Quantifying Voice Change After Hydration Treatment in Primary Sjögren’s Syndrome Using the Cepstral Spectral Index of Dysphonia (CSID)

Alison Miner
Brigham Young University - Provo

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Quantifying Voice Change After Hydration Treatment in Primary Sjögren’s Syndrome

Using the Cepstral Spectral Index of Dysphonia (CSID)

Alison Miner

A thesis submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of
Master of Science

Kristine Tanner, Chair
Ron Channell
Shawn L. Nissen

Department of Communication Disorders
Brigham Young University
September 2014

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ABSTRACT

Quantifying Voice Change After Hydration Treatment in Primary Sjögren’s Syndrome Using the Cepstral Spectral Index of Dysphonia (CSID)

Alison Miner
Department of Communication Disorders, BYU
Master of Science

Primary Sjögren’s Syndrome (SS) is an autoimmune disease that causes dehydration of the eyes, mouth, and throat. Individuals with Primary SS are at risk for voice problems associated with vocal fold dehydration. Topical hydration treatments show promise in reducing the negative effects of vocal fold dehydration on voice production. However, no studies have examined the preventive effects of topical hydration treatments on voice production in individuals at risk for vocal fold dehydration. The purpose of this study was to quantify the effects of a topical vocal fold hydration treatment on voice production in individuals with Primary SS using the Cepstral Spectral Index of Dysphonia (CSID). Eight participants with Primary SS completed an eight-week study involving twice-daily audio recordings of sustained vowels and the Rainbow Passage. Participants received 9 mL of nebulized isotonic saline (0.9% Na’Cl’) immediately following morning and evening voice recordings during weeks 3, 4, 7, and 8 using an ABAB within-subjects experimental design. Baseline CSID values were in the mild range. Although CSID values decreased (improved) during the treatment phases of the study, no statistically significant changes were observed from baseline to treatment. Statistically significant correlations were observed among CSID values and patient-based ratings of vocal effort and dryness, which did improve with treatment (p < .05). These results indicate that topical saline treatments may prevent and treat some voice problems associated with vocal fold dehydration in at-risk populations.

Keywords: Sjögren’s Syndrome, CSID, laryngeal hydration, vocal effort, nebulized saline
ACKNOWLEDGMENTS

Above all, I would like to thank my thesis chair, Kristine Tanner, who has been both a personal and professional mentor throughout this process. Her grasp of the speech-language pathology field and her zeal for excellence constantly left me in awe, and full of appreciation for the opportunity to work with her. I would also like to thank my thesis committee for their encouragement and continued reminders of the big picture, even in times when I felt we were under pressure. Finally, I would like to thank my family and friends for having confidence I could do this and faith I could do it well. They repeatedly provided a listening ear for me to discuss my research with, and that made all the difference.
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DESCRIPTION OF STRUCTURE AND CONTENT

The body of this thesis was written as a manuscript suitable for submission to a peer-reviewed journal in speech-language pathology. This thesis is part of a larger collaborative project, portions of which may be submitted for publication, with the thesis author being one of multiple co-authors. The participant consent form, materials related to the study, and an annotated bibliography are presented as noted in the List of Appendices.
Introduction

Sjögren’s Syndrome (SS) is an autoimmune disease that affects the lacrimal and salivary glands, causing extreme dryness of the eyes and mouth (Allec et al., 2011; Kassan & Moutsopoulos, 2004; Ogut et al., 2005). These dryness or sicca symptoms may also affect other areas of the body, including the throat, lower airway, intestines, and vagina. Primary SS occurs in the absence of another autoimmune condition, whereas Secondary SS is the result of, or is secondary to, another autoimmune disease such as rheumatoid arthritis, lupus, or mixed connective tissue disease (Kassan & Moutsopoulos, 2004). Because Secondary SS results from other more common autoimmune diseases, Primary SS is more rare. SS most frequently occurs in females after menopause, though males may also develop SS; incidence rates of SS are approximately nine females to one male (Freeman, Sheehan, Thorpe, & Rutka, 2005). Recent reports indicate that approximately four million individuals in the US have SS, though only four in 100,000 are diagnosed with Primary SS (Kruszka & O’Brien, 2009; Pillemer et al., 2001).

Individuals with SS may experience voice, speech, and swallowing problems (Freeman et al., 2005; Heller et al., 2014; Kassan & Moutsopoulos, 2004; Ogut et al., 2005). Voice-related auditory-perceptual features include varying degrees of hoarseness, breathiness, huskiness, and strain (Allec et al., 2011; Ogut et al., 2005). Voice symptoms can include increased vocal effort and vocal fatigue (Tanner et al., 2013). Laryngostroboscopic studies have documented vibratory abnormalities, including reduced mucosal wave, amplitude of vibration, phase symmetry, and glottal closure (Allec et al., 2011; Ogut et al., 2005). Individuals with SS may demonstrate differences in traditional peak-picking acoustic measures, including shimmer, jitter, pitch perturbation quotient, and amplitude perturbation quotient (Ogut et al., 2005).
In addition to voice-related changes, individuals with SS may experience speech-motor problems related to dry mouth and peripheral neuropathy. An oral clicking sound may be noted due to decreased salivary production, causing the tongue to stick to the roof of the mouth when speaking (i.e., lingual-palatal diglossia). Nervous system alterations may also contribute to mild dysarthria of the moving articulators. Poor dentition due to xerostomia-related tooth loss may also contribute to articulatory changes (Kruszka & O’Brien, 2009; Sheehan, 2008).

One of the most common SS symptoms includes oropharyngeal and esophageal dysphagia, with symptoms reported in approximately 75% of cases. This is likely due to the combination of decreased saliva production causing oropharyngeal dryness as well as esophageal dysmotility (Kjellen, Fransson, Lindström, Sökjer, & Tibbling, 1986; Sheehan, 2008). The decrease in saliva production can lead to difficulty with chewing and swallowing, particularly with dry foods and pills. Esophageal dysmotility also results from nervous system alterations. Approximately one-third of those with SS have abnormal esophageal peristalsis leading to severe dysphagia, while the decreased salivary production intensifies the discomfort of the dysphagia (Anselmino et al., 1997). Studies showing a lack of correlation between dysphagia and salivary secretion in SS indicate that other unknown factors may also be responsible for dysphagia in this population (Anselmino et al., 1997; Sheehan, 2008). Chronic, non-productive cough has also been noted (Allec et al., 2011; Kassan & Moutsopoulos, 2004).

Collectively, research involving SS populations indicates that voice, speech, and swallowing symptoms may be related, in part, to the nature and severity of their sicca symptoms. Laryngeal dryness is known to be associated with voice problems. Vocal fold vibration depends on the state of the vocal fold mucosa, which in turn depends on the hydration level of this tissue (Verdolini-Marston, Titze, & Druker, 1990; Verdolini-Marston, Titze, & Fennell, 1994).
Hydration of the vocal folds improves voice production by promoting efficient vibration (Leydon, Wroblewski, Eichorn, & Sivasankar, 2010). The viscosity, or thickness, of the fluid within the vocal folds influences their biomechanical properties. As the viscosity of the fluid inside the vocal folds increases, vibratory efficiency decreases. Similarly, vibratory efficiency decreases as the fluid on the surface of the vocal folds increases in viscosity. Therefore, hydration of the vocal fold surface and of the fluid inside the vocal folds is important for efficient, healthy voice production (Verdolini-Marston et al., 1990; Verdolini-Marston et al., 1994).

Internal vocal fold hydration is maintained systemically and is supported by liquid consumption. The renal system metabolizes this fluid, which is then delivered to cells throughout the body. Vocal fold surface fluid is maintained by systemic and surface tissue mechanisms (Sivasankar & Fisher, 2007). The mechanisms that maintain vocal fold surface fluid are similar to those that regulate surface fluid in the lungs, bronchi, trachea, and nose (Leydon, Sivasankar, Falciglia, Atkins, & Fisher, 2009). The surface of the vocal folds is covered with water and mucus layers. The water, or sol, layer is deepest to the mucosa and is approximately 15 microns deep (Widdicombe, 1997). Superficial to the sol layer is the mucus layer. The sol and mucus layers on the vocal fold surface are continuous with the fluid that lines the rest of the respiratory tract and airway. Vocal fold surface fluid is maintained, in part, by water and ion fluxes across the vocal fold epithelia (Leydon et al., 2009). Numerous in vivo and in vitro studies have shown the negative effects of dehydration on optimal vocal fold functioning and the mechanisms behind this (Sivasankar & Fisher, 2007; Sivasankar & Fisher, 2008; Witt, Taylor, Regner, & Jiang, 2011).

Recent research indicates that individuals with SS are specifically at risk for voice problems associated with laryngeal dehydration (Tanner et al., 2013). Following a desiccation
challenge involving eleven patients with Primary SS, patients reported significant increases in mouth dryness, throat dryness, and vocal effort. The Voice Handicap Index (VHI, Appendix C; Jacobsen et al., 1997) showed a positive correlation with the dryness and vocal effort measures at baseline. Patients also rated self-perceived vocal effort and mouth and throat dryness using a 10 cm visual analog scale (VAS) as shown in Appendixes D and E, and reported their self-perceived SS severity using the ESSPRI (EULAR Sjögren’s Syndrome Patient Reported Index, Appendix F; Seror et al., 2012). Phonation threshold pressure (PTP), the minimum amount of pressure required to initiate and sustain vocal fold oscillation (Titze, 1994), also increased significantly. Following nebulized saline treatment, improvement in throat dryness and PTP were noted, with values below, or better than, those observed at baseline. Similar findings were observed for individuals with normal voices (Tanner, Roy, Merrill, & Elstad, 2007; Tanner et al., 2010). These foundational works demonstrate that the manipulation and increase of surface vocal fold hydration is possible through topically administered treatments. Supporting the functionality and efficiency of laryngeal hydration may be beneficial in helping those who suffer from systemic or superficial vocal fold dehydration.

Other studies provide additional evidence for the relationship between vocal fold dehydration and self-perceived vocal effort ratings. Sivasankar and Erickson-Levendoski (2012) found that PTP was significantly affected by mouth breathing during exercise and in environments of varying humidity. Even in short-term trials, oral breathing has been shown to increase PTP and self-perceived vocal effort (Sivasankar & Fisher, 2002), providing support for the assumption that the surface layer of the vocal folds responds to the humidity of inhaled air. This increase in PTP was also noted in trials of prolonged, loud speech (Solomon, Glaze, Arnold, & van Mersbergen, 2003; Solomon & DiMattia, 2000).
Traditionally, PTP has been used to indirectly estimate changes in pulmonary effort related to vocal fold hydration. These studies have shown that as vocal fold hydration increased, PTP decreased (Leydon et al., 2010). However, much variability exists in PTP measurement. It is possible that acoustic measures may also be useful in detecting changes in vocal fold vibration following hydration treatment. Hemler and colleagues have documented a significant increase in perturbation measures, including parameters of jitter and shimmer, following dry air exposure (Hemler, Wieneke, & Dejonckere, 1997). However, these time-based acoustic measures apply peak-picking algorithms, which are not always sensitive to aperiodic voices (Titze, 1995).

In contrast to time-based measures, the Cepstral Spectral Index of Dysphonia (CSID) is a spectral measure computed using frames of signal data rather than cycle boundary identification (Peterson et al., 2013). This acoustic analysis measure gives a graphic display in which a highly periodic sample shows a greater cepstral peak (i.e., a clearly defined harmonic and fundamental frequency). A signal with more noise and decreased periodicity, such as that likely found in a dysphonic voice, shows a signal with a lesser cepstral peak. This measure not only allows for an estimate of dysphonia severity in sustained vowels but may also be applied to connected-speech samples. CSID values usually range from 1 to 100, but may exceed these boundaries, with lower numbers representing more normal, or periodic, voicing and higher numbers representing more aperiodic voicing.

This study examined the effects of a topical hydration treatment on voice production in Primary SS using the CSID. These CSID values were compared to self-perceived effort and dryness ratings collected as part of a larger investigation. It was hypothesized that CSID values would demonstrate voice improvement as observed in the patient-based ratings. It was further
hypothesized that CSID values would correlate with patient-based ratings of vocal effort and dryness.

**Method**

**Participants**

Eight females (mean age = 57; range 36 to 74 years) with Primary SS participated in this study. All participants were identified and recruited at The University of Utah Division of Rheumatology. A rheumatologist with expertise in SS assigned the diagnosis, including clinical evaluation of sicca symptoms and anti-nuclear antibody testing with or without lip biopsy. Mean number of years with sicca symptoms was 14 (range 3 to 30 years), and mean number of years since diagnosis was 11 (range 2 to 32 years). Significant medical history factors for each participant are presented in Appendix G. The University of Utah and Brigham Young University Institutional Review Boards approved all procedures related to this study (IRB_00061835).

Prior to initiating the study, participants completed the ESSPRI (Seror, 2012), the Sicca Symptoms Inventory (SSI; Bowman, Booth, Platts, Field, & Rostron, 2003), and the VHI (Jacobsen et al., 1997). The ESSPRI and SSI were used to quantify patient-based SS disease severity; the VHI quantified patient-reported voice handicap related to the possible presence of a voice problem, with 0 being no handicap and 120 being an extreme handicap. The ESSPRI involves a 10-point equal-appearing interval scale for three domains, including dryness, limb pain and fatigue; the final score is the mean of each domain. The SSI utilizes four domains, including ocular, oral, vaginal, and cutaneous dryness. The SSI scale ranges from 0 to 7 for each item, with 0 being no problem and 7 being an extreme problem; the final score is the sum of the four domains.
Study Design

This study involved an eight-week within-subjects, repeated measures ABAB design. The study included four two-week phases. A study timeline is provided in Appendix H. Weeks one and two (i.e., the A phase) consisted of baseline audio recordings and patient-based perceptual ratings of vocal effort and dryness. Weeks three and four (i.e., the B phase) incorporated a twice-daily topical hydration treatment. During weeks five and six (i.e., second A phase and treatment withdrawal) participants continued audio recordings and perceptual ratings, but received no treatment. In weeks seven and eight (i.e., the B phase) participants resumed nebulized saline treatment.

Study Procedures

Twice-daily audio recordings included the first paragraph of the Rainbow Passage (Fairbanks, 1960), three sustained vowels, select sentences from the Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V; Zraick et al., 2011), and single-word lists (see Appendix I). Only the sustained vowels and excerpts from the Rainbow Passage were examined in the present study. Participants were given written instructions and photos to guide audio-recording acquisition. Recordings were obtained in a quiet environment using the Zoom Handy Recorder, model H1, and an Audio Technica head-mounted microphone (model ATM 75-SP-NP). Participants received additional instructions to monitor the VU meter and avoid peak-clipping. Recordings were saved to a SanDisk 32GB Ultra Micro SD card. Immediately after each audio recording, participants rated self-perceived vocal effort, mouth dryness, and throat dryness using 10 cm VASs. The extreme left of the scale represented no effort or dryness and the extreme right represented significant effort or dryness. VAS rating scales and corresponding participant instructions are included in Appendixes D and E.
Upon completion of each two-week phase (i.e., on days 14, 28, 42, and 56), participants again completed the VHI, ESSPRI, and SSI. During weeks three and four (i.e., the first B phase) participants continued to complete audio recordings and VAS ratings each morning and evening. Participants then nebulized 9 mL of Simply Saline™ isotonic saline (Na\(^+\)Cl\(^-\)) twice daily, using the Omron MicroAir Vibrating Mesh Nebulizer™ (Model NE-U22V). Participants were instructed to perform recordings and VAS ratings prior to nebulized saline treatment to avoid possibly documenting only the short-term effects of nebulized saline on voice production and dryness (Tanner et al., 2013). During weeks five and six, participants continued to collect voice recordings and VAS ratings twice daily, but the nebulized saline treatment was withdrawn. During weeks seven and eight, participants again resumed the twice-daily nebulized saline treatments immediately following audio recordings and VAS ratings.

**CSID Analysis**

Original audio recordings from each Micro SD card were transferred to an iMac computer via a Micro USB cable. Recordings were downsampled to 25 kHz (16-bit), trimmed, coded, and saved as .wav files using Adobe Audition, v. 5.0 (Adobe, Inc.). Sample tokens for CSID analysis included (a) the central three seconds of the second of three sustained vowels and (b) the second and third sentences of the Rainbow Passage. Samples were excluded if significant background noise was present, if recording protocols were not followed, or if the participant omitted one or more words from the Rainbow Passage. Of the possible 896 sustained vowel and 896 sustained vowel recordings in this study (i.e., 8 participants x 56 days x 2 daily recordings), 124 were excluded due to the above factors, 108 of which were from a single participant who did not follow the sustained vowel recording protocol. Additionally, 40 tokens (21 sustained vowel
and 19 Rainbow Passage tokens) were not recorded by participants. Therefore, 768 sustained vowel and 860 Rainbow Passage tokens (i.e., 1628 total tokens) were included for analysis.

Using the Analysis of Dysphonia in Speech and Voice (ADSV™), batch file commands were used to generate the cepstral peak prominence, the low-to-high spectral ratio, and the standard deviation of the low-to-high spectral ratio required for CSID calculation. These variables were used to calculate the CSID for vowel tokens (Awan, Roy, & Dromey, 2009) and Rainbow Passage tokens (Peterson et al., 2013). To ensure no differences existed between the batch command-derived values and those produced during individual sample analysis via the ADSV™ program interface, 10% of vowels were re-analyzed individually. These CSID calculations were identical to the batch file-derived CSID values, or were within .01, a difference likely due to rounding. All Rainbow Passage CSID values were calculated from the batch command-derived cepstral peak prominence, the low-to-high spectral ratio, and the standard deviation of the low-to-high spectral ratio, as Rainbow Passage CSID calculations are not yet commercially available in the ADSV™ program; however, the batch-derived values were identical or within .01 to those generated during individual sample analysis for the 10% re-analyzed Rainbow Passage tokens via the ADSV™ program interface.

**Statistical Analysis**

Descriptive summary statistics were used to describe participants at baseline on acoustic and patient report measures. Treatment effects over time were examined using the Friedman nonparametric analysis of variance. Missing data points were replaced by adjacent samples from the same participant, treatment phase, and time of day. Relationships among CSID and VAS ratings were examined using Spearman correlations. Fourth-order polynomial modeling was
used to evaluate temporal trends. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, v. 21, IBM, Armonk, NY).

Results

Patient-Based Measures of Voice and Disease Severity

Mean, standard deviation, median, and range for the VHI, ESSPRI, and SSI on days 1, 28, 42, and 56 are presented in Table 1. Baseline patient-based ratings of voice handicap related to their voice problems were in the mild to mild-to-moderate range (Jacobsen et al., 1997). Baseline patient-based ratings of disease severity were in the moderate range (Bowman et al., 2003; Seror et al., 2012). Freidman tests for related samples detected no significant changes in VHI (p = .298), ESSPRI (p = .300), or SSI (p = .902) across study phases.

Table 1

Participants Perceptual Ratings

<table>
<thead>
<tr>
<th>Measure</th>
<th>Day 1</th>
<th>Day 28</th>
<th>Day 42</th>
<th>Day 56</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VHI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>32.5</td>
<td>31.1</td>
<td>28.0</td>
<td>26.9</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>16.8</td>
<td>23.8</td>
<td>20.2</td>
<td>15.4</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>29.0</td>
<td>23.8</td>
<td>25.0</td>
<td>25.0</td>
<td>.298</td>
</tr>
<tr>
<td>Range</td>
<td>12.0-62.0</td>
<td>7.0-74.0</td>
<td>8.0-63.0</td>
<td>10.0-56.0</td>
<td></td>
</tr>
<tr>
<td>ESSPRI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>5.3</td>
<td>4.8</td>
<td>5.7</td>
<td>4.7</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>1.0</td>
<td>1.7</td>
<td>0.8</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>5.0</td>
<td>4.8</td>
<td>5.7</td>
<td>4.2</td>
<td>.300</td>
</tr>
<tr>
<td>Range</td>
<td>4.0-6.7</td>
<td>2.7-7.3</td>
<td>4.3-7.0</td>
<td>2.7-7.0</td>
<td></td>
</tr>
<tr>
<td>SSI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>13.1</td>
<td>12.6</td>
<td>12.8</td>
<td>12.5</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>3.2</td>
<td>5.2</td>
<td>4.2</td>
<td>4.6</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>12.8</td>
<td>12.4</td>
<td>12.9</td>
<td>13.2</td>
<td>.902</td>
</tr>
<tr>
<td>Range</td>
<td>8.0-16.8</td>
<td>5.7-22.3</td>
<td>8.4-20.4</td>
<td>5.1-19.1</td>
<td></td>
</tr>
</tbody>
</table>

Note. Total scores for the Voice Handicap Index (VHI), the EULAR Sjögren’s Syndrome Patient Reported Index (ESSPRI), and the Sicca Symptoms Inventory (SSI), including mean, standard deviation (SD), median, and range, for days 1, 28, 42, and 56.
CSID

Mean, standard deviation, median, and range for CSID sustained vowel and Rainbow Passage analyses on days 1, 28, 42, and 56 are presented in Table 2. Baseline CSID values were in the mild-to-moderate range of voice disorder severity based on previously reported severity criteria (Awan et al., 2009; Petersen et al., 2013). CSID values decreased by approximately 20%, on average, during nebulized treatment weeks, and began increasing during treatment withdrawal weeks; these changes were more apparent for sustained vowels versus Rainbow Passage tokens. For sustained vowels, Freidman tests for related samples detected no significant changes in CSID values across days 1, 28, 42, and 56 for morning (p = .615) or evening (p = .116) recordings.

Table 2

CSID Values

<table>
<thead>
<tr>
<th>Measure</th>
<th>Day 1</th>
<th>Day 28</th>
<th>Day 42</th>
<th>Day 56</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSID vowel (AM)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>10.9</td>
<td>7.8</td>
<td>6.7</td>
<td>9.2</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>8.1</td>
<td>10.6</td>
<td>9.7</td>
<td>11.3</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>10.8</td>
<td>7.5</td>
<td>7.1</td>
<td>13.1</td>
<td>.615</td>
</tr>
<tr>
<td>Range</td>
<td>2.6-26.2</td>
<td>-5.5-23.5</td>
<td>-7.3-21.1</td>
<td>-4.9-22.0</td>
<td></td>
</tr>
<tr>
<td>CSID vowel (PM)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>17.0</td>
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<tr>
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Note. Cepstral Spectral Index of Dysphonia (CSID) values for morning (AM) and evening (PM) sustained vowel and Rainbow Passage recordings.
Trend analyses for morning and evening sustained vowel recordings are presented in Figures 1 and 2.

*Figure 1. Cepstral Spectral Index of Dysphonia (CSID) for morning (AM) sustained vowels.*
Figure 2. Cepstral Spectral Index of Dysphonia (CSID) for evening (PM) sustained vowels.
Trend analyses for morning and evening Rainbow Passage recordings are presented in Figures 3 and 4.

Figure 3. Cepstral Spectral Index of Dysphonia (CSID) for morning (AM) Rainbow Passages.
Figure 4. Cepstral Spectral Index of Dysphonia (CSID) for evening (PM) Rainbow Passages.
VAS Ratings

Mean, standard deviation, median, and range for VAS ratings of vocal effort, mouth dryness, and throat dryness on days 1, 28, 42, and 56 are presented in Table 3. Friedman tests for related samples detected significant changes in evening ratings of mouth dryness ($p = .024$) and throat dryness ($p = .018$), but not for vocal effort. To accomplish post-hoc comparisons between day 1 and days 28, 42, and 56, Wilcoxon Signed Ranks Tests were undertaken using a Bonferroni correction for multiple comparisons (alpha $.05/3 = .016$). For mouth dryness, no significant differences between days 1 and 28 ($p = .025$), days 1 and 42 ($p = .035$), or days 1 and 56 ($p = .05$) were observed. For throat dryness, a significant difference was observed between days 1 and 28 ($p = .012$), but not between days 1 and 42 ($p = .208$) or between days 1 and 56 ($p = .036$). No other significant differences were observed.

Correlations

Spearman correlations were used to quantify the strength of relationships among CSID values and patient-based ratings of vocal effort, mouth dryness, and throat dryness. CSID values for sustained vowel and Rainbow Passage tokens were significantly correlated for evening ($r = .320, p = .016$) but not morning ($r = .189, p = .164$) recordings. Morning CSID values for sustained vowels were significantly correlated with morning ratings of vocal effort ($r = .327, p = .014$), mouth dryness ($r = .302, p = .024$), and throat dryness ($r = .355, p = .007$). Morning CSID values for Rainbow Passage were significantly correlated with morning ($r = .411, p = .002$) and evening ($r = .416, p = .001$) ratings of vocal effort, morning ($r = .366, p = .005$) and evening ($r = .293, p = .028$) ratings of mouth dryness, and morning ($r = .367, p = .005$) and evening ($r = .383, p = .004$) ratings of throat dryness. Evening CSID values for sustained vowel and Rainbow Passage tokens were not significantly correlated with patient ratings.
Table 3

VAS Ratings

<table>
<thead>
<tr>
<th>Measure</th>
<th>Day 1</th>
<th>Day 28</th>
<th>Day 42</th>
<th>Day 56</th>
<th>p value</th>
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<td><strong>Vocal Effort (PM)</strong></td>
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<tr>
<td><strong>Mouth Dryness (AM)</strong></td>
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<td>4.1</td>
<td>3.9</td>
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<td><strong>Mouth Dryness (PM)</strong></td>
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<tr>
<td><strong>Throat Dryness (AM)</strong></td>
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<td></td>
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</tr>
<tr>
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<td>3.5</td>
<td>4.5</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
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</tr>
<tr>
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<td>3.9</td>
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<td>4.0</td>
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Notes. Visual analog scale (VAS) ratings for vocal effort, mouth dryness, and throat dryness in the morning (AM) and evening (PM), including mean, standard deviation (SD), median, and range, for days 1, 28, 42, and 56. *statistically significant at alpha < .05
Discussion

The current study attempted to quantify the acoustic changes in voice production following nebulized saline treatments in individuals with Primary SS. As part of a larger investigation, eight individuals with Primary SS received twice-daily doses of nebulized saline treatment during two-week intervals using an eight-week ABAB withdrawal experimental design. This investigation was the first to examine effects of a larger 9 mL dose of nebulized isotonic saline, delivered regularly over a two-week period, using low-airflow ultrasonic nebulization. Analysis of the results from the larger investigation revealed significant improvements (i.e., reductions) in vocal effort, mouth dryness, and throat dryness based on perceptual ratings. Similarly, the current study also documented a 20% improvement in voice production, on average, with the nebulized saline treatment based on CSID acoustic analysis. These findings were more pronounced for sustained vowels versus connected speech samples. Significant correlations were observed among CSID analyses and patient-based ratings of effort and dryness.

The lack of statistical significance for baseline to treatment comparisons necessitates some caution when interpreting trends. However, the present study does shed light on the potential benefits of nebulized saline treatments in this population. Previous studies have documented one-time benefits of nebulized isotonic saline (Tanner et al., 2007; 2010) in Primary SS following laryngeal desiccation challenge (Tanner et al., 2013), but the prophylactic, long-term benefits were not tested at that time. Additionally, the low-flow ultrasonic nebulizer employed in this study facilitated delivery of nebulized saline without the potential drying effects of traditional jet nebulizers. Therefore, the current study results support the theory that nebulized saline may improve voice production over time in individuals at risk for vocal fold dehydration. These results also support previous findings that hydration treatments may be used to treat vocal
fold dehydration in the absence of an explicit laryngeal desiccation challenge (Hemler et al., 1997; Leydon et al., 2010; Verdolini-Marston et al., 1994).

Several findings in the current study offer a strong contribution to the literature in vocal fold hydration treatment and warrant discussion here. First, it is important to consider the significance of the prophylactic nature of the saline treatment applied in this study. It was theorized that a laryngeal desiccation challenge was not necessary due to the already dry nature of SS, further supported by studies showing positive hydration treatment effects occurring when not preceded by a desiccation challenge (Leydon et al., 2010; Roy, Tanner, Gray, Blomgren, & Fisher, 2003; Verdolini-Marston et al., 1994). Conceptually, a twice-daily nebulized saline treatment might be analogous to other topical hydration treatments for the eyes, mouth, and skin; as such, these treatments may be expected to have immediate, short-term, and long-term benefits to treating and preventing dryness. In a similar vein, these treatments might be quantified physiologically as well as subjectively, using patient-based ratings of comfort or dryness. It is important to note that all observed effects were obtained in participants’ natural environment. Additionally, it is noteworthy that audio recordings were obtained prior to each nebulized treatment, to avoid repeatedly measuring only short-duration nebulized saline benefits that have been documented in previous studies (Tanner et al., 2010, 2007, 2013). Participants’ perceptual ratings indicated moderate vocal effort, mouth dryness, and throat dryness. These ratings improved during the third and fourth weeks (i.e., during the first phase of treatment). Subsequently, the ratings worsened during the treatment withdrawal. This study documented short-term, long-term, and carry-over effects of nebulized saline treatment by the fact that although ratings worsened during the second treatment withdrawal phase, they were not as severe as ratings obtained during initial baseline data collection. Collectively, these findings
indicate that nebulized saline is an effective treatment for vocal fold dehydration and adverse effects from dehydration. Although these changes from baseline to treatment were not statistically significant, it is important that these treatment effects have now been demonstrated over time.

A second important finding involves the significant correlations among CSID values and patient-based ratings of effort and dryness. Analysis of the results revealed significant correlations among all morning CSID values and morning ratings of vocal effort, mouth dryness, and throat dryness; morning CSID values for the Rainbow Passage were also significantly correlated with evening patient-based ratings. However, it is interesting that no significant correlations were observed between evening CSID values and patient ratings. It is possible that other factors, such as voice use practices, might have influenced the CSID values differently than the patient-based ratings. Previous studies have demonstrated somewhat poor relationships between patient-based and physiologic measures of vocal effort (Sivasankar & Fisher, 2002; 2003; Tanner et al., 2010). Recently, McHenry, Evans, and Powitzky (2013) observed a pronounced lack of correlation between ratings of vocal effort and PTP in a study involving 48 singers. Therefore, it is not entirely surprising that CSID values were not always correlated with perceptual ratings. What is interesting is the fact that morning CSID values were correlated with perceptual ratings, while evening CSID values were not. More strikingly, morning CSID values for the Rainbow Passage were correlated with both morning and evening perceptual ratings. One possible explanation for this would be that the CSID is more sensitive to dynamic voice changes associated with voice quality changes with use and fatigue, whereas perceptual ratings are based on many factors, such as sensory or psychological factors. Another consideration would be the fact that participants were aware they were in a treatment study, and it is possible that the ABAB
design was subject to participant expectations regarding recurrence of dryness and effort symptoms during the withdrawal phase. However, the strong correlations between CSID and morning patient ratings suggest that notable acoustic benefits resulted from the nebulized hydration treatments. It is also possible that dryness accounted for a greater proportion of the participants’ ratings in the morning versus evening, when other SS disease factors such as pain, fatigue, or neuropathy might have influenced voice production (Allec et al., 2011; Kassan et al., 2004; Kruszka & O’Brian, 2009). Regardless of the predictive factors that distinguish physiological measures from patient-based measures of voice, the current study results underscore the value of several forms of measurement in evaluating potential treatment effects of nebulized saline on voice production.

A third point of consideration when evaluating the CSID findings in this study relates to the severity level of the participants at baseline. Given that individuals with SS generally have normal to mild-to-moderate voice severities, the task of quantifying acoustic change with treatment in this population is inherently difficult due to treatment ceiling effects. This task becomes even more complex when considering the multiple factors — structural, functional, and neurological — that might account for voice problems in this population (Allec et al., 2011; Heller et al., 2014; Kassan et al., 2004; Kruszka & O’Brian, 2009). Yet, the CSID has been shown to track voice improvement with treatment in voice severities from mild to severe (Awan et al., 2009; Peterson et al., 2013). Therefore, the results from the present study are particularly impressive, given that the 20% average improvement with treatment shifted CSID values from the mild to normal range over time. Thus, even a minor improvement with hydration treatment, as indicated by the CSID values, could have a major effect in symptom relief. It is possible that
this change also explains some of the differences in magnitude of the effects on patient-based perceptual ratings versus acoustic findings.

Also of note, the improvement in CSID values was more apparent for sustained vowel samples than for Rainbow Passage samples. This difference in improvement could be due to a number of factors. The nature of connected speech and the variation of consonants could lead to more variability. Though connected speech samples have been connected to voice problems, measurements of connected speech samples may not be quite as sensitive as measures of sustained vowel samples. Or, the nature of the CSID analysis may be over-sensitive to typical speaker variations that are not picked up in a sustained vowel analysis. This can lead to greater variability, resulting from such differences as intonation patterns, prosody, stress, and linguistic loading (Maryn, Corthals, Cauwenberge, Roy, & Bodt, 2010). Speech problems found in SS, such as the 50% likelihood of tongue click (Allec et al., 2011) would also lead to more variability in connected speech samples over sustained vowel samples. However, dysphonic symptoms are more likely to emerge in connected speech samples, and the combination of both measures ultimately provides the greatest insight into severity. This is particularly so when utilizing cepstral-based measures, as in the current study, versus time-based parameters such as jitter (Maryn et al., 2010).

In addition to the patient-based ratings of vocal effort and dryness, patient-based measures of voice and disease severity provide interesting insight. The mean VHI of approximately 32 is consistent with previous work showing that voice problems within the SS population typically fall in this range of mild to mild-to-moderate severity (Tanner et al., 2013). The VHI improved over time (decreased across observations), but changes were not statistically significant. Therefore, interpretation of the results is somewhat guarded, and should be looked at
with the recognition that the VHI captures many aspects of voice problems, including social, occupational, and environmental difficulties due to voice problems. For this reason, the VHI was not expected to change significantly with a single treatment aimed at addressing dryness — not aimed at addressing voice problems as a whole. However, it is encouraging to note that the VHI ratings did not increase with the frequency of nebulized treatments. This finding supports that the treatment protocol itself is not detrimental to the voice. While traditional asthma therapy involving inhaled corticosteroids can affect the larynx through deposits on the vocal folds leading to irritation (Erickson & Sivasankar, 2010; Mirza, Kasper-Schwartz, & Antin-Ozerkis, 2004), nebulizing saline alone does not cause an adverse effect. This is an important finding because future nebulized treatments for the vocal folds will need to be compared to a standard or baseline treatment, such as nebulized saline. Further, nebulized saline may serve as a delivery medium for future drug therapies that address vocal fold hydration.

Similar to the VHI ratings, the patient-based ESSPRI and SSI ratings did not display significant changes. This finding offers evidence that the changes in patient-based ratings of vocal effort and dryness with treatment were not exclusively related to a placebo effect. The ESSPRI ratings did improve slightly with treatment, but these findings were not significant. Additionally, it is important to consider that one of the subscales of both the ESSPRI and SSI involves patient-based ratings of dryness; thus some movement with dryness treatment was anticipated. Collectively, the patient-based disease severity and voice handicap scales indicate that while acoustic voice severity, vocal effort, and mouth and throat dryness improved with nebulized saline treatment, the overarching impact of the disease did not.

Finally, this is the first study comparing CSID and patient-based ratings over time. Previously, the CSID has been standardized on auditory-perceptual ratings, but not on patient-
based ratings (Awan et al., 2009; Peterson et al., 2013). Therefore, it is important to keep in mind that patients in this study were asked to rate effort and dryness, not to rate their voice quality. As discussed previously, it is likely that different factors predict voice quality versus vocal effort and dryness ratings. Related to the collection of CSID values over time, this study offers evidence for the feasibility of high quality at-home audio recordings to monitor voice change with treatment. This form of treatment effect monitoring has numerous potential clinical applications.

The consideration of several qualifications and caveats is also warranted in the current study. Of necessity, this study permitted participants to view previous perceptual ratings when making new judgments of current vocal effort and dryness severity. This may have reduced the possibility for variability to some extent. Furthermore, due to the complexity of this study, time commitment, and rarity of SS, only a small number of participants were utilized and statistical significance was not found, therefore, caution should be exercised when interpreting the results. These participants also knew they were part of a study, making the study somewhat at risk for a placebo effect; however, this would be more likely to affect perceptual ratings versus acoustic measures. Acoustically, some variation was expected, as the CSID varies depending on voice context and diagnosis (Peterson et al., 2013). Connected speech samples likely had more variation, which might explain the stronger correlations between CSID vowel values and perceptual ratings. It should be noted that some correlations, though statistically significant, were not strong, limiting potential clinical significance. Participants also varied in their procedures for recording acoustic data, despite detailed instructions and training; corresponding missing data replacement due to these issues could potentially influence the results. Finally, the saline dosage
and concentration for nebulization were selected fairly arbitrarily, creating the possibility that other dosages or concentrations could prove more effective.

**Conclusion**

Until now, previous hydration studies had yet to explore long-term effects of nebulized hydration treatments. Additionally, most clinical studies utilized dehydration challenges in a controlled experimental environment (Hemler et al., 1997). This study evaluated participants with pre-existing sicca symptoms in their natural environment, maximizing this study’s generalizability. It is the first study to look at long-term effects of nebulized hydration treatment, particularly in a population already at risk for dryness symptoms. Confusion and postponement of diagnosis and treatment often occur because of the systemic nature and clinical manifestations of SS. Yet dysphonia is often an early indicator of SS and other autoimmune disorders (Sanz et al., 2011). In SS and other diseases such as Parkinson’s disease, where diagnosis time is frequently lengthy (Kassan & Moutsopoulos, 2004), dysphonia may possibly be the first sign of disease, and hence should be readily quantifiable. Therefore, the opportunity to quantify dysphonia objectively while simultaneously correlating it with a patient’s perceptions is invaluable. The need for greater treatment modalities to improve the quality of life for these individuals is apparent. Future research should examine effects of vocal fatigue and changes in saline concentration and dosage in regard to this promising vocal fold hydration treatment. This data lays the groundwork for future development of nebulized drug therapies for treating vocal fold dehydration.
References


Appendix A: Consent and Authorization Document

BACKGROUND
You are being asked to take part in a research study. People with Sjögren’s Syndrome may be more likely to experience voice problems and throat dryness. The University of Utah Health Care Voice Disorders Center is studying the effects of throat dryness and hydration in individuals with Sjögren’s. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends and relatives if you wish. Ask the research doctor or staff if there is anything that is not clear or if you would like more information. Take time to decide whether or not to volunteer to take part in this research study.

STUDY PROCEDURES
This research study will examine the effects of a hydration treatment on the voice and throat dryness. All participants will be individuals with Sjögren’s. If you agree to participate in this study, you will participate in an 8-week home program including the hydration treatment, research paperwork, and audio recordings. You will do all research tasks in your own home, and will not need to travel to participate. The hydration treatment is inhaled saline mist. The mist is similar to fluid in the cells in your body.

The study is divided into 4, 2-week phases. The first 2 weeks will be the baseline phase. You will complete daily ratings of your voice and dryness, and recordings of your voice using the portable recorder we send you. The next 2 weeks will be the first treatment phase. You will continue all the ratings you did during the first phase, but will add the daily hydration treatment in the morning and evening. The treatment involves breathing saline using a personal nebulizer. The treatment is 9 mL, and takes approximately 15 minutes to administer.

The next phase of the research study involves withdrawing the nebulized treatment. During this 2-week phase, you will not receive the hydration treatment, but will continue completing daily ratings and audio recordings. The final phase includes 2-weeks of the hydration treatment, ratings, and recordings. You will mail ratings in a prepaid envelope at the end of each 2-week phase. When the study is completed, you will return the audio equipment in a prepaid envelope.

Your participation is outlined in the table below:

<table>
<thead>
<tr>
<th>Study Phase</th>
<th>Participation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1 = Baseline 2 weeks</td>
<td>Daily ratings of voice and dryness; Daily recording of voice</td>
</tr>
<tr>
<td>Phase 2 = Treatment 2 weeks</td>
<td>Daily ratings of voice and dryness; Daily recordings of voice; Twice-daily nebulized treatment</td>
</tr>
<tr>
<td>Phase 3 = Baseline 2 weeks</td>
<td>Daily ratings of voice and dryness; Daily recording of voice</td>
</tr>
<tr>
<td>Phase 4 = Treatment 2 weeks</td>
<td>Daily ratings of voice and dryness; Daily recordings of voice; Twice-daily nebulized treatment</td>
</tr>
</tbody>
</table>

You will receive detailed instructions on how to perform the ratings and recordings. The study coordinator will call you before you begin the study to review the instructions with you and answer questions. Also, the study coordinator will be available by telephone to answer any questions you might have.
RISKS
It is possible that you may experience occasional coughing associated with the inhaled mist. This coughing should be infrequent, and should not continue after the treatment is completed. The nebulizers used in this study have been used to treat asthma and have not been reported to be uncomfortable.

REPRODUCTIVE RISKS
If you are pregnant or think you might be pregnant, you should not participate in the study. The inhaled mist is not believed to have adverse effects in pregnancy. However, changes to the voice during pregnancy could influence the research study outcomes. Therefore pregnant women are not being included in this study.

BENEFITS
There are no direct benefits to you from your taking part in this study. The information we get from this study may help us provide better recommendations to address throat dryness in people with Sjögren’s.

ALTERNATIVE PROCEDURES
There are no similar alternative treatments to the inhaled treatments being studied in this research.

CONFIDENTIALITY
The results of this study will be stored on a password-protected computer on a University of Utah network drive with restricted access. Only the investigators and research assistants will have access to the results and confidentiality and privacy will be maintained. You will be assigned a code number and your name will not appear on any written or computer documents. All identifying information will be stored separately, preventing any link between you and the results. The results of this study may be published for scientific purposes. By Federal Law, the information gathered in this study may be reviewed by the United States Food and Drug Administration. We will do everything we can to keep your records private, but cannot guarantee this.

PERSON TO CONTACT
If you have questions, complaints or concerns about this study, you can contact Dr. Kristine Tanner at (801) 633-7471. If you think you may have been injured from being in this study, please call Dr. Mark Elstad, MD or Dr. Kathy Kendall, MD at (801) 587-8368. The doctors can be reached at this number during the hours of 8:30 am to 4:30 pm.

Institutional Review Board: Contact the Institutional Review Board (IRB) if you have questions regarding your rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at irb@hsc.utah.edu.

Research Participant Advocate: You may also contact the Research Participant Advocate (RPA) by phone at (801) 581-3803 or by email at participant.advocate@hsc.utah.edu.

RESEARCH-RELATED INJURY
If you are injured from being in this study, medical care is available to you at the University of Utah, as it is to all sick or injured people. The University of has not set aside any money to pay the costs for such care. The University will work with you to address costs from injuries. Costs would be charged to you or your insurance company (if you have insurance), to the study sponsor or other third party (if applicable), to the extent those parties are responsible for paying for medical care you receive. Since this is a research study, some health insurance plans may not pay for the costs. By signing this consent form you are not giving up your right to pursue legal action against any parties involved with this research.
The University of Utah is a part of the government. If you are injured in this study, and want to sue the University or the doctors, nurses, students, or other people who work for the University, special laws may apply. The Governmental Immunity Act of Utah is a law that controls when a person needs to bring a claim against the government, and limits the amount of money a person may recover. See sections 63G - 7-101 to -904 of the Utah Code.

**VOLUNTARY PARTICIPATION**

It is up to you to decide whether or not to take part in this study. If you decide to take part you are still free to withdraw at any time and without giving a reason. Refusal to participate or the decision to withdraw from this study will involve no penalty or loss of benefits to which you are otherwise entitled. If you don’t take part, you can still receive all standard care that is available to you. This will not affect the relationship you have with your doctor or other staff, nor decrease the standard of care that you receive as a patient.

**UNFORESEEABLE RISKS**

In addition to the risks listed above, you may experience a previously unknown risk or side effect.

**COSTS AND COMPENSATION TO PARTICIPANTS**

There is no cost associated with your participation in this study. You will be compensated in the amount of $160 after completing the study. A check will be mailed after you have completed the 8-week program and have returned the ratings and recording equipment. Compensation is not available to participants who do not complete the study. Brigham Young University, Provo, Utah is funding this study, and will retain your name and citizenship status for accounting purposes. If you prefer not to have your information retained by Brigham Young University, you may still participate in the study and can choose not to receive compensation.

**NUMBER OF PARTICIPANTS**

We expect to enroll 15 individuals with Sjögren’s in this study at The University of Utah.

**AUTHORIZATION FOR USE OF YOUR PROTECTED HEALTH INFORMATION**

Signing this document means you allow us, the researchers in this study, and others working with us to use information about your health for this research study. You can choose whether or not you will participate in this research study. However, in order to participate you have to sign this consent and authorization form.

This is the information we will use:

- Name
- Address
- Telephone number
- Participant’s prior medical history (self-report)
- Sjögren’s Syndrome diagnosis medical records
- Vocal measures and throat dryness ratings that will be performed in the study

Others who will have access to your information for this research project are the University’s Institutional Review Board (the committee that oversees research studying people) and authorized members of The University of Utah Health Sciences Center who need the information to perform their duties (for example: to provide treatment, to ensure integrity of the research, and for accounting or billing matters).
If we share your information with anyone outside The University of Utah Health Sciences Center you will not be identified by name, social security number, address, telephone number, or any other information that would directly identify you, unless required by law.

You may revoke this authorization. This must be done in writing. You must either give your revocation in person to the Principal Investigator or the Principal Investigator’s staff, or mail it to Kristine Tanner, Ph.D., Voice Disorders Center, 729 Arapeen Dr., Salt Lake City, UT, 84108. If you revoke this authorization, we will not be able to collect new information about you, and you will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research.

You have a right to information used to make decisions about your health care. However, your information from this study will not be available during the study; it will be available after the study is finished.

This authorization does not have an expiration date.

**CONSENT**
I confirm that I have read this consent and authorization document and have had the opportunity to ask questions. I will be given a signed copy of the consent and authorization form to keep.

I agree to take part in this research study and authorize you to use and disclose health information about me for this study, as you have explained in this document.

________________________
Participant’s Name

________________________             ____________
Participant’s Signature             Date

________________________
Name of Person Obtaining Authorization and Consent

________________________             ____________
Signature of Person Obtaining Authorization and Consent             Date

Would you like to receive information on future studies involving Sjögren’s Syndrome?
Yes _____ (we will retain your name, telephone number, and mailing address to provide information)
No _____
Appendix B: Study Outline

Thank you for participating in this study! We have outlined the steps you will perform during the next 8 weeks below. Please contact Dr. Kristine Tanner at (801) 633-7471 with questions at any time during your participation.

1. Complete Voice Handicap Index, Sjögren’s Questionnaires, and Medical History the day before you begin the study.

2. Read Zoom instruction manual. Watch Omron nebulizer instructional DVD.

3. **Weeks 1-2:** Complete baseline audio recordings and ratings every morning and evening at similar times of day. Track completion on the Participant Log (Note: track any additional information, protocol deviations, and illnesses/colds on the participant log throughout the study). Purchase distilled water and white vinegar. Clean nebulizer following manufacturer instructions.

4. Complete the Voice Handicap Index and Sjögren’s Questionnaires again on the last day of Week 2.

5. **Weeks 3-4:** Complete audio recordings and ratings prior to nebulizing. Nebulize 9 mL of saline TWICE daily, immediately following recording and ratings. (Note: Spray saline into medicine cup and fill to black 9mL line. Pour into nebulizer per manufacturer instructions. The nebulizer holds about 6 mL, so you will need to pour saline in 2 stages to reach 9 mL. It should take 15-20 min to breathe the saline. **It is essential that you breathe in and out continuously with your lips around the nebulizer mouthpiece. Don’t remove the nebulizer during exhalation like the woman does in the DVD! You should breathe continuously, in and out, at your normal respiration rate.** Stop nebulizing when the mist runs out.). Track completion on the Participant Log. Clean nebulizer daily per manufacturer instructions.

6. Complete Voice Handicap Index and Sjögren’s Questionnaires again on the last day of Week 4.

7. **Weeks 5-6:** Complete baseline audio recordings and ratings. Track completion on the Participant Log. **Do not use the nebulizer during these weeks.**

8. Complete Voice Handicap Index and Sjögren’s Questionnaires again on the last day of Week 6.

9. **Weeks 7-8:** Complete audio recordings and ratings prior to nebulizing. Nebulize 9 mL of saline TWICE daily, immediately following recording and ratings. Track completion on the Participant Log. Clean nebulizer daily per manufacturer instructions.

10. Complete Voice Handicap Index and Sjögren’s Questionnaires on the last day of Week 8.

11. Return the portable recorder, head-mounted microphone, and all study forms in the pre-addressed, postage-paid box. Please use bubble wrap from the original shipment to protect the equipment. **You will need to ship this package from the Post Office counter.** Please keep the nebulizer as this is a personal medical device and cannot be reused.
# Appendix C: Voice Handicap Index

**NAME________________________ Date________________________**

**Voice Handicap Index (VHI)**

Instructions: These are statements that many people have used to describe their voices and the effects of their voices on their lives. Check the response that indicates how frequently you have the same experience. (Never=0 points, Almost Never=1 point, Sometimes=2 points, Almost Always=5 points, Always=4 points)

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Almost Never</th>
<th>Sometimes</th>
<th>Almost Always</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>My voice makes it difficult for people to hear me</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F2</td>
<td>I run out of air when I talk</td>
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<tr>
<td>F3</td>
<td>People have difficulty understanding me in a noisy room</td>
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<tr>
<td>F4</td>
<td>The sound of my voice varies throughout the day</td>
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<tr>
<td>F5</td>
<td>My family has difficulty hearing me when I call them</td>
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<tr>
<td>F6</td>
<td>I use the phone less often than I would like</td>
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<tr>
<td>F7</td>
<td>I’m tense when talking with others because of my voice</td>
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<tr>
<td>F8</td>
<td>I tend to avoid groups of people because of my voice</td>
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<tr>
<td>F9</td>
<td>People seem irritated with my voice</td>
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<tr>
<td>P10</td>
<td>People ask, “What’s wrong with your voice?”</td>
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<tr>
<td>F11</td>
<td>I speak with friends, neighbors or relatives less often because</td>
<td></td>
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<tr>
<td>F12</td>
<td>People ask me to repeat myself when speaking face-to-face</td>
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<td></td>
<td></td>
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<tr>
<td>P13</td>
<td>My voice sounds creaky and dry</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>P14</td>
<td>I feel as though I have to strain to produce voice</td>
<td></td>
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<tr>
<td>E15</td>
<td>I find other people don’t understand my voice problem</td>
<td></td>
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<tr>
<td>F16</td>
<td>My voice difficulties restrict my personal and social life</td>
<td></td>
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<tr>
<td>P17</td>
<td>The clarity of my voice is unpredictable</td>
<td></td>
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<tr>
<td>P18</td>
<td>I try to change my voice to sound different</td>
<td></td>
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<tr>
<td>F19</td>
<td>I feel left out of conversations because of my voice</td>
<td></td>
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<tr>
<td>P20</td>
<td>I use a great deal of effort to speak</td>
<td></td>
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<tr>
<td>P21</td>
<td>My voice is worse in the evening</td>
<td></td>
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<tr>
<td>P22</td>
<td>My voice problem causes me to lose income</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E23</td>
<td>My voice problem upsets me</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E24</td>
<td>I am less outgoing because of my voice problem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E25</td>
<td>My voice problem makes me feel handicapped</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P26</td>
<td>My voice “gives out” on me in the middle of speaking</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>E27</td>
<td>I feel annoyed when people ask me to repeat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E28</td>
<td>I feel embarrassed when people ask me to repeat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E29</td>
<td>My voice makes me feel incompetent</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E30</td>
<td>I’m ashamed of my voice problem</td>
<td></td>
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</tr>
</tbody>
</table>

***Please circle the word that matches how you feel your voice is today: No Problem  Mild Problem  Moderate Problem  Severe Problem***

On a scale of 1-10, with 1 being least talkative and 10 being most talkative, how would you rate yourself?

On a scale of 1-10, with 1 being most soft and 10 being most loud, how would you rate yourself?

For Clinician Use Only:

P Scale __________ F Scale __________ E Scale __________ Total ________

Appendix D: Patient-based Rating (Weeks 1, 2, 5, and 6)

RATINGS

Participant #: 

WEEK 1 (Baseline)

Instructions: Please rate your level of vocal effort, mouth dryness, and throat dryness every morning and evening using the rating scales below. You may refer to previous ratings.

For vocal effort, please rate the amount required during the recorded reading task by placing a vertical line on the scale. The extreme left of the scale represents “no effort” and the extreme right represents “extreme effort”.

For mouth and throat dryness, please rate your current level of dryness by placing a vertical line on the scale below. The extreme left of the scale represents “no dryness” and the extreme right represents “extreme dryness”.
(*note: lines not to scale)

Date: ___ AM

No Vocal Effort  ____________________________ Extreme Vocal Effort
No Mouth Dryness __________________________ Extreme Mouth Dryness
No Throat Dryness __________________________ Extreme Throat Dryness

PM

No Vocal Effort  ____________________________ Extreme Vocal Effort
No Mouth Dryness __________________________ Extreme Mouth Dryness
No Throat Dryness __________________________ Extreme Throat Dryness
Date: ___ AM

No Vocal Effort ____________________________ Extreme Vocal Effort

No Mouth Dryness __________________________ Extreme Mouth Dryness

No Throat Dryness __________________________ Extreme Throat Dryness

PM

No Vocal Effort ____________________________ Extreme Vocal Effort

No Mouth Dryness __________________________ Extreme Mouth Dryness

No Throat Dryness __________________________ Extreme Throat Dryness

Date: ___ AM

No Vocal Effort ____________________________ Extreme Vocal Effort

No Mouth Dryness __________________________ Extreme Mouth Dryness

No Throat Dryness __________________________ Extreme Throat Dryness

PM

No Vocal Effort ____________________________ Extreme Vocal Effort

No Mouth Dryness __________________________ Extreme Mouth Dryness

No Throat Dryness __________________________ Extreme Throat Dryness

Date: ___ AM

No Vocal Effort ____________________________ Extreme Vocal Effort

No Mouth Dryness __________________________ Extreme Mouth Dryness

No Throat Dryness __________________________ Extreme Throat Dryness

PM

No Vocal Effort ____________________________ Extreme Vocal Effort

No Mouth Dryness __________________________ Extreme Mouth Dryness

No Throat Dryness __________________________ Extreme Throat Dryness
No Vocal Effort __________________________ Extreme Vocal Effort
No Mouth Dryness _________________________ Extreme Mouth Dryness
No Throat Dryness ________________________ Extreme Throat Dryness

Date: ___ AM

No Vocal Effort __________________________ Extreme Vocal Effort
No Mouth Dryness _________________________ Extreme Mouth Dryness
No Throat Dryness ________________________ Extreme Throat Dryness

Date: ___ AM

No Vocal Effort __________________________ Extreme Vocal Effort
No Mouth Dryness _________________________ Extreme Mouth Dryness
No Throat Dryness ________________________ Extreme Throat Dryness

Date: ___ AM

No Vocal Effort __________________________ Extreme Vocal Effort
No Mouth Dryness _________________________ Extreme Mouth Dryness
No Throat Dryness ________________________ Extreme Throat Dryness

Date: ___ AM

No Vocal Effort __________________________ Extreme Vocal Effort
No Mouth Dryness _________________________ Extreme Mouth Dryness
No Throat Dryness ________________________ Extreme Throat Dryness

*Screenshot of Visual Analog Scales, not to scale
Appendix E: Patient-based Rating (Weeks 3, 4, 7, and 8)

RATINGS

Participant #: ___

WEEK 3 (Treatment)

Instructions: Please rate your level of vocal effort, mouth dryness, and throat dryness every morning and evening using the rating scales below. You may refer to previous ratings.

**For vocal effort,** please rate the amount required during the recorded reading task by placing a vertical line on the scale. The extreme left of the scale represents “no effort” and the extreme right represents “extreme effort”.

**For mouth and throat dryness,** please rate your current level of dryness by placing a vertical line on the scale below. The extreme left of the scale represents “no dryness” and the extreme right represents “extreme dryness”.

(*note: lines not to scale)

Please complete all ratings BEFORE nebulizing.

<table>
<thead>
<tr>
<th>Date: ___</th>
<th>AM</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Vocal Effort</td>
<td>Extreme Vocal Effort</td>
</tr>
<tr>
<td>No Mouth Dryness</td>
<td>Extreme Mouth Dryness</td>
</tr>
<tr>
<td>No Throat Dryness</td>
<td>Extreme Throat Dryness</td>
</tr>
</tbody>
</table>

**FM**

| No Vocal Effort | Extreme Vocal Effort |
| No Mouth Dryness | Extreme Mouth Dryness |
| No Throat Dryness | Extreme Throat Dryness |
Date: ___ AM

No Vocal Effort ____________________________ Extreme Vocal Effort
No Mouth Dryness __________________________ Extreme Mouth Dryness
No Throat Dryness __________________________ Extreme Throat Dryness

PM

No Vocal Effort ____________________________ Extreme Vocal Effort
No Mouth Dryness __________________________ Extreme Mouth Dryness
No Throat Dryness __________________________ Extreme Throat Dryness

Date: ___ AM

No Vocal Effort ____________________________ Extreme Vocal Effort
No Mouth Dryness __________________________ Extreme Mouth Dryness
No Throat Dryness __________________________ Extreme Throat Dryness

PM

No Vocal Effort ____________________________ Extreme Vocal Effort
No Mouth Dryness __________________________ Extreme Mouth Dryness
No Throat Dryness __________________________ Extreme Throat Dryness

Date: ___ AM

No Vocal Effort ____________________________ Extreme Vocal Effort
No Mouth Dryness __________________________ Extreme Mouth Dryness
No Throat Dryness __________________________ Extreme Throat Dryness

PM

No Vocal Effort ____________________________ Extreme Vocal Effort
No Mouth Dryness __________________________ Extreme Mouth Dryness
No Throat Dryness __________________________ Extreme Throat Dryness
Date: ___ AM

No Vocal Effort ................................................. Extreme Vocal Effort
No Mouth Dryness ........................................... Extreme Mouth Dryness
No Throat Dryness ........................................... Extreme Throat Dryness

PM

No Vocal Effort ................................................. Extreme Vocal Effort
No Mouth Dryness ........................................... Extreme Mouth Dryness
No Throat Dryness ........................................... Extreme Throat Dryness

Date: ___ AM

No Vocal Effort ................................................. Extreme Vocal Effort
No Mouth Dryness ........................................... Extreme Mouth Dryness
No Throat Dryness ........................................... Extreme Throat Dryness

PM

No Vocal Effort ................................................. Extreme Vocal Effort
No Mouth Dryness ........................................... Extreme Mouth Dryness
No Throat Dryness ........................................... Extreme Throat Dryness

Date: ___ AM

No Vocal Effort ................................................. Extreme Vocal Effort
No Mouth Dryness ........................................... Extreme Mouth Dryness
No Throat Dryness ........................................... Extreme Throat Dryness

PM

No Vocal Effort ................................................. Extreme Vocal Effort
No Mouth Dryness ........................................... Extreme Mouth Dryness
No Throat Dryness ........................................... Extreme Throat Dryness

*Screenshot of Visual Analog Scales, not to scale
Appendix F: Sjögren’s Symptom Severity Scale Questionnaires

Instructions: Please complete the following questions.

Participant # ____
Date: ____

Please consider the past 2 weeks when rating the following:

Sore Eyes

0 1 2 3 4 5 6 7
0=No problem at all 7=As bad as imaginable

Eye Irritation

0 1 2 3 4 5 6 7
0=No problem at all 7=As bad as imaginable

Poor Vision

0 1 2 3 4 5 6 7
0=No problem at all 7=As bad as imaginable

Difficulty Eating

0 1 2 3 4 5 6 7
0=No problem at all 7=As bad as imaginable

Dry Throat/Bad Breath

0 1 2 3 4 5 6 7
0=No problem at all 7=As bad as imaginable

(Difficulty) Wetting Mouth (e.g., needing to drink fluid often)

0 1 2 3 4 5 6 7
0=No problem at all 7=As bad as imaginable

Oral Problems (e.g., ulcers, swollen salivary glands, taste altered)

0 1 2 3 4 5 6 7
0=No problem at all 7=As bad as imaginable
<table>
<thead>
<tr>
<th>Condition</th>
<th>Scale</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal Dryness (females only)</td>
<td>0  1  2  3  4  5  6  7</td>
<td>0=No problem at all 7=As bad as imaginable</td>
</tr>
<tr>
<td>Skin Dryness</td>
<td>0  1  2  3  4  5  6  7</td>
<td>0=No problem at all 7=As bad as imaginable</td>
</tr>
<tr>
<td>Systemic Discomfort/Arthralgia (joint pain)</td>
<td>0  1  2  3  4  5  6  7</td>
<td>0=No problem at all 7=As bad as imaginable</td>
</tr>
</tbody>
</table>

**Sjögren’s Questionnaire 2**

Please rate the items below, where 0=no dryness and 10=maximum dryness.

<table>
<thead>
<tr>
<th>Item</th>
<th>Scale</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dryness</td>
<td>0  1  2  3  4  5  6  7  8  9  10</td>
<td></td>
</tr>
<tr>
<td>Limb Pain</td>
<td>0  1  2  3  4  5  6  7  8  9  10</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>0  1  2  3  4  5  6  7  8  9  10</td>
<td></td>
</tr>
</tbody>
</table>
## Appendix G: Select Medical History Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
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<tr>
<td>Female</td>
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<tr>
<td><strong>Age</strong></td>
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<tr>
<td>36 to 45</td>
<td>x</td>
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<tr>
<td>46 to 55</td>
<td></td>
<td>x</td>
<td></td>
<td>x</td>
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<tr>
<td>56 to 65</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>66 to 75</td>
<td></td>
<td></td>
<td>x</td>
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<td>x</td>
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Appendix H: Overview of Study

Study Onset: Complete Medical History, VHI, ESSPRI, & SSI

Baseline Weeks 1-2
- AM & PM Voice Recordings & VAS

Day 14: Complete VHI, ESSPRI, & SSI

Treatment Weeks 3-4
- AM & PM Voice Recordings & VAS
- Nebulized Isotonic Saline

Day 28: Complete VHI, ESSPRI, & SSI

Baseline Weeks 5-6
- AM & PM Voice Recordings & VAS

Day 42: Complete VHI, ESSPRI, & SSI

Treatment Weeks 7-8
- AM & PM Voice Recordings & VAS
- Nebulized Isotonic Saline

Day 56: Complete VHI, ESSPRI, & SSI
Appendix I: Recording Instructions

Recordings will be performed twice daily, at similar times of day, for 8 weeks. You will read a paragraph, sentences, a list of words (3 times) and sustain “ah” (3 times for 5 seconds each), during each recording. It is very important that recordings are made under similar conditions, with the same mouth-to-microphone distance, and in quiet environments. Recordings are made with you speaking at comfortable pitch and loudness.

Please read the Zoom H1 instruction manual prior to performing recordings. Recording steps have been summarized here:

1. Put on the headset microphone with the pads over the temples. The silver microphone should be facing your lips, approximately 3 inches away, like the photos enclosed. The microphone puff should be covering the mic (see photo 2).
2. Be sure the mic is plugged into the mic/line in slot on the recorder (see diagram #1).
3. Turn on the recorder by holding the power lever to the left for 2 seconds (see diagram #2). The LCD screen will say “Hi” (see diagram #3).
4. Check the battery level on the upper right of the LCD screen. If the battery is low, replace with another AA battery (enclosed).
5. Test the record level by reading the first sentence of the reading passage (below), watching the moving bars on the left side of the LCD screen (see diagram #4). They should range between 50-75% of the scale. If you are “too loud”, a red light will flash (see diagram #5). If this happens, adjust the mic slightly away from your lips (don’t just get softer; keep the comfortable pitch and loudness and adjust the mic instead).
6. When you are ready, press the “record” button (see diagram #6).
At the beginning of each recording, say your participant number, day of the week, date and time.

Then read: “WHEN THE SUNLIGHT STRIKES RAINDROPS IN THE AIR THEY ACT LIKE A PRISM AND FORM A RAINBOW. THE RAINBOW IS A DIVISION OF WHITE LIGHT INTO MANY BEAUTIFUL COLORS. THESE TAKE THE SHAPE OF A LONG ROUND ARCH WITH ITS PATH HIGH ABOVE, AND ITS TWO ENDS APPARENTLY BEYOND THE HORIZON. THERE IS, ACCORDING TO LEGEND, A BOILING POT OF GOLD AT ONE END. PEOPLE LOOK, BUT NO ONE EVER FINDS IT. WHEN A MAN LOOKS FOR SOMETHING BEYOND HIS REACH, HIS FRIENDS SAY HE IS LOOKING FOR THE POT OF GOLD AT THE END OF THE RAINBOW.”

“The blue spot is on the key again.” (pause briefly)
We were away a year ago. (pause briefly)
We eat eggs every Easter.” (pause briefly)

Read the 3 lists of words at normal rate:

<table>
<thead>
<tr>
<th>List 1</th>
<th>List 2</th>
<th>List 3</th>
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<tbody>
<tr>
<td>“Bye”</td>
<td>“Boy”</td>
<td>“Bay”</td>
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<tr>
<td>“Heat”</td>
<td>“Hoot”</td>
<td>“Hat”</td>
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<tr>
<td>“Bow” (like “go”)</td>
<td>“Bay”</td>
<td>“Bow” (go)</td>
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<tr>
<td>“Hat”</td>
<td>“Hot”</td>
<td>“Hot”</td>
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<tr>
<td>“Bough” (like “cow”)</td>
<td>“Bough” (cow)</td>
<td>“Bye”</td>
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<tr>
<td>“Hot”</td>
<td>“Hat”</td>
<td>“Hoot”</td>
</tr>
<tr>
<td>“Bay”</td>
<td>“Bow” (go)</td>
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<tr>
<td>“Boy”</td>
<td>“Bye”</td>
<td>“Boy”</td>
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<tr>
<td>“Hut”</td>
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Say and hold “ah” for at least 5 seconds at a comfortable pitch and loudness. Do this 3 times, pausing in between.

7. Press the “record” button again to stop recording. Remaining record time available will be indicated on the LCD screen.
8. Turn off the recorder by holding the power lever to the left for 2 seconds. The LCD screen will say “bye”.
Appendix J: Medical History

Instructions: Please complete the following questions on the first day of week 1.

Participant # ____
Date: ____

Medical History

1. How long have you had Sjögren’s symptoms (# years)?

2. How long have you been diagnosed with Sjögren’s (# years)?

3. Please list all treatments tried for Sjögren’s, if they helped, and if you are still using this treatment:

4. Please list other health conditions:

5. Do you have asthma or other pulmonary disease (if yes, please describe and list meds/inhalers/oxygen use/CPAP)?

6. Do you smoke, or have you ever smoked (if yes, frequency, # years)?

7. Date of your last menstrual period (possible effect on voice quality):

8. Do you have acid reflux/heartburn (if yes, # years)?

9. Do you have seasonal allergies (if yes, please list, including medications taken for allergies)?

10. What (other) medications do you take, and why?

11. Have you had voice training (if yes, number of years, type of training)?
Appendix K: Participant Tracking Sheet

PARTICIPANT LOG

On the day before beginning the study, complete:

- Voice Handicap Index
- Siagram's Symptom Severity Scales
- Medical History

**Week 1 (Baseline)**

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On the last day of week 2, complete:

- Voice Handicap Index
- Siagram's Symptom Severity Scales

**Week 3 (Treatment)**

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On the last day of week 4, complete:

- Voice Handicap Index
- Sjögren's Symptom Severity Scales

Week 5 (Baseline)

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On the last day of week 6, complete:

- Voice Handicap Index
- Sjögren's Symptom Severity Scales

Week 7 (Treatment)

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Week 8 (Treatment)

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On the last day of week 8, complete:

- Voice Handicap Index
- Sjögren's Symptom Severity Scales
Appendix L: Annotated Bibliography


**Purpose of the Study:**
Many subjective reports such as dysphagia and pharyngeal dryness exist among people with SS. This study set out to identify objective, specific impairments associated with speech, voice, and swallowing in people with SS.

**Method:**
Thirty-one patients with SS (4 Primary, 26 Secondary, 30 female) participated in perceptual analysis of dysphonia, nasofibro-laryngeal endoscopy, video laryngostroboscopy, fiberoptic endoscopic evaluation of swallowing (FEES), and acoustic analyses.

**Results:**
Dysphagia was the most common problem, mainly in pharyngeal efficiency. Mild dysphonia was seen in most cases and did not interfere with speech intelligibility. Lingual-palatal diglossia (causing the clicking during speech) was seen in about 50% of those tested. Among all patients with SS, 67% had alterations in the lower cranial nerves suggesting that neurological involvement is likely playing a role in speech, voice and swallowing changes in these patients. This study did not find laryngeal lesions such as vocal nodules.

**Conclusion:**
The primary abnormalities in speech, voice and swallowing in those with SS were related to xerosis. Other alterations seen, such as decreased gag reflex and tongue deviation, not explicable by xerosis, may be related to neurological involvement. Whatever the cause, those with SS warrant a multidisciplinary approach to their treatment.

**Relevance to the Current Work:**
There was a clear difference from the norm in patients’ mucosal wave vibration. Further research relating this to dryness or a neurological component is needed. The acoustic parameters showed few altered formants, but many reports of aperiodic segments.


**Purpose of the Study:**
This study set out to determine if environmental relative humidity affects the voice. More specifically, the study examined if there would be measurable effects with short-term changes in the humidity of the environmental air.

**Method:**
Eight participants inhaled, by mouth, three varieties of air on three different days: dry, standard room, and humidified, followed by production of a sustained /a/ twelve times. This was analyzed for perturbation and noise-to-harmonic parameters.
Results:
Participants reported greater strain with the desiccated air. Statistical significance in absolute jitter and shimmer were seen between the dry and normal air, but not between the normal and humidified air. No significant differences were seen in the noise-to-harmonic ratio.

Conclusion:
Dry air produced statistically significant increases in perturbation measures following dry air exposure. Three hypotheses for the lack of a decrease in perturbation following the humidified air were offered. First, a longer provocation period may be necessary to see an effect. Second, perhaps perturbation cannot physically decrease any further (at baseline). Third, there may be no effect of inhalation of humidified air.

Relevance to the current work:
Even after short-term exposure, desiccated air produces subjective and objective voice changes. This includes subjects’ report of ease of phonation, and objective data regarding perturbation. This study outlines the need for further investigation of hydration challenges.


Purpose of the work:
This work gives increased understanding of the autoimmune disease SS, both primary and secondary varieties.

Summary:
SS is a systemic disease that can occur independently or in connection with other autoimmune diseases, such as thyroid dysfunction. The disease is often under-diagnosed or treated at the individual symptom level. Therefore, diagnosis time is frequently very long. Females are much more likely to have SS, and approximately one million have a diagnosis (though many go undiagnosed). Other problems can include fatigue, joint problems, dermatological problems, and gastroenterologic, neurologic, oncologic, and renal involvement. Often women attribute symptoms to menopause. Symptoms are outlined in this work.

Conclusion:
SS is often under-diagnosed though refined criteria are assisting in this area. Most treatments assist with symptom relief rather than recovery. SS is not a life threatening disease, but it can have a significant effect on quality of life.

Relevance to the Current Work:
Xerostomia can produce dryness in the nose, throat, and trachea. Treatments and modalities in this area are needed for the sustained and improved quality of life of individuals with SS.

**Purpose of work:**
This summary asserts that increasing vocal fold hydration can be beneficial to both typical speakers and those with voice disorders through efficient oscillation and voice quality. This work goes further in understanding the cellular mechanisms behind this, asserting that those mechanisms are similar to the mechanisms maintained in the lungs, bronchi, trachea, and nose.

**Summary:**
Details are given regarding the liquid layer covering the vocal folds. Part of the layer’s maintenance is from water and ion fluxes across the vocal fold epithelia. In vitro and in vivo studies are outlined regarding the negative effects of dehydration on optimal vocal fold functioning and the mechanisms that may be causing this.

**Conclusion:**
The outlined models of how the vocal fold surface maintains liquid homeostasis provide a theoretical basis for how these fluxes are regulated in desiccation challenges and how supporting this transport may be helpful to those suffering from systemic or superficial dehydration. Other mechanisms for vocal fold hydration are also possible.

**Relevance to the current work:**
Changes in the liquid layer covering the vocal folds both before and after nebulized hydration treatments may be indirectly, acoustically measurable depending on the effect those changes have on voice production.


**Purpose of Work:**
This work involved meta-analysis of studies using PTP as a measure related to vocal fold hydration, either systemically or superficially. The extent and effects of vocal fold hydration across numerous studies were evaluated.

**Summary:**
Of 39 articles found, nine fit the criteria of quality studies for this analysis. Most of the studies reviewed showed that as vocal fold hydration increased, PTP decreased. Due to the large amount of variability in types of hydration intervention, it is not surprising for this meta-analysis to find a wide array of outcomes. This coupled with pitch factors in PTP measurements and vocal health solidifies the chances of having varying outcomes.

**Conclusion:**
Among numerous studies, it was observed that hydration treatment did reduce PTP, though not at a significant level. Variability in pitch tasks and study participants could account for a portion of the wide variability in findings. Factors surrounding the PTP measurement techniques as applied to hydration treatments need further research.
Relevance to the Current Work:
Previous studies of hydration therapies in relation to measures of vocal effort show the need for more knowledge regarding type of therapy, including duration, extent, and dosage. Though a trend in PTP reduction was noted in these studies, it was not of a significant nature. Acoustic measures may provide more evidence regarding the effects of vocal fold hydration.


Purpose of the Study:
This study was designed to determine the validity of the CSID in quantifying dysphonia severity in connected speech and sustained vowels before and after treatment. This was done in an effort to provide a more objective measurement in voice disorders without relying on time-based analyses.

Method:
Patient voice samples of the Rainbow Passage and sustained vowels were measured pre- and post-treatment (n=112). Comparison was made between the CSID score and perceptual voice ratings. Voice samples included a continuum of mild, moderate, and severe dysphonia from six different diagnostic categories. Treatment technique was not considered relevant so long as some type of change occurred. Twenty-two of the samples were reanalyzed for reliability.

Results:
Regression analysis was used to compare the listeners’ perceived ratings and the CSID severity. CSID severity tended to be lower than the listener ratings and a greater correlation was observed for the pre-treatment recordings. This measurement provided a fairly accurate measure of dysphonia severity, while also being sensitive enough to detect changes following treatment. Greater correlation was found among sustained vowels than connected speech. The CSID underestimated dysphonia in mutational falsetto.

Conclusion:
This study supports the use of the CSID as an objective measure. There was a strong relationship between the CSID and listener-perceived dysphonia severities. This relationship existed among various diagnoses and levels of severity. This measure may be useful as an objective tool in clinical practice alongside trained clinical judgment.

Relevance to the Current Work:
The CSID acoustic measure significantly mirrors that of listeners’ perceived dysphonia severity ratings, making it a useful tool in objective assessment of treatment effects. Specifically in the present study following nebulized treatment, the CSID provides a non time-based measure of voice dysfunction.

**Purpose of work:**
This work provides a review of the benefits of hypertonic saline in treating cystic fibrosis, an airway condition characterized by thick mucus and poor mucociliary clearance.

**Summary:**
Cystic fibrosis is outlined as a severe example of extreme dehydration of the airway surface liquid layer. One treatment for this is aerosolized hypertonic saline. A number of proposals have been given as to how effective this treatment is, one proposal being increasing airway surface liquid hydration. The salt concentration promotes osmosis of water into the airway surface liquid, thereby providing rehydration. One study showed long term lung function improvement related to use of this treatment. The treatment’s ability to increase mucus clearance has not been shown in children. Effectiveness varies by dosage, with an optimal dosage yet to be determined. Mannitol is another osmotic agent shown to improve airway surface hydration when nebulized.

**Conclusion:**
Hypertonic saline solution, in addition to restoring the liquid layer of the airway, may also serve an immune and an anti-inflammatory function, thereby providing further therapeutic benefits. The hypertonic saline solution is also an inexpensive treatment option. Optimal dosage and specific working mechanisms are still under investigation.

**Relevance to the current work:**
Hypertonic saline has been shown to restore the liquid layer lining the airway, which is likely the same properties lining the vocal folds. More broadly, this work adds support for the use of saline therapies in treating respiratory airway dryness, particularly in patients with immune system dysfunction.


**Purpose of the Study:**
Due to varying conditions that lead to vocal fold dryness, and the minimal evidence of current treatment effects, this study examined three possible vocal fold surface treatments. The article also gives a summary of superficial and systemic studies of note.

**Method:**
Eighteen female participants with normal voices engaged in three separate nebulization treatments (i.e., laryngeal lubricants), including 2 mL of Mannitol, water, and Entertainer’s Secret Throat Relief over a three-week period. PTP was measured at baseline and four times following each treatment at normal and high fundamental frequency levels.

**Results:**
No significant trends were noted at the comfortable pitch level. At the high pitch level, the Mannitol treatment lowered PTP after five minutes, approaching statistical significance. It had no significant effect from 20 minutes onward. Water and Entertainer’s Secret Throat
Relief™ did not show a significant effect. PTP fluctuated frequently — including the baseline measurements — for the Entertainer’s Secret Throat Relief condition.

**Conclusion:**

The effect of Mannitol was assumed to be due to physical changes resulting in more efficient phonation and less effort during phonation. This effect was not long lasting. The treatments were done on vocally healthy individuals and may have different effects on those with laryngeal pathologies.

**Relevance to the Current Work:**

This work demonstrated the effects of nebulized treatments to decrease dryness in females with no voice complaints. Specifically, the study demonstrates that effects may be observed without including a laryngeal desiccation challenge in the experimental design.


doi: 10.1016/j.voice.2011.02.003

**Purpose of the Study:**

This study analyzed predominance of dysphonia in patients with Rheumatoid Arthritis (RA), SS, and Systemic Lupus Erythematosus (SLE). The study specifically looked at the biochemical parameters of each.

**Method:**

Eighty participants had a diagnosis of one or more of the above-mentioned diseases, four of whom had SS, thirty-two with SLE, and forty-four with RA. Sixty participants constituted a control group with no voice problems or presence of rheumatic disease. Each participant completed the Voice Handicap Index and an item outcomes scale. Forty patients from the RA and SLE groups also had a biochemical analysis completed.

**Results:**

Dysphonia in the control group was in the 5 to 8% range, while those with the specific diagnoses ranged from 32 to 38%. There were no significant differences found in the biochemical analysis. The SS patients did not show statistically significant different results from the control group, likely due to the small sample size.

**Conclusion:**

An increased risk of dysphonia was seen with all the rheumatic diseases observed in this study. This study asserts that it may be an initial sign of an autoimmune disease and that the autoimmune diseases may cause voice disorders.

**Relevance to the Current Work:**

Dysphonia is likely occurring among those with SS. It is also likely to affect their quality of life. Accurate measurement of this through procedures such as the CSID may be beneficial in determining the level of dysphonia following hydration treatments.

**Purpose of the Study:**
This study looked at everyday behaviors, including mouth breathing during exercise and during loud reading, as well as different levels of environmental humidity, that may lead to vocal fold dryness, thereby increasing effort in vocal production.

**Method:**
Sixty-three participants, about half of whom had reported voice trouble with extensive voice use, participated in mouth breathing, loud reading, and exercise with oral breathing. PTP and self-perceived phonatory effort were measured before and after each oral breathing challenge. Humidity was also controlled with participants in either low or high humidity conditions.

**Results:**
PTP was significantly affected by the vocal behavioral and environmental challenges at both low and high humidity. There was no marked difference between the two groups in any of the challenges. There were no significant effects shown in the self-perceived phonatory effort measurements.

**Conclusion:**
This study showed that both exercise and loud reading increased PTP, but did not conclude if the same underlying mechanisms are responsible for this increase. Also, longer durations of mouth breathing may be necessary to show a difference between the two groups of participants. The lack of significant finding from self-perceived phonatory effort is noted.

**Relevance to the Current Work:**
This study provides additional evidence for the relationship between vocal fold dehydration and patient-perceived vocal effort ratings. Similar rating scales are incorporated as a primary outcome measure in the present investigation.


**Purpose of the Study:**
This study proposed that ovine vocal fold epithelia respond to perturbations on the luminal surface, both ionic and osmotic, measured by bioelectric parameters of potential difference (PD) and short circuit current (I_{sc}). Detection of the luminal composition of ovine vocal folds was present immediately following perturbation, regardless of denervation of vocal folds.

**Method:**
Fifty adult ovine larynges were bisected for bioelectric data. They were exposed to one of five vocal challenges: ionic, sham, osmotic, or one of two combined ionic-osmotic solutions. PD and I_{sc} were measured.

**Results:**
The isosmotic sodium-substituted solution, the hyperosmotic sodium-substituted solution, and the ionic-osmotic challenge reduced PD. The hyperosmotic sodium chloride significantly
reduced PD. Sham and osmotic challenges did not significantly affect the exposed tissues over time. $I_{sc}$ showed significant decreases following the ionic and combined ionic-osmotic challenges, but not the sham or only osmotic challenges.

**Conclusion:**
Due to the $I_{sc}$ results, vocal folds may be sensitive to ionic species but not osmolarity. This study showed detectable perturbations to ionic composition of luminal surface liquid (less so to osmolarity). Cells likely respond to these perturbations to restore homeostasis of surface fluid important in voice production and protection from laryngeal irritants.

**Relevance to the Current Work:**
Sodium-substituted solution ionic challenge reduced the bioelectric parameters. Changes following ionic perturbations were independent of the concentration or osmolarity. This study establishes a theoretical framework for why saline solutions might influence transepithelial water flux and increase vocal fold surface hydration.


**Purpose of the Study:**
The importance of superficial vocal fold hydration on vocal fold oscillation and ease is assumed. This study looked at how the vocal fold epithelium would act in response to increases in transepithelial water fluxes creating surface hyperosmotic perturbations.

**Method:**
Thirty-six ovine vocal folds underwent exposure to either 150 mOsm Mannitol luminal hyperosmotic or isosmotic sham perturbations. Baseline, 10, 20, and 30 minutes post-challenge measurements were taken. Measurements included water fluxes, including luminally-directed and basally-directed transepithelial fluxes, and checks on vocal fold viability.

**Results:**
Electrophysiological capability of the vocal folds was maintained throughout osmotic perturbation for more than two hours. Sixty percent of vocal folds showed an increase in luminally-directed water flux following the osmotic challenge, though was not statistically significant. The main difference from the sham exposure was at 10 minutes post-exposure, such that the sham treatment decreased luminally-directed water flux. No difference was seen at 20 or 30 minutes. No significant changes in basally-directed water fluxes were noted.

**Conclusion:**
The ovine vocal folds detected osmotic perturbations and responded. Epithelia reduced hyperosmotic surface fluid by increasing luminally-directed water flux within the first 10 minutes following the osmotic challenge. This may be important in maintaining homeostasis of fluid on the vocal fold surface during times such as respiration and phonation where osmotic perturbations are taking place.

**Relevance to the Current Work:**
Inability to detect or respond to changes in the surface fluid of the vocal folds may decrease ease of phonation, reduce the clearance of mucus, and/or trigger cough in some persons. This study shows how typical vocal folds should regulate changes in superficial vocal fold hydration. This foundational work is important to demonstrate that manipulation of surface vocal fold hydration is possible through topically administered treatments.

**Purpose of the Study:**
This study examined oral and nasal breathing and their respective effects on PTP—referred to in this study as “$P_{th}$”—and vocal effort in order to provide more direction in treatments to help those who routinely breathe exclusively transorally.

**Method:**
Twenty females with no voice problems participated in 15 minutes of oral breathing or 15 minutes of nasal breathing. $P_{th}$ and perceived vocal effort were measured at three different pitches.

**Results:**
At the low, comfortable, and high pitches, oral breathing increased mean $P_{th}$ and nasal breathing decreased $P_{th}$. Overall, perceived vocal effort increased following the oral breathing task and decreased following the nasal breathing task, though four subjects reported a decrease or no change in effort following oral breathing and three nasal breathers reported no change in effort.

**Conclusion:**
Oral breathing was shown to increase $P_{th}$ and perceived vocal effort, even in a short-term 15-minute trial, likely due to superficial dehydration. Increased nasal breathing could possibly assist in preventing vocal fold pathologies and other adverse effects of oral breathing resulting in dehydration of the vocal folds.

**Relevance to the Current Work:**
This study provides the support for the previous assumption that vocal fold hydration, specifically the depth of the sol layer, responds to the humidity of inhaled air as determined by oral versus nasal inhalation. Not only is this important during singing and physical exercise, but also for individuals with chronic dryness conditions. This study also involved lower humidity levels, therefore more likely to approximate normal versus humidified environments during activities of daily living.


**Purpose of the Study:**
Following prolonged loud speech, untrained speakers are likely to have increased acoustic changes and laryngeal changes, measured by increased PTP. This study examined the effect of external hydration on PTP as well as functional changes in the larynx following long periods of loud reading.

**Methods:**
Vibratory closure patterns from laryngeal imaging, PTP, and phonatory effort visual analog scale ratings were measured in four females following two hours of reading loudly. Hydration was monitored two days before and during data collection. Baseline measurements were taken with ten minutes of comfortable reading. The experimental data was taken at least
two days following baseline and included two separate hours of loud reading. The low hydration condition included .5 L of water per day for the two days before measurements. The high hydration condition included at least 2.5 L per day for the same duration.

**Results:**

PTP generally increased at varying degrees of pitch range. In three of the four participants, drinking water helped lower the elevation of PTP, more so at the 80% pitch percentile. Phonatory effort seemed to correlate with loud reading, decreasing following vocal rest. Three participants also displayed some spindle-shaped vibratory patterns of vocal fold closure following two hours of loud reading. Vocal effort ratings were similar across subjects for the experimental sessions, in both high and low hydration conditions.

**Conclusion:**

This study offered preliminary support for increasing water intake to assist phonation following prolonged loud speaking. Hydration before and during speaking tasks produced consistent results in three out of four patients. The study suggested that PTP is a sensitive measure to changes in vocal fold hydration.

**Relevance to the Current Work:**

Utilizing PTP as a measurement, differences were noted with increased systemic hydration during prolonged phonation versus prolonged phonation with low hydration. This study gives fundamental support to the effect hydration can have on vocal effort.


**Purpose of the Study:**

This study was a follow-up replication of an earlier work (Solomon & DiMattia, 2000) that examined PTP and vocal fatigue following sustained loud reading. However, in this study, four men participated as the previous study involved only female subjects.

**Methods:**

PTP was measured at various vocal pitches in an effort to more closely match phonatory effort. Subjects were compared to their own baseline data, not in comparison to each other. Participants attended five sessions including training, two typically hydrated sessions, one low hydration, and one high hydration session. Laryngeal imaging and effort ratings were also obtained.

**Results:**

PTP increased after one hour of loud reading in 79% of trials and in 88% of trials after two hours of loud reading, with the greatest change at the highest pitch percentile. Changes in hydration did not have a consistent effect on PTP, with two subjects showing an increase during the low hydration session and two showing a decrease. Self-perceived phonatory effort also increased after the loud reading trials.

**Conclusion:**

No clear correlation was demonstrated between drinking water and improved vocal function. There was a significant effect of prolonged loud talking on vocal effects. This study hypothesized that a more global manipulation of hydration would likely have a greater effect. The data collection in this study had much greater variability than that of the authors’ previous study (Solomon & DiMattia, 2000).
Relevance to the Current Work:

Some changes in PTP were noted when hydration levels were manipulated. This study is helpful in documenting variability that may exist based on individual or sex differences.


Purpose of the Study:

This study examined results of three treatments of varying osmotic properties following a laryngeal desiccation challenge. This study also looked at the correlation between PTP and self-perceived phonatory effort.

Method:

Sixty females participated in a 15-minute laryngeal desiccation challenge followed by receiving nebulized isotonic saline, hypertonic saline, sterile hypotonic water, or a no-treatment control condition. PTP and self-perceived phonatory effort measures were administered immediately following the desiccation challenge and at four intervals after the nebulized treatments.

Results:

PTP values increased significantly following the desiccation challenge, but did not significantly change after the treatments. After 50 minutes the participants did not return to their initial pre-desiccation baseline. Self-perceived phonatory effort ratings decreased following the desiccation challenge.

Conclusion:

The low correlation between PTP and self-perceived phonatory effort demonstrated that these measures might not be as closely correlated as assumed. Though there was a worsening in PTP values following treatment with no significant improvement, there was a delayed worsening in the isotonic and saline solution groups compared to the control group. This suggested that isotonic saline might offset the negative effects associated with vocal fold dehydration.

Relevance to the Current Work:

This study gives results for three types of nebulized treatments with specific quantities and durations of each. It gives a foundation for further studies in that significant results showed PTP significantly increases following laryngeal desiccation.


Purpose of the Study:

This study examined the effects of two nebulized vocal fold hydration treatments in patients with SS as measured with PTP, self-perceived vocal effort, and mouth and throat dryness.

Method:

Eleven participants with SS participated in a 15-minute desiccation challenge, followed by one of two nebulized treatments. The treatments were either 3 mL of isotonic saline or sterile water. Measures were taken post-desiccation and at three intervals after treatment.
Results:
As expected, PTP, vocal effort, mouth dryness and throat dryness all showed significant increases after the desiccation challenge. Following the nebulized treatments, no significant effects were shown, however there was a decrease in PTP, vocal effort, and mouth and throat dryness. Sub-baseline levels were reached with the saline treatment at 35 minutes post-treatment for both PTP and throat dryness, though these differences were not statistically significant. Also, PTP correlated strongly with self-perceived throat dryness.

Conclusion:
The increase in laryngeal dryness following the desiccation challenge was significantly greater than that seen in individuals with typical voices following a desiccation challenge. Though the effect of the nebulized treatments was not statistically significant, the effect size was greater than that observed with typical voices in previous studies.

Relevance to the Current Work:
This study shows the effects of dryness and the potential benefits of nebulized treatments in individuals with SS. It gives a base from which to determine future dosage, frequency, concentration, and types of nebulized treatments. The patient-based rating scales and their relationships with PTP are also relevant to the current study.


Purpose of the Study:
This study examined the relationship between phonatory effort and hydration level by measuring phonatory effort following various treatments using PTP and direct magnitude estimation of self-perceived phonatory effort.

Methods:
This study used a double-blind placebo controlled design. Twelve participants received four hours of a hydration treatment, a dehydration challenge, and a placebo treatment. The treatment phase consisted of high humidity, two doses of a mucolytic, and encouragement to drink water throughout the session. The placebo treatment involved administration of a cherry syrup in a moderately humid environment. The dehydration condition included low humidity, the administration of a decongestant, and no fluid intake. PTP was sampled at high, low, and conversational pitches.

Results:
An inverse relationship was shown between hydration level and phonatory effort, mainly at high pitches. Across all three groups, PTP was highest at high pitches. PTP was highest for the dehydration group overall, and lowest for the hydration group. Self-perceived effort was rated higher overall in the dehydration group. Control and hydration groups did not differ considerably for effort measures.

Conclusion:
Though the exact physiological mechanisms involved in these tasks were not quantified, assumptions regarding hydration and PTP were found to support those from previous studies. PTP varied with hydration level and pitch level. This supports the authors’ theory that PTP increases with thinned and stiffened vocal folds, as observed at higher pitches.
Relevance to the Current Work:
Laryngeal hydration treatments were shown to have an effect on both PTP and self-perceived effort in a typical population. This work shows the need for studies that evaluate perceived effort in relation to objective measures as well as the need for hydration studies in clinical populations.


Purpose of the Study:
This study sought to establish evidence for the assertion that hydration treatments improve voice production. Specifically, it examined whether hydration changes occurred in those with laryngeal nodules or polyps, and whether those changes were greater compared to changes from placebo treatments.

Method:
Six females with vocal fold nodules received a hydration treatment and a placebo treatment. Each treatment lasted five consecutive days. The hydration treatment included approximately eight glasses of water a day and one tsp of a mucolytic three times daily. Participants were also exposed to high humidity in the clinic for two hours daily. The placebo group performed 20 bilateral forefinger flexions each day and took 1 tsp of cherry syrup, which they were told was an herbal medication. During their two-hour clinic time they were exposed to filtered air and scented candles. Measures were taken prior to start of program and one day following the end of the program, and included phonatory effort, PTP, auditory-perceptual ratings, acoustic measures and laryngoscopic views of the larynx.

Results:
Voice improvements as well as laryngeal improvements were noted in both the placebo and the hydration treatments as compared to baseline measures, with greater effects following the hydration treatment. Participants stated that their voice symptoms improved “somewhat” after both the placebo and the control conditions. Voice was “somewhat to quite a bit” clearer and easier following the hydration treatment. On average, performance on all measures was best following the hydration treatment.

Conclusion:
Due to the small sample size, large generalizations were not made. However, this study offered initial support to the positive effects of hydration treatments, specifically suggesting that they may reduce the viscosity of fluid within the vocal folds. In this study, greater differences were seen using self-perceived effort measures as compared to PTP, possibly resulting from variability in the PTP measure. Improvement during placebo phases could have been related to carryover from the hydration treatment; however, this possibility was not explicitly studied.

Relevance to the Current Work:
To some extent, combined topical and systemic hydration treatments were shown to have an effect on disordered voice. It provides support to utilizing similar treatments in other clinical populations such as SS.

**Purpose of the Study:**
This seminal work was the first study to examine the effects of hydration treatments on PTP in vivo. It lays the foundation for theories related to vocal fold fluid viscosity and its effect on PTP.

**Method:**
PTP was measured in six participants at low, medium, and high pitches following no-treatment, hydrated and slightly dehydrated conditions. It should be noted that four of the participants knew the hypotheses before participating. Dry conditions included dehumidification, administration of a decongestant, and no water drinking. The “wet” condition included humidified air, administration of a mucolytic, and ample water drinking.

**Results:**
The lowest pressure at all pitches was observed following the hydrated condition. Changes were significant, especially at high pitches. PTP increased as vocal fold length increased, corresponding with physiologic reductions in vocal fold thickness and increases in stiffness. Minimal changes were observed at the intermediate pitch.

**Conclusion:**
Although this study included a small participant group, these results support the theory that PTP varies with changes in the viscosity of vocal fold surface fluid in vivo. It also shows a relationship between PTP sampling pitch and PTP magnitude.

**Relevance to the Current Work:**
This study laid a foundation for future work in vocal fold surface tissue hydration and voice production.


**Purpose of the Study:**
This study examined the effects of vocal fold surface dehydration in excised canine larynges as indicated by vibratory parameters measured during high-speed video.

**Method:**
Eight excised canine larynges were recorded with high-speed video while exposed to dehumidified air. Two excised canine larynges were recorded while exposed to humidified air. No saline solution was applied to the dehumidified group. Saline (0.9% Na⁺Cl⁻) was applied in 30-second intervals to the two control group larynges. Amplitude and frequency were measured.

**Results:**
As the level of dehydration increased, amplitude and frequency tended to decrease. The percent change for these parameters was also measured. All of these results were statistically significant.
Conclusion:
Dehydration caused a decrease in mucosal wave amplitude and frequency, which would likely lead to voice worsening in vivo. This study served as a reference to which future ex vivo studies of vocal fold dehydration have been compared.

Relevance to the Current Work:
Surface tissue dehydration of the vocal folds influenced vibratory frequency and amplitude. This work supports the theory that vocal fold fluid viscosity has an inverse relationship with mucosal wave, vibratory amplitude, and vibratory frequency.