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Influence of exercise intensity and nasal flow resistance on activities of human nasal dilator muscles

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INFLUENCE OF EXERCISE INTENSITY AND NASAL FLOW RESISTANCE ON ACTIVITIES OF HUMAN NASAL DILATOR MUSCLES

by

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ABSTRACT

Ten healthy subjects exercised on a cycle ergometer at 60, 120, and 150 - 180 W while breathing nasally. Nasal inspiratory flow, nasal dilator muscle (alae nasi; A.N.) EMG activities, and alveolar CO_2 and O_2 were measured at rest and at each work rate. On separate days six of the subjects exercised at 30 - 60, and 60 - 120 W while nasal airway resistance was measured by anterior rhinomanometry. In both protocols, 12 - 15 breaths of a He:O_2 (79:21%) gas mixture were substituted surreptitiously for air under each condition. He:O_2 breathing resulted in a decrease in flow turbulence and intranasal pressure, and therefore, resistance, as indicated by lower calculated Reynold's numbers. He:O_2 evoked an increase in nasal inspiratory flow, and reductions in nasal pressure and A.N. EMG activities (25 - 50%) at each work rate. These results suggest that A.N. EMG during exercise is controlled by increases in intranasal pressure, not by nasal flow. Thus, the data suggest that sensory information from pressure sensitive nasal receptors in the nasal lumen serve to modulate A.N. EMG during exercise.

INTRODUCTION

The mechanisms controlling the distribution of nasal and oral breathing routes have not been elucidated. In fact, most researchers and clinicians use noseclips to measure ventilation in human subjects, thereby eliminating airflow through the upper airways. This is significant in that most of the airflow in normal subjects enters the lungs via the upper airways at rest and with light exercise. The upper airway, as defined by Proctor (21), consists of the external nares and the nasal passages, the nasopharynx and pharynx, and in some circumstances the mouth. The nasal passages serve to adjust the temperature and the humidity of inspired air, and to participate in the absorption of foreign gases and dust; consequently, the nose has been described as a defense organ (21). Because of these defensive mechanisms, approximately 80% of adult humans breathe nasally at rest and during light exercise (12). Moreover, human infants and lower mammals breathe through the nose only. In 1981 Niinimaa et al. (18) found that 20 out of 30 subjects breathed nasally at rest and during mild exercise, but switched to an oronasal breathing pattern when total pulmonary ventilation reached about 35 L/min. A 1991 study by Wheatley et al. (32) reported similar results in five subjects who breathed nasally at rest, but switched to an oronasal pattern when ventilation reached about 22 L/min.

However, the mechanisms controlling the switch from a nasal to an oronasal breathing pattern are poorly understood. In fact, Niinimaa et al. (18) reported that five of 30 subjects continued to breathe nasally even during maximal exercise.

Proctor (21) described the pattern of airflow through the nose using a biophysical model (Fig. 1). He found that air flows primarily between the septum and the meatus nasi medius, with a small amount of flow passing along the most caudal portion of the nasal chamber. Nasal airflow is largely turbulent, and nasal flow resistance accounts for about half of the total pulmonary resistance and work of breathing in healthy human subjects at rest (1, 6). Inspiratory nasal airflow limitation or collapse has been shown to occur when nasal flow rates approach 1 - 2.5 L/sec in subjects performing voluntary nasal breathing maneuvers (21). Average nasal flow rates of 1.9 L/sec at a total nasal ventilation of 58 L/min have been reported during exercise in subjects breathing nasally (31), and nasal ventilation values in excess of 78 L/min have been reported in some subjects that failed to switch to an oronasal breathing pattern during heavy bicycle exercise (24). Although it seems clear that the maintenance of nasal airway patency must be actively regulated under these conditions, the mechanisms that serve to maintain nasal airway patency during exercise are also poorly understood.

The dilator naris muscles ("alae nasi" muscles, A.N.) are thought to play a significant role in the regulation of nasal airway patency. The A.N. muscles are innervated by the facial nerve (cranial nerve VII), and sensory innervation is by the opthalmic branch of the trigeminal nerve (cranial nerve V) (10). The A.N. muscles originate on the lateral aspect of the greater alar cartilage and insert on the anterior aspect of the skin of the nostril. Thus, activation of the A.N. muscles increases the diameter of the nasal airway by enlarging the aperture of the nares (12), guards against collapse of the nasal lumen by stiffening the compliant nasal walls (12), and reduces nasal airflow resistance by up to 30% (26). Indeed, unilateral paralysis of the A.N. muscles after facial nerve palsy has been associated with an increase in ipsilateral nasal airway resistance in one subject (7, 29).

Wheatley et al. (31) showed that A.N. EMG and nasal ventilation are tightly correlated during exercise, independently of the rate of flow through the mouth. In addition, they found that A.N. EMG increased as a function of exercise intensity. These results led Wheatley et al. (31) to hypothesize that the A.N. EMG may be regulated reflexively by changes in the rate of nasal inspiratory airflow. Similar results were found in a study by Fregosi et al. (8) who studied seven healthy males during

progressive submaximal exercise, and found nasal ventilation increased linearly as a function of exercise intensity, but reached a maximum and plateaued at a value of about 40 L/min (Fig. 2). The pattern of the corresponding change in A.N. EMG activities was similar, as indicated by the high correlation between nasal airflow and A.N. EMG activities (Fig. 2). However, progressive increases in nasal airflow are accompanied by monotonic increases in flow turbulence and intranasal pressure swings. Thus, Fregosi et al. (8) hypothesized that intranasal pressure and/or nasal airway resistance may be more important determinants of A.N. muscle activity than the rate of nasal inspiratory airflow. Indeed, animal studies have shown that EMG activities of the genioglossus, posterior cricoarytenoid, and A.N. muscles increased as a function of intranasal pressure (13, 30). However, a recent study in human subjects has shown that A.N. EMG fail to increase when increased external nasal resistances are applied (33). Consequently, whether A.N. EMG is modulated by inspiratory nasal airflow or by intranasal pressure swings remains controversial.

Nasal pressure and flow have not been measured simultaneously with A.N. EMG during exercise in human subjects (4, 23, 31). Moreover, although it is well known that nasal resistance decreases after an exercise bout in both nasal passages, the changes in nasal resistance during

exercise have not been determined. Richerson and Seebohm (23), and Dallimore et al. (4) have found that the decrease in nasal resistance after exercise persists for up to thirty minutes, and Richerson and Seebohm (23) found that stellate ganglion blockade abolishes the post-exercise decrease in nasal resistance. These observations suggest that cervical sympathetic vasoconstriction of the nasal mucosa increases the diameter of the nasal passages, leading to the decrease in nasal resistance.

In summary, it seems that A.N. EMG is highly correlated with nasal ventilation (8, 31). However, with increased nasal ventilation, intranasal pressure swings and turbulent airflow increase simultaneously. Thus, whether A.N. EMG is modulated by changes in nasal inspiratory airflow or nasal resistance is uncertain. Accordingly, the purpose of the present studies was to quantify the changes in nasal resistance during submaximal exercise, and to assess the separate effects of nasal airflow and resistance on A.N. EMG under these conditions. Specifically, we tested the hypothesis that A.N. muscle activities are regulated by changes in nasal flow resistance, independently of the rate of flow through the nose. Nasal inspiratory airflow and nasal resistance were changed reciprocally by substituting a mixture of He:O_2 for air in subjects breathing nasally at rest and during progressive cycle ergometer exercise. The

lower density and greater kinematic viscosity of the He:O_2 mixture compared to air allowed for a satisfactory test of our hypothesis, as it reduced flow turbulence leading to higher nasal flow rates and much lower levels of nasal resistance.

METHODS

Ten healthy volunteers (7 males, 3 females) were studied after giving their written informed consent. The age range of 9 subjects was 23 - 37 years; the 10th subject was 60. Eight of the subjects had no knowledge of the experimental aims or anticipated results, but the remaining two were well acquainted with the purpose of the experiments. All subjects were recreationally active, and two were varsity swimmers. All subjects were free of cardiopulmonary disease and allergies, and had no history of trauma to the nose or deviation of the nasal septum. Finally, all subjects had normal lung mechanics: thus, forced vital capacity (FVC) averaged 101.7 $\pm$ 5.9% (mean $\pm$ S.D.) of the age predicted value, and the forced expiratory volume in 1.0 second ($FEV_{1.0}$) was equal to 86.9 $\pm$ 3.4% of the FVC.

Resting and exercise measurements were obtained while the subjects were seated on a mechanically braked cycle ergometer in an air-conditioned laboratory maintained at 22 degrees Celsius, and with a barometric pressure range of 695

- 705 mmHg. Silver-silver chloride electrodes (4 mm diameter) were placed bilaterally on the anterolateral aspect of the nose for the measurements of A.N. EMG. The EMG of the diaphragm muscle (DIA EMG) was also measured in two of the subjects with an esophageal electrode attached to a stiff catheter. The electrode was positioned at the point where the signal to noise ratio was the most satisfactory. The catheter was then taped to the mandible and anchored by the seal of the breathing mask that the subjects wore. The mask was a modified continuous positive airway pressure (CPAP) mask with the valves removed. One valve opening was permanently sealed, and non-rebreathing valve with a low dead space (12 ml) was attached to the other opening. The electrode wires passed under the seal, which was inflated with air and checked for leaks by instructing the subjects to hyperventilate while an investigator ensured that the CO_2 concentration around the seal was approximately zero. Subjects breathed either air or a mixture of He:O_2 (79:21%) from two meteorological balloons; both gases were warmed and humidified by adding several liters of warm water to the balloons.

A short length of tubing and a pneumotachometer were placed on the inspiratory side of the breathing valve for the measurement of inspiratory nasal airflow. The pressure drop across the pneumotachometer was measured with a

differential transducer (Validyne MP 45). The resistance of the breathing circuit, from meteorological balloons to the mask interior, was 1.1 and 1.2 $cmH_2O/L/sec$ with air and 0.67 and 0.55 $cmH_2O/L/sec$ with $He:O_2$ at flow rates of 1.0 and 2.0 L/sec, respectively. The pneumotachometer:pressure transducer system was calibrated for each gas using the method described by Sullivan and Chang (27). A 9.0 liter spirometer (Collins) was filled with known volumes of air or $He:O_2$, and the gases were expelled through the pneumotach at constant flow rates (0.31 to 0.89 L/sec) by placing weights on the spirometer. Flow was integrated digitally (see below) to derive volume. For air, the volumes derived by integrating the pneumotach output were always equal to the actual volumes measured with the spirometer. In contrast, integration of the flow signal derived with the $He:O_2$ gas mixture resulted in a 12% overestimation of the actual volume. The 12% increase reflects the greater pressure drop consequent to the greater kinematic viscosity of humidified $He:O_2$ compared to air, and is consistent with values reported by Wood et al. (36) and Sullivan and Chang (27). Accordingly, a 12% correction factor was applied to the volumes derived during $He:O_2$ breathing. The percentages of end tidal CO_2 and O_2 were measured at the mouth with rapidly responding analyzers.

Nasal airway resistance was measured in a separate

study on six of the ten subjects by measuring flow, as described above, and intranasal pressure with an anterior rhinomanometric technique. A piece of small diameter tygon tubing was inserted through a stopper, which was placed in one nostril, and the other end of the tubing was connected to a pressure transducer (Grass PT 5). All signals were monitored on a Grass chart recorder and stored on VCR tapes following pulse code modulation (Vetter).

PROTOCOLS

Protocol 1: The influence of exercise intensity on nasal ventilation and nasal dilator EMG during nasal breathing. The aim of this protocol was to determine the influence of progressive intensity exercise, at normal and reduced nasal airway resistances, on inspired nasal ventilation, and on A.N. and diaphragm EMG during nasal breathing. Thus, this paradigm was designed to test the hypothesis that the A.N. muscles are regulated by changes in nasal resistance or intranasal pressures, independently of nasal airflow.

The ten subjects were instructed to breathe through their nose only, and to maintain a pedal rate of 60 rpm for the entire exercise bout. A three minute resting control period was followed by cycling exercise performed at three different work rates. The duration of each work rate ranged from three to six minutes. Five of the male subjects

exercised at 60, 120, and 180 W, two male and two female subjects exercised at 60, 120, and 150 W, and one female subject exercised at 60 and 90 W only. After resting steady state conditions were established, the $He:O_2$ mixture was substituted surreptitiously for air. After 12 - 15 breaths of $He:O_2$ were taken, air breathing resumed and continued for another 1 - 2 minutes. The above protocol was repeated at each of the exercise work rates, which were completed without intervening periods of rest.

Protocol 2: The influence of CO_2 rebreathing at rest on nasal dilator EMG during nasal breathing. Four subjects also performed a CO_2 rebreathing test. This study was conducted in an effort to determine the CO_2 sensitivity and thresholds of the A.N. EMG during nasal breathing. Inspiratory and expiratory nasal flows were measured by attaching a 5.0 liter bag directly to the pneumotach which was in turn connected directly to the CPAP mask; about 4 liters of O_2 were added to the bag. After a sufficient rest period, the subjects began rebreathing from the bag and continued to do so until the end-tidal CO_2 reached 7.0 - 8.0%, or until the subjects became too uncomfortable to continue.

Protocol 3: Determination of nasal airway resistance at rest and in progressive exercise during nasal breathing. The aim of this protocol was to estimate nasal resistance at

rest and during progressive exercise while breathing air or $He:O_2$. Six subjects (four males and two females) completed this protocol. Because the nostrils are arranged in parallel, two experimental sessions were required so that the resistance of each nostril could be determined separately. Inspiratory nasal flows (pneumotach) and intranasal pressures (anterior rhinomanometry) were measured at rest and during exercise as described above. The four male subjects exercised at 60 and 120 W, and the two females exercised at 30 and 60 W. As in Protocol 1, 12 - 15 breaths of the $He:O_2$ mixture was substituted surreptitiously for air in each condition. The same six subjects repeated this protocol on a different day, and nasal pressure was measured on the opposite nostril. Resistance is frequently described by Rohrer's constants, K_1 and K_2, derived from his equation: $P = K_1V + K_2V^2$, or in the linear form, where K_1 is the intercept, and K_2 is the slope: $P/V = K_1 + K_2V$. K_2 represents resistance to turbulent airflow, and K_1 represents resistance to laminar airflow (3).

Analysis of Data

EMG was amplified and filtered (0.1 - 5 kHz) with AC coupled differential amplifiers (AM systems). The filtered and amplified EMG was passed through a circuit which full-wave rectified and integrated the activities with a time constant of 150 ms. The airflow signals and the integrated

EMG were digitized at 25 Hz and stored on a microcomputer disc for further analysis (Dataq/Codas). The durations of inspiration (T_I) and expiration (T_E) were measured from the inspiratory flow signal, and the volume of each inspiration (tidal volume, V_T) was derived by integrating the flow signal digitally; the volumes, measured under ATPS conditions, were converted to BTPS using standard methods. These measurements were used to calculate inspired minute ventilation (V_I), breathing frequency (f), and the average rate of inspiratory airflow (V_T/T_I).

The peak height, area, and duration of each integrated EMG burst were also computed. The average EMG per burst ("mean EMG activity") was calculated by dividing the area of each burst by the burst duration. Measurements of mean and peak A.N. EMG gave similar results, so only the former were used for analysis. Finally, the percentages of end-tidal CO_2 measured proximal to the non-rebreathing valve were analyzed by hand. The derived percentages of CO_2 were converted to partial pressures, assuming full saturation with water vapor and an airway temperature of 37 degrees Celsius. For each variable, the average of the six breaths of air preceding the He:O_2 transition was computed and taken as the "control" point in each of the conditions. A breath-by-breath analysis was conducted on each of the first 12 breaths of He:O_2. This analysis was performed on the data

from each subject, and the data from all subjects were then averaged.

Inspired nasal airway resistance for each nostril was calculated using a technique described by Mead and Whittenberger (15). Inspiratory nasal pressure and flow were displayed on the x and y coordinates of a storage oscilloscope after the signals were balanced with a time delay circuit. The slope of the pressure-flow relationship derived in this way is equal to the average inspiratory nasal flow resistance (Fig. 13). The nose was modeled as a simple parallel resistance circuit, and total nasal resistance was calculated as: $1/R_T = 1/R_R + 1/R_L$ where R_T, R_L, and R_R represent total, left, and right nasal resistances, respectively. For each variable, the average of the six breaths prior to $He:O_2$ transition was computed and taken as the "control" point in each condition. Breath-by-breath analysis was conducted on each of the first 12 breaths of $He:O_2$ for all variables except nasal airway resistance. For the latter, the average resistance of the six normoxic breaths was compared to the average of the first six breaths of $He:O_2$. The individual data from each subject were then averaged to obtain the composite group averages.

Statistical Analysis.

The statistical significance of the changes evoked with

$He:O_2$ was assessed by applying a nonparametric, distribution-free, multiple-comparison analysis of variance test, based on the Friedman rank-sum procedure (5). For each variable, the average of each breath of $He:O_2$ was compared to the average value of the air breathing control point that preceded the transition to $He:O_2$ (Figs. 5 - 10). Differences were considered significant if the P value was < 0.05. All values in the text and figures are means and SEM.

RESULTS

Protocol 1: The influence of exercise intensity on nasal ventilation and nasal dilator EMG during nasal breathing. During air breathing, nasal ventilation and A.N. EMG increased monotonically as a function of the exercise intensity (Fig. 3). As a result, A.N. mean EMG activity and nasal V_I were highly correlated under these conditions ($r = 0.998$; Fig. 4). An example of the influence of $He:O_2$ on nasal V_I and A.N. EMG at rest and during exercise in one subject is shown in Fig. 3, and the average data are given in Figs. 5 and 6. As shown in Fig. 3, the transition from air to $He:O_2$ breathing (or $He:O_2$ to air; middle panel) increased nasal V_I, and led to a rapid and marked reduction in A.N. EMG at each exercise work rate for this subject, and the entire group of subjects (Figs. 5 and 6). The changes occurred by the first or second breath following the transition to $He:O_2$ breathing in all subjects. In contrast,

the influence of $He:O_2$ on these variables at rest was inconsistent and highly variable (Figs. 5 and 6).

The increase in nasal V_I evoked by $He:O_2$ was mediated entirely by increases in frequency (f) (Fig. 7), as nasal V_T did not change (Fig. 8). The increased f was the result of reductions in both T_I and T_E (data not shown). The influence of $He:O_2$ breathing on nasal V_T/T_I is shown in Fig. 9. Note that nasal V_T/T_I increased with $He:O_2$ breathing despite the marked reductions in A.N. EMG (and also in the activity of the diaphragm, which was measured in two of the subjects; Fig. 3).

The end-tidal $P_{ET}CO_2$ increased as a function of the exercise intensity during air breathing, from 38.2 $\pm$ 1.2 at rest to 44.2 $\pm$ 1.1 mmHg at 150 - 180 W (Fig. 10). The increase in nasal V_I evoked by $He:O_2$ breathing during exercise resulted in decrease in $P_{ET}CO_2$ that was statistically significant by the second breath. The reduction in $P_{ET}CO_2$ evoked by $He:O_2$ breathing at rest, although small, was reduced significantly by the sixth breath. The decrease in $P_{ET}CO_2$ was sustained throughout the period of $He:O_2$ breathing both at rest and during exercise.

Protocol 2: The influence of CO_2 rebreathing at rest on nasal dilator EMG. We determined the influence of $P_{ET}CO_2$ on A.N. mean EMG in four of the subjects by conducting CO_2 rebreathing tests under resting conditions. Fig. 11 shows

the changes in A.N. EMG as a function of the $P_{ET}CO_2$. The mean A.N. EMG was expressed as a percent of the maximal activity observed at any time during the rebreathing trial. Note that A.N. EMG did not increase until the $P_{ET}CO_2$ was greater than 43 mmHg. In addition, the magnitude of the increase in A.N. EMG at the highest level of $P_{ET}CO_2$ examined was much less than the increase evoked by even mild exercise (compare Fig. 11 with Fig. 3).

Protocol 3: Determination of nasal airway resistance at rest and in progressive exercise during nasal breathing. An example of the influence of $He:O_2$ breathing on intranasal pressure and inspiratory nasal airflow during exercise at 60 W in one subject is shown in Fig. 12. In this trial intranasal pressure was measured in the right nostril, so that the subject was breathing through the left nostril only. The transition to $He:O_2$, depicted by the black tick mark on the time base, reduced intranasal pressure and A.N. EMG, while nasal flow and V_T increased. As a result, inspiratory nasal airway resistance fell markedly.

$He:O_2$ breathing led to a decrease in nasal airway resistance in all subjects, as indicated by the calculated average Reynolds numbers (Fig. 14). A comparison of inspiratory nasal resistance while breathing air or $He:O_2$ during exercise at 60 W is shown for one subject in Fig. 13. Note that $He:O_2$ reduced resistance at all flows greater than

0.25 L/sec and allowed the subject to achieve greater peak flows at lower pressures. The average inspiratory nasal resistance values, measured at a flow rate of 0.5 l/sec, were less while breathing He:O_2 as compared to air during exercise, but not at rest (Fig. 15). Furthermore, exercise did not change nasal resistance significantly during air breathing (Fig. 15). The reduction in airflow turbulence evoked by He:O_2 resulted in significant reductions in K_2 values during exercise (Fig. 16).

DISCUSSION

The primary aims of the study were to quantify the changes in nasal airflow resistance evoked by submaximal exercise during nasal breathing, and to separate the effects of nasal airflow and intranasal pressure on A.N. EMG at rest and during exercise in healthy human subjects breathing nasally. The studies were conducted at rest and during exercise so that a wide range of spontaneous flow rates could be examined. He:O_2 breathing induced reciprocal changes in nasal flow and resistance because of its lower density and greater viscosity (3). A.N. EMG increased linearly as a function of the increase in nasal V_I evoked by air breathing exercise. The surreptitious administration of He:O_2 under these conditions led to a small increase in nasal flow and V_I, but an abrupt and substantial decrease in A.N. EMG. The results indicate that the control of A.N.

muscle activity during nasal breathing is not a simple function of the rate of flow through the nose. Rather, the activity appears to be controlled by the nasal airway resistance.

Critique of Methods.

Before discussing the results of the study, we wish to address four technical concerns relating to our experimental paradigm and methods. First, subjects were allowed to breathe through the nose alone because nasal breathing produced larger and more consistent changes in nasal airflow and A.N. EMG, thereby, improving the ability to resolve changes in these variables. Furthermore, the route of breathing has been shown to influence the activity of A.N. muscles markedly (31). Thus, changes in breathing route during exercise would have made interpretation of the findings considerably more complicated. Nevertheless, most subjects generally adopt an oronasal breathing pattern when total pulmonary ventilation exceeds about 35 - 40 L/min. (18, 24). Although a recent study reported that the switch from nasal breathing to the oronasal pattern occurred at a total V_I of 22 L/min. (32). Our subjects exceeded this value at the two highest work rates, indicating that the normal pattern of breathing may have been constrained, particularly at the highest work rate.

Second, a mixture of He:O_2 was used to evoke reciprocal

changes in intranasal airflow and resistance. He:O_2 increases nasal airflow and decreases nasal airway resistance at rest and during exercise (Fig. 12). However, He:O_2 also has a higher thermal conductivity than air, and subjects may have perceived airway cooling and changed their breathing patterns voluntarily. The "cooling" sensation was minimized by warming and humidifying both gases. As a result, only one of the subjects stated that he sensed "coolness" at any time during the test. A recent study has shown that inhalation of hot or cool air through the nose did not change A.N. EMG (33). Furthermore, cool airflow through the nasal passage has been shown to decrease breathing frequency in humans (14). Since He:O_2 consistently increased breathing frequency in our subjects, the influence of thermally mediated sensations on the pattern of breathing was minimal or absent.

Third, the $P_{ET}CO_2$ increased significantly during air breathing exercise, particularly at the two highest work rates, indicating that the subjects were hypoventilating slightly. The modest increase in nasal V_I accompanying the switch to He:O_2 reduced $P_{ET}CO_2$ back to resting levels. Thus, it is possible that the small decrease in $P_{ET}CO_2$ rather than the reduction in nasal airway resistance, lead to the decrease in A.N. EMG activity. This issue was addressed by conducting CO_2 rebreathing tests in four

subjects. As shown in Fig. 10, increasing the CO_2 sensitivity by 6 mmHg above the resting level (from 37 - 43 mmHg) failed to change A.N. EMG activity significantly. Thus, the CO_2 sensitivity of the A.N. muscles is low, a finding that is consistent with the results reported previously by Redline and Strohl (22). However, the exercise, itself, may have increased the CO_2 sensitivity, and that changes in CO_2 may have influenced the results in some way. Nevertheless, these effects were probably insignificant. Furthermore, the changes in A.N. EMG activity that occurred within the first few breaths after the transition to $He:O_2$ was probably independent of changes in CO_2, because a step change in CO_2 at the mouth is not sensed at the central chemoreceptors for several seconds (19).

Fourth, to the best of our knowledge, the anterior rhinomanometric technique has not been used to measure nasal resistance during exercise. Most investigators have used posterior rhinomanometry as the method of choice (2, 4, 23, 26, 34). In a comparison of anterior and posterior rhinomanometry, Mygrind (17) found that the major disadvantage of anterior rhinomanometry is the fact that only one nostril remains patent. This disadvantage is not a factor in our study because it is well known that adult humans have a normal unilateral nasal cycle that occurs

because of continuous turbinate engorgement in one nasal passage (20). Consequently, adults breathe from one nostril at a time and switch to the other nostril every 30 to 240 minutes (20), although we do not know how the nasal cycle is influenced by exercise. In our study subjects always used the nostril that was judged to be the most patent prior to the exercise bouts. Despite of these potential limitations, we used the anterior rhinomanometric technique for three reasons. First, our subjects were healthy and free of septal deviations and allergies, and other nasal obstructions. Second, subjects were performing submaximal exercise, and the anterior technique was more comfortable than the posterior technique under these conditions. Third, the anterior technique allowed intranasal pressures to be measured close to the A.N. muscles; thus, the pressures in this region may accurately reflect those that the A.N. muscles are subjected to during exercise.

Influence of He:O_2 breathing on nasal airflow and resistance. He:O_2 breathing delays the onset of turbulent airflow through the nasal passage because of its greater kinematic viscosity and lower density in comparison to air. Thus, higher flow rates can be obtained with He:O_2 breathing than with air at any given pressure, as indicated by the lowered Rohrer's constant (K_2) which represents the onset of turbulent airflow. The onset of turbulent airflow in a

straight, rigid smooth-walled cylindrical tube is thought to occur when the Reynold's number (N_{RE}) exceeds approximately 2,000 (25). The N_{RE} and flow rates associated with turbulent flow in the nose are not known with certainty, and the geometry of the nasal airway is complex. It is clear that a N_{RE} above 3,000 indicates that nasal flow is largely turbulent (25). We estimated the N_{Re} associated with air and He:O_2 breathing at rest and during exercise, to gain some insight into the nasal flow conditions while breathing nasally. Fig. 14 shows the estimated N_{RE} for air and He:O_2 as a function of the corresponding average nasal airflow rates obtained at rest and during the exercise bouts. Note that air breathing was associated with marked nasal airflow turbulence under all exercise conditions (i.e., N_{RE} > 4,000). In contrast, with He:O_2 breathing N_{RE} did not exceed 3,000 until the flow rates exceeded 1.5 L/sec, corresponding to exercise at 150 - 180 W. Moreover, nasal resistance at a flow rate of 0.5 L/sec was significantly reduced with He:O_2 breathing at both exercise work rates (Fig. 15). Thus, the switch to He:O_2 breathing during exercise was associated with substantial reductions in intranasal pressure, flow turbulence, and flow resistance. Finally, nasal resistance was unchanged with air breathing at rest and during exercise. Other investigators have measured nasal resistance pre- and post-exercise and have

found a decrease in resistance post-exercise (4, 23). Our results indicate that nasal resistance at 0.5 L/sec during air breathing does not change during exercise under these conditions.

Influence of nasal flow and intranasal pressure on A.N. EMG activity. The close correspondence between A.N. EMG and nasal V_I during normoxic exercise (Fig. 4) is in accord with the results of a recent study by Wheatley et. al (31), who hypothesized that the close coupling between two variables was mediated by receptors sensitive to the rate of nasal airflow. This hypothesis was tested in this study by substituting a mixture of $He:O_2$ for air at rest and during exercise, thereby increasing the rate of nasal flow, but decreasing nasal resistance simultaneously. Results show that the increase in nasal V_I with $He:O_2$ breathing was consistently associated with a decrease in A.N. EMG, which is directionally opposite to the change that would have been predicted by flow regulated control. Furthermore, the increased nasal airflows were associated with more negative pressures and increased flow resistances. This suggests that nasal flow resistance and/or intranasal negative pressure, rather than the flow rate per se, are the primary determinants of the monotonic increase in A.N. EMG observed during progressive intensity exercise (31). Thus, the changes in A.N. EMG observed with $He:O_2$ breathing are

probably mediated by receptors sensitive to changes in intranasal pressure or resistance. Furthermore, these results are consistent with the results of studies in anesthetized dogs by vanLunteren (30), in rabbits by Mathew (13), and in awake humans by Mezzanotte and Strohl (16, 26). All of these investigators agreed that experimentally induced increases or decreases in the magnitude of upper airway negative pressures led to respective increases or decreases in A.N., posterior cricoarytenoid, and genioglossus EMG.

In contrast, Wheatley et al. (33) found that increases in nasal pressures had no influence on A.N. EMG during light exercise. They used five healthy males exercising at a constant work rate of 100 - 150 W for 5 - 7 min. The investigators applied an external inspiratory resistance during exercise which increased nasal pressures swings from -3.2 ± 0.2 to -14.7 ± 1.8 cmH_2O, but failed to change A.N. EMG significantly. There are some apparent differences between Wheatley's study and the present one that may possibly explain the differences. First, Wheatley et al. (33) used an external inspiratory resistance which did not alter the transmural pressure across the nasal wall, whereas in the study by vanLunteren (30) and in the present one, the more negative intranasal pressures produced collapsing transmural pressures. Second, in Wheatley's

study the five subjects were instructed to maintain constant nasal flow by using visual feedback of their flow signals during exercise; the flow rates of our subjects were not restricted. It is possible that the voluntary input to facial motoneurons, by maintaining a constant flow rate, influenced the automatic control by mechanisms that would not be operative in the conditions of the present study. Third, the A.N. EMG did increase by 28% in the study of Wheatley et al., and although this change was not statistically significant, only five subjects were studied. Thus, it is possible that a physiological difference was masked by the combination of a small sample size and the rigorous parametric statistical model used. Finally, although application of an external nasal resistance increased the driving pressure markedly during exercise, the airflow dynamics should have been unchanged inasmuch as the subjects maintained a constant voluntary ventilatory rate (33). In contrast, He:O_2 decreases nasal resistance by reducing both flow turbulence (Fig. 14 and 15) and the magnitude of intranasal pressure swings (Fig. 13). This raises the possibility that the human nasal passage has sensory nerve endings sensitive to the level of flow turbulence or intranasal pressure. Redline and Strohl (22) studied A.N. EMG activity during CO_2 rebreathing tests in six normal subjects, with and without topical anesthesia

(2 - 4 ml of viscous lidocaine in each nares). They found that topical anesthesia in the nasal passage did not influence A.N. EMG activity. The results suggested that rapidly adapting upper airway receptors have no influence on A.N. EMG activity during CO_2 rebreathing. The authors hypothesized that A.N. EMG is controlled by the same mechanisms that control the diaphragm and other inspiratory muscles. Similarly, Wheatley et al. (33) found that local anesthesia applied in the nares had no significant influence on A.N. EMG during exercise. The authors concluded that A.N. EMG activity is not sensitive to changes in nasal airflow or surface pressure.

The idea that central respiratory drive potentials are conveyed in parallel to the motoneurons of upper airway and inspiratory pumping muscles cannot be ruled out by the results of the present investigation. Indeed, parallel changes in diaphragm and A.N. EMG activities in each of the two subjects in which diaphragm activities were measured (Fig. 3). Thus, it is possible that the consistent reduction in A.N. EMG that we observed with He:O_2 breathing was the result of a global decrease in central respiratory drive that was transmitted proportionately to all spinal and cranial respiratory muscle motoneuron pools. However, we hypothesize that the decrease in respiratory drive accompanying He:O_2 breathing is reflexogenic rather than

feed-forward, and is initiated by sensory receptors in the upper airway or in other parts of the respiratory system.

This is in accord with the results of a study by Hussain et al. (11), that showed an abrupt reduction in diaphragm EMG activities in healthy human subjects following a switch from air to $He:O_2$ breathing during exercise. These authors also concluded that the decrease in diaphragmatic electrical activity was reflexogenic, and was mediated by receptor mechanisms sensitive to the change in pulmonary resistance or the time constant of the respiratory system. Thus, it appears that a reduction of the normal resistance to airflow results in a global, reflex-mediated reduction in respiratory motor output; determining the location and functional properties of the receptors that initiate this reflex will require further study. Moreover, determining the relative influences of this mechanism and the role of upper airway sensory receptors on the decrease in A.N. EMG activity with $He:O_2$ breathing will require further study.

Physiological Significance.

The maximal rate of nasal airflow that can be achieved during exercise with nasal breathing is unknown. However, maximal nasal ventilation rates of 78 L/min have been reported in subjects that could freely choose their route of breathing during exercise (24). Although inspiratory nasal flow limitation has been shown to occur at flow rates

ranging from 1 - 2.5 L/sec (22), the average flow rates observed in the present study were in this range at the two highest work rates (Fig. 5). Nevertheless, higher flows could always be obtained when He:O_2 was substituted for air. Thus, the factor limiting nasal airflow is not flow per se, but the high resistive pressure that must be overcome under these conditions. The parallel changes in nasal airflow resistance, and A.N. EMG activity suggest that activation of these muscles serve to reduce nasal flow resistance, and may prevent collapse of the nasal passages during exercise and other hyperpneas. This idea is consistent with the observation that voluntary "flaring" of the nostrils at rest can decrease nasal airflow resistance by 30% (26).
Thus, preservation of a normal breathing pattern at rest and during exercise is dependent upon the functional integrity of the A.N. dilator muscles.

Fig. 1. Proctor's Biophysical Model of the Pathways for Nasal Inspiratory Airflow. According to Proctor's model, nasal inspiratory flow enters the nostril traveling superiorly and posteriorly to the nasal valve region, the narrowest segment. At that point, the majority of air flows through the middle nasi meatus, while a small portion flows through the base of the nasal chamber. Inspiratory airflow from these two regions is then combined at the nasopharynx.

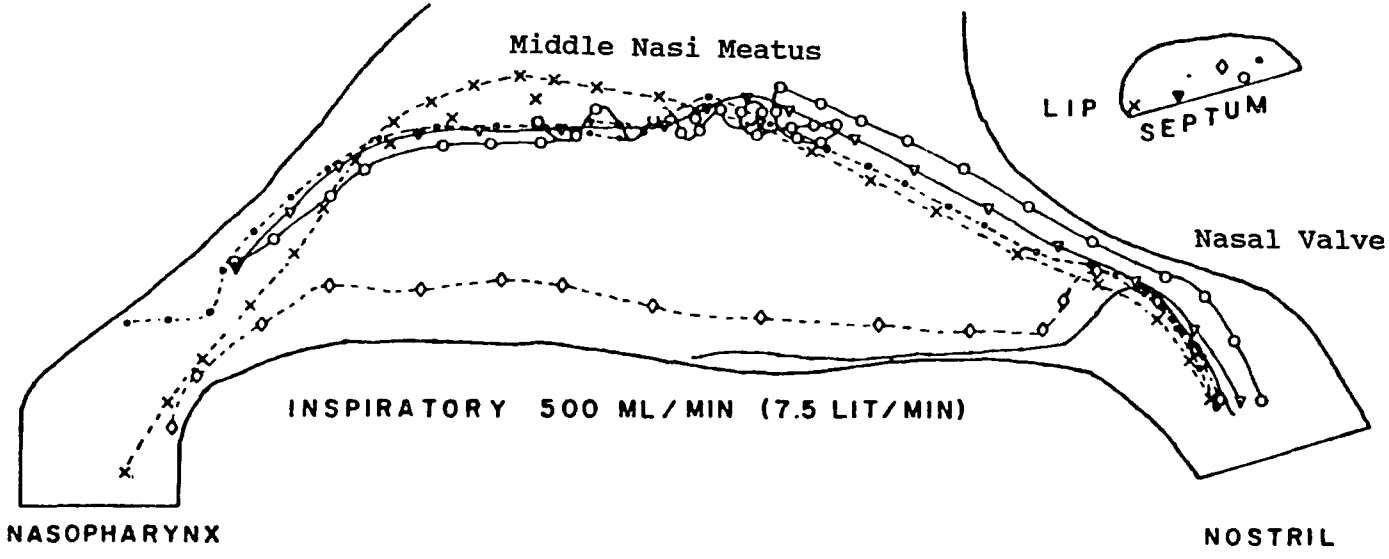

Fig. 1. Proctor's Biophysical Model of the Pathways for Nasal Inspiratory Airflow.

Fig. 2. Inspiratory Nasal Ventilation (V_I) and Alae Nasi (A.N.) EMG During Progressive Intensity Exercise. Total ventilation (oral plus nasal) increased linearly as a function of exercise intensity, while nasal V_I increased up to a total V_I of approximately 40 L/min or 60% peak power, and then plateaued. Note that the A.N. EMG also increased linearly up to 60% peak power, and then plateaued. These data suggest that the A.N. EMG is regulated by nasal V_I. Data points represent the mean $\pm$ SEM of the seven subjects.

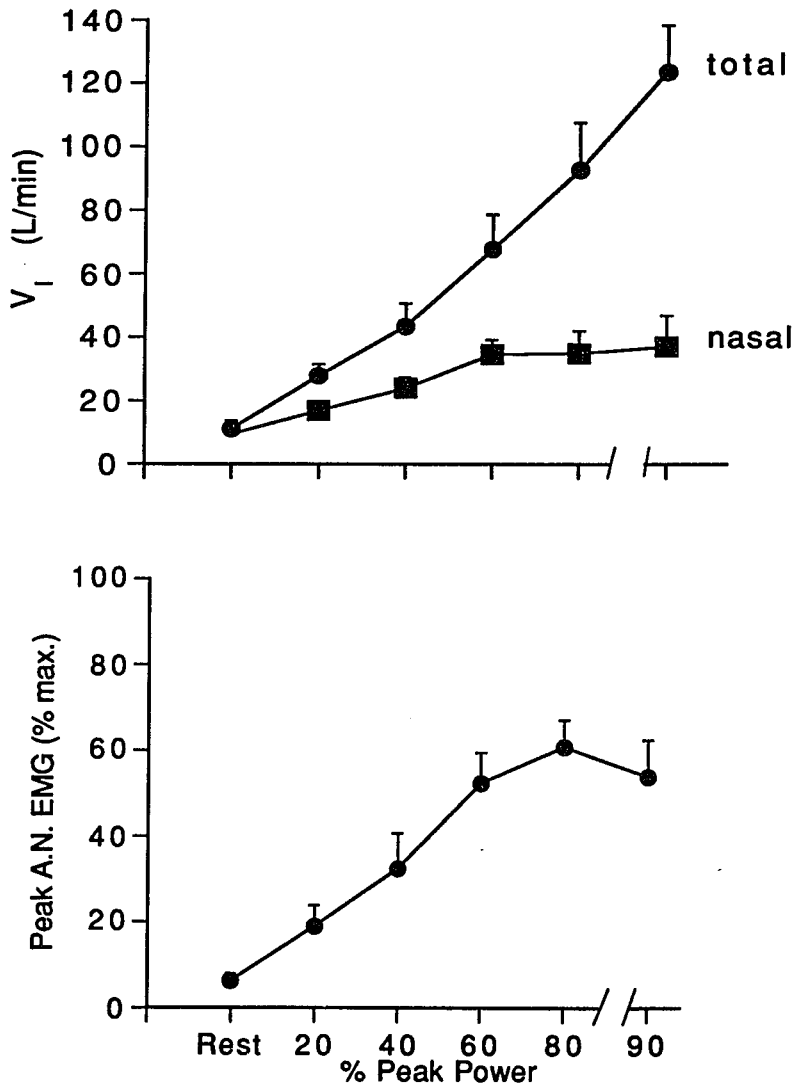

Fig. 2. Inspiratory Nasal Ventilation (V_I) and Alae Nasi (A.N.) EMG During Progressive Intensity Exercise.

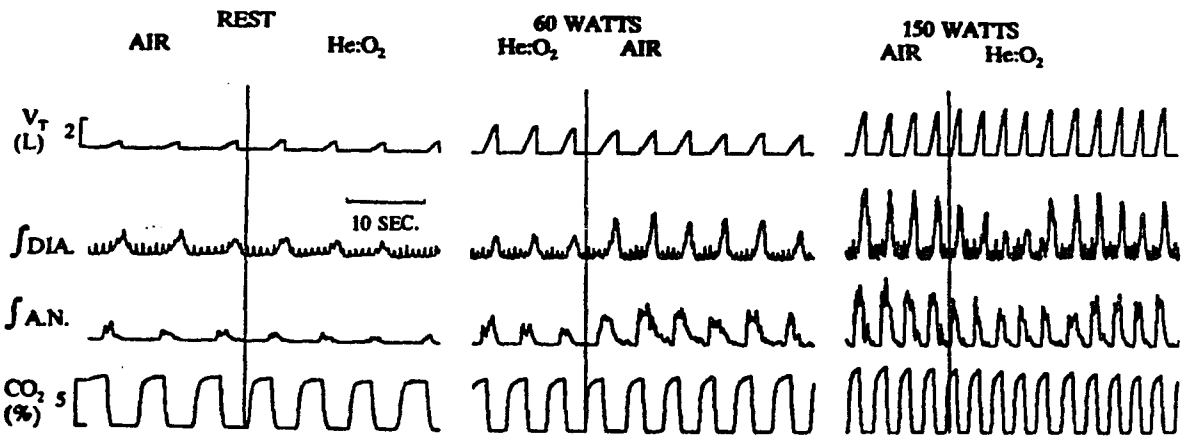

Fig. 3. Original Recordings Showing the Influence of $He:O_2$ Breathing on Tidal Volume (V_T), and on Diaphragm (DIA) and Alae Nasi (A.N.) Integrated EMG.at Rest and During Exercise. Tracings from the top to the bottom include nasal tidal volume (V_T), integrated A.N. and DIA EMG, and CO_2 measured at the breathing mask, in one subject, at rest and during exercise at 60 and 150 W. The point of transition from air to $He:O_2$ breathing (or $He:O_2$ to air, middle panel) is indicated by the vertical line in each panel. Note that $He:O_2$ caused a slight increase in V_T and frequency, and reduced A.N. and DIA EMG. Furthermore, these influences of gas density on ventilation and A.N. and DIA EMG were usually present by the first or second breath, and are similar whether the transition was from air to $He:O_2$ (rest and 150 W) or $He:O_2$ to air (60 W, middle panel).

Fig. 4. Alae Nasi (A.N.) Mean EMG Activity as a Function of Inspired Nasal Ventilation (Nasal V_I) During Air Breathing at Rest and During Exercise. Each point represents the average value ($\pm$ S.E.M.) at rest, or during exercise at 60, 120, and 150 - 180 W. Mean EMG activity is expressed as a percent of the maximal activity, which always occurred at the subjects highest work rate. Nasal V_I was also maximal at the highest work rate performed by each subject. As a result, these two variables were highly correlated: A.N. Mean EMG activity (%) = 1.90 (Nasal V_I) + 3.20, $r = 0.99$, $P < 0.002$. *, different than rest, $P < 0.05$.

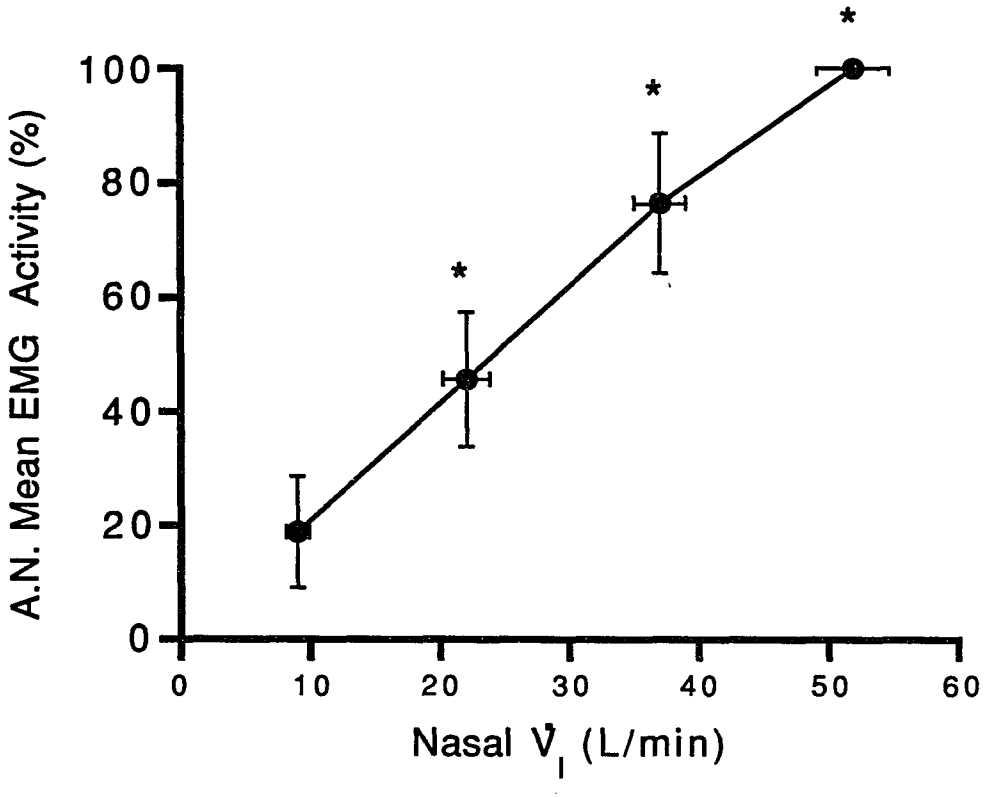

Fig. 4. Alae Nasi (A.N.) Mean EMG Activity as a Function of Inspired Nasal Ventilation (Nasal V_I) During Air Breathing at Rest and During Exercise.

Fig. 5. Influence of $He:O_2$ on Nasal V_I at Rest and During Exercise. Each panel represents the influence of $He:O_2$ breathing on nasal V_I at rest and during exercise at 60, 120, and 150 - 180 W. In each panel, the point to the left of the line, parallel to the y axis, is the average of the six breaths of air immediately preceding the switch to $He:O_2$, and represents the "control" value. The average of each of the first twelve breaths of $He:O_2$ lie to the right of the line. Note that $He:O_2$ breathing caused a significant (but small and variable) increase in nasal V_I during exercise, but little change at rest. *, different than control ($P < 0.05$).

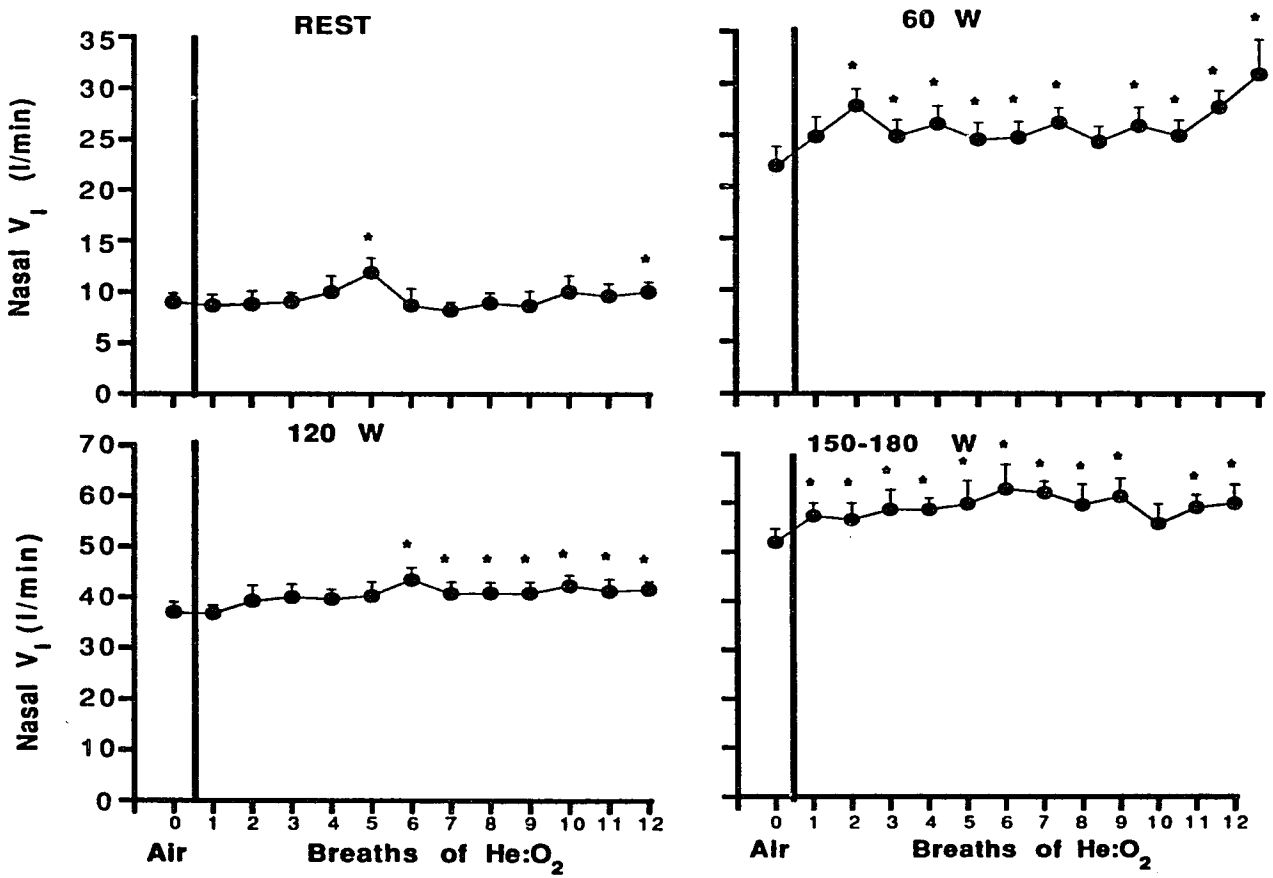

Fig. 5. Influence of He:O_2 on Nasal V_I at Rest and During Exercise.

Fig. 6. Influence of $He:O_2$ on A.N. Mean EMG Activity at Rest and During Exercise. Each panel represents the influence of $He:O_2$ breathing on A.N. mean EMG activity at rest and during exercise at 60, 120, and 150 - 180 W. In each panel, the point to the left of the line, parallel to the y axis, is the average of the six breaths of air immediately preceding the switch to $He:O_2$, and represents the "control" value. The average of each of the first twelve breaths of $He:O_2$ lie to the right of the line. Note that $He:O_2$ breathing caused a significant decrease in A.N. EMG during exercise, but changes were variable at rest. *, different than control ($P < 0.05$).

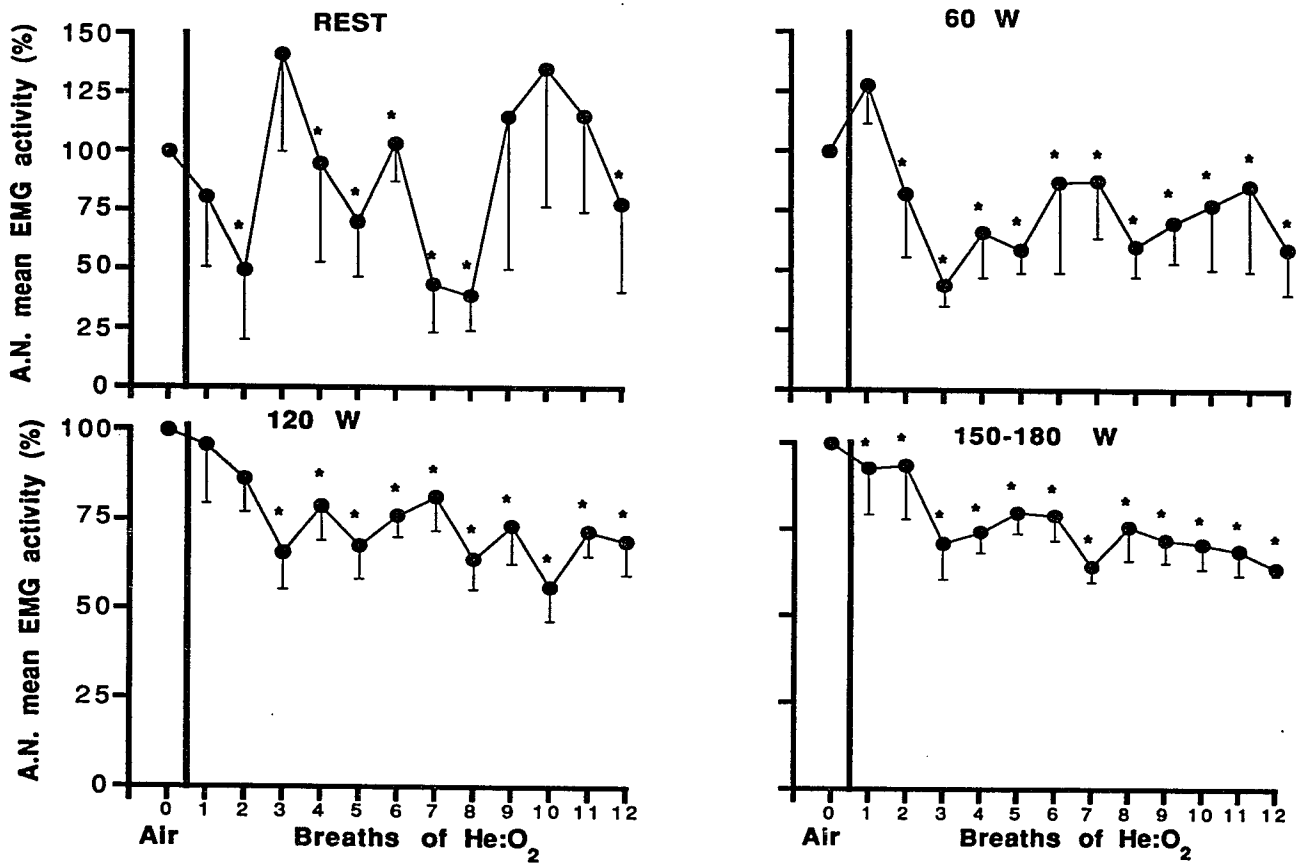

Fig. 6. Influence of He:O2 on A.N. Mean EMG Activity at Rest and During Exercise.

Fig. 7. Influence of $He:O_2$ on Breathing Frequency at Rest and During Exercise. Each panel represents the influence of $He:O_2$ breathing on frequency (breaths/min) at rest and during exercise at 60, 120, and 150 - 180 W. In each panel, the point to the left of the line, parallel to the y axis, is the average of the six breaths of air immediately preceding the switch to $He:O_2$, and represents the "control" value. The average of each of the first twelve breaths of $He:O_2$ lie to the right of the line. Note that $He:O_2$ breathing caused a significant increase in frequency during exercise, but not at rest. *, different than control ($P < 0.05$).

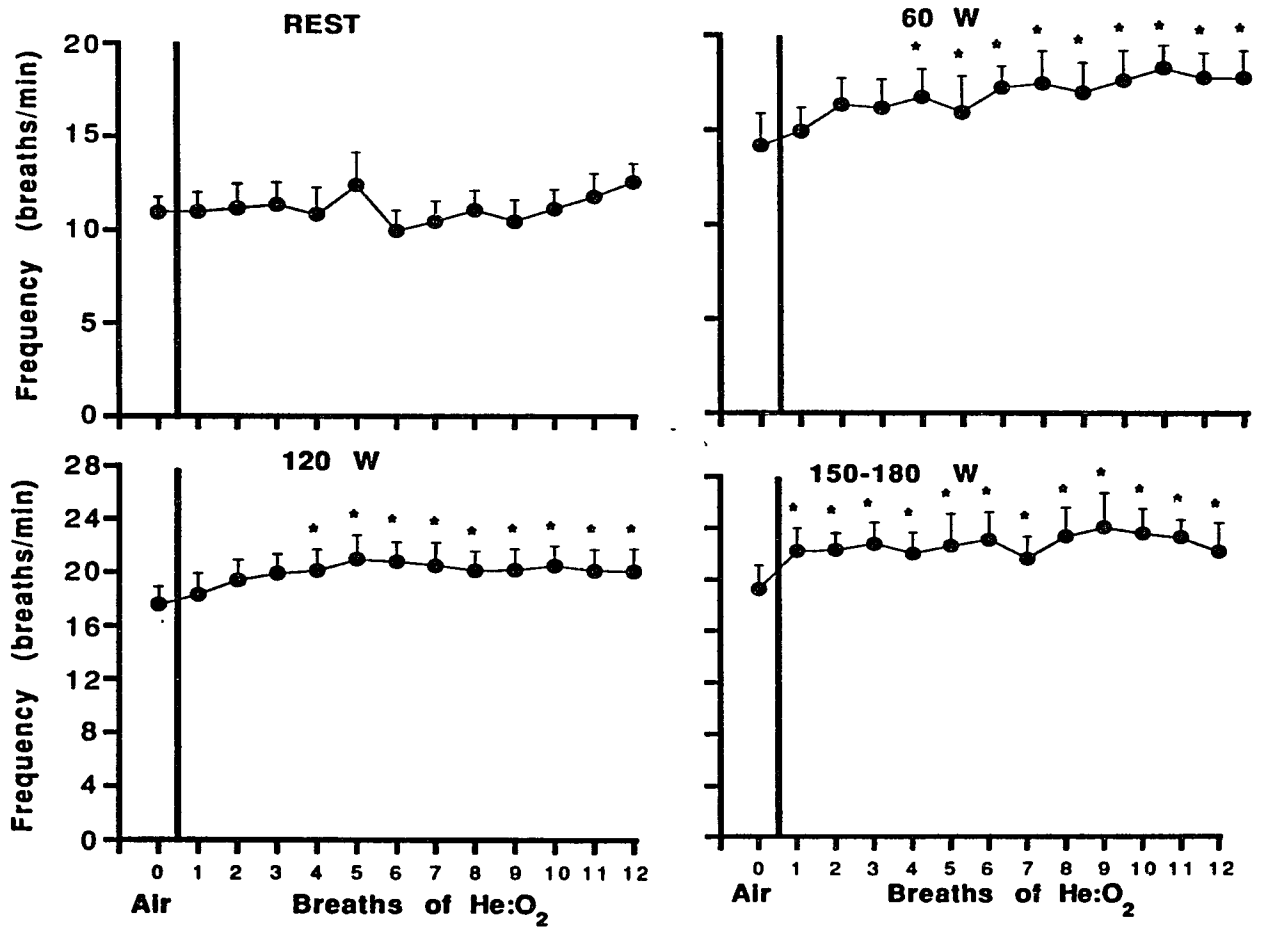

Fig. 7. Influence of $He:O_2$ on Breathing Frequency at Rest and During Exercise.

Fig. 8. Influence of $He:O_2$ on Nasal Tidal Volumes (Nasal V_T) at Rest and During Exercise. Each panel represents the influence of $He:O_2$ breathing at rest and during exercise at 60, 120, and 150 - 180 W. In each panel, the point to the left of the line, parallel to the y axis, is the average of the six breaths of air immediately preceding the switch to $He:O_2$, and represents the "control" value. The average of each of the first twelve breaths of $He:O_2$ lie to the right of the line. Note that $He:O_2$ breathing failed to alter nasal V_T at rest or during exercise. *, different than control ($P < 0.05$).

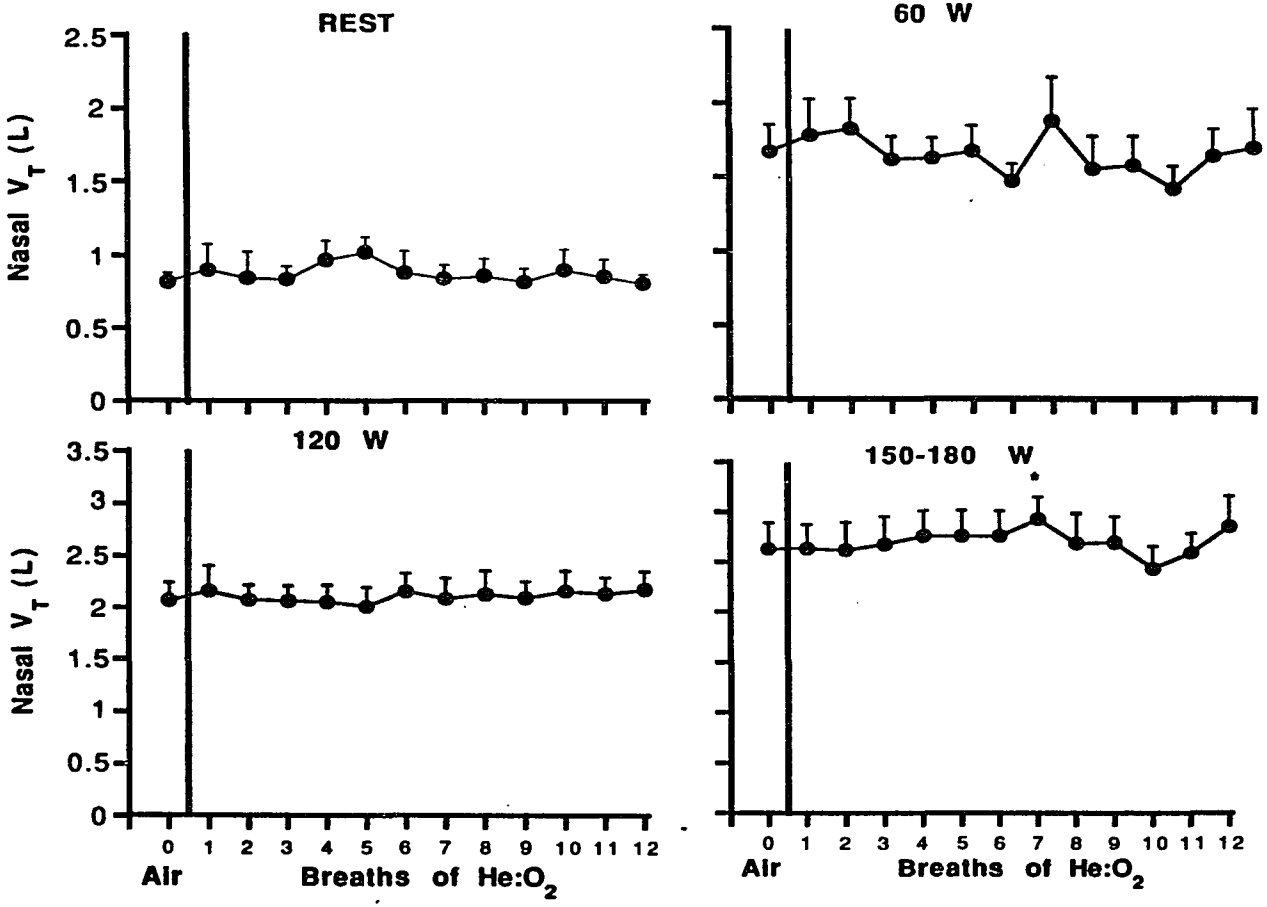

Fig. 8. Influence of He:O_2 on Nasal Tidal Volume (Nasal V_T) at Rest and During Exercise.

Fig. 9. Influence of $He:O_2$ on the Mean Inspiratory Flow Rate (V_T/T_I) at Rest and During Exercise. Each panel represents the influence of $He:O_2$ breathing on V_T/T_I at rest and during exercise at 60, 120, and 150 - 180 W. In each panel, the point to the left of the line, parallel to the y axis, is the average of the six breaths of air immediately preceding the switch to $He:O_2$, and represents the "control" value. The average of each of the first twelve breaths of $He:O_2$ lie to the right of the line. Note that $He:O_2$ evoked a significant increase in V_T/T_I during exercise, but not at rest. *, different than control ($P < 0.05$).

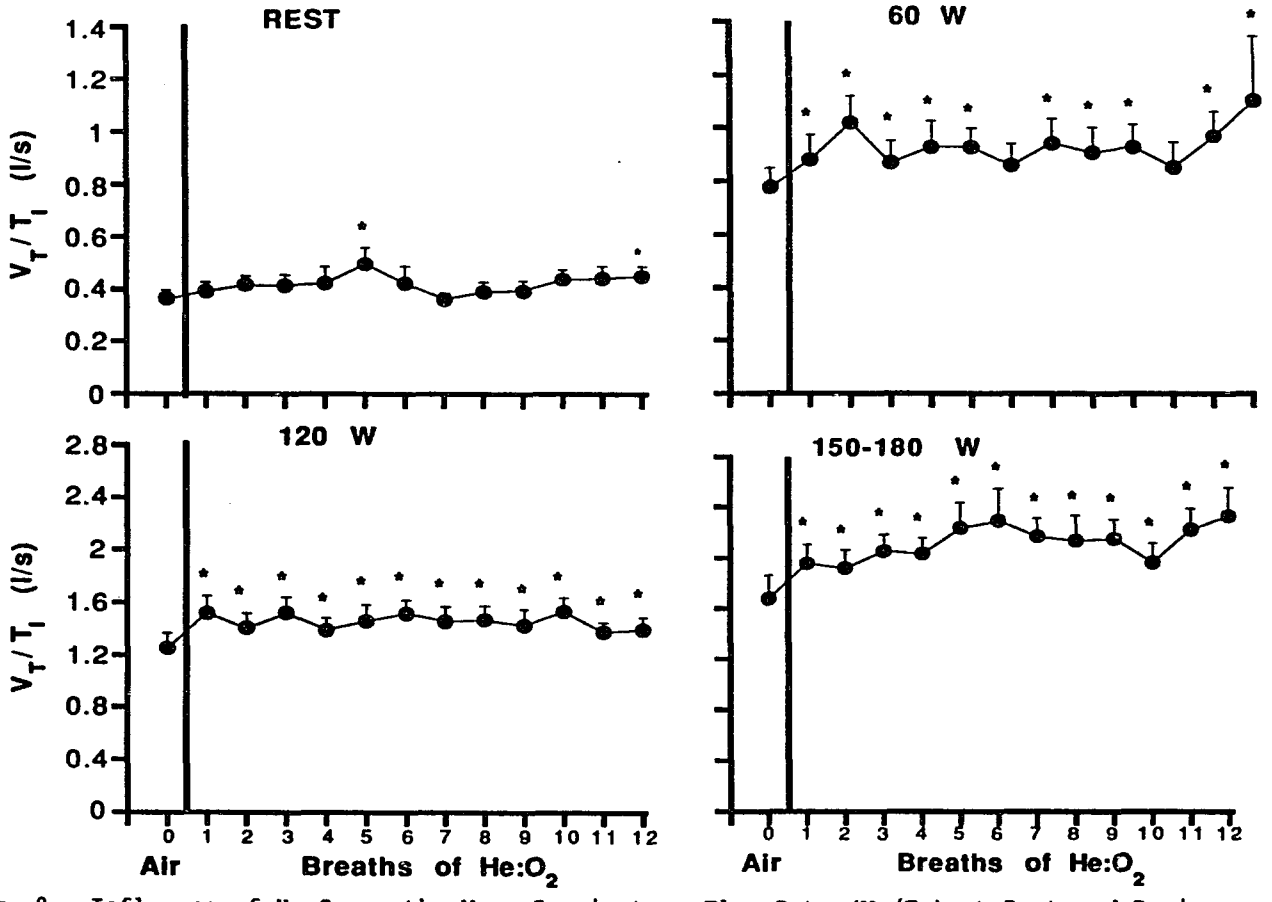

Fig. 9. Influence of $He:O_2$ on the Mean Inspiratory Flow Rate (V_T/T_I) at Rest and During Exercise.

Fig. 10. Influence of $He:O_2$ on the Partial Pressure of End-Tidal CO_2 ($P_{ET}CO_2$) at Rest and During Exercise. Each panel represents the influence of $He:O_2$ breathing on the $P_{ET}CO_2$ at rest and during exercise at 60, 120, and 150 - 180 W. In each panel, the point to the left of the line, parallel to the y axis, represent the average of six breaths of air immediately preceding the switch to $He:O_2$, and represents the "control" value. The average of each of the first twelve breaths of $He:O_2$ lie to the right of the line. Note that $He:O_2$ evoked a significant decrease in $P_{ET}CO_2$ by the second breath during each of the exercise conditions, and by the sixth breath under resting conditions. In addition, the decrease in $P_{ET}CO_2$ was sustained throughout the period of $He:O_2$ breathing. *, different than control ($P < 0.05$).

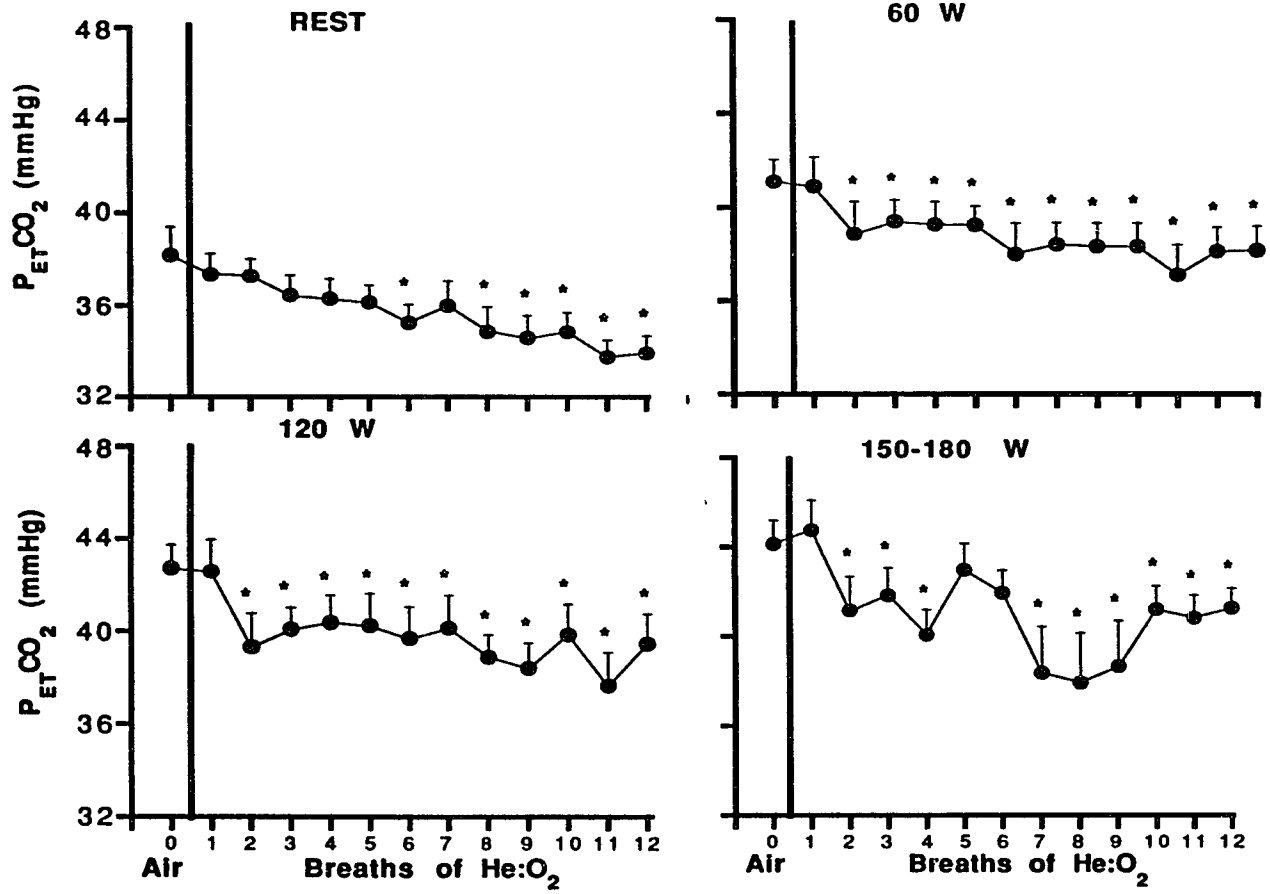

Fig. 10. Influence of $He:O_2$ on the Partial Pressure of End-Tidal CO_2 ($P_{ET}CO_2$) at Rest and During Exercise.

Fig. 11. Influence of CO_2 Rebreathing on A.N. Mean EMG Activity. This graph represents A.N. mean EMG activities in four subjects during CO_2 rebreathing studies. The mean EMG activity (average values $\pm$ S.E.M.) at six specific $P_{ET}CO_2$ levels is expressed as a percent of the maximal activity obtained during exericse. Note that A.N. EMG activity did not increase significantly until the $P_{ET}CO_2$ exceeded 43 mmHg. *, different than the value at $P_{ET}CO_2$ of 37 mmHg ($P < 0.05$).

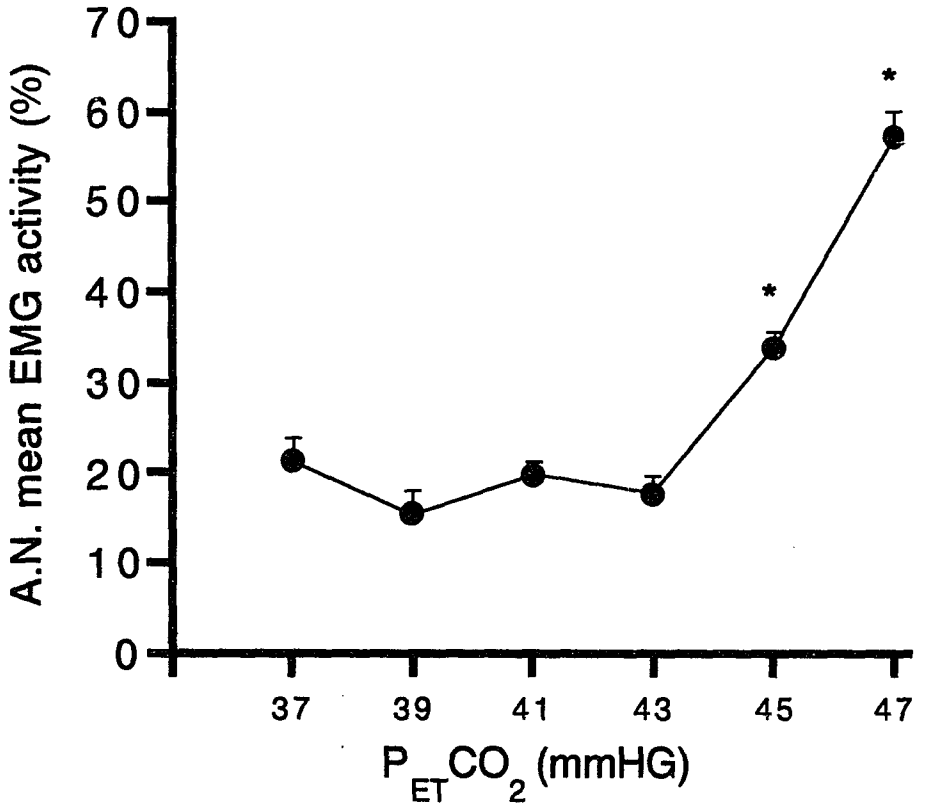

Fig. 11. Influence of CO2 Rebreathing on A.N. Mean EMG Activity

Fig. 12. Original Recordings From One Subject Showing the Influence of $He:O_2$ on A.N. EMG and on Inspiratory Nasal Flow During Exercise at 60 W. The tracings are from one subject exercising at 60 W during a transition from air to $He:O_2$ breathing, as depicted by the black tick mark on the time base beneath the first trace. Tracings from the top to bottom include nasal tidal volume (L), nasal flow (L/sec), left and right integrated A.N. EMG, intranasal pressure (cmH_2O), and $\%CO_2$. Note that with $He:O_2$ breathing, nasal V_T and nasal flow increased while A.N. EMG and intranasal pressure decreased.

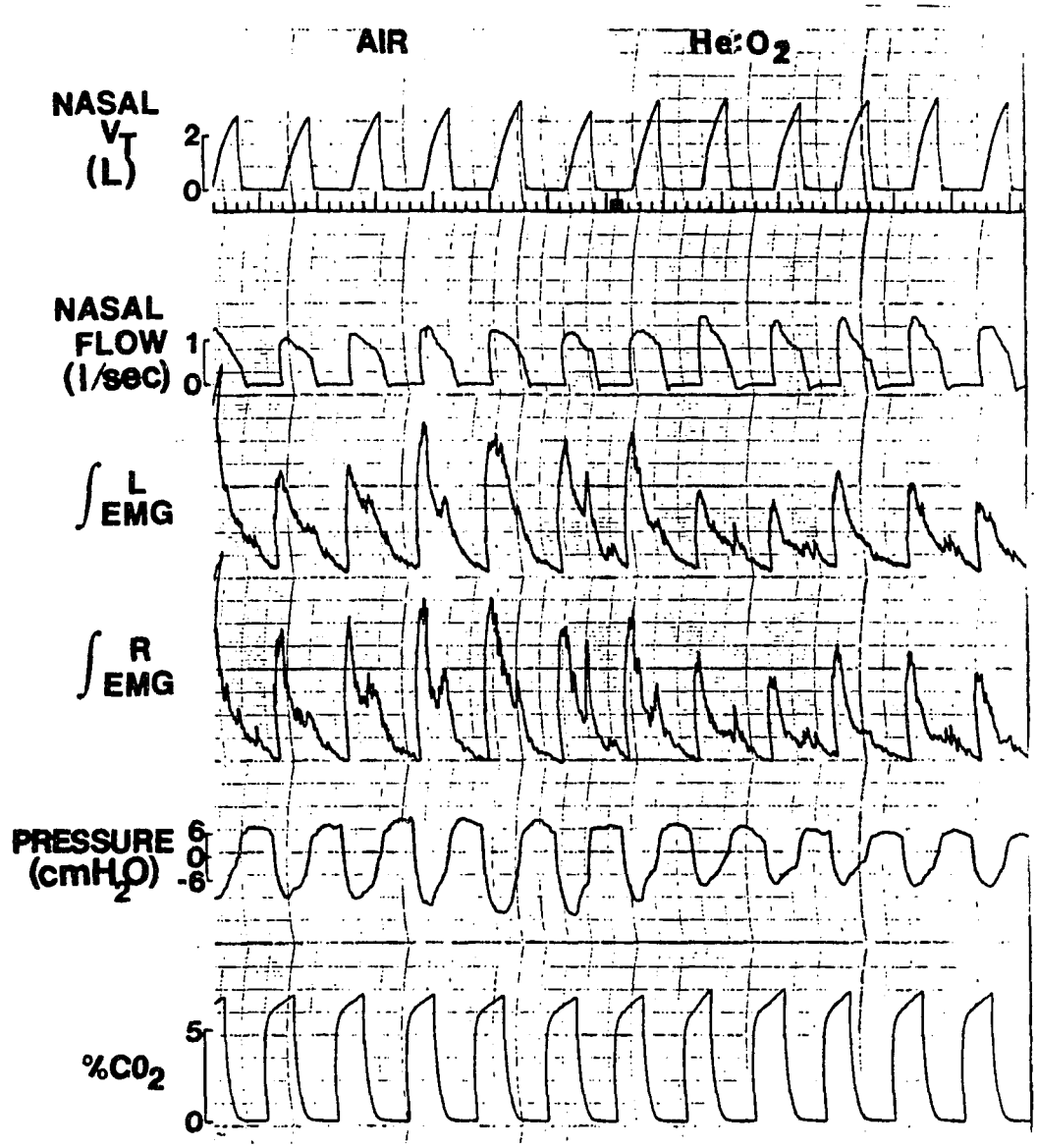

Fig. 12. Original Recordings From One Subject Showing the Influence of He:O_2 on A.N. EMG and on Inspiratory Nasal Flow During Exercise at 60 W.

Fig. 13. Oscilloscope Tracing of the Pressure-Flow Relationship While Breathing Air or He:O_2 in One Subject During Exercise at 60 W. These tracings represent intranasal pressure plotted as a function of nasal flow while breathing air or He:O_2 in one subject during exercise at 60 W. Note that during He:O_2 breathing nasal flow is greater as compared to air breathing at any given intranasal pressure. Thus, the slope of the line, which is proportional to nasal resistance, is less during He:O_2 breathing as compared to air breathing.

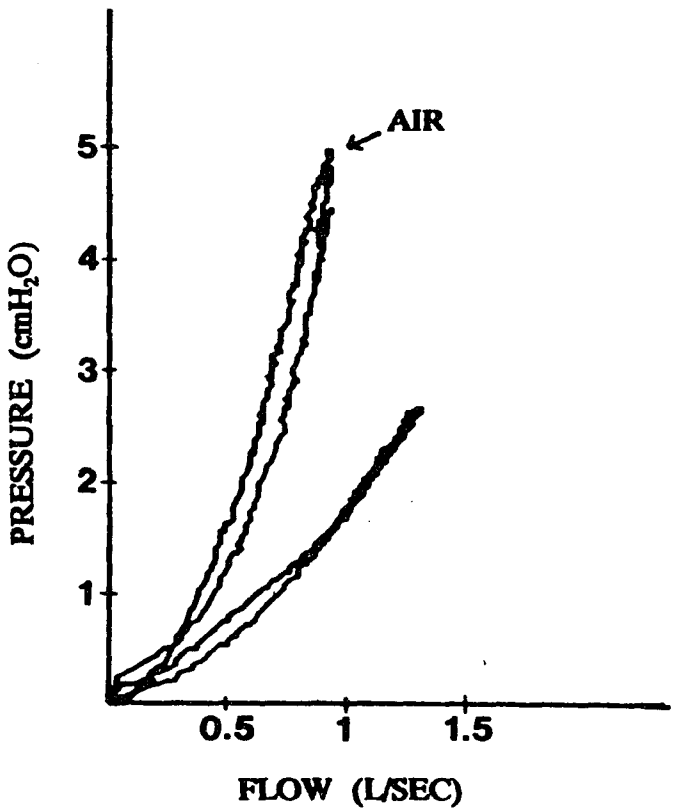

Fig. 13. Oscilloscope Tracing of the Pressure-Flow Relationship While Breathing Air or He:O2 in One Subject During Exercise at 60 W.

Fig. 14. Influence of $He:O_2$ on the Average Reynolds Numbers (N_{RE}) Calculated at Different Average Nasal Airflow Rates (V_T/T_I). Calculated Reynolds numbers (N_{RE}) at different mean inspiratory nasal airflow rates (V_T/T_I) evoked by progressive intensity exercise while breathing air or $He:O_2$. N_{RE} were calculated with the following equation: N_{RE} = pDU / u, where p = gas density, D = airway diameter, U = average airflow velocity (V_T/T_I / airway area), and u = gas viscosity. The V_T/T_I values used represent the average values derived at rest and in each of the exercise conditions; for $He:O_2$, the values represent the average of 12 breaths of $He:O_2$. The averages for nasal diameter and area were taken from estimates in healthy adult subjects by Sullivan and Chang (27). Values for one nostril were multiplied by two to derive the diameter and area of both nostrils; thus, the N_{RE} calculated represents the airflow profiles in the normal nasal airflow pathway with two nostrils in parallel. Note that $He:O_2$ reduced airflow turbulence at any given airflow rate, and that the difference in N_{RE} between air and $He:O_2$ increases as a function of flow rate.

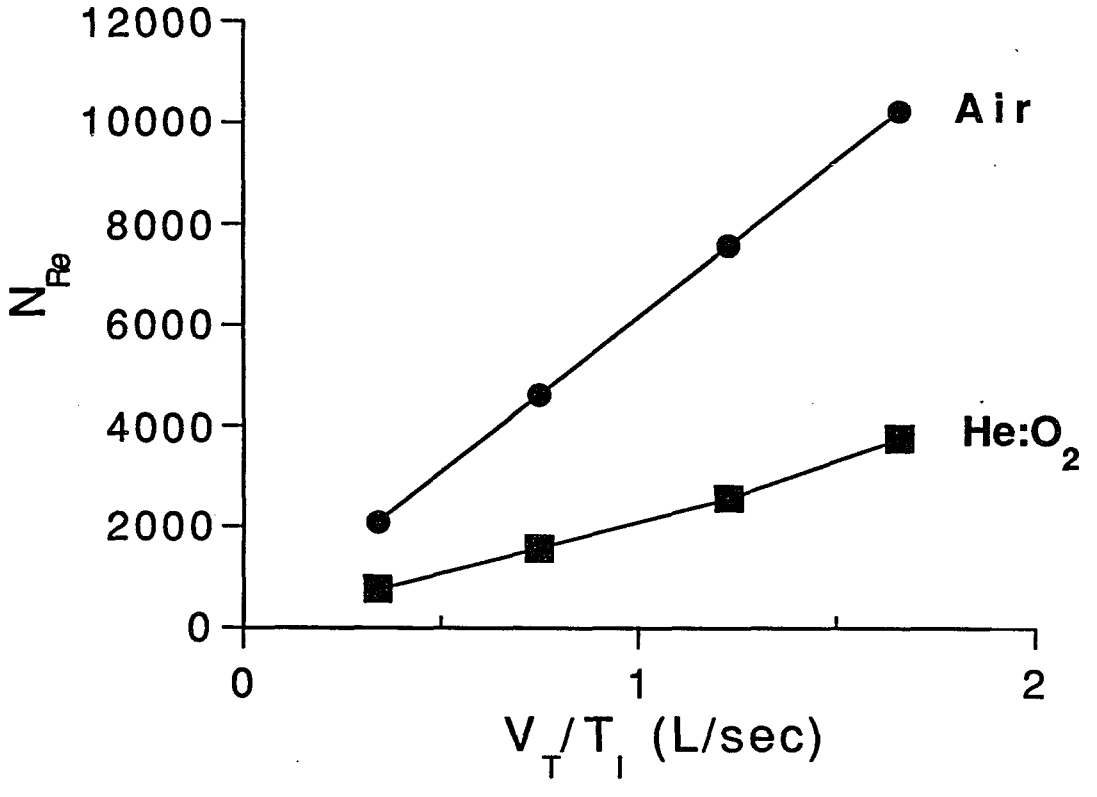

Fig. 14. Influence of He:O_2 on the Average Reynolds Numbers (N_{RE}) Calculated at Different Average Nasal Airflow Rates (V_T/T_I).

Fig. 15. Influence of $He:O_2$ and Exercise on Nasal Airway Resistance (Nasal R_N). Nasal R_N was calculated at a flow rate of 0.5 L/sec at rest and at each work rate. Data points represent the mean $\pm$ SEM values of the six subjects under each condition. Note that $He:O_2$ breathing significantly decreased nasal resistance, not at rest, but during exercise. Exercise failed to alter nasal resistance (nasal R_N) during air breathing. *, different than $He:O_2$ breathing ($P < 0.05$).

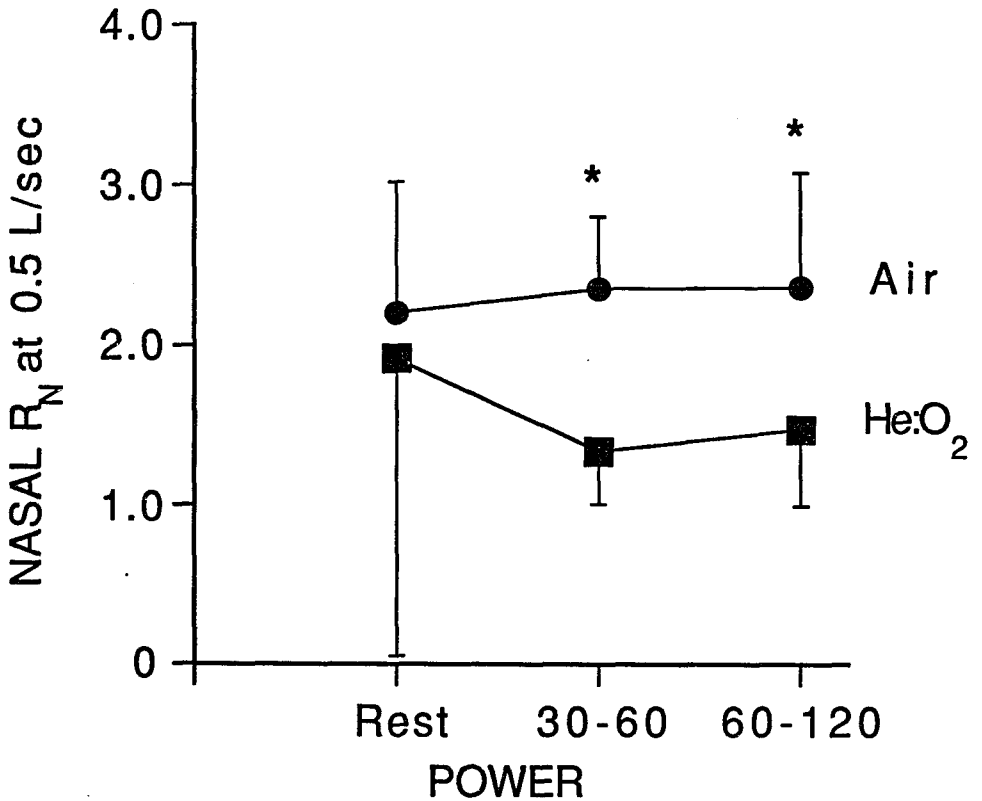

Fig. 15. Influence of He:O_2 and Exercise on Nasal Airway Resistance (Nasal R_N).

Fig. 16. Influence of Exercise and $He:O_2$ on the Estimates of Nasal Airway Resistance (Nasal R_N) Based on the Method of Rohrer ($P = K_1V + K_2V^2$). K_2, which represents resistance to turbulent airflow, was calculated at rest and at each work rate while breathing air or $He:O_2$. Data points represent the mean $\pm$ SEM for the six subjects. Note that $He:O_2$ breathing decreased K_2 relative to sir breathing at rest and at each work rate, although not significantly. *, different that the $He:O_2$ breathing value ($P < 0.05$).

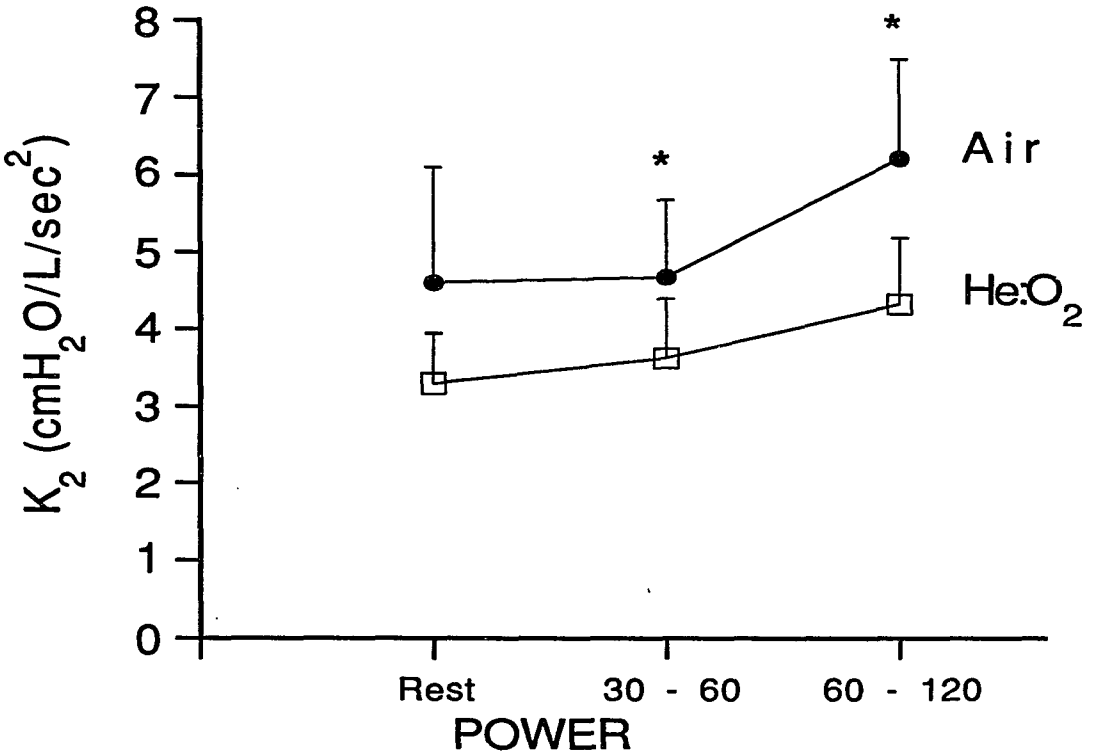

Fig. 16. Influence of Exercise and He:O_2 on the Estimates of Nasal Airway Resistance (Nasal R_N) Based on the Method of Rohrer ($P = K_1V + K_2V^2$).

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