Effects of tongue electrical stimulation on pharyngeal mechanics in anaesthetized patients with obstructive sleep apnoea

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ABSTRACT: The tongue plays a significant role in the maintenance of a patent airway. The purpose of this study was to examine the effects of tongue musculature contraction on the static mechanical properties of the pharynx in patients with obstructive sleep apnoea (OSA).

During hyperventilation-induced apnoea in seven OSA patients anaesthetized with sevoflurane, the static pressure/area relationships of the oropharynx were obtained by means of step changes in airway pressure while endoscopically measuring cross-sectional area. At each airway pressure, the tongue was electrically stimulated *via* electrodes placed bilaterally.

Tongue electrical stimulation (TES) did not further dilate the oropharyngeal area at higher airway pressure (3.2 ± 1.9 versus 3.0 ± 2.1 cm²), although the narrowed oropharyngeal area at lower airway pressures increased during TES (0.8 ± 9.0 versus 1.7 ± 1.8 cm², $p < 0.05$). Accordingly, the slope of the pressure/area relationship decreased during TES (0.24 ± 0.20 versus 0.12 ± 0.09 cm²·cmH₂O⁻¹, $p < 0.05$).

In conclusion, electrical stimulation of the tongue stiffens the retroglossal airway wall in patients with obstructive sleep apnoea.

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Reduction of pharyngeal muscle activity unmasks abnormally high collapsibility of the pharynx leading to significant narrowing or complete closure of the pharynx during sleep in patients with obstructive sleep apnoea (OSA), whereas augmented activity of the pharyngeal muscles appears to compensate for the anatomical abnormalities in order to maintain a patent airway during wakefulness [1–3]. Although there is no doubt that pharyngeal muscles play a significant role in maintaining pharyngeal airway patency, the primary function of the contraction of these muscles has yet to be sufficiently investigated in humans.

Although a number of previous studies have reported an increase in whole hypoglossal nerve activity in response to hypoxia and hypercapnia [4–6], FULLER *et al.* [7] simultaneously recorded electromyograms of both tongue protruder and retractor muscles in an anaesthetized rat preparation, and found that there was coactivation of both muscles during chemoreceptor stimulation. SCHWARTZ *et al.* [8] reported that pharyngeal collapsibility, assessed by means of the upper airway critical pressure (P_{crit}), was decreased by electrical stimulation of the whole hypoglossal nerve in anaesthetized cats with isolated upper airways. More recently, HIDA *et al.* [9] examined the effects of electrical stimulation of the whole hypoglossal nerve on the upper airway pressure/volume relationship in anaesthetized dogs, and found that the slope of the relationship, *i.e.* the compliance of the upper airway, decreased with the electrical stimulation. These animal studies strongly suggest that both the tongue protruder and retractor muscles act as stiffeners of the pharynx for airway maintenance, regulating the compliance of the

pharyngeal wall. Although EISELE *et al.* [10] also demonstrated that electrical stimulation of the main trunk of the hypoglossal nerve improved maximum inspiratory airflow in sleeping patients with OSA, there is no direct evidence indicating that coactivation of the tongue protruder and retractor muscles stiffens the pharyngeal airway wall in unconscious humans. Accordingly, this study was designed in order to test the hypothesis that electrical stimulation of both the tongue protruder and retractor muscles decreases the compliance of the retroglossal airway wall in anaesthetized patients with OSA.

Materials and methods

Subjects and overnight oximetry

Seven male patients with OSA who chose uvulopalatopharyngoplasty as a treatment for their apnoea were included in this study. All had histories of excessive daytime sleepiness, habitual snoring and witnessed repetitive apnoea. Sleep-disordered breathing (SDB) was evaluated using a pulse oximeter (Pulsox-5; Minolta, Tokyo, Japan). All subjects were instructed to attach an oximetry finger probe before sleep and to remove the probe upon awakening. Digital readings of arterial oxygen saturation (Sa_{O_2}) and pulse frequency were stored every 5 s on a memory card. The stored data were displayed on a computer screen to check the quality of the recordings. The computer-calculated oxygen desaturation index defined as the number of oxygen desaturations $>4\%$ from baseline per hour,

and the percentage of time spent at S_{a,O_2} of <90%. Table 1 lists all nocturnal oximetry data and anthropometric characteristics. Although the oximetry evaluation alone does not clarify the nature of the SDB, it is believed that all patients can be safely diagnosed as having OSA based on oximetry results and clinical symptoms.

Informed consents were obtained from all subjects after the aim and potential risks of the study were fully explained to each. The investigation was approved by the Hospital Ethics Committee.

Electrical stimulation of the tongue

After clearing off secretions on the surface of the tongue, two electrocardiogram electrodes (1 cm^2) were attached bilaterally to the tongue at the mucosal fold level, and connected to an electric stimulator (SEN 3201; Nihon Kohden, Tokyo, Japan). The tongue was stimulated with a pulse width of 0.2 ms, frequency of 100 Hz and burst duration of 2–3 s. The voltage was set at 20–30 V and apparent tongue movement was confirmed by pharyngeal endoscopy during tongue electrical stimulation (TES). Based on the anatomy of the pharyngeal muscles, it was believed that the current applied through these electrodes spread into the tongue protrudors such as the genioglossus as well as the tongue retractors such as the hyoglossus and the styloglossus.

Pharyngeal endoscopy under general anaesthesia

Preparation of the subjects. The subjects were premedicated with 0.5 mg atropine 30 min before induction of anaesthesia. Studies were performed with each subject in a supine position on an operating table, with the neck in a neutral position. A modified tight-fitting nasal continuous positive airway pressure or modified anaesthetic nasal mask was fitted on to each subject. The possibility of air leaks between the mask and face was carefully examined, particularly at airway pressurization to 20 cmH₂O. General anaesthesia was induced by intravenous administration of thiopentone ($4\text{ mg}\cdot\text{kg}^{-1}$), and was maintained by inhalation of 2–4% sevoflurane in oxygen. S_{a,O_2} , electrocardiography and blood pressure were continuously monitored. The subject was hyperventilated at positive pressure through an anaesthetic machine. Electrical stimulation electrodes were placed bilaterally on the tongue as described above and connected to a stimulator. A slim endoscope (FB15H or FB10H; Pentax, Inc., Tokyo, Japan, 3 mm and 4.5 mm outside diameter, respectively) was inserted into the nasal

mask and naris. The tip of the endoscope was positioned to visualize the velopharynx (VP; retropalatal space) or the oropharynx (OP; retroglossal space). A closed-circuit camera (ETV8; Nisco, Saitama, Japan) was connected to the endoscope and pharyngeal images were recorded on videotape.

Experimental procedure. In order to determine the pressure/area relationship of the pharynx, the anaesthetic machine was disconnected from the nasal mask, which was then connected to a pressure control system capable of accurately producing a constant preselected airway pressure (P_{aw}) ranging -20–20 cmH₂O in steps of 1 cmH₂O. Cessation of mechanical ventilation resulted in apnoea due to hyperventilation and the respiratory depressant effect of sevoflurane. P_{aw} measured by means of a water manometer was immediately increased and maintained at 20 cmH₂O. While the subject remained apnoeic for 2–3 min, P_{aw} was slowly reduced from 20 cmH₂O to the velopharyngeal closing pressure, *i.e.* the pressure at which the VP was seen to close completely. At each P_{aw} , TES was performed for ~2–3 s. In all subjects, S_{a,O_2} remained >99% throughout the test. This hyperventilation-induced apnoea procedure allowed construction of pressure/area relationships of the visualized airway with and without (control) TES. The apnoeic tests were terminated at the restarting of spontaneous breathing or with unexpected movement of the pharyngeal wall. The distance between the endoscope tip and the narrowing site was measured by means of a wire passed through the aspiration channel of the endoscope. The apnoeic tests were performed at the oropharyngeal and velopharyngeal airways.

After evaluation of the influence of TES on the static pressure/area relationship of the pharynx, a completely paralysed condition was induced by intravenous administration of a muscle relaxant (vecuronium $0.2\text{ mg}\cdot\text{kg}^{-1}$) allowing evaluation of the static mechanics of the atonic pharynx as previously reported [11]. Briefly, the apnoeic test mentioned above was repeated in this paralysed condition while observing the VP or the OP.

Data analysis

In order to convert the monitor image to an absolute value of pharyngeal cross-sectional area, the magnification of the imaging system was estimated at every 1.0 mm distance between the endoscope tip and the object at a range of 10–30 mm. At the defined P_{aw} , the pharyngeal lumen image was outlined on tracing paper ($50\text{ g}\cdot\text{m}^{-2}$), cut out and weighed (ER120; AND, Tokyo, Japan). The area

Table 1. – Patient characteristics and results of oximetry

Patient No.	Age yrs	BMI $\text{kg}\cdot\text{m}^{-2}$	ODI events $\cdot\text{h}^{-1}$	CT90	Baseline S_{a,O_2} %	Nadir S_{a,O_2} %	Lowest S_{a,O_2} %
1	40.0	31.1	27.7	10.0	96.1	87.2	72.0
2	40.0	35.7	11.6	1.0	97.8	92.0	86.0
3	45.0	33.2	63.4	72.0	94.0	80.5	44.0
4	51.0	28.7	48.1	47.0	96.5	84.5	62.0
5	59.0	26.9	14.3	1.0	96.5	91.3	86.0
6	61.0	18.6	7.6	0.0	98.3	92.9	85.0
7	53.0	27.0	17.1	3.5	97.2	90.4	77.0

BMI: body mass index; ODI: oxygen desaturation index, defined as the number of oxygen desaturations >4% from baseline per hour; CT90: the percentage of time spent at an arterial oxygen saturation (S_{a,O_2} of <90%; nadir S_{a,O_2} : mean of lowest S_{a,O_2} during desaturation events; lowest S_{a,O_2} : lowest S_{a,O_2} during recording.

of the paper was converted to pharyngeal cross-sectional area according to the distance/magnification relationship. For a constant distance, the area measurements were validated to be accurate within 8% (difference between actual and measured areas: $-0.1 \pm 4.6\%$, range 6.5–7.6%) using known-diameter tubes (4–9 mm inner diameter). In addition, anterior/posterior distance and the lateral width of the airway were also measured in order to evaluate the influence of TES on the shape of the pharyngeal airway.

The measured luminal cross-sectional area was plotted as a function of P_{aw} . The maximum cross-sectional area (A_{max}) for each condition was determined as the mean of the measured areas at the three highest P_{aw} (18, 19 and 20 cmH₂O). The minimum cross-sectional area (A_{min}) was determined at the lowest P_{aw} for each condition. Since the nature of the obtained pressure/area curves of the pharynx in the non-paralysed condition was not necessarily exponential as previously reported for the completely paralysed condition [11], only the pressure/area relationship at the six lowest P_{aw} was assessed using a linear regression model. The quality of the fitting was provided by the coefficient R^2 of the regression. The effects of TES on the pressure/area relationship at the lower P_{aw} were assessed *via* changes in the slope of the model representing com-

pliance of the pharynx for the lower P_{aw} range and changes in the x-intercept of the model, representing the closing pressure of the pharynx.

The static pressure/area relationships of the atonic pharynx in the completely paralysed condition were fitted using an exponential function: $A = A_{max} - Be^{-KP_{aw}}$ where A is area and K and B are constants [11]. The closing pressure (P_{close}) was estimated by $P_{close} = \ln(B/A_{max})K^{-1}$ where B is a constant and the static airway compliance (C_{st}) for a given area was calculated from the following equation: $C_{st} = K(A_{max} - A)$.

Statistical analysis

All values are expressed as means $\pm$ SD. The Wilcoxon signed rank test was used for the comparison of control and TES conditions. A p-value < 0.05 was considered significant.

Results

Oropharyngeal airway images before and during TES at higher and lower P_{aw} in one patient (No. 1) are shown in figure 1. TES narrowed the oropharyngeal airway at 20 cmH₂O, but dilated the airway at 3 cmH₂O.

Influence of tongue electrical stimulation on pressure/area relationships of the oropharynx

The influences of TES on the oropharyngeal pressure/area relationships in each patient are illustrated in figure 2. The curves are not exponential, but rather linear. At higher P_{aw} , the cross-sectional area of the OP decreased in four of seven patients (Nos. 1, 2, 3, and 4), remained unchanged in patients No. 5 and No. 6, and increased in patient No. 7. A_{max} did not statistically differ before and during TES (fig. 3). In contrast, TES increased the oropharyngeal area at lower P_{aw} except patients No. 4 and No. 6, thereby producing a significant increase in A_{min} (fig. 3). Accordingly, reduction of the slope of the pressure/area relationship was most commonly observed during TES.

Dimensional analyses of the oropharyngeal airway

The influence of TES on oropharyngeal airway shape was evaluated by measuring anterior/posterior distance and the lateral width of the airway before and during TES. As illustrated in figure 4, TES did not significantly change lateral width at either the higher or the lower P_{aw} . TES significantly increased anterior/posterior distance at lower P_{aw} whereas the distance did not change at higher P_{aw} . Accordingly, TES primarily prevented anterior/posterior narrowing.

Oropharyngeal wall properties at lower airway pressure

The individual pressure/area relationships of the OP at lower P_{aw} were satisfactorily fitted by linear regression models (mean R^2 range 0.94–0.99). The x-intercept before

Fig. 1. – Oropharyngeal images: a, b) before (control); and c, d) during tongue electrical stimulation at an airway pressure of: a, c) 20 cmH₂O; and b, d) 3 cmH₂O in patient No. 1. e) Diagrammatic representation of c.

Fig. 2. – Static oropharyngeal pressure/area (A) relationships before (control, $\circ$) and during tongue electrical stimulation ($\bullet$) in each patient. Patient No.: a) 1; b) 2; c) 3; d) 4; e) 5; f) 6; and g) 7. P_{aw} : airway pressure.

TES (0.43 ± 5.7 cmH₂O) significantly decreased during TES (-12.7 ± 20.8 cmH₂O) (fig. 5). The slope of the linear regression model (0.24 ± 0.20 cm²·cmH₂O) significantly decreased during TES (0.12 ± 0.09 cm²·cmH₂O), indicating a reduction in the compliance of the oropharyngeal airway wall during TES. Since the absolute value of the compliance depends upon the size of the airway, the reduction rate of the compliance was calculated. Interestingly, it was found that the reduction rate of the compliance varied little among the patients ($51 \pm 9\%$ reduction in the slope, 43–69%). The oropharyngeal compliance decreased by a half during TES in patient No. 6, with the fewest SDB events and the lowest body mass index although the OP significantly narrowed during TES, resulting in an increase in P_{close} in this patient.

Influence of tongue electrical stimulation on the velopharyngeal segment

The influence of TES on the upstream adjacent segment to the OP, *i.e.* the VP, was variable, and no statistically significant difference was indicated in static mechanical parameters between with and without TES, as shown in figures 3 and 5. However, it should be noted that the statistical insignificance does not necessarily indicate no influence of TES on static mechanical properties in each of the patients. Figure 6 demonstrates two extreme patterns of velopharyngeal airway responses to TES. The pressure/area relationships of the VP in the control condition (fig. 6) and the responses of the oropharyngeal

Fig. 3. – Influence of tongue electrical stimulation (TES) on: a) maximum (A_{max}); and b) minimum cross-sectional area (A_{min}) at the velopharynx (VP) and the oropharynx (OP). $\square$: control; hatched : TES. *: $p < 0.05$ versus control.

Fig. 4. – Influence of tongue electrical stimulation (TES) on maximally (A_{max}) and minimally dilated airway (A_{min}) dimensions of the oropharynx: a) anterior/posterior distance; and b) lateral width. $\square$: control; hatched : TES. *: $p < 0.05$ versus control.

Fig. 5. – Influence of tongue electrical stimulation (TES) on the mechanical characteristics of the velopharynx (VP) and oropharynx (OP) assessed by: a) the x-intercept; and b) the slope of the regression lines of the static pressure/area relationship at lower airway pressures. □ : control; ▨ : TES. *: $p < 0.05$ versus control.

segments to TES (fig. 2) were similar between the patients. Nevertheless, the velopharyngeal airway was dilated at the lower P_{aw} and the compliance of the pharyngeal wall was decreased by TES in patient No. 1 whereas TES narrowed the velopharyngeal airway without influencing the compliance of the pharyngeal wall in patient No. 5.

Static pharyngeal mechanics in the completely paralyzed condition

Table 2 presents individual static mechanical parameters obtained in the completely paralyzed condition. Velopharyngeal and oropharyngeal A_{max} in paralyzed conditions did not differ from the control A_{max} in nonparalyzed control conditions. Although estimation methods differ between P_{close} and the x-intercept, the individual P_{close} for each pharyngeal segment in the paralyzed condition was similar to the x-intercept value in nonparalyzed control conditions. The C_{st} of the OP in the paralyzed condition at lower P_{aw} , estimated by $K(A_{max} - A_{min})$ did not differ from that in the nonparalyzed control condition, estimated as the slope of the pressure/area relationship at lower P_{aw} , (0.31 ± 0.26 versus 0.24 ± 0.20 $\text{cm}^2 \cdot \text{cmH}_2\text{O}$).

Fig. 6. – Two patterns of the velopharyngeal airway response to tongue electrical stimulation (TES): velopharyngeal area (A) in patients number: a) 1; and b) 5. ○ : control; ● : TES. P_{aw} : airway pressure.

Discussion

In this study, it was demonstrated that TES dilated the oropharyngeal area at lower P_{aw} , but not at higher P_{aw} , and that the compliance of the OP assessed by the slope of the pressure/area relationship decreased during contraction of the tongue at lower P_{aw} .

Limitations of the study

Inhalational anaesthetics are known to depress hypoglossal nerve activity more than phrenic nerve activity [12], and the influence of chemical stimulation of the diaphragm is always greater than that on the upper airway muscles despite differences in the consciousness state. [13]. It was, therefore, believed that the static mechanical properties of the hypotonic pharynx could be evaluated during hyperventilation-induced apnoea under general anaesthesia before initiation of spontaneous breathing. This is supported by the findings that the P_{close} and compliance of the oropharyngeal airway in completely paralyzed conditions did not differ from those in non-paralyzed control conditions. However, there is no direct evidence available to deny the suggestion that carbon dioxide accumulation during apnoea might have increased pharyngeal muscle activity since pharyngeal muscle activity was not measured. The control pressure/area relationship of the pharynx obtained in this study may not represent passive mechanical properties, particularly at lower P_{aw} , and the compliance at lower P_{aw} may possibly be underestimated. SCHWARTZ *et al.* [14] examined the effects of CO_2 accumulation on pharyngeal collapsibility in anesthetized dogs, and found that an increase in arterial carbon dioxide tension (P_{a,CO_2}) of ~ 10.0 kPa (~ 75 mmHg) resulted in a decrease in P_{crit} of 5 cmH_2O . In anesthetized humans, P_{a,CO_2} is considered to increase by 0.4–0.8 kPa (3–6 mmHg) during an apnoea for 1 min [15]. During the 2–3 min apnoeic test in the present study, therefore, P_{close} could be speculated to decrease by ~ 1 cmH_2O . The effect of TES on P_{close} were possibly underestimated during the present study, partly due to lack of P_{a,CO_2} control during the apnoeic tests. In addition, surface adhesive forces on the pharyngeal mucosa may possibly have influenced pressure/area relationships since reopening of the narrowed or closed airway has been reported to be impaired by the mucosal effect [16]. Therefore, the observed dilation of the pharynx during TES at lower P_{aw} may be underestimated, and compliance of the pharynx with TES is possibly overestimated. Accordingly, these uncontrolled factors are considered to alter the pharyngeal pressure/area relationships and to obscure the distinct difference of the pressure/area relationships between passive and active pharynx.

Another limitation of this study would be the lack of evaluation of the dose-dependent effects of TES on static pharyngeal mechanics. Although the stimulation intensity was set based on apparent tongue movement identified by pharyngeal endoscopy, lower intensity stimulation, which is possibly more physiological in terms of the contraction strength of the tongue musculature, could have influences on the pharyngeal wall other than the stiffening effect.

Table 2. – Static mechanical properties of the pharynx in the paralysed condition

Patient No	Velopharynx			Oropharynx			
	$A_{\max}$ cm ²	P_{close} cmH ₂ O	C_{st} at P_{close} cm ² ·cmH ₂ O ⁻¹	$A_{\max}$ cm ²	P_{close} cmH ₂ O	C_{st} at P_{close} cm ² ·cmH ₂ O ⁻¹	C_{st} at $A_{\min}$ cm ² ·cmH ₂ O ⁻¹
1	0.8	0.2	0.14	1.6	2.5	0.19	0.19
2	0.8	0.5	0.15	2.0	0.5	0.22	0.19
3	0.5	8.3	0.11	3.7	6.5	1.92	0.82
4	0.2	7.3	0.05	2.1	4.1	0.57	0.46
5	1.0	-0.2	0.13	3.9	-2.3	0.46	0.24
6	0.8	2.4	0.17	1.0	6.4	0.23	0.23
7	1.0	2.4	0.09	1.2	-25	0.17	0.03
Mean	0.72	3.0	0.12	2.2	-1.1	0.54	0.31
SD	0.29	3.4	0.04	1.1	11	0.63	0.26

$A_{\max}$: maximum cross-sectional area (A) determined as the mean of the measured areas at the three highest airway pressures (P_{aw}) (18, 19 and 20 cmH₂O); P_{close} : closing pressure estimated by $\ln(B/A_{\max})K^{-1}$ where K and B are constants obtained *via* curve fitting analysis ($A=A_{\max} - Be^{-KP_{\text{aw}}}$); C_{st} : static airway compliance calculated as $C_{\text{st}}=K(A_{\max} - A)$; $A_{\min}$: minimum cross-sectional area observed during apnoeic test.

Mechanical influences of co-activation of the tongue protrudor and the retractor muscles

The tonic as well as the phasic activities of the genioglossus, a major tongue protrudor muscle, significantly depend upon consciousness state, and a reduction in the activities has been reported to be associated with an increase in upper airway resistance or obstructive apnoea, particularly in patients with OSA [1, 2]. Recently, KOBAYASHI *et al.* [17] examined the relationship between genioglossus activity and tongue movement in laryngectomized subjects who breathed through a tracheal stoma, therefore eliminating the effects of P_{aw} on tongue position. They found that increased genioglossal activity enlarged the retroglossal airway space. Based on this evidence, the primary function of the genioglossus in breathing has been believed to be as a dilator of the pharynx. FREGOSI and coworkers [7, 18], however, questioned the simple dilator theory and proposed that the coactivation of tongue protrudor and retractor muscles was important in regulating the compliance of the pharyngeal wall since they found an increase in tongue retraction force during coactivation of the tongue muscles. Their idea was in complete agreement with the results of other previous animal studies evaluating the effects of electrical stimulation of the whole hypoglossal nerve on upper airway collapsibility [8, 9]. In this context, consideration of possible coactivation of the tongue retractor muscles might give new insights into the interpretation of previous human studies, in which only protrudor muscle activity was measured. The observed anterior movement of the tongue in the study of KOBAYASHI *et al.* [17] could have resulted from a balance between tongue protrudor and retractor muscles during mechanical loading. EISELE *et al.* [20] reported that electrical stimulation of the whole hypoglossal nerve increased maximum inspiratory flow in association with tongue retraction in patients with OSA during sleep. SCHWARTZ *et al.* [19] further demonstrated that electrical stimulation of the tongue protrudor increased maximum inspiratory flow, whereas electrical stimulation of the tongue retractor decreased maximum inspiratory flow in sleeping apnoeics. Although these human studies were in agreement with the concept proposed by FREGOSI and coworkers [7, 18] no study ex-

amined the effect of coactivation of the tongue muscles on pharyngeal wall properties in humans. Accordingly, examination of the precise mechanical influences of coactivation of the tongue protrudor and retractor muscles may answer the important question as to whether the primary mechanical function of the tongue muscles is dilation of the retroglossal airway or stiffening the airway wall in humans [20]. In a static pressure/area relationship, a simple dilating effect would result in a shift of the curve to the left without changing the slope of the curve, but an increase in the area for a given P_{aw} . In contrast, stiffening of the airway would be determined by a decrease the slope of the curve. Both dilation and stiffening effects were found at lower P_{aw} . The authors believe that dilation and stiffening of the airway are not mutually exclusive, but rather compatible, as clearly shown by the changes in static pressure/area relationships (fig. 2).

Anatomical consideration of tongue movement during tongue electrical stimulation

Although previous animal and human studies found tongue retraction during coactivation of the protrudor and retractor muscles, significant dilatation of the retroglossal airway was observed during the present study at lower P_{aw} during TES. The position of the tongue is considered to be determined by the balance of contraction force between the tongue protrudor and the retractor muscles. The anatomical arrangement of these muscles in the airway and their force/length relationship may possibly account for the seeming disagreement between the present findings and previous observations. FULLER *et al.* [7] measured tongue force while pulling the tongue forward, indicating that retroglossal airway space was not decreased. Since EISELE *et al.* [10] gave positive nasal airway pressure, maintaining stable inspiratory flow limitation during electrical stimulation of the hypoglossal nerve, the pharyngeal airway was not significantly narrowed at the onset of the stimulation. All these experimental settings are considered to lengthen the retractor muscle fibres, and, therefore, favour retraction of the tongue during coactivation of the protrudor and retractor muscles. In contrast, significant dilatation of the retroglossal airway during TES was observed in the present study only when the genioglossus muscle fibres were considered to be lengthened in

significantly narrowed or closed airway at lower P_{aw} . Accordingly, coactivation of the protruder and retractor muscles would cause narrowing of the retroglossal airway in an already dilated airway and cause dilatation of the airway in a significantly narrowed airway.

Interaction between the oropharynx and the velopharynx

Although no consistent influence of TES on the velopharyngeal pressure/area relationship was found in the present study, TES certainly modulated the mechanical properties of the VP supporting the notion of SCHWARTZ *et al.* [19]. Considering the anatomical arrangement of the OP and VP, interaction between the two segments can be speculated during TES. First, electric current may stimulate the palatoglossus muscle fibres, which influence velopharyngeal airway size and compliance. Secondly, mechanical connection between the segments through the palatoglossal arch possibly allows movement of the soft palate together with the tongue base. Thirdly, the tongue may have gravitational impact on the soft palate, the anterior wall of which attaches to the base of the tongue. Further studies are necessary for clarification of the mechanisms since the VP is the most common site of occlusion in patients with OSA during sleep [21], and, therefore, successful treatment of OSA by electrical stimulation may depend on the response of the velopharyngeal airway to the stimulation.

Clinical implication of the study

Since MIKI *et al.* [22] successfully reversed OSA by submental electrical stimulation, electrical stimulation of the upper airway muscles has been proposed as a possible new therapeutic approach to OSA. Succeeding studies in other laboratories, however, failed to obtain favourable responses to the procedure, although methodological differences exist among the studies [23–25]. The major criticisms include that electrical stimulation of the upper airway possibly resulted in restoration of a patent airway as a result of an arousal response to painful stimulation rather than the direct effect of electrical stimulation on the pharyngeal muscles. The technical difficulty in recording cortical activity during electrical stimulation has limited further examination of the possible contribution of the arousal response to airway patency. In this context, SCHWARTZ *et al.* [19] successfully stimulated the genioglossus only during inspiration without arousal by placing the electrodes into the musculature away from sensory nerves, and demonstrated an improvement in airflow dynamics as well as a reduction in the number of obstructive episodes in patients with OSA. In accordance with the results of SCHWARTZ *et al.* [19], the present study demonstrated that electrical stimulation of the tongue musculature improved pharyngeal collapsibility without interference from non-specific activation of the genioglossus in association with cortical arousal. The results, however, may not indicate that electrical stimulation of the upper airway is a useful alternative treatment for OSA since whether the intensity of the applied electrical stimulation level would not cause cortical arousal during natural sleep was not evaluated. Upper airway characteristics evaluated during the experimentally-induced apnoea in anaesthetized patients might differ from those during apnoeas in natural sleep.

In conclusion, contraction of the tongue musculature induced by electrical stimulation stiffened the oropharyngeal airway wall.

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