

Relief of Upper Airway Obstruction With Hypoglossal Nerve Stimulation in the Canine

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Hypoglossal nerve stimulation was investigated as a method to relieve an induced upper airway obstruction. Six dogs were implanted with a cuff electrode applied to each hypoglossal nerve and a pulse generator. After 4 weeks, the hypoglossal nerve was stimulated (50% duty cycle) for up to 8 weeks. At 12 weeks a double tracheotomy was placed, with a negative pressure intermittently applied to the upper limb, simulating inspiratory airway pressure. Unilateral hypoglossal nerve stimulation improved peak upper airway flow from an average of 0.1 L/s to 1.6 L/s ($P = 0.0001$). Seventy-seven percent of the maximum possible flow (explanted tracheotomy tube) was obtained with unilateral stimulation. Histopathological evaluation revealed no nerve damage secondary to chronic stimulation. This study provides support for clinical trials of hypoglossal stimulation for obstructive sleep apnea.

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INTRODUCTION

Occlusion of the upper airway during sleep is a distinguishing feature of obstructive sleep apnea (OSA).¹ Despite continued respiratory effort, obstruction of the pharyngeal airway prevents effective ventilation. The resulting hypoxia and hypercapnea progress until arousal occurs and airway patency is reestablished.² Obstructive sleep apnea increases the patient's susceptibility to cardiovascular disease and hypoxic complications. Excessive daytime sleepiness associated with OSA impairs work

and social functioning and increases the risk of accidents while driving or at work.³

The pharynx is the only area of the upper respiratory tract that lacks substantial bony or cartilaginous support. The position and stiffness of the anterior and lateral pharyngeal walls and the patency of the pharyngeal airway depend on the activity of pharyngeal dilator muscles.⁴ The most common sites of pharyngeal obstruction are at the level of the soft palate and behind the tongue.⁵ In each individual the relationship between the anatomic size of the pharyngeal airway and the activity of the pharyngeal dilator muscles determines the ability of the pharynx to maintain patency.⁶

The genioglossus muscle is the tongue protrusor muscle and its activity is responsible for anterior positioning of the tongue and tongue base. Genioglossus muscle fibers contract during inspiration⁷ as part of a reflex that is initiated by the presence of negative pharyngeal airway pressure.⁸ Pharyngeal dilator muscles that respond to negative pressure during inspiration, such as the genioglossus, tend to maintain their activity during non-rapid eye movement (non-REM) sleep.⁷ Pharyngeal dilator muscles that exhibit little respiratory change in activity, such as the tensor palatini, demonstrate a progressive decrease in electromyogram (EMG) activity with deepening levels of non-REM sleep.⁹ The cumulative result is an increase in upper airway resistance during non-REM sleep.

Obstructive sleep apnea is an anatomic problem. Patients with OSA have a structurally smaller pharyngeal airway than nonapneic control patients.¹⁰ The phasic activity of the genioglossus muscle is increased approximately three times normal during wakefulness in OSA patients to compensate for the anatomic restriction of flow.¹¹ In nonapneic individuals during sleep the inspiratory phasic activity of the genioglossus muscle is maintained at normal awake levels. In individuals with OSA, there is a large reduction of genioglossus muscle activity during sleep from the elevated levels seen when awake.^{1,12} Reduced genioglossus activity can also be seen after sleep deprivation and use of alcohol or sedatives. The loss of genioglossus muscle activity is associated with a decrease in airway patency and collapse of the pharyngeal airway.

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Electrical stimulation of the hypoglossal nerve, which innervates the genioglossus muscle, can potentially compensate for the decrease in genioglossus muscle activity seen in OSA patients during sleep. Functional electrical stimulation has been used therapeutically for ventilatory insufficiency, upper and lower extremity neuromuscular-assist devices, control of intractable pain, control of incontinence, and inhibition of epileptic seizures.¹³ In acute experiments, electrical stimulation of the lingual musculature improved inspiratory airflow in animals¹⁴ and patients with OSA.^{15,16} Application of hypoglossal nerve stimulation for the treatment of OSA would require long-term electrode implantation.

The purpose of the current study is to determine the feasibility of chronic implantation of an electrode on the hypoglossal nerve in a canine model. The ability of the chronically implanted electrode to improve pharyngeal airflow during an induced apnea is studied and the hypoglossal nerve-electrode interface is examined.

MATERIALS AND METHODS

Six adult dogs weighing 19 to 26 kg were used in the study. Animals were cared for according to the Physiologic Research Laboratories Standard Operating Procedures and *The Guide for Care and Use of Laboratory Animals*. The protocol was approved by the Institutional Animal Care and Use Committee of the Physiologic Research Laboratories Division of Medtronic, Inc.

Implantation

After a standard quarantine and overnight fast, the animals were sedated with 0.2 mg/kg of acepromazine. Hair was shaved in the anterior cervical and right chest regions. An intravenous catheter was placed and approximately 20 mL of a 2.5% thiopental sodium solution was given. The animal was intubated, given isoflurane to effect, and mechanically ventilated. A midline vertical incision was made in the neck and the hypoglossal nerve was exposed bilaterally. A tripolar cuff electrode (Model 3990A, Medtronic Inc., Minneapolis, MN) (Fig. 1) was placed around the medial branch of each hypoglossal nerve. One electrode was secured to the muscle underlying the hypoglossal nerve with a 4-0 prolene suture in each animal. The electrode on the contralateral hypoglossal nerve was placed without an anchoring suture. The side of the sutured electrode (right vs. left) was alternated between animals. A separate skin incision was made over the right chest wall and a subcutaneous pocket was created. The lead body of both stimulating electrodes was passed through a subcutaneous tunnel to the subcutaneous pocket in the chest wall. A strain relief loop was made in each lead body and the lead body anchored to underlying tissue. Both lead bodies were connected to a single implantable pulse generator (IPG) (Itrel 3, Medtronic Inc.) via a lead connector (Model 5866-40M, Medtronic Inc.). The cervical and chest incisions were closed in two layers and a Penrose drain was placed in the neck via a separate stab incision.

Unipolar and tripolar thresholds for each electrode were obtained by programming the implantable pulse generator with a console programmer (Model 7432, Medtronic Inc.) and monitoring tongue movement visually and by palpation of the suprahyoid region. A stimulus frequency of 30 Hz with a 90- μ s pulse width was used. Thresholds were determined by averaging the lowest voltage producing palpable suprahyoid movement with serially increasing (up threshold) and decreasing (down threshold) 0.1 volt steps. Fluoroscopic images were recorded (Model 9600 digital fluoroscope, OEC Medical Systems, Inc., Salt Lake City, UT) to confirm electrode position. The animals were

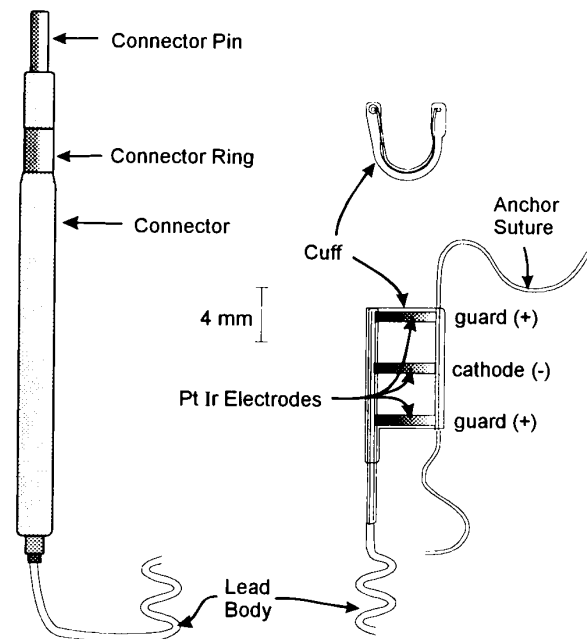


Fig. 1. The Medtronic Model 3990A electrode used to stimulate the hypoglossal nerve. The half-cuff configuration contains three platinum iridium (Pt Ir) electrodes, two outer anodes (guards), and one central cathode. The electrode cuff is 3 mm in diameter and 9 mm long. The lead body is 45 cm in length and joins the cuff to the lead connector, which inserts into the implantable pulse generator.

bandaged and recovered. The drain was removed on postoperative days 2 to 4.

Implant Monitoring

Awake, sedated monitoring of the IPG and stimulating electrode was performed at 1, 2, 3, 4, 6, 8, and 10 weeks after implantation and at the terminal experiment (12 weeks). The animals were given 0.2 mg/kg of acepromazine. Unipolar-center (center electrode foil vs. IPG), unipolar-guard (outside guard foil vs. IPG), and tripolar up and down thresholds were averaged for each electrode with the method used immediately after implantation.

Chronic Stimulation

Chronic, unilateral stimulation of the hypoglossal nerve was begun at 4 weeks after implant. Chronic stimulation was maintained for 8 hours per day, 7 days per week. The stimulus frequency was 30 Hz, with a 90- μ s pulse width and a 50% duty cycle of 5 seconds on and 5 seconds off. Voltage amplitude was placed at a level at which visible tongue movement occurred but caused no visible discomfort. The stimulus amplitude was set and recorded daily. The animal was stimulated on the left side on weeks 4 to 6 and 8 to 10. Right-sided stimulation was performed on weeks 6 to 8 and 10 to 12. Chronic stimulation was not performed in the event of electrode failure on the side scheduled for stimulation.

Terminal Experiment

The animals were sedated with 0.2 mg/kg of acepromazine. An intravenous catheter was placed and approximately 20 mL of a 2.5% thiopental sodium solution was given. The animal was in-

tubated, given isoflurane to effect, and mechanically ventilated. Glycopyrrolate (0.01 mg/kg) was given to control airway secretions. A final implant monitoring was performed and fluoroscopic images were recorded to confirm electrode position. Fluoroscopic images were recorded of electrode and tongue position in one animal with and without stimulation. A midline vertical incision was made exposing the cervical trachea. A double tracheotomy was performed with the caudal endotracheal tube passed into the lower trachea and used to ventilate the animal. A second endotracheal tube was passed through the cephalad tracheotomy with the distal tip at the level of the vocal cords. The jaw was opened to an angle of 30° with short lengths of plastic tubing acting as a bite block. The stimulating electrode connections to the implanted pulse generator were exposed and attached to an external stimulator (Model 3625, Medtronic, Inc.). In the event of electrode failure, hypoglossal stimulation was achieved by stimulating proximal to an electrode lead break or by unipolar stimulation in the case of an electrode foil break or partial electrode displacement.

A pneumotachograph (Hans Rudolph, model 3700, Kansas City, MO) and a vacuum generator (Eureka Mighty Mite vacuum cleaner) controlled by a waveform generator (Model 75, Wavetek, Inc., San Diego, CA) were attached to the cephalad endotracheal tube. All pneumatic and electrical signals were synchronized from a single wave form generator. Hypopharyngeal pressure was measured using a pressure transducer (Model PDM 205, Air-Neotronics, LTD, Oxford) attached to a side pressure port attachment to the upper endotracheal tube. Hypopharyngeal pressure, hypoglossal stimulation, and pharyngeal airflow were measured and recorded on a chart recorder (Model ES2000, Gould Instrument Systems, Inc., Cleveland, OH) and on digital cassette tape (TEAC RD-111).

The vacuum generator was adjusted to deliver a maximum negative pressure of 12 to 18 cm of water against an obstructed rostral endotracheal tube. The waveform generator applied a smooth (raised cosine) pressure wave with a duration of 6 seconds. Hypoglossal nerve stimulation was synchronized with the start of the vacuum cycle and maintained for 4 seconds (40 Hz, 100 μ s pulse). Stimulation was begun at 0 milliamperes (mA) and gradually increased in approximately 2 mA steps until a maximum airflow was obtained. After a maximum airflow had been obtained for each side, the cephalad endotracheal tube was removed from the trachea. Negative pressure was applied and airflow recorded to determine the maximum potential airflow for the system.

Following collection of airflow data, the animals were killed with a potassium chloride solution. The electrode cuffs and sections of hypoglossal nerve were removed and placed in a 10% buffered formalin solution. All 12 specimens were sectioned and stained with hematoxylin and eosin (H & E) and Trichrome. Two transverse sections of each nerve and electrode cuff were examined.

RESULTS

The experiment was completed in all six animals. All animals tolerated the stimulation and maintained their preoperative weight. One animal (dog #6926) had a seroma noted at the time of explantation. No other wound complications occurred.

Lead Failure

The number of functioning implantable stimulation systems over the course of the experiment is presented in Figure 2. Electrode failure was defined as no detectable tongue movement with 12-volt stimulation or an impedance of greater than 4000 Ω , which implies an incomplete circuit. Two nonsutured electrodes were displaced from the

hypoglossal nerve. This occurred prior to implant monitors #6 (dog #6926) and #7 (dog #6911). One sutured electrode was partially displaced off the hypoglossal nerve (dog #6943). The remaining failures occurred secondary to breakage of the lead body, electrode cuff foil, or both (Table I). Implanted stimulation systems with a sutured cuff lasted an average of 9 weeks, with two systems functioning at termination, while systems with a nonsutured cuff lasted an average of 8 weeks (one system functioning at termination). The different methods of securing the electrode cuff did not affect the longevity of the stimulating system ($P > 0.05$, paired T-test).

Chronic Stimulation

Because of electrode breakage the animals received an average of 5 weeks of chronic stimulation (range, 2 to 8 weeks). The average stimulus amplitude applied during chronic stimulation was 2 volts (range, 1 to 2.9 volts). Chronic stimulation was performed at an average of 0.7 volts over threshold (range, 0.4 to 1 volt). The animals quickly adapted to the induced tongue movement and were able to easily maintain oral intake. No discomfort secondary to stimulation was observed.

Stimulation Threshold During Implant Monitoring

The average stimulation threshold of intact electrode systems during each monitoring session is presented in Figure 3. At implantation, the stimulation thresholds were low at 0.19 ± 0.12 volts tripolar. By week 1 the tripolar stimulation threshold had increased to 1.13 ± 1.34 volts. After week 2 the average tripolar stimulation threshold of functioning units stabilized between 1.38 and 2.24 volts. No trend toward increasing threshold was seen between weeks 2 and 12. Unipolar stimulation thresholds using the center foil or the two outside guard foils as cathode and the IPG as an anode followed a similar pattern and allowed incorporation of a larger number of electrode systems.

Effect of Stimulation on Induced Pharyngeal Airway Obstruction

Hypoglossal stimulation was able to be performed in 11 of the 12 electrode-hypoglossal nerve units. The only failure occurred in a displaced electrode (dog #6926, left side, nonsutured). A stimulation threshold was obtained in the other displaced cuff (dog #6911, left side, nonsutured) with unipolar-guard stimulation. Hypoglossal stimulation was achieved in other failed electrodes by stimulating proximal to an electrode lead break or by unipolar stimulation in the case of an electrode foil break. The hypopharyngeal pressure, pharyngeal airflow, and stimulus timing for an animal with and without unilateral hypoglossal nerve stimulation are demonstrated in Figure 4. The maximum airflow obtained with and without unilateral hypoglossal nerve stimulation in each trial is presented in Figure 5. An average of 7.7 ± 3.3 mL was required to achieve maximum airflow with stimulation. Unilateral hypoglossal nerve stimulation improved peak upper airway flow from an average of 0.1 ± 0.08 L/s to 1.6 ± 0.5 L/s ($P = 0.0001$, paired t-test). An average of 77% of the maximum possible flow (ex-

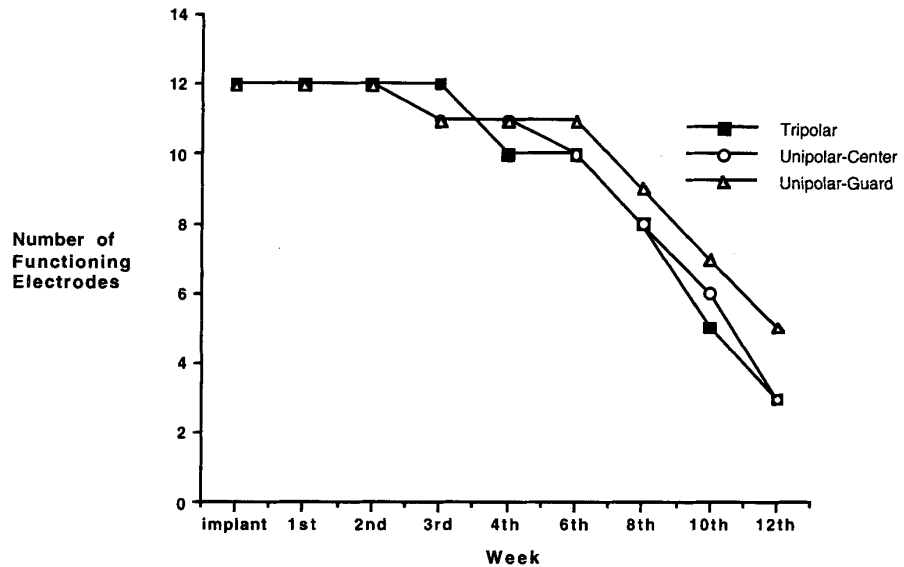


Fig. 2. The number of electrodes functioning over the 12-week implantation. Electrodes were monitored for tripolar stimulation and unipolar stimulation using the center foil and the two outside guard foils as cathode and the implantable pulse generator as an anode.

planted endotracheal tube) was obtained with unilateral stimulation. Termination of the stimulus resulted in an abrupt decrease in airflow to nonstimulation levels.

Fluoroscopic Examination

Fluoroscopic imaging of the electrode cuffs during a 50% duty cycle stimulation in one animal revealed bilateral electrode movement. The stimulated electrode moved 1.4 cm and the contralateral electrode moved 0.9 cm with each stimulation. Slight deformation of the electrode cuff was observed during stimulation. Lateral fluoroscopic images of the tongue base in the animal studied demonstrated a forward displacement of the posterior tongue base with stimulation. The posterior pharyngeal wall remained in stable position, resulting in an increased pharyngeal space.

Histologic Results

All 12 nerves and electrode cuffs were examined histologically. An example is presented in Figure 6. The in situ location of the electrode cuff (represented by a C-shaped clear space) was delineated by a fibrous sheath having an inner wall (along the concave surface) and outer wall (along the convex surface). The outer sheath wall consisted of dense fibrous tissue 0.08- to 0.4-mm thick that was discontinuously lined at the device interface by an infiltrate of histiocytes. The inner sheath wall

closely circumscribed the nerve and was contiguous with collagenous fibers of the outer epineurium. The inner sheath wall consisted of a thin rim of fibrous tissue near the arms of the cuff, with progressively thicker (0.4 to 1.7 mm) fibrous ingrowth at the concave surface. Histologic evidence of active fibrous tissue growth between the nerve and electrode cuff was present in seven of the 10 specimens in which this could be adequately evaluated. No significant histologic lesions were noted in the hypoglossal nerve, endoneurium, or perineurium.

DISCUSSION

In this study we examined the feasibility of chronic hypoglossal nerve stimulation in a canine model. The canine hypoglossal nerve tolerated the electrode implantation and an average of 5 weeks of unilateral daily stimulation with no detectable neuropathic changes. Although the half-cuff electrode design was safe, problems with electrode stability occurred. Stimulation of the hypoglossal nerve was effective in improving airflow in an induced pharyngeal airway obstruction model 3 months after implantation of a half-cuff stimulating electrode. In intact electrodes, the stimulation threshold remained stable after 2 weeks.

Postimplantation Neurohistopathology

The hypoglossal nerve showed only minimal histologic changes as a result of the study protocol. Functional electrical stimulation subjects the nerve to both mechanical and electrical trauma. The mildest form of mechanically induced neuropathy consists of a thickening of the epineurium due to the accumulation of connective tissue along the inner surface of the electrode. Increases in subperineurial and endoneurial connective tissue are found with additional trauma. With severe damage, endoneurial edema, demyelination, axonal degeneration, and axonal loss can occur. Subperineurial crescents of thickened connective tissue are commonly seen when a mild abrasive

TABLE I.
Number of Electrode Failures by Site and Implant Method.

	No Breaks (Functional)	Foil Break Only	Lead Break Only	Foil and Lead Break	Displaced Off Nerve*
Suture	1	2	2	1	1 (partial)
Nonsuture	2	1	2	1	2 (1 complete)

*Displaced electrodes also demonstrated foil or lead breaks.

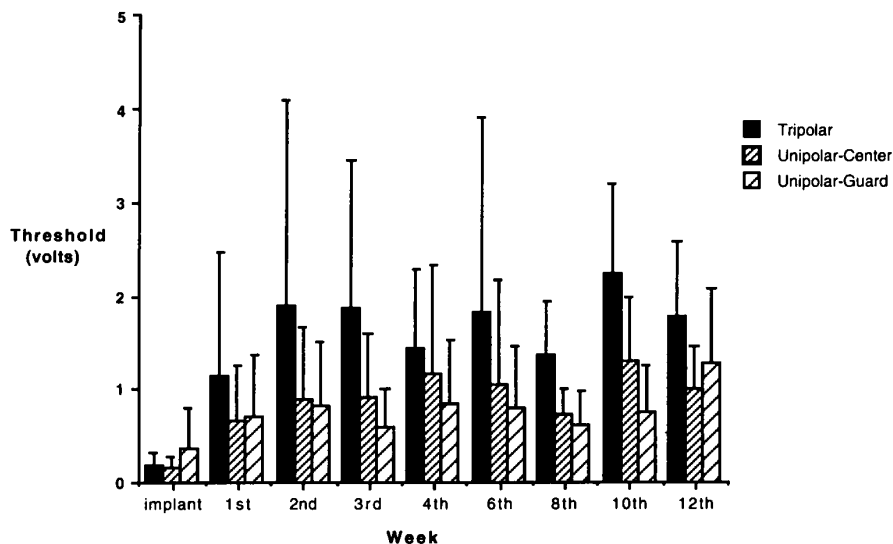


Fig. 3. Average stimulation threshold in volts to obtain tongue movement over the 12-week implantation. Averages include threshold measurements from functioning electrodes. (See Figure 2.)

injury, rather than a compressive injury, occurs.¹³ Histologic examination of the hypoglossal nerve in the present study revealed only a thickening of the epineurium with no endoneurial changes. Functional nerve stimulation was accomplished in all hypoglossal nerves with a cuff in position after a 3-month implantation.

Surgical manipulation of the nerve was kept to a minimum and less than a 2-cm section of nerve was circumferentially dissected to place the electrode cuff around the hypoglossal nerve. Preservation of the perineurial vasculature of a peripheral nerve is important in reducing postsurgical neuropathy.¹⁷ Naples et al.¹⁸ recommended a

number of electrode cuff characteristics that reduce mechanically induced neuropathy for peripheral nerves in general. First, the electrode should avoid nerve compression by allowing for postimplantation edema. Second, the electrode should closely approximate the nerve so that it moves with the nerve during stimulation, avoiding abrasion of the epineurium. Third, the lead body should apply minimal traction to the electrode cuff, which could torque or compress the nerve. The half-cuff electrode used in this study was designed to avoid compression of the nerve secondary to postoperative edema. Problems that we observed with electrode displacement necessitate further re-

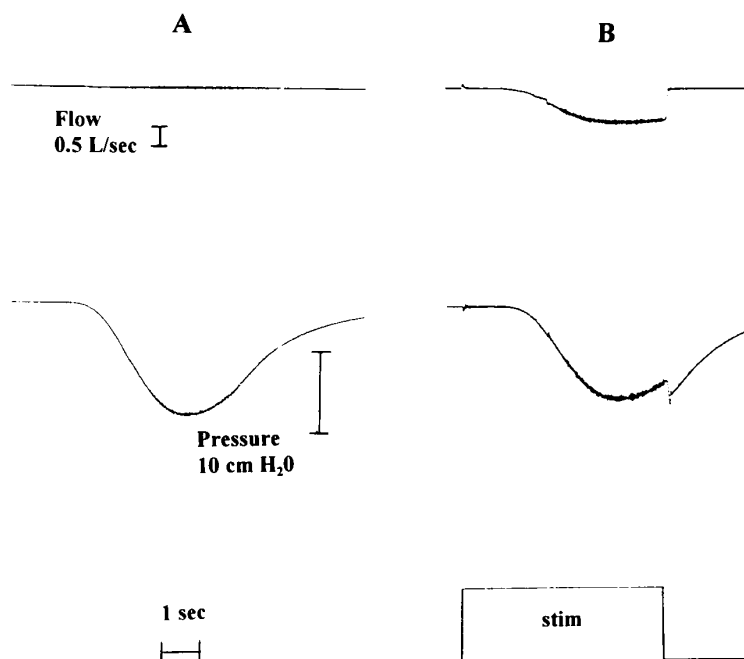


Fig. 4. Pharyngeal airflow, hypopharyngeal pressure, and hypoglossal stimulation timing (dog #6926, trial #7 in Figure 5). A negative deflection denotes inspiratory air flow (top row) and decreased subglottic pressure (second row). Note that without stimulation, the airway is completely occluded (A). Maximal stimulation (B) opened the airway, but the pressure/flow relationship was nonlinear. Flow was limited to about 860 mL/sec, and independent of further increases in hypopharyngeal pressure. Note also that the airway immediately closed when stimulation ceased.

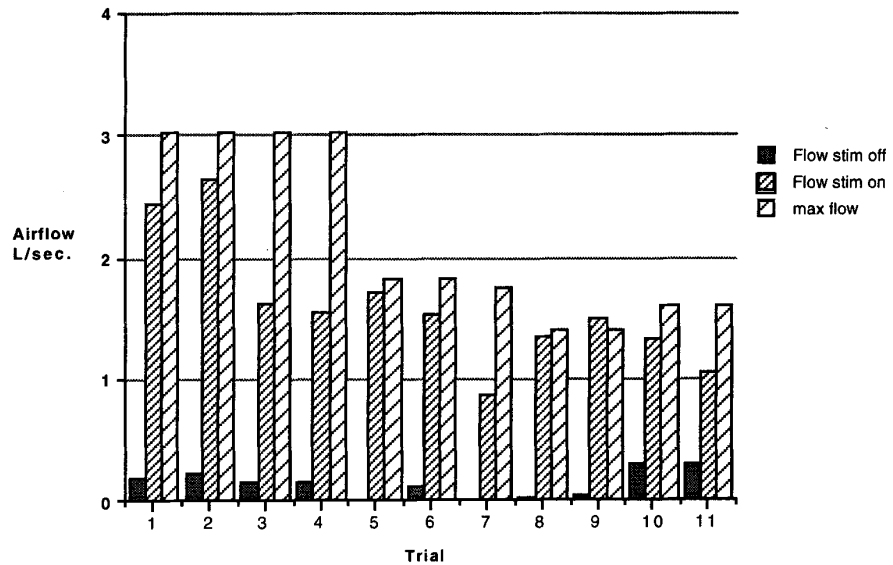


Fig. 5. Pharyngeal airflow in liters per second during induced pharyngeal obstruction for each of the 11 trials. Each trial represents air flow results with one of the 11 electrodes able to produce hypoglossal stimulation during the terminal experiment (see text). Flow stim off = airflow without hypoglossal stimulation; flow stim on = airflow with hypoglossal stimulation; max flow = airflow through endotracheal tube removed from pharynx.

finement in electrode design to insure long-term contact between the nerve and electrode.

Prolonged electrical stimulation (8 to 16 hours) at high frequency (50 to 100 Hz) and pulse amplitude (2.5 mA) produces irreversible axonal injury in the cat peroneal and sciatic nerve.¹⁹ Irreversible injury is characterized by endoneurial edema at 48 hours and early axonal degeneration at 1 week after stimulation. Two to 3 weeks after damaging electrical stimulation, axonal degeneration and fiber loss is present along with an endoneurial infiltration of macrophages. Long-term stimulation of the canine phrenic nerve has been performed without morphologic changes detected by light or electron microscopic examination.²⁰ A narrow pulse duration, reduced stimulation frequency, and intermittent duty cycle tend to reduce the chances for neural damage.¹³ A short pulse duration was chosen to increase stimulus efficiency and to increase the threshold differences between larger nerve fibers and smaller sensory fibers.²¹ The intermittent nature of respiration was modeled by using a 50% stimulation duty cycle. These adjustments to the stimulation protocol further reduced the potential for nerve injury.

Electrode Failure

Hypoglossal nerve stimulation in the canine model resulted in considerable stress applied to the electrode. This was manifested by the high number of electrode foil and lead breaks that occurred during the study. In electrodes that withstood the protocol, the stimulation threshold was maintained at levels similar to that seen 2 weeks after implantation. The majority of electrodes, however, failed during the study. The canine model is therefore felt to be a severe test of electrode stability. The movements of the head and neck were not restricted during the duration of the experiment other than by a circumferential bandage during the first 2 to 4 days. Comparing anthropometric data²² with animal data obtained in the laboratory, the estimated expansion of the lead with cervical exten-

sion and rotation in the canine was estimated to be at least twice what is seen in humans. Lack of adequate strain relief results in breakage of the lead body.¹³ Although strain relief loops were placed at the time of implantation, these loops were often found to be fibrosed where the lead body crossed itself, negating some of the effectiveness of the loop. No lead breaks were detected until the fourth implant monitor (4 weeks after implantation). It is at this time when wound tensile strength is increasing.²³ It is likely that encapsulated and adherent strain relief loops became less effective at this time. A resulting increased strain on the lead body with similar changes in neck position could result in eventual lead failure.

Chronic stimulation of the hypoglossal nerve was delayed until 4 weeks after implantation in our study. This amount of time was chosen to allow fibrosis to form around the electrode cuff to hold it in position and reduce abrasion from the relative movement between the nerve and electrode. Despite this, a significant strain was applied to the electrode cuff. Movement of the cuff with ipsilateral or contralateral hypoglossal stimulation produced a repetitive shearing force on the half-cuff electrode design. Distortion of the electrode cuff was confirmed in the one animal that underwent fluoroscopic examination during a stimulation trial. That shearing stress on the cuff was greater with repetitive hypoglossal stimulation than spontaneous tongue movement is implied by the absence of cuff displacement prior to the onset of chronic stimulation. Gradual deposition of fibrous tissue within the electrode over the course of the experiment likely increased the ease of cuff displacement.

Pharyngeal Airflow

The tongue is a major determinant of upper airway collapsibility.¹ Anterior displacement of the tongue will widen the pharyngeal luminal size and overcome a pharyngeal airway obstruction.²⁴ Dental appliances²⁵ and surgical procedures³ designed to position the tongue ante-

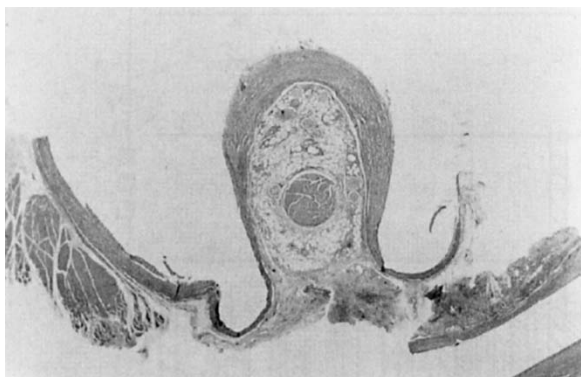


Fig. 6. Histologic section of hypoglossal nerve and surrounding electrode cuff space (H&E stain, original magnification $\times 15$). Note thickening of inner wall sheath fibrous tissue in concavity of electrode cuff and lack of endoneurial changes.

riorly can reduce airflow obstruction during sleep. Anterior displacement of the tongue base was a prominent effect of hypoglossal stimulation in the one canine undergoing fluoroscopic examination in the present study. Protrusion of the tongue was seen in all animals during hypoglossal stimulation. Active displacement of the tongue base and enlargement of the pharyngeal airway occurs during normal respiration to position the tongue and optimize pharyngeal airflow.⁵ The increase in size of the pharyngeal airway is directly related to the degree of genioglossus muscle activity.²⁶

In patients with OSA, a substantial reduction in genioglossus activity occurs with the onset of sleep.^{1,12} The anterior position of the tongue seen during wakefulness is lost and pharyngeal collapse and airflow obstruction occurs. Functional electrical stimulation of the hypoglossal nerve has the potential to increase genioglossus activity and reposition the tongue base anteriorly, allowing improved pharyngeal airflow. Because the primary anatomic problems of OSA are left intact, pharyngeal airflow would be improved only during periods of hypoglossal nerve stimulation. Nerve stimulation would need to coincide with inspiration.

Electrical stimulation of the feline hypoglossal nerve resulted in a decrease in pharyngeal collapsibility and an increase in pharyngeal airflow.¹⁴ Intramuscular stimulation of the genioglossus and direct stimulation of the hypoglossal nerve in patients with OSA was also found to increase inspiratory airflow during sleep.^{15,16} Complete elimination of airflow limitation in humans, however, could not be obtained without supplemental continuous positive airway pressure. Effective genioglossal stimulation was able to be performed without arousing the patient from sleep or causing changes in the EEG pattern. Airflow improvement was seen in patients whether the

pharyngeal obstruction was localized to the oropharynx or nasopharynx.

The present study confirms the effectiveness of hypoglossal nerve stimulation in opening the pharyngeal airway in an animal model. The current protocol produced consistent lingual movement at stable stimulation thresholds in intact electrodes over a 3-month period. The effectiveness of hypoglossal nerve stimulation in the treatment of OSA can only be determined in patient studies. The safety of long-term hypoglossal nerve stimulation is supported by the present study. The half-cuff design and stimulation parameters were well tolerated by the hypoglossal nerve and animal as a whole. Difficulties in electrode stability were related to the increased movement of the animal model as well as electrode design characteristics. Our results suggest that with some electrode design modification, hypoglossal nerve stimulation has the potential to be an important adjunct in the treatment of OSA in patients that are not adequately relieved by current noninvasive therapies.

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