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EVIDENCE FOR REFLEX UPPER AIRWAY DILATOR MUSCLE ACTIVATION BY SUDDEN NEGATIVE AIRWAY PRESSURE IN MAN

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SUMMARY

1. To determine if negative upper airway pressure causes reflex pharyngeal dilator muscle activation, we used intra-oral bipolar surface electrodes to record genioglossus electromyogram (EMG) activity in response to 500 ms duration pressure stimuli of 0, −2·5, −5, −15, −25 and −35 cmH_2O (0–90 % rise time < 30 ms) in ten normal, conscious, supine subjects.

2. With the subjects relaxed at end-expiration, stimuli were applied in each of three conditions: (i) glottis open (GO), (ii) glottis closed (GC) and (iii) controls with the mouth and nose closed.

3. Six rectified and integrated EMG responses were bin averaged for each pressure in each experimental condition. Response latency was defined as the time when the EMG activity significantly increased above pre-stimulus levels. Response magnitude was quantified as the ratio of the EMG activity for 80 ms post-stimulus to 80 ms pre-stimulus; data from after the subject's voluntary reaction time (for tongue protrusion) were not analysed.

4. Negative airway pressure activated the genioglossus. The median latency of activation (34 ms) was much faster than the time for voluntary activation (184 ms) indicating a reflex response.

5. Significant activation, compared to 0 cmH_2O controls *and* controls with mouth and nose closed, occurred with pressures of at least −5 cmH_2O (GC) and −15 cmH_2O (GO). At −25 and −35 cmH_2O, responses with GO were significantly greater than with GC.

6. The magnitude ('strength') of the responses differed between subjects; these differences were repeatable.

7. We conclude that negative airway pressure causes reflex pharyngeal dilator muscle activation in man. Responses with GC suggest that upper airway receptors can mediate the response but larger responses with GO indicate a contribution from subglottal receptors.

INTRODUCTION

During inspiration, the upper airway is subjected to negative pressure generated by the respiratory pump. Central respiratory activation of upper airway dilator muscles opposes this airway collapsing effect (Bartlett, 1986). In addition to this

central mechanism promoting upper airway patency, recent studies have shown that negative pressure applied to the isolated upper airway in anaesthetized animals causes reflex activation of upper airway dilator muscles, particularly the genioglossus (Mathew, Abu-Osba & Thach, 1982*a*, *b*; van Lunteren, van de Graaff, Parker, Mitra, Haxhiu, Strohl & Cherniack, 1984). This muscle is thought to play a dominant role in the maintenance of upper airway patency (Remmers, de Groot, Sauerland & Anch, 1978; Bartlett, 1986); activation of the genioglossus pulls the tongue forward and opens up the pharyngeal airspace (Abd-El-Malek, 1938; Bennett & Hutchinson, 1946). The presence of this reflex response to negative airway pressure in animals has given rise to the concept that sensory feedback from the upper airways summates with central respiratory drive to activate upper airway dilator muscles; this may play an important role in maintaining upper airway patency in the presence of subatmospheric inspiratory pressures.

In man, activation of the genioglossus muscle in response to subatmospheric upper airway pressures may also be an important mechanism for the maintenance of upper airway patency. Sauerland & Mitchell (1975) demonstrated increased tonic and phasic genioglossus electromyogram (EMG) activity in man moving from the upright to the supine posture and Sauerland & Harper (1976) demonstrated increased inspiratory genioglossus EMG activity during periods of loud snoring, compared to quiet snoring, in an obese subject during sleep. In addition, Remmers *et al.* (1978) have shown that during naturally occurring obstructive apnoeas, increased supraglottic negative pressures, generated below the level of the oropharyngeal obstruction, are associated with increased genioglossus EMG activity. These observations taken together suggest that increased upper airway negative pressure generated during inspiration may activate the genioglossus muscle in man. The purpose of the present study was to determine whether such a reflex response to negative upper airway pressure exists in man. Some of the results of this study have been reported in preliminary form (Guz, Horner & Innes, 1990; Innes, Horner & Guz, 1990).

METHODS

Studies were performed on ten normal, non-obese, supine subjects (eight male). Anthropometric data for all subjects are presented in Table 1. No subject had taken any alcohol on the day of the study. The protocol was approved by the Ethical Committee of Charing Cross Hospital.

Genioglossus EMG recording. Genioglossus EMG recordings were made using intra-oral bipolar surface electrodes (Doble, Leiter, Knuth, Daubenspeck & Bartlett, 1985); a grounding electrode was placed on the forehead. The EMG signal was amplified, filtered (100–1000 Hz), rectified and integrated using an integrator (time constant = 10 ms) which was reset every 10 ms. Preliminary studies showed that each electrode only picked up EMG activity when the tongue was actively protruded. In one subject, no change in EMG activity was recorded following small passive movements of the electrode plate relative to the tongue.

Application of negative pressure stimuli. A schematic diagram of the apparatus is shown in Fig. 1. The subjects breathed through a tight-fitting face mask (covering nose and mouth) attached to a circuit open to atmosphere. The inspiratory port of the breathing circuit was arranged so that inspiration occurred through a solenoid valve (Martonair/Beech, B/6SP5/122M10) whilst expiration took place near the face mask to minimize rebreathing. At end-expiration, activation of the solenoid valve rapidly switched the circuit (manufacturer's specifications for full opening time of solenoid = 10 ms) from atmosphere to a 50 l volume reservoir which previously had been partially evacuated to a negative pressure < -100 cmH_2O. By this method, rapid decreases in pressure were created in the breathing circuit. To constrain the negative pressure in the circuit to

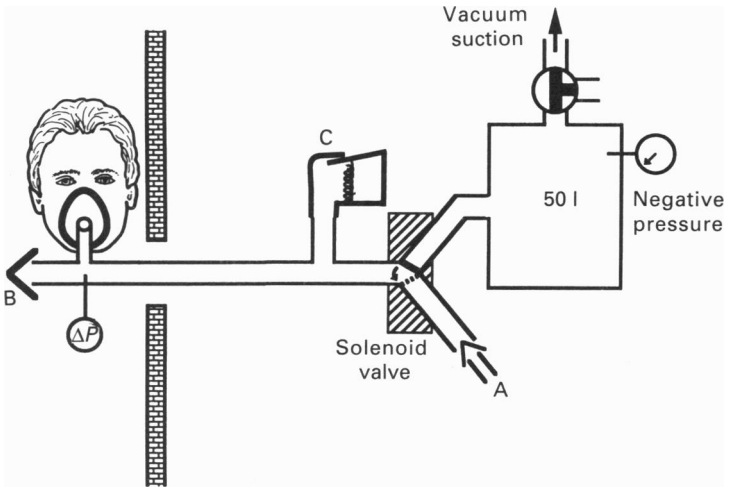

Fig. 1. The experimental apparatus used to produce rapid decreases in airway pressure. The subject lies supine, with a mask over nose and mouth, in a room separate from the investigator and equipment. The subject inspires (via valve A) through the solenoid valve and expires through valve B located near the face mask (< signifies the direction of airflow through the valves). ΔP shows the site of pressure measurement. At end-expiration, the solenoid was activated to switch the circuit from atmosphere to a 50 l volume reservoir in which a negative pressure had been established by vacuum suction. Spring-loaded valves (at C) constrain the pressure change experienced by the subject to that desired for the test.

TABLE 1. Subject details

Subject number	Gender	Age (years)	Height (m)	Weight (kg)
1	M	35	1·58	70
2	M	29	1·75	70
3	M	27	1·75	64
4	M	28	1·72	72
5	F	30	1·64	70
6	F	27	1·61	58
7	M	39	1·78	72
8	M	33	1·69	61
9	M	29	1·80	72
10	M	34	1·78	78

predetermined levels, we used spring-loaded valves (Vital Signs Inc.) to vent the excess negative pressure to atmosphere. By changing these valves, different values of negative pressure could be reproducibly applied. Using this apparatus, pressures of −35, −25, −15, −5 and −2·5 cmH_2O were applied to each subject. The duration of the pressure stimulus was 500 ms; a gated pulse generator (Digitimer, Devices 3290) activated and deactivated the solenoid valve.

Pressure changes were recorded on one side of a differential pressure transducer (±80 cmH_2O, MP45-30-871, Validyne Inc.) referenced to atmosphere. The 0–90 % response time of the transducer to an instantaneous pressure change (bursting a balloon) was < 2 ms, with 700 Hz resonance. The transducer was connected to the face mask by 52 cm length of manometer line (R84, Ayon

Medicals, Redditch). With a subject attached to the apparatus, the 52 cm length of manometer tubing did not significantly alter the shape of the pressure change when compared to simultaneous changes recorded with a catheter-tip pressure transducer (Type 16CT, Gaeltec Ltd, Isle of Skye) whose resonant frequency was > 15 kHz (manufacturer's specifications). The complete system

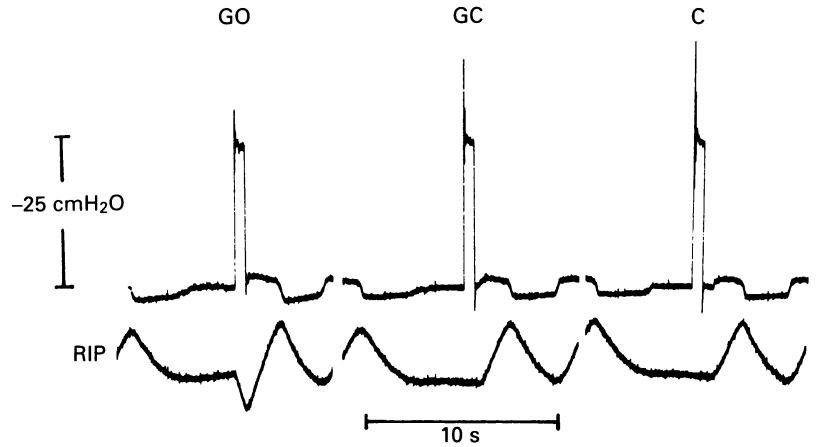

Fig. 2. Typical changes in lung volume, recorded by respiratory inductance plethysmography (RIP, inspiration upwards, uncalibrated) following application of negative pressure at end-expiration with the glottis open (GO), glottis closed (GC) and controls (C) with the mouth and nose closed. With GO, -25 cmH_2O pressure change decreases lung volume by approximately half the tidal volume; no such change occurs with GC or C.

(Fig. 1) was capable of producing pressure changes in an individual with a 0–90% response time of < 30 ms if the pressure stimuli were applied with the glottis open (GO) and < 10 ms if the glottis was closed (GC).

All interventions were performed with the subjects in the supine position and relaxed at end-expiration, i.e. during an expiratory pause. A DC-coupled respiratory inductance plethysmograph (RIP, Respitrace) was used to monitor movements of the chest wall and abdomen to allow accurate timing of the stimulus; the RIP signals were not calibrated for volume. Interventions were performed in each of two conditions; with the glottis open and voluntarily closed. To train each subject to voluntarily close his or her glottis before each study, the subjects breathed through a pneumotachograph and were instructed to abolish the cardiac oscillations in airflow observed on an oscilloscope trace whilst relaxed at end-expiration. During the experiment, each subject was asked to close his or her glottis before the pressure stimuli were applied. In one of the authors, the glottis was observed directly via a bronchoscope. In this subject, instruction to close the glottis was seen to be accompanied by closure of the vocal cords and functional isolation of the upper airway above that level.

During the experiments with the subjects relaxed at end-expiration, deflections in the baseline level of the RIP signal were almost always observed following application of the negative pressure (Fig. 2) indicating that the glottis was open. Data for interventions with the glottis closed were analysed only if no deflection in the baseline level of the RIP signal was observed following application of negative pressure (Fig. 2).

Responses to upper airway negative pressure. Pressures of -35, -25, -15, -5 and $-2{\cdot}5$ cmH_2O were applied to each subject both with the glottis open and closed. The controls for this study included (i) application of 0 cmH_2O and (ii) application of all the pressure stimuli to the outside of the face and not the airways; for these latter controls, each subject wore a nose clip and closed his or her mouth before the pressure stimuli were applied. Data for these interventions were analysed only if no deflection in the baseline level of the RIP signal was observed (Fig. 2).

Repeatability of responses to upper airway negative pressure. To study the repeatability of the responses to upper airway negative pressure (-15 and -25 cmH_2O) within a subject with the glottis open and closed, studies were performed (on separate days) in seven subjects (numbers 1, 2 and 6–10, Table 1). Interventions for each subject were performed between two and five times depending on how many times each subject visited the laboratory.

Sequence of interventions and recording of data. At least six interventions were performed (in succession) for each pressure change in each experimental condition (glottis open, glottis closed and controls). The order in which the conditions were presented was random. Each intervention was separated by about five breaths.

The pressure signal and the EMG signals were recorded on a computer-based data capture/signal averaging system operating at 5000 Hz (Cambridge Electronic Design, Cambridge, 1401 interface), magnetic tape (Store 14DS, Racal Ltd) and chart recorders. The genioglossus EMG was recorded in three forms consisting of (a) the raw, (b) the rectified and (c) the rectified and integrated activity.

Data capture and activation/deactivation of the solenoid valve were manually triggered by the gated pulse generator (Digitimer, Devices 3290) which co-ordinated time alignment of all signals. Data were sampled for a period of 500 ms which included 115 ms preceding the pressure change (pre-stimulus control period) and 385 ms following the pressure change. Averaging and subsequent analyses were performed off-line at the end of the experiment.

Voluntary reaction time. To distinguish voluntary from reflex responses to the pressure change, the voluntary reaction time taken to protrude the tongue was measured for each subject. The subjects were asked to 'voluntarily protrude the tongue as quickly as possible' in response to a visual stimulus given with the subjects relaxed at end-expiration. Six responses were recorded and then the reaction time was computed from the bin-averaged data.

Data analyses. For each pressure stimulus in each experimental condition, the EMG responses to the repeated interventions were time–bin averaged. Computations were performed on this average for the time period following the transient phase of the pressure change and were continued to include the time period up to the voluntary reaction time measured for that subject. This analytical approach was thought to exclude 'behavioural' responses.

Latency of EMG responses. The latency of genioglossus muscle activation was taken as that time, following the onset of the pressure change, when the post-stimulus integrated EMG activity increased above two standard deviations of the pre-stimulus activity and remained above that level for at least 30 ms. Due to the nature of the resetting integrator, latencies could only be determined to the nearest 10 ms.

Magnitude of EMG responses. The magnitude of the EMG response was taken as the ratio of the integral of the rectified EMG activity over an 80 ms post-stimulus period (before voluntary reaction time) to the integral of the EMG activity for an 80 ms period before the pressure stimulus. Preliminary analyses of the data relating to the magnitude of the EMG response showed that for larger values of the calculated ratio, the variability associated with that measurement also increased. Statistical analyses were therefore performed on the natural logarithm of the calculated ratio of post/pre-stimulus integrated EMG activity (Petrie, 1978) to normalize the data for statistical analyses.

Statistical analyses. The analyses performed for each statistical test are included in the text where appropriate. Where two-way analyses of variance (ANOVA) were used for statistical comparisons, the analyses were performed only after the initial ANOVA (with all conditions and pressures) showed a significant interaction ($P < 0{\cdot}05$). For all statistical tests, differences were considered significant if the null hypothesis was denied at a level of $P < 0{\cdot}05$.

RESULTS

All subjects reported that they did not fall asleep, were able to tolerate the intra-oral recording electrode and were able to voluntarily close the glottis when required during the study.

Responses to upper airway negative pressure

Following a stimulus of negative pressure, activation of the genioglossus muscle occurred both with the glottis open and closed. A typical example of such a response is shown in Fig. 3 where activation of the genioglossus muscle occurs 45 ms from the onset of the pressure change.

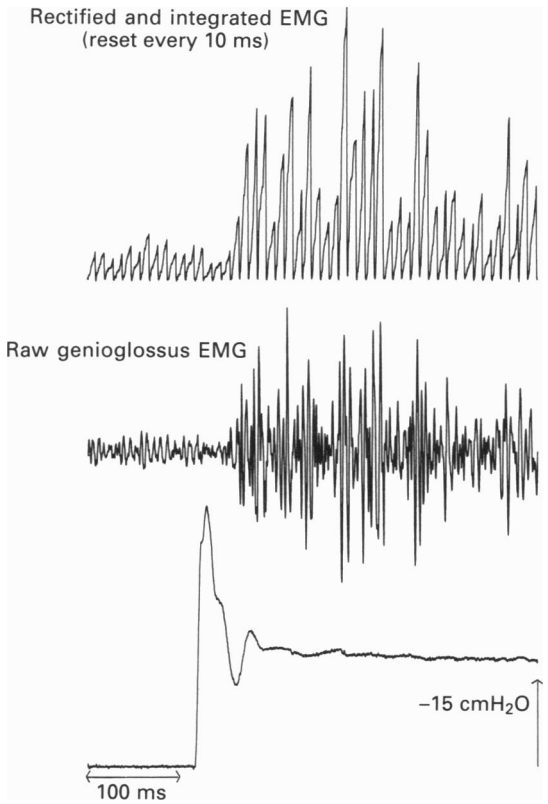

Fig. 3. Single response in subject 1 showing activation of the genioglossus muscle following a 15 cmH_2O negative pressure change with the glottis closed. Note the rapidity of the pressure change (0–90 % time = 4 ms) and the short latency of activation from the onset of the pressure change (45 ms).

Magnitude of EMG response

The magnitude (together with its variability) of genioglossus muscle activation, following each stimulus of negative pressure in each experimental condition, is shown in Fig. 4 for one subject. This figure shows that with the glottis both open and closed, the magnitude of the EMG response increased with the magnitude of the pressure change and that the responses to negative pressure with the glottis open were greater than those recorded with the glottis voluntarily closed. However, when the pressure stimuli were confined to the outside of the face only, little activation of the genioglossus was observed.

For any given pressure change, the magnitude of the EMG response varied between subjects. The bin-averaged magnitude of EMG response for each subject is shown in Fig. 5. From this figure it is clear that each subject tends to behave in a similar fashion to the subject shown in Fig. 4 but that there is a variability between subjects in the 'strength' of the EMG responses to the stimuli of negative pressure.

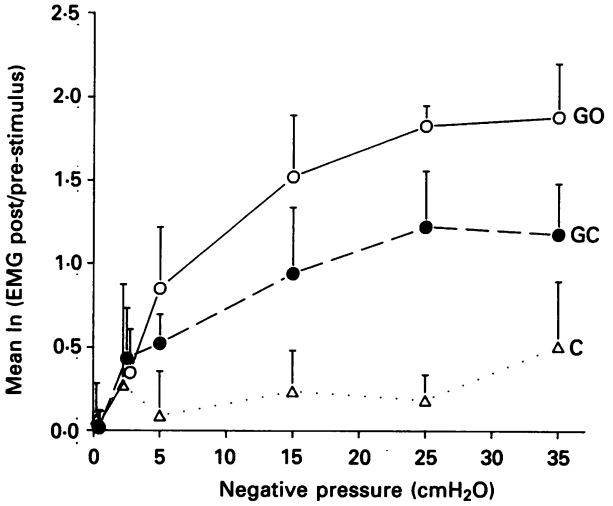

Fig. 4. Magnitude of genioglossus activation in subject 1 for each pressure change in each condition (glottis open (GO, ○), glottis closed (GC, ●) and control interventions (C, △) with the mouth and nose closed. The magnitude of response (for this figure) was calculated for each intervention ($n = 6$) for each pressure change in each condition; a ratio > 0 indicates muscle activation. The means, with +1 S.D., are shown to illustrate the variability associated with repeated single interventions. In all subsequent analyses, the magnitude of responses was calculated after bin averaging data from repeated interventions for each pressure change in each condition (see Methods).

Group results

The mean EMG responses for the group of ten subjects plotted against the stimulus of negative pressure for each experimental condition is shown in Fig. 6.

Responses within a condition

Significant activation of the genioglossus, compared to 0 cmH_2O controls, occurred at pressure changes of at least -5 cmH_2O with the glottis closed, and at least -15 cmH_2O with the glottis open, whilst at least -25 cmH_2O was needed when the pressure stimuli were confined to the outside of the face ($P < 0{\cdot}05$, Dunnett's test; (Dunnett, 1955) using one-way ANOVA).

Responses between conditions

With pressure changes of increasing magnitude, the activation of the genioglossus was significantly different both when the glottis was open and closed compared to the

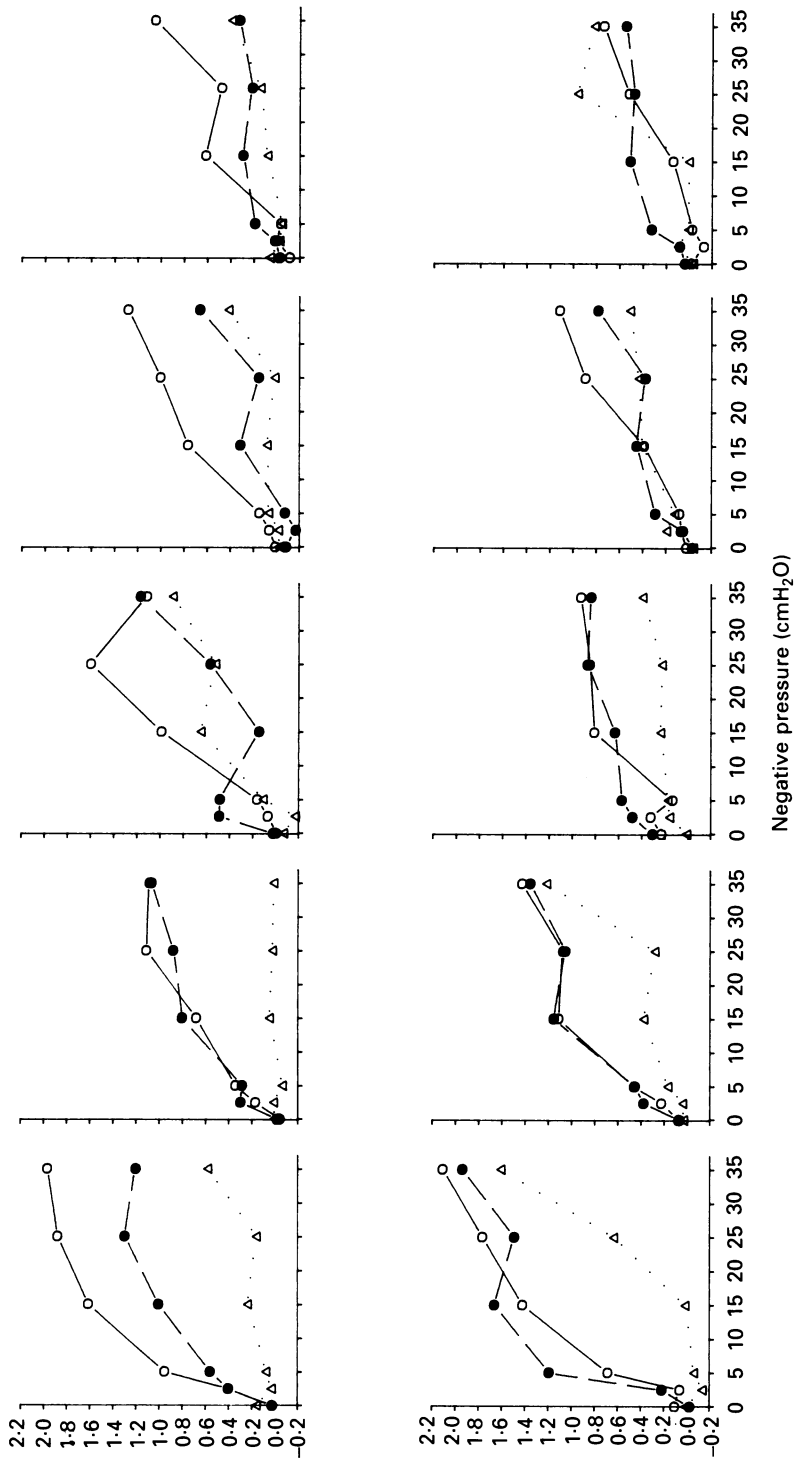

Fig. 5. Magnitude of genioglossus activation in all subjects (1 to 5 top of figure, left to right) for all pressures in each experimental condition. Magnitude of response was calculated from bin-averaged data (see Methods); symbols as for Fig. 4. Note that the axes for the dependent variable are the same for all subjects. This figure shows that there is a variability in the 'strength' of response between subjects.

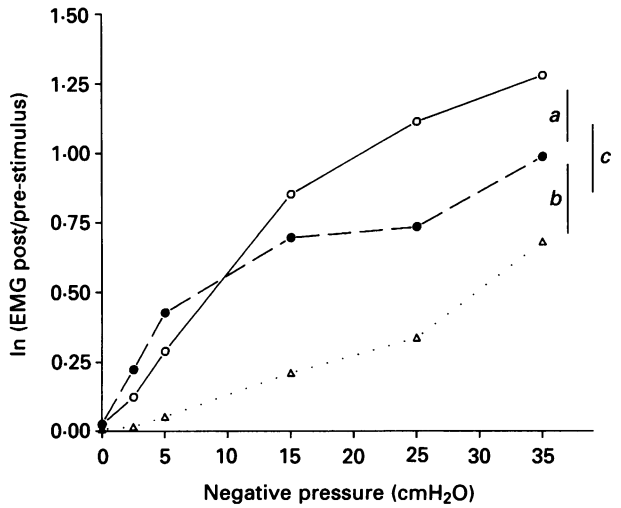

Fig. 6. Magnitude of genioglossus activation following negative pressure stimuli in each experimental condition; each point is the mean response from ten subjects. Symbols and abbreviations as for Fig. 4. Fisher's least significant differences ($P < 0{\cdot}05$) between the three conditions are shown (GO−GC = *a*, GC−C = *b* and GO−C = *c*).

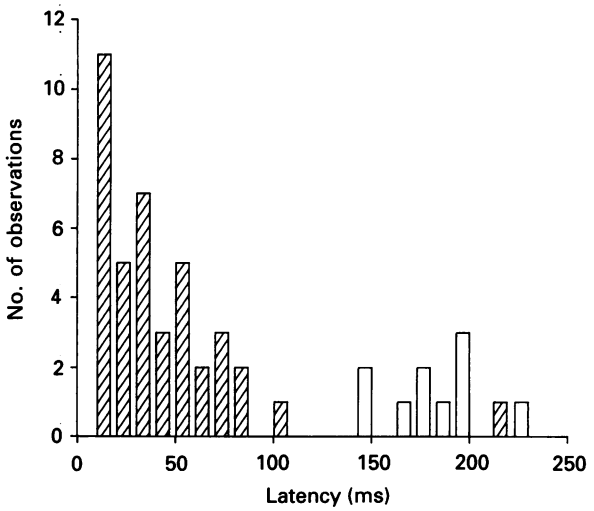

Fig. 7. Frequency histogram of the latency of genioglossus activation following stimuli of negative airway pressure (−25 and −35 cmH_2O with the glottis open and closed). Note that the latencies of activation following the pressure stimuli (▨) are much shorter than the time for voluntary activation (□).

control interventions when the pressure was confined to the outside of the face ($P < 0{\cdot}0001$ and $< 0{\cdot}05$ respectively, two-way ANOVA). Calculation of Fisher's least significant difference between pairs of conditions (separate two-way ANOVAs) showed that for pressures between −15 and −35 cmH_2O (glottis open) and −5 and −35 cmH_2O (glottis closed), the activation of the genioglossus was significantly increased compared to these controls ($P < 0{\cdot}05$, see Fig. 6).

With pressure changes of increasing magnitude, the degree of genioglossus activation was significantly different when the glottis was open compared to when the glottis was closed ($P < 0{\cdot}001$, two-way ANOVA). Calculation of Fisher's least significant difference (two-way ANOVA) showed that these differences became

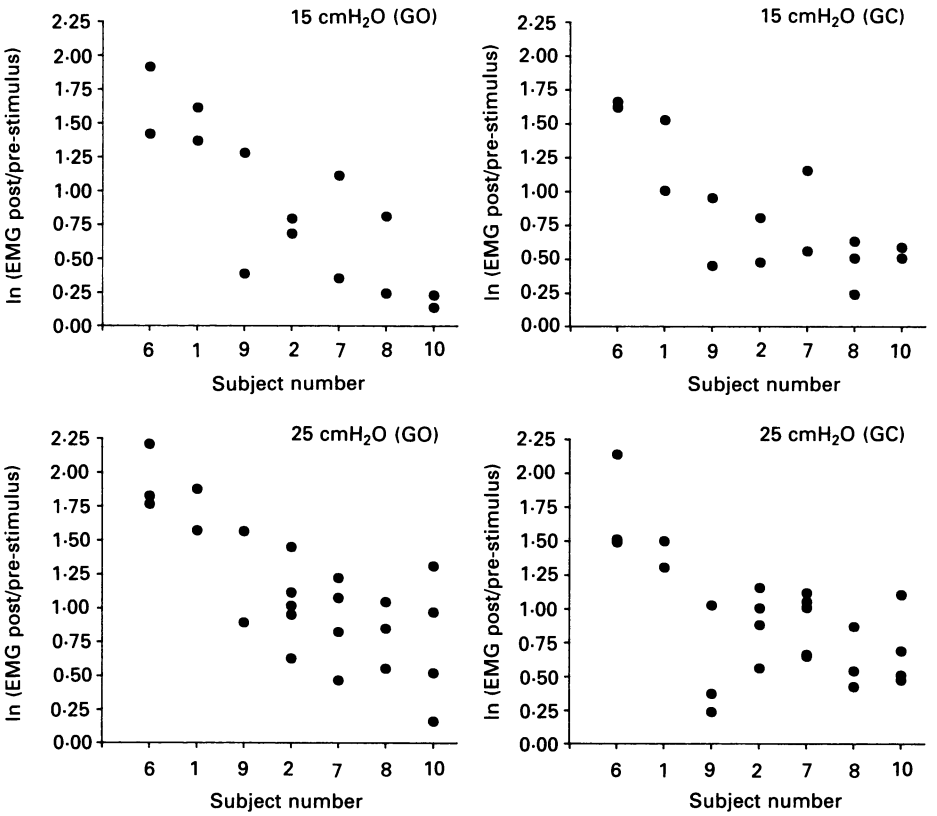

Fig. 8. Repeatability of bin-averaged responses within an individual (seven subjects) to negative pressure (-15 and -25 cmH_2O) with the glottis open (GO) and closed (GC) on separate days. The number of points for each subject varies according to the number of times they visited the laboratory. Subjects are ranked on the abscissa according to the 'strength' of response for -15 cmH_2O, GO. Analysis of these data show that responses within an individual are more similar than those between individuals, suggesting that each subject has a characteristic 'strength' of response.

apparent only at the larger values of negative pressure; i.e. -25 and -35 cmH_2O applied with the glottis open caused greater activation of the genioglossus compared to responses when the glottis was closed ($P < 0{\cdot}05$, see Fig. 6).

Latency of EMG response

Figure 7 shows the latency of genioglossus muscle activation following stimuli of negative pressure (-25 and -35 cmH_2O, glottis open and closed) in the group of ten subjects. The median latency of genioglossus muscle activation for negative pressures of -25 and -35 cmH_2O was 34 ms. This latency was much quicker than the

voluntary reaction time taken to protrude the tongue (median latency 184 ms, range 150–230 ms).

Repeatability of responses to upper airway negative pressure

Observation of the bin-averaged responses for each individual (see Fig. 5) suggests that there is a variability between subjects in the 'strength' of the EMG response for a given stimulus of negative pressure. The repeatability of the magnitude of the bin-averaged EMG response within a subject to pressure stimuli of -15 and -25 cmH_2O (glottis open and closed) is shown in Fig. 8 for seven subjects. 'Individuality' of responses was assessed by calculating the pooled within-subject variance (from repeated measures within a subject and condition) and comparing this to the pooled between-subject variance (from the S.D. of the mean results for each condition, between subjects). The ratio of the between-subject response variance to the within-subject response variance (F ratio = 2·10) was significantly greater than 1 ($P < 0·05$). This result showed that the responses observed within an individual, in each experimental condition, on separate days, were more characteristic of that individual compared to the responses observed in all others, i.e. each individual has a characteristic 'strength' of EMG response to upper airway negative pressure.

DISCUSSION

The results of the present study demonstrate that sudden upper airway negative pressure, applied at end-expiration, activates the genioglossus muscle in man. Greater reductions in upper airway pressure caused a greater degree of muscle activation, the latency of which was of the order expected in a reflex. Furthermore, when the subglottic airways were included in the negative pressure change, the degree of muscle activation was greater than that observed when the pressure change was confined to the airways above the glottis only. These results suggest that in conscious man, a reflex pathway is present that results in pharyngeal dilator muscle activation in the presence of intrapharyngeal forces that otherwise may narrow or close the pharynx.

Although many muscles may act to maintain the upper airway as an effective conduit for airflow (van Lunteren & Strohl, 1988), the genioglossus muscle has been the most studied and is considered the most important pharyngeal dilator (Bartlett, 1986). For this reason, and because the genioglossus is easily accessible for recording, this muscle was chosen for study in the present experiments. However, in animals the activation of upper airway dilator muscles by upper airway negative pressure is not unique to the genioglossus. In the dog, upper airway negative pressure has been shown to cause activation of the alae nasi, genioglossus and posterior cricoarytenoid (van Lunteren *et al.* 1984), geniohyoid, thyrohyoid and sternohyoid (van de Graaff, Gottfreid, Mitra, van Lunteren, Cherniack & Strohl, 1984). The present study was not extended to investigate the responses of other muscles because of a wish to make the protocol non-invasive.

Activation of the genioglossus muscle results in tongue protrusion in animals (Abd-El-Malek, 1938; Bennett & Hutchinson, 1946) and man (Sauerland & Mitchell, 1975) and is associated with an increased ability of the upper airway to resist collapse by

negative pressure in animals (Brouillette & Thach, 1979). In man, upper airway obstruction during sleep tends to occur with reduced or abolished genioglossus EMG activity whereas at the termination of the obstruction this EMG activity increases (Remmers *et al.* 1978). These observations suggest that activation of the genioglossus causes an increase in the size of the pharyngeal airspace (due to tongue protrusion) and/or an increased ability of this airspace to resist collapse (due to increased stiffness).

The observed activation of the genioglossus by sudden negative airway pressure in the present study indicates the presence of a mechanism which may act to maintain and/or re-establish the pharyngeal airspace as an effective conduit for airflow in the presence of upper airway collapsing pressure. Such a mechanism has been previously demonstrated in anaesthetized animals (Mathew *et al.* 1982*a*; van Lunteren *et al.* 1984) and there is evidence that sleeping neonates also show a similar reflex (Carlo, Miller & Martin, 1985). The presence of such a mechanism in conscious man has remained speculative due to the small number of studies designed to test this hypothesis and the nature of the applied stimulus in those studies (Kuna & Smickley, 1988; Aronson, Onal, Carley & Lopata, 1989; Weigand, Zwillich & White, 1989; Leiter & Daubenspeck, 1990). For example, studies on the response of the genioglossus muscle to inspiratory resistive loading (Weigand *et al.* 1989) and inspiration against an occluded nasal airway (Kuna & Smickley, 1988) are complicated since in conscious subjects, the observed activation of this muscle may have been due to increased central respiratory activation either mediated voluntarily, mediated by sensory feedback effects from the upper airways and/or mediated by reduced vagal inhibitory activity from lung stretch receptors. Aronson *et al.* (1989) and Leiter & Daubenspeck (1990) have used negative pressure stimuli more like those used in the present study. However, it is difficult to determine the mechanism of the observed activation of the genioglossus in those studies because of the different protocol used and because the 0–90 % time for the pressure change was slow; approximately 2000 ms in the study reported by Aronson *et al.* (Fig. 1 of that paper) and even slower (20 s) in the study reported by Leiter and Daubenspeck. Our experiments differ from these previous studies in that we chose to perform our interventions at end-expiration (i.e. during an expiratory pause) since only then could we simply apply the negative pressure with the glottis closed. In addition, performing the interventions at this phase of the breathing cycle simplified the calculation of the magnitude and latency of response by avoiding problems resulting from varying background EMG activity depending on central inspiratory drive. Furthermore, we focused on the need to establish, as close as possible, a 'square-wave' input function, i.e. a very rapid pressure change, to allow physiologically relevant determinations of latency and magnitude of the EMG response to be made. Moreover, calculations of the magnitude of the EMG responses to stimuli of negative pressure were made within the voluntary reaction time taken to protrude the tongue in response to a visual cue, the objective being to quantify the responses within the time uninfluenced by 'behaviour'.

Latency of genioglossus muscle activation to negative pressure

In the present study, the activation of the genioglossus muscle following changes in airway pressure was of short latency (Fig. 3). The use of an integrator that reset

every 10 ms facilitated measurements of latency but introduced an error of 10 ms. Despite this error, the activation of the genioglossus was much quicker than the voluntary reaction time taken to protrude the tongue in each subject. Therefore, it is unlikely that the early responses had a 'behavioural' component. The median latency of response observed in the present study (34 ms) is consistent with the EMG response being of reflex origin; it is of the same order as the latency of onset of other reflexes in man, e.g. the electrically induced corneal reflex ($36 \pm 1{\cdot}3$ ms (1 S.E.M.); Berardelli, Rothwell, Day & Marsden, 1988) and the stretch reflex in peripheral muscles (40 ms; Marsden, Merton & Morton, 1971). Furthermore, a similar latency has been demonstrated for the changes in breathing pattern of sleeping human neonates in response to upper airway negative pressure applied via a tracheostomy (42 ms; Thach, Menon & Schefft, 1989).

Responses with glottis closed

The activation of the genioglossus muscle with the glottis closed (i.e. an 'isolated' upper airway segment) is consistent with the findings previously reported for animals (Mathew *et al.* 1982*a*; van Lunteren *et al.* 1984). Since the responses in animals (with surgically isolated upper airways) are abolished by bilateral section of the superior laryngeal nerves and topical anaesthesia of the pharyngeal mucosa (Mathew *et al.* 1982*b*; van Lunteren *et al.* 1984), it is reasonable to postulate from the findings of the present study that upper airway receptors mediate the observed activation of the genioglossus by negative pressure with the glottis closed. The afferent pathways for this activation are considered in more detail in the accompanying paper (Horner, Innes, Holden & Guz, 1991) where an attempt has been made to localize the upper airway receptors mediating the response by using upper airway anaesthesia.

Responses with glottis open

The results have shown that responses with the glottis open (-25 and -35 cmH_2O) were significantly greater than those with the glottis closed (Fig. 6). The facilitatory effect on genioglossus of stimulating with negative pressure with the glottis open suggests activation of a larger number of airway receptors in this condition, i.e. activation of receptors below the level of the vocal cords in addition to upper airway receptors. However, on the basis of the present experiments it is not possible to determine the nature of these receptors nor their adequate stimulus (slowly adapting or rapidly adapting receptors responding to transmural pressure, lung deflation or deformation of the airway walls).

Responses with stimuli applied to outside of face only

An interesting finding of the present study was that stimuli of negative pressure applied solely to the outside of the face activated the genioglossus. The responses in this condition were small (and with a higher threshold) compared to the responses elicited from the airways but the presence of such responses necessitated the sequence of control interventions used in this study. The trigeminal nerves are most likely to mediate the responses to negative pressure in this condition. In this respect, the trigeminal nerves have been shown to mediate activation of the genioglossus muscle following negative pressure applied to the inside of the nasal cavity in animals (Mathew *et al.* 1982*b*; Hwang, St John & Bartlett, 1984). The interpretation of a

response elicited from the outside of the face depends critically on the pressure change having no access to the airways. The validity of this assumption depended on the mouth having remained closed during the pressure change (according to verbal instruction) and the careful positioning of the nose clip. We believe that the pressure change had no access to the inside of the nose since the nose clip was placed firmly on the nostrils. In addition, we have indirect evidence that the mouth remained closed during the pressure change since the lung volume did not change during the stimulus (Fig. 2).

Repeatability of EMG responses within an individual

The results of the present study have shown that the 'strength' of the EMG response to airway negative pressure varies between individuals significantly more than within an individual. Therefore, it would appear that there are those individuals who characteristically have a large degree of upper airway dilator muscle activation in response to airway collapsing pressures whilst there are others who characteristically have a small degree of activation. It is tempting to speculate that those individuals with a low strength of EMG response would be more prone to upper airway collapse by negative pressure developed during sleep. A reduced strength of EMG response to collapsing pressures in the upper airways may explain the existence of snoring or obstructive sleep apnoeas in some individuals. This hypothesis is testable, as is the alternative hypothesis that the activation of pharyngeal dilator muscles by negative pressure may be reduced in individuals with a stiffer pharynx, i.e. less receptors stimulated by mechanical distortion of the mucosa. There was also not enough variation in anthropometric parameters (particularly body weight) to test the hypothesis that more obese people may have smaller (or larger) EMG responses.

Conclusion

The results of the present study suggest that sensory feedback from the upper airway (and from the airways below the level of the vocal cords) in response to subatmospheric pressure may mediate activation of upper airway dilator muscles in man. The afferent pathway(s) of this reflex has been studied and the results are presented in the accompanying paper (Horner *et al.* 1991).

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