Breathing route dependence of upper airway muscle activity during hyperpnea

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The nasal route of breathing is important in ventilatory control (3, 6, 8), and nasal obstruction can lead to an increase in both central and obstructive apneas in healthy sleeping humans (16). In addition, the breathing route influences the level of upper airway dilator muscle electromyographic (EMG) activity (2, 4, 7, 13). For the alae nasi (AN) muscle, it is clear that the EMG activity during nasal breathing is much greater than that during oral or oronasal breathing, both at rest (2, 4, 7) and during exercise (13). However, the evidence in favor of route-dependent genioglossus (GG) muscle EMG activity remains controversial.

Basner et al. (2) reported increased GG EMG activity during nasal breathing, whereas Douglas et al. (5) reported the opposite; i.e., EMG activity was greater during oral breathing compared with the nasal route. Recently, we were unable to detect a breathing-route difference for GG muscle EMG activity during hyperpnea stimulated by progressive exercise (13). Thus it remains unclear whether all upper airway muscles exhibit the same breathing-route dependence (i.e., EMG activity during nasal breathing greater than that during oral breathing) or whether the breathing-route dependence can vary between different upper airway muscles. In addition, it has not been established whether there is a breathing-route dependence of GG or AN EMG activity during hyperpnea stimulated by progressive hypercapnia.

The breathing-route dependence of AN EMG activity is better demonstrated during exercise-induced hyperpnea than during quiet tidal breathing (13). Therefore, we reasoned that the breathing-route dependence of EMG activity for all upper airway muscles would be more readily demonstrated under conditions of increased ventilation. Thus, during hyperpnea stimulated by both progressive exercise and hyperoxic hypercapnia, we measured the AN and GG muscle EMGs in normal subjects during nasal-only and oral-only breathing. This maximized the likelihood of demonstrating a consistent breathing-route dependence of EMG activity for both muscles. In addition, by using both exercise and hypercapnia to increase ventilation, we were able to evaluate the effect of different respiratory stimuli on the breathing-route dependence of upper airway muscle EMG activity.

METHODS

Seven healthy normal male subjects [age 30.0 ± 5.4 (SD) yr, height 177 ± 9 cm, weight 69 ± 11 kg] were studied. The subjects were all nonsmokers, with no recent upper airway infection and no cardiovascular or pulmonary disease. Informed consent was obtained from each subject, and the protocol was approved by the Ethics Committee of the Western Sydney Area Health Service.

Measurements

The study was performed by using both progressive exercise and hyperoxic hypercapnia, with the EMG activity of the AN and GG muscles being recorded while subjects breathed separately via the nose-only and mouth-only breathing routes. For each run, the subjects were seated on a bicycle ergometer and breathed via a partitioned face mask (model 7390, Hans Rudolph), which was modified to permit separate measurements of nasal and oral airflow. Both mask compartments were tested for air leaks before and after each run. After detection of a leak, the mask was readjusted until an airtight seal was obtained. Care was taken to avoid any pressure on the nares or any obstruction to nasal airflow. The mask was securely strapped to the subject’s face and connected to the breathing circuits. There were two identical low-resistance circuits (Fig. 1), one each for the nose and mouth mask compartments (dead space ≈ 230 ml for each mask compartment and circuit). Flow was measured separately in each circuit with a heated pneumotachograph (Fleisch no. 2) coupled to a differential pressure transducer (Validyne MP 45; ± 10 cmH2O). A three-way stopcock (Hans Rudolph) was connected to each pneumotachograph to permit external occlusion of either breathing route. The AN EMG was measured by using bipolar-surface electrodes placed ~1 cm apart over the lateral wall of one external naris. The GG...
EMG was measured by using two stainless steel Teflon-coated fine-wire electrodes (single strand, 36 gauge) inserted into the GG muscle with a 25-gauge needle, following the method of Sauerland and Harper (9). Both raw EMG signals were displayed on an oscilloscope (Tektronix) and were amplified, band-pass filtered between 100 and 1,000 Hz, rectified, and passed through a “leaky integrator” with a time constant of 100 ms (Neotrace NT 1900) to give a moving time-average (MTA) EMG. The concentration of CO2 in each mask compartment was monitored by using an infrared CO2 analyzer (Datex Normocap CD-101). Nasal and oral flows together with AN MTA EMG, GG MTA EMG, and CO2 level were simultaneously recorded on a strip-chart recorder (Hewlett-Packard 7758B), digitized at a sampling rate of 100 Hz (ADC 488/164, Iotech), and stored in real time on a Macintosh computer (Centris 750). In addition, all signals were recorded together with the raw AN and GG EMGs on videotape by using an analog-to-digital converter (Medical Systems, Green- vale, NY).

Protocol 1: Hyperoxic hypercapnia. Hypercapnia was induced by having the subjects rebreathe from a 12-liter Douglas bag connected to either the nasal or oral breathing route via the three-way stopcock. Subjects rebreathed from a gas mixture of between 4 and 6% CO2 in O2 (CO2 concentration individually predetermined as that required to increase ventilation above 40 l/min over 3–4 min) while O2 saturation was monitored.

Protocol 2: Exercise. Exercise runs were performed by using the bicycle ergometer. Each run consisted of 30-W increments every 45 s until ventilation exceeded 40 l/min (over a 3- to 4-min time period).

For each run, an initial 1-min period of resting breathing was recorded as a control immediately before either exercise or hypercapnia. Each subject performed four exercise runs and four hypercapnia runs, with paired runs under each condition by using the following two breathing routes: 1) nasal-only breathing with the mouth route occluded externally (3-way stopcock) and 2) oral-only breathing with the nasal route occluded externally (Fig. 1). Hypercapnia runs were alternated with exercise runs. There was a 20- to 30-min recovery time between each run.

Data Analysis

The peak inspiratory MTA EMGs were quantified in arbitrary units above electrical zero. They were then expressed as a percentage of the maximum activity recorded either during the stimulated breathing or during maximal voluntary nasal flares (for the AN) or during maximal voluntary tongue protrusions against the upper dentition (for the GG). Peak inspiratory MTA EMG for each breath was defined as the maximum MTA EMG activity maintained for at least 140 ms during the inspiration.

The inspiratory nasal and oral flow signals were integrated separately to give nasal and oral inspired tidal volumes, respectively. Mean inspiratory flow (VT/TI), where VT is tidal volume and TI is inspiratory time, was calculated as the total inspiratory volume divided by the inspiratory time for each breath. Inspiratory ventilation was calculated separately from the tidal volume and breathing-frequency data. Breath-by-breath measurements of peak MTA EMG were plotted against VT/TI (as a measure of respiratory output) for each run (including the control period). Because the relationships were not usually linear, a power function (of the form y = ax^b + c, where a, b, and c are constants, y = MTA EMG, and x = VT/TI) was fitted to each relationship (15), and the values of AN EMG and GG EMG were then calculated from the function at a VT/TI of both 0.5 and 1.5 l/s. The VT/TI of 1.5 l/s was the highest common VT/TI reached by all seven subjects.

Statistical analysis was made by using Students t-test for paired samples. Data were expressed as means ± SD. Multiple comparisons (stimulus and breathing route) were made by using a one-way analysis of variance with a Tukey test for significance (10).

RESULTS

During resting tidal breathing before either hypercapnia or exercise, no significant differences were observed in minute ventilation, peak AN EMG activity, or peak GG EMG activity whether the subjects breathed nasally or orally (Table 1). Phasic inspiratory AN EMG activity was seen in all subjects during nasal breathing.

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<tr>
<th>Table 1. Ventilatory and EMG parameters at rest</th>
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<td>Ventilation, l/min</td>
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<td>Peak AN EMG, % maximum</td>
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<td>Values are means ± SD. AN EMG and GG EMG, inspiratory moving timing-average EMG activity of alae nasi and genioglossus muscles, respectively.</td>
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Fig. 1. Experimental setup for studies of breathing route during either hypercapnia or exercise, showing subject seated on a bicycle ergometer and breathing through a partitioned face mask. Nasal (Vn) and oral (Vo) flows were measured separately with 2 pneumotachographs. Breathing route could be selected by the operator, by utilizing 3-way taps for external occlusion of either nasal or oral routes. Three-way taps were also utilized to select room-air breathing during exercise or rebreathing bag during hypercapnia.

1 Whenever AN EMG and GG MG are specified in text, tables, and figures, they are MTA EMGs.
Phasic inspiratory GG EMG activity was recorded in five subjects during both nasal and oral breathing. At the highest common VT/TI during hypercapnia or exercise (1.5 l/s), no significant differences were observed in ventilation, tidal volume, inspiratory time, or breathing frequency whether the breathing was nasal or oral (Table 2).

Breathing-Route Effects

At mean flows above the resting levels, the AN EMG activity during nasal breathing was greater than that during oral breathing (Figs. 2 and 3). However, there was no difference in GG EMG activity between nasal and oral-route breathing (Figs. 2 and 3).

Peak AN EMG activity (at 1.5 l/s) with nasal breathing during both hypercapnia (81.2 ± 23.1% maximum) and exercise (69.2 ± 24.3% maximum) was greater than activity with oral breathing (30.2 ± 18.1 and 27.2 ± 19.9% maximum, respectively; both P < 0.01; Fig. 4). The effect of breathing route on AN EMG activity (at 1.5 l/s) was consistent for each subject during both hypercapnia and exercise (Fig. 5). In contrast, peak GG EMG activity (at 1.5 l/s) with nasal breathing during either hypercapnia (35.6 ± 19.3% maximum) or exercise (37.6 ± 22.6% maximum) did not differ from activity with oral breathing (26.0 ± 16.5 and 35.9 ± 26.4% maximum, respectively; both P > 0.2; Figs. 6 and 7). Thus AN EMG activation demonstrated significant breathing-route dependence, whereas GG EMG activation was not substantially influenced by the route of breathing during hyperpnea.

Stimulus Effects

Both peak AN and peak GG MTA EMG activity increased as a function of ventilation during both hypercapnia and exercise (Fig. 3). For equivalent VT/TI values, the GG EMG activity during hypercapnia did not differ from that during exercise, nor did the AN EMG activity differ between hypercapnia and exercise (Fig. 3).

At the highest common VT/TI reached by all subjects (1.5 l/s), peak inspiratory EMG activity of both the AN and GG muscles was consistently greater than activity at a flow of 0.5 l/s (Figs. 4 and 6). At VT/TI of 1.5 l/s, there was no difference in AN EMG activity between hypercapnia and exercise whether the subjects were breathing nasally or orally (both P > 0.3; Fig. 4). Similarly, peak GG EMG activity (at 1.5 l/s) did not differ between hypercapnia and exercise, whether the subjects were breathing nasally or orally (both P > 0.05; Fig. 6).

DISCUSSION

This study demonstrates that, in normal subjects during exercise and hyperoxic hypercapnia, increasing ventilation is associated with progressive rises in both inspiratory AN and GG EMG activity, whether the subjects were breathing via the nasal or oral route. Furthermore, the increases in AN and GG activity are

![Fig. 2](https://example.com/fig2.png)
quantitatively similar for exercise and hypercapnia when the subjects are breathing via the same route. However, the peak inspiratory AN activity during nasal breathing is greater than that during oral breathing at the same mean inspiratory flow, irrespective of the respiratory stimulus. In contrast, the peak inspiratory GG activity is similar for both the nasal and oral breathing routes during hyperpnea.

Nasal breathing during both exercise and hypercapnia was consistently associated with higher levels of AN EMG activity than was oral breathing. Although a similar trend was observed during resting breathing, no significant breathing-route dependence was detected, due mainly to interindividual variability. Previous investigators have clearly demonstrated that nasal breathing is associated with increased levels of AN activity compared with oral breathing (2, 4, 7, 13). The original observation of Mann et al. (7) demonstrated a semiquantitative difference in AN EMG activity at rest (in both humans and dogs) that was related to the route of breathing. Cole et al. (4) reported that AN EMG activity was increased by nasal-only breathing during exercise but not by oral-only breathing. Basner et al. (2) were the first to quantitate the difference in AN activity when breathing was done via the nasal and oral routes. However, this required enhancement of the phasic EMG activity at rest by adding CO2 to the inspired gas mixture. Subsequently, Wheatley et al. (13) demonstrated that during exercise AN EMG activity and nasal ventilation were tightly correlated, independently of flow through the mouth. Our present results for AN activity are consistent with these previous observations and extend them further by simultaneously studying the GG muscle and by comparing two different respiratory stimuli, which are both known to increase upper airway muscle activity.

The evidence supporting breathing-route dependence of GG muscle activity is more controversial. Basner et al. (2) demonstrated a decrease in phasic GG activity on transition from nasal breathing to oral breathing in normal subjects during mild hypercapnia. In a subsequent study of breathing route and GG EMG activity during steady-state exercise, Wheatley et al. (13) were unable to detect any difference in GG activity on change from nasal to oral breathing. More recently, Douglas et al. (5) demonstrated a slightly decreased...
level of GG activity during nasal breathing compared with oral breathing in normal subjects at rest. However, in sleep apnea patients, GG activity was greater with nasal than oral breathing (5). In contrast, the present study did not demonstrate any consistent breathing-route dependence of GG activity, either at rest or during moderate levels of hyperpnea stimulated by either exercise or hypercapnia. These contrasting results could be due to methodological differences, because Basner et al. (2) used a tight-fitting, single-compartment face mask, whereas our study employed a double-compartment-partitioned face mask and that of Douglas et al. (5) used a noseclips with no face mask. Subject posture together with head and neck position also differed among the studies (2, 5, 13) and may have influenced the route-dependent EMG activity. The different methods for controlling breathing route, in addition to varying postures, may have permitted subjects to adopt variable mouth and jaw positions during oral breathing, and these factors may have influenced the level of GG activity.

Because of our sample size (n = 7), we cannot exclude a small difference in GG EMG activation due to the breathing route. However, for the same respiratory output, oral breathing resulted in consistent 60–80% decreases in AN EMG compared with nasal breathing but in smaller inconsistent changes in GG EMG. Thus we believe that any route-dependent effect on GG EMG during hyperpnea would be small and inconsistent compared with the AN EMG breathing-route dependence, implying different mechanisms and physiological significance.

The use of hypercapnia in the study of Basner et al. (2) was not responsible for the breathing-route dependence of GG activity. Our results during hypercapnia did not demonstrate any difference in GG activity when the subjects were breathing nasally compared with orally, and the end-tidal CO2 levels in our study were substantially greater than those of Basner et al. These facts combined with the similarity of the exercise and hypercapnia responses virtually exclude any stimulus-specific role for hypercapnia in producing the breathing-route dependence of upper airway muscle activity.

Recently, some investigators have reported that soft palate muscles demonstrate a route-dependent pattern of activation (11, 12). Palatoglossus activity was always greater during nasal respiration than during oral respiration (12). In contrast, levator veli palatini activity was always greater during oral respiration than during nasal respiration (12). Importantly, these patterns of activity are appropriate to help maintain airway patency of the chosen breathing route. For example, activation of the levator veli palatini during nasal breathing would not be appropriate, because this would elevate the soft palate and impede nasal respiration. Thus studies of the soft palate muscles suggest that breathing-route dependence of palate muscle activity is appropriate to maintain patency of the chosen breathing route. In addition, the AN muscles are activated during nasal inspiration to help prevent collapse of the nasal vestibule (unpublished observations) but are not activated to the same degree during oral-route inspiration, when their activity is not required to maintain breathing route patency. However, the issue of appropriate route-dependent activation for the GG muscle is more controversial. The GG muscle forms the floor of the oral cavity and the anterior wall of the oropharynx below the junction of the nasal and oral airways. Therefore, activity of this muscle can influence the patency of both the oral and oropharyngeal airways. For the oropharyngeal airway, there is no advantage in route-dependent activation of the GG, because this segment of the airway is common to both nasal and oral breathing. For the oral cavity airway, it is not known whether increased GG activity improves the oral airway patency. Indeed, airway patency of the oral cavity may depend more on jaw position and soft palate muscle activity than on GG activity. Therefore, with the obvious importance of the GG muscle in maintaining oropharyngeal airway patency, below the junction of the nasal and oral airways, route-dependent activation may not be appropriate for this upper airway muscle. This hypothesis is consistent with the observed variability of GG activity in relation to breathing route and may help to explain the discordant results from
different studies. Therefore, we believe that consistent breathing-route dependence of upper airway muscles will only be demonstrated for the nasal and soft palate muscle groups.

Our data do not explain the mechanism(s) responsible for the breathing-route dependence of the AN muscles. The finding of identical breathing-route responses for the AN during both exercise and hypercapnia indicates that the response is not stimulus specific. Other possible mechanisms for the breathing-route dependence include upper airway pressure or flow reflexes with feedback to selected upper airway muscles (1, 2) or a centrally imposed feedforward system related to flow route (14).

We were concerned that artifacts related to local effects of the mask (e.g., inhibition of jaw movement) may have influenced our results. The oral mask compartment was quite compliant and did not physically restrict mouth position except to prevent a very large degree of opening. However, the mouth mask may have altered the normal degree of mouth opening during the oral runs. Hence we cannot exclude the possibility that the lack of breathing-route dependence for GG activity may have been related to the mouth mask and an altered degree of jaw opening.

We conclude that, in normal subjects during both progressive exercise and hypercapnia, there is a breathing-route dependence of AN activity that is appropriate to the chosen route (i.e., increased for nasal breathing compared with oral breathing). In addition, this breathing-route dependence is independent of the type of stimulus used to increase respiration. In contrast, increases in GG activity are independent of both the breathing route and the type of stimulus. This demonstrates that breathing-route dependence of upper airway muscle activity during hyperpnea is not a feature that is common to all upper airway muscles under the conditions of our study. This does not exclude breathing-route dependence of GG activity under other conditions or in different postures. However, we speculate that consistent breathing-route dependence of upper airway muscle activity only occurs for muscles in which the activity is appropriate to maintain patency of the upper airway breathing route, such as occurs for the nasal and soft palate muscles.

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