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IEEE Trans Biomed Eng. Author manuscript; available in PMC 2010 April 1.

Published in final edited form as:
IEEE Trans Biomed Eng. 2009 April ; 56(4): 1154–1159. doi:10.1109/TBME.2008.2007968.

Design of a New Somatosensory Stimulus Delivery Device for Measuring Laryngeal Mechanosensory Detection Thresholds in Humans

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Abstract

Laryngeal control is essential for airway protection, breathing, deglutition, speech, and voice. Unfortunately, integration of laryngeal sensory assessment in research and clinical practice is limited by technical and practical limitations of commercially available technology. A commercial device is available, but reported limitations include procedural complexity requiring two or three individuals to operate, limited stimulus dynamic range, device generated noise, and questionable stimulus reproducibility. The objective of this study was to design a new laryngeal somatosensory stimulus delivery device that provides direct, reliable control over the timing, duration, and dynamic range of stimulus presentation, and test the device in individuals who may manifest a laryngeal sensory deficit. The new device operates silently and has more than four times greater stimulus dynamic range than the commercial device. Testing with the new device revealed laryngeal mechanosensory detection thresholds in an individual with Parkinson's disease that were seven times higher than those of healthy controls. These data would have otherwise gone undetected due to limited stimulus dynamic range in the commercial device. The new design resulted in a new assessment instrument that is simple to use for routine clinical assessment, yet sufficiently versatile for integration within rigorous clinical research protocols.

Index Terms

Assessment; detection thresholds; larynx; mechanoreceptor; Parkinson's disease (PD); sensory

I. Introduction

Laryngeal control is essential for airway protection, breathing, deglutition, speech, and voice. Evidence suggests that rapidly adapting mechanoreceptors located within the laryngeal mucosa [1]–[6], innervated by the tenth cranial nerve, may serve as the primary somatosensory organs for encoding and guiding laryngeal movements [7]–[13]. In animal studies, impaired laryngeal somatosensation has been associated with movement errors, abnormal patterns of vocalization and deglutition, and aberrant changes in contractile properties and fiber type of the intrinsic laryngeal muscles [14]–[17]. However, the role of somatosensation in human laryngeal control remains poorly understood.

A better understanding of afferent-guided laryngeal control in humans will be useful in designing appropriate assessment and intervention related to deficits in airway protection, ventilatory regulation, deglutition, speech, and voice. Sources of aberrant laryngeal sensory

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function in humans may include gastroesophageal reflux, medication, neuropathy, oncologic intervention, and trauma. Similarly, such causes of abnormal sensation have also been associated with a variety of upper airway abnormalities, and increased risk of airway obstruction, dysphagia, dysarthria, and respiratory infection [16], [18], [19]. These types of deficits increase morbidity and mortality and can occur across the life span from infancy through senescence. Unfortunately, integration of laryngeal sensory assessment in both research and clinical practice has been relatively limited in part due to technical and practical limitations of commercially available technology. Reported device limitations include procedural complexity requiring two or three individuals to operate, limited stimulus dynamic range, device-generated noise, and questionable stimulus reproducibility [20]–[24].

Laryngoscopic stimulus delivery is a valuable option to assess laryngeal sensory function [25]. In this approach, a brief pulse of pressurized air passes through the port of a transnasal laryngoscope to stimulate the mucosa surrounding the larynx. Given the nature of aerodynamic events (e.g., air pressure, air-flow) available for encoding by the mucosal sensorium of the larynx, a pressure-calibrated air pulse is a logical choice as a natural stimulus that minimizes potential risk. In response to the air pulse stimulus, the participant may acknowledge feeling the stimulus by raising a hand or pushing a button, or the examiner may record the participant's laryngeal reflexive response to the stimulus.

In clinical practice, a commercially available device (Pentax AP-4000) commonly exhibits stimulus pressure instability and may fail to generate a stimulus [24]. During stimulus presentation, the solenoid valve within the commercial device generates a mechanical noise, providing an auditory cue. Patients may report confusion as to whether they feel the somatosensory stimulus or simply hear the noise. In addition, constant background noise generated by an air compressor in the commercial device may make it difficult for patients to hear instructions from the examiner. Finally, the distance between the stimulus control dial on the chassis of the commercial device and the laryngoscope necessitates two or three examiners to achieve laryngeal visualization, stimulus delivery, and adjustments to the stimulus gain. These and other limitations provided the impetus for a new instrument (Table I). Therefore, the objective of this study was to design a new laryngeal somatosensory stimulus delivery device that provides direct and reliable control over the timing, duration, and dynamic range of stimulus presentation, and to test the device in individuals who may manifest laryngeal sensory deficits.

II. Methods

A. Circuit Design

Fig. 1 is a block diagram of the stimulus delivery paradigm. Two primary electrical circuits are used as the backbone of the new laryngeal somatosensory stimulus delivery device: 1) a pressure control circuit and 2) a solenoid driver control circuit. The purpose of the *pressure control circuit* is to manually control stimulus pressure by hand using a ten-turn knob potentiometer fastened to the housing of the laryngoscope. A pressurized air source (pressurized medical grade air cylinder) is coupled in series to the input port of the pressure control device. The output port of the pressure control device is connected in series to an air reservoir (two 2-L laboratory vacuum bottles) and is coupled to a normally closed solenoid valve (Parker). Adjustments made to the ten-turn potentiometer knob result in a dc voltage between 0.00 and 10.00 V. This voltage control signal is applied to the electronic control input of the pressure control unit. Adjustments to this input voltage result in a proportional change of the inline reservoir air pressure between 0.00 and 10.00 psi (0.00–68.93 kPa). This stimulus-pressure-control dial is affixed to the transnasal laryngoscope, and enables the examiner to adjust the stimulus pressure while visualizing the larynx.

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The *solenoid driver control circuit* utilizes the Texas Instruments DRV-102 solenoid driver [26] and is activated by a +5-V TTL input signal received from a pulse generator (Berkley Nucleonics, 565). When the solenoid valve is opened, a burst of air at the selected pressure is released to atmosphere, or through the port of the transnasal laryngoscope, for the duration the solenoid is in the open position. This design feature enables the investigator to custom-select the stimulus duration. The *circuit control box* is designed with an ON/OFF switch on the front panel and contains all associated electrical components for the pressure control and solenoid valve control circuits. A connector on the front panel of the circuit control box provides a voltage output signal that is calibrated in proportion to the stimulus pressure level. In addition, the new device includes a foot switch to interrupt the presentation of stimuli when adjusting between stimulus levels. Each of these design features provides direct and reliable control over the timing, duration, and dynamic range of stimulus presentation, and requires only one individual to operate.

B. Noise Attenuation

In order to attenuate the noise generated by the activation of the solenoid valve, the solenoid, tubing, and reservoir of the new device are contained within a triple-walled enclosure of 0.75 in (19.05 mm) medium-density fiberboard, and are surrounded by layers of sound damping material (Sonex). Use of the sound attenuating enclosure prevents any potential acoustic cues of the device from imposing a bias on participant responses.

C. Bench Testing

For comparison, bench testing was performed using the new device and the commercial device (Pentax AP-4000). Bench tests were performed using both the FNL-13RAP and FNL-10RAP transnasal laryngoscopes (Pentax) positioned 2 mm from a calibrated pressure sensor (MPX2010D, Freescale Semiconductor). The length and diameter of the air pulse channel of each laryngoscope was identical (1.2 mm ID, 350 mm length), but the overall diameter of the FNL-13RAP (4.1 mm) was greater than that of the FNL-10RAP (3.4 mm), providing more fiberoptic bundles for improved illumination and imaging of the larynx.

D. Human Testing

For additional comparison, one adult with Parkinson's disease (PD) and a group of five healthy adult controls participated in testing using each device. Four additional adults with PD were also tested using the new device. Each participant provided informed consent to participate. This study was conducted in accordance with the National Institutes of Health (NIH) regulations for the ethical treatment of human subjects and was approved by the local institutional ethics committee for the safety of human subjects. PD1 was 67 years old and at Hoehn and Yahr Stage III [28], indicating moderate severity of PD at the time of testing, and had a 12-year history of PD. PD1 participated in testing under two conditions: "medication OFF" and "medication ON." Medication dosage included carbidopa-levodopa (Sinemet) 50/200 and ropinirole hydrochloride (Requip) 24 mg. The four additional PD participants were at Hoehn and Yahr Stage III, and were also tested OFF and ON medication.

1) Signal of Interest—Laryngeal Mechanosensory Detection Threshold—The primary signal of interest for laryngeal mechanosensory detection threshold (LMDT) testing was the pressure (mm Hg) of the air burst stimulus applied to the laryngeal mucosa overlying the superior surface of the arytenoid cartilage at which the participant acknowledged feeling the stimulus by pressing a hand-held switch.

2) Triggered Stimulus Delivery—All stimulus presentations were triggered by the initiation of the expiratory phase of respiration as transduced using inductance

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plethysmography (Respiratory Monitoring, Inc.). During the onset of expiration, the TTL from a threshold discriminator (Coulbourn LabLinkV) triggered a control pulse from a pulse generator (Berkley Nucleonics 565) resulting in event-related triggering of the air burst stimulus. Because the commercial device did not contain a triggered input, the investigator installed one prior to testing. The new device design included a triggered input. A stimulus duration of 135 ms was selected to provide a more salient stimulus and avoid potential problems with temporal summation that may also have accounted for previous difficulties in obtaining thresholds with the commercial device that provided a fixed stimulus duration of only 50 ms.

A topical decongestant (e.g., neosynepherine) was used with each participant. A transnasal laryngoscope (Pentax FNL-13RAP) was placed into the most patent naris of each participant (see Fig. 1). No anesthesia was administered to maintain mucosal sensitivity that would be diminished with topical anesthesia [19] and given the demonstrated minimal discomfort accompanying transnasal laryngoscopy in the absence of topical anesthesia [27]. Visual guidance from a display monitor was used to direct the distal end of the laryngoscope to the mucosa overlying the superior surface of the arytenoid cartilage. The air burst port of the laryngoscope was luer-lock coupled to the end of a 3-ft-long (91.44 cm) rigid polyethylene tube (1.2 mm ID). The opposite end of the tubing was luer-lock coupled to the air burst output port of the commercial or new device.

Each participant was instructed to press a hand-held switch as soon as a stimulus was detected. Pressing the switch resulted in a +5-V signal displayed on an oscilloscope (Tektronix TDS 2004) and digitized at 1000 Hz. A “positive response” was defined as a +5-V response by the participant within a 2.5-s window beginning at the midpoint of the stimulus control signal. All participants found the hand-held switch easy to use. The time interval between stimulus presentations was randomized, with a minimum of 5 s between stimuli. The stimulus level of the air burst source was decreased by 1.00 mm Hg until no response was elicited from the participant. Once no response was elicited, the stimulus level was increased by 0.50 mm Hg until a “positive response” was elicited. Then, the stimulus was decreased by 0.10 mm Hg. This process continued until the threshold level was reached. The LMDT was defined as the level of stimulus pressure at which the participant responded 50% of the time following six crossings of the same stimulus level.

For each participant, the investigator’s index finger was positioned on the scope tube at the nasal inlet during stimulus presentation once the target position was achieved in an attempt to maintain a constant distance from scope tip to arytenoid mucosa of 2 mm. Adjustments to scope position were made between stimulus presentations as necessary. Within a scope tip to tissue distance of 2–3 mm, individual blood vessels within the vocal fold became very easy to visualize [23]. Based on preliminary bench top calibration and stimulus testing, the air burst stimulus output from the laryngoscope appeared to be laminar with little to no variation in output delivered to targets within 2–5 mm from the scope tip. Therefore, an additional attempt to standardize distance was made by ensuring that at least 50% of the monitoring screen was occupied by the arytenoid unit during each stimulus presentation. Verification was accomplished using two excised human adult cadaveric larynges. Within a scope tip to arytenoid mucosa distance of 2 mm, the arytenoid body occupied between 50% and 65% of the monitor screen.

III. Results

A. Bench Testing

Bench testing was performed using the new device and the commercial device (Pentax AP-4000). Bench test results were identical for both laryngoscopes (FNL-13RAP and FNL-10RAP). Table II and Fig. 2 display a comparison of the stimulus dynamic range between

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the new and commercial devices. In summary, the new device provides an increased dynamic range by a factor of 4.31.

In clinical practice, the commercial device commonly exhibits stimulus pressure instability and may fail to generate a stimulus [24]. In bench tests, the commercial device failed to deliver a stimulus an average of 17% and as many as 25% of trials. When a given stimulus level was selected, an average of 11 attempts, and as many as 24 attempts were required for the commercial device to actually deliver the selected stimulus level. Mean drift was 10%, with up to 20% error between selected and delivered stimulus level. Error magnitude was 2–3 mm Hg or more. The new device never failed to generate a stimulus, and instabilities in stimulus pressure were not observed.

Table III displays a comparison of noise levels generated by each device using a sound level meter (Bruel & Kjaer Model 2260). The high basal noise level of the commercial device primarily results from a mechanical air compressor. Additional transient noise results from activation of the solenoid valve. The new device design used a compressed air cylinder and a sound enclosure to effectively eliminate all device-generated noise from the ambient test environment.

B. Human Testing

1) Results With Commercial Device—In the “medication OFF” condition, PD1 responded less than 25% of the time at the highest stimulus level of the commercial device (10.0 mm Hg), making measurement of the LMDT impossible (Fig. 3). In the “medication ON” condition, PD1’s LMDT was 2.2 mm Hg for the right arytenoid and 4.0 mm Hg for the left arytenoid. In a group of five healthy control participants, each individual perceived the lowest stimulus generated by the commercial device (2.0 mm Hg) 100% of the time, also making measurement of the LMDT impossible.

2) Results With New Device—In the “medication OFF” condition, PD1 exhibited LMDT of 8.16 mm Hg (left) and 7.29 mm Hg (right). In the “medication ON” condition, PD1’s LMDT was 3.63 mm Hg (left) and 5.37 mm Hg (right). In contrast, thresholds for the healthy control group were 1.18 mm Hg (left) and 1.07 mm Hg (right). A group comparison (Fig. 4) was performed between the group of five healthy controls and the group of five PD participants (“medication ON” and “medication OFF”). LMDTs for both PD conditions were significantly higher than the controls (two-sample *t*-test), with a nonsignificant trend for lower LMDTs in the medication ON versus medication OFF condition (paired *t*-test). These trends were consistent with those observed with the commercial device. However, actual LMDT values could be reported as a result of improvements in the new device design.

IV. Discussion and Conclusion

Implementation of laryngeal sensory assessment has been restricted in part due to technical and practical limitations of commercially available technology including procedural complexity requiring two or three individuals to operate, limited stimulus dynamic range, device-generated noise, and questionable stimulus reproducibility. The goal of this study was to design a new laryngeal somatosensory stimulus delivery device and test the device in individuals who may manifest a laryngeal sensory deficit. The new device provided silent operation, direct and reliable control over the timing, duration, and dynamic range of stimulus presentation, and required only one individual to operate.

In attempting to test LMDT in an individual with PD and a group of healthy controls with an available commercial device (Pentax AP-4000), the clinical participant’s true threshold (unmedicated) exceeded the dynamic range of the commercial device. In addition, the threshold

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of the healthy controls fell below the lower limit of the dynamic range of the commercial device. The limited stimulus dynamic range of the commercial apparatus significantly limited the investigator's ability to accurately estimate LMDT for both healthy and clinical participants. However, because of the increased dynamic range of the new device, the investigator was able to measure LMDT in each participant. In the unmedicated state, PD1 exhibited thresholds that were seven times greater than healthy controls. Without the new device, these data might have otherwise gone undetected. It should be noted that the stimulus duration for the new device of 135 ms was selected to provide a more salient stimulus and avoid potential problems associated with temporal summation. The commercial device presented only a brief and fixed stimulus duration of 50 ms that may account for PD1's lower LMDT for the new device versus the commercial device. Testing with the new device revealed that a group of moderately severe PD participants had significantly higher LMDTs that were five times greater than healthy controls. There was a nonsignificant trend for LMDTs to decrease in PD following medication.

Challenges faced in the present design included careful control of laryngoscope position and calibration. In the present investigation, great care was taken in an attempt to maintain a constant distance of 2 mm between the laryngoscope and the laryngeal mucosa. In addition, negligible variation was observed in output delivered to targets within 2–5 mm from the laryngoscope tip. Future work will attempt to improve control of laryngoscope to target distance. An additional challenge concerned use of a compressed air cylinder. The air cylinder was effective in minimizing noise levels, but added bulk and weight to the experimental setup. Therefore, a small-size cylinder is recommended to maintain portability of the paradigm. Given the relatively finite air supply available in a compressed air cylinder, future device design should also consider integrating an active air compression source with adequate sound attenuation.

The new device described in this paper will enable greater flexibility and efficiency in studies of laryngeal sensory function. Based on results from this study, the improved dynamic range of the new device (0.07–29.09 mm Hg) should be more than sufficient to estimate LMDT for both healthy and clinical participants. In addition to increased dynamic range, the ability to increase stimulus duration with the new device, compared with the fixed stimulus duration of the commercial device (50 ms), will enable the investigator to adjust stimulus duration to examine the effects of temporal integration on thresholds. Because the new device design includes silent operation, it is easier for the examiner to provide instructions to a participant, and the participant will not be distracted or biased by mechanical noises triggered during stimulus delivery. Finally, designing the new device with the stimulus control dial fastened to the housing of the laryngoscope enables the examiner to adjust stimulus pressure while visualizing the larynx.

These design improvements provide a new assessment instrument that is adequately simple for use in routine clinical assessment, yet sufficiently versatile for integration within rigorous clinical research protocols. Laryngoscopic stimulus delivery will be employed in future studies to compare upper airway sensory thresholds in pediatric development, healthy aging, and neurological disease. This device may provide a helpful tool in assessing the effects of intervention on upper airway sensory function. The new device will enable future experiments to formally examine the effects of stimulus duration and stimulus magnitude on LMDT and somatosensory evoked laryngeal myogenic reflexes. This device can also be easily modified to assess cutaneous receptive fields of orofacial and limb regions in an attempt to provide a more comprehensive assessment of somatosensory function.

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Acknowledgements

The author would like to thank Dr. N. P. Connor and Dr. J. G. Webster for their valuable suggestions during the preparation of this manuscript.

This work was supported in part by the National Institutes of Health grants DC007260 and RR025012, by the American Speech-Language-Hearing Foundation, and by the Council of Academic Programs in Communication Sciences and Disorders.

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Biography

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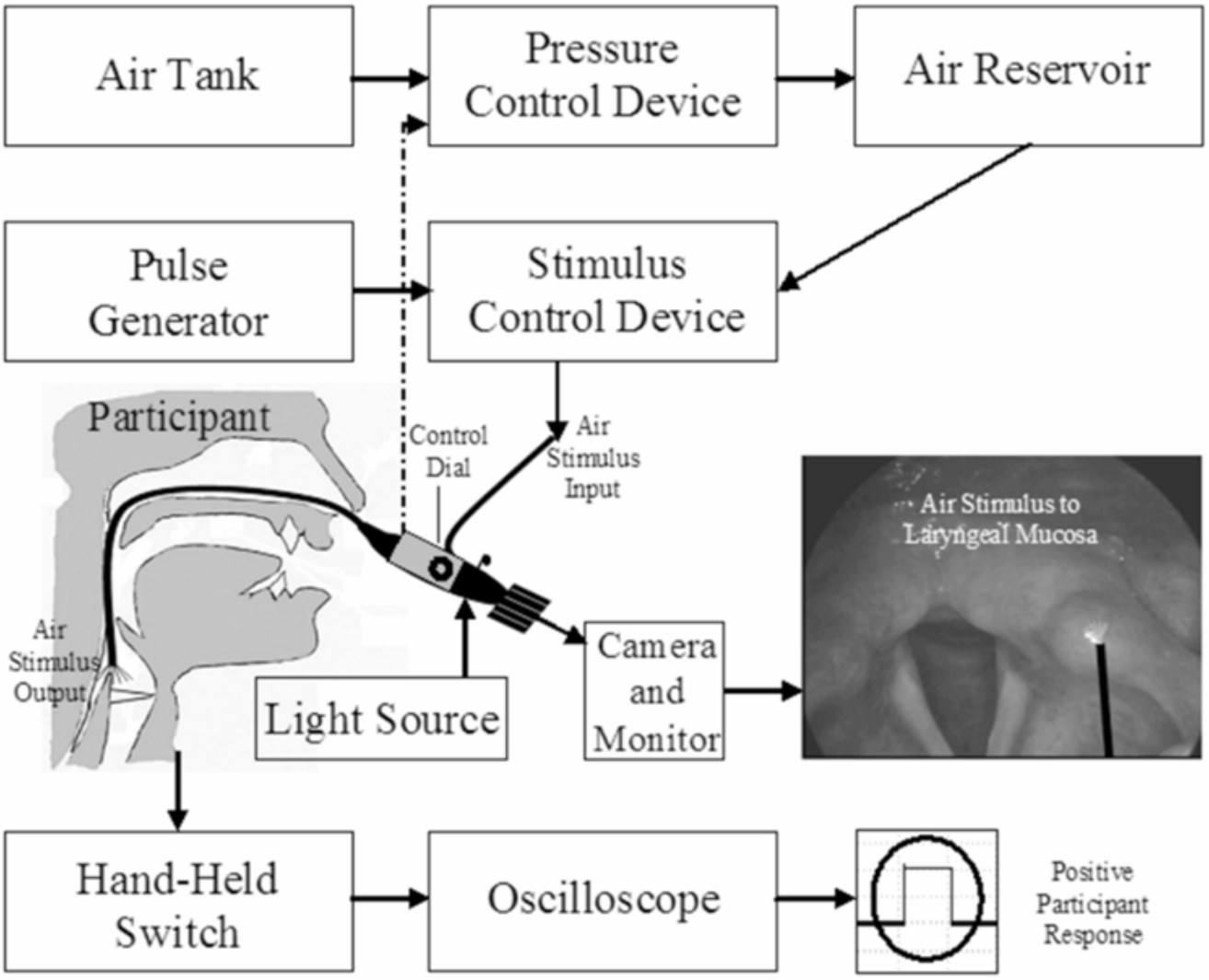

Fig. 1.

Block diagram of the stimulus delivery paradigm. The air stimulus is directed to the laryngeal mucosa through a port in the laryngoscope as visualized on the monitor. The +5-V signal from a hand-held switch indicates when the participant feels the laryngeal somatosensory stimulus.

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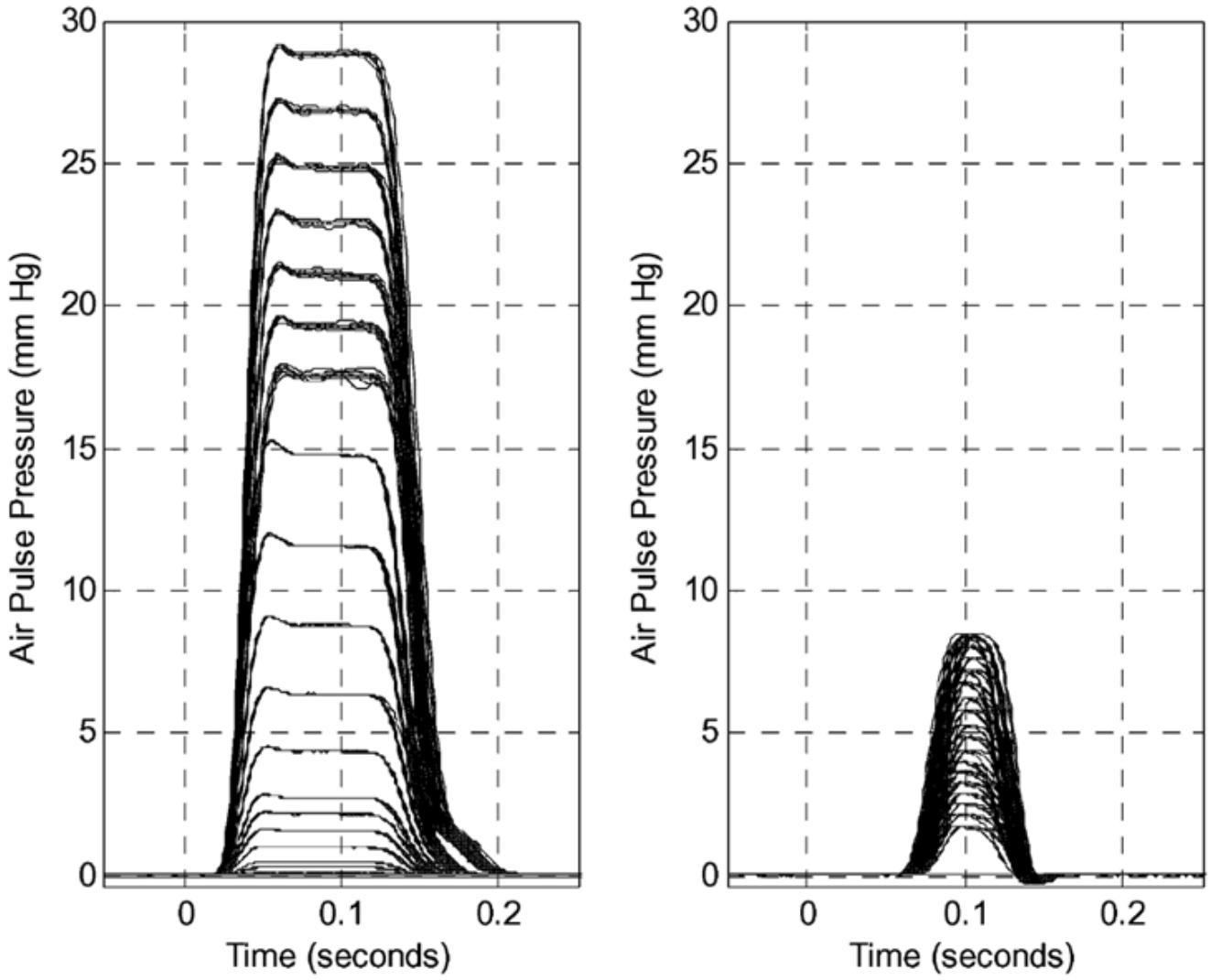

Fig. 2.
Stimulus waveforms for the new laryngeal somatosensory stimulus delivery device (left panel) and the commercial device (right panel).

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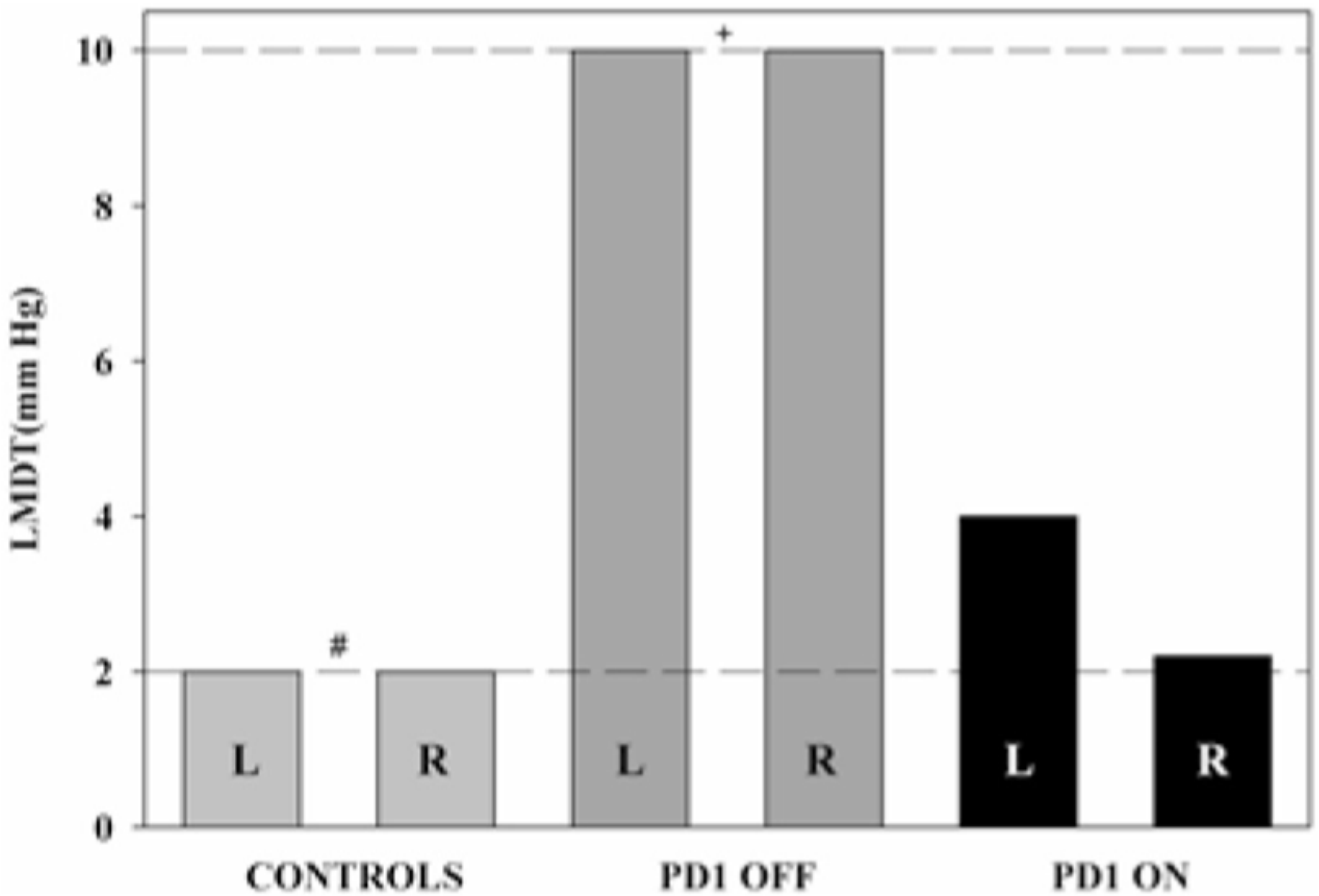

Fig. 3.

LMDT was measured for five healthy controls and PD1 using the commercial device (L: left arytenoid mucosa; R: right arytenoid mucosa). Stimulus duration was fixed at 50 ms. LMDT was not measurable (#) because controls felt the lowest stimulus of the commercial device (2 mm Hg) 100% of the time. LMDT was not measurable (+) because PD1 OFF felt the highest stimulus of the commercial device (10 mm Hg) <25% of the time. PD1 (ON) exhibited a lower and measurable LMDT with medication. Dashed lines represent the extent of the reported dynamic range of the commercial device (2.0–10.0 mm Hg).

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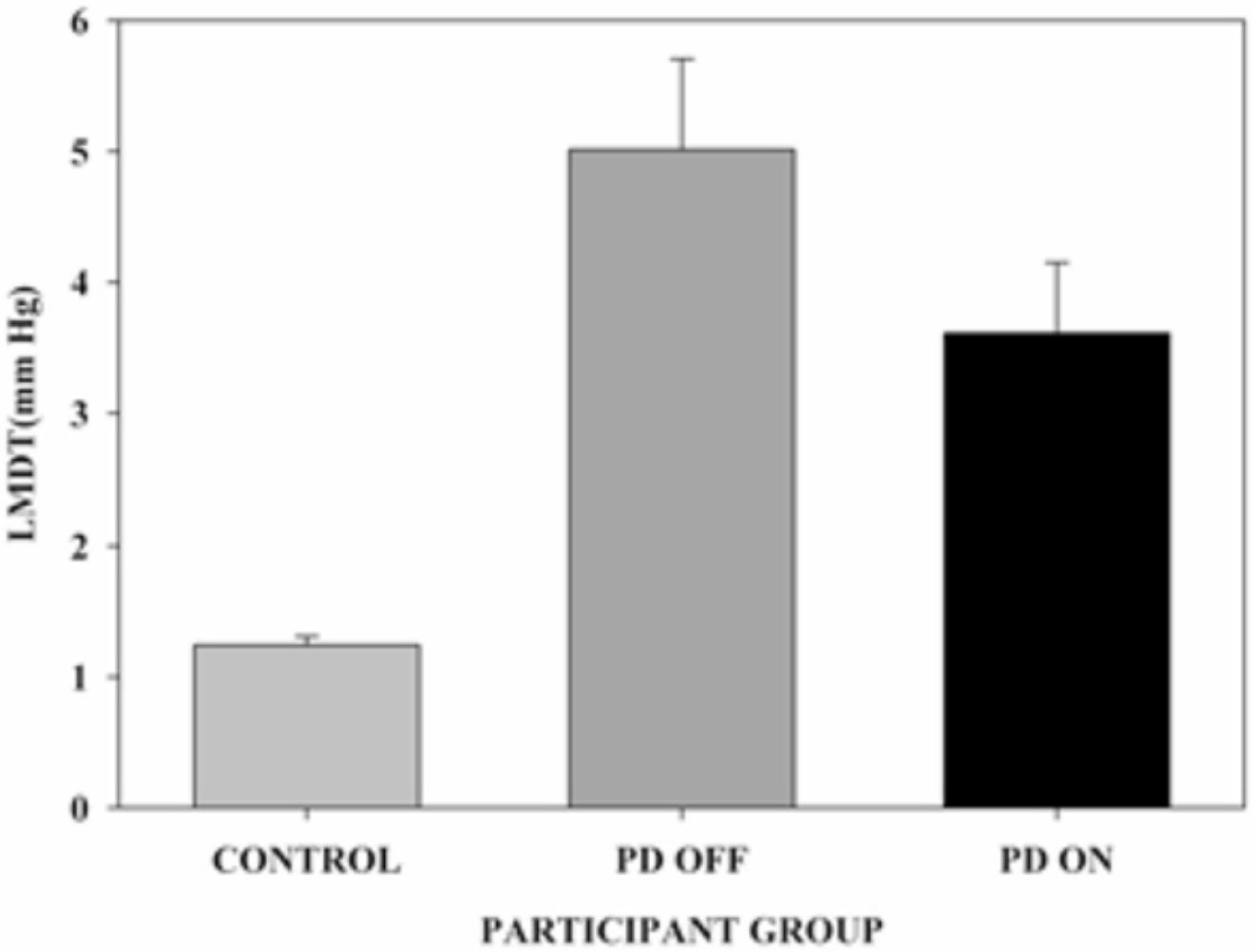

Fig. 4.

LMDT was measured for five healthy controls and five participants with PD using the new device. A 135-ms stimulus duration was used. LMDT was measurable for all participants. Bar height represents mean LMDT with standard error of the mean for each condition. LMDT for PD-OFF and PD-ON were each significantly higher than controls ($p < 0.01$). There was a nonsignificant trend for LMDTs to decrease (PD-OFF versus PD-ON) following medication ($p > 0.01$).

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TABLE I

Limitations of Commercial Stimulus Device

Constant noise generated by device	Limited dynamic range (2.0 to 10.0 mm Hg)
Transient noise by opening solenoid valve	Limited step resolution (0.1 mm Hg)
Minimum 2 experimenter operation	No input for triggered stimulus control
Single fixed pulse width (50 ms)	Questionable stimulus output pressure
Limited stimulus repetition rate (2/s)	Limited output pulse waveform shape

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TABLE II

Magnitude of Stimulus Output

Stimulus output range of new device	0.07 mm Hg to 29.09 mm Hg
Stimulus output range of commercial device (measured)	1.76 mm Hg to 8.49 mm Hg
Factor increase in maximum output	3.43
Factor increase in dynamic range	4.31

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TABLE III

Acoustic Measurement of Commercial and New Device

All dB SPL measurements with reference to 20 μPa (Bruel & Kjaer Model 2260 Observer)			
Commercial Device			
	Ambient Room Noise	**Device ON**	**Activation of Solenoid**
At Device	47.6 dB	80.4 dB	82.9 dB
At Chair 97 cm from Device	45.3 dB	61.0dB	64.2 dB
New Device			
	Ambient Room Noise	Device ON	Activation of Solenoid
At Device	47.6 dB	47.6 dB	47.6 dB
At Chair 97 cm from Device	45.3 dB	45.3 dB	45.3 dB

Unlike the commercial device, the new device design eliminates all device-generated noise from contaminating the ambient acoustic environment.