

Electrical stimulation of the lingual musculature in obstructive sleep apnea

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Schwartz, Alan R., David W. Eisele, Anil Hari, Roy Testerman, Donald Erickson, and Philip L. Smith. Electrical stimulation of the lingual musculature in obstructive sleep apnea. *J. Appl. Physiol.* 81(2): 643–652, 1996.—The influence of lingual muscle activity on airflow dynamics in the upper airway was examined in nine patients with obstructive sleep apnea. Muscles that retract the tongue (hyoglossus and styloglossus) and protrude the tongue (genioglossus) were selectively stimulated electrically during sleep with fine wire electrodes placed intramuscularly transorally. We confirmed that stimulation with 50 Hz and 40- μ s pulse duration did not elicit changes in electroencephalographic patterns or heart rate or alter airflow after the stimulation burst had ceased. The highest stimulus intensity that did not arouse patients from sleep was then utilized to examine the effect of lingual muscle recruitment on airflow dynamics during steady-state periods of inspiratory airflow limitation. When applying a stimulus burst during single inspirations, maximal inspiratory airflow decreased by 239 ± 177 ml/s ($P < 0.05$) during retractor stimulation, whereas maximal inspiratory airflow increased by 217 ± 93 ml/s during protrusor stimulation ($P < 0.001$) compared with breaths immediately before and after the stimulated breath. When consecutive inspirations were stimulated repeatedly, protrusor stimulation decreased the frequency of obstructive breathing episodes in four patients breathing at 3.9 ± 3.4 (SD) cmH₂O nasal pressure. The findings suggest that stimulation of the lingual muscles can increase or decrease airflow depending on the specific muscles stimulated without arousing patients from sleep.

genioglossus; upper airway; pharynx; hypoglossus; styloglossus; electrical stimulation

OBSTRUCTIVE SLEEP APNEA is due to periodic pharyngeal airway occlusion during sleep (10). The development of occlusion in this disorder has been related to prolapse of the tongue into the pharynx. Tongue prolapse, in turn, has been attributed to diminished neuromuscular activity in the genioglossus that protrudes the tongue when it is activated (16). Thus pharyngeal occlusion in obstructive sleep apnea may be due to reductions in genioglossal activity during sleep.

If a fall in genioglossal activity leads to pharyngeal occlusion, it should be possible to maintain pharyngeal patency by stimulating this muscle electrically. In fact, several groups of investigators have attempted to stimulate the genioglossus with transcutaneous (7, 15), percutaneous (6, 9), and intraoral electrodes (12). Although several different methods have been utilized, the influence of stimulating the genioglossus on pharyngeal patency is still not clear for two reasons. First, it is

not certain whether the genioglossus was recruited with each stimulation technique. Second, patients were reported to have aroused frequently when stimulation was applied (6, 9, 12). During arousal, improvements in pharyngeal patency can be attributed to nonspecific activation of the pharyngeal musculature (14, 20, 21, 33) rather than to a direct effect of electrical stimulation on the genioglossus. Therefore, the response in airway patency to selective electrical stimulation of the genioglossus during sleep is still not certain.

We therefore set out to stimulate the genioglossus selectively during sleep in apneic patients. Initially, stimulating electrodes were placed transorally near the proximal hypoglossal nerve trunk. We observed that electrical stimulation at this site caused the tongue to retract, suggesting that the hyoglossus and styloglossus rather than the genioglossus were recruited. After characterizing the effect of stimulating lingual retractors on airflow dynamics during sleep, we then placed electrodes transorally directly into the genioglossus. Recruitment of this muscle was suggested by the fact the tongue protruded when stimulated. Further evidence obtained during direct intra- and postoperative stimulation of these muscles confirms that our methods allowed us to selectively stimulate these muscles and will be reported separately. The present report discusses how selective stimulation of lingual muscles that retract (hyo- and/or styloglossus) and protrude (genioglossus) the tongue influence airflow dynamics during sleep in apneic patients. Our findings suggest that lingual muscles can play a prominent role in the control of airflow dynamics and the degree of pharyngeal obstruction during sleep.

METHODS

Subject Selection

Patients with obstructive sleep apnea referred to the Johns Hopkins Sleep Disorders Center were recruited for this study. Patients were eligible if they had an apnea-hypopnea index of >10 obstructive hypopneic and apneic episodes/h of non-rapid-eye-movement (NREM) sleep on a screening overnight sleep study. Patients with concomitant medical illnesses were excluded. Written informed consent for this study was obtained from each patient for a protocol that was approved by the Johns Hopkins Medical Institutions Human Investigations Review Board.

Experimental Techniques

Electrical stimulation. Fine-wire Teflon-coated stimulating electrodes (0.007 in., A-M Systems, Everett, WA) were uti-

lized for intramuscular stimulation. The stimulating electrodes were connected to a constant-current electrical stimulator (Dynex transcutaneous electrical stimulator, Medtronic, Minneapolis, MN). The muscles were stimulated with a pulse width of 40 μ s, a frequency of 30 Hz, and a burst duration of 1–1.5 s. The current level was then increased stepwise. The recruitment threshold was considered to be the lowest current level at which stimulation elicited tongue movement. When patients reported discomfort during stimulation at the recruitment threshold, the electrode pair was removed and other electrodes were repositioned. As current was increased further, tongue movement was observed. At still higher current levels, stimulation produced discomfort. The electrode pair that resulted in the greatest tongue movement without discomfort was then utilized for stimulation trials during sleep.

During sleep, the lingual musculature was stimulated during the inspiratory phase of the respiratory cycle. Synchronization with inspiration was achieved by triggering the stimulator when pressure in the hypopharynx or esophagus began to fall early in inspiration. The current level was then increased stepwise to maximize the effect of electrical stimulation on inspiratory airflow without arousing the patient from sleep. Results obtained at the highest level of electrical stimulation that did not arouse patients (see *Assessment of arousal*) are presented.

Stimulation site. A transoral approach was utilized to stimulate the lingual retractors and protrusors intramuscularly. Each muscle group was stimulated with two fine-wire Teflon-coated steel electrodes. As many as four electrodes were placed.

RETRACTOR MUSCLES. Electrodes were placed under topical anesthesia in the posterior gingivolabial sulcus. Single-hook wire electrodes were directed inferoposteriorly ~2 cm below the oral mucosa under local anesthesia. We speculated that the hyoglossus and styloglossus were recruited when stimulation led to tongue retraction and deviation toward the stimulated side (ipsilateral tongue deviation) (1–3). It has recently been confirmed that the tongue retracts and deviates ipsilaterally when direct intraoperative stimulation of the hyo- and/or styloglossus muscles is performed (Eisele, unpublished observations).

PROTRUSOR MUSCLES. Single-hook wire electrodes were placed just lateral to the frenulum and directed inferiorly ~2 cm below the oral mucosa under local anesthesia. Likewise, we speculated that the genioglossus was recruited when stimulation led to tongue protrusion and deviation away from the stimulated side (contralateral tongue deviation) (1–3). It has recently been confirmed that the tongue protrudes and deviates contralaterally when direct intraoperative stimulation of the genioglossus is performed (Eisele, unpublished observations).

Polysomnography. Standard polysomnographic techniques were employed to monitor respiratory responses to electrical stimulation during sleep. In brief, surface C₃-A₂ and C₃-O₁ electroencephalographic (EEG) electrodes, submental surface electromyographic (EMG) electrodes, and left and right electrooculograms were used to stage sleep. Electrocardiographic (ECG) electrodes were placed to monitor heart rate and rhythm. To monitor respiratory responses, each subject breathed through a tight-fitting nasal mask with a fixed leak and a variable airflow source at the inflow port (Respironics, Murrysville, PA). Pressure in the nasal mask (P_n) was measured with the catheter connected to a port. Airflow was monitored with a pneumotachometer connected to the breathing circuit. Esophageal pressure (P_{es}) was measured with an esophageal balloon, or pharyngeal (P_{ph}) and hypopharyngeal

pressures (P_{hp}) were monitored with saline-filled catheters at the rim of the soft palate and in the supraglottic space, respectively. All pressures, flows, and polysomnographic parameters were recorded continuously on a polygraph recorder.

All patients were monitored to assure that oral breathing did not occur in two ways. First, the patients were monitored visually with infrared video cameras to ensure that the mouth remained closed. Second, the level of biased airflow through the nasal continuous positive airway pressure (CPAP) circuit was examined as follows. Initially, the level of bias flow was established in each patient over a range of nasal CPAP pressures when the mouth was closed. Thereafter, a deviation in the bias flow level from these preestablished levels was taken to indicate that mouth and/or mask leaks had occurred. When this occurred, the sleep study was interrupted to refit the mask and seal the mouth with a chin strap or tape over the lips.

Assessment of arousal. Several parameters were examined to determine whether electrical stimulation produced an arousal from sleep. First, arousal was considered to have occurred if any change in the EEG (alpha rhythm, K complexes, or blocking artifact) or EMG (amplitude or blocking artifact) occurred either during or immediately after the stimulation period. Second, when stimulation did not produce EEG or EMG evidence for arousal, the effect of stimulation on heart rate and airflow was measured for the inspiration immediately preceding, during, and immediately after the stimulated breath. Because electrical artifacts from stimulation obscured the EEG and EMG patterns in selected patients, changes in the EEG and EMG patterns were examined during the expiration immediately after the stimulation period. Stimulated inspirations that were associated with EEG or EMG evidence for arousal were not analyzed.

Intramuscular Stimulation Protocols During NREM Sleep

Single-breath stimulation (lingual retractors and protrusor). **PROTOCOL.** The P_n was first raised to nearly eliminate inspiratory airflow ($\dot{V}_I$) limitation (for retractor stimulation) and to achieve steady-state periods of $\dot{V}_I$ limitation (for protrusor stimulation) during NREM sleep. $\dot{V}_I$ limitation was defined by the presence of a plateau in $\dot{V}_I$ at a maximal level as the pressure downstream in the hypopharynx or esophagus continued to fall (25). Stimulation was initiated at the onset of inspiration and was maintained for 1–1.5 s during the inspiration. Stimulation was performed during single inspirations in NREM sleep.

ANALYSIS. The level of maximal inspiratory airflow ($\dot{V}_{I_{max}}$) was then measured for each stimulated inspiration and for the inspirations immediately before and after stimulation. Patterns in the airflow and in the P_{hp} or P_{es} tracings were also examined during the stimulated inspiration to determine the presence or absence of $\dot{V}_I$ limitation, as previously described (24, 25, 31). Upper airway resistance (R_{ua}) was calculated as the pressure difference between P_n and P_{hp} at the point of $\dot{V}_{I_{max}}$ divided by the level of $\dot{V}_{I_{max}}$ (25).

Repeated stimulation (lingual protrusor only). **PROTOCOL.** Thereafter, P_n was lowered to a level associated with the development of recurrent apneas and hypopneas during NREM sleep and maintained at this level for ~10–15 min. Protrusor stimulation was then performed for each inspiration repeatedly for ~10–15 min of NREM sleep. Thereafter, another 10- to 15-min baseline period of nonstimulated breathing was obtained. This sequence was then repeated for as long as the patient was able to maintain sleep.

Table 1. *Anthropometric data*

Patient	Muscles Stimulated	Age, yr	Sex	Weight, kg	Height, m	BMI, kg/m ²
JL	HS	45	M	142.7	1.80	43.9
JaL	HS, G	30	F	139.5	1.78	44.1
JN	HS, G	37	M	104.0	1.76	33.0
MW	HS, G	46	M	116.8	1.73	39.2
DB	G	47	M	104.6	1.75	34.0
GC	G	59	M	163.6	1.71	56.2
LM	G	56	M	121.8	1.76	39.4
EP	G	39	M	106.4	1.75	34.6
SW	G	27	M	145.5	1.93	39.0

HS, hyo and/or styloglossus; G, genioglossus; M, male; F, female; BMI, body mass index.

ANALYSIS. During periods with and without stimulation, each disordered breathing episode (apnea or hypopnea) was scored with standard polysomnographic criteria, as previously described (30). In brief, the duration of each episode [disordered breathing time (DBT)], duration of apnea during each episode [apnea time (AT)], and baseline and low oxyhemoglobin saturation (Sa_{O_2}) were tabulated for each episode. The apnea-hypopnea index (episodes/h), the mean episode duration [AT-to-DBT ratio (AT/DBT)], and baseline and average low Sa_{O_2} values were then calculated for the entire sample periods with and without electrical stimulation.

Statistical Analysis

Repeated-measures analysis of variance or paired *t*-tests were employed to detect significant differences between stimulated and unstimulated periods as appropriate. Where significant differences were detected by analysis of variance, *t*-tests were performed to isolate these treatment effects.

RESULTS

Anthropometric and Polysomnographic Characteristics of Study Patients

The effect of stimulating the lingual musculature was examined in nine patients, eight men and one woman. Anthropometric characteristics of these patients appear in Table 1. The patients' age was 42.9 ± 10.8 (SD) yr and body mass index was 40.4 ± 7.2 kg/m². The retractor muscles were stimulated in four of these

patients, and the protruder was stimulated in eight of these patients.

Baseline polysomnographic data for these patients are shown in Table 2. Patients had evidence for severe obstructive sleep apnea with a NREM apnea-hypopnea index of 93.2 ± 20.3 episodes/h. All patients had been using nasal CPAP for therapy, which had been titrated to a mean level of 13.7 ± 3.1 cmH₂O, as previously described (31).

Polysomnographic Findings During Stimulation

Single-breath stimulation. To maintain relatively steady-state levels of inspiratory airflow during periods of airflow obstruction, Pn was set at levels associated with $\dot{V}_I$ limitation but no oxyhemoglobin desaturations or arousals from sleep. Stimulation of the retractors was performed at a mean Pn of 7.9 ± 2.6 cmH₂O and stimulation of the protruder muscle was performed at a Pn of 6.6 ± 3.2 cmH₂O. In one patient in whom the retractor muscle stimulation completely occluded the airway (JaL), Pn was raised to a level that nearly eliminated $\dot{V}_I$ limitation to fully assess the effect of stimulation. Representative polysomnographic recordings are illustrated for single stimulated inspirations in Figs. 1 (retractor stimulation) and 2 (protruder stimulation). In Fig. 1, the effect of retractor stimulation is illustrated for one patient (JaL) at a Pn of 16.8 cmH₂O. Stimulation was associated with a marked reduction in airflow and a more negative swing in Pnp (middle breath) compared with the nonflow limited breaths immediately before and after stimulation and was not associated with any change in EEG patterns. Protruder stimulation was associated with increases in $\dot{V}_{I_{max}}$ and reductions in Pnp compared with levels immediately before and after stimulation (Fig. 2). Such increases in $\dot{V}_{I_{max}}$ are shown for a brief stimulus burst (~ 0.5 – 0.75 s) within a single flow-limited inspiration (Fig. 2A) and for stimulus bursts of 2 and 3 s (Fig. 2, B and C, respectively) compared with breaths immediately before and after stimulation. In each example shown in Figs. 1 and 2, stimulation did not alter EEG patterns.

Prolonged periods of stimulation. Stimulation of lingual retractor muscles was maintained for longer than

Table 2. *Baseline polysomnographic data*

Patient	AHI, no./h		AT/DBT		SaO ₂ , %				Site of Obstruction	Therapeutic CPAP, cmH ₂ O
	NREM	REM			Baseline		Average low			
			NREM	REM	NREM	REM				
<i>JL</i>	122	107	0.11	0.06	96.9	94.9	83.4	75.4		12.0
<i>JaL</i>	124	105	0.75	0.55	92.8	94.3	68.9	59.3	NP	12.0
<i>JN</i>	82	73	0.05	0.07	97.0	96.8	91.9	88.8	NP	10.0
<i>MW</i>	99	78	0.48	0.67	96.1	96.2	92.4	72.9	NP	10.0
<i>DB</i>	88	80	0.38	0.90	97.8	97.8	89.5	81.0	OP	18.0
<i>GC</i>	82	63	0.25	0.48	91.9	90.9	70.9	67.6	NP	16.0
<i>LM</i>	59	55	0.79	0.71	94.2	92.3	73.5	61.5	OP	12.5
<i>EP</i>	95	77	0.30	0.20	95.0	95.4	81.9	85.3	NP	15.0
<i>SW</i>	88	84	0.63	1.00	91.2	88.0	72.8	68.8		18.0
Mean ± SD	93 ± 20	80 ± 17	0.42 ± 0.27	0.52 ± 0.35	94.8 ± 2.4	94.1 ± 3.1	80.6 ± 9.3	73.4 ± 10.2		13.7 ± 3.1

AHI, apnea-hypopnea index; AT/DBT, ratio of apnea time to disordered breathing time; Sa_{O_2} , oxyhemoglobin saturation; CPAP, continuous positive airway pressure; NREM, non-rapid eye movement; REM, rapid eye movement; NP, nasopharynx; OP, oropharynx.

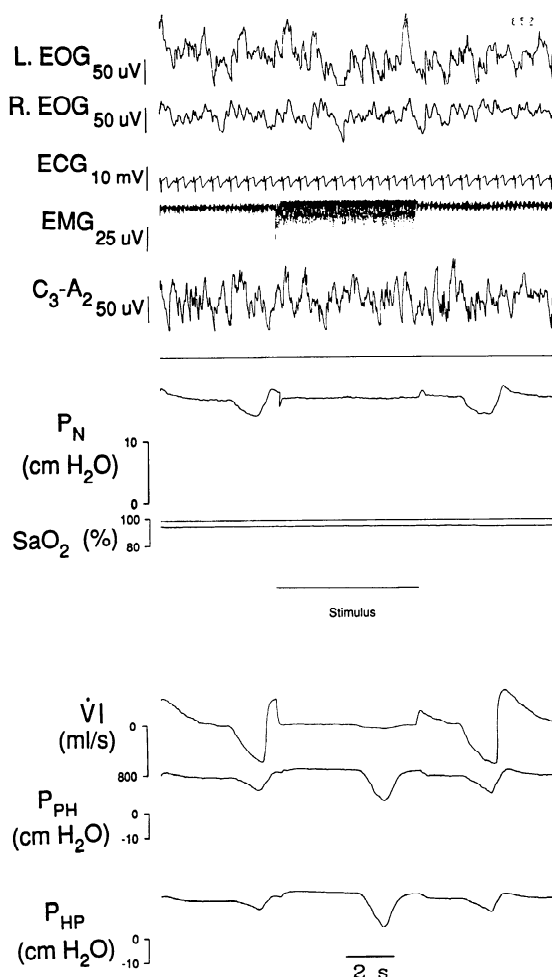


Fig. 1. Stimulation of lingual retractors for a single breath (*middle* inspiration). L.EOG and R.EOG, left and right electrooculogram, respectively; Pn, nasal pressure; SaO₂, oxyhemoglobin saturation; Vi, inspiratory airflow; Pph, pharyngeal pressure; Pph, hypopharyngeal pressure. Stimulus period (solid line) produced artifact in EMG trace. Vi was markedly reduced during stimulated inspiration compared with inspirations immediately before (*left*) and after (*right*) stimulation at 16.8 cmH₂O Pn. During stimulated inspiration, Pph and Pph swings increased. During stimulation, inspiratory Pph paralleled Pph and diverged from the signal, indicating that obstruction occurred in nasopharynx.

a single inspiration only once in one patient because it reduced airflow markedly (Fig. 3A). In this patient, a sustained 24.5-s period of stimulation (see high-amplitude high-frequency artifact in EMG trace) resulted in a near-complete cessation of airflow for four obstructed inspirations (Fig. 3A, compare *middle* with *left* part of tracing). In fact, an obstructive apneic episode with progressively negative swings in Pes, oxyhemoglobin desaturation, and an arousal from sleep (Fig. 3A, see change in EEG pattern in *right* part of Vi tracing) resulted. Airflow resumed during the arousal despite the fact that electrical stimulation was maintained for two breaths after the onset of arousal.

The lingual protruder was stimulated repeatedly during inspiration in four patients. In one patient,

electrical stimulation was discontinued for two breaths during periods of repeated electrical stimulation. A polysomnographic recording is shown for this patient in Fig. 3B. Of the six inspirations that appear in Fig. 3B, the first and last two were electrically stimulated (see high-frequency stimulation artifact in EEG, electrooculographic, and submental EMG channels). $\dot{V}_{I_{max}}$ was maintained at ~ 400 ml/s during the stimulated inspirations, whereas $\dot{V}_{I_{max}}$ fell to zero in the unstimulated breaths. The $\dot{V}_I$ plateaued during inspiration as Pes continued to fall, indicating the presence of airflow limitation in the stimulated (as well as unstimulated) breaths.

Stimulation and Arousal

EEG, ECG, and $\dot{V}_I$ signals were assessed for evidence of arousal in response to electrical stimulation as follows. First, no alterations in the EEG patterns were observed during or immediately after stimulus bursts (see examples in Figs. 1–3). Second, the R-R interval during the stimulated inspiration was 0.99 ± 0.25 s and was not significantly different from that during the inspirations immediately before (0.98 ± 0.25 s) or after (0.98 ± 0.24 s) the stimulus burst. Third, the level of $\dot{V}_{I_{max}}$ in the breath immediately after stimulation was not significantly different from that in the inspiration immediately preceding stimulation (326 ± 156 vs. 312 ± 131 ml/s; $P = 0.55$) for the entire group of nine patients. In fact, airflow returned to prestimulus levels even when a brief stimulus burst was applied within a single flow-limited inspiration (Fig. 2A). Therefore, changes in airflow during stimulation were closely related temporally in onset, duration, and offset to the stimulus burst period. Conversely, sustained retractor muscle stimulation maintained airway occlusion during sleep until a clear-cut EEG arousal occurred (Fig. 3A), suggesting that the effect of stimulation on airflow was independent of arousal from sleep. Moreover, the lack of any EEG or heart rate response to stimulation suggests that the responses in airflow were due to direct stimulation of the lingual muscles or to subcortical reflex activation rather than to generalized cortical activation of the pharyngeal muscles via central neural pathways.

Effect of Stimulation on Airflow

Lingual retractor stimulation. During single stimulated inspirations, a decrease in $\dot{V}_{I_{max}}$ was observed in each of four patients compared with the unstimulated breaths immediately before and after stimulation (Fig. 4). In the four patients, $\dot{V}_{I_{max}}$ decreased significantly ($P < 0.05$) during stimulation, whereas no significant change in R_{ua} was detected ($P = 0.40$). Stimulation was also associated with a nonsignificant increase in the percentage of flow-limited inspirations. These data are summarized in Table 3.

Lingual protruder stimulation. During single stimulated inspirations, an increase in $\dot{V}_{I_{max}}$ was observed in each of eight patients compared with the unstimulated breaths immediately before and after stimulation (Fig.

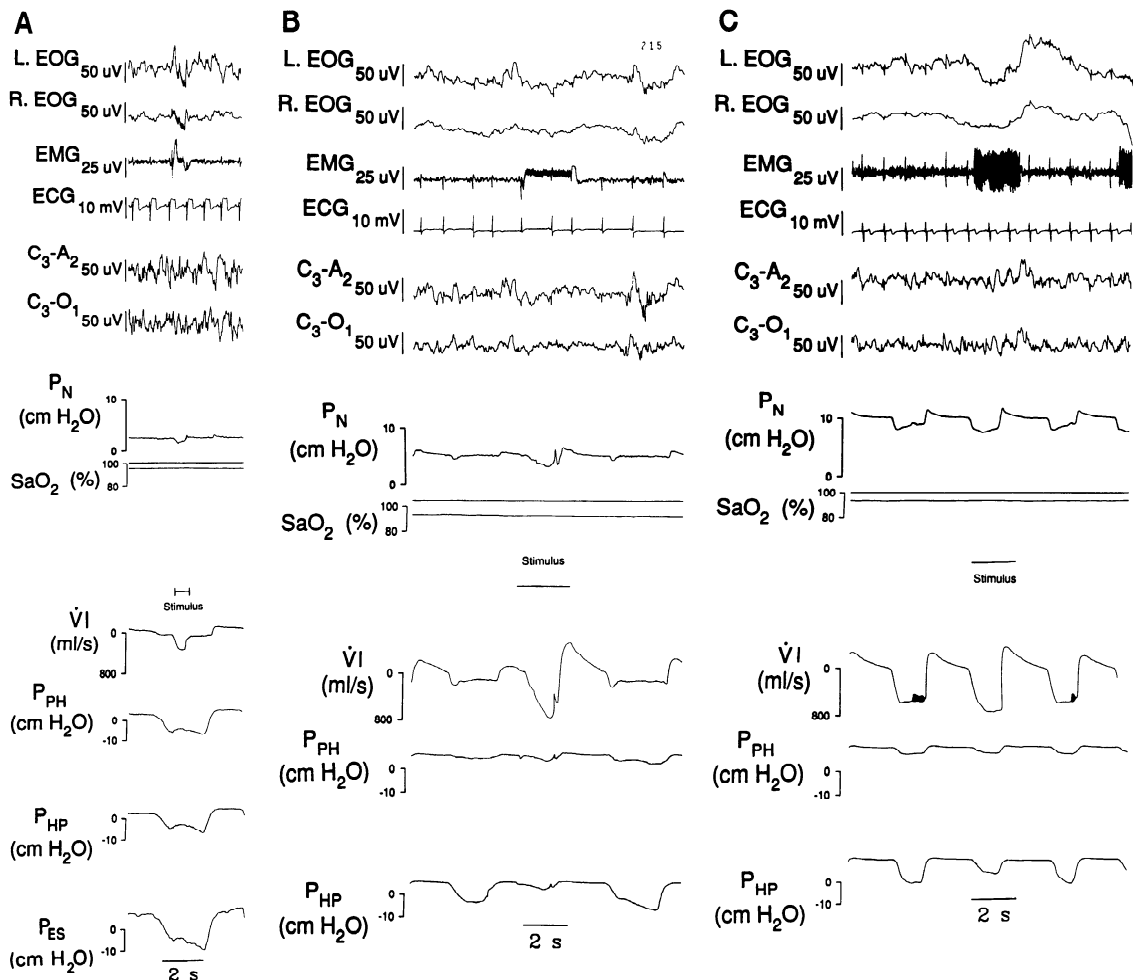


Fig. 2. Protrusor stimulation applied within a flow-limited inspiration (A) and for an entire inspiration (B and C) during non-rapid-eye-movement (NREM) sleep. Stimulation burst duration is shown, and stimulation artifact appears in EMG traces. In A, stimulus within a breath produced a prompt increase in $\dot{V}_I$ that returned to unstimulated levels when burst was over. Stimulation also attenuated rapid fall in P_{PH} , P_{HP} , and esophageal pressure (P_{ES}). In B and C, $\dot{V}_I$ increased during stimulated breath compared with breath immediately before and after stimulation. P_{PH} and P_{HP} swings during stimulation were reduced. In A–C, no changes in EEG pattern were observed during or after stimulation. In B and C, inspiratory P_{PH} paralleled P_n and diverged from P_{HP} signal during flow-limited unstimulated breaths, indicating presence of airflow obstruction in oropharynx.

5). In this patient group, $\dot{V}_{I_{max}}$ increased significantly ($P < 0.001$) and R_{ua} decreased significantly ($P = 0.03$). Stimulation was associated with a decrease in the percentage of flow-limited inspirations ($P < 0.001$). These data are summarized in Table 4.

Effect of Lingual Protrusor Stimulation on Apnea Severity

In four patients, electrical stimulation was performed repeatedly during consecutive inspirations for 34.0 ± 12.6 min at a P_n of 3.9 ± 3.4 cmH₂O. Polysomnographic characteristics of apneas for periods of on- and off-stimulation at the same level of P_n are reported in Table 5. Repetitive stimulation of each inspiration resulted in a decrease in the apnea-hypopnea index during the ~30-min stimulation period from $65.6 \pm$

11.5 to 9.0 ± 5.8 episodes/h in this group (Fig. 6). No significant changes in event duration, AT/DBT, or baseline or average low SaO_2 values were observed during electrical stimulation.

DISCUSSION

In this study, we examined how lingual muscles control upper airway airflow dynamics during sleep by electrically stimulating these muscles in apneic patients. The major findings were as follows. First, it was possible to selectively stimulate muscles that both retract and protrude the tongue. The motor movement produced by stimulation in each of two sites was consistent with recruitment of the hyoglossus and styloglossus when the tongue retracted ipsilaterally and with recruitment of the genioglossus when the

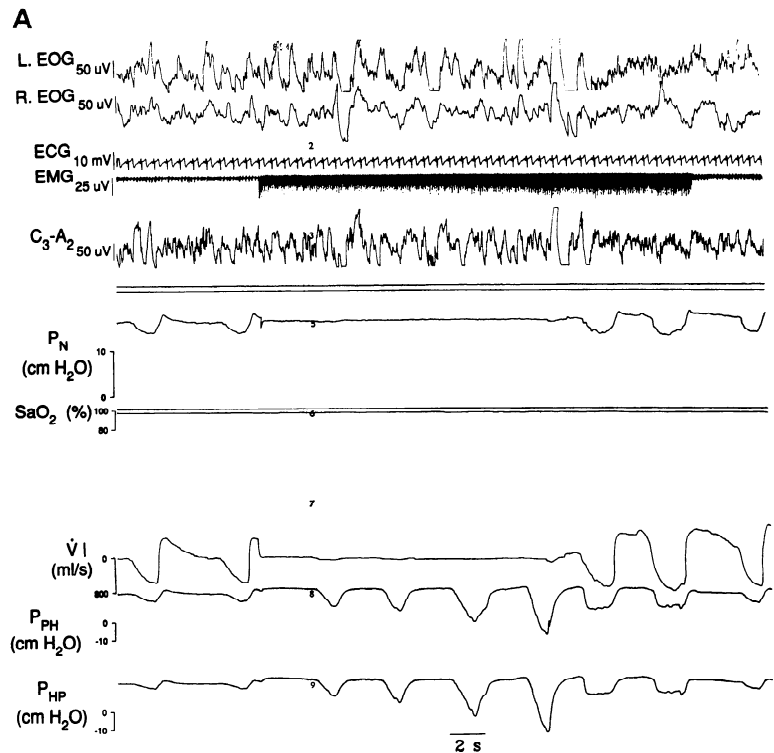
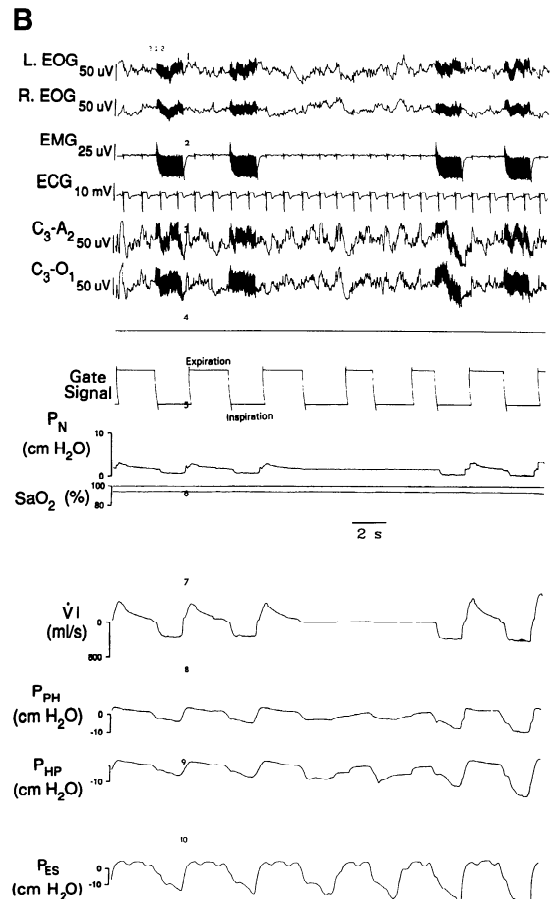


Fig. 3. Effect of continuous electrical stimulation. A: stimulation of lingual retractors in an apneic patient breathing at 16.8 cmH₂O P_N. In *left* one-third of tracing, airflow is normal during NREM sleep. Stimulation was maintained continuously during *middle* one-third of tracing (see high-amplitude stimulus artifact in EMG tracing). It resulted in near cessation of airflow for 4 breaths. An EEG arousal then occurred. Airflow resumed for 2 breaths despite continued stimulation and was maintained in final breath after turning stimulation off. During obstructed breaths, inspiratory P_{ph} diverged from and paralleled P_{hp} signal, indicating presence of nasopharyngeal obstruction. B: repetitive protrusor stimulation in a patient breathing at 1.6 cmH₂O P_N. Stimulation was applied during inspiration (see gate signal and high-frequency stimulus artifact in EOG, EMG, and EEG channels) for 1st 2 and last 2 breaths illustrated. $\dot{V}_I$ was maintained during these breaths compared with *middle* 2 unstimulated breaths in which airflow is zero. During obstructed breaths, inspiratory P_{ph} diverged from P_N and paralleled P_{hp} signal, indicating presence of nasopharyngeal obstruction.



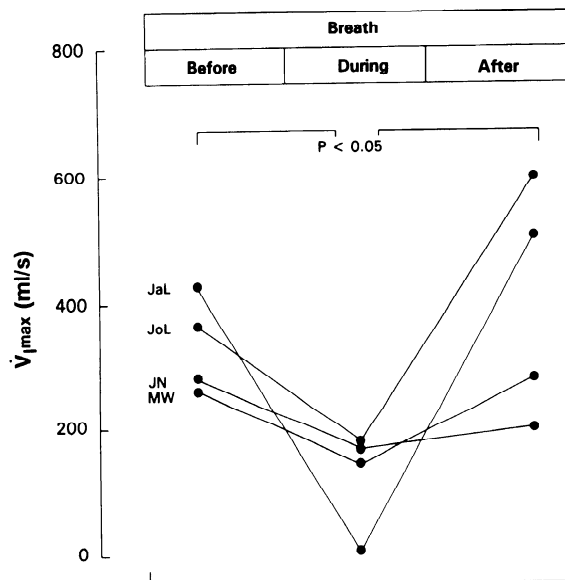


Fig. 4. Mean maximal $\dot{V}_I$ ($\dot{V}_{I_{\max}}$) levels for each of 4 patients before, during, and after retractor stimulation.

tongue protruded contralaterally. Second, our analysis of EEG, heart rate, and airflow patterns suggests that electrical stimulation did not arouse patients from sleep, thereby excluding nonspecific generalized activation of the pharyngeal musculature. Third, intramuscular stimulation of the hyo- and/or styloglossus muscles decreased $\dot{V}_{I_{\max}}$ during sleep, whereas stimulation of the genioglossus increased $\dot{V}_{I_{\max}}$ significantly and abolished $\dot{V}_I$ limitation in nearly one-half of the stimulated inspirations. Reductions in R_{ua} during genioglossal stimulation suggest that stimulation dilated the upper airway. During extended periods of repetitive genioglossal stimulation, apnea severity was attenuated in a subgroup of our patients who were exposed to low levels of nasal CPAP. Our results suggest that the tongue and its musculature play a major role in the control of pharyngeal airflow dynamics during sleep.

There are two reasons we believe it possible to attribute observed changes in airflow dynamics to the action of specific lingual muscles. First, both anatomic and functional considerations point to the recruitment of specific lingual muscles. Specifically, the stimulating electrodes were positioned anatomically in the region of muscles known to retract and protrude the tongue. When these sites were stimulated, tongue movements were consistent with the known actions of the genioglossus and hyo- and/or styloglossus muscle groups (1–3).

Table 3. Hyo- and/or styloglossal stimulation

	Before	During	After
$\dot{V}_{I_{\max}}$, ml/s	345 ± 77	137 ± 79*	407 ± 187
R_{ua} , cmH ₂ O · l ⁻¹ · s	11.6 ± 3.5	61.6 ± 89.9	17.1 ± 14.6
%Flow-limited inspirations	94.5 ± 11.0	100 ± 0	87.3 ± 21.1

Values are means ± SD; $n = 4$ patients. $\dot{V}_{I_{\max}}$, maximal inspiratory airflow; R_{ua} , upper airway resistance. Nasal pressure during stimulation was 7.9 ± 2.6 cmH₂O. * $P < 0.005$ vs. before and after stimulation.

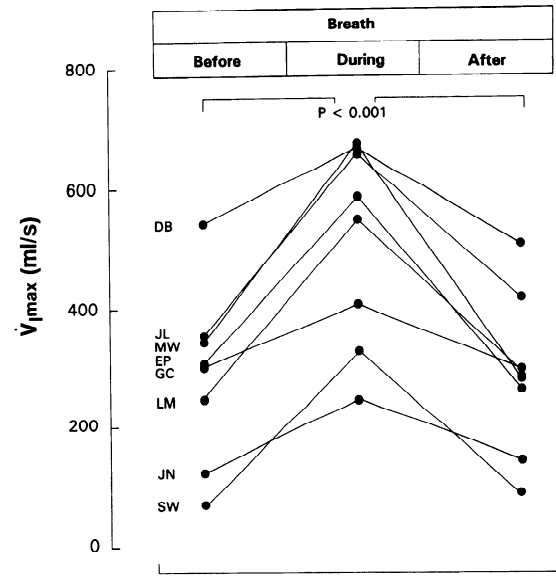


Fig. 5. Mean $\dot{V}_{I_{\max}}$ levels for each of 8 patients before, during, and after protrusor stimulation.

Moreover, we have since found that direct intraoperative stimulation of the hypoglossal nerve branches that innervate these muscles produced identical tongue movements. Therefore, we have good evidence that specific muscles known to protrude (genioglossus) and retract (hyoglossus and styloglossus) the tongue were stimulated with our intramuscular electrodes.

Second, electrical stimulation of the lingual muscles was performed without arousing patients from sleep. In fact, we demonstrated that it was possible to stimulate without changes in EEG patterns, $\dot{V}_{I_{\max}}$, and heart rate between breaths immediately before and after stimulation. Our findings stand in contrast to those of others (6, 9) who demonstrated sustained changes in airflow with stimulation when cortical arousal occurred. When patients arouse, increases in airflow may be attributed to generalized activation of the pharyngeal musculature rather than to isolated recruitment of the lingual musculature. Therefore, these findings support the notion that stimulation altered pharyngeal airflow dynamics by selectively recruiting specific lingual muscles. Moreover, the effect of lingual muscle activation on the severity of pharyngeal airflow obstruction in apneic patients suggests that the tongue plays a major role in controlling pharyngeal patency during sleep.

Table 4. Genioglossal stimulation

	Before	During	After
$\dot{V}_{I_{\max}}$, ml/s	288.1 ± 176.2	501.4 ± 195*	284.3 ± 162.1
R_{ua} , cmH ₂ O · l ⁻¹ · s	25.7 ± 32.4	13.3 ± 12.8†	27.2 ± 34.8
%Flow-limited inspirations	100 ± 0	52.9 ± 23.9‡	99.3 ± 2.1

Values are means ± SD; $n = 8$ patients. Nasal pressure during stimulation was 6.6 ± 3.2 cmH₂O. * $P < 0.001$ vs. before and after stimulation. † $P \leq 0.03$ vs. before and after stimulation. ‡ $P < 0.001$ vs. before and after stimulation.

Table 5. *Effect of genioglossal stimulation on apnea severity*

Patient	Nasal Pressure, cmH ₂ O	Time, min		AHI, no./h		Event Duration, s		AT/DBT, %		SaO ₂ , %			
		Off		On		Off		Off		Baseline		Average low	
		Off	On	Off	On	Off	On	Off	On	Off	On	Off	On
JN	2.0	46.0	36.0	57.4	3.3	22.0	28.0	11	0	98	95	93	93
EP	8.9	11.5	24.0	73.0	5.0	12.2	20.0	0	0	95	96	92	94
LM	1.5	18.5	25.0	77.8	12.2	18.4	19.0	0	0	96	95	89	91
SW	3.0	10.5	51.0	54.3	15.4	28.6	28.0	16	10	98	98	97	97
Mean $\pm$ SD	3.9 $\pm$ 3.4	21.6 $\pm$ 16.6	34.0 $\pm$ 12.6	65.6 $\pm$ 11.5	9.0 $\pm$ 5.8	20.3 $\pm$ 6.9	23.8 $\pm$ 4.9	6.8 $\pm$ 8.1	2.5 $\pm$ 5.0	97 $\pm$ 2	96 $\pm$ 1	93 $\pm$ 3	94 $\pm$ 3

It is noteworthy that our stimulation methods allowed us to recruit the lingual muscles without arousing patients from sleep because other investigators have reported a high frequency of arousal during electrical stimulation. Our success may be attributed to differences in stimulation methods that allowed us to recruit lingual muscles without sensory activation. Discomfort was avoided presumably by positioning the electrodes in close proximity to motor nerve fibers. Better anatomic positioning of the stimulating electrodes allowed motor recruitment during stimulation without current spread to sensory nerves. Indeed, we also found that patients predictably aroused from sleep when higher levels of current were applied (see METHODS). Thus we conclude that our stimulation techniques allowed us to examine the effect of motor recruitment without sensory stimulation or cortical arousal from sleep.

The precise mechanism for changes in pharyngeal airflow dynamics during lingual muscle stimulation is largely unknown. Recently, Edmonds et al. (7) confirmed that the pharynx widened when apneic patients voluntarily protruded their tongue. The fact that Rua declined in our patients strongly suggests that the pharyngeal airway indeed widened during genioglossal stimulation. These observations are also consistent with the notion that the genioglossus dilates the pharynx by pulling the tongue forward, as has been shown in previous observations in anesthetized humans (18, 19, 29) and experimental animals (32). Indeed, airflow

obstruction decreases when apneic patients wear dental appliances (5, 8) and undergo surgical procedures (17) that passively pull the tongue forward. Thus both active and passive maneuvers that protrude the tongue dilate the pharynx and relieve airflow obstruction during sleep.

In theory, muscles that dilate the pharynx can increase $\dot{V}_{I_{max}}$ in two ways. These muscles may decrease either pharyngeal collapsibility [critical pressure (P_{crit})] and/or the nasal resistance (R_n) upstream to the site of pharyngeal collapse (25–28). In fact, the relationship between genioglossal activity and $\dot{V}_{I_{max}}$ has already been examined in several experimental systems. In the isolated rabbit upper airway, Brouillette and Thach (4) found that P_{crit} rose as genioglossal activity fell with progressive deepening in the level of anesthesia and postulated that the genioglossus modulates pharyngeal collapsibility. In the isolated feline upper airway, Schwartz et al. (27) demonstrated significant decreases in P_{crit} and increases in $\dot{V}_{I_{max}}$ during hypoglossal nerve stimulation. In this study, it was possible to attribute observed increases in airflow to a fall in pharyngeal collapsibility (P_{crit}) because R_n remained constant or actually increased during stimulation. Thus there is good evidence in animals that increased airflow during genioglossal stimulation was due to a reduction in pharyngeal collapsibility. Although P_{crit} and R_n were not measured in the present study, current evidence suggests that the alterations in $\dot{V}_{I_{max}}$ during lingual muscle stimulation were probably due to changes in pharyngeal collapsibility.

We note that airflow obstruction was localized to the oropharynx in two of our patients and to the nasopharynx in five other patients (see Table 2 and Fig. 5). Despite differences in the site of obstruction between patients, we observed a similar directional change in airflow in each patient and little variability in the response of airflow to stimulation. Similarities in the response of oropharyngeal and nasopharyngeal obstructors to stimulation suggest that the tongue modulates collapsibility at both sites. The influence of the tongue on nasopharyngeal collapsibility probably stems from the fact that the tongue overlies the soft palate in the supine patient. Depending on the force exerted by lingual protrusor or retractor muscles, the tongue may either decrease or increase collapse of the nasopharyngeal segment, respectively. Similarly, the tongue is thought to modulate oropharyngeal collapsibility because lingual retractors compress and protrusors tether

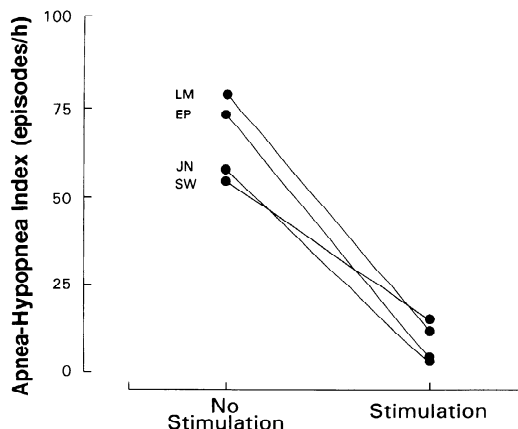


Fig. 6. Effect of repetitive protrusor stimulation on apnea-hypopnea index in 4 patients.

this segment. Thus it is likely that the lingual musculature modulates the collapsibility of each pharyngeal segment by altering the direction and magnitude of radial forces applied to the airway lumen.

Although measurements of pharyngeal collapsibility (P_{crit}) were not made, it is still possible to estimate the magnitude of the change in pharyngeal collapsibility from the alterations in $\dot{V}_{I_{max}}$ that we observed. In the present study, we noted a mean decrease in $\dot{V}_{I_{max}}$ during hyo- and/or styloglossal stimulation of 239 ml/s and a mean increase in $\dot{V}_{I_{max}}$ during genioglossal stimulation of 215 ml/s. These findings suggest that stimulation of the lingual musculature can produce changes in $\dot{V}_{I_{max}}$ over a dynamic range of nearly 500 ml/s, a level of $\dot{V}_{I_{max}}$ that is comparable in magnitude to that during normal tidal breathing. Based on previous studies in our laboratory, we would predict that such a change in $\dot{V}_{I_{max}}$ would be caused by a 13- to 16-cmH₂O difference in P_{crit} (11, 24). In fact, the magnitude of the P_{crit} difference during sleep is comparable to that previously demonstrated between normal and apneic individuals (24, 31). Our approximation may underestimate the dynamic range in P_{crit} produced by lingual muscle stimulation because these muscles were only stimulated unilaterally. Regardless of the precise magnitude of the changes, our findings strongly suggest that the tongue and the tension generated by its muscles can play a major role in modulating pharyngeal airflow dynamics during sleep.

The fact that $\dot{V}_{I_{max}}$ increased by >200 ml/s during genioglossal stimulation has clinical implications for the treatment of obstructive sleep apnea. An increase in $\dot{V}_{I_{max}}$ of this magnitude would imply a fall in P_{crit} of ~4.8 (22) to 9.8 cmH₂O (11). When P_{crit} falls by this amount, significant reductions in the apnea-hypopnea index and complete remission of obstructive apnea have been documented (22, 23). Our finding that apnea severity diminished during short-term repeated stimulation of the genioglossus is consistent with the notion that some therapeutic benefit may be derived from this approach. Nevertheless, the response to genioglossal stimulation was obtained on moderate levels of nasal CPAP and $\dot{V}_I$ limitation was not completely abolished by stimulation. The persistence of airflow obstruction during stimulation may be attributed to incomplete recruitment of the genioglossus with our unilateral fine-wire needle electrodes or may suggest that other muscles including the contralateral genioglossus, cervical strap (13), and palatal (33) play a role in maintaining airway patency during sleep. With further studies, the role of the genioglossus in maintaining airway patency at specific sites of pharyngeal obstruction, as well as the potential therapeutic utility of electrical stimulation, should be examined.

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