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ALAE NASI AND UPPER AIRWAY PATENCY

BY

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ABSTRACT

The hypotheses tested in this thesis were that the alae nasi muscle was influenced by a peripheral feedback loop related to pressure and flow in the nasal passage, and secondly that the alae nasi muscle was important in influencing nasal resistance. Breathing was stimulated by CO_2. Alae nasi muscle EMG (Ean) was recorded from surface electrodes glued to the nose and flow and volume by a pneumotachymeter attached to a scuba mask. Lidocaine was applied to the nasal passage and the rest of the upper airway to try to block postulated superficial receptors in the upper airway that might be sensitive to pressure or flow and influence alae nasi activity independent of central respiratory drive to this muscle. The data showed no difference in Ean activity before and after lidocaine application to the upper airways, but there was a great deal of scatter in the data. The experimental design was therefore refined by using steady state CO_2 stimulation with CO_2 adjusted to achieve the same ventilation; Ean pre and post lidocaine were then compared. The results showed that after lidocaine application there was less Ean activity at the same ventilation suggesting the presence of pressure receptors which modulated Ean activity and were blocked by lidocaine.

To study the effect of Ean on nasal resistance, resistance was calculated by measuring transnasal pressure by posterior rhinometry and inspired flow by pneumotachymeter. Increase in nasal resistance was shown to be associated with decreased Ean and vice versa. The mechanism whereby the alae nasi muscle could influence nasal resistance was investigated by locating the point of maximum nasal resistance using a small

tube inserted into the nasal passage to measure pressure and resistance at various sites of the nasal passage. The greatest resistance was noted 2 cm inside the nares at the site of the alae nasi muscle. Hence by contracting the muscle pressure flow relationships could be changed at this site.

Finally two masks (a scuba and an anaesthesia mask) were compared to find out how different stimuli from these masks affected Ean activity. It was shown that the effect of cold air breathing on the alae nasi activity with the scuba mask was much less compared to its effect when an anaesthesia mask was used. This was probably related to the smaller dead space of the anaesthesia mask which made the air cooler in it than in the scuba mask. Hence cooler air in the anaesthesia mask may have depressed Ean.

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DEDICATION

GEETA

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

List of Figures (Cont'd.)

I. BACKGROUND

Introduction

Maintainance of upper airway patency is vital for life (Remmers et al. 1978). An obstruction in the upper airway may cause well known disorders like sleep apnea and sudden infant death syndrome (Strohl et al. 1978). The maintainance of this patency is dependent on the muscles, the nerves, and possible receptors on the muscles of the upper airways (Van de Graff et al. 1982). The mechanism by which the airway is kept open is elaborate because there are 24 sets of muscles innervated by four cranial nerves and three cervical nerves (Proctor 1983). This thesis focuses on the most accessible muscle of the upper airway, the alae nasi, its control mechanism, and function. (The "upper airway" refers to the structures in the larynx and above.)

Activation of upper airway muscles, of which the alae nasi is one, normally occurs just prior to phrenic electroneurographic activity and prevents collapse of the upper airway when the inspiratory muscles develop a negative intraluminal pressure during inspiration (Strohl 1980). Activity of the upper airway muscle increases with increasing minute ventilation (Strohl 1980). This could be due to increased activity of the respiratory centre and/or feedback loops from various receptors in the upper airways. Figure 1 is a diagram representing the possible neural mechanisms which modulate alae nasi EMG activities in humans.

The role of alae nasi in influencing nasal resistance is controversial. Previous literature (Dallimore & Eccles 1977) made no mention of the alae nasi in the study of nasal resistance. Recently Strohl (1982)

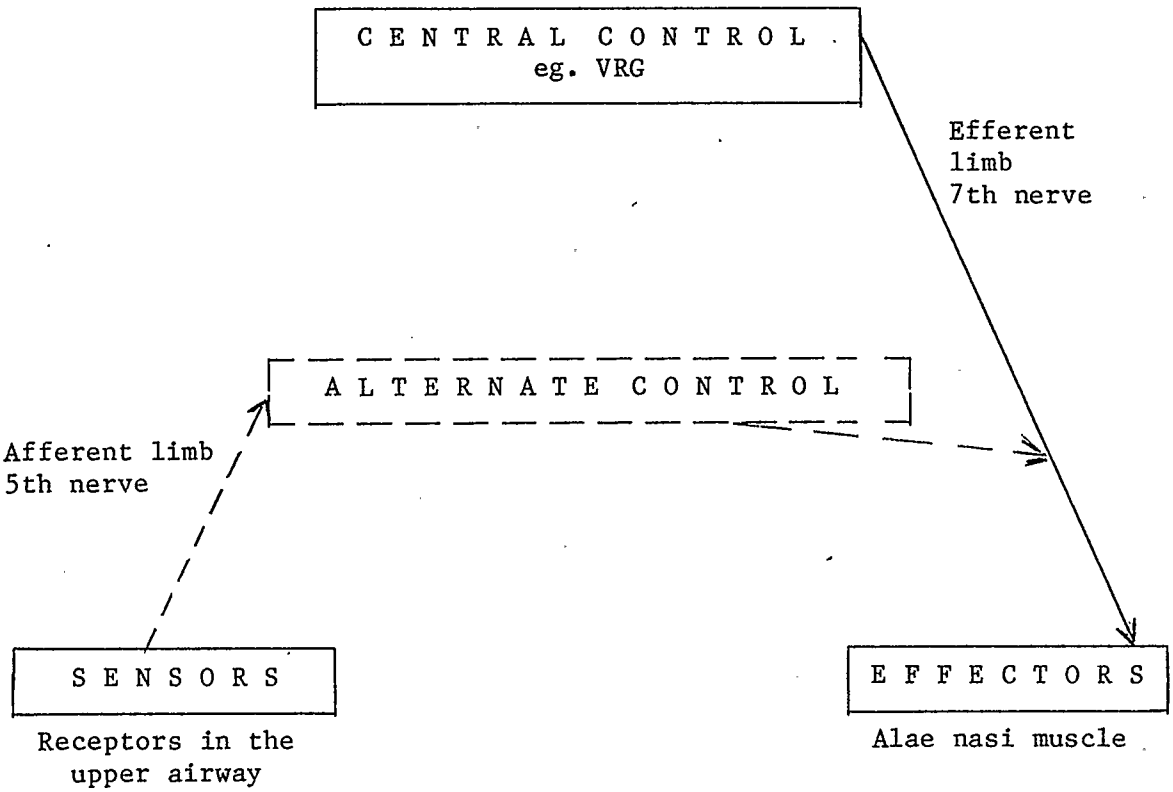


Figure 1 - The Reflex Loop

There is a direct control from the respiratory centre to the alae nasi muscle (unbroken line). The hypothesis tested in this thesis is that an afferent limb from the receptors in the upper airway modulates the central respiratory drive to the alae nasi muscles.

showed a significant role for this muscle in changing resistance. However, other recent investigators (Haight & Cole 1983) argue otherwise by suggesting that the main nasal passage which is beyond the region of alae nasi muscle is normally the main site of resistance. Therefore an experiment was designed to study the influence of alae nasi on nasal resistance.

Control of Upper Airway Muscles

1) Some pathways for possible control of upper airway muscles

i. Sensors

a. Pressure Receptors

Recent evidence (Van de Graff, Strohl 1982) has appeared which shows that negative pressures (-10 cm H_2O) created in the larynx and nasal areas in the tracheostomized dog causes increased genioglossus and alae nasi activity, as evidenced by increased EMG activity in these muscles. Lidocaine applied to the nasal passage nullified this effect on the alae nasi EMG. This evidence favors the existence of pressure receptors in the upper airways.

Adzaku and Wyke (1979) reported in cats a detailed microdissection and neurohistological study of the innervation of the subglottic mucosa and its possible relevance to phonation and airway pressure changes. In the past, many investigators such as Kirchner and Suzuke (1968), and Wyke (1974) had suggested that receptors in the subglottic portion of the larynx were important in the reflex control of the activity of laryngeal musculature during respiratory cycle and during phonation. Adzaku and Wyke found that the mucous

membrane lining of the subglottic larynx was liberally provided with corpuscular and noncorpuscular nerve endings resembling pressure receptors. Three varieties of corpuscular nerve endings were identified: (1) most numerous were corpuscles identical to Ruffini corpuscles which were innervated by a pair of myelinated afferent fibers, (2) less numerous were thinly encapsulated corpuscles innervated by fine myelinated afferent fibers and even less numerous were (3) conical corpuscles. Noncorpuscular nerve endings were represented by dense plexuses and the terminals of unmylinated nerve fibers. The silver staining of nerve endings showed myelinated fibers ramifying beneath the surface epithelium and sending branches between the epithelial cells, testifying to the superficial location of these receptors. They suggested that whilst the reflexogenic influence of the subglottic mucosa appeared to be slight in normal quiet breathing because of small subglottic pressures associated with this, the reflexogenic influence might become more significant in the presence of augmented breathing which created more negative pressures, for example, exercise or airway obstruction.

b. Temperature (Flow) Receptors

Airflow through the nose probably exerts effects on breathing by cooling the mucosa. McBride & Whitelaw (1981) showed that a gentle stream of cold air through the nose during breath holding prolonged the breath hold time and reduced the frequency of the involuntary respiratory muscle contractions that occur during these experiments at FRC. This effect was absent when air was humidified at 37°C and was also absent with topical lidocaine spray. An

explanation for this was the presence of cold air receptors which may be part of a reflex arc which in this case depresses ventilation. When there was a depression of ventilation, the mucles of the upper airways would also be less activated.

c. Other Stimuli

Various physiological changes have been noted with different nasal stimuli, for example, water, cigarette smoke, chemical gases, etc. (Widdicombe 1964). The usual change in breathing with these nasal stimuli is apnea in the expiratory phase. Although sneezing is the most obvious respiratory reflex from the nose, this is not noted in experimental animals, probably because it is blocked by anesthesia.

ii. Afferent Limb

The afferent limb of the nose and nasal mucosa is the trigeminal nerve (Grays Anatomy 15th Edition). The nasal branch of the ophthalmic nerve, which is one of the divisions of the trigeminal nerve, supplies the tip and septum of the nose. The maxillary division of the trigeminal nerve, through its branches, supplies the cavity of the nose and the integument of the side of the nose. Increases in impulse traffic in the branches of the trigeminal nerves have been described by But and Klimova-Cherkasova (1967) after nasal insufflation of ammonia and ether. Cigarette smoke into the nasal passages of rabbits has been shown to cause apnea through trigeminal nerve activity (White and McRitchie 1973).

The internal branch of the superior laryngeal nerve is sensory

to the supraglottic portion of the larynx and adjacent pharynx. The recurrent laryngeal nerve innervates the infraglottic portion of the larynx. Reduction of resiratory frequency following intralaryngeal carbon dioxide exposure was abolished through bilateral transection of superior and recurrent laryngeal nerves (Boushey and Richardson 1973). Electrical stimulation of the superior laryngeal nerve consistently reduced respiration by inhibiting inspiration (Lucier et al. 1979).

The ninth cranial nerve is the major sensory nerve innervating the pharyngeal mucosa. As a result the sensory limb of the gag reflex is the ninth cranial nerve and the motor limb the tenth cranial nerve. Investigations into diving apnea in the duck have identified fibers from a branch of the glossopharyngeal nerve that respond to the specific temperature ranges of water (Bamford and Jones 1974).

iii. Central Control

Sessle et al. (1978), recording from the solitary tract nucleus in the medulla identified a population of cells possessing an inherent rhythmic discharge pattern that was linked to respiration. From this population, eleven neurones responded to stimulation of the upper respiratory airways with a reduction in discharge frequency. Stimulation of the superior laryngeal and glossopharyngeal nerves produced similar inhibition in the same eleven neurones. Iscoe et al. (1979) have shown similar effects on stimulating the superior laryngeal nerve and vagus nerves. These results suggests

that afferent impulses in the superior laryngeal nerve, glossopharyngeal nerve, and vagus can directly affect respiration through the respiratory centres.

iv. Efferent Limb

Branches of the facial nerve, which is the motor nerve of all the muscles of expressions in the face, are the efferent supply to the alae nasi muscle. Seventh nerve paralysis causes alae nasi paralysis with a resulting collapse (alar collapse) of the outward opening of the nose of that side. Cases have been described (May et al. 1977) where alar collapse led to increased resistance during inspiration and surgical correction had to be undertaken.

v. Effectors

a. The Role of Upper Airway Muscles

The evolution of the lung and chest wall muscles in man has been accompanied by the development of a complex upper airway structure and function quite different from other animals such as the fish. For example, in the fish, the gill functions as a water pump to facilitate the gas exchange while nutrients are being filtered by one gill at the same time. There is no problem of aspirating food stuff as in human beings which have a more complex respiratory mechanism.

In humans as the bolus of food is pushed back by the tongue and propelled into the pharynx, a wave of involuntary contractions of the pharyngeal muscles (for example, the superior, middle, and

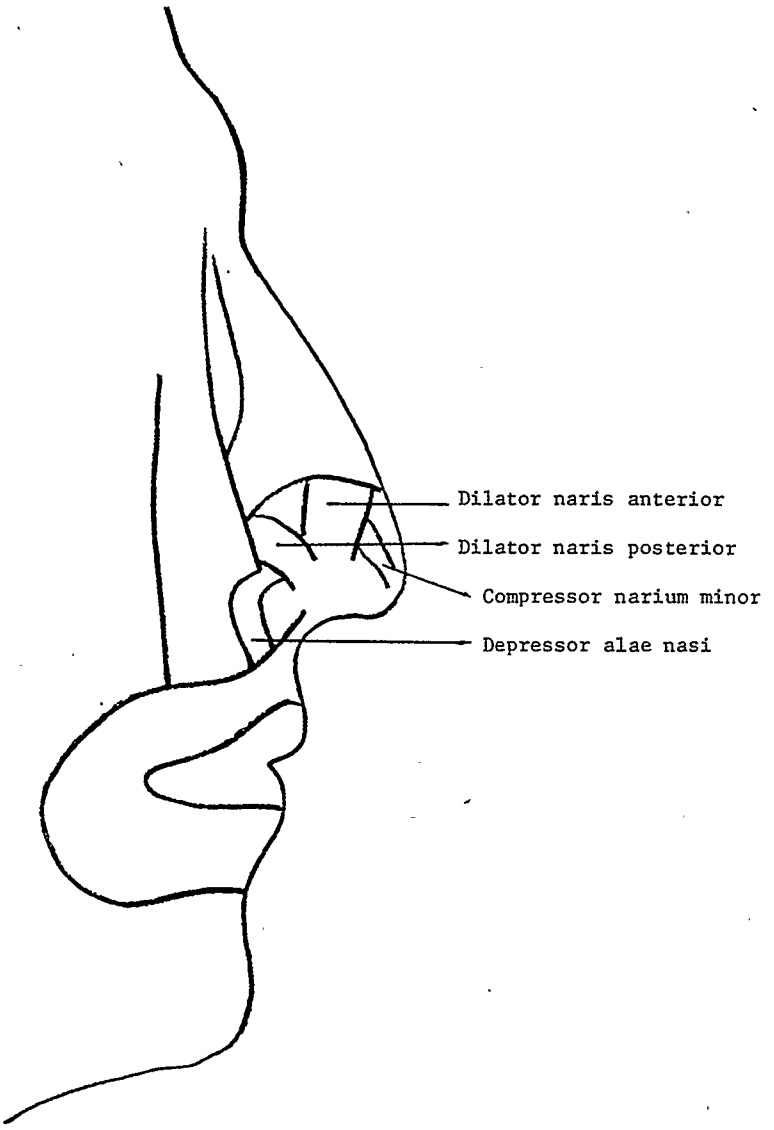


Figure 2 - Alae Nasi Muscle System (Side View of Face)

The dilator naris is the main muscle in the system. The afferent supply is the 5th nerve and the efferent nerve is the 7th nerve for these muscles.

inferior constrictors which are part of the upper airway muscle system) pushes the material into the oesophagus. Inhibition of respiration and glottic closure by laryngeal muscles takes place at the same time. In humans upper airway muscles are also used for phonation and speech.

Hence upper airway muscles have very important roles, but another important function which has recently come to light is their role in maintaining airway patency and this is a theme this thesis tries to address. The patency of the upper airway can be dependent on the contraction of the muscles of the upper airways like the pharyngeal, laryngeal, and possibly the dilator naris muscles. The contraction of these muscles will help maintain airway patency by overcoming possible collapse in the upper airways by negative pressure generated by contraction of diaphragm and chest wall muscles (Remmers et al. 1978, Strohl et al. 1978). These studies have shown that episodes of obstruction in sleep apnea patients are accompanied by diminished EMG activity in muscles of upper airways and that the activity which is present is ineffective and uncoordinated with efforts of the chest wall muscles.

Remmers et al. (1978) postulated that during sleep there is a decrease in neural respiratory output of the oropharyngeal muscles which cause a narrowing of the pharynx. They studied the genioglossus and a pharyngeal muscle, tensor palatini, and found that a striking decrease in the EMG activity of these muscles coincided with the onset of oropharyngeal occlusion. Both these muscles are located in the vicinity of the oropharyngeal opening. They also

showed that release of oropharyngeal occlusion depended on arousal and activation of the genioglossus muscle.

b. Alae Nasi

As shown in figure 2, the alae nasi consists of a pair of dilator naris, a pair of compressor naris, and a pair of depressor alae nasi. The two dilators enlarge the aperture of the nose. Their action in ordinary breathing is to resist the tendency of the nostrils to close from atmospheric pressure. If the nostrils closed there would obviously be airway obstruction. When breathing is difficult they may be noticed to be in violent action, possibly to increase the aperture of the nose to maintain airflow and prevent pharyngeal collapse (Carlo et al. 1983). The other muscles of the nose draw the alae of the nose downwards, and thereby constrict the aperture of the nares. The compressor nasi depresses the cartilaginous part of the nose and compresses the alae together. As mentioned earlier, the afferent supply of these muscles is the trigeminal nerve and the efferent is the facial nerve.

c. "Hyoid Apparatus" Muscles

The hyoid bone is suspended from the styloid process of the skull and is stabilized by supra and infrahyoid muscle groups. The suprahyoid muscles pull the hyoid both ventrally and cranially, whereas the infrahyoid muscle pull the hyoid caudally (Mathew 1984). Therefore when both muscle groups act together there is a forward displacement of the hyoid bone causing greater patency of the upper airways. The one difference from suprahyoid muscles and laryngeal muscles that can be seen in the infrahyoid muscles (for

example, sternohyoid and sternothyroid) is a rapid decline in EMG activity in these muscles when negative pressures are maintained. The laryngeal and suprahyoid muscles have a gradual decline in activity when negative pressures are maintained (Mathew 1984). The reasons for this difference are not clear. The posterior cricoarytenoid is an important laryngeal muscle which abducts the vocal cords during inspiration and negative pressure in the larynx will produce EMG activity in this muscle (Van de Graff et al. 1981).

The genioglossus, a suprahyoid muscle, is a commonly studied upper airway muscle (Brouillette and Thach 1982). It is a flat, fan shaped muscle which is parallel to the median plane. It arises from the symphysis menti and is attached to the hyoid bone. The action of this muscle is to pull the hyoid bone forward during contraction so that airway patency is maintained. The nerve supply to this muscle is the hypoglossal nerve.

vi. Normal patterns of activation of upper airway muscles

The alae nasi, genioglossus, posterior cricoarytenoid and other muscles of the upper airway have a phasic inspiratory activity (Onal et al.; Brouillette and Thach 1980). Investigators (Strohl et al. 1980) have noticed that when phasic genioglossus activity is present, its time of onset is generally coincident with the alae nasi phasic burst. This enabled them to suggest that the alae nasi EMG may be of value in timing of upper airway muscle activation. Strohl et al. (1980) were also able to show that the muscles (alae nasi EMG, genioglossus EMG, diaphragmatic EMG) were activiated in a

parallel fashion, as respiration was stimulated by hypoxia, hypercapnia, and increased inspiratory resistance.

2) Known and Hypothesized Control of Upper Airway Muscles

Activity in upper airway muscles has been thought to be an index of central respiratory drive from the medulla. In 1927 Heymans and Heymans measured the respiratory displacement of the larynx as an index of respiratory drive in an isolated canine head. These authors suggested that movements of numerous muscles, particular structures of the face, the nasopharnx, and the larynx correlated with respiratory rate and depth. Recent studies have shown that there is increased EMG activity of the upper airway muscles (including alae nasi) accompanying an increased drive (Patrick et al. 1982). Beside central control to the muscles there may be peripheral feedback which detects imminent collapse of the upper airway caused by excessive resistance to airflow by whatever cause. This local detection of pressure change may form the beginning of a reflex arc which maintains an airflow conduit.

Many voluntary muscles in the human body have a peripheral reflex control in addition to the control from the brain. Strohl et al. (1981) have indicated that the alae nasi muscles are important in the control of nasal resistance and it is in the control of nasal resistance, that such a non-central reflex loop may come into play. For example if the nasal resistance increased then this local reflex loop acting on the alae nasi muscle in response to pressure or flow could counter balance this by decreasing the resistance without a direct effect from the respiratory centre. The first objective was to investigate the presence of such a

reflex loop in humans.

Such a reflex loop for the alae nasi in animals has been demonstrated by many investigators. Mathew et al. (1982) demonstrated in rabbits that negative pressure caused marked increased in EMG activity of the genioglossus muscle but topical anaesthesia on the genioglossus produced no change in EMG activity after applying negative pressure. Van Lunteren et al. (1984) did similar experiments in spontaneously breathing, anaesthetized dogs. They put a tracheostomy tube in place and applied posterior nasal packs thus dividing the upper airway into three compartments: mouth, nose, and larynx. Negative pressures (around -15 cm of water) were separately applied in the different compartments which increased EMG activity in the muscles studied: the alae nasi, posterior cricoarytenoid, and genioglossus. However, nasal negative pressure affected Ean more than posterior cricoarytenoid EMG while laryngeal negative pressure had the opposite effect. The effects of nasal negative pressure were abolished by local anaesthesia to the nasal passage whereas local anaesthesia to the larynx abolished laryngeal negative pressure effects. An interesting finding which some of these investigators showed was that electrical stimulation of the superior laryngeal nerve (afferent nerve for larynx above the vocal cords) depressed posterior cricoarytenoid EMG activity, unlike the results seen after applying negative pressure. This effect of the nonspecific stimulation of the nerve shows that there might be other receptors in the larynx which when stimulated may have a depressant effect on the muscles there.

There has not been any study in humans where the possibility of the existence of pressure receptors has been shown by studying an upper air-

way muscle, applying lidocaine anaesthesia to it as in animals, and observing to see if that alters the EMG activity of that muscle. Such a study would help better define the role of upper airway muscles in maintaining extrathoracic airway patency by a peripheral reflex arc.

Nasal Resistance

i. Resistance in the Vestibule

The nose accounts for one-half of the total respiratory resistance to airflow during nasal breathing (Proctor 1977). The alae nasi muscles may be playing a significant part in that half of the total respiratory resistance (Strohl et al. 1982). This was the second hypothesis tested in these experiments.

If the alae nasi does play an important role in controlling nasal resistance, this may be due to its strategic location. Indeed, in models and cadavers the first 2-3 cms in the nasal passage (vestibule) has been shown to be where the greatest pressure drop in nasal passage takes place (figure 3). The first 2-3 cms of nasal passage is the site of the alae nasi muscle. Dilating or compressing the alae nasi could alter the pressure drop and change resistance. Because of the vascular factors in the nasal passage and the changing tone of the alae nasi muscle in live subjects, the findings in models and cadavers had to be verified in live subjects. Recently Cole and Haight (1983) studied six healthy subjects and reported that the greatest pressure drop was not in the region of the alae nasi muscle but actually several millimetres within the main nasal cavity in the region of the inferior turbinate. If this were the case it would be reasonable to expect the alae nasi to play only a minor role in

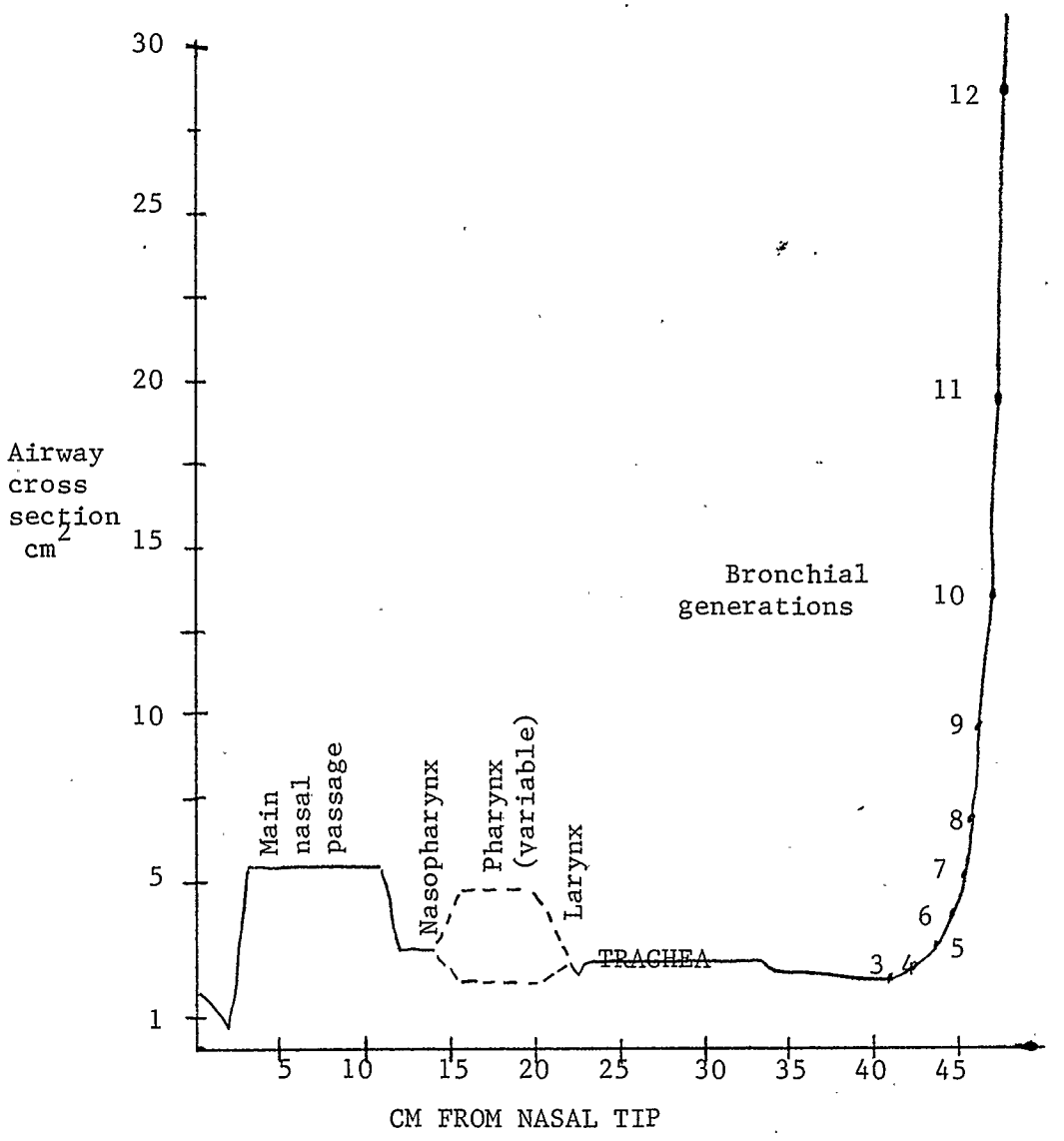


Figure 3 - Airway Cross Section and Distance from External Nasal Opening from Models and Cadaver Data, (Proctor et al. 1977).

The narrowest point in the respiratory system is in the first 2.5 cm of the nasal passage.

nasal resistance.

ii. Nose breathing

Nasal resistance may vary among different subjects (figure 4) by as much as fivefold (Proctor 1977). The resistance can also vary within the same individual in relation to changes in nasal vascular congestion, posture and exercise. In these instances one main factor for altering resistance is change in the size of the blood vessels in the main nasal passage which changes the width and therefore the resistance in the passage.

If we were to breathe through our mouth only, the total respiratory resistance would be half, yet we breath through our nose under most circumstances (Uddstromer 1940). Although the resistance encountered is greater, the instinct to breathe through our nose serves us in two main ways. Firstly, nasal breathing humidifies the air and helps adjust its temperature to body temperature. The temperature is approximately 23°C at the nasal opening, 30°C by mid nasal passage, 33°C in the nasopharynx, and slightly above that in the trachea. The relative humidity is nearly 100 per cent (Proctor 1977). Humidifying and temperature adjustment capacity of the nose are closely linked because with each increment in temperature additional water vapor is required to reach full saturation.

Secondly, large amounts of inhaled foreign materials are removed by the nose. Removal takes place due to the high linear velocity and the bend in the airstream in the anterior nares resulting in impaction of a large proportion of particles on to the nasal passage (Brain 1970). Particles of aerodynamic size of 5 to 10 micrometers are deposited on the

nasal passage. A significant proportion of even very small particles are deposited in the nose, although many particles smaller than 2 micrometers pass with the inspired air into the lung. Of those in the size range 2 to 4 micrometers, which probably includes droplet nuclei carrying infections microorganisms, not much is known.

In many animals, approximation of the epiglottis to the palate allows nasal breathing even when the mouth is open to ensure operation of the olfactory defence mechanism, which carries the sense of smell through the cribiform plate of the ethmoid via the first nerve.

iii. Nasal Cycle

This is a relative vascular congestion and decongestion which occurs rhythmically in some individuals sometimes resulting in what appears to be a systematic raising and lowering of resistance to airflow first on one side of the nose and then the other. It is unlikely that any such cycling is a vital part of nasal function since it is not found in all persons (Proctor & Swift 1977); and, when it occurs, the number of hours involved in a cycle is highly variable. The total nasal resistance does not change during the cycle.

iv. Nasal Resistance in Infants

Carlo et al. (1983) have shown that in healthly pre term infants alae nasi activity reduced nasal resistance. This was important because newborn infants are considered obligate nose breathers and nasal resistance may be a major determinant of airflow to the lungs. Futhermore, a decrease in nasal resistance may reduce the negative inspiratory pharyn-

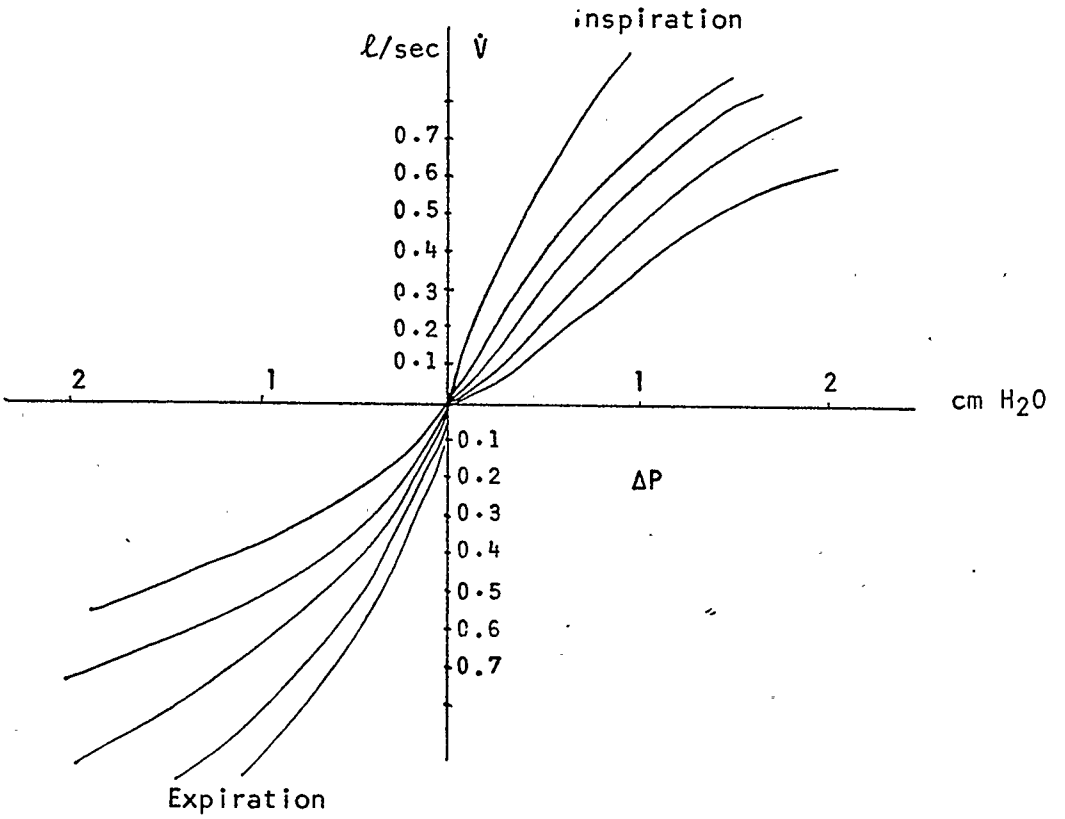


Figure 4 - The Difference in Nasal Resistance (cm H_2O/L/sec) in Normal Subjects. Resistance is change in pressure upon flow. (From Proctor 1977)

Each line represents a different subject. There is a wide range of variation in normal nasal resistance in different individuals.

geal pressure and thus prevent collapse of the pharyngeal air passage. This is indirectly supported by studies of partial nasal occlusion in which negative pharyngeal pressure during inspiration was augmented (Tonkin et al. 1979). Small changes in pharyngeal pressure may be critical to the development of upper airway obstruction (Wilson et al. 1980).

v. Resistance in Main Nasal Passage

The main nasal passage extends backwards from the vestibule approximately 6-8 cm to the posterior end of the turbinates and the arch of the septum (figure 5). The passage is divided by the nasal septum and the lateral walls are made up of the folds of the turbinates and the meati are in between the turbinates (Proctor 1977). In the main nasal passage there is a rich supply of secretory cells and complex vasculature in the nose which has erectile capabilities comparable to the corpus cavernosus and corpus spongiosus in the genitalia (Batson 1954, Swindle 1935). The vasculature helps the nose adapt to ambient changes in the atmosphere so that damage to the alveoli is prevented. As in the genitalia, the autonomic nervous system acts on the smooth muscles in the blood vessels to account for the increased blood flow, the alterations in the width of the airway (Anggard 1974), and the variability of nasal passage diameter which will obviously influence resistance. Investigators (Proctor 1977; Cole and Haight 1983) are agreed that during congestion of the nose the main passage of the nose especially in the region of the inferior turbinate offers the greatest amount of resistance and this can be appreciated with the vasculature of the main nasal passage set up as described.

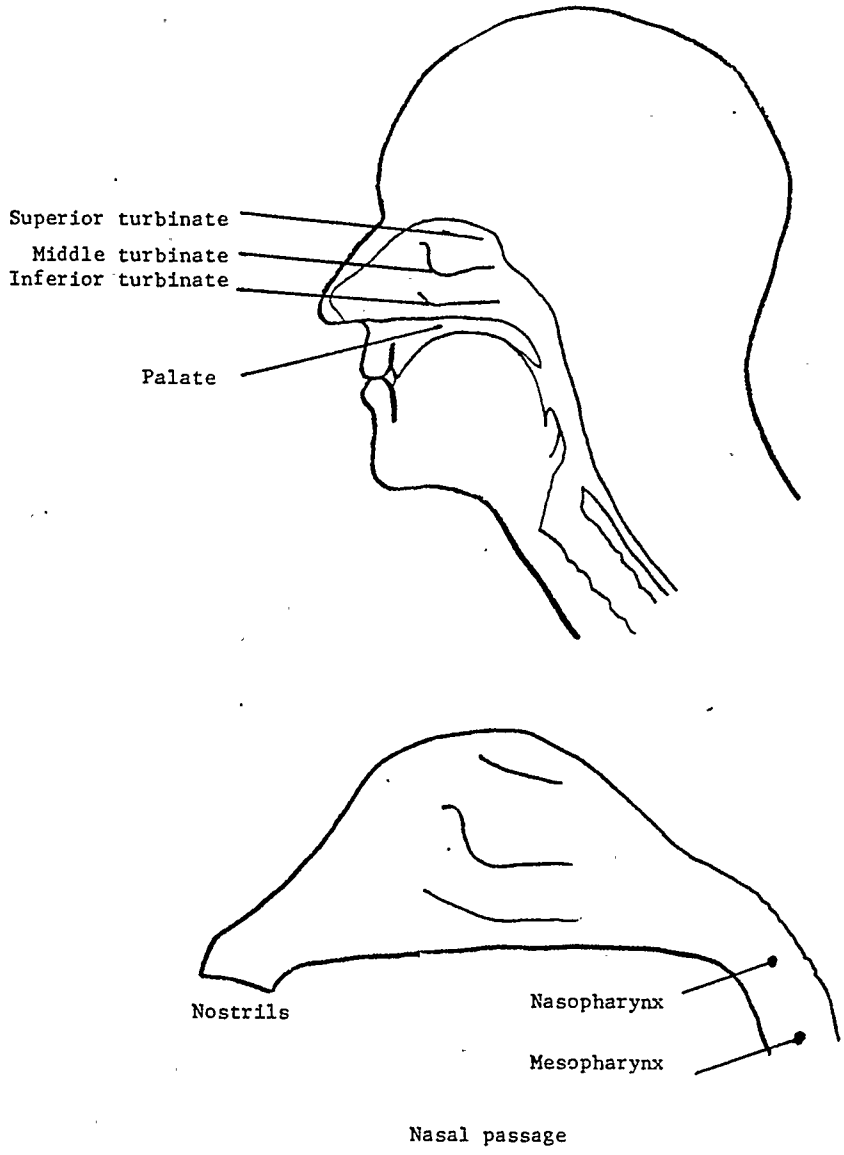


Figure 5 - Saggital Section of the Face and Nasal Passage

The main nasal passage can be the site for maximum nasal resistance when the turbinates become congested.

II. HYPOTHESES

Various investigators have demonstrated in animals the presence of a reflex loop which partly controls the activity of some of the upper airway muscles and thus help maintain extrathoracic airway patency (Van de Graff et al. 1982, Mathew 1984). Such a reflex loop has not been demonstrated in humans.

The **first hypothesis** therefore stated that there were superficially located receptors in the upper airway which formed part of a reflex arc that modulated the drive supplied by the main respiratory centre to an upper airway muscle, the alae nasi.

The **second hypothesis** stated that the alae nasi was significant in the control of nasal resistance.

III. EXPERIMENTAL OUTLINE

To test the first hypothesis, Read's rebreathing technique (Read 1967) was used to stimulate respiration while studying the relation between alae nasi activity and ventilation, and how this relation was affected when possible peripheral feedback was interrupted by lidocaine anaesthesia. For various reason the data obtained in rebreathing experiments turned out to be difficult to compare from one condition to another, and hence steady state CO_2 stimulated breathing was chosen to make this comparison possible and examine the first hypothesis. The experimental design was also altered to include a cold air breathing circuit to examine the possibility of a peripheral feedback loop involving temperature receptors (McBride and Whitelaw 1981) which might affect the alae nasi muscles.

The second hypothesis stated that the ale nasi was important in the control of nasal resistance. The experiments were exactly the same as the first set of experiments with the focus of attention on transnasal pressures which were being monitored to calculate nasal resistance and correlate it with alae nasi activity.

Another set of experiments were carried out to see where the resistance was maximum in the nasal passage of live human beings. This was done to confirm or challenge Proctor's cadaver data (1977) and thus study the importance of the strategic position of the alae nasi.

Finally, during the course of my experiments, another investigator in our laboratory who was using an anaesthetic face mask (figure 19) for his experiments was obtaining very different Ean (alae nasi EMG) activity

from what I was obtaining using a scuba mask (figure 10). A comparison study of the results of Ean obtained from the two masks at a particular ventilation was carried out in five subjects to try to resolve the discrepancy and understand more about alae nasi EMG (Ean) activity.

IV EXPERIMENT 1:

Existence of a reflex loop in humans

1) Rebreathing Technique:

i) Rationale

In addition to the control of the main respiratory centre in the medulla, there may be a neural reflex arc which influences the activity of the alae nasi muscle of the nose. To test this hypothesis it had to be shown that the activity of alae nasi muscles as seen by EMG recordings could be varied independently of the overall output of the respiratory centres. To do this it was necessary to produce a specified output from the respiratory centre. The centre had to be driven with CO_2 which would help override other inputs to the respiratory centre including those from higher centres. As an alternative to giving CO_2 to drive the respiratory centre, the subject could be made to exercise; but giving CO_2 would be more convenient. CO_2 stimulation produced large Ean activity and this was useful because, as will be seen in the results, there is a range of breath to breath variation in alae nasi EMG (figure 8) which would be less important as percent of the signal when the alae nasi activity was large.

The most desirable method of measuring output from respiratory centre would be to do it directly but since that is not possible it was decided to measure minute ventilation (V_E) (Milic-Emili et al. 1981). A control run would be done without a receptor blocker and then a receptor blocker would be used to prevent the receptor in the upper airway from transmitting signals. If this in any way altered alae nasi activity while leaving V_E unchanged, one could then postulate a peripheral

reflex loop independent of central drive.

In brief, EMG of the alae nasi (Ean) would be measured to detect changes in the activity of the alae nasi muscle and ventilation (V_E) would be measured to monitor central drive (output from the medulla). CO_2 would be used to drive the respiratory centre in the medulla. Lidocaine would be used to block the upper airway receptors in the mucosa.

ii. Methods

Five healthy male volunteers with a mean age of 28 years, who had no history of recent cold or nasal allergy were studied. The septum of the nose was also checked because a deflected nasal septum would interfere with resistance measurements of the nose. The subjects sat comfortably on a chair and the apparatus was set up as shown in figure 6.

EMG of the alae nasi (Ean) was measured by means of two brass electrodes 0.7 mm in diameter. Collodion glue was used to stick one electrode on the side of a dilator naris and the other electrode was stuck on the midline at the tip in close proximity to the first electrode. The electrical activity obtained at these positions is more specific for nasal flaring than for other facial movements (Carlo 1983).

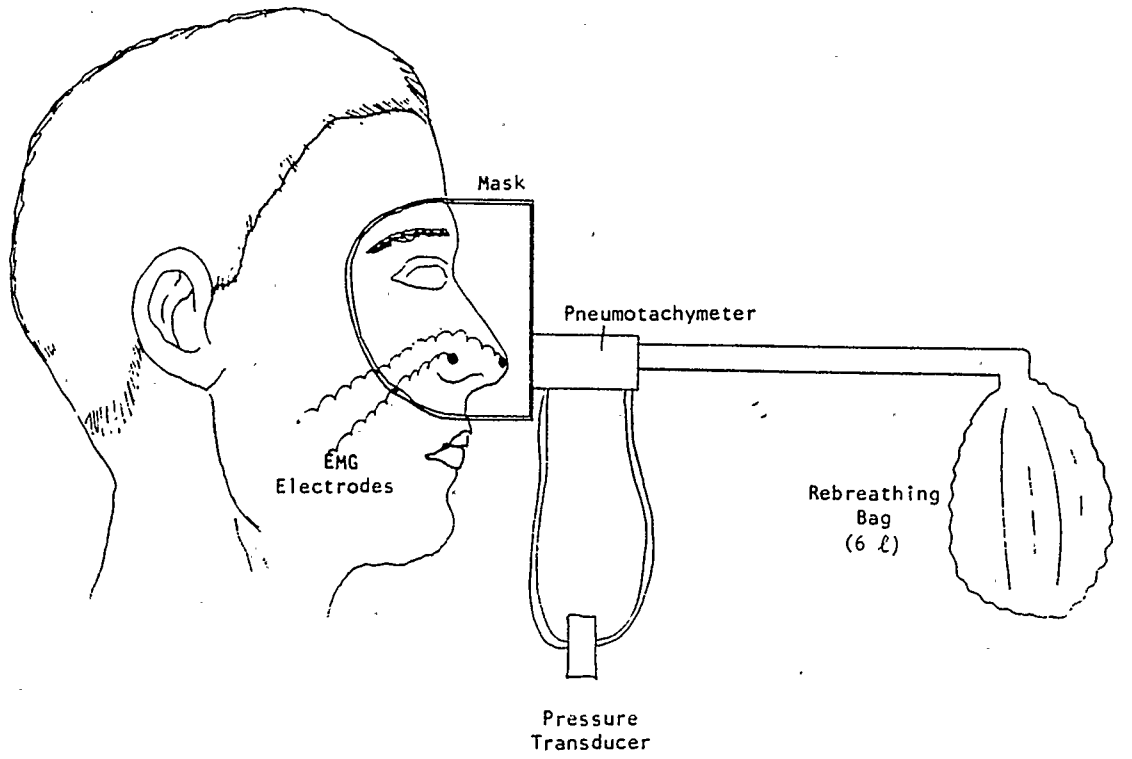


Figure 6 - Apparatus for the Read's Rebreathing Technique
ET_{CO_2} was being sampled from the external nares and monitored by a CO_2 analyzer (Beckman LBII) (see text).

It is difficult to be certain if the electrical activity of the compressor naris or the depressor naris (both antagonistic to the dilator) was not also being picked up. But since the dilator naris makes up the main part of anterior naris it can probably be said that most of the EMG activity was from this muscle.

The raw Ean signal was full wave rectified and time averaged (Strohl et al. 1982). Measurements were made of peak electrical activity during inspiration. The duration from the onset of activation to the time of peak activity was not measured as there is a linear relationship between the rate of rise and the height of EMG activity (Strohl et al. 1982).

A scuba mask similar to the one pictured in figure 6 created an air tight seal around the nose and the eyes but the mouth was uncovered. The subject was asked to breathe only through his nose and the mouth was kept closed. To the mask was attached a Fleish No. 2 pneumotachymeter. Pressure difference in the pneumotachymeter was conveyed to a Validyne transducer (± 2 cm H_2O) by means of plastic tubes 5 mm in internal diameter and 50 cm in length. Volume was obtained by electrically integrating flow by a Hewlett Packard respiratory integrator 8815A.

The pneumotachymeter was connected by a tube (8 cm in internal diameter and 30 cm long) to a rebreathing bag (Read 1966). This was a small bag originally containing 7.75 percent carbon dioxide. The rest of the gas in the bag was oxygen. The expired air was continuously mixed in the rebreathing bag until the concentration rose to 10% CO_2. Frequency, tidal volume, $ETCO_2$ (end tidal CO_2), and integrated EMG activity were monitored continuously by a Honeywell recorder (1858 Visicorder).

From the frequency and tidal volume, minute ventilation was

derived. ET_{CO_2} was measured by a CO_2 analyzer (Beckman LBII). Graphs of V_E and Ean were plotted.

Following a 10 minute break, 4% lidocaine 4 mg/Kg was administered into the nasal passage in spray form by a De Vilbiss nebulizer to anesthetize the upper airways. While applying the lidocaine, the subject was asked to breath hold at total lung capacity. This was intended to prevent deposition of anesthesia below the vocal cords and confine anesthesia to the upper airways. After 5 minutes, a small piece of cotton with a pointed end was inserted into the nose to see if the subject would sneeze. If there was sneezing, 10 squirts of lidocaine (about 0.4 mg/Kg) from the same nebulizer were administered and the sneeze reflex checked again. It is important to point out that checking for the sneezing could be irrelevant, as the type of receptors which were being anethesized may not have been irritant receptors. Whether these other receptors were also anesthetized at the same time cannot be certain. Before and after lidocaine anesthesia, the subject's pulse rate was monitored to check for bradycardia, which could be a sign of lidocaine toxicity. After lidocaine application, the same experiment was repeated.

iii. Results

The tracings were analyzed by hand; ten breaths were averaged to derive one point for ventilation and EMG. Ean activity was plotted on the y axis and V_E on the x axis. It can be seen in figure 7 that for three subjects (GF, BB, and BR) ventilation was at least 30 L/min before Ean activity could be detected. The other two subjects had ventilations of about 20 L/min before Ean was detected. The slopes of the lines drawn

by linear regression analysis by least square method were not significant and as can be seen from Table 1, the difference in slopes pre and post lidocaine are not significant, although by just observing the data it would seem to indicate that the post lidocaine Ean was slightly less for a given V_E where comparisons can be made. Also Table 1 shows y intercepts when x=40. In three subjects the post lidocaine values at that point were less than prelidocaine values.

iv. Discussion

In most of the subjects in figure 7 it seemed there was a small slope of EMG present before and after lidocaine. However for all the subjects except one the slope increased less than proportionately as demonstrated by the confidence interval for the y intercept in figure 8 which had a possible zero value for only one subject (BB). The y intercepts for pre and post lidocaine values combined were calculated as there was no significant difference between the pre and post lidocaine runs.

It was decided that if Ean could be studied at a lower ventilatory range than perhaps the slope would be steeper and the comparisons easier to make.

There was a breath by breath variation of EMG recordings at the same $ETCO_2$, as illustrated in figure 8. No definite cause for this could be ascertained. The movement of the electrode during inspiration was not the cause of the breath by breath variation. Although carbon dioxide was used to override the higher control influence on the medulla, it still seemed possible that this was not completely accomplished as psychological factors could probably influence the respiratory control. The breath

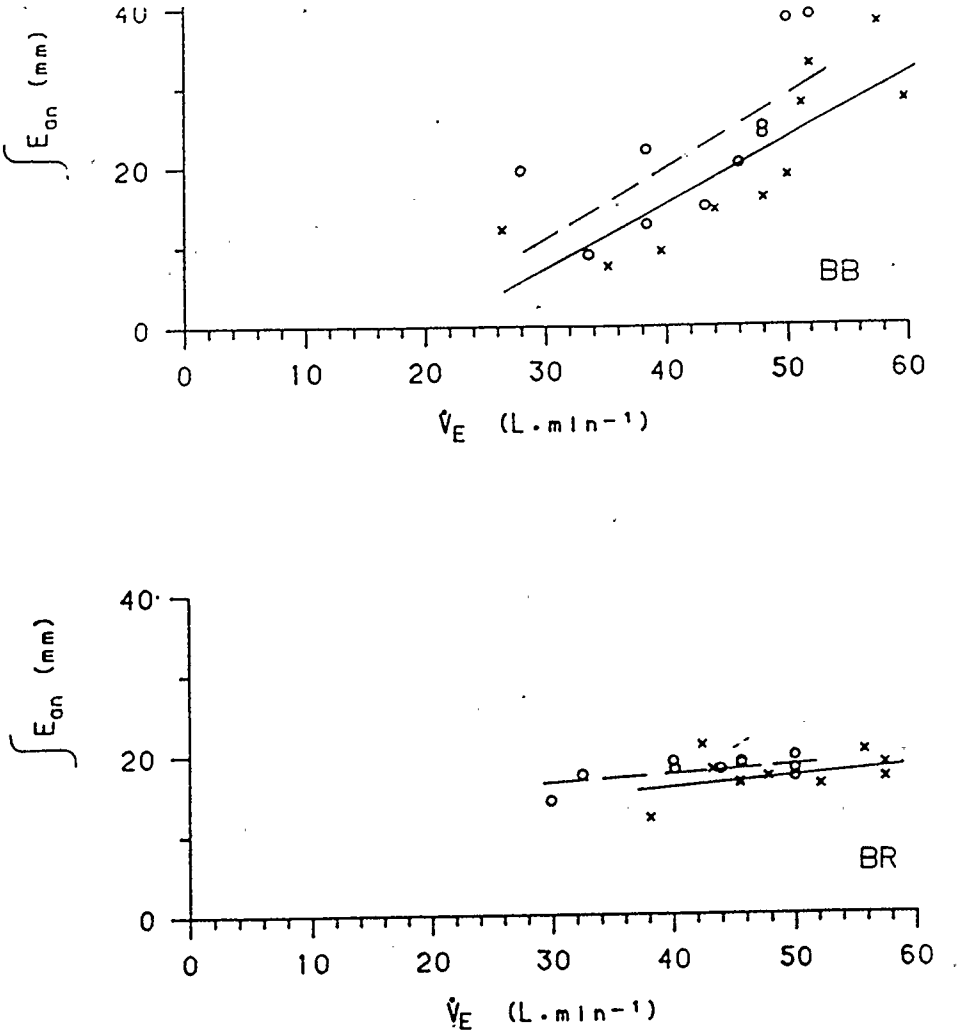


Figure 7 - Results of the Rebreathing Technique

Open circles represent prelidocaine runs and the crosses represent postlidocaine runs. The lines were fitted by least square regression technique. Ventilation ($\dot{V}_E$) is on the x axis and time averaged, full wave rectified EMG on the y axis.

(Fig. 7 continued . . . .)

. . . Figure 7 (continued)

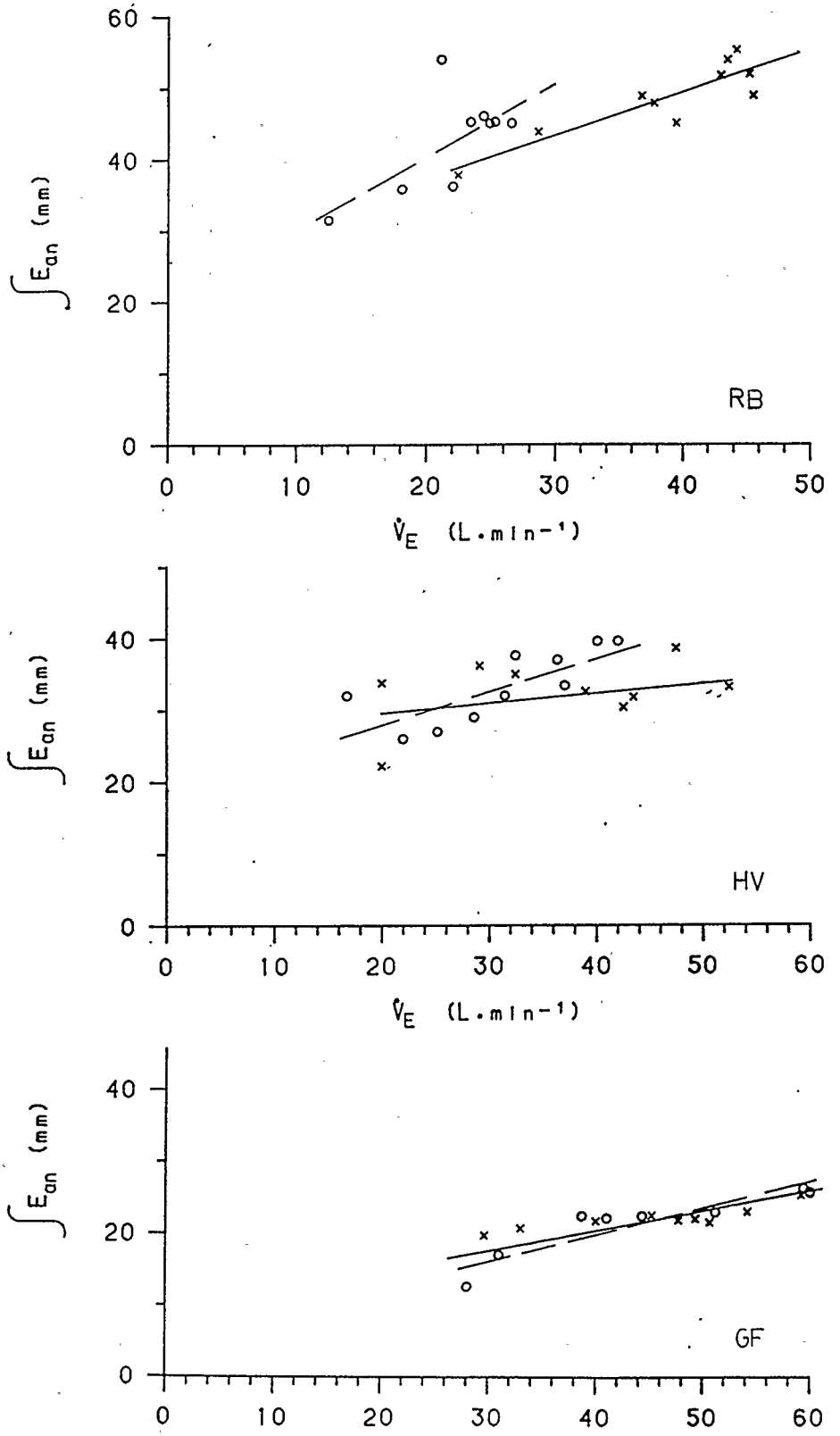


Table 1

Slope, intercept, and r values of response lines of subjects shown in figure 7.

	Slope	Intercept at x=40	r Value
HV			
Pre-lidocaine	0.45	36.9	0.76
Post-lidocaine	0.14	32.6	0.36
BB			
Pre	0.89	19.7	0.70
Post	0.81	14.9	0.81
BR			
Pre	0.11	17.2	0.59
Post	0.13	15.6	0.38
RB			
Pre	0.41	37.8	0.42
Post	0.58	48.5	0.88
GF			
Pre	0.36	19.4	0.92
Post	0.27	19.9	0.87

by breath variation in alae nasi EMG could also have been due to reflexes brought about by the positioning of the mask or other parts of the apparatus. Whatever the cause may have been the scatter made it necessary to average EMG from many breaths to obtain clear data.

Although the rebreathing runs failed to support the hypothesis of a peripheral feedback loop, there were three technical factors that might have obscured a sizable effect.

One, and most important: there was a small slope, and when the stimulus increased, EMG did not increased proportionately. Very few readings fell on a steep portion of the curve where comparisons might have been more easily observed. In the rebreathing technique there was no way of maintaining the stimulus during the early steep portion of the curve for purposes of comparison. A different method of stimulation was needed.

Two: instead of one constant ventilation, the rapidly increasing ventilation of the rebreathing technique made comparisons difficult since groups of crosses and circles were scattered at two quite different ranges of ventilation, as was the case with subject RB in figure 7. Hence it was not possible to tell if the increase in Ean after lidocaine was due to increased ventilation or due to the receptor blocking effect of lidocaine which altered Ean. Ideally if the V_E could be made constant and Ean, after applying the blocker, shown to be different from the control run, the peripheral relfex arc hypothesis could be invoked.

Three: In the rebreathing technique the subjects breathed humidified air from the rebreathing bag which did not activate cold air receptors. Previous work in the lab (McBride and Whitelaw 1981) had shown

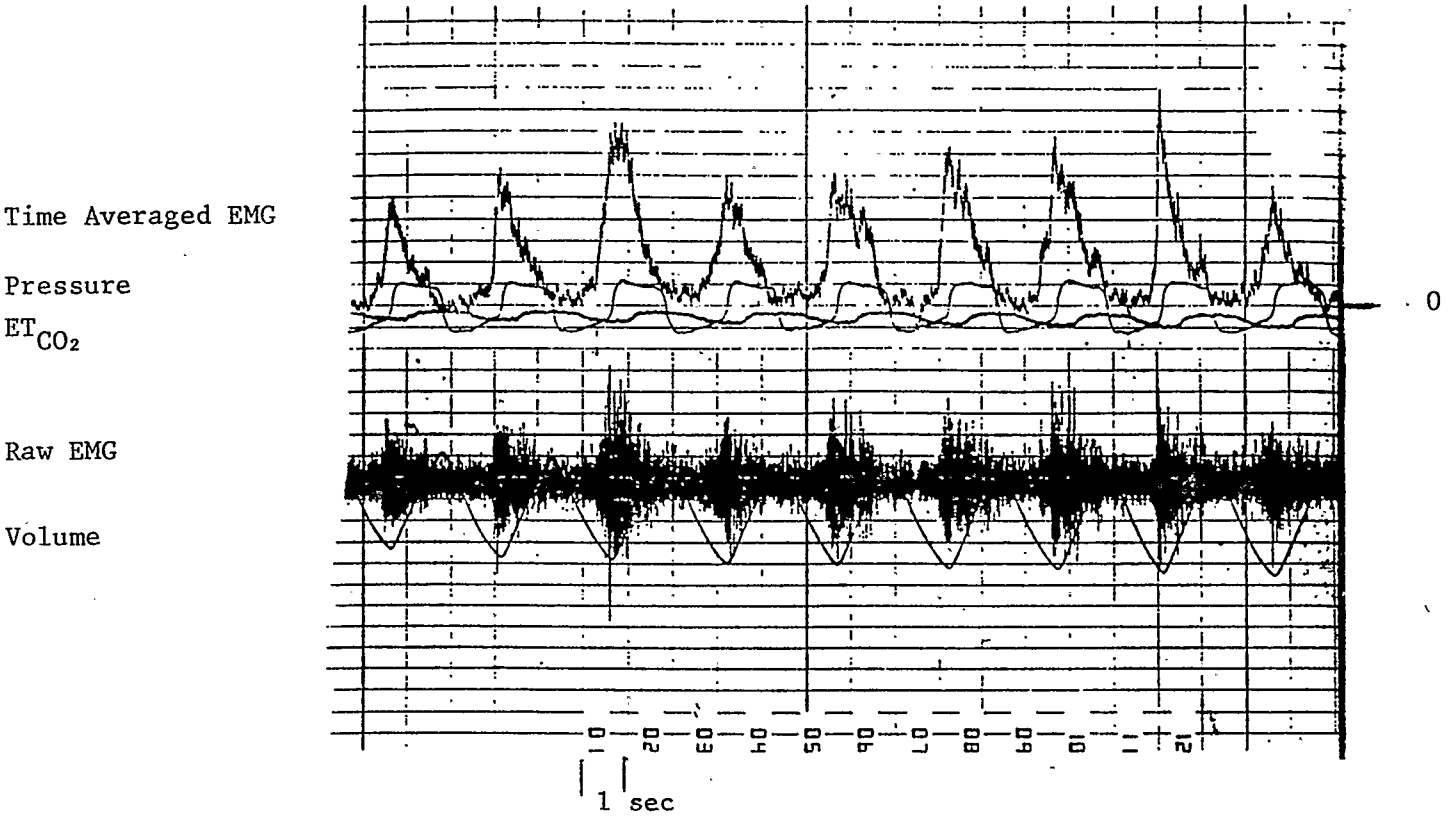


Figure 8 - Illustration of breath-by-breath variation in EMG in spite of constant ventilation in the rebreathing runs. Traces are from above downward
- Time average full wave rectified EMG
- Transnasal Pressure 1 division = 5 cm H_2O
- End tidal CO_2 1 dividion = 3.1 mm Hg (mean value = 50 mm Hg)
- Raw EMG
- Volume (inspiration down) 3.5 divisions = 1 ℓ

that breathing cold air depressed ventilation by possibly activating cold air receptors. Hence the experiment was redesigned so that subjects were made to breathe cold air before and after the administration of a blocker (lidocaine) in the upper airways and comparisons between Ean and V_E were carried out.

2) Steady State Technique:

i. Rationale

The same hypothesis about the presence of a peripheral reflex arc was being tested. The solution to the problems outlined seemed to be best dealt with by this method.

A steady state of P_{CO_2} was attained after 3-4 minutes of breathing the same level of CO_2 at which point an equilibrium existed between end tidal P_{CO_2} and chemoreceptor tissues with the values being nearly equal (Lambertsen, 1953).

The ET_{CO_2} was manipulated in such a way that the same ventilation was achieved in the control run as in the test run with the blocker.

Comparisons then could be made to see if the blocker altered alae nasi EMG, when the central output drive as measured by the V_E was constant.

With the steady state technique a steeper slope at lower ventilation could be expected. In order to do this as soon as reasonable EMG activity was observed the ventilation was not driven any further with carbon dioxide but allowed to stabilize and only then were readings of Ean taken. The same procedure was repeated at the same ventilation after using the blocker. In this steady state technique the subject was made

to breathe cold air as mentioned earlier. For purposes of comparison the subject was also made to breathe warm, humid air. It was thought that breathing warm, humid air would be suitable for testing the action of pressure receptors (Van de Graff et al. 1982) before and after a blocker because unlike cold air, warm air is not known to provide any stimulus in breathing.

ii. Methods

Six male volunteers with a mean age of 29 years, who were healthy and had no relevant nasal problems as described for rebreathing runs were used. The apparatus was set up as shown in figure 9. A Scuba mask (figure 10) was attached to the subject's face and covered the nose and the eyes, leaving the mouth and most of the forehead exposed. A Fleish No. 2 pneumotachymeter measured the inspiratory flow and was mounted on the mask, as shown in figure 9. A one way valve attached to the pneumotachymeter permitted inspiration through the pneumotachymeter and prevented expired air from entering the circuit. Another one way valve allowed expired air to leave the mask and prevented inspiration of fresh air. The gas sample from the mask was analyzed by means of a mass spectrometer (Medspec II, Chemtron, Missouri). The spectometer probe was placed in front of the nostils as shown in figure 9.

Warm air (30 ± 3°C) and cold air (0 ± 3°C) were fed alternately into the mask. Continuous temperature readings were obtained from a thermistor probe near the valve. The source of the warm air, which was saturated with water vapour was a humidifier heater as shown, and the source of the cold air, which was dry, was alcohol cooled by dry ice in a

tank and made to circulate through a coil around which the mixture of gases passed, as shown in the diagram. There was a valve to switch from the cold to the warm air. During both the warn and cold runs, flow, ventilation, Ean and ET_{CO_2} were measured as before. It was made sure that the pneumotachymeter was heated only during the warm runs. During the course of the experiment the subject was breathing only through his nose.

As before, after a 10 minute break, 4% lidocaine 4 mg/kg was administered to the nasal passage in the same fashion with similar precautions. The constant ventilation was determined after the first run in the experiment which could be either a cold or warm run. Then an effort was made to arrive at approximately the same ventilation for all the other runs by manipulating the ET_{CO_2}.

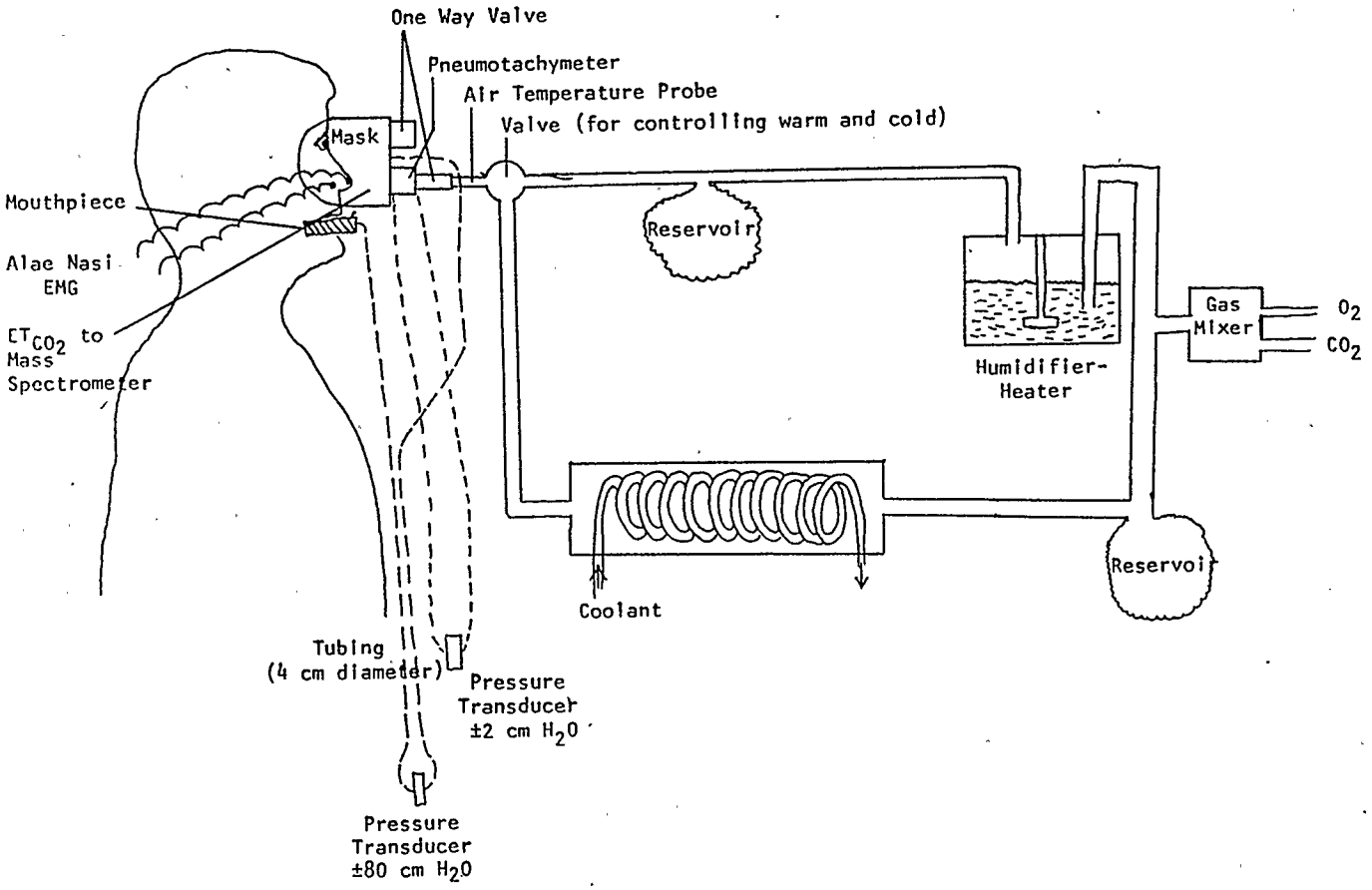


Figure 9 - Apparatus for the Steady State Runs and Nasal Resistance

ET_{CO_2} was sampled near the external nares. The two one-way valves prevented rebreathing.

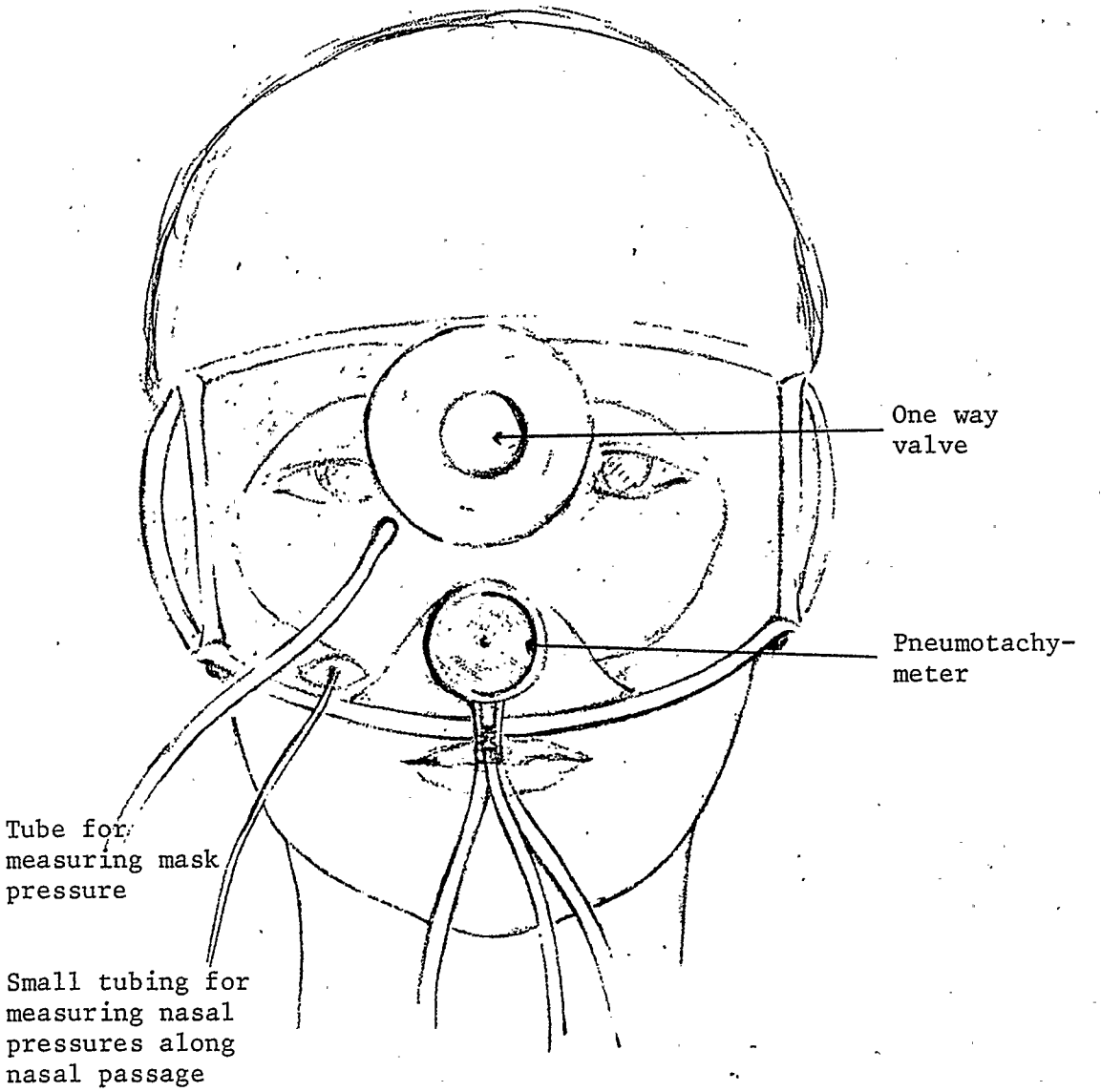


Figure 10 - Scuba Mask (Anterior-Posterior View)
This was used in the steady state experiments. The one way valve was for the expired air.

iii. Results

The raw tracings from the steady state runs are shown in figure 11. Ten breaths were averaged at peak inspiratory EMG activity for ventilation and Ean pre and post lidocaine. Table 2 charts the results obtained from the six subjects, showing their $ETCO_2$, V_E, and Ean before and after lidocaine. Bar graphs showing integrated activity in arbitrary units during pre and post lidocaine warm runs are shown in figure 12. The hatched bars are post lidocaine warm runs and the clear bars are pre lidocaine warm runs. Standard error bars are as indicated at the top of the bars. The range of ventilation in any one subject was not more than 3.6 L/min in the various runs for that subject. All the subjects decreased their integrated EMG activity after the lidocaine, except subject TM in whom the standard error bars overlap considerably.

Although inspired CO_2 was manipulated to derive constant ventilation, the latter was very difficult to achieve. And, indeed, there was a statistical difference ($p < 0.05$) in warm pre lidocaine and warm post lidocaine ventilations, i.e., minute ventilation decreased after lidocaine administration. However, when the normalized Ean activity was corrected for ventilation by dividing it by V_E for each individual subject, the Ean still decreased after lidocaine administration in the warm run independent of the decrease in ventilation ($P<0.05$)

There was no statistical change in the warm and cold Ean, nor was there any change in the cold pre and post lidocaine runs.

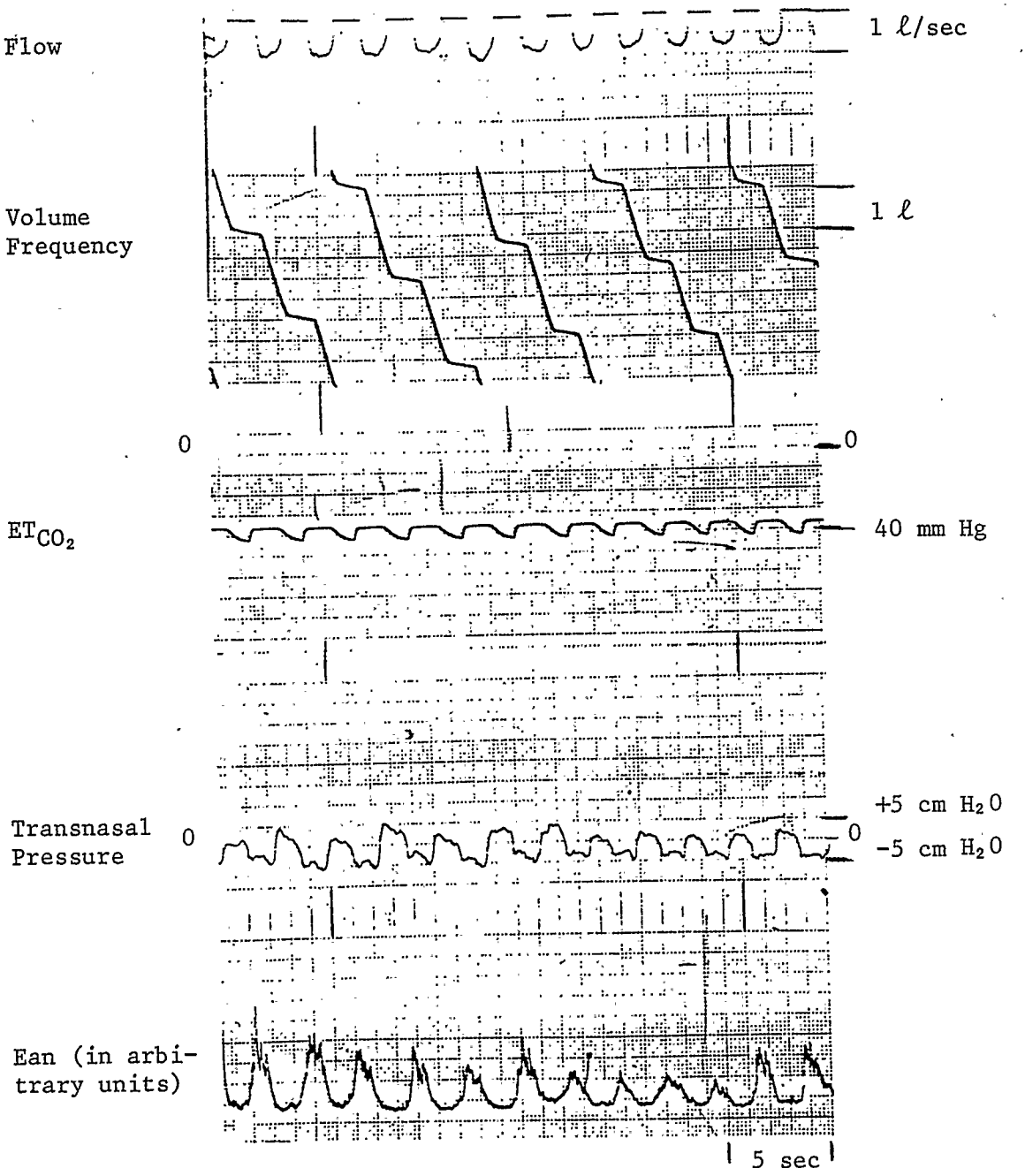


Figure 11 - Tracings from the Steady State Runs

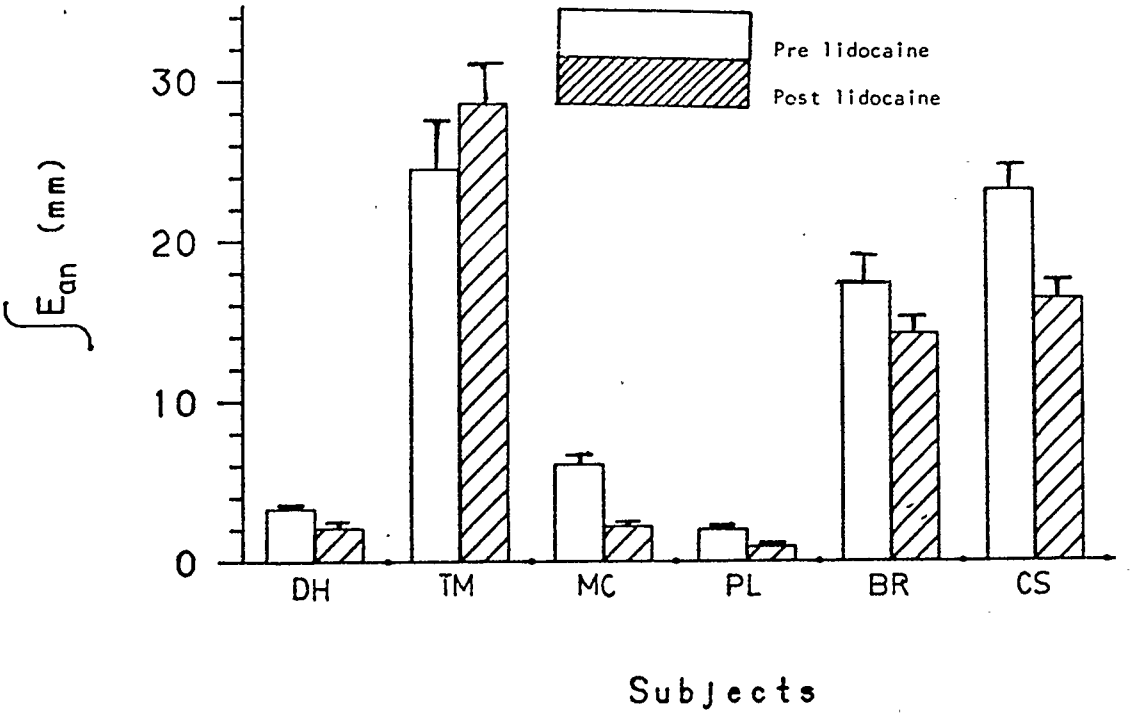


Figure 12 - Bar Graph Showing Integrated EMG Activity During Warm Pre and Postlidocaine Runs ($P<0.05$).

Ventilation differed by not more than 3.6 L/min during the comparisons (see Table 2 and text).

Table 2 - Results of Steady State Runs

		PRE LIDOCAINE			POST LIDOCAINE		
SUBJECT	TEMP.	$EtCO_2$ mm/Hg	VE L/Min/BTPS	EMG (not normalized)	$EtCO_2$	VE	EMG (not normalized)
DH	Cold	38	27.3	2.4	38	27.6	2.5
	Warm	38	34.1	3.3	38	32.8	2.1
TM	Cold	56	43.6	29.1	60	49.8	28.9
	Warm	46	49.8	24.5	48	47.3	28.6
MC	Cold	62	43.9	10.5	67	53.1	7.3
	Warm	48	53.3	6.0	52	51.2	2.0
PL	Cold	52	39.1	0.8	52	45.9	1.1
	Warm	52	48.6	2.0	52	48.4	0.9
BR	Cold	46	36.9	21.7	45	39.9	23.9
	Warm	46	39.5	17.5	46	39.9	14.2
CS	Cold	43	36.5	23.1	43	37.7	16.8
	Warm	47	39.0	23.2	43	36.6	16.4

iv. Discussion

Ean, ET_{CO_2}, and ventilation were studied in six subjects, with warm and cold air runs before and after lidocaine anesthesia of the upper airways. The most significant result was the post lidocaine warm run which showed a small but significant decrease in Ean when compared to pre lidocaine warm run. This relative decrease in Ean after the lidocaine anaesthesia suggests there may be receptors which influence the activity of the alae nasi besides the direct control from respiratory centre in the medulla. It is felt that these receptors which may be present in the upper airways are superficially located as it is assumed the action of the lidocaine spray does not penetrate into the deeper layers of muscles and tissues. These receptors probably fire when they are exposed to negative pressures. When these receptors fire due to negative pressure, for example, during inspiration, the afferent nerve (the fifth nerve in the case of nasal mucosa) carries this signal either to the respiratory centre in the medulla or to another location, for example, to the seventh nerve nucleus in the medulla from where an efferent pathway reaches the alae nasi. Lidocaine blocked the pressure receptor pathway during the warm run, hence decreased Ean activity.

The idea of pressure receptors in the upperways is appealing because this would mean that when pharyngeal collapse tended to occur during sleep apnea (Remmers et al. 1978), these pressure sensors would come to the rescue as soon as abnormal pressure drops were detected to activate the respiratory centre or other alternate pathways to stiffen the muscles to maintain an air conduit. Sleep apnea has also been known to be caused by seasonal allergic rhinitis increasing nasal resistance (McNicholas et

al. 1982). Strohl et al. (1980) showed that in human beings there was activation of alae nasi EMG even before inspiration. Animal experiments (Green and Neil 1955) have also demonstrated activation of pharyngeal and laryngeal muscles prior to intercostal and diaphragm activity. Hence there is a central drive to alae nasi muscle independent of a reflex loop. This was also borne out in the experiments described here where even after anesthesia to the nasal passage, Ean activity was present. Hence the effect of the pressure sensing mechanism in the upper airway would be to amplify the contraction of the upper airway muscles. In my experiments, because nasal resistance was normal in these subjects, intranasal and transnasal pressures were low throughout the experiment, so that it is not surprising that the effect of anesthetising such receptors, although significant, is quite small.

Although there was a significant decrease in warm post lidocaine Ean, when compared to the warm prelidocaine runs, no such decrease was noted in the cold runs. If we assume that pressure receptors are excitatory (Van de Graaff et al. 1982) and cold air receptors are inhibitory (McBride and Whitelaw 1981; Burgess and Whitelaw 1984), the statistically unchanged difference in Ean during the pre and post lidocaine cold runs can be explained on the basis that lidocaine blocked both the temperature (cold air) receptors and the pressure receptors. As a result, both inhibition and excitation were checked, which lead to no difference in EMG activity.

Patrick et al. (1982) studied nine subjects whose ventilation was being driven by carbon dioxide and who had a 15 cm H_2O/L/sec resistive load in the inspiratory line. They studied the activity of the alae nasi

EMG with the activity of the diaphragmatic EMG. They found that with inspiratory resistive loading the electrical activity of both the muscles was increased when compared to different level of carbon dioxide during the control run without resistive loading and that there was no statistical difference in the increased electrical activity of these muscles when compared to each other. Their findings suggest pressure sensitive feedback loops in the upper airways or in the lower airways or chest wall muscles. It could be that the muscle spindles or tendon organs of the diaphragm may be reacting to increased resistive loading by causing a greater contraction of the diaphragm. However, unlike the animal experiments (Van Luntern et al. 1984; Van de Graff et al. 1982) in these experiments in humans the negative pressure was being applied outside the mask which meant that transmural pressures across the alae nasi and nasal passage, would not be affected, although the transmural pressure across the pharyngeal airway may have changed. Because the transmural pressures did not change, the receptors in the nasal passage sensitive to collapsing pressure, if present, would not be activated. Hence these experiments in humans did not simulate animal experiments where transnasal pressure were also changed. It is also not clear in their experiments if the subjects activated flow (temperature) receptors in the nasal passage, as was the case in the rebreathing experiments, which would have had an inhibitory effect on Ean.

3. Alae Nasi and Nasal Resistance

As mentioned this experiment was part of the first experiment which has just been described. For purposes of clarity the first experiment has been broken down into two parts. The second part which relates to nasal resistance is being discussed here.

i. Rationale

The alternate neural control of the alae nasi may be important in the context of nasal resistance. The second hypothesis states that the alae nasi plays an important role in determining nasal resistance. The experiment would have to be done in a way which showed that increasing the alae nasi activity as seen by the EMG recordings would decrease nasal resistance. For this nasal resistance would have to be measured by a suitable method.

ii. Methods

Resistance was calculated by dividing pressure measurement (trans-nasal pressure) by a constant peak inspired flow. Ean was compared with the resistance to see if an increase or decrease in Ean had any effect on resistance. Resistance in the warm and cold run, before and after lido-caine was also studied.

a. Pressure Flow Curves

The pressure flow relationship in the nasal passage has a curvilinear relationship (figure 4, Proctor 1977). Resistance varies with the flow rate. Four different methods have been used to determine resistance from pressure flow curves (figure 13).

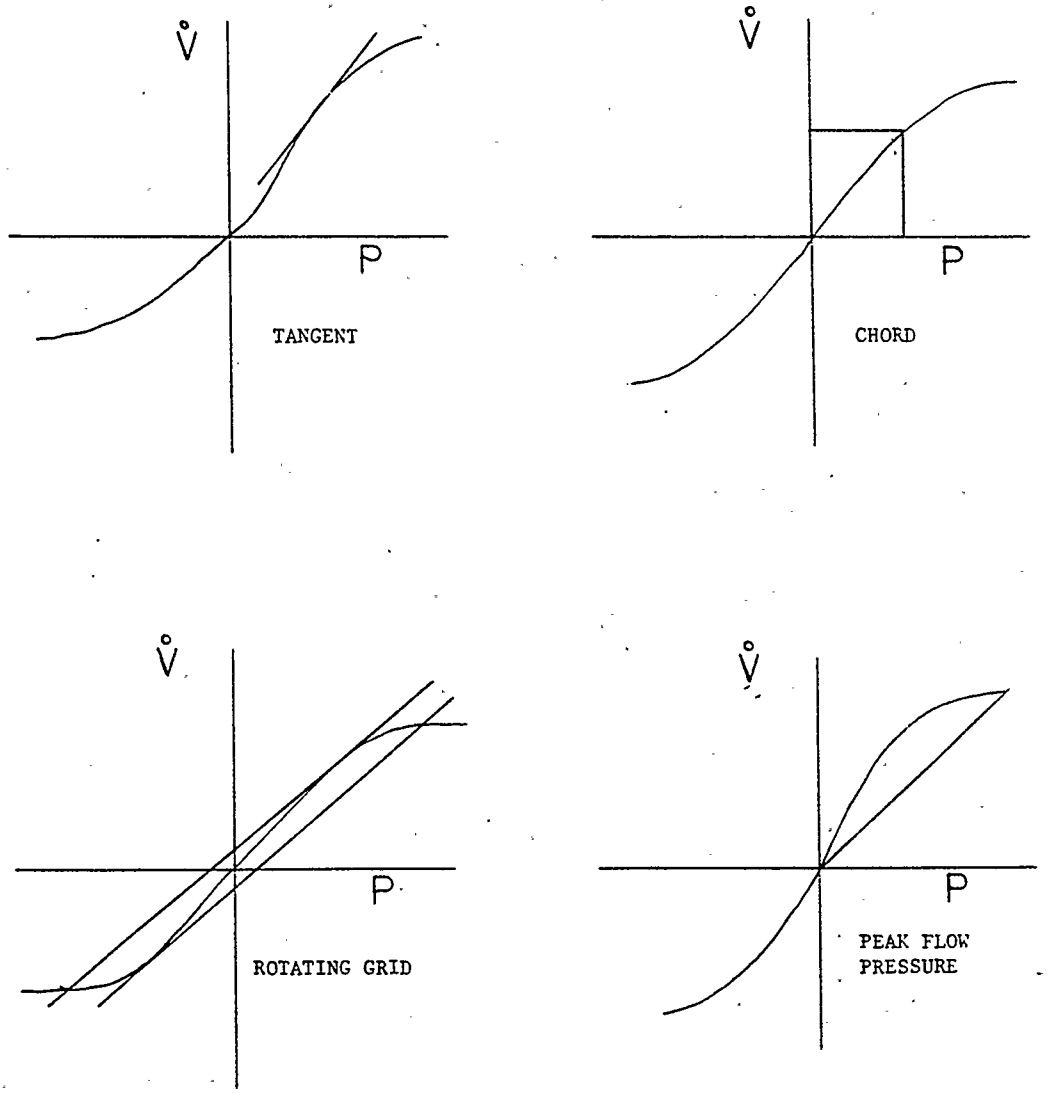


Figure 13 - Four common methods of determining nasal resistance from a pressure flow curve. Pressure is on the x axis and flow is on the y axis (see page 49).

Tangent

This does not measure resistance as defined since the tangent measures the slope of the pressure flow curve.

Rotating Grid

The whole pressure flow curve is averaged by means of the grid to give resistance. Since the resistance is always changing, this gives only an approximation of resistance.

Peak Flow Pressure

This method gives arbitrary resistance at high flows.

Chord

This method defines resistance at a particular flow and this is the method used here.

b. Pressure Measurements

Many different methods of measuring pressures to calculate nasal resistance have been used:

Anterior rhinometry

Plethysmography

Posterior rhinometry (posterior rhinomanometry)

Anterior Rhinometry

This is the measurement of pressure at one nostril as a function of airflow through the other nostril (figure 14) (Kortekangas

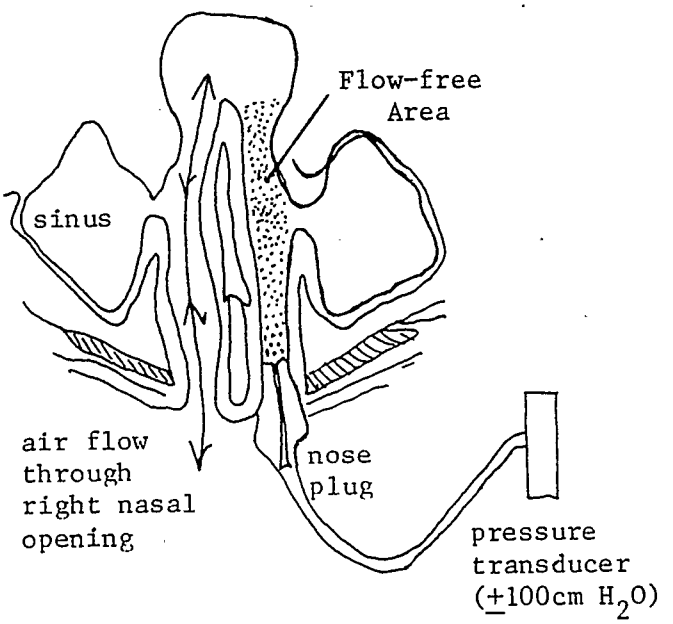


Figure 14 - Anterior Rhinomanometry (Transverse Section Through the Nose)
The arrow depicts airflow and the dotted area depicts a flow free area. The pressure difference between the nasopharynx and the atmosphere is measured.

1972). Because of the difficulty some subjects have in keeping the back of the mouth open during post rhinometry, this method may be an alternative.

In this method, the pressure difference between the nasopharynx and ambient pressures is recorded; in posterior rhinometry, the pressure difference between the mesopharynx (figure 5) and ambient pressure is recorded. The difference of the anatomical measuring points is, however, not significant since the posterior part of the "nasal respiratory tube" contributes very little to the pressure fall or rise which are mostly due to more anterior parts of the tube (Kortekangas 1972).

The disadvantage in this method is the possible distortion of the nostril and the fact that directing the entire airstream through one side of the nose is not physiological (Proctor 1977). Because of the distortion of the nostril the activity of the local receptors inside the nose would also have to be considered. Nolte and Luder-Luhr (1972) found that, unlike post rhinomanometry, precision and accuracy in this method were lacking and that the main concern, according to these investigators, may be the unsolved difficulty to compute resistance from two measured partial resistances.

Body Plethysmography

Airway resistance is the pressure difference between the alveoli and the mouth per unit of airflow. There are two steps in calculating resistance by the body plethysmography as originally described (Dubois 1956). In the first step the subject sits in the airtight box, and his airflow and pressure changes in the box as he

inspires and expires are measured by a pneuomotachometer and a manometer respectively. During inspiration inside the box alveolar pressure has to be less than the box pressure and during expiration the reverse is true. The second step involves a process whereby the pressure change in the box is related to mouth pressure when there is no flow. No flow is created by the subject inspiring and expiring against an occluded airway. During a no flow situation mouth pressure reflects alveolar pressure. The first step gives a plot of pressure change in the box and airflow and the second step gives a plot of pressure change in the box and mouth pressure (or alveolar pressure). The total airway resistance is calculated by taking the ratio of the two slopes derived from the two plots.

Nolte et al. (1968) explained that the total resistance between alveoli and nose openings consists of two partial resistances: R_{aw} (airway resistance) and R_n (nasal resistance). R_{aw} can be obtained during mouth breathing, and the sum of R_{aw} and R_n can be obtained during breathing by nose. The difference gave them R_n, as shown in figure 15. They used a fixed value for flow (0.5 L /sec) to calculate the resistance because the relation between pressure and flow is not linear, as presumed in the definition of flow resistance.

While measuring nasal resistance, there seem to be one drawback. During the measurement of airflow in the plethysmograph, the subject was to perform a panting maneuver. If the greatest resistance in the nasal passage was at the level of the dilator naris, then depending on how vigorously the subject used his dilator naris,

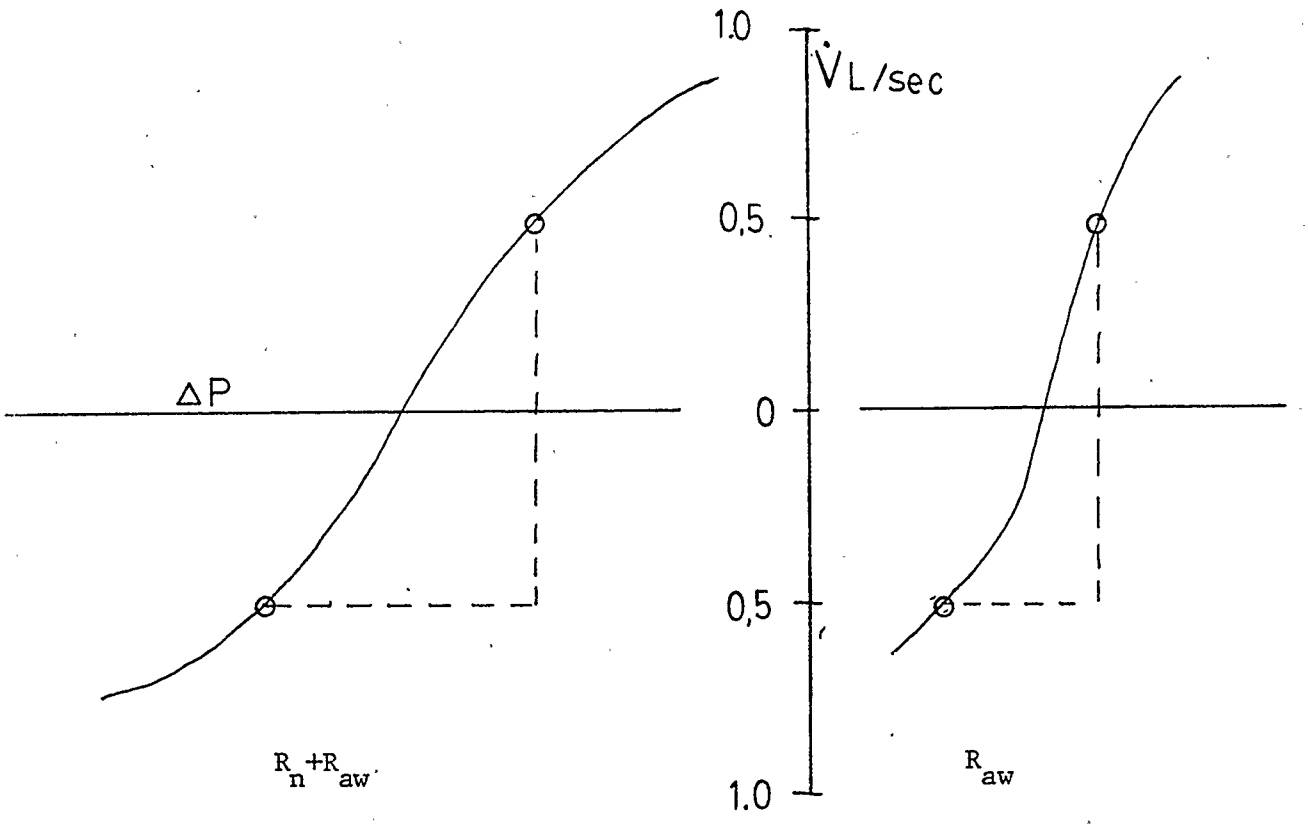


Figure 15 - Resistance During Mouth and Nose Breathing

Nasal resistance (R_n) can be obtained by subtracting the result during mouth breathing (right side) from the result during nose breathing (left side). The S shape of the pressure flow characteristic demands the calculation of resistance values for a fixed flow. R_{aw} = airway resistance (Nolte and Lüder-Lühr, 1968).

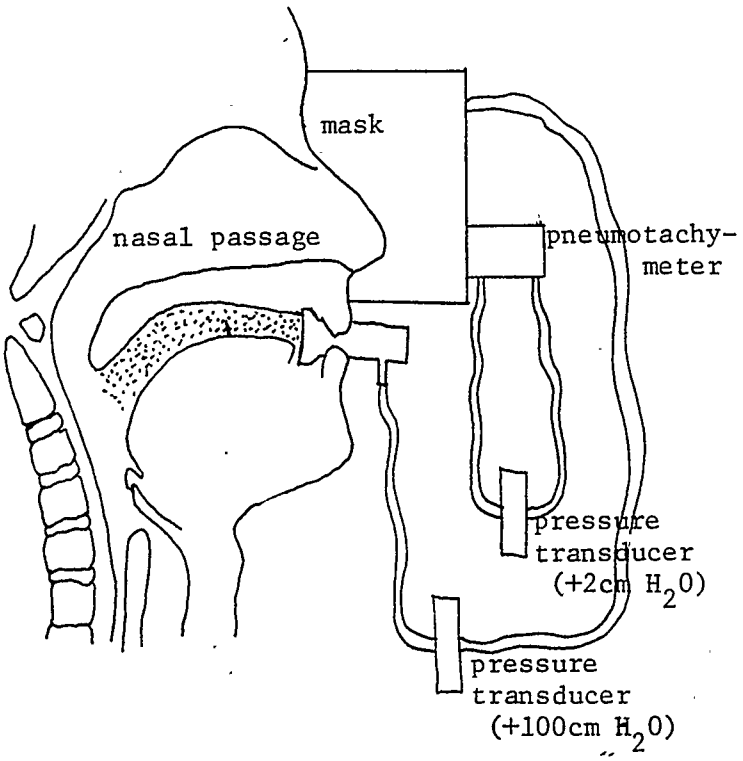


Figure 16 - Posterior Rhinomanometry (Saggital Section of the Face)
The dotted area depicts a flow free area. The pressure difference between the mesopharynx and the mask (transmural pressure) is being calculated. The pneumotachymeter measures flow. If the back of the mouth is occluded, no pressure will be registered in the tube coming out of the mouthpiece.

the pressure difference could be variable, hence, the resistance would also change.

iii. Posterior Rhinometry: The method chosen

This method was chosen here to measure pressure since it was a relatively simple and accurate procedure to perform (figure 16). Many investigators felt this to be the most effective method (Proctor 1977).

A mouthpiece (21 cm in diameter, No 1077 Godart Statham BV) was attached to the mouth. The mouthpiece was held by the teeth and it was not advanced beyond the teeth. A plastic tubing 5 mm in internal diameter was attached to the end of the mouthpiece. This tubing was connected to one end of the Validyne transducer (±80 cm H_2O) and to the other end of the transducer the same diameter plastic tubing from the front of the mask was attached as shown. The pressure difference gave the transnasal pressure.

Posterior rhinometry was hard to perform for some subjects because of their inability to keep the back of their mouth open during the experiment, so that no pressure was registered from the back of the mouth. But because this was a more natural method for measuring pressure than the other simple alternative, anterior rhinometry, I stuck to posterior rhinometry. It was not possible to perform posterior rhinometry recordings on three of the six original subjects because the back of the mouth was kept closed even after a suitable trial, so for the purposes of measuring resistance and Ean before and after the lidocaine during warm and cold runs, two other

healthy male subjects, mean age 28 years, with no relevant nasal problems, were brought into the study.

iii. Results

To calculate flow and pressure five breaths were averaged. Corresponding peak EMG activities were also noted. This was done for pre and post lidocaine runs so that there were ten readings.

On the y axis (figure 17) was plotted warm resistance - cold resistance and on the x axis was plotted $\frac{\text{warm Ean - cold Ean}}{\text{cold Ean}} \times 100$.

The latter was done for normalizing. A percent change in Ean had to be calculated but it did not matter if the change was from warm to cold or vice versa.

The points indicate the percent change in normalized Ean to the corresponding change in resistance. For a total of five subjects there are ten points because pre and post lidocaine runs for individual subjects have been included. Open circles are pre lidocaine and closed circles are post lidocaine.

Eight out of the ten points fall in diagonally opposite quadrant indicating that when the Ean increased the resistance decreased. Neither warm and cold runs nor pre and post lidocaine studies showed a significant pattern concerning nasal resistance.

iv. Discussion

As the results have shown alae nasi does seem to influence nasal

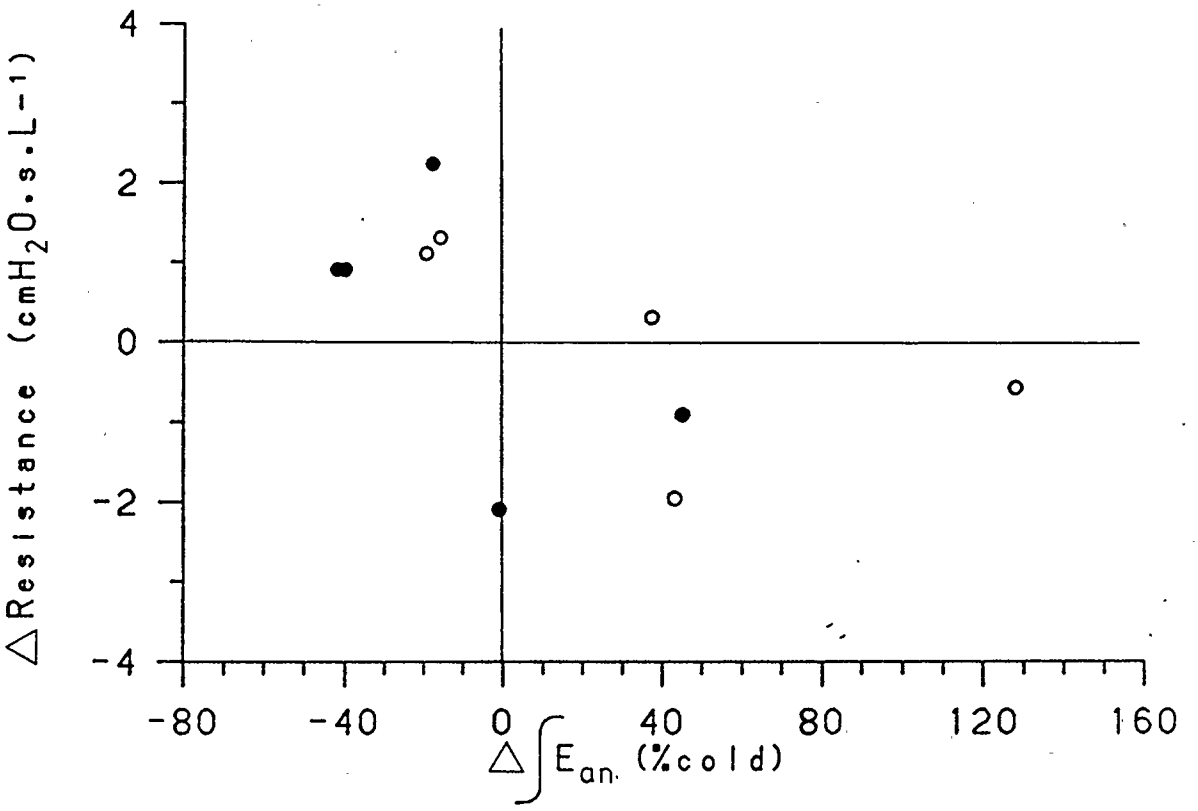


Figure 17 - Relationship of Ean and Nasal Resistance

The change in resistance between the warm and cold runs is plotted on the y axis and the change in time averaged normalized EMG on the x axis. Open circles denote prelidocaine runs; closed circles denote postlidocaine runs.

Table 3 - Results of Nasal Resistance Experiments

		PRE-LIDOCAINE					POST LIDOCAINE			
SUBJECT		$EtCO_2$	$\dot{V}E$	EMG	R+		$EtCO_2$	$\dot{V}E$	EMG	R
BF	Cold	46	29.9	11.4	5.25		47	30.1	30.2	1.98
	Warm	45	35.2	16.3	3.93		46	39.9	17.5	2.88
DH*	Cold	38	27.3	2.4	7.40		38	27.6	2.55	8.32
	Warm	38	34.1	3.3	7.70		38	32.8	2.09	10.56
JM	Cold	40	17.5	13.5	4.04		38	16.5	9.7	5.58
	Warm	39	28.7	30.8	3.46		38	18.3	14.1	4.67
TM*	Cold	56	43.6	29.1	3.5		60	49.8	28.9	4.0
	Warm	46	49.8	24.5	4.8		48	47.3	28.6	1.9
BR*	Cold	46	36.9	21.7	15.3		45	39.9	23.9	13.9
	Warm	46	39.5	17.5	16.4		46	39.9	14.2	14.8

*These subjects also appear in steady state CO_2 experiment
+Calculated from five breaths at a specified inspiratory flow (average 0.6 ℓ/sec)

resistance in quiet breathing.

The most likely explanation for this could be that the contraction of these muscles changes the cross sectional area of the nasal passage at the narrowest point in the respiratory passage where these muscles are situated (Fig. 18). This in turn would change the existing pressure and flow relationships of the nasal passage.

Another explanation for the decrease in resistance could be CO_2 itself. Investigators have shown that nasal resistance falls with inhalation of gas mixtures containing CO_2 (Dallimores and Eccles 1977; Tagaki et al. 1969). However Strohl et al. (1982) could not demonstrate an effect of CO_2 on resistance independent of alae nasi activity and nasal flaring. Dallimore and Eccles suggested that a decrease in nasal resistance during exercise (or CO_2 stimulation) was due to an increase in sympathetic tone in the main nasal passage. However there was no direct proof of this and therefore Strohl proposed that alae nasi may be the principal means of decreasing nasal resistance.

Another less likely explanation for the observed relationship between Ean and resistance could be that increase in alae nasi activity may be only coincidental to decrease in nasal resistance and that some other mechanism, for example, the nasal cycle may be causing the changes in resistance. Nasal cycle occurs in only some individuals and the duration of the cycle is uncertain. It was difficult to control for this in the experiment, although the patency of the nasal passage of all the subjects was checked by ruling out cold, stuffy nasal passage on either side. Nasal resistance, however, remains relatively constant during nasal cycle.

As can be seen in the resistance and Ean graph, warm R - cold R can be + or - and the explanation for this seems to be that ventilation was not controlled for during these experiments, increasing or decreasing the ventilation may have changed resistance from + to -. It should be pointed out that flow was controlled for every individual while measuring the resistance.

The right bottom quadrant in figure 17 has a point with change in Ean about 130 and R about -0.5. Why is there such a large change in Ean for a relatively small change in resistance? The answer maybe that the region of the anterior nares, where the narrowest point is located, may be of a sizable calibre in this subject so that even a substantial change in Ean did not make much difference to the resistance.

Haight and Cole (1983) studied ten subjects and found inconsistent changes in nasal resistance after the subjects were made to contract their alae nasi voluntarily without the use of carbone dioxide as stimulus. These inconsistent changes could be due to various reasons.

First of all the alae nasi is a complex set up of muscles. For example when voluntary contraction of the alae nasi is taking place and the dilator naris is trying to widen the opening, the compressor naris and the depressor naris may both be trying to narrow the opening (figure 2). When carbon dioxide is being used for causing contraction of alae nasi, this contraction is presumably done in the right way to widen the narrowing. We can voluntarily try to contract the alae nasi and realize that there are many different ways of contracting this muscle - some ways of contracting may increase resistance, others may decrease and so on. Hence the importance of a physiological flare by using CO_2, which the

investigators did not use.

Secondly, as in one of the subjects (figure 17, the furthest point to the right on the lower right quadrant) there is a large change in Ean for a relatively small change in resistance. This means that some subjects may have a relatively large opening in the region of the narrowest point in their nose in which case flaring the alae nasi would not make a significant difference to resistance. Perhaps some of their subjects had a large opening at this point to account for their inconsistent results.

Thirdly, one of the obvious factors which would affect nasal resistance is posture (Wilson et al. 1980). If any of their subjects had their heads excessively flexed or extended, this would affect nasal resistance.

V. EXPERIMENT 2:

Location of greatest respiratory resistance

i. Rationale

It has been shown in models and cadavers that the greatest narrowing and thus the greatest pressure drop of the nasal passage takes place in the region of the dilator naris. If that is the case then flaring or collapsing of this part of the nasal passage can make a large difference in nasal resistance.

There are differences in resting tone of alae nasi muscle and vasomotor influences in the nasal passage between live human subjects and models or cadavers, therefore, it is important to confirm that the greatest narrowing and pressure drop takes place in the region of the dilator naris even in live subjects. Vasomotor influences in the nose obviously contribute a great deal to nasal resistance. The main part of the nasal passage can, due to elaborate vascularity, easily provide the largest resistance in the nasal passage. The vascular component was probably collapsed in the models studied.

In the living the alae nasi tone and vascularity of the nasal passage would be constantly changing and consequently altering nasal resistance. Hence similar studies to those in cadavers and models had to be documented in live subjects. The next section deals with how this was investigated.

ii. Methods

A polyethylene tube 1 mm in internal diameter was used to measure the pressure at various points in the nasal passage. The nasal passage.

was anesthestized with 15 to 20 puffs of lidocaine spray (4%) and the sneezing reflex on the same side of the nose was tested for; lidocaine was administered here so that the tube would not irritate the nasal mucosa, and reflex nasal discharge, when the polyethylene tube was advanced, would be minimal. The polyethylene tube was attached to a Validyne transducer (±100 cm H_2O) by means of plastic tubing 5 mm in internal diameter. The other side of the pressure transducer was open to the atmosphere. The depth the tube penetrated was measured from an ink-mark at the junction of the nasolabial angle with the midpoint of the floor of the external nasal opening. A cotton plug was used to block off the other nostril which did not have the nasal tube. If the cotton plug was not used, the flow would be divided between the two nostrils. This would create an error when the resistance was calculated because flow through only one nostril was being measured. A total of five subjects participated in this experiment. All were healthy males with a mean age of 29, with no relevant nasal problems as described above. Their ventilation was not driven by CO_2. The subjects were made to practice breathing through their nose at a mean flow of 0.6 L/min. before the actual run. There was no Ean activity in all the subjects except one who maintained the same level of Ean throughout the experiment. Therefore Ean was not considered to be a concern. The flow was kept constant so that resistance could be comparable at various parts of the nasal passage at a particular flow. To clear the nasal secretions which sometimes collected inside the polyethylene tube, a three-way valve with a syringe was attached to the tube so that before each measurement, air was blown through the tube from the syringe to clear any secretions. The tube was

advanced 10-12 cm along the nasal passage up to the nasopharynx. It was slowly withdrawn and pressure measurements were made after every 2 cm.

iii. Results

Figure 18 has nasal resistance on the Y axis and distance from anterior nares on the X axis. These are the mean values of the resistance measurements of five subjects. Each subject was breathing through the nose at a constant flow for the subject during the whole experiment. The mean peak inspiratory flow rate for all the five subjects was 0.6 l/sec. With this fixed flow rate the resistance was then calculated by using the formula:

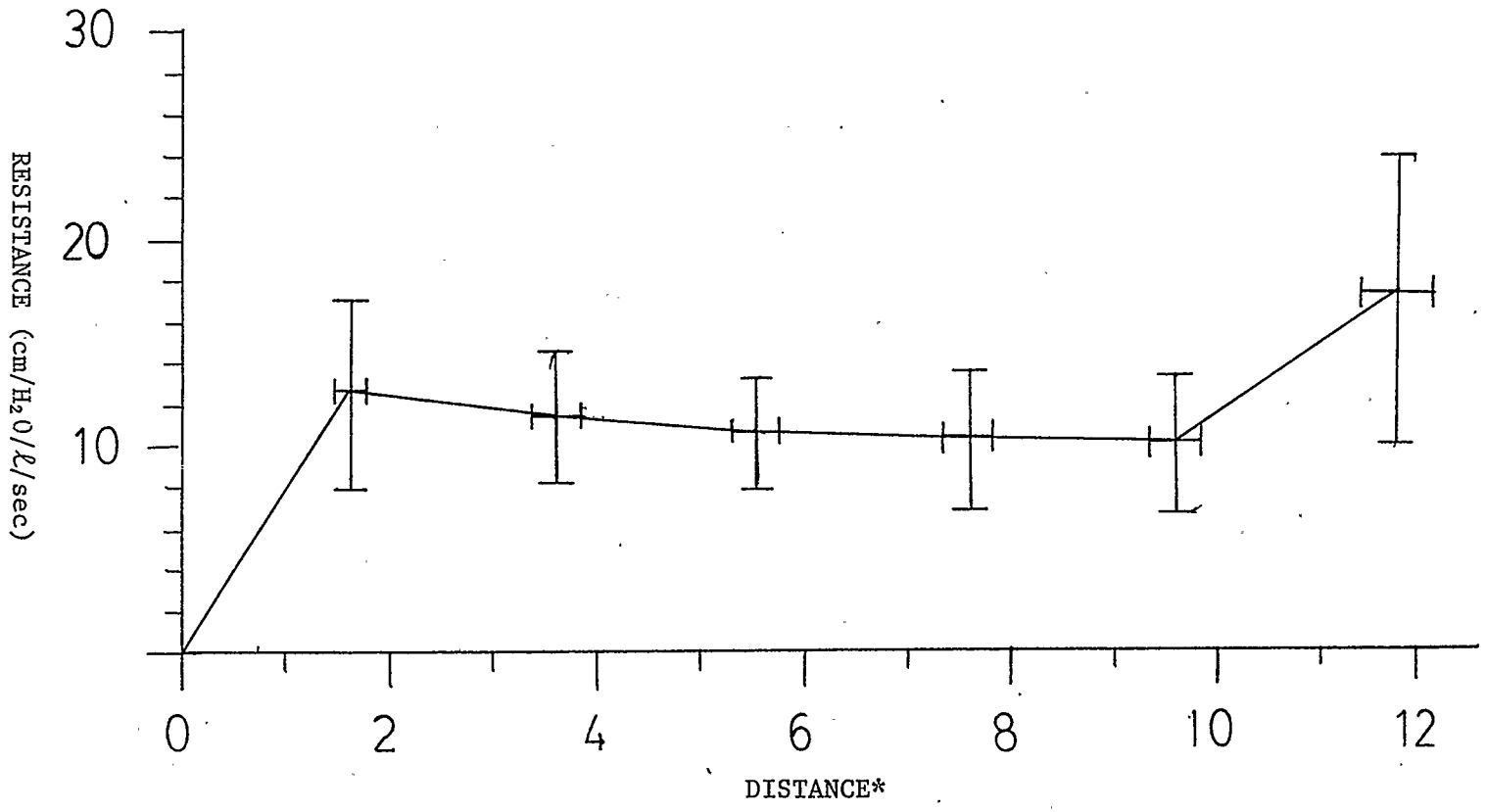
$$\text{Resistance} = \frac{\text{Change in pressure}}{\text{Flow}}$$

The readings of the pressure drop between the position of the polyethylene tube and atmosphere were taken every 2 cm ± 1/2 cm. Five breaths were averaged for pressure and flow.

As can be seen from figure 18, a significant resistance was encountered in the first two centimeters in the vestibular passage and then the resistant remained more or less unchanged in the main nasal passage until the nasopharynx was reached around 12 cm, when the mean resistance increased but the standard error was also larger at the 12 cm mark.

iv. Discussion

The results were similar to the cadaver data of Proctor (1977). The cadaver data was presented by the authors in a slightly different manner as shown in figure 18. However, a rough estimate can be made by assuming



*Distance from external nasal opening (cm)

Figure 18 - Resistance at Various Points of the Nasal Passage

Measurements were begun from the junction of the nasolabial angle with the midpoint of the floor of the external nasal opening.

that Poiseuille's Law holds for the nose and deriving resistance from the cross section area by using the formula:

(i) $R \propto \frac{1}{\text{Radius } 4}$

(ii) $R \propto \frac{1}{\text{area}^2}$

The resistance was calculated from the area and a graph similar to the human experiments was seen which is not shown here.

The resistance at various parts of the nasal passage has been shown in figure 18. The biggest pressure drop was in the first 2 cm of the dilator nares, which seems to bear out the anatomic narrowing at this point (less than 1 cm^2). At the narrowest point of the nasal passage the total cross section area was about 0.6 cm^2 from the cadaver data and the cross-section area of the polyethylene tube was 0.07 cm^2. Therefore the tube itself at this point contributed to 22% of the resistance. Hence the tube did not significantly influence the measurements.

The main nasal passage offered a relatively unchanging resistance because the nasal passage here was wide. One reason why the resistance was higher again at the nasopharynx may have been that the tube in some subjects went right to the nasopharynx where the passage was again narrower (figure 5).

Although Bridger and Proctor (1970) have mentioned pressure drops being the greatest in the region of the alae nasi, no documented experiments confirming their data such as this in live human subjects could be found. The excess nasal discharge and accompanying discomfort may have

been a determining factor. The lidocaine spray made this experiment comfortable enough to take pressure recordings but did not completely abolish mucous discharge. Lidocaine has no known effects on the vasculature of the nose and on nasal resistance in general, as shown by the unchanging resistance before and after lidocaine in my experiments.

As can be seen in figure 18, on observation resistance seemed to be decreasing slightly although the difference is not significant in the main nasal passage as compared to the highest resistance point in the first 2 cm. Theoretically that is an impossibility. However, due to small changes in turbulence caused by the canges in position of the tube or by some mucosal congestion increasing slightly over the course of the experiment could result in a small rise in resistance. Haight and Cole (1983) also measured such decreases in resistance in the main nasal passage during their measurements. They studied human subjects in whom they passed a catheter in the floor of the nose and took pressure recordings as done here. They found the greatest pressure drop to be just within the main nasal cavity past the alae nasi muscle. This distance was almost consistently 3 cm inside the nose, measurements being taken from a junction made by the naso labial angle with the midpoint of the floor of the external opening of the nose. This was also the starting point where my measurements were taken. The results from my experiments however, showed the narrowest point to be within 2 cm from the starting point at the site of the alae nasi muscle and probably not into the main nasal cavity. The cadaver data of Proctor (1977) showed that greatest pressure drop was also within the area of the alae nasi muscle and not in the main nasal passage. In the cadaver data there were no mucosal secretions of

the nose to deal with. In my experiments the muscosal secretions were minimized greatly by the usage of a local anaesthetic so that there would be very little irritation as the tube was being inserted. Haight and Cole did not use any local anaesthesia and they conceded that in some of their subjects it caused marked irritation. Irritation would certainly cause the inferior turbinate to swell up and increase nasal resistance within the main nasal passage thus perhaps creating an important artifact. During congestion the inferior turbinate plays an important role in determining the magnitude of resistance in the nasal passage (Bridger and Proctor 1970).

VII. EXPERIMENT 3:

Comparison of Masks

i. Rationale

Other workers in the lab who used a No. 6 anesthesia mask (figure 19) to study Ean for a different set of experiments, had very much more depressed Ean activity in the cold runs than experiments described here. A scuba mask (Scuba pro supervision 24-220-000) (figure 10) was used in the experiments decribed here. It was decided to document this difference in Ean activity at the same ventilation with the two different masks given that all other conditions remained the same. The scuba mask had 430 ml dead space and the anesthetic mask had 150 ml dead space. The scuba mask covered the eyes and the nose but left the mouth and most of the forehead uncovered. The anesthetic mask covered the nose and the mouth, but the eyes were uncovered.

ii. Methods

The comparison study was done in five healthy male subjects with a mean age of 28 with no relevant nasal problems, who breathed through the two different masks utilizing the same apparatus as in figure 9 without posterior rhinometry. With each mask a warm and cold run was carried out in the same subject while V_E, Ean, ET_{CO2} were recorded. The V_E was kept as constant as possible, (see results).

Lidocaine was not administered because the main aim of the experiment was to document the large difference in Ean between the warm and cold runs in one mask (anesthesia mask) compared to the other (scuba mask) at a similar ventilation.

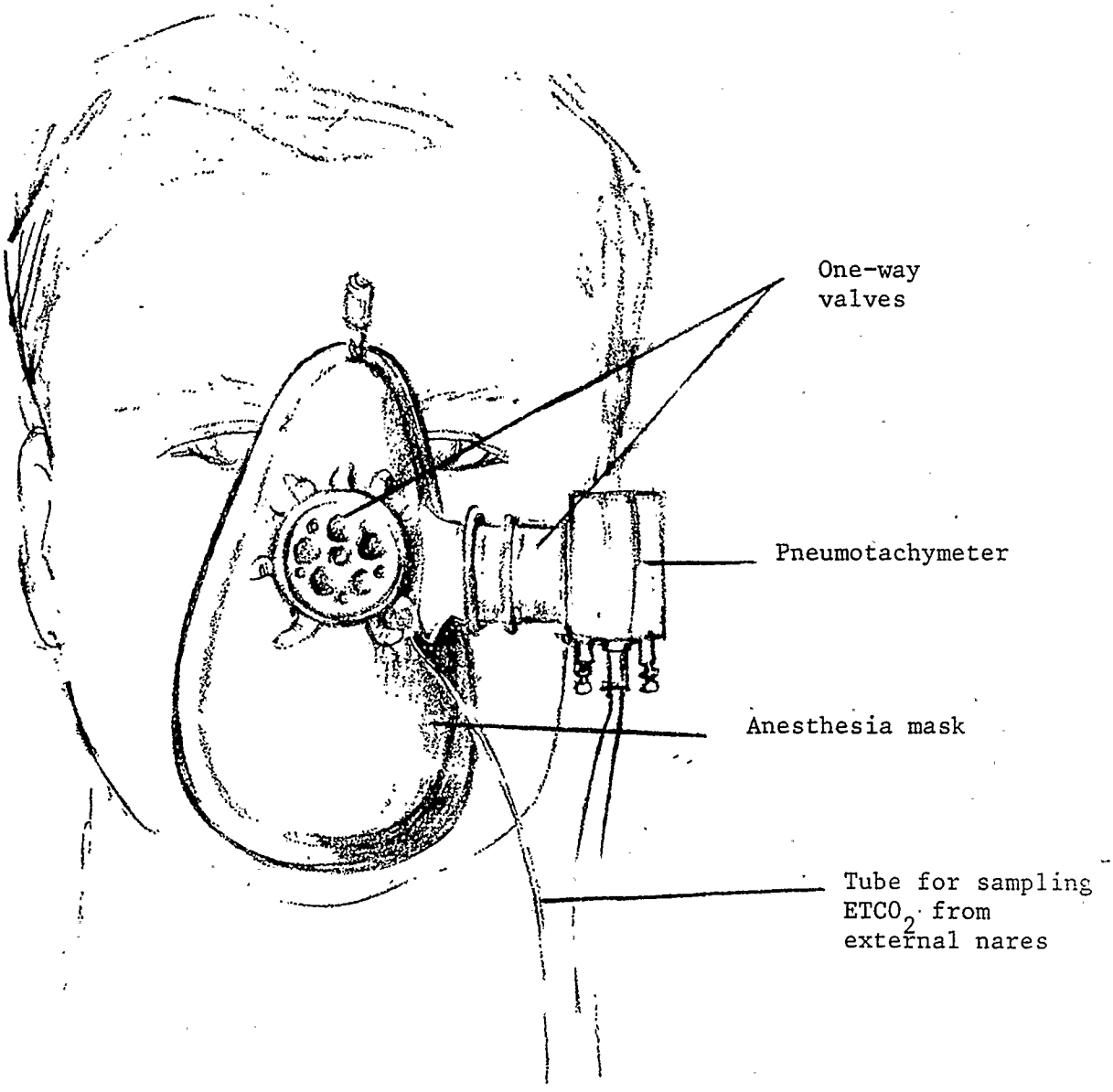


Figure 19 - Anesthesia Mask

The two one-way valves prevented rebreathing. The pneumotachymeter measured inspired flow.

iii. Results

There were five male subjects who breathed through two different masks, the scuba and anesthesia mask. The percent change in normalized EMG activity from cold to warm runs is illustrated in Figure 20. The open bars represent the scuba mask and the hatched bars are the anesthesia mask. The percent changed was derived as follows:

$$\frac{\text{Warm EMG} - \text{Cold EMG}}{\text{Cold EMG}} \times 100$$

A paired t test was done on the percent change in normalized Ean of the two masks. The test showed a p of < 0.1. The standard error values are as marked on the bar graph. Paired t test was also done on the absolute percent change regardless of direction of trend (subject BR) in the normalized Ean of the two masks and p value was <0.05. Although by manipulating inspired CO_2 attempts were made to narrow the range of VE it was very difficult to derive similar ventilation during the warm and cold runs for both masks (see Table 4). But even when the EMG was corrected for VE by dividing it by V_E, the p value was < 0.1. Paired t test was again done on the absolute percent change of Ean, regardless of direction of trend, after EMG was divided by ventilation and the p value was <0.05. Subject BR did exactly the opposite, as compred to other subjects but, the pattern was the same because the percent change was greater with the anesthesia mask.

As can be seen in figure 20, the percent change in normalized alae nasi EMG activity is greater with the anesthesia mask than the scuba mask. All subjects except BR have a significant percent increase in the alae nasi EMG activity from cold to warm with the anaesthesia mask, but not with the scuba mask. Subject BR had greater EMG increase in going

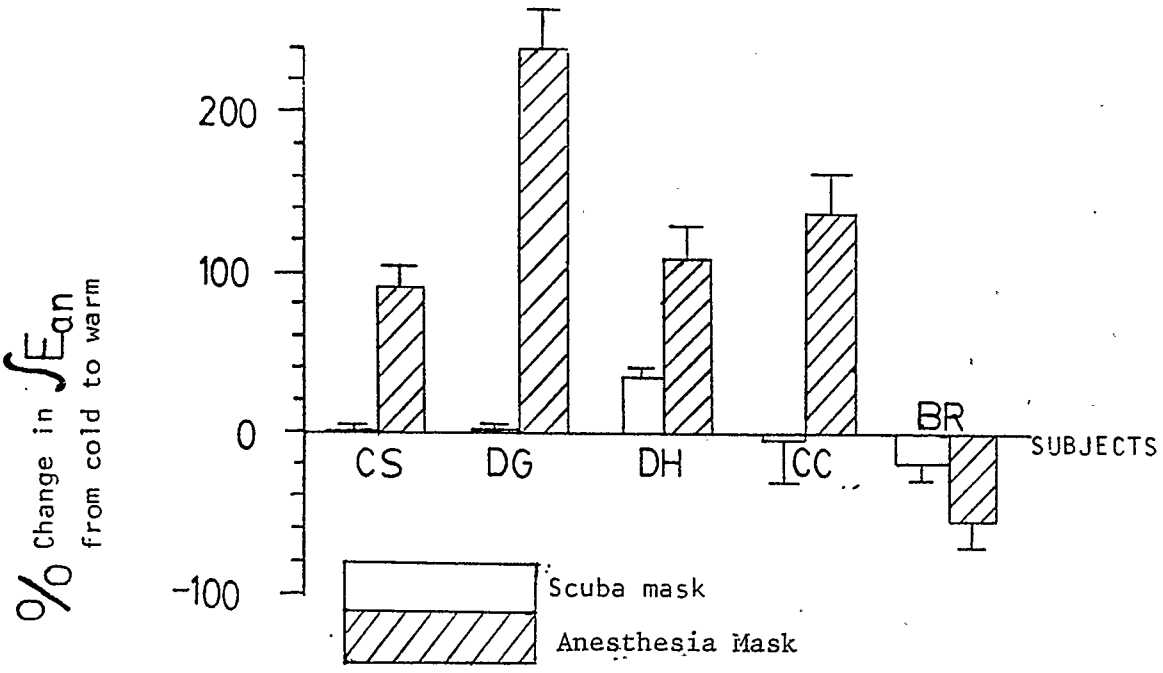


Figure 20 - Comparison of Masks ($p<0.1$)

An attempt was made to study the % change in Ean at a constant ventilation (see text).

Table 4 - Results of Comparison of Masks

SUBJECT	TYPE OF MASK		VE 1/min	EMG mm	$ETCO_2$ mm of Hg
CS	Scuba	Cold	36.5	23.1	43
		Warm	39	23.2	47
	Anesthesia	Cold	26.3	6.7	53
		Warm	32.9	12.6	48
BR	Scuba	Cold	36.9	21.7	46
		Warm	39.5	17.5	46
	Anesthesia	Cold	32.05	15.75	40
		Warm	27.76	6.75	34
DG	Scuba	Cold	16.9	1.64	46
		Warm	18.8	1.7	46
	Anesthesia	Cold	15.9	3.7	34
		Warm	27	12.6	40
DH	Scuba	Cold	27.3	2.4	38
		Warm	34.1	3.3	38
	Anesthesia	Cold	24.7	13.7	40
		Warm	23.2	28.5	40
CC	Scuba	Cold	36	17	46
		Warm	37	16	46
	Anesthesia	Cold	38.3	6.3	41
		Warm	39.3	15	40

from warm to cold for both the masks. But, again, the percent increase was more with the anesthesia mask.

iv. Discussion

Since the only variable in the experiments was the mask, it seems as though the dead space of the two masks and the different areas of the face covered by the two masks would play an important role in explaining this discrepancy of dilator nares activity. The dead space of the scuba diving mask was 430 ml, whereas the dead space in the anesthesia mask was 150 ml. In these experiments the thermistor which measured the temperature was placed outside the mask (figure 9) near the valve for controlling the warm and cold. As the person breathed out into the scuba mask, expired air mixed with the cool air coming in, and because of the larger dead space in the scuba mask the temperature of the cold air inside the mask may have been warmer than the recorded temperature of the incoming cool air. In the anaesthesia mask with the much samller dead space the temperature recorded by the thermistor may have been closer to temperature in the mask. Hence because the aneathesia mask probably stimulated more cold air receptors in the face (Zotterman 1959) and possibly in the nasal passages, the stimulation of these cold air receptors depressed ventilation (McBride and Whitelaw 1981; Burgess and Whitelaw 1984) and Ean. Hence the greater change in ventilation for the anaesthesia mask in going from cold breathing to warm breathing, as warm air breathing does not seem to stimulate or depress ventilation.

The next question to be addressed was the area of the face exposed

for the two masks and their effect on Ean. Parfrey and Seehan (1975) have shown that the area of the face exposed to cold water (15°C) may also make a difference on the inhibition of heart rate and increase in peripheral vascular resistance; and, by analogy, breathing, as breath holding had to be carried out in these experiments in order to find out the cardiovascular effects without interference by breathing. Breathing may also be inhibited like heart rate because the trigeminal nerve from the face which conveys the cold water stimulus to the medulla, may reflexly cause both decrease in the heart rate, ventilation, and an increase in peripheral vascular resistance as demonstrated in the diving reflex (Bamford and Jones 1974; Gooden 1970). Parfrey and Seehan showed that when the whole face was immersed in water (15°C), the heart rate decreased and peripheral vascular resistance increased significantly. Selective immersion of individual facial areas was not particularly effective in producing bradycardia, and again by analogy this may hold true for breathing. They suggested that the total area of the trigeminal skin exposed to water determined the cardiac slowing. Since the sensory supply of the whole face and the nasal passage is by the trigeminal nerve, the amount of area covered by each mask would seem to make a difference. The scuba mask covered more facial area than the anesthesia mask and yet there was more inhibition with the anaesthesia mask. The much smaller dead space (almost 3 times) of the anaesthesia mask which presumably helped keep the temperature of the air in the mask cooler, must have been a more important factor than the area of the face covered. One could speculate that the cooler gas in the anesthesia mask activated more receptors in the nasal mucosa than the scuba mask,

although the latter mask covered a larger facial area. Perhaps the temperature receptors in the nasal mucosa if present are more susceptible to activation at lower temperatures than the receptors on the face.

It would also be possible that with the scuba mask, which needed to be fitted right under the nose, the mask in some way physically restricted tha alae nasi movement. But even if this were true, the electrical activity should be unchanged. Therefore, it seems that the difference in the physical restraint of the masks had little to do with the actual results.

A logical question would be: why can't it be true that there are warm air receptors which are excitatory [illegible]nce cause increase in ventilation during the warm experiments? The understanding of the diving reflex supports the idea of cold air receptors in the face and nasal passage, and Zotterman (1959) has shown that the highest density of thermosensitive spot (cold air) receptors are in the face. Such data is lacking for warm air receptors. In fact, Hansel, Andres and Dunning (1974) after studying the skin of a cat's nose, showed the absence of a nerve terminal at the side of a warm "spot" and suggested that the warm sensitive structures were located in a deeper layer of the skin. The cold spots, which were more superficial and revealed a myelinated fiber beneath them, would be more quickly activated by a cold stimulus on the face.

If there was a difference in the resistance to breathing offered by the two masks this might have affected Ean as increased resistance to breathing decreases ventilation (Lopata et al. 1977) and hence Ean. The resistance offered by the system when using the two masks was negligible.

A well known cause of decreased EMG activity in the cold is decreased firing from both the annulospiral and flower spray muscle spindles when the temperature of these sensory organs is lowered to 10°C to 15°C below normal body temperature. The decreased firing from these muscle spindles would cause decreased activity of the extrafusal fibres (Eldred et al. 1960). However, thermal receptors on the skin overlying the muscle may also cause a decrease in EMG activity of the muscle as shown by Wolf and Letbetter (1975). They cooled the skin over the gastronemious muscle of ten cats. The skin temperature was 10°C but the temperature drop within the substance of the gastrocnemius was only 16°C after two minutes. Cooling the skin over the muscle was follwed by a decrease after 1-5 sec in the EMG activity of the muscle. Hence although decreased spindle firing from the muscle may cause decreased EMG activity, cutaneous receptors as in the study of Ean, may play a part in decreasing EMG activity. In my experiments it is unlikely that the spindle temperture would fall below 10°C from normal. From all this it is possible that Ean activity was depressed with the anaesthesia mask while breathing cold air because of a depressant effect of cold air receptors on Ean.

VII CONCLUSIONS

1. The rebreathing experiments revealed that the relationship of alae nasi EMG and ventilation was not proportional.

   Therefore:

   Future studies of Ean activity must take this disproportionality into account.

2. The steady state experiments before and after lidocaine suggested the presence of pressure receptors in the upper airways which increased alae nasi EMG activity by means of a reflex loop.

   Therefore:

   Local anaesthesia does affect the activity of Ean in breathing even when the pressure stimulus to nasal receptors is small. Hence local feedback loops seem to exist and may be important in situations where the system is stressed, for example, sleep apnea where pharyngeal pressures may drop abnormally.

3. Comparison studies which showed a decrease of Ean activity after lidocaine were made at constant ventilations in the steady state experiments.

Therefore:

Nasal receptors are capable of modulating respiratory drive to the alae nasi muscles.

4. The nasal resistance experiments suggested that increase in alae nasi EMG activity decreases nasal resistance. The site of greatest respiratory resistance is about 2 cm from the nasal vestibule.
Therefore:

The strategic location of the alae nasi muscle in this vestibular area accounts for its influence on nasal resistance by being able to dilate the narrow site.

5. The experiment on the comparison of masks demonstrated the possibility of cold air receptors from the face and possibly the upper airways depressing alae nasi EMG activity.
Therefore:

There may be at least two types of receptors influencing alae nasi EMG activity.

VIII FUTURE RESEARCH

To further bolster the argument for the presence of pressure receptors in the upper airways and especially in the nasal passage, experiments could be designed in human subjects which changed transnasal pressure; experiments described so far in the literature in humans have included resistive loading in the inspiratory line outside the mask into which subjects were breathing, but this did not greatly change transnasal pressure. By applying negative pressure at the site of the external nasal opening and greatly increasing transnasal pressure, pressure receptors in the upper airways could be activated maximally; and by applying posterior nasal packs of cotton or gauze, the nasal passage could be segregated to study negative pressure effects only in the nasal compartment and its effect on alae nasi EMG. This would closely simulate animal experiments in which there were EMG activity of alae nasi on application of negative pressure to the nasal cavity.

In a group of patients with leprosy who had a lack of sensation in the nasal passage, studies could be done by applying negative pressure to the nasal passage and studying the EMG effects on the alae nasi muscle. If a similar depressant effect on Ean, as seen after lidocine anaesthesia were noticed it would give a difinitive answer to the existence of pressure receptors in the upper airways.

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