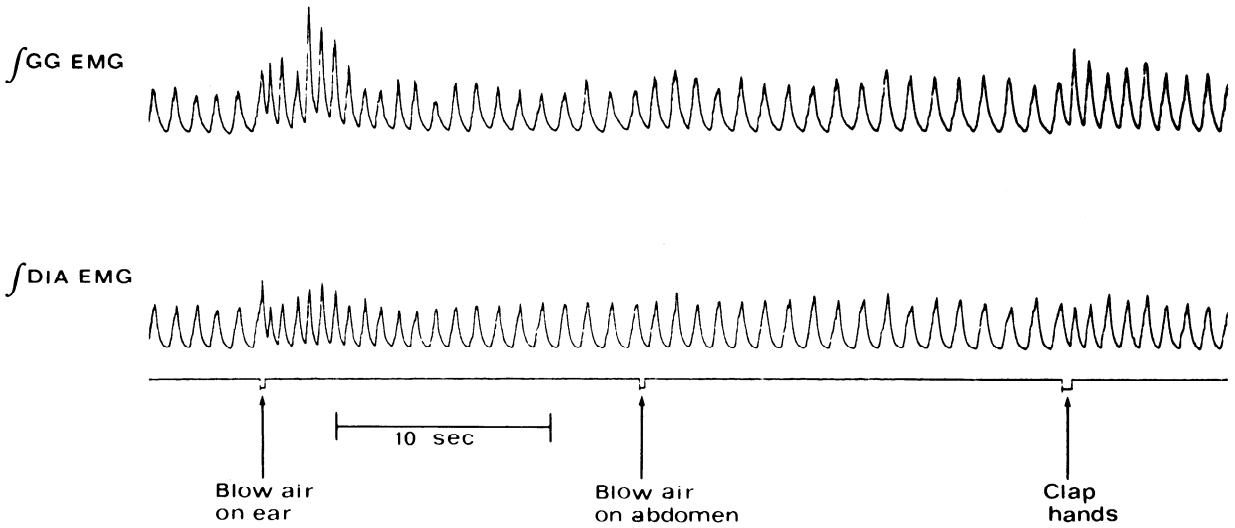

FIG. 10. Three stimuli are presented to one animal. GG EMG increases after each stimulus; DIA EMG increases after first two stimuli but not after third. In each case increase in GG EMG is more marked as a percent of base-line activity than increase in DIA EMG. Respiratory rate increases after each stimulus.

reduction (26) was observed by us to occur as reduced EMG activity in both GG and DIA.

Increased GG activity during hypercapnia and decreased GG activity during hypocapnia suggest that the central chemoreceptors influence the level of phasic inspiratory GG activity. This conclusion is supported by the finding of decreased GG inspiratory activity with hyperventilation even in the carotid body-denervated animal. Two findings suggest that GG apnea occurs at a higher CO_2 than DIA apnea: *1*) during hyperventilation, phasic inspiratory EMG activity was lost in the GG before the DIA; and *2*) during recovery from hypocapneic apnea, phasic inspiratory GG activity returned after DIA activity. However, during hypercapnia, integrated GG EMG increased more, as a percentage of base-line activity, than integrated GG EMG. Thus, as compared to the DIA, the GG appears to have a higher CO_2 apneic point but a more marked increase in activity with hypercapnia.

The peripheral chemoreceptors apparently affect phasic inspiratory activity in the GG and DIA in qualitatively similar, but quantitatively different, ways. Nitrogen breathing and cyanide injection, which stimulate ventilation via peripheral chemoreceptors (11, 24), increased phasic inspiratory activity in the GG more than in the DIA. Conversely, preferential depression of GG activity compared to DIA activity by oxygen breathing probably resulted from decreased peripheral chemoreceptor drive (24). Abolition of these responses after carotid body denervation further supports these conclusions.

Previously (4) it was shown that the asphyxia of a prolonged airway occlusion maneuver increases GG activity more than inspiratory pressure-generating muscular activity. Prolonged occlusions in the present series confirmed that asphyxia preferentially activates GG EMG compared with DIA EMG. Furthermore, the present studies suggest that both central and peripheral chemoreceptors participate in this preferential GG activation. That preferential GG activation or depression is relevant to the actual maintenance of pharyngeal patency can be inferred from our previous observations (4) that pharyngeal collapse occurs only when GG EMG activity is preferentially depressed by anesthetics or by hypoglossal nerve section. Moreover, this phenomenon appears to be analogous to the pharyngeal obstruction seen with anesthesia (22) and with the various obstructive apnea syndromes mentioned in the introduction.

Increased GG activity after vagotomy and on the first breath after airway occlusion maneuvers and abolition of phasic inspiratory GG activity after lung inflation maneuvers are consistent with known pulmonary mechanoreceptor inhibition of inspiratory muscle activity (8). Interestingly, we were not able to demonstrate preferential effects of vagal stretch receptors on GG EMG unlike the effects of other respiratory afferents reported here.

In three of five vagotomized animals, DIA, but not GG, EMG activity decreased on the first inspiration after airway occlusion. Inhibition of the phrenic electroneurogram on the first occluded breath has been ascribed to an inhibitory intercostal-to-phrenic reflex (20). Apparently the intercostals do not affect the GG muscles in a similar manner.

Clinical relevance to obstructive apnea. We found that various nonspecific respiratory stimuli (light, sound, touch) preferentially increase phasic inspiratory GG activity. Similar abrupt increases in GG EMG, associated with behavioral or electroencephalographic arousals, have been noted at the termination of obstructive sleep apneas at points of falling arterial oxygen tension (21, 25). Thus, asphyxial excitation of central arousal mechanisms may preferentially activate the GG muscles, which then pull the tongue forward unobstructing the pharyngeal airway.

Because pharyngeal airway obstruction acutely threatens survival, it should be expected that several mechanisms may assist in reestablishment of airway patency. The present experiments suggest four such protective mechanisms: *1*) participation of the GG muscles in the Hering-Breuer inflation-inhibition reflex; *2*) preferential activation of the GG muscles (compared to DIA) by hypoxia; *3*) preferential GG recruitment by hypercapnia; and *4*) preferential GG recruitment by nonspecific respiratory stimuli. On the first obstructed breath, loss

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of inhibitory input from pulmonary mechanoreceptors would increase both GG and DIA activity. Depending on the relative strengths of GG and DIA on this inspiration, obstruction would continue or be relieved. With continued obstruction, hypoxic and/or hypercapnic preferential activation of GG should eventually unobstruct the airway. Alternatively, arousal, either asphyxial or associated with a nonspecific stimulus, might intervene to preferentially activate the GG and terminate the obstruction.

The periodic recurrence of obstructive and mixed apneas during sleep has been noted above. Recently, Cherniak et al. (7) suggested mechanisms for periodic breathing that may apply to periodic airway obstruction as well. Oscillations in respiratory muscle activity, ventilation, and blood gas tensions occur when one or more of the physiological mechanisms that normally damp the respiratory control system fail: prolonged lung-to-chemoreceptor circulation time, a shift of the respiratory controller towards peripheral chemoreceptor drive, or abrupt increases in respiratory controller gain. In mixed apnea, quantitative differences in GG and DIA responses to central or peripheral chemoreceptor drive may explain the association of obstructed breaths with a central apnea. Characteristically, these obstructed breaths come just before and/or just after a period of central or diaphragmatic apnea (25, 27). This pattern might be expected because increasing arterial oxygen tension and decreasing carbon dioxide tension after a ventilatory phase should depress GG activity before DIA. Thus, obstructed inspiratory efforts preceding a central apnea would occur because DIA activity, generating negative pharyngeal pressure, would not be counterbalanced by GG activity. Similarly, with decreasing oxygen tension and rising carbon dioxide tension near the end of an apneic interval, the DIA might resume activity before the GG; these breaths would also be obstructed for the same reason. Likewise, periodic obstructive apnea could be explained using this model if the GG was periodically depressed by lowered central and/or peripheral chemoreceptor drive while DIA activity was never completely abolished.

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