

Alae nasi activation decreases nasal resistance during hyperoxic hypercapnia

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Shi, Yong-Xin, Margaret Seto-Poon, and John R. Wheatley. Alae nasi activation decreases nasal resistance during hyperoxic hypercapnia. *J. Appl. Physiol.* 85(1): 294–300, 1998.—It has been proposed that decreases in nasal resistance (Rn) during hypercapnia are entirely due to vasoconstriction in the nasal cavity. We hypothesized that alae nasi (AN) muscle activity dilates the nasal vestibule and contributes to the decrease in Rn during hypercapnia. Nine normal subjects were studied during hyperoxic hypercapnia (HH). Rn and vestibular resistance (Rvest) for one nasal passage were measured simultaneously with the AN electromyogram before and after nasal decongestion. HH decreased Rvest from 1.6 ± 0.6 to 0.8 ± 0.9 cmH₂O·l⁻¹·s (predecongestant) and from 1.3 ± 0.8 to 0.6 ± 0.7 cmH₂O·l⁻¹·s (postdecongestant; both $P < 0.01$). Nasal decongestant decreased Rn but not Rvest. Significant inverse linear relationships between Rvest and AN electromyogram were demonstrated for all subjects. We conclude that in normal subjects during HH 1) decreases in Rvest are predominantly due to increases in AN activity; and 2) decreases in Rn are due to a combination of mucosal vasoconstriction and AN activation.

upper airway physiology; hyperpnea; alae nasi electromyogram; nasal resistance; nasal vestibule

DECREASES IN NASAL AIRWAY RESISTANCE (Rn) have been well documented during hyperpnea induced by either exercise or hypercapnia (3, 4, 6, 9, 13, 15). The principal mechanism attributed to the decreased Rn is an increase in sympathetic nerve discharge, which results in vasoconstriction within the nasal cavity. However, the precise site and mechanism responsible for the decrease in Rn remain unclear (3, 10, 12, 19), and other possible explanations include passive redistribution of blood away from the nasal mucosal vasculature and contraction of the alae nasi (AN) muscles (12, 19).

A number of experimental observations have clearly shown that the AN are capable of influencing Rn independently of vascular structures within the nasal passages. Studies in animals have clearly shown that neural activation of the alar muscles is associated with shortening of the muscle length (21) with presumed dilatation of the nasal vestibule. These effects are enhanced during hyperoxic hypercapnia with increased neural activation (17) and increased muscle shortening during both inspiration and expiration (22). Similar results have been obtained in humans, in whom the dilating force exerted by the nasal dilator muscles closely parallels the increased electromyographic (EMG) activity of the muscles during hyperpnea produced by progressive exercise (7). It is well documented that maximal voluntary activation of the AN muscles, which results in nostril flaring, can decrease Rn both at rest

and during hypercapnia (19). In addition, paralysis of the AN muscles can lead to inspiratory collapse of the nasal vestibule and results in increased Rn (8). Thus it is well documented that contraction of AN muscles can reduce Rn. However, the contribution of increased AN activity to the decrease in Rn seen during exercise and hypercapnia remains controversial (3, 10, 12, 19). The study by Strohl and co-workers (19) demonstrated that hypercapnia caused both decreases in Rn and increases in AN activity. Furthermore, they reported that voluntary nostril flaring decreased Rn during the flaring maneuver. However, they failed to demonstrate that any of the spontaneous decrease in Rn during hypercapnia (without flaring) was due to AN muscle contraction. A subsequent study by Cole et al. (3) demonstrated that the decrease in Rn during exercise was abolished by application of topical vasoconstrictor agents to the nasal mucosa while the nasal vestibule was splinted widely open. They concluded that AN activity made no contribution to the changes in Rn during exercise. However, splinting of the nasal vestibule may have prevented any dilation of the vestibule due to muscle activity. Thus, while some authors suggest that AN muscle activity dilates the nasal vestibule during hyperpnea (7, 12, 19, 22), others maintain that the AN muscles only act as stabilizers to prevent dynamic inspiratory collapse of the nasal cartilages (3, 6). Therefore, it remains unclear from the current literature whether the increased activity of the AN muscles during hypercapnia or exercise actually alters the nasal vestibule size (causing a decrease in total Rn) or merely prevents vestibule collapse (no change in resistance).

Bridger and Proctor (1) were the first to document that resistance of the bony nasal cavum did not substantially contribute to the overall nasal pressure-flow relationship, suggesting that most of the resistance to nasal airflow occurs within the nasal valve region. This was confirmed by Haight and Cole (8), who demonstrated that about two-thirds of the total nasal airflow resistance occurred in the region of the ostium internum and the remaining one-third in the cartilaginous nasal vestibule. The remainder of the bony cavum did not contribute significantly to the measured nasal airflow resistance. Thus measurements of total Rn (using bulk flow) will largely reflect the narrowest segment of the nasal passages, which generally occurs in the region of the ostium internum (or nasal valve) and which is mainly influenced by vascular changes. This suggests that the contribution of the AN to lowering nasal vestibule resistance (Rvest) may not easily be measured by total Rn, as the vestibule is not generally

the narrowest segment of the nasal passage and measures of bulk flow do not provide regional information. Therefore, separate resistance measurements of the nasal vestibule are required to fully evaluate the contribution of the AN muscles in dilating the nasal vestibule (where AN dilator action will be maximal).

Therefore, we hypothesized that inspiratory AN muscle activity dilated the nasal vestibule and caused a decrease in R_n during moderate increases in ventilation. To investigate this, we measured R_{vest} separately from R_n during progressive hyperoxic hypercapnia both before and after nasal decongestion. This allowed us to determine the decrease in R_{vest} due to AN activation independently from changes in nasal vascular structures. In addition, we attempted to partition the decrease in R_n during hyperoxic hypercapnia into muscular (AN) and vascular components.

MATERIALS AND METHODS

Nine healthy male subjects [age 32.0 ± 6.4 (SD) yr] participated in this study, and none of them had chronic nasal disease or recent upper airway infection. Informed consent was obtained from each subject, and the protocol was approved by the Ethics Committee of the institution.

Subjects were studied while they were seated in a dental chair with the head supported. They breathed nasally through a nasal continuous positive airway pressure mask (Rescare), with the mouth sealed shut. The mask was modified to allow connection to a pneumotachograph. Care was taken to avoid any contact with the compliant portion of the nose or obstruction of nasal airflow. R_n and R_{vest} were measured both during quiet breathing and during hyperpnea induced by hyperoxic hypercapnia.

Unilateral nasal airway and nasal vestibular airway resistances (i.e., R_n and R_{vest} , respectively) were measured by using the technique of anterior rhinomanometry for one nasal passage. Flow was measured with a heated pneumotachograph (Fleisch no. 2) coupled to a differential pressure transducer (Validyne MP45, ± 5 cmH₂O) and connected to the mask. Flow was calibrated with a rotameter. Pressures in the mask, ipsilateral nasal vestibule (P_{vest}), and posterior nasal choanae (P_{pc}) were measured simultaneously with differential pressure transducers (Validyne MP45, ± 50 or 100 cmH₂O). P_{vest} (used to calculate R_{vest}) was measured by using a side-holed catheter located inside the ipsilateral patent nasal vestibule at 1 cm from the external naris (which was just proximal to the nasal valve/ostium internum region). P_{pc} (used to calculate total R_n) was measured by using a side-holed catheter located >1 cm inside the contralateral nasal passage, with that external nostril occluded by dental-impression material (Coltene President Heavy Body) to provide an airtight seal. The pressure in the occluded nasal passage was then equivalent to P_{pc} of the patent nasal passage. The pressure transducers were calibrated with a water manometer. The pressure and flow signals were all phase matched up to 7 Hz by adjusting the length of the pressure catheters. The AN EMG of the unoccluded nostril was recorded from bipolar surface electrodes placed ~ 1 cm apart over the lateral wall of the external naris, with a reference electrode placed on the forehead. The raw EMG was 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 produce a moving time average (MTA) EMG. Airway CO₂ concentration was

monitored at the mask by using an infrared CO₂ analyzer (Datex Normocap).

Nasal flow together with the pressures, AN MTA EMG, and CO₂ level were simultaneously recorded on a strip-chart recorder (Hewlett-Packard 7758B). In addition, all signals were recorded together with the raw AN EMG on videotape by using an analog-to-digital converter (Medical Systems, Greenvale, NY) for later off-line analysis. Nasal and vestibular pressure-flow curves were monitored on-line by displaying X-Y plots of transvestibular and transnasal pressure vs. flow on a storage oscilloscope (Tektronix) during the study.

Subjects breathed nasally for between 3 and 5 min until stable ventilation was achieved. After 1 min of quiet breathing at rest was recorded, progressive hyperoxic hypercapnia was induced by having the subject rebreathe from a 6-liter bag containing 8% CO₂ in 50% O₂. The run was terminated after 3–5 min, when peak inspiratory flow reached a plateau and flow limitation had occurred. Two further runs were performed in each subject 15–20 min after the end-tidal CO₂ concentration had returned to resting values. After this, each subject's patent nasal passage was decongested with xylo-metazoline nasal spray (0.1%). After 30 min, the three hypercapnic runs were repeated, separated by 15- to 20-min periods during which the subjects were breathing room air.

Data analysis. After the study, recorded data were digitized at a sampling rate of 100 Hz (Iotech ADC 488/164) and stored on a Macintosh IIcx computer. Transnasal and transvestibular pressures were calculated by subtraction of P_{pc} and P_{vest} , respectively, from mask pressure. Tidal volume was determined by integration of the flow signal, and the inspiratory minute ventilation (\dot{V}_i) was calculated from tidal volume and breathing frequency data. The AN MTA EMG was quantified in arbitrary units above electrical zero.

Both transnasal and transvestibular inspiratory pressure-flow plots were then constructed for each recorded breath. Where hysteresis of the pressure-flow relationship was apparent during hyperpnea, it was anticlockwise in direction, with an ascending and descending pressure-flow curve (16). The inspiratory transnasal and transvestibular resistances were calculated from the ascending limb of the pressure-flow curves at a flow rate of 0.5 l/s. In addition, the AN MTA EMG was measured at an inspiratory flow of 0.5 l/s for the corresponding breaths at rest and during hyperpnea. Data were analyzed for five consecutive breaths both before hypercapnia and at maximum \dot{V}_i during each hypercapnic run. Data from all the runs either before or after decongestion were meaned for analysis.

Results are expressed as means \pm SE. Statistical analysis included Student's *t*-test for paired samples and one-way analysis of variance by using a Fisher paired least significant difference test for significance. For each rebreathing run, the relationship between AN MTA EMG activity and either R_n or R_{vest} was analyzed by plotting data for all breaths during the run and fitting linear regressions.

RESULTS

Each subject performed three rebreathing runs both before and after nasal decongestant. However, the data from the first run before decongestant were excluded because of irregular breathing patterns during the first performance of the breathing maneuver. Therefore, only the second and third rebreathing runs before nasal decongestant were analyzed.

\dot{V}_i during resting breathing after nasal decongestant was not statistically different (Fig. 1). \dot{V}_i increased during hypercapnia to 33.4 ± 2.3 l/min ($P < 0.001$)

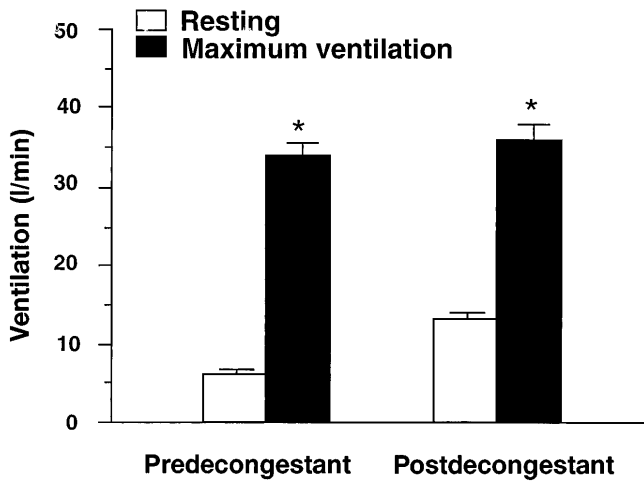


Fig. 1. Mean ventilation during resting breathing and at maximum ventilation during hypercapnia both before and after nasal decongestant. Each histogram is the average of 2–3 runs in all subjects. Bars represent +1 SE. * $P < 0.05$ relative to resting values. Note that ventilation increased to a similar level during hypercapnia both pre- and postdecongestant.

before decongestant and to 35.4 ± 3.4 l/min ($P < 0.001$) after decongestant (Fig. 1). There was no systematic difference in maximum \dot{V}_I achieved either before or after decongestant ($P > 0.2$). AN MTA EMG activity was similar for runs before and after decongestant, both during resting breathing and at maximum \dot{V}_I (Fig. 2; $P > 0.2$). AN EMG activity increased by a similar amount during hypercapnia under both conditions (Fig. 2; both $P < 0.001$).

There was a substantial variation in resting total Rn before decongestant (Fig. 3), presumably due to the unilateral nature of the measurement. After decongestant, total Rn fell from 5.3 ± 1.3 to 2.4 ± 0.8 cmH₂O·l⁻¹·s ($P < 0.05$) during resting \dot{V}_I (Fig. 3). At maximum \dot{V}_I

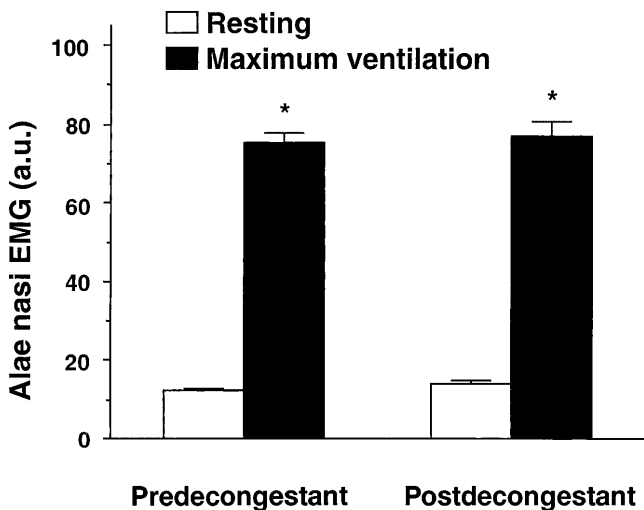


Fig. 2. Alae nasi (AN) moving time average EMG activity during resting breathing and at maximum ventilation during hypercapnia, both before and after nasal decongestant. Each histogram is the average of 2–3 runs in all subjects. Bars represent +1 SE. * $P < 0.01$ relative to resting values. Note that AN EMG activity increased by a similar amount at maximum ventilation both pre- and postdecongestant. au, Arbitrary units.

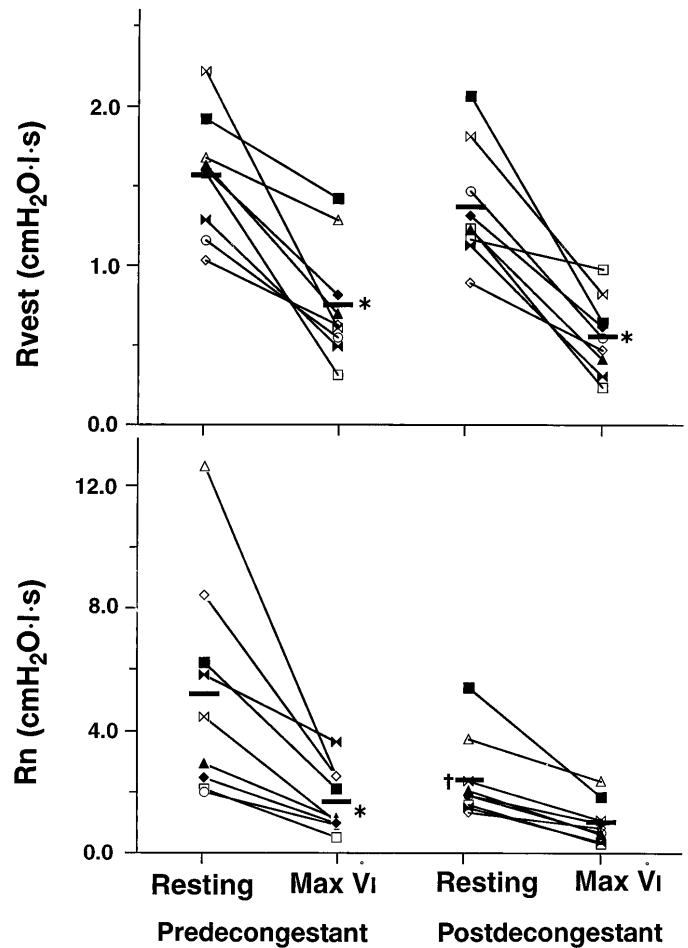


Fig. 3. Nasal (Rn) and vestibular (Rvest) resistances during resting breathing and at maximum ventilation (Max \dot{V}_I) during hypercapnia, both before and after nasal decongestant. Each symbol represents the average of 2–3 runs in an individual subject. Note for Rvest: 1) resting values are not altered by nasal decongestant; and 2) resistance falls during hypercapnia by a similar amount both pre- and postdecongestant. Note for Rn: 1) resting values decrease after nasal decongestant; and 2) resistance falls during hypercapnia both pre- and postdecongestant, although the latter does not reach statistical significance. Group mean values are indicated by horizontal bars. * $P < 0.001$ relative to resting values; † $P < 0.01$ relative to predecongestant values (ANOVA).

during hypercapnia, Rn decreased to 1.9 ± 0.8 cmH₂O·l⁻¹·s ($P < 0.01$) before decongestant, but the resistance decrease was not statistically different postdecongestant (1.4 ± 0.6 cmH₂O·l⁻¹·s; Fig. 3). Resting Rvest before decongestant (1.6 ± 0.6 cmH₂O·l⁻¹·s) represented $31 \pm 13\%$ of the total Rn and did not change significantly after decongestant (1.3 ± 0.8 cmH₂O·l⁻¹·s; $P > 0.1$; Fig. 3). In general, Rvest represented a greater proportion of the total Rn in subjects with a lower total Rn. At maximum \dot{V}_I during hypercapnia, Rvest fell to a similar level both predecongestant (0.8 ± 0.9 cmH₂O·l⁻¹·s) and postdecongestant (0.6 ± 0.7 cmH₂O·l⁻¹·s; both $P < 0.01$; Fig. 3). Before decongestant, the fall in Rvest represented a larger percentage of the fall in total Rn in those subjects whose total Rn was low before hypercapnia (range was 5–75% of the total decrease in Rn).

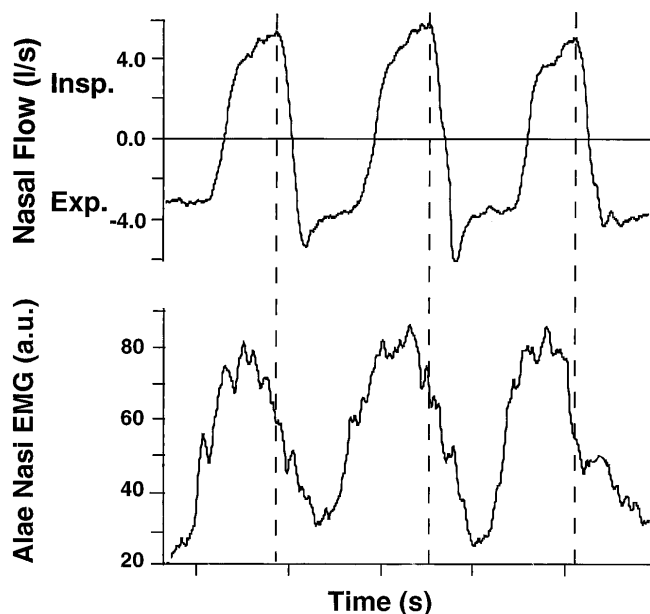


Fig. 4. Representative strip-chart recording of nasal flow and AN moving time average EMG in 1 subject during hypercapnia. Inspiratory flow (Insp) is positive. Each time interval is 1 s. Dashed vertical lines denote peak inspiratory flow. Note that peak AN EMG activity precedes peak inspiratory flow. Exp, expiratory flow.

To assess the effect of AN muscle activity on R_{vest} , we considered the timing of EMG activity in relation to inspiratory flow during hypercapnia. The onset of AN EMG activity preceded inspiratory flow and generally reached maximal values during the increasing flow portion of inspiration (Fig. 4). Therefore, measurements of AN EMG activity and both R_{vest} and total R_n were made simultaneously during the increasing flow portion of inspiration at 0.5 l/s. At this time, the AN EMG was close to maximal values for the inspiration. Both R_n and R_{vest} (at 0.5 l/s) were examined as a function of the AN MTA EMG activity (at 0.5 l/s) for each subject on a breath-by-breath basis as \dot{V}_I increased during hypercapnia (Fig. 5). For the group, each relationship was well fitted by a linear regression. Significant inverse linear relationships between inspiratory resistance and AN EMG activity were demonstrated in all subjects for both R_{vest} (Fig. 5, Table 1) and total R_n (Table 1). Analysis of expiratory R_{vest} did not show any systematic effect of AN activation.

DISCUSSION

The findings of this study demonstrate that decongestion of the nasal passages in normal subjects decreases total R_n but has little influence on R_{vest} . In addition, both R_{vest} and total R_n decrease during progressive hypercapnic hyperpnea. For total R_n , this decrease after decongestant is less than that before decongestant. However, the decrease in R_{vest} is similar both pre- and postdecongestant. In addition, the decreases in both R_{vest} and total R_n during hypercapnia are inversely related to an increase in AN EMG activity, both before and after decongestant. These findings support the hypothesis that AN muscle activity causes

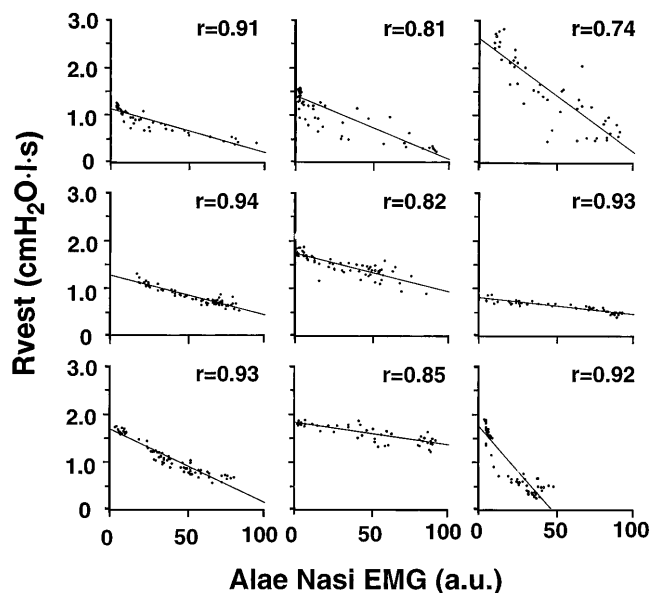


Fig. 5. R_{vest} as a function of AN moving time average EMG activity (both measured at an inspiratory flow of 0.5 l/s) on a breath-by-breath basis for 1 hypercapnia run in each subject before nasal decongestant. Linear regressions and correlation coefficient (r) values are shown for each subject (all $P < 0.001$). The mean r value for all hypercapnia runs before decongestant is 0.83 ± 0.02 . Note the significant inverse linear relationships between R_{vest} and AN EMG activity for all subjects.

dilatation of the nasal vestibule, which contributes to the decrease in R_n seen during the increased ventilation stimulated by hyperoxic hypercapnia.

The nasal airway is 10–14 cm long, divided in two by a septum, often narrow in width but large in cross section, and convoluted by the superior, middle, and inferior turbinates. The funnel-shaped vestibule leads from the external nostril to the nasal valve. The skeleton of the vestibule is cartilaginous and consists of the septum medially and paired alar cartilages laterally. Several groups of voluntary muscle fibers act on the vestibular walls and can alter the shape of the vestibular lumen. These muscles may exert both dilator and compressor action on the compliant anterior nasal walls. Thus the nasal vestibule is compliant, and vestibular airway patency is dependent on soft tissue and cartilage resistance to deformation of lateral walls, in addition to dilator muscle activity that opposes negative transmural collapsing pressures. The major airflow-resistive segment of the nasal airway is situated in the nasal valve region (8). It is confined to a

Table 1. Correlation coefficients of linear regression analysis between alae nasi EMG activity and resistance

	Predecongestant	Postdecongestant
R_n /AN EMG	$0.89 \pm 0.02^*$	$0.89 \pm 0.02^*$
R_{vest} /AN EMG	$0.83 \pm 0.02^*$	$0.89 \pm 0.02^*$

Data are means \pm SE. R_n /AN EMG and R_{vest} /AN EMG are the linear regressions between alae nasi EMG activity (AN EMG) and total nasal (R_n) and vestibular (R_{vest}) resistances, respectively. * $P < 0.001$.

short, narrow segment from the caudal end of the vestibular cartilages to the anterior end of the long inferior turbinate. In the nasal valve, there are capacitance vessels that line the anterior septum, inferior turbinate, and the inferior portion of the middle turbinate, and these erectile tissues in the nasal valve regulate its airflow resistance. The erectile tissues extend from the bony cavum to the nasal vestibule but appear to be absent proximal to the nasal valve region (2). Hence, the nasal valve forms the narrowest segment of the nasal passage, and its cross-sectional area is largely determined by vascular capacitance vessels inside a fixed bony passage. In contrast, the cross-sectional area of the compliant nasal vestibule is less influenced by vascular structures and much more dependent on the stiffness of the vestibular walls, contraction of alar dilator muscles, and the degree of negative transmural collapsing pressure generated during inspiration (2). The major dilator muscles of the nasal vestibule are the AN, which originate from the maxillae, insert into the ala of the nose, and pull the ala laterally. The AN muscles exhibit phasic inspiratory EMG activity in humans (3, 18, 19, 23), but the functional significance of this activity remains uncertain, particularly during exercise and hypercapnic hyperpnea (3, 12, 19).

A number of previous studies have demonstrated that Rn can decrease substantially during CO₂ inhalation (4, 11, 19, 20). Initial studies did not attempt to elicit the mechanism for the decrease in resistance (4, 11, 20) but proposed reflex vasoconstriction of the nasal vascular bed mediated by sympathetic nervous system stimulation as the most likely cause (11). However, recent work has questioned this assumption (10) and concluded that Rn cannot be simply correlated with vascular resistance or blood flow, implying that other factors must be involved. Strohl et al. (19) proposed that the AN played a significant role in reducing Rn during hypercapnia. A number of observations support the contention that the AN muscles do modulate Rn. First, paralysis of the normal phasic inspiratory contraction of the AN muscle can lead to inspiratory collapse of the nasal vestibule (5, 8). Second, there is a 40% reduction in Rn after the external nares are propped open with stiff tubes (14). Third, sonomicrometry studies demonstrate a shortening in AN muscle length during inspiration, which correlates with AN EMG activity (21). The degree of muscle shortening is increased during hyperoxic hypercapnia (22). This suggests that AN EMG activity does lead to muscle shortening, which has the potential to increase the nasal vestibule airway cross-sectional area and, hence, reduce airway resistance. Fourth, Fuller et al. (7) demonstrated that the dilating force exerted by the human AN muscles during progressive exercise closely paralleled the increased EMG activity of the muscles. Finally, Strohl et al. (19) investigated the effect of AN activation on Rn and convincingly demonstrated that maximal voluntary activation of the AN can decrease Rn both before and after vasoconstrictive nasal spray. They also studied Rn during CO₂ inhalation and demonstrated

that, although Rn fell during hypercapnia, maximal flaring maneuvers resulted in further decreases in Rn (independent of the level of CO₂). All the above observations clearly demonstrated that the AN can modulate Rn independently from the vascular structures within the nasal passages. However, no previous investigations have demonstrated that Rvest actually decreases during hypercapnia or exercise at physiological levels. The study by Strohl et al. (19) was not able to partition the measured decrease in Rn during hypercapnia into muscular and vascular components, as it only examined the contribution of the AN muscles during maximal voluntary maneuvers. The levels of EMG activity seen during maximal voluntary maneuvers are generally far greater than those seen during moderate hypercapnia (19) and, hence, cannot be used to infer normal physiological activity during CO₂ inhalation. In contrast to these previous studies, Cole et al. (3) stated that the respiratory function of the alar muscles was to prevent vestibule collapse during inspiration by restraining alar movement, and they concluded that physiological decreases in Rn were entirely vascular in origin. However, in this study, the nasal vestibules were splinted widely open by springs, which would have removed any potential for reduction in Rn by muscular mechanisms affecting the vestibules. Therefore, the relative contribution of AN muscle contraction to the normal physiological decrease in Rn during hypercapnia remains controversial.

The major problem that confounds previous studies has been that increases in AN activity and nasal mucosal vasoconstriction tend to occur in parallel during both hypercapnia and exercise. In addition, the only variable that has been monitored during hyperpnea is total Rn, which can be decreased by either vascular or muscular factors. Our study is unique compared with previous investigations, as we have independently measured Rvest together with total Rn. Although our technique only measured unilateral Rn, we do not believe that this would have significantly influenced our results. Previous work has shown that both nasal cavities respond similarly to decongestant (2) and that AN activity is similar for both nasal passages (7). Although resistance may be unequal between the two nostrils (2), this would not cause any measurement error or affect the nasal responses to hypercapnia. However, the results obtained will not necessarily reflect resistance values that might be measured were both nasal passages patent.

Previous work has demonstrated that the effects of nasal decongestion on airway resistance are only detected when a catheter measuring nasal pressure is advanced >2 cm along the floor of the nostril (8). This is in the region of the nasal valve, where vascular changes are known to influence Rn. We reasoned that the AN can only decrease Rn in the segment of the airway proximal to the nasal valve, which is the region of the nasal vestibule. Therefore, to measure the effect of AN muscle contraction on Rn, we placed a pressure catheter at only 1-cm depth within the nasal vestibule. This had two major benefits, the first being the measure-

ment of resistance changes in a short segment of the airway where AN action was likely to be maximal. Normally, the nasal vestibule airway only contributes ~30% of the total R_n (8), and the majority of the total resistance arises in the short nasal valve segment. These values agree well with the data obtained in our study. Therefore, measurements of total R_n will predominantly reflect the resistance changes due to the nasal valve region, and relatively small changes in R_{vest} (due to muscular action) may not significantly influence the measurement of total resistance. This emphasizes the importance of making resistance measurements in the segment of the airway where the muscle action will be maximal, i.e., the nasal vestibule. The second major benefit of our approach is that resistance changes due to vascular effects are not likely to significantly influence the initial 1-cm segment of the vestibule airway. This is supported both by previous data (8) and by the results of our study, which demonstrate no significant change in resting R_{vest} after nasal decongestion.

The major new findings of the present study are that there is a real fall in R_{vest} during hyperoxic hypercapnia, that this fall is not due to vascular effects, and that the decrease in R_{vest} is a significant component of the overall decrease in total R_n . In addition, our data demonstrate that the $\sim 0.8 \text{ cmH}_2\text{O}\cdot\text{l}^{-1}\cdot\text{s}$ fall in R_{vest} (before and after decongestant) is likely caused by normal physiological levels of AN muscle contraction that occur during moderate hypercapnic hyperpnea. This is supported by the good correlations between an increase in AN EMG activity and a decrease in R_{vest} , in addition to the lack of any other likely mechanism by which R_{vest} could decrease. Furthermore, following decongestion, the decrease in total R_n during hypercapnia is almost entirely due to the decrease in R_{vest} mediated by AN activity. In addition, the correlations between EMG and resistance were not substantially altered by nasal decongestion, which suggests that AN muscle contraction is a significant factor in the decrease of R_{vest} . Thus our data clearly demonstrate that normal physiological AN muscle activity contributes to the overall decrease in R_n during hypercapnia.

It is clear that AN EMG activity varies phasically throughout the respiratory cycle, with onset of activity before inspiratory flow and peak activity occurring before peak inspiratory flow (18, 24). In this study, we measured inspiratory AN EMG activity at the same time as the resistance was measured (i.e., at an inspiratory flow of 0.5 l/s) rather than using a measure of peak activity. This simultaneous measurement improved the accuracy of our assessment of the relationships between EMG activity and R_{vest} . However, this measurement does not address the role of AN activity during the remainder of an inspiration. As the level of muscle activity decreases during an inspiration at a faster rate than inspiratory flow decreases, this may result in an imbalance of the collapsing negative airway pressures and the dilating muscular forces. This leads to increases in R_{vest} during the latter phase of an inspiration. During quiet breathing, the relative timing of flow

and EMG activity does not appear to cause increases in R_{vest} . However, during hypercapnic hyperpnea, there is a progressive increase in R_{vest} during an inspiration, resulting in pressure-flow hysteresis (16). This hysteresis can be decreased by high levels of AN EMG activity maintained throughout an inspiration, suggesting that reduced levels of AN EMG activity during the second half of an inspiration result in increased R_{vest} (16). Therefore, whereas AN EMG activity significantly decreases R_{vest} during the first one-half of an inspiration, this decrease may not be maintained during the second half of an inspiration. This may explain why Cole et al. (3) were unable to visually demonstrate any abduction of the lateral alar walls of the vestibule during inspiration. They did not relate their measurements to the timing of inspiratory flow or AN EMG activity and may have failed to detect any early inspiratory abduction of the alar walls. In a second study, which concluded that alar muscles did not dilate the nasal vestibule, there were no direct measurements made of either R_{vest} or AN EMG activity (6). In fact, the study provided no data on the activity of the AN muscles during exercise and relied on changes in R_n due to topical decongestant to make conclusions about the role of the AN muscles. Therefore, we believe that our study is the first to directly measure the effect of AN activity on R_{vest} during hypercapnic hyperpnea and to demonstrate that an increase in EMG activity is correlated with decreases in R_{vest} . As AN EMG activity also increases progressively during exercise (23), it is likely that AN muscle contraction has a similar effect on R_{vest} during exercise.

Although the decrease in R_{vest} must be due to AN muscle contraction, this does not necessarily mean that there is dilatation of the nasal vestibule. We did not directly measure vestibule size or shape, so we cannot conclude that the vestibule enlarges during hyperoxic hypercapnia. Although the most likely mechanism for the decrease in R_{vest} is vestibule dilatation, it remains possible that AN contraction altered the shape of the vestibule in such a way as to decrease overall airflow turbulence, without any change in minimum cross-sectional area. Hence, the effect of AN muscle contraction on nasal vestibule flow regime, cross-sectional area, or both may be the mechanism responsible for the decrease in inspiratory R_{vest} (16).

Despite the significant effect of AN muscle activity on R_n , vascular changes are responsible for the majority of the decrease in R_n that occurs during hypercapnia. Based on the values obtained in our study, moderate hypercapnia results in a 65% decrease in total R_n . Of this decrease, only 25% could be apportioned to AN muscle activity. However, in subjects with a low total R_n , the proportion of the total decrease due to muscle contraction was much greater and could be more significant clinically. After nasal decongestant, nearly 70% of the decrease in total R_n was due to AN muscle contraction. Although these data were obtained from a unilateral measurement of R_n , our overall results are consistent with the published data, suggesting that the major

influence on Rn during increased ventilation is vascular, not muscular (3, 6, 13).

The clinical significance of the reduction in Rn due to AN activity is debatable. However, decreases in total Rn during exercise and in patients with nasal disease may be important in preserving the air-conditioning function of the nose at higher ventilation. To the extent that this occurs, AN activity will improve nasal patency during exercise and will help maximize the nasal fraction of ventilation during oronasal breathing. Our study also provides some support for the use of external nasal dilator strips. If AN contraction can contribute to the decrease in total Rn during hypercapnia or exercise, then an external nasal dilator strip may be equally effective in reducing Rvest. Indeed, given that the dilator strips would exert the same dilating force throughout the whole of inspiration, the strips may be more effective in reducing total Rn than is the normal contraction of the AN muscles.

In conclusion, we have demonstrated that during moderate hypercapnic hyperpnea in normal subjects Rvest is reduced by AN muscle activity, with no significant contribution to the reduction by nasal mucosal vascular structures. In addition, decreases in total Rn during hypercapnia are due to a combination of AN muscle activation and nasal mucosal vascular responses. Therefore, our data support the hypothesis that physiological levels of AN muscle activity can reduce both Rvest and total Rn during moderate increases in ventilation, such as may occur during hypercapnia and exercise.

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