




Effects of Thyroarytenoid Activation Induced Vibratory Asymmetry on Voice Acoustics and Perception

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Introduction: Asymmetry of vocal fold (VF) vibration is common in patients with voice complaints and also observed in 10% of normophonic individuals. Although thyroarytenoid (TA) muscle activation plays a crucial role in regulating VF vibration, how TA activation asymmetry relates to voice acoustics and perception is unclear. We evaluated the relationship between TA activation asymmetry and the resulting acoustics and perception.

Methods: An in vivo canine model of phonation was used to create symmetric and increasingly asymmetric VF vibratory conditions via graded stimulation of bilateral TA muscles. Naïve listeners ($n = 89$) rated the perceptual quality of 100 unique voice samples using a visual sort-and-rate task. For each phonatory condition, cepstral peak prominence (CPP), harmonic amplitude (H1-H2), and root-mean-square (RMS) energy of the voice were measured. The relationships between these metrics, vibratory asymmetry, and perceptual ratings were evaluated.

Results: Increasing levels of TA asymmetry resulted in declining listener preference. Furthermore, only severely asymmetric audio samples were perceptually distinguishable from symmetric and mildly asymmetric conditions. CPP was negatively correlated with TA asymmetry: voices produced with larger degrees of asymmetry were associated with lower CPP values. Listeners preferred audio samples with higher values of CPP, high RMS energy, and lower H1-H2 (less breathy).

Conclusion: Listeners are sensitive to changes in voice acoustics related to vibratory asymmetry. Although increasing vibratory asymmetry is correlated with decreased perceptual ratings, mild asymmetries are perceptually tolerated. This study contributes to our understanding of voice production and quality by identifying perceptually salient and clinically meaningful asymmetry.

Key Words: cepstral peak prominence, mucosal wave asymmetry, thyroarytenoid muscle, vocal fold paresis, voice quality.

Level of Evidence: N/A (Basic Science Study)

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INTRODUCTION

The thyroarytenoid (TA) muscle is the primary intrinsic laryngeal muscle (ILM) involved in regulating vocal fold (VF) thickness. Specifically, the TA plays an important role in maintaining VF adduction, regulating glottal closure, and modulating voice quality.¹ Neuro-muscular activation of the TA and ILMs narrows the glottic inlet to facilitate sufficient rise of subglottal pressure required for phonation.² Often, malfunctioning of these muscles is related to laryngeal diseases causing dysphonia. For example, the ILM adductors are

found to be hyperfunctional in laryngeal dystonia and are hypofunctional in paresis and paralysis conditions.² The most common clinical finding in paresis conditions is VF vibratory asymmetry captured by laryngeal videostroboscopy.^{3,4} Although the observed VF asymmetry may reflect a broad range of denervation conditions from subtle paresis to complete paralysis,⁵ it is also frequently encountered in the normophonic, asymptomatic population. In Haben et al., for example, a 10.5% prevalence rate of mucosal wave asymmetries was reported in normophonic speakers.⁶

Distinguishing clinically meaningful VF vibratory asymmetries from benign ones is therefore important in the effective management of voice disorders. However, previous studies relating asymmetry to acoustic correlates are diverse and often conflicting. For example, Verdonck-de Leeuw et al.'s study of laryngeal videokymography with a small sample of patients found that the presence of left–right phase asymmetry was associated with auditory perception of roughness as measured by noise-to-harmonic ratio (NHR).⁷ Conversely, Zhang et al. showed that left–right vibratory asymmetry did not produce significant changes in voice quality metrics such as NHR and source spectral slopes unless the vibratory asymmetry was significant and accompanied by a change in vibratory mode.⁸

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Further limitations come from the use of measures that carry no perceptual importance to determine listeners' preference of pathologic voices. Traditional measures of dysphonia, such as the aforementioned NHR, as well as jitter (frequency perturbation), and shimmer (amplitude perturbation), each reflects only one perturbation measure and, by themselves, have been shown to be inconsistent predictors of dysphonia⁹ and are thus not clinically useful indices of voice quality.¹⁰ In contrast to traditional quality assessment protocols, voice research has utilized a comprehensive, psychoacoustic model of voice quality to capture the greatest acoustic variability across voices.¹³ Model components include harmonic and inharmonic voice source, loudness of the signal, pitch, and vocal tract information. This study with a canine phonation model utilizes the following indices of the psychoacoustic model: cepstral peak prominence (CPP),^{9,12} root-mean-square (RMS) energy,^{11,13} and the amplitude difference between the first and second harmonics (H1-H2),¹⁴ which are perceptually relevant acoustic measures of voice quality.¹¹

Finally, manipulating the degree of VF asymmetry was unavailable in many previous studies. An *in vivo* canine model with graded nerve stimulation, which is a validated method for a direct manipulation of individual laryngeal muscle stimulation,¹ can offer insights on compensatory neuromuscular rescue of vibratory asymmetry.^{15,16} However, no prior studies have examined the role of the individual ILMs responsible for VF asymmetry. Despite its importance in voice production, little is known about their contributions in producing VF asymmetries.

In this study, we use an *in vivo* canine model of phonation to produce graded levels of VF vibratory asymmetry via stimulation of the bilateral TA muscles. Furthermore, we utilize a validated subset of acoustic metrics from a psychoacoustic model of voice quality that analyzes all samples of normal and disordered voice appropriate for our canine phonation model.¹¹ We aim to investigate (1) the role of the TA in producing vibratory asymmetry, (2) the impact of asymmetric VF stimulation on voice acoustics, and (3) its subsequent impact on perception of voice. We hypothesize that increasingly asymmetric TA vibration results in decreasing quality of voice acoustic metrics, which, in turn, leads to decreased listener preference.

MATERIAL AND METHODS

In Vivo Canine Phonation Model

This study was approved by the Institutional Animal Research Committee of the University of California, Los Angeles. Using an *in vivo* canine model, surgical exposure of the larynx and distal nerve branches of the individual laryngeal nerves was performed as previously described.^{17,18} The internal (sensory) branches of the SLNs and RLN nerve branches to the posterior cricoarytenoid muscle were divided bilaterally to eliminate their effects during nerve stimulation. Tripolar cuff electrodes were applied to the respective nerve branches to simulate the TA and LCA/IA. Nerves were stimulated

with 0.1 ms cathodic pulses at 100 Hz for 1,500 ms. A subglottal tube provided rostral airflow at a constant rate of 500 mL/s until stable phonation was achieved. Audio samples from each phonatory condition were recorded using a probe microphone (Model 4128; Brüel and Kjær, Norcross, GA) mounted flush against the inner wall of the subglottic tube.

We modeled TA vibratory asymmetry through graded neuromuscular activation of the left and right TA muscles. Nerves to each TA muscle were tested across 10 levels of graded stimulation from threshold to maximum muscular contraction, resulting in a total of 100 unique activation combinations. Concurrently, the LCA/IA was maximally stimulated across all stimulation conditions to achieve improved glottal closure. Vibratory symmetry was visually assessed by three trained clinicians and the left/right activation combination that produced opening phase symmetry was labeled as asymmetry level "0." Subsequent steps of neuromuscular activation beyond asymmetry level 0 were designated as increased levels of asymmetry. For example, if left/right TA activation of 5/4 were evaluated as symmetry, left/right TA activation of 5/5 would be labeled "1." Larger values thus reflect greater degrees of asymmetry, which ranged from 0 (symmetry) to 8. Asymmetry level assignment is given in Table I. Absolute values of asymmetry level were used for analysis.

Acoustic Analysis

Measurements included CPP, RMS energy, and H1-H2. CPP is a measure of signal periodicity, which has been consistently demonstrated in listener perception as a robust measure of dysphonia.^{9,12} Increasing values of CPP are associated with higher quality voice. RMS energy was calculated by taking the square root of the average sum of the squares of the amplitude of the signal samples.¹⁹ Although influenced by many factors, the auditory perception of loudness is related to the amplitude of the voice signal, with greater amplitudes being perceived as louder voice. As a measure of amplitude or intensity of the voice signal, increasing RMS energy is therefore related to a louder percept.¹³ Lastly, H1-H2 is associated with a quality continuum from "breathy" to "modal" to "strained," and a decreasing amplitude difference between the first and second harmonics indicates a less breathy voice.²⁰ The variables were sampled every 5 ms from a 1-s portion of stable phonation of each audio sample using VoiceSauce.²¹ To validate our model, we additionally measured the resulting fundamental frequency and the subglottal pressure required for sustained phonation. Ranges for both measured 59 to 101 Hz and 1.18 to 2.56 kPa, respectively, which are within ranges of physiologic canine voice production.^{18,22,23}

Perceptual Study

Eighty-nine naïve listeners participated in the perceptual study. Participants were undergraduate students from the University of California Los Angeles, consisting of 68 females and 21 males (mean age = 19.2 years). The

TABLE I.
Left/Right TA Activation Combinations with Level of Asymmetry.

| Left TA | Right TA | | | | | | | | | | |
|---------|-----------------------|----|----|----|----|----|----|----|----|----|----|
| | Grades of Stimulation | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| | 1 | -1 | -2 | -2 | -3 | -3 | -4 | -4 | -5 | -6 | -7 |
| | 2 | 0 | -1 | -1 | -2 | -2 | -3 | -3 | -4 | -5 | -6 |
| | 3 | 1 | 0 | 0 | -1 | -1 | -2 | -2 | -3 | -4 | -5 |
| | 4 | 2 | 1 | 1 | 0 | 0 | -1 | -1 | -2 | -3 | -4 |
| | 5 | 3 | 2 | 2 | 1 | 1 | 0 | 0 | -1 | -2 | -3 |
| | 6 | 4 | 3 | 3 | 2 | 2 | 1 | 1 | 0 | -1 | -2 |
| | 7 | 5 | 4 | 4 | 3 | 3 | 2 | 2 | 1 | 0 | -1 |
| | 8 | 6 | 5 | 5 | 4 | 4 | 3 | 3 | 2 | 1 | 0 |
| | 9 | 7 | 6 | 6 | 5 | 5 | 4 | 4 | 3 | 2 | 1 |
| | 10 | 8 | 7 | 7 | 6 | 6 | 5 | 5 | 4 | 3 | 2 |

Note: Ten levels of graded stimulation were performed for each TA to produce 100 L/R activation combinations. The combination that produced symmetry was labeled "0" and each step away from symmetry received increasingly higher levels of asymmetry, ranging from 0 to 8.
TA = thyroarytenoid.

perception study was conducted using the same visual sort-and-rate task as in our prior study implemented in Microsoft PowerPoint (Fig. 1).¹⁶ This study design has been previously validated with adequate inter and intra-rater reliability.

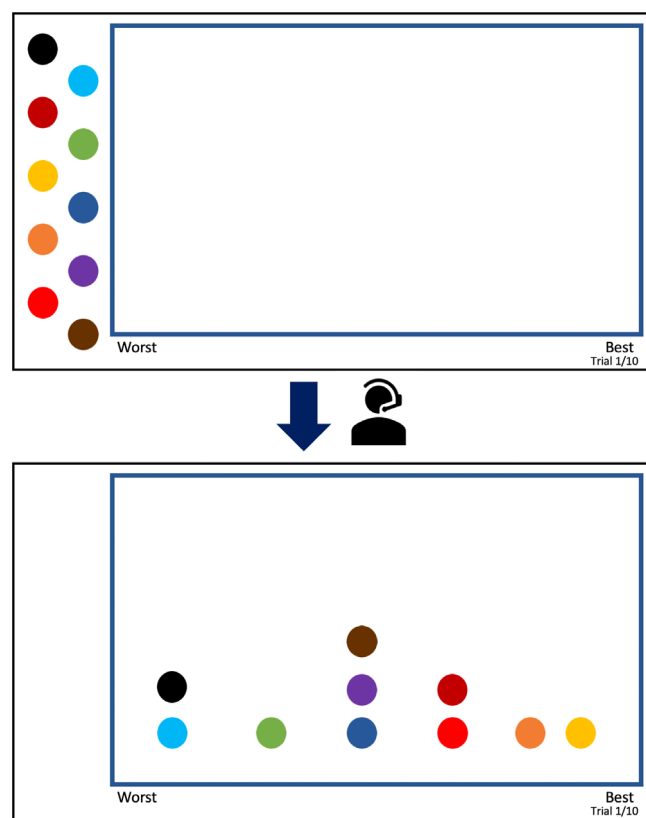


Fig. 1. Visual sort-and-rate task implemented in Microsoft PowerPoint. Each colored icon represents an audio file that listeners would click to listen to. Listeners subsequently dragged each icon from left to right, indicating worst to best in the box provided. All icons in the slide belong to a fixed level of left TA activation with graded Right TA activation. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

Each presentation consisted of 10 slides (blocks), and each slide contained 10 audio samples in randomized order, totaling 100 audio samples tested. Each slide contained audio samples produced from a fixed right TA level coupled with graded left TA stimulation. Each participant was instructed to listen to each sound sample and rate it from "worst" to "best" by dragging the corresponding icon from left to right. If multiple audio samples were perceived to be equally acceptable, participants stacked the icons on top of one another. Matlab (version R2022a) was used to rank each audio file from 1 to 10, indicating worst to best.

Data Analysis

SPSS (Version 27; Chicago, IL) was used for statistical analysis. Relationships between perceptual ratings, CPP, H1-H2, and RMS energy were analyzed using Pearson correlation (Table II). Relationships between acoustic metrics and degree of asymmetry were analyzed using Spearman correlation. One-way ANOVA was used to evaluate the effect of asymmetry levels (0 = symmetric, 1, 2, 3, 4, 5, 6, 7, 8) on voice acoustic and perception metrics. Significant ANOVA results were further analyzed using post hoc Tukey's tests. For this analysis, asymmetry level 8 was grouped with level 7 given only one audio file was produced for level 8. Significance was defined as $p < 0.05$.

RESULTS

Acoustic Correlates of Vibratory Asymmetry

Mean CPP across each level of asymmetry is shown in Table III. The highest mean CPP was produced with symmetric (level 0) stimulation conditions (mean = 25.29) and the lowest mean CPP was produced with asymmetry level 6 (mean = 22.87). Spearman correlation demonstrated a negative correlation between CPP values and asymmetry level ($r = -0.349$, $p < 0.001$) (Table IV). As asymmetry level increased, CPP values decreased. H1-H2

TABLE II.
Correlation Between all Sound Metrics.

| | | CPP | H1H2 | Energy | Asymmetry | Listener Preference |
|---------------------|-----------------|--------|--------|--------|-----------|---------------------|
| CPP | <i>r</i> | 1 | | | | |
| | <i>p</i> -value | | | | | |
| H1H2 | <i>r</i> | -0.365 | 1 | | | |
| | <i>p</i> -value | <0.001 | | | | |
| Energy | <i>r</i> | -0.608 | 0.49 | 1 | | |
| | <i>p</i> -value | <0.001 | <0.001 | | | |
| Asymmetry | <i>r</i> | -0.349 | 0.104 | -0.095 | 1 | |
| | <i>p</i> -value | <0.001 | 0.301 | 0.346 | | |
| Listener preference | <i>r</i> | 0.343 | -0.219 | 0.270 | -0.213 | 1 |
| | <i>p</i> -value | <0.001 | < 0.05 | < 0.01 | < 0.05 | |

Note: Pearson correlation was used for continuous metrics and Spearman correlation was used for ordinal metrics (level of asymmetry).
CPP = cepstral peak prominence; RMS = root-mean-square.

TABLE III.
Mean Values of Acoustic Metrics for Each Level of Asymmetry.

| Asymmetry Level | CPP | H1-H2 | RMS Energy | Listener Preference |
|-----------------|-------|-------|------------|---------------------|
| 0 | 25.29 | 17.12 | 123.72 | 5.92 |
| 1 | 25.17 | 15.99 | 116.23 | 5.63 |
| 2 | 25.19 | 14.51 | 108.70 | 5.83 |
| 3 | 24.87 | 14.61 | 110.98 | 5.62 |
| 4 | 24.40 | 14.15 | 109.83 | 5.33 |
| 5 | 24.10 | 15.30 | 113.46 | 5.15 |
| 6 | 22.87 | 15.56 | 132.83 | 4.99 |
| 7 | 23.42 | 14.67 | 123.90 | 4.44 |
| 8 | 23.75 | 17.35 | 120.24 | 4.04 |

CPP = cepstral peak prominence; RMS = root-mean-square.

and RMS energy did not demonstrate a significant association with asymmetry level.

There was a significant main effect of symmetry levels on CPP ($p < 0.01$). Post hoc analysis revealed that symmetric (level 0) and mildly asymmetric (levels 1, 2) conditions were significantly different from asymmetry level 6 ($p < 0.05$).

Acoustic Correlates of Perception

All three variables were significantly correlated with listener preference (Table V). Increasing CPP ($r = 0.343$, $p < 0.001$), increasing RMS energy ($r = 0.27$, $p < 0.01$) and

TABLE IV.
Spearman Correlation of Sound Metrics Versus Asymmetry Level.

| | Correlation Coefficient (<i>r</i>) | <i>p</i> Value |
|---------------------|--------------------------------------|------------------|
| CPP | -0.349 | <0.001 |
| H1-H2 | 0.104 | 0.301 |
| RMS energy | -0.095 | 0.346 |
| Listener preference | -0.213 | 0.034 |

Note: Bolded values reached statistical significance at $p < 0.05$.
CPP = cepstral peak prominence; RMS = root-mean-square.

TABLE V.
Pearson Correlation of Sound Metrics Versus Listener Preference (Average Rank).

| | Correlation Coefficient (<i>r</i>) | <i>p</i> Value |
|------------|--------------------------------------|-------------------|
| CPP | 0.343 | < 0.001 |
| H1-H2 | -0.219 | 0.029 |
| RMS energy | 0.270 | 0.007 |

Note: Bolded values reached statistical significance at $p < 0.05$.
CPP = cepstral peak prominence; RMS = root-mean-square.

decreasing H1-H2 ($r = -0.219$, $p < 0.05$) were associated with greater listener preference. As shown in Figure 2, CPP ($r = 0.343$, $p < 0.001$) demonstrated the strongest relationship with listener preference among all acoustic metrics.

Vibratory Asymmetry and Perception

Symmetric conditions (level 0) were rated the most favorably. With the exception of asymmetry level 1, increasing asymmetry showed a stepwise decrease in mean perceptual ratings. Moreover, there was a negative

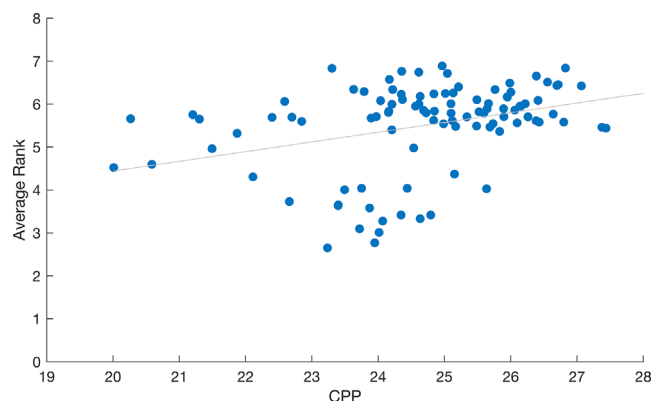


Fig. 2. Scatter plot of listener preference (average of rank) versus CPP. Pearson correlation value is 0.343 ($p < 0.001$). CPP = cepstral peak prominence. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

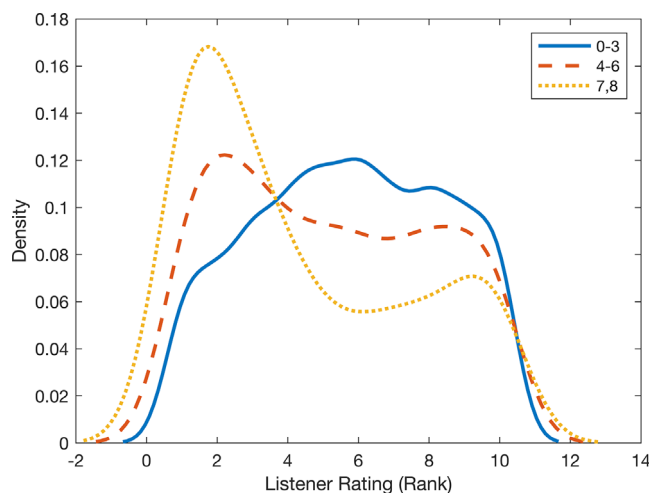


Fig. 3. Kernel density plot displaying distributions of perceptual ratings by level of asymmetry. Symmetric and mildly asymmetric levels (0–3) are shown in blue (solid line). Moderately asymmetric levels (4–6) are shown in orange (dashed line). Severely asymmetric levels (7, 8) are shown in yellow (dotted line). Higher listener rating (rank) indicate greater preference for the audio sample. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

correlation between asymmetry level and listener preference ($r = -0.213$, $p < 0.05$) (Table IV).

One-way ANOVA showed a significant main effect of asymmetry level on listener preference ($p < 0.001$). Listener preference declined as asymmetry level increased. Post hoc analysis revealed that whereas symmetric (level 0) and mildly asymmetric conditions (levels 1–3) were not different from each other, they were rated significantly higher than severely asymmetric conditions (levels 5–8) ($p < 0.05$) (Fig. 3).

DISCUSSION

This study systematically investigates the effects of TA asymmetry on voice acoustics and perception using an in vivo canine model of phonation. As hypothesized, increasingly asymmetric activation of left/right TA muscles generated increasingly poorer quality voice as indicated by CPP. This study therefore suggests that TA asymmetry alone is sufficient to produce changes in voice quality and thus plays a pivotal role in producing VF asymmetries.

The present study also examines what degree of VF asymmetries results in perceivable voice changes. It has been suggested that minor laryngeal asymmetries are relatively common and also clinically irrelevant and represent asymmetries found in vocally normal speakers.^{4,8,24} Evaluation of CPP in relation to degree of TA asymmetry in this study suggests that mild asymmetries are resilient to a decline in voice quality. Indeed, it is not until asymmetry level 6 is reached that a significant difference in CPP between groups is detected. Because asymmetry level 6 represents six (of ten) graded steps away from symmetric VF vibration, our findings suggest that a

significant degree of neuromuscular insult is required before consequences in voice quality take place, consistent with Zhang's assessment of VF asymmetry using a two-layer physical model.⁸ Of note, CPP values obtained across all levels of asymmetry indicate seemingly high-quality voice, as previous studies have reported CPP values as low as 10 as cutoffs for dysphonia.²⁵ However, we suggest that CPP values need to be relatively evaluated within a study of well-balanced experimental conditions. Our results demonstrate that increasing asymmetry results in a significant decline in voice quality in our in vivo model.

Additional voice quality metrics used in this study included H1-H2 and RMS energy, both of which were not significantly correlated with degree of TA asymmetry. H1-H2 generally corresponds to open quotient (OQ) in which an increase in OQ results in breathier voice.²⁶ Furthermore, H1-H2 is heavily dependent on VF medial surface thickness with additional influences from resting glottal angle, anterior–posterior stiffness, and subglottal pressures.²⁷ Therefore, a significant relationship between H1-H2 and TA asymmetry may not have been captured in this study due to changes in various physiologic parameters that were not accounted for. For instance, previous computational analyses showed significant effects on H1-H2 when modulating VF left–right body stiffness even during symmetric conditions.⁸ Our current schema for relating vibratory asymmetry and acoustic metrics would therefore not capture variations in H1-H2 given left/right symmetry is not differentiated between soft/soft and stiff/stiff conditions, which would influence H1-H2 according to these previous findings. Further exploration of VF vibratory asymmetry and its influence on the above VF parameters and resulting changes in H1-H2 is required to fully identify the relationship between this acoustic metric and vibratory asymmetry.

Similarly, variations in RMS energy are also impacted by varying stimulation conditions. Previously, Zhang found decreasing energy as measured by sound pressure level (SPL) with increasing VF vertical thickness in symmetric conditions.²⁸ Again, a complex interplay between numerous parameters including resting glottal angle and transverse and anterior–posterior stiffness impacted the resulting acoustic signal. As changes in neuromuscular stimulation ultimately affect additional parameters such as medial surface shape in addition to VF approximation,²⁹ both impacting RMS energy, a systematic understanding of the effects of asymmetry and RMS energy warrants further exploration.

To validate quantification measures, results must be related to perception of voice quality to be clinically meaningful.^{7,15,30} Our results confirm that CPP is a reliable correlate of perceptual measures of dysphonia, as listeners are most sensitive to changes in CPP among all acoustic metrics measured. Despite the lack of significant correlations found between H1-H2 and RMS energy with degree of asymmetry, these acoustic metrics demonstrate significant relationships with listener preference, and their utility in perceptual evaluation of dysphonia remain important complements to CPP. The negative correlation between H1-H2 and perceptual preference in the current

study indicates that, unsurprisingly, listeners prefer less breathy voices. The positive correlation between RMS energy and preference similarly indicates listeners prefer louder voices.

Finally, we demonstrate a significant relationship between degree of asymmetry and listener preference, in which symmetric conditions are preferred over asymmetric conditions. Our model of vibratory asymmetry is therefore perceptually validated and clinically meaningful. A more nuanced finding is that our perceptual study corroborates the above notion that mildly asymmetric vibrations are clinically benign; only severely asymmetric conditions are perceptually salient in naïve listeners, resulting in a nonlinear relationship between asymmetry and perception. That is, symmetric and mildly asymmetric conditions are not perceptually different from each other, and only severely asymmetric conditions are rated significantly poorly. Therefore, not only are mild asymmetries resistant to an objective decline in voice quality as measured by CPP, but they are also importantly resistant to a subjective, *perceived* decline in voice quality.

Although this study contributes to our understanding of the causal link between VF vibratory asymmetry and voice quality, limitations exist. TA activation plays only one role in modulating VF vibratory asymmetry and, ultimately, the acoustic metrics of the voice signal. Future work may include investigating the combined effects of modulating TA asymmetry with other ILMs, for example, to account for the unexplained variance in acoustic measures in this study.

CONCLUSION

To our knowledge, this study is the first to explore vibratory asymmetry as a function of asymmetric TA muscle activation and evaluate its subsequent effects on voice quality and perception. Results suggest that asymmetric TA activation plays an important role in modulating voice quality, as increasing TA asymmetry results in worsening quality metrics. Increasing asymmetry is further correlated with decreased perceptual ratings. However, mild asymmetries are perceptually tolerated. In fact, a substantial amount of vibratory asymmetry is required before consequences in both objective metrics and subjective perception of voice quality result. This study contributes to our understanding of voice production and quality by identifying perceptually salient and therefore clinically meaningful laryngeal vibratory asymmetry.

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