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Authors

Pillutla, Pranati
Zhang, Zhaoyan
Kreiman, Jody
et al.

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Effects of Laryngeal Vibratory Asymmetry and Neuromuscular Compensation on Voice Quality

Pranati Pillutla, MD[1], **Zhaoyan Zhang, PhD**[1], **Jody Kreiman, PhD**[1,2], **Holly Wilhalme, MS**[3], **Dinesh K. Chhetri, MD**[1]

[1]Department of Head and Neck Surgery, University of California, Los Angeles; Los Angeles, CA.

[2]Department of Linguistics, University of California, Los Angeles; Los Angeles, CA.

[3]Department of Medicine, Statistics Core, University of California, Los Angeles; Los Angeles, CA.

Abstract

Introduction: Vibratory asymmetry and neuromuscular compensation are often seen in laryngeal neuromuscular pathology. However, the ramifications of these findings on voice quality are unclear. This study investigated the effects of varying levels of vibratory asymmetry and neuromuscular compensation on cepstral peak prominence (CPP), an analog of voice quality.

Study Design: *In vivo* canine phonation model.

Methods: Varying degrees of vocal fold vibratory asymmetry were achieved by stimulating one recurrent laryngeal nerve (RLN) over 11 levels from threshold to maximal muscle activation. For each of these levels, phonation was induced at systematically varied combinations of neuromuscular compensation: three levels each of contralateral RLN stimulation (80%, 90%, 100% of maximal), superior laryngeal nerve (SLN) activation (0%, 50%, 100% of maximal), and airflow levels (500, 700, 900 ml/s). Vocal fold symmetry was determined by assessing the opening phase of the vibratory cycle in high-speed video recordings. Voice quality was estimated acoustically by calculating CPP for each voice sample.

Results: 822 phonatory conditions with varying degrees of vibratory asymmetry were evaluated. CPP was highest at vibratory symmetry. Increasing levels of asymmetry resulted in significant decreases in CPP. CPP increased significantly with increasing contralateral RLN activation. CPP was significantly higher at 50% SLN activation than 0% or 100% SLN activation.

Conclusion: Voice quality, as approximated by CPP, is best at vibratory symmetry and deteriorates with increasing degrees of asymmetry. Voice quality may be improved with neuromuscular compensation by increased adduction of the contralateral vocal fold or increased vocal fold tension at mid-levels of SLN activation.

Level of Evidence: N/A, Basic Science

Keywords

in vivo phonation; canine phonation model; voice quality; voice acoustics; vibratory asymmetry

Corresponding Author: Dinesh K. Chhetri, MD, Department of Head and Neck Surgery, 62-132 CHS, UCLA Medical Center, 10833 Le Conte Ave, Los Angeles, CA 90095, DChhetri@mednet.ucla.edu, Phone: (310) 794-4225.

INTRODUCTION

Symmetry of the vocal fold vibratory phase, amplitude, and mucosal wave are hallmarks of normal laryngeal vibration and voice quality.[1] Symmetric vocal fold vibration requires congruent parameters, such as mass and tension. Laryngeal pathology characterized by mass and tension asymmetry may lead to abnormal vibration and voice quality. Vibratory phase asymmetry is present in many clinical conditions such as vocal paresis,[2–4] yet is also seen in the normophonic, asymptomatic population.[5–8] Haben et al. reported a 10.5% prevalence of mucosal wave asymmetries in normophonic, asymptomatic adults.[5] Distinguishing between innocent and significant asymmetries represents the greatest challenge in defining vocal fold paresis.[2] Therefore, investigations of vibratory asymmetry and voice quality are necessary to identify clinically meaningful asymmetries.

Speakers may attempt to mitigate vocal fold asymmetry and its adverse voice quality effects by compensating with activation of other intrinsic laryngeal muscles.[9] Compensation may develop subconsciously, such as the compensatory falsetto observed in neurogenic paresis and paralysis. Activation of the intact cricothyroid (CT) muscle tenses, stiffens, and adducts the vocal fold, limiting flaccidity and decreasing air loss during phonation.[10] Improving neuromuscular compensation may also be a targeted goal, such as in voice therapy.[11] Compensation by the contralateral adductor muscles facilitates phonation by decreasing the glottal gap and subglottal pressure requirements.[12] However, neuromuscular compensation and its consequent effects on voice quality have not been systematically studied.

Clinical observation of laryngeal asymmetry ranges from an incidental finding in an asymptomatic patient to dense paresis or paralysis causing functional voice deficits. The associations between the degree of asymmetry, neuromuscular compensation, and voice quality changes are unclear. Exploring these interactions would improve our understanding of the clinical relevance of the observed asymmetry and subsequent compensation. To this end, we used an established animal model capable of graded neuromuscular stimulation to investigate (1) the degree of vocal fold asymmetry that results in significant changes in voice quality, and (2) the role of neuromuscular compensation in improving voice quality. The cepstral peak prominence (CPP), a quantitative acoustic measure of the relative amount of noise versus harmonic energy in voice, was used as an analog for voice quality.[13] We hypothesized that (1) increasing laryngeal vibratory asymmetry would increase the relative amount of inharmonic energy (noise) in the voice, thus decreasing CPP, and (2) increasing neuromuscular compensation would reduce spectral noise and increase CPP by enhancing the energy in the harmonic source spectrum.

METHODS

In vivo Canine Model of Phonation

The Institutional Animal Care and Use Committee approved this protocol. Three male mongrel canines were used for this investigation. The recurrent laryngeal nerves (RLNs) and superior laryngeal nerves (SLNs) were exposed as previously described.[14,15] The nerves to the posterior cricoarytenoid muscles, Galen’s anastomosis, and internal (sensory) branches

of the SLNs were divided bilaterally to eliminate their effects during neuromuscular stimulation. Tripolar cuff electrodes (Ardiem Medical, Indiana, PA) stimulated the RLNs and SLNs to activate the laryngeal adductors and cricothyroid (CT) muscles, respectively. The laryngeal nerves were stimulated with 5 ms cathodic pulses at 80 Hz for 1,500 ms in neuromuscular combinations detailed below. A subglottal tube attached to the upper trachea provided rostral airflow for phonation. A humidifier (HumiCare 200, Gruendler Medical, Freudenstadt, Germany) warmed air at the glottic level to 37.5 °C and 100% relative humidity.

Neuromuscular Conditions Tested

Speakers with vocal fold paresis can compensate (1) neuromuscularly by activating intact intrinsic laryngeal muscles in various combinations, or (2) aerodynamically with increased airflow.[12] To simulate this, two neuromuscular compensation models (Figure 1) and three flow levels were tested. These models were intended to generate a broad range of symmetric and asymmetric laryngeal activation conditions. In both models, the left RLN was tested as the paretic side by stimulating the nerve across a range of graded activation levels, ranging from just a hint of muscle activation (level 1, observed as subtle muscle twitch, near paralysis) to maximal activation (level 11, observed as full contraction). In Model 1, the compensatory right RLN was stimulated at three constant levels (80%, 90%, and 100% of maximum activation), while bilateral SLNs were stimulated symmetrically at three constant levels (0%, 50%, and 100%). In Model 2, the compensatory right RLN and SLN were stimulated together at three constant levels (80%, 90%, and 100% of maximum activation), while the left SLN was stimulated at three constant levels (0%, 50%, and 100%). Each neuromuscular compensation model was phonated at three airflow levels (500, 700, and 900 mL/s).

Measurement of Experimental Parameters

In all phonatory conditions, a probe tube microphone (Model 4128; Brüel & Kjær North America, Norcross, GA) and pressure transducer (MKS Baratron 220D; MKS Instruments, Andover, MA) mounted flush with the inner wall of the subglottic airflow tube measured acoustic and subglottal pressure signals. A high-speed video (HSV) camera (Phantom v210, Vision Research Inc., Wayne, NJ) captured laryngeal posture and vibration at 3,000 frames/s. Multiple dots tattooed on the superior vocal fold surface using India ink served as reference points for glottal gap and vocal fold strain measurements, which were obtained from HSV images 1,000 ms following nerve stimulation. Glottal gap was measured as the distance, in pixels, between the India ink landmarks at the vocal processes. Strain was determined by measuring each vocal fold length from the anterior commissure to its respective vocal process at baseline (L_0) and final posture (L_i). Strain (ε) was then calculated as the percent length change from baseline, $\varepsilon = (L_i - L_0)/L_0$.

Determination of Laryngeal Vibratory Symmetry

Vibratory symmetry/asymmetry was determined via frame-by-frame analysis of the glottal opening phase from high-speed video recordings as described by Haben et al.[5] Vibratory conditions were deemed symmetric when both glottal edges opened simultaneously and asymmetric when the glottis opened first on one side. The symmetric condition was

labeled “0,” and the remaining phonatory conditions within the set were labeled to reflect levels away from vibratory symmetry. For example, if RLN stimulation level 5 resulted in vibratory symmetry, then stimulation levels 4 and 6 would be labeled −1, levels 3 and 7 would be labeled −2, and so on. Thus, more negative values represent greater degrees of opening phase vibratory asymmetry.

Measurement of Cepstral Peak Prominence (CPP)

CPP quantifies the relative strength of the harmonic versus inharmonic components of an acoustic sample.[13] Measurement does not require a stable fundamental frequency, unlike jitter, shimmer, and harmonics-to-noise ratio measures.[13,16] CPP is a reliable correlate to perceptual ratings of voice quality[17] and the severity and duration of voice disorders,[18] even for severely aperiodic signals such as tracheoesophageal voice.[19] Given these advantages and the large number of conditions in our study, we used CPP as an analog for voice quality. CPP was calculated for each phonatory condition from a 700 ms segment of stable phonation with Praat (Version 6.1.09)[20] using parameters described by Watts et al.[21]

Data Presentation and Interpretation

Statistical analysis was conducted using RStudio (Version 1.1.463, Boston, MA). Data from both neuromuscular compensation models were aggregated since both models resulted in a range of symmetric and asymmetric conditions. Pearson correlation explored correlations between CPP values and laryngeal posture measures. One-way between-subjects ANOVA compared CPP values across flow, contralateral RLN, and SLN groups. Post hoc analysis was performed using two-tailed t-tests to compare each asymmetric condition (−1 to −11) to the symmetric condition (0). Post hoc Tukey tests were used to compare contralateral RLN and SLN groups. Predictors of CPP were investigated using a linear mixed effects model with a random effect for animal. Significance was defined as $p < 0.05$.

RESULTS

A total of 822 phonatory conditions were evaluated. Successful neuromuscular stimulation was confirmed by reviewing high-speed video and aerodynamic data. RLN activation resulted in increased subglottal pressure and decreased glottal gap and vocal fold strain. SLN activation resulted in increased vocal fold strain. These findings confirmed appropriate graded neuromuscular activation.

CPP was evaluated as a function of vibratory symmetry, laryngeal posture measures, and flow. Figure 2 illustrates mean CPP values as a function of vibratory symmetry. One-way ANOVA showed significant differences in mean CPP across degrees of vibratory symmetry [$F(11, 532) = 3.835$, $p < 0.001$]. Post hoc two-tailed t-tests showed that the symmetric condition and mildly asymmetric condition did not differ significantly in CPP [Symmetric Condition 0: M = 12.3, SD = 4.7; Asymmetry Degree −1: M = 12.4, SD = 4.5; $p = 0.89$]. However, CPP decreased significantly compared to the symmetric condition when the degree of asymmetry was −2 or greater [e.g., Asymmetry Degree −2: M = 10.9, SD = 3.6; $p = 0.02$)]. No meaningful correlation was found between CPP and laryngeal posture measures such as vocal fold strain or glottal gap ($r = −0.34$ and 0.02, respectively). There were no

statistically significant differences in CPP group means across flow conditions [F(2, 819) = 0.806, p = 0.447].

CPP was also evaluated as a function of neuromuscular compensation by the contralateral RLN and bilateral SLNs. Increasing contralateral RLN activation significantly increased CPP values (one-way ANOVA; F(2, 819) = 25.41, p = 0.04; Figure 3). Post hoc Tukey comparisons showed that all contralateral RLN conditions differed significantly (80%: M = 10.5, SD = 4.0; 90%: M = 11.3, SD = 4.3; 100%: M = 12.9, SD = 3.6; $p < 0.05$). CPP values also varied significantly with bilateral SLN activation level (0%, 50%, and 100%) (one-way ANOVA; F(2, 819) = 23.25, $p < 0.01$). Post hoc Tukey comparisons showed that mean CPP for the 50% bilateral SLN group differed significantly from the 0% and 100% groups (0%: M = 10.6, SD = 4.4; 50%: M = 12.9, SD = 4.0; 100%: M=11.4, SD=3.5; $p < 0.001$; Figure 4). There was no significant difference in mean CPP between the 0% and 100% bilateral SLN conditions (p = 0.08).

A linear mixed effects multivariable model was developed to identify the neuromuscular parameters that were most predictive of CPP (Table 1). Increasing contralateral RLN activation level increased CPP, so contralateral RLN level was modeled as a continuous variable. CPP showed a non-linear relationship with SLN level, so SLN level was modeled as a categorical variable with 0% SLN level defined as the reference condition. The effect estimate indicates the magnitude of CPP increase by neuromuscular activation level. For example, our model showed that increasing contralateral RLN activation from 80% to 90% would increase CPP by 1.15. In comparison, increasing the graded RLN level from 1 to 2 was predicted to increase CPP by approximately 10% of that magnitude, 0.19. SLN activation of 50% was expected to increase CPP by 2.07 compared to 0% SLN. SLN activation of 100% was predicted to increase CPP by 0.56 compared to 0% SLN. Of all neuromuscular factors studied, SLN level of 50% and increased contralateral RLN activation were most effective in increasing CPP as predicted by this model.

DISCUSSION

This study systematically investigated the effects of laryngeal asymmetry on voice quality, as measured by CPP. The results were consistent with our hypothesis that CPP is determined by two key factors: vibratory symmetry and neuromuscular compensation. While CPP was highest (i.e., least spectral noise) in symmetric and slightly asymmetric conditions, larger asymmetries resulted in significantly lower CPP values. These findings are consistent with prior reports that minor laryngeal asymmetries can be clinically negligible, and small temporal and spatial asymmetries often result in normal, unexceptional voice quality.[5,22,23]

While several studies have associated vocal fold asymmetries with increased noise (e.g., jitter, shimmer, harmonics-to-noise ratio),[24–26] our findings suggest that significant worsening in these measures (corresponding to declining voice quality) only occurs at larger degrees of vibratory phase asymmetry. This decrease in the voice quality measure (CPP) is due to increased noise within the acoustic signal. For example, highly asymmetric neuromuscular activation of the laryngeal nerves results in an increasingly chaotic vibration and aperiodic acoustic signal.[27,28] While CPP differences between minor and major

asymmetries in our results are statistically significant, these values may be of limited clinical relevance due to varying proposed cutoffs for CPP values in dysphonia evaluation.[29] Perceptual assessments are also needed to corroborate these findings in clinical settings.

CPP was affected by neuromuscular compensation from the SLNs or contralateral RLN. Mid-level (50%) activation of the SLNs was associated with improved CPP. SLN activation provides vocal fold tension and stiffens the cover layer,[27] which generates a restraining force and prevents the vocal folds from being blown apart by aerodynamic forces during phonation.[12,30] Thus, SLN activation is often used to compensate for a flaccid vocal fold in vocal paresis and paralysis. Patients with unilateral vocal fold paralysis have higher fundamental frequencies compared to age- and sex-matched controls.[31] Lundy and Casiano theorized that a “compensatory falsetto” may “represent an unconscious attempt by the patient to improve vocal quality.”[32] We find that mid-level SLN stimulation improved the acoustic quality of voice and CT activation may be an appropriate compensation strategy for those with vocal fold paresis and paralysis. However, very high levels of SLN stimulation significantly increased vocal fold tension and glottal gap, requiring more subglottal pressure and airflow to achieve phonation.[12] At maximal SLN activation in an asymmetrically activated larynx, increased aerodynamic forces may add noise to the acoustic signal, leading to worsening voice quality.[33]

CPP increased as contralateral compensatory RLN activation increased. Increasing contralateral RLN activation stiffens and stabilizes the vocal fold in a more adducted position, which excites more harmonics within the acoustic signal and leads to a perceptually improved voice.[23] Our findings are consistent with the notion that increased contralateral RLN compensation improves glottal insufficiency, decreases noise, and increases harmonic energy in voice, thus improving CPP.[33] In our study, compensation by the contralateral adductors was a primary driver of CPP improvement in the setting of vocal paresis and paralysis (Table 1). Thus, the present study supports using multifaceted approaches to improving glottal closure in laryngeal paresis and paralysis. For example, surgical medialization to treat the ipsilateral vocal fold may be combined with voice therapy to ensure appropriate and effective use of neuromuscular compensation to maximize voice quality. Targeting neuromuscular compensation has been shown to be an effective strategy to improve voice quality in patients with laryngeal pathology. For example, patients who underwent injection laryngoplasty combined with voice therapy showed improvement in multiple acoustic voice parameters (jitter, shimmer, noise-to-harmonics ratio, mean phonation time) compared to patients who underwent injection laryngoplasty without voice therapy.[34]

Limitations of this study include the use of an animal model along with the asymmetry and voice quality measures used. Although the *in vivo* canine model is non-human, the canine larynx reasonably approximates the human larynx in anatomy and physiology[35,36] and allows systematic activation of the intrinsic laryngeal muscles not possible in humans. The neuromuscular activation conditions we tested may not reflect all possible patterns or combinations of individual muscle control or neuromuscular compensation in physiologic phonation. We also based our rating of vibratory asymmetry on the graded RLN activation level and did not parameterize the degree of vocal fold asymmetry based on opening phase

lateral displacement or glottal area waveforms. While quantitative measurement of lateral phase asymmetry could be helpful in clinical practice, technical complexities involved in gathering accurate measurements have limited applicability. Finally, the amount of change in CPP needed for listeners to perceive a change in voice quality is unknown and certainly interacts with the structure of the harmonic voice source.[37] Future perceptual experiments are required to evaluate clinically meaningful changes in CPP.

CONCLUSION

This study investigated the effects of vibratory opening phase asymmetry and neuromuscular compensation on CPP, an analog of voice quality. We found that slight vibratory asymmetries resulted in CPP values comparable to those characterizing symmetric vibration, while further increases in vibratory asymmetry led to significant decreases in CPP, implying a decline in vocal quality. Compensation by the superior and recurrent laryngeal nerves improved CPP. These findings support the clinical observations that mild degrees of laryngeal asymmetry may result in normal voices, and hoarseness in the setting of mild laryngeal asymmetry may require further investigation. Additionally, neuromuscular compensation by the intact cricothyroid or laryngeal adductor muscles is an appropriate strategy to maintain or improve voice quality in the setting of laryngeal asymmetry.

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Conflicts of Interest:

The authors have no other funding, financial relationships, or conflicts of interest to disclose.

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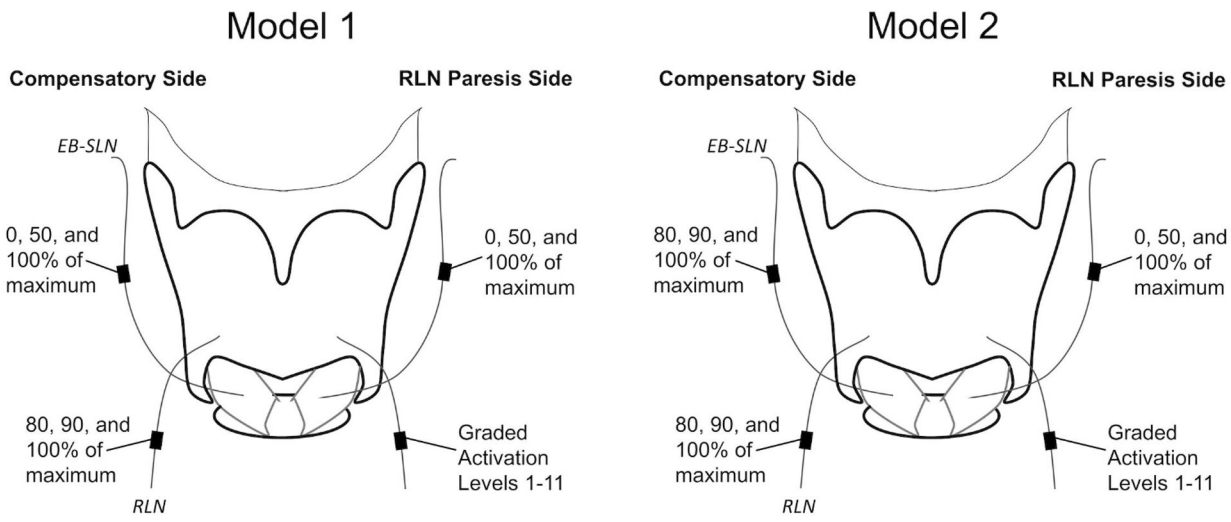

Figure 1.

Schematic diagram of *in vivo* neuromuscular activation parameters used. Black boxes indicate stimulation via tripolar cuff electrodes. RLN = recurrent laryngeal nerve. EB-SLN = external branch of superior laryngeal nerve.

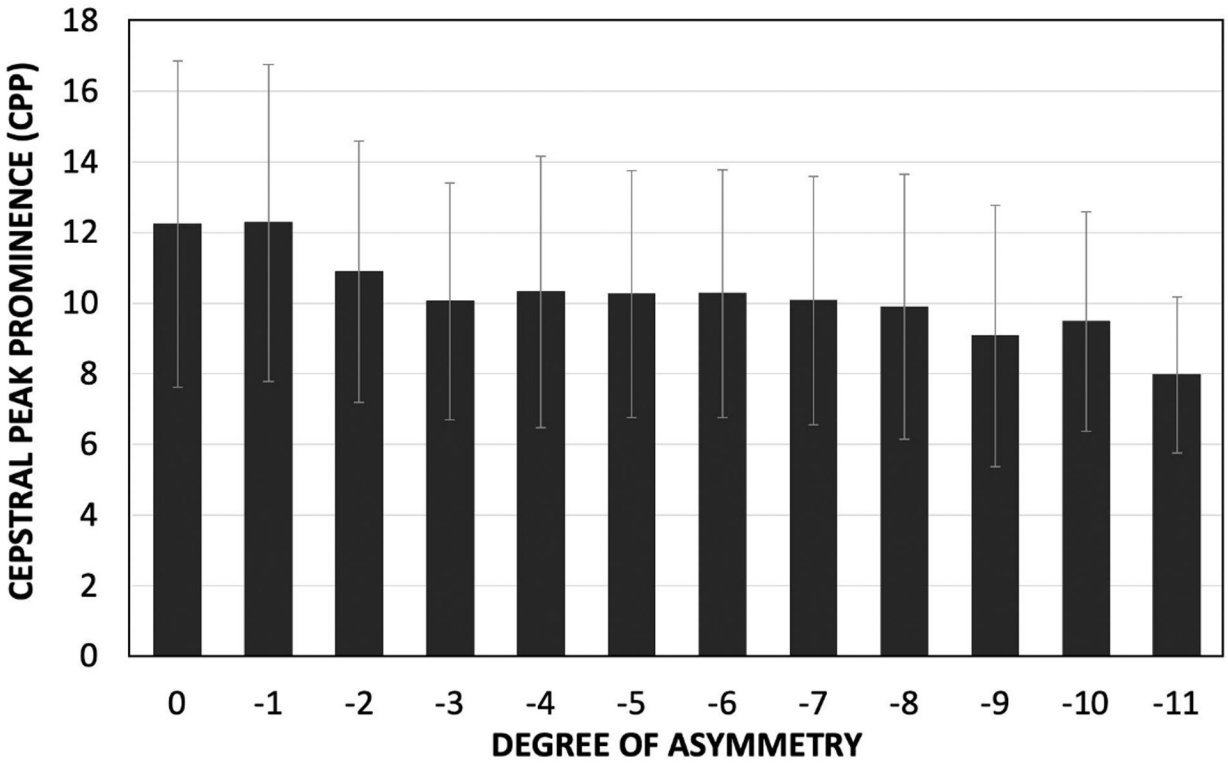

Figure 2.

Mean and standard deviation of cepstral peak prominence (CPP) as a function of vibratory phase asymmetry. CPP was comparable between conditions with symmetric (0) and mildly asymmetric (−1) vibratory phase. Further increases in vibratory phase asymmetry led to a statistically significant decrease in CPP.

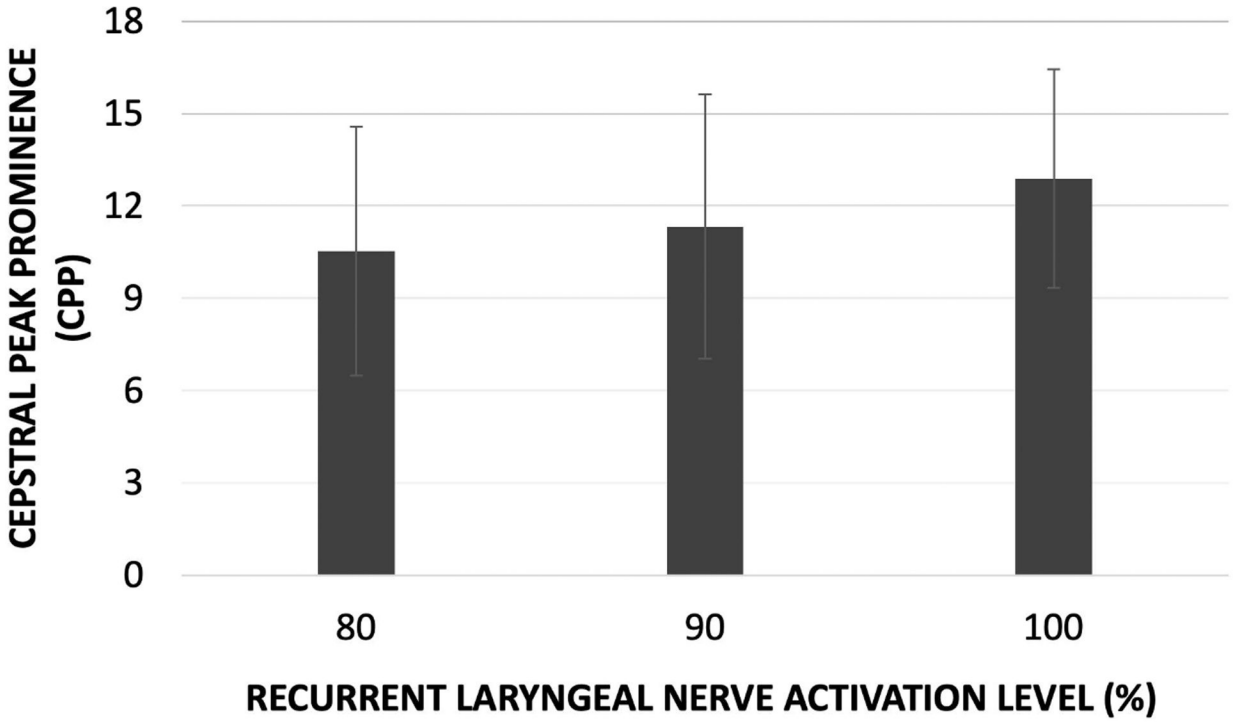

Figure 3.
Cepstral peak prominence (CPP) as a function of compensatory recurrent laryngeal nerve (RLN) activation level. CPP increased as the contralateral RLN activation level increased.

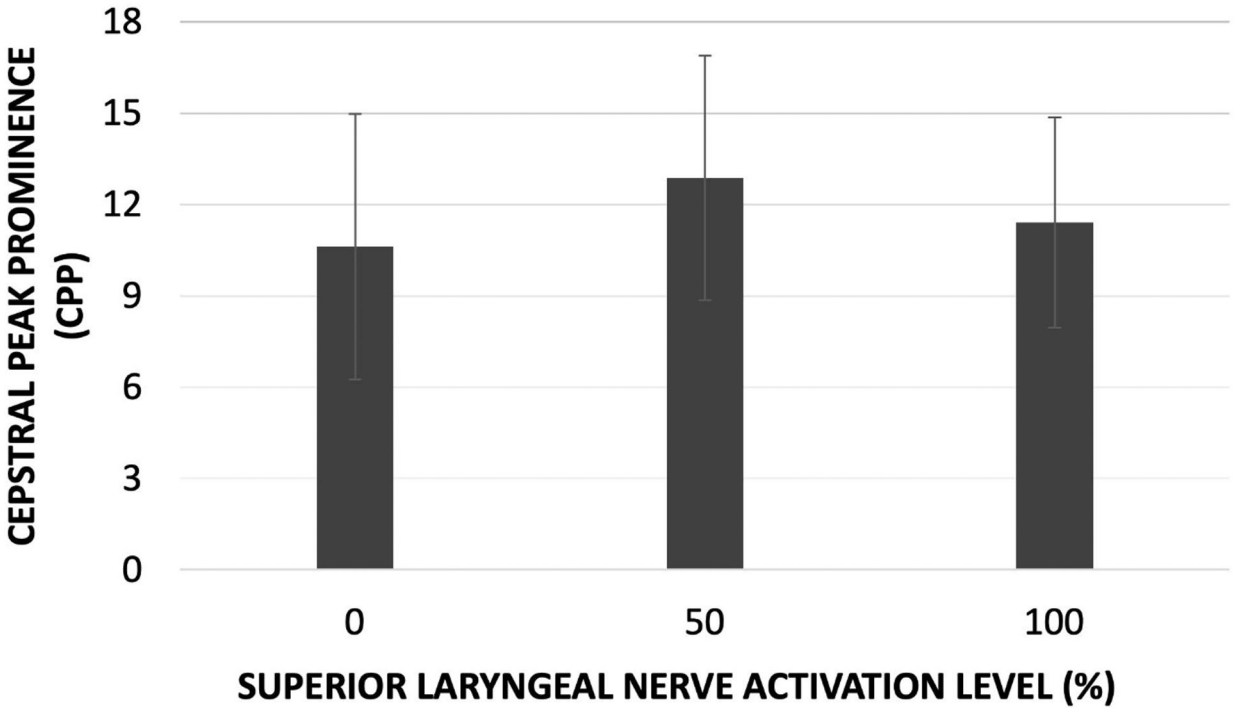

Figure 4.
Cepstral peak prominence (CPP) as a function of bilateral superior laryngeal nerve (SLN) activation levels. CPP was highest at mid-level (50%) activation of the SLNs.

Table 1.

Linear Mixed Effects Multivariable Model of Cepstral Peak Prominence Predictors.

Variable	Category	Effect Estimate (SE)	P Value
Graded RLN	--	0.19 (0.035)	< 0.0001
Contralateral RLN	--	1.15 (0.133)	< 0.0001
SLN	0%	Reference	--
	50%	2.07 (0.262)	< 0.0001
	100%	0.56 (0.266)	0.0347

SE = standard error, RLN = recurrent laryngeal nerve, SLN = superior laryngeal nerve.