A LONGITUDINAL STUDY OF THE EFFECT OF PUBERTY ON VOICE QUALITY IN CHILDREN WITH BILATERAL VOCAL FOLD LESIONS

By

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ABSTRACT

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Dysphonia related to bilateral vocal fold lesions can have a lasting negative effect on a child's education, self-esteem and quality of life (Connor et al., 2008). The aim of this study was to investigate the progression of dysphonic symptoms of pediatric bilateral vocal fold lesions as they progress through puberty to facilitate a better understanding of pediatric voice disorders. This study evaluated the current voice quality of children diagnosed with bilateral vocal fold lesions post-puberty using acoustic and aerodynamic measurements. It compared the current quantitative measures to the measures taken pre-puberty. This study also collected subjective data in the form of the self-assessment, Pediatric Voice Handicap Index (pVHI), and compared these data pre- and post-puberty. Descriptive analyses were utilized to compare data from two male subjects. The results, though not statistically significant, support all three hypotheses. Both subjects showed a decrease in Mean Fundamental Frequency (Fo) and Mean Peak Air Pressure (MPAP) as well as an increase in Maximum Phonation Time (MPT), Cepstral Peak Prominence (CPP), Cepstral Spectral Index of Dysphonia (CSID), and Average Airflow. Scores of the pVHI also decreased or remained at 0, indicating a possible relationship between the decrease or increase in quantitative measures and the decrease or increase in qualitative measures, though inferential statistics could not be used to confirm this. The initial results from this study are highly encouraging, suggesting that this line of research should be continued to use inferential statistics.

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Introduction

Symptoms of Bilateral Vocal Fold Lesions

Vocal lesions are often the result of continuous collision of the vocal folds during phonation and are the most common cause of dysphonia, or difficulty speaking, in children (Ribeiro et al., 2012). Vocal lesions are described as small fibrous bumps that develop on the vocal folds. Vocal lesions appear red or pink at first and appear white as they become more fibrous over time. They can be unilateral; however, vocal fold lesions are typically bilateral and are placed directly across one another (Hegde & Roseberry-McKibbin, 2016). *Figure 1* shows healthy vocal folds while *Figure 2* shows bilateral vocal fold lesions. These lesions are thought to be caused by hyperactivity, impulsiveness or excessive crying (Ribeiro et al., 2012). While children are at play, they frequently increase their voice intensity, causing irritation to the vocal folds and the muscles surrounding them. Dysphonia caused by vocal lesions in children is chronic in nature. This persistence is due in part to the misperception of a child's voice quality by his/her parents as well as a delay in diagnosis and treatment (Ribeiro et al., 2012).

Figure 1: Picture of Normal, healthy vocal folds (voicedoctor.net)

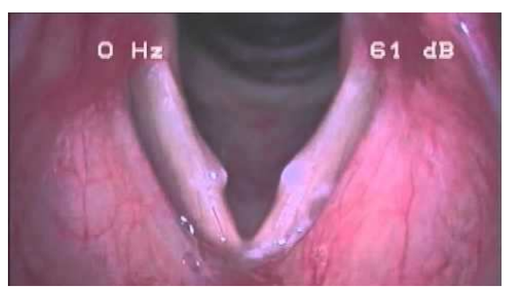


Figure 2: Picture of bilateral vocal fold lesions (WEVOSYS Reference of Organic Voice Disorders *ROVD*)

Symptoms of dysphonia in children include roughness, breathiness, vocal strain, and reduced vocal range (Connor et al., 2008). Dysphonia has been reported to be associated with a "negative impact on communicative effectiveness, social development, and self-esteem" (Connor et al., 2008). These psychosocial effects can have a direct impact on a child's education and overall social development when they have a compromised self-esteem. The voice quality of children with dysphonia can influence an adult's perception of the child's overall behavior in a negative connotation (Ruscello et al., 1988; Hooper, 2004). Teachers are more likely to associate these children with having more behavioral issues and being more aggressive than their peers. Having dysphonia can affect a child's ability to function in a classroom or to make friends, where the use of oral communication is necessary (Hooper, 2004). Moreover, children with dysphonia are likely to have other co-occurring deficits correlated with their voice disorder (Hooper, 2004). Articulation disorders, language disorders, and mild hearing problems are likely to coexist with voice disorders while respiratory tract infections, allergies, and asthma are likely to co-occur with hoarseness in children (St. Loise et al., 1992; Greene & Mathieson, 2001; Hooper, 2004).

Persistence of Bilateral Vocal Fold Lesions

Many studies have shown that dysphonia in young boys is more prevalent than in young girls. In a study by Ribeiro et al. (2012), of 304 children participants, ages 4-18, who presented with dysphonia, 64% were male and 36% were female. This prevalence is theorized by the different tendencies in behavior among adolescent boys and girls. Boys are more likely to be impulsive, aggressive, or hyperactive. Such behavior is linked to the abuse of vocal folds, leading to the development of vocal fold lesions and dysphonia.

The previously mentioned effects of dysphonia can change for some children as they endure puberty, but these changes are dissimilar among boys and girls due to their different growth hormones. As the larynxes in boys develop, they undergo structural changes that result in larger vocal folds (1 cm longer) and a more acute angle of the thyroid cartilage. These structural changes are induced by masculine hormones during puberty. As the vocal folds increase in size, vocal fold lesions and symptoms of dysphonia tend to decrease.

As girls endure puberty, their feminine hormones also elicit growth and structural changes in the larynx; however, the growth of the vocal folds is less drastic (3-4 mm elongation vs 1 cm in males) than that of boys. This amount of growth does not cause a decrease in dysphonic symptoms as it does in boys. In a study conducted by De Bodt et al. (2007), symptoms of dysphonia such as hoarseness were observed in 21% of children post-puberty while the other 79% of children no longer presented with dysphonic symptoms. Of the children who still presented with dysphonic symptoms post-puberty (21%), there was a statistically significant difference ($p \leq 0.001$) between boys (8%) and girls (37%) in that more girls persisted with symptoms than boys (De Bodt et al., 2007). Regardless of sex, chronic and insidious manifestation of vocal symptoms is the most frequently observed pattern amongst children with voice disorders (Ribeiro et al., 2012).

Current Supporting Data

There are major discrepancies among data that best estimates the number of children who have dysphonia (Hooper, 2004). According to Smith (2013), the prevalence of pediatric voice disorders is around 6-9%, but can also be estimated up to 38%. The high variance of numbers is likely due to a "lack of consistency in measurement, as well as variability in listener perceptual judgement" (Hooper, 2004). It is not uncommon for two patients with similar levels of impairment to perceive different levels of disablement (Awan et al., 2014). Many factors can contribute to the variability in voice perception including the individual's occupation, for example, if they use their voice as a primary tool of trade, they are likely to perceive their voice disorder as a more serious condition than others. Several similar studies have highlighted the importance of incorporating objective measures such as acoustics and aerodynamics in conjunction with perceptual voice quality to help improve the diagnostic and treatment steps for pediatric voice disorders (Yardeni et al., 2007).

The most common management programs for children with voice disorders include secondary prevention/vocal hygiene programs, direct voice therapy, and surgery; though, surgery is the least commonly recommended form of treatment (Hooper, 2004). The most common age for surgical intervention for children with bilateral vocal fold lesions is between 9 and 11 years (Hooper, 2004). Voice therapy is the primary treatment recommended for bilateral vocal fold lesions; however, the data to document the efficacy of voice therapy for bilateral vocal lesions are sparse (Smith et al., 2013). Data to validate the efficacy of voice therapy can increase with more studies that investigate pre- and post-measurements using assessment protocols such as the Voice Handicap Index (VHI) and the Pediatric Voice Handicap Index (pVHI) (*see Appendix E)* (Hooper, 2004).

Self-assessments of voice quality such as the pVHI are commonly used to collect outcome measures in children through the perspective of the parent. Like the VHI (for adults), the pVHI focuses on three elements of functional, physical, and emotional aspects of the children's perceived voice quality (Zur et al., 2006). The survey is used to measure pre- and post-surgical, medical and behavioral treatment effects by comparing the child's quality of life and well-being in each of these areas on the pVHI. The pVHI consists of 23 questions, which parents are asked to answer using a 5-point scale (Schindler et al., 2011). The pVHI provides a more effective tool in measuring the outcome of a child's surgical, medical or behavioral treatment interventions compared to an assessment using only objective measures. The most recently developed voice assessment approach is based on perception, endoscopic examination, acoustic and aerodynamic measurements and subjective self-assessments such as the pVHI (Schindler et al., 2011).

A clinician's perceptual evaluation of voice quality is generally considered the golden standard for assessment; however, due to the subjective nature of this assessment method, various levels of bias can occur (Maryn et al., 2010). These biases can include the experience of the listeners, their exposure to voice disorders, the degree of the patient's dysphonia, the type of auditory-perceptual rating scale, and the speaking task or stimulus type. Due to these possible errors, researchers have investigated different methods for "objectively quantifying" the patients' overall voice quality. Acoustic and aerodynamic assessments are non-invasive means of collecting quantitative data and are considered an important component of a pediatric voice disorder evaluation (Brehm et al., 2009). Acoustic and aerodynamic analyses provide numerical outputs to define the severity of dysphonia as well as provide an easy way to communicate the diagnosis and severity of dysphonia to third-parties, for example, parents or physicians (Maryn et al., 2010). Acoustic and aerodynamic measurements are known for their consistency in measuring voice quality and can provide a more comprehensive analysis of voice quality to better measure the effects of dysphonia through puberty.

Aerodynamic Measures

Aerodynamic analysis can be used to measure airflow rate and subglottic air pressure, and can also provide information about glottal efficiency (Brehm et al., 2009). Some of the more common aerodynamic measures used in voice assessment are the average airflow rate during voicing and mean peak air pressure (MPAP). Average airflow during sustained vowel production ranges from 40 to 320 cc/sec in post-pubertal males and 50 to 220 cc/sec in post-pubertal females (Sapienza & Hoffman-Ruddy, 2013). An average airflow signal provides a general idea of laryngeal function but does not provide any details about the flow modulated at the level of the glottis. When extracted from a voicing signal that is other than a sustained vowel prolongation, such as connected speech, it not only estimates glottal airflow but also the airflow that is modulated by other articulators within the oronasal-pharyngeal cavities (Sapienza & Hoffman-Ruddy, 2013). MPAP is the average of the pressure peak values and is often used to estimate subglottic pressure. These objective measures of voice quality can supplement other aspects of the voice evaluation such as perceptual measurement by allowing clinicians to compare subjective and objective data to enhance their understanding of how vocal fold lesions are affected by laryngeal growth and puberty (Brehm et al., 2009).

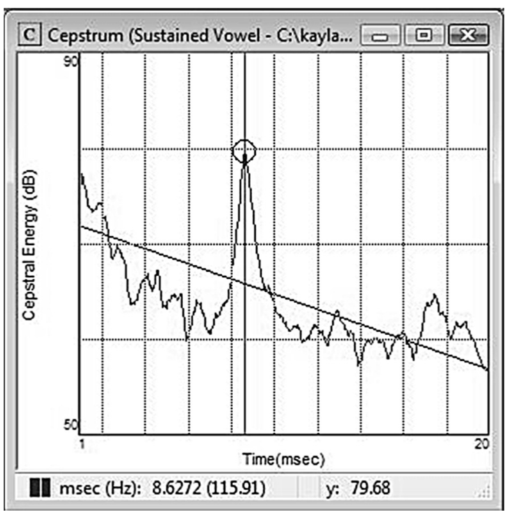
Acoustic Measures

Some of the most common acoustic measures used in voice assessment include Fo and maximum phonation time (MPT). Fo is a parameter measured from the acoustic signal of voice that reflects the rate of vocal fold vibrations (Sapienza & Hoffman-Ruddy, 2013). Most software used for the acoustic analysis of voice provide more than one algorithm for computing Fo from a connected speech sample. This measure reflects the number of vibratory cycles per second and is perceptually related to pitch. MPT measures the ability to sustain a vowel sound for as long as possible (Sliiden et al., 2017). This measure can roughly estimate things like breath control and vocal proficiency. MPT is correlated to various types of voice disorders and is frequently used to help in assessing progress of treatment, surgery, and voice therapy (Sliiden et al., 2017).

Before we can assess the effects of puberty on vocal fold lesions and dysphonia, we must first understand how a normal pediatric voice develops. Without an understanding of how acoustic measures of the normal pediatric voice change over time, our ability to use these objective measures in evaluating children with voice disorders is limited (Infusino et al., 2015). A study by Infusino, et al. (2015) found there are specific periods of transition in the Fo during the natural development of both males and females. In males, this shift begins at age 12 and has fully matured by age 16. In females, the transition begins at age 11 and has reached maturation by age 14.

Acoustic measurements have always relied on time-based measures to estimate dysphonia severity in patients, meaning these measures require cycle boundary identification to accurately determine measures like Fo and amplitude (Peterson et al., 2013). This limits the assessment to sustained vowels, such as a prolonged /a/, since these time-based measures cannot be applied to connected speech and severely disordered voices. Connected speech is important for voice assessment because it contains rapid onsets and offsets, shorter vowel durations, voiced and voiceless phonemes, amplitude variation, Fo variation related to prosody, as well as speech rate, phonetic contexts, vocal pauses, and stress (Peterson et al., 2013). Recent studies investigating the relationship between perceptual and acoustic measures found that measures derived from the cepstrum were the best predictors of dysphonia severity and provide a suitable alternative to time-based measures.

Cepstral analysis uses frequency-domain algorithms to examine continuous speech (Infusino et al., 2015). The cepstrum is the Fourier transform of the logarithmic signal spectrum where spectrum is the RMS of the Fourier transform of a signal. The cepstrum graphically displays the extent to which the harmonics are present within the patient's Fo during speech (Peterson et al., 2013). The Cepstral Peak Prominence (CPP), is an acoustic measure calculated from the cepstrum of an acoustic signal. CPP is then defined as a measure of cepstral peak amplitude corresponding to the Fo normalized to the overall amplitude (Hillenbrand et al., 1994). In a normal voice, a highly periodic signal will show a well-defined Fo and harmonic structure, corresponding to a more prominent cepstral peak. In contrast, a dysphonic voice will show disturbed periodicity and/or increased spectral noise, which are associated with a decrease in amplitude of the cepstral peak (Peterson et al., 2013). *Figure 3* is taken from Peterson, et al. (2013) to demonstrate a graphic display of CPP.



"FIGURE 1. Typical cepstral frame from a typical male sustained vowel production. The cepstral peak is circled—the cepstral peak corresponds to the fundamental frequency (115.91 Hz) and a quefrency (x-axis value in time) of approximately 8.63 milliseconds. The ratio of the automatically identified cepstral peak to the expected amplitude of the cepstral peak estimated via linear regression is referred to as the CPP (Peterson et al., 2013)."

Figure 3: An excerpt from Peterson et al. (2013) explaining a graphic display of Cepstral Peak Prominence

The results of the Infusino et al. (2015) study showed a small but significant increasing trend in CPP in male participants, which aligns with previous findings that males were more likely to present with decreased dysphonic symptoms as they developed through puberty. A possible explanation is that as age increases, phonation is better controlled during speech, which leads to a higher CPP. In female participants, however, the trend of an increasing CPP as age increased was less obvious.

The study by Infusino et al. investigated the normal development of healthy voices, and found that these normative data can be used to better understand the progression of vocal fold lesions through puberty (Infusino et al., 2015). Studies like this have highlighted the importance to know the cepstral norms in the natural development of children before using it to assess dysphonic children. Similarly, the current study aims to find a pattern of development of the voice in children with vocal fold lesions as they progress through puberty; thus, helping accurately evaluate and treat these voice disorders (Infusino et al., 2015).

Other spectral and cepstral measures for the estimation of dysphonia severity have been recently incorporated into an acoustic analysis program called the *Analysis of Dysphonia in Speech and Voice* (ADSV model 5109; KayPENTAX, Montvale, NJ). The estimate generated by the *ADSV* program is called the Cepstral Spectral Index of Dysphonia (CSID) and it represents a quantitative, multivariate, dysphonia summary tool that incorporates spectral and cepstral measures extracted from a continuous speech or sustained vowel sample. The CSID estimate of dysphonia severity is theoretically a number between 0 and 100, with 100 being rated the most severe. At times, the CSID can generate a number below 0 or above 100 representing an extremely normal and periodic voice or a profoundly abnormal and aperiodic voice, respectively (Peterson et al., 2013).

Purpose

In a study designed by Skyler Nellesen in coordination with Stephanie Zacharias PhD, CCC-SLP, and the Cincinnati Children's Hospital Medical Center (CCHMC) staff, pediatric voice center patients, ages 15 and older, who had been previously diagnosed with bilateral vocal fold lesions pre-puberty (at CCHMC), were asked to complete the pVHI. The information from the pVHI has supplied us with a subjective perception of the patients' voice qualities pre/post-puberty.

However, these data only describe the qualitative individual perceptions, which, as previously stated, is not always a reliable source of information (Ribeiro et al., 2012). To perform a more comprehensive assessment, and thereby to increase diagnostic precision and develop treatment plans for dysphonia in children, acoustic and aerodynamic measurements are often included to serve as objective data. The acoustic measures that were used in this study include MPT, Fo of connected speech, CPP, and CSID. Aerodynamic measures to be assessed include average airflow during voicing and MPAP.

This study evaluated the current voice quality of children diagnosed with bilateral vocal fold lesions post-puberty using the previously mentioned acoustic and aerodynamic measures. It compared these current measures to the measures taken pre-puberty. This study also collected subjective data in the form of self-assessments (pVHI) and compared these data pre- and post-puberty. Finally, Ad Hoc analysis of the relationship between the measurements of voice quality and subjective self-assessment (pVHI) were performed.

Hypotheses and Research Questions

1. How do quantitative measures (i.e., acoustic and aerodynamic) change in children diagnosed with bilateral vocal fold lesions from pre- to post- puberty?

   Hypothesis (1a): acoustic and aerodynamic measures of pre-pubertal children diagnosed with bilateral vocal fold lesions will show the following changes post-puberty: Fo, CSID and subglottic pressure (MPAP) will decrease while CPP, MPT, and average airflow rate will increase.

   Hypothesis (1b): the pre-post changes in acoustic and aerodynamic measures will be greater for males than females.

2. How do pVHI scores change in children diagnosed with bilateral vocal fold lesions from pre- to post-puberty?

   Hypothesis (2a): scores of the pVHI (Emotional, Functional, Physical and Total) will decrease from pre- to post-puberty.

   Hypothesis (2b): scores of pVHI (Emotional, Functional, Physical and Total) will decrease more from pre-to post-puberty in males than in females.

3. How does change in acoustic voice quality as measured through CPP relate to the change in pVHI scores from pre- to post- puberty in both males and females?

   Hypothesis (3a): the pre-post puberty change in CPP will show strong negative correlation with pre-post puberty change in total pVHI scores.

Methods

Delaney Hurst, the primary investigator, with the assistance of Dr. de Alarcon and the CCHMC staff, conducted this study. Participants are administered an acoustic and aerodynamic assessment of their voice. The objective data collected from these more current (post-puberty) measurements are compared to each participant's pre-puberty measurements. Secondly, the current perception of their voice quality as measured by the pVHI is compared to their previous perception of their voice quality taken at the time of diagnosis (pre-puberty). This study and its procedures are approved by the Institutional Review Board of CCHMC and are permitted as follow-up care through the Voice Registry at the CCHMC Center for Pediatric Voice Disorders.

Participants

This study is a continuance of the previously mentioned study conducted by Skyler Nellesen. The same participants used in Nellesen's study are used in the current study along with other participants from the CCHMC data who meet inclusion criteria. Approximately 42 patients are invited, aged 14 years and older, who previously underwent a voice evaluation at CCHMC pre-puberty, and were diagnosed with bilateral vocal fold lesions. Each participant is older than 14 years (post-puberty) at the time of data collection for the current study and must have visited CCHMC Voice Center pre-puberty (age 9 or younger) for the diagnosis of bilateral vocal fold lesions.

Procedure

A letter is sent to the household of each patient as well as a phone call, requesting their participation in this study (*see Appendices B & C)*. Participants are asked to make an appointment at CCHMC Voice Center, where they are administered the acoustic and aerodynamic assessments per CCHMC protocol. Because these participants are asked to make an appointment that is not required for their specific treatment under the care of the clinic, CCHMC is required to offer compensation for their participation in the study. A grant has been awarded to this research team through CCHMC and the Michigan State University Communicative Sciences and Disorders department for $2000 to fund this project (*see Appendix A)*. The funds allow each participant to receive a $25 VISA gift card (*see Appendix D)*.

The CCHMC protocol includes a perceptual evaluation using the pVHI, acoustic assessment using the Kay Elemetrics Computerized Speech Lab (CSL) (Kay Elemetrics Corp., Pinebrook, NJ) and aerodynamic assessment using the KayPENTAX *Phonatory Aerodynamic System* (PAS) Model 6600 (KayPENTAX Corp., Lincoln Park, NJ) (Zacharias, et al., 2016). ADSV is used to evaluate CPP and CSID of connected speech (Infusino et al., 2015).

The CCHMC protocol required that several samples of the following acoustic and aerodynamic measures be collected and used to determine an average measure during an evaluation: 1) Glide to Low Pitch (Hz), 2) Glide to High Pitch (Hz), 3) MPT (/a/) (secs), 4) Mean Fo (/a/) (Hz), 5) Mean Fo (sentences) (Hz), 6) Mean Intensity (/a/) (dB SPL), 7) Maximum Intensity (/a/) (dB SPL), 8) Mean Airflow During Voicing (mL/sec), and 9) MPAP (cmH2O). For this study, a few selected measures were utilized in the data analysis. These measures included MPT (/a/) (sec), Mean Fo (sentences) (Hz), CPP (sentences), CSID of connected speech (sentences), Mean Airflow during Voicing (mL/sec), and MPAP (cmH2O).

Preceding the collection of acoustic and aerodynamic measures, the participants' parents were asked to complete the pVHI. If the participant was not accompanied by their parents, they were asked to complete the survey on their own behalf. To collect the acoustic and aerodynamic measures, the participant was seated inside a sound booth, where the speech pathologist assisted them with the recordings. A detailed account of each measurement is listed below:

Each acoustic measure was taken using CSL. A unidirectional microphone was held approximately 15cm from the participant's mouth. *Average MPT (/a/) (sec):* The participant was given the following instructions: "take a deep breath, hold out /a/ as long as you can in a normal speaking voice until you're out of breath." The participant did this at least three times. An average measure is calculated from the three samples. *Average of the Mean Fo (sentences) (Hz):* The participant was instructed to read the following Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V) sentences once (6 sentences) in a normal speaking voice:

(a)The blue spot is on the key again.

(b) How hard did he hit him?

(c) We were away a year ago.

(d) We eat eggs every Easter.

(e) My mama makes lemon muffins.

(f) Peter will keep at the Peak.

If necessary, the speech pathologist read the sentences one by one to have the participant repeat the sentences. The ADSV software was used to calculate *CPP (sentences)* and *CSID of connected speech (sentences)* measures from three of the CAPE-V sentences: *(b), (c), and (d)*. These three sentences were used because they represent three different types of voice effort, as follows: *(b)* is an Easy-Onset Consonants Sentence, *(c)* is an All-Voiced Consonants Sentence, and *(d)* Hard Glottal Attack Voicing Sentence. CPP and CSID were computed for each separate sentence and reported separately for each type of sentence.

For each aerodynamic measure, the participant placed the face mask tightly over his/her nose and mouth, grasping the handles on either side of the mask to hold it up. The speech pathologist assisted the participant in holding the mask and monitoring for a sufficient seal of the mask around the participant's mouth and nose for both of the following tasks. *Average of the Mean Airflow during Voicing (mL/sec):* The participant was given the following instructions: "Take a deep breath and hold out the sound /a/ for about 4-5 seconds. Then take another breath and do the same thing. We will do this for 5 breaths." Each of the five breaths were considered five samples of /a/ held for 4-5 seconds. The middle three samples were used to calculate the average of the mean airflow. Once the participant completed the 5 breaths, the task was complete.

Average of the MPAP (cmH2O): The MPAP measures were used in the study to estimate the subglottic air pressure. For this task, a small plastic tube protruded from the face mask and was placed between the participants' lips, slightly inserted into their mouth about 2-3 cm. The participants were able to feel the tube between their lips when producing a /pa/ sound. The participants were given the following instructions: "Take a deep breath and say /pa-pa-pa-pa-pa/ on that one breath. Then take another breath and do the same thing. Five samples of the syllable train /pa-pa-pa-pa-pa/ were collected and the middle three syllable trains, or middle three samples were used to calculate an average of the MPAP. Once the participant completed 5 rounds, the task was complete.

Data Analysis

Data was collected on site at CCHMC Pediatric Voice Center and planned to be analyzed using a variety of parametric and non-parametric tests. For the first hypothesis, a parametric ANOVA test was planned to be used. An ANOVA (analysis of variance), was selected to determine whether the mean of two groups were significantly different from each other. As shown in *Figure 4*, hypothesis 1 consists of six dependent variables (acoustic and aerodynamic measures): CPP, CSID, MPT, Fo, MPAP, and Mean Airflow. These 6 dependent variables were measured using ratio scales and are expected to be normally distributed. Therefore, parametric statistics shall be applicable. Six separate two-way ANOVA analyses was planned to be utilized to study the interaction and significance of the data collected from the acoustic and aerodynamic measures. All six ANOVA analyses used the same two independent variables: pre/post- puberty and sex. This study aimed to demonstrate significant differences in both acoustic and aerodynamic measures between pre- and post-puberty with an anticipated sex interaction.

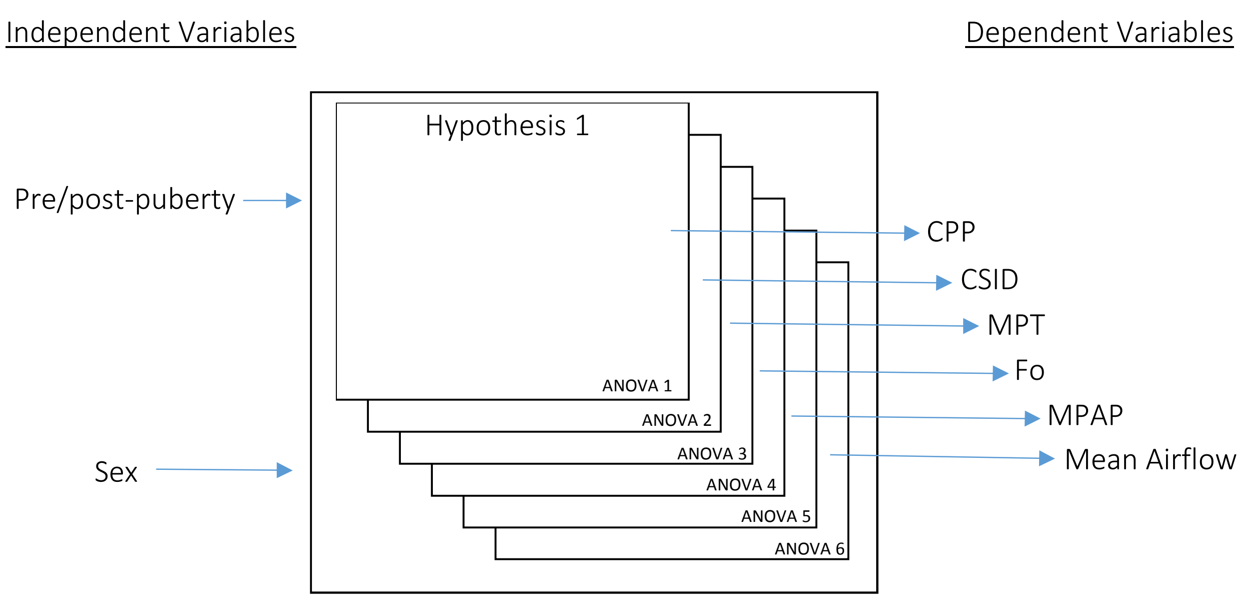


Figure 4: Block diagram of the ANOVA analysis to test hypothesis 1a and 1b.

For the second hypothesis, a non-parametric test was planned to be utilized. The Wilcoxon Signed-Rank Test was proposed to be used to compare the overall pVHI scores pre- and post-puberty. The Wilcoxon Signed-Rank Test is the equivalent to the dependent t-test and was selected used to compare two sets of scores that come from the same participants. The Mann-Whitney Test was planned to be used to determine the impact of sex. The Mann-Whitney Test was selected to compare differences between two independent variables when the dependent variable is ordinal or continuous. The total pVHI score is an ordinal scale and the total combined score of all participants could have ranged from 0-92. As shown in *Figure 5*, hypothesis 2 consists of just one dependent variable: total pVHI score and two independent variables: pre/post- puberty and sex. This study aimed to demonstrate differences in each pVHI scores from pre- to post-puberty and among males and females.

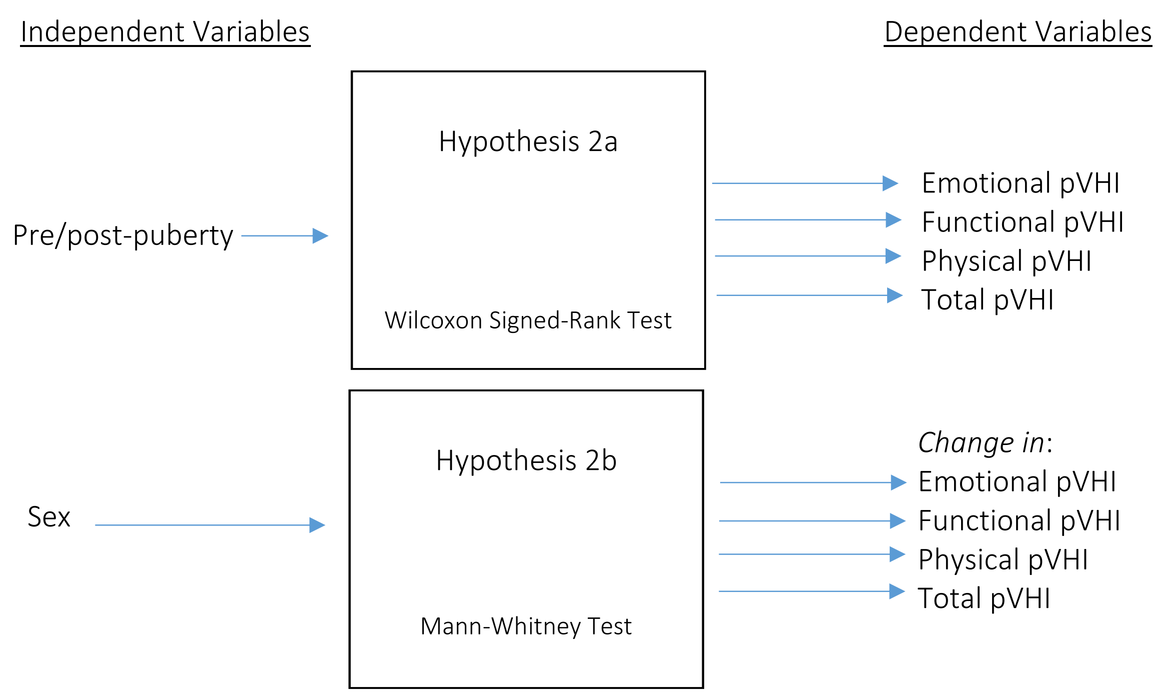


Figure 5: Block diagram of the non-parametric analyses to test hypothesis 2a and 2b.

For the third and final hypothesis, a parametric Ad Hoc analysis such as the Pearson Correlation analysis was planned to be used. A Pearson Correlation is a measure of the strength of a linear association between two variables and is commonly presented as a dot-graph with a line of best fit to display the nature of the correlation. The two variables are change in CPP and change in Total pVHI. This hypothesis aimed to demonstrate a significant negative correlation between the change in CPP from pre- to post-puberty and the change in Total pVHI scores from pre- to post-puberty among both males and females.

Results

Participants

Due to various reasons, the results of only two participants were utilized in this study. Approval from the Institutional Review Board was granted to this team in January 2018 at which time letters were sent to the homes of 42 prospective participants. Shortly thereafter, phone calls were made using the listed contact number in the CCHMC database. Addresses and phone numbers listed in the CCHMC database were provided by the parents or guardians of the participants likely when they first sought diagnosis, at which time they were minors living with their parents. Some parents who were contacted reported their children no longer lived with them and provided updated contact information. Furthermore, some contact information was outdated and families were unable to be reached due to relocation or a new phone number.

The majority of participants contacted never responded though multiple attempts were made to reach them. Those who did answer phone calls gave different reasons for declining the invitation to participate in the study, including busy work schedules restricting the parents from being able to drive their child or attend the appointment with them. Others stated that their child was away at college and was unable to return home to participate. Parents of two participants expressed interest in the study, stating they would “think about it”, however when contacted a second or third time to schedule an appointment, they gave no definitive yes or no confirmation. One parent scheduled an appointment, cancelled and rescheduled it, and did not show for the scheduled time nor did they give a reason for the missed appointment. *Table 1* displays the responses from each of the 42 prospective participants and/or their families.

Table 1: The reported reasons of the participants and/or their families for choosing not to participate in the study

Response to Letter/Phone Calls	Number of Participants Contacted
Accepted and assessed*	2
Accepted - no show to appointment	1
Expressed interest- no appointment made	2
Declined- live too far away	2
Declined- busy schedule	1
Declined -away at school	1
No response to mail and phone calls	30
Returned mail and/or disconnected phone number	3
Total Participants Contacted	*42*

Results of Two Participants

Due to the small size of the sample, inferential statistical tests were not performed as originally planned. Instead, descriptive statistics were utilized. Data from 2 subjects are compared using bar graphs to display pre- and post- puberty acoustic and aerodynamic measures as well as pre- post puberty scores of each pVHI category including the total.

The two participants included in this study were two males ages 22 years; 11 months and 18 years; 2 months at the time the post-puberty measurements were obtained in February and March 2018. Both subjects were male and each had received voice therapy for a period following their original diagnoses. Acoustic and aerodynamic measurements were obtained and compared to the pre-pubertal data of each participant. Results for Maximum Phonation Time (s), Mean Fo (Hz), Mean Airflow (ml/s), MPAP (cmH2O), CPP, CSID and Emotional, Functional, Physical and Total pVHI scores are represented in the following graphs:

Acoustic & Aerodynamic Measures: Hypothesis (1a):

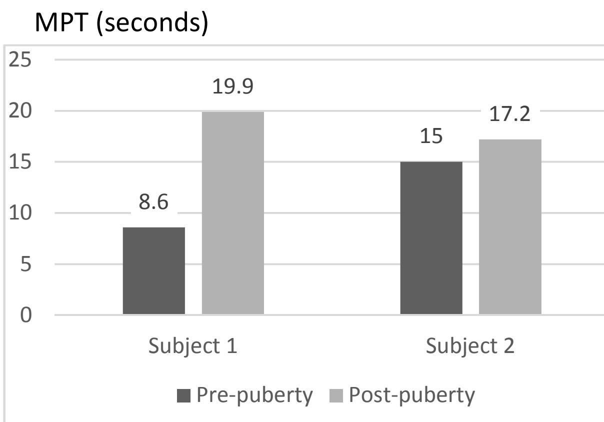


Figure 6: Bar graph displaying pre-post measurements of Maximum Phonation Time.

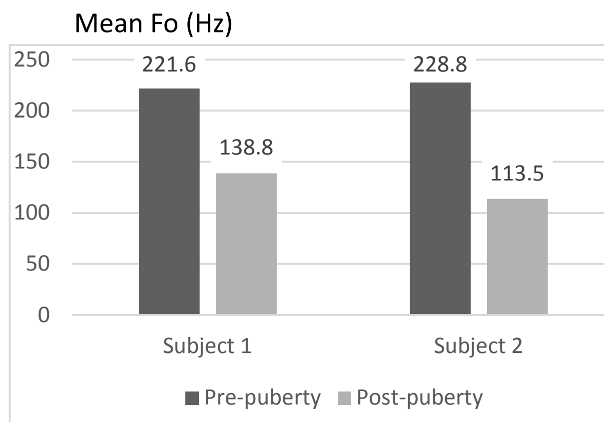


Figure 7: Bar graph displaying pre-post measurements of Mean Fundamental Frequency

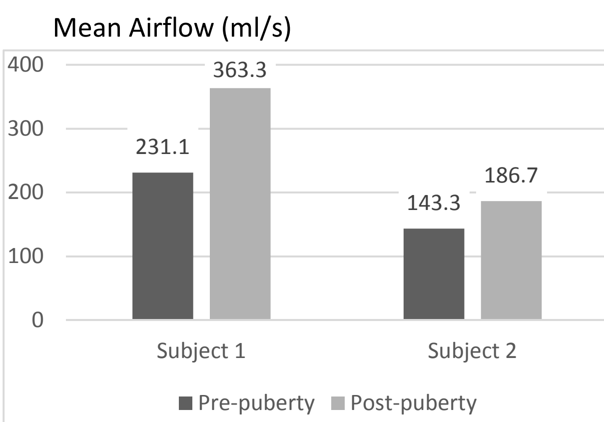


Figure 8: Bar graph displaying pre-post measurements of Mean Airflow

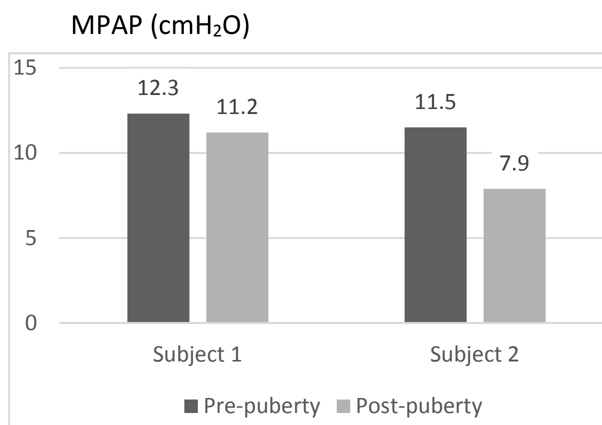


Figure 9: Bar graph displaying pre-post measurements of Mean Peak Air Pressure

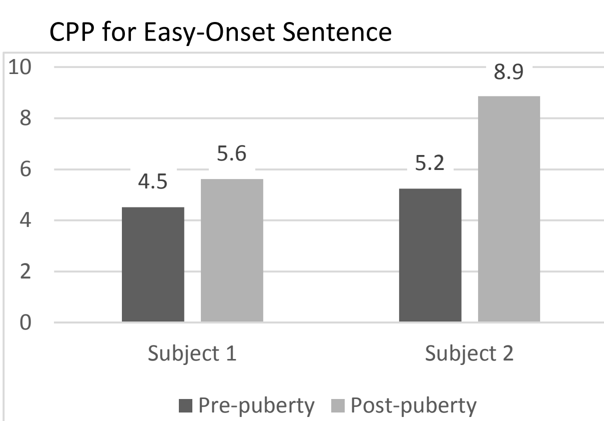


Figure 10: Bar graph displaying pre-post measurements of Cepstral Peak Prominence for CAPE-V Easy Onset Sentence (b): *"How hard did he hit him?"*

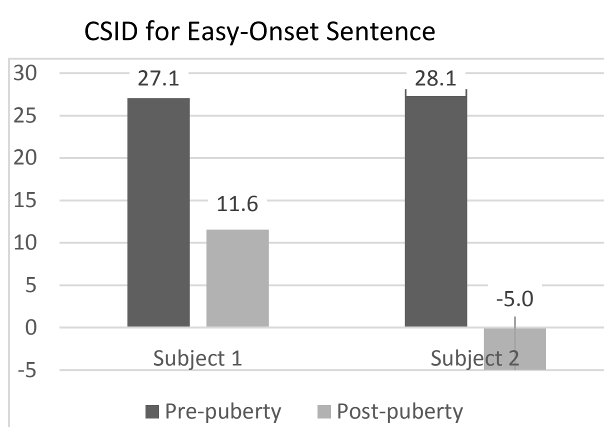


Figure 11: Bar graph displaying pre-post measurements of Cepstral Spectral Index of Dysphonia for CAPE-V Easy Onset Sentence (b): *"How hard did he hit him?"*

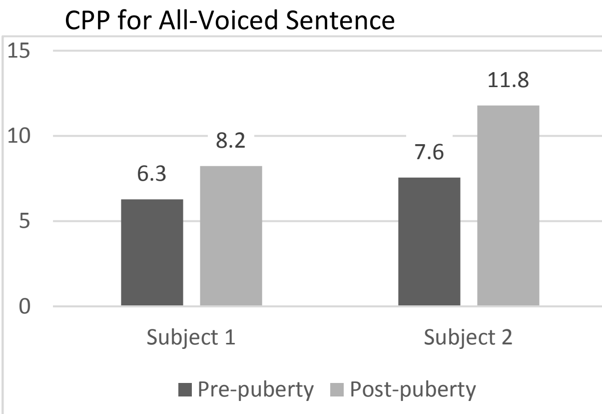


Figure 12: Bar graph displaying pre-post measurements of Cepstral Peak Prominence for CAPE-V All-Voiced Sentence (c): *"We were away a year ago"*

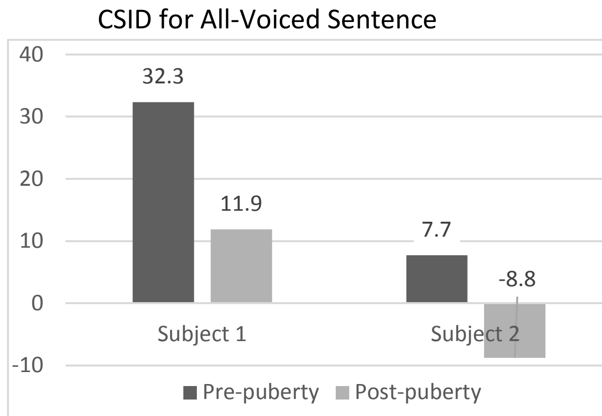


Figure 13: Bar graph displaying pre-post measurements of Cepstral Spectral Index of Dysphonia for CAPE-V All-Voiced Sentence (c): *"We were away a year ago"*

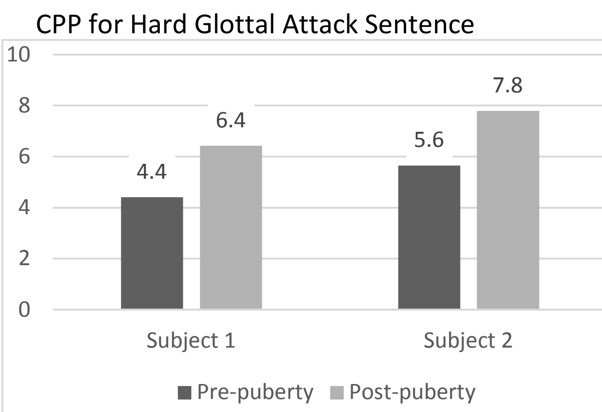


Figure 14: Bar graph displaying pre-post measurements of Cepstral Peak Prominence for CAPE-V Hard Glottal Attack Sentence (d): *"We eat eggs every Easter."*

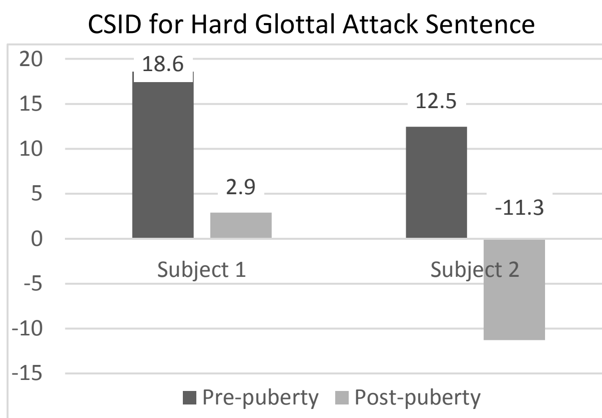


Figure 15: Bar graph displaying pre-post measurements of Cepstral Spectral Index of Dysphonia for CAPE-V Hard Glottal Attack Sentence (d): *"We eat eggs every Easter."*

As seen in *Figure 6*, both Subject 1 and Subject 2 show an increase in MPT (seconds) from pre- to post- puberty. Subject 1 increased by 11.3 seconds while Subject 2 increased by 2.2 seconds. This increase in MPT aligns with Hypothesis 1(a), stating that MPT would increase post-puberty. *Figure 7* shows a pronounced decrease in Mean Fo (Hz) in both subjects by 82.8 Hz and 115.3 Hz respectively. This decrease in Mean Fo is also consistent with the anticipated results stated in Hypothesis (1a).

Aerodynamic measures are displayed in *Figures 8 and 9.* Mean Airflow, as seen in *Figure 8*, shows that each subject's post-puberty measurement increased from their pre-puberty measure. Subject 1 increased by 132.2 ml/s, while Subject 2 increased by 43.4 ml/s. *Figure 9* shows a decrease in MPAP in both subjects. For Subject 1 MPAP decreased by 1.1 cmH_2O and for Subject 2 by 3.6 cmH_2O.

CPP and CSID were calculated using the ADSV software, which computed individual CPP and CSID score for each of the three CAPE-V voicing sentences: *(b), (c), and (d)*. As shown in *Figures 10, 12 and 14*, CPP for all three sentences increased for both subjects as expected in Hypothesis (1a). For Subject 1 and Subject 2, CPP increased by approximately 2 units and 3 units, respectively, for all three sentences. As shown in *Figures 11, 13 and 15*, a pronounced decrease in CSID was observed for all 3 sentences also aligning with Hypothesis (1a), of which post-puberty measurements reached negative units for Subject 2. These negative measurements are consistent with a normal voice quality as a negative score is considered an improvement. The largest decrease of CSID was seen for the Easy-Onset Sentence *(b)*, as Subject 2 decreased by 33 units; however, for Subject 1, the largest decrease was seen for the All-Voiced Sentence *(c)*, by 20.4 units. While each sentence reveals differing changes in CSID for both subjects, there is no consistent pattern in both subjects that might suggest one of the three sentences would elicit greater change in CSID or CPP for that matter. However, all subjects had pronounced decrease in CSID in all sentences.

pVHI Scores: Hypothesis (2a):

Data for pVHI scores are depicted in *Figures 17-20*. The Emotional pVHI score for Subject 2 decreased post-puberty from 2 to 0 (*Figure 17*). Subject 1's Emotional pVHI score could not decrease because his pre-puberty score was already at 0 and remained at 0 post-puberty. Functional pVHI scores, as seen in *Figure 18*, decrease by 8 and 7 points, respectively, each scoring a 0 post-puberty. Physical scores (*Figure 19*) also show a pronounced decrease for each subject, yet did not reach a score of 0 like the Emotional and Functional scores did. Both subject's Physical pVHI score dropped by 12 and 19 points, respectively. Finally, the Total pVHI scores (*Figure 20*) for both subjects decreased to a total of 6 and 2 out of 92 points possible, respectively.

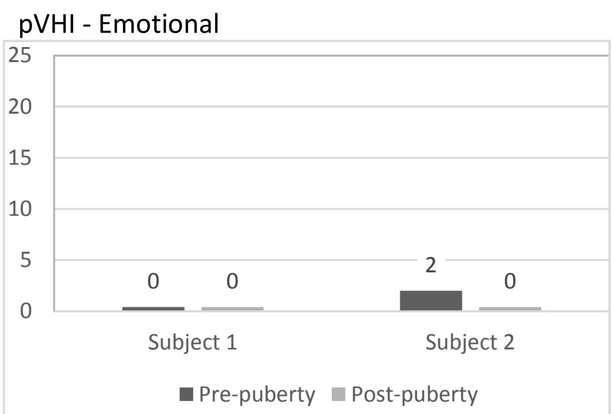


Figure 16: Bar graph displaying pre-post measurements of pVHI Emotional scores

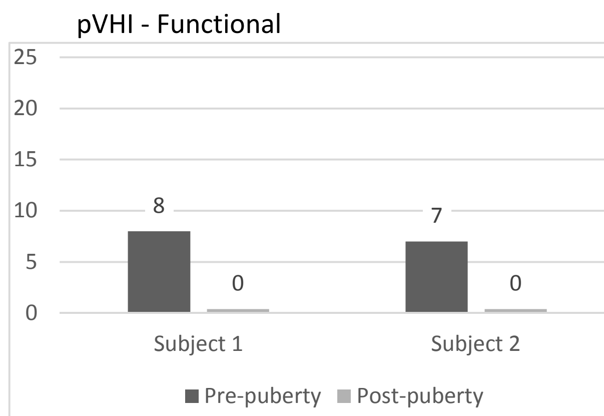


Figure 17: Bar graph displaying pre-post measurements of pVHI Functional scores

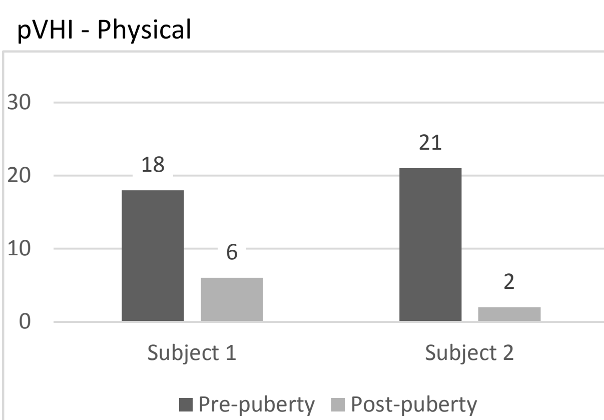


Figure 18: Bar graph displaying pre-post measurements of pVHI Physical scores

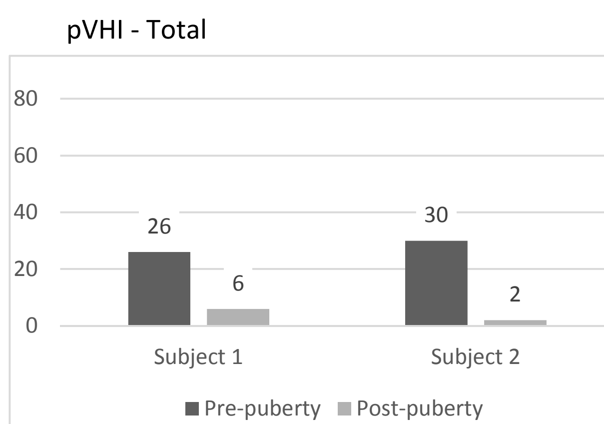


Figure 19: Bar graph displaying pre-post measurements of pVHI Total scores

Discussion

Both subjects have shown post-puberty anticipated changes for each objective and subjective measure; however, due to the small sample size and the lack of female subjects, certain hypotheses could not be tested at this stage of the study. Inferential statistics were not applicable due to the small sample size, therefore, statistical significance could not be determined. The results were informally observed to support our Hypotheses.

Hypothesis (1a) is supported by these data as Mean Fo, CSID, and subglottic pressure (estimated by MPAP) each decreased across both subjects, while CPP, MPT, and Mean Airflow all increased across both subjects. The prominent decrease in Mean Fo is within the typical range for developing males post-puberty, and while this decrease supports Hypothesis (1a), without data from female subjects, it is difficult to determine whether or not this change occurred because of typical physical development of males. The increased MPT and Mean Airflow measures are consistent with the expected growth and lung capacity that takes place during puberty. Hypothesis (1b) anticipated greater changes in these measures for male subjects compared to female subjects, however, this hypothesis could not be tested due to the absence of female subjects.

Hypothesis (2a), involving pVHI scores, was supported by the data presented from both subjects. Scores from Emotional, Functional, Physical and Total categories showed a marked decrease with the exception of Subject 1's Emotional scores, which remained a 0 from pre- to post-puberty. Once again, due to the lack of female subjects, Hypothesis (2b) which predicted greater changes in males than in females could not be tested.

Finally, Hypothesis (3a), regarding the correlation between the change in CPP and the change in Total pVHI scores was tested. Though inferential statistics were not able to be used to confirm a correlation between quantitative and qualitative scores Hypothesis (3a) was observed to be supported by the reported changes in CPP as well as changes in Total pVHI scores.

During the informal analysis of these date, the possibility of subject bias arose. Subject 1 is the child of a speech-language pathologist employed by CCHMC. Upon receiving the letter inviting them to participate in this study, his mother promptly responded via email with noted enthusiasm to contribute to research. The greatest limitation of this study was the difficulty in recruiting participants to return to CCHMC. The fact that so few participants chose to partake in the study may suggest a lack of enthusiasm to contribute to scientific research in this particular population, even though that research could potentially help others with the same diagnoses. Other possibilities include a great inconvenience for participants to make an appointment considering the busy schedules and tight budgets of the average family. Initially, a $25 gift card was thought to increase the incentive for patients to participate in the study, especially aimed toward late high school and college-aged participants. It is possible that $25 was simply not worth the inconvenience of coming into CCHMC for an appointment. Perhaps, in the future, more patients would be willing to participate if they are offered a larger compensation. Given the limitations of the study, the reported data seem to support Hypotheses (1a), (2a) and (3a).

Clinical Implications

The initial results from this study are highly encouraging suggesting that this line of research should be continued. The structure of this study could be easily replicated for future students to continue this project in the hopes of finding statistically significant results as well as to investigate differences among sexes. This study shows promise for a great contribution to science of communicative disorders, specifically to better understand typical development of voice quality through puberty of children with bilateral vocal fold lesions, which could in turn help clinicians to better determine a prediction of outcome and conduct more accurate diagnoses. In future studies, we suggest to further study how the objective acoustic and aerodynamic data relate to developmental changes in vocal fold vibratory patterns by having subjects participate in the full diagnostic exam including a fiberoptic scope to view the vocal folds.

APPENDICES

Appendix A: APPROVED GRANT

Proposal Aims:

Vocal lesions are often the result of continuous collision of the vocal folds during phonation. These lesions are most likely due to hyperactivity, impulsiveness or excessive crying making vocal lesions the "major diagnosed lesion in dysphonic children" (Ribeiro et al., 2012). Symptoms of dysphonia in children include roughness, breathiness, vocal strain, and reduced vocal range. Dysphonia has been reported to be associated with a "negative impact on communicative effectiveness, social development, and self-esteem" (Connor et al., 2008). These effects of dysphonia can change for some children as they endure puberty. As the larynxes in boys develop, they are typically larger than the larynxes of girls. Boys undergo structural changes that result in longer vocal folds and the typical symptoms of dysphonia in them tend to decrease during adolescence (Ribeiro et al., 2012). Girls instead develop only slightly longer vocal folds and are more likely to exhibit symptoms of dysphonia such as hoarseness post-puberty. Regardless of sex, chronic and insidious manifestation of vocal symptoms is the most frequently observed pattern amongst children with voice disorders (Ribeiro et al., 2012).

Self-assessments of vocal quality such as the pediatric Voice Handicap Index (pVHI) are commonly used to collect outcome measures in children through the perspective of the parent. The pVHI consists of 23 questions, which parents are asked to answer using a 5-point scale (Schindler et al., 2011). In a study designed by Skylar Nellesen in coordination with Stephanie Zacharias PhD, CCC-SLP, and Cincinnati Children's Hospital staff, approximately 25 pediatric voice clinic patients, ages 15 and older, who had been previously diagnosed with bilateral vocal fold lesions pre-puberty (at CCHMC), were asked to complete the pVHI. This information has supplied us with a subjective perception of the patients' voice qualities pre/post-puberty, however, these data only describe the qualitative individual perceptions. Acoustic and aerodynamic assessments are non-invasive means of collecting quantitative data and are considered to be an important component of a pediatric voice disorder evaluation, because they provide a more comprehensive analysis of vocal quality to better measure the effects of dysphonia through puberty (Baker Brehm et al., 2009). Aerodynamic analyses can measure average airflow rate, estimated subglottic air pressure, and provide information about glottal efficiency, while acoustic measurements analyze fundamental frequency and frequency range. These objective measurements of vocal quality can supplement other aspects of the voice evaluation such as perceptual measurement, by allowing us to compare subjective and objective data, to enhance our understanding of how bilateral vocal fold lesions are affected by laryngeal growth and puberty, as well as effects of various treatment options (Baker Brehm et al., 2009).

The goals of this study are to evaluate the current vocal quality of children diagnosed with bilateral vocal fold lesions pre-puberty, who have since undergone puberty, using acoustic and aerodynamic measurements and compare them to the measurements taken pre-puberty. We will also compare the subjective data of their perceived vocal quality to the objective data of their vocal quality as measured by acoustic and aerodynamic analyses post-puberty. Research questions include the following, but are not limited to:

1. How do quantitative measurements change post-puberty, in children diagnosed with bilateral vocal fold lesions pre-puberty?
   Hypotheses: (1a) quantitative measurements of pre-pubertal children diagnosed with bilateral vocal fold lesions will show improvement post-puberty and **(1b)** improvements in quantitative measurements will be greater in males than in females.

2. Do the subjective perceptions of voice quality (pVHI) match that of quantitative measurements post-puberty?
   Hypotheses: (2) the post-puberty subjective perceptions of vocal quality will ultimately align with the findings of the post-puberty acoustic and aerodynamic measurements.

Delaney Hurst, the primary investigator, with the assistance of Stephanie Zacharias PhD, CCC-SLP, and the CCHMC staff, will conduct this study. We intend to invite an estimated 30 patients, 15 and older, who previously underwent a voice evaluation at CCHMC (including acoustic and aerodynamic measurements) pre-puberty, and were diagnosed with bilateral vocal fold lesions. These participants will be administered an acoustic and aerodynamic assessment of their voice including, but not limited to the following: average airflow, estimated subglottic air pressure, and fundamental frequency. The objective data collected from these measurements will ultimately be used to compare to each participant's pre/post-puberty objective data as well as pre/post-puberty subjective data.

We are asking Cincinnati Children's Hospital to grant this team $2,000 to conduct this study. Most of this budget will be allocated for patient incentives to participate in our study. A total of $25 will be given to an expected 30 participants. Other funds will go toward reimbursement for those participants who are required to travel long distances to CCHMC. Attached is an example of a letter and phone-call script to each participant as well as a detailed explanation of the budget.

On behalf of our team, I would like to thank you for the consideration of awarding this grant to fund this research endeavor.

Sincerely,

Delaney Hurst
Graduate Student, Michigan State University

References:

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Appendix B: LETTER

<Date>
<Contact Name>
<Company>
<Address>
<City, State, Zip>

To Whom It May Concern,

You are receiving this letter on behalf of follow-up care for the Pediatric Voice Center at Cincinnati Children's Hospital. You or one of your children was identified as being previously seen at Cincinnati Children's Hospital for complaints of a hoarse, raspy, or breathy voice.

We would like to invite you and your child to participate further in our research by scheduling an appointment to return to our clinic. Your child's voice will be analyzed with the same assessments they have previously undergone at the time of their original visit to the clinic. These measurements will be taken in a sound booth and should require approximately 20 minutes total. The measurements taken will be compared to your child's past measurements. If you and your child decide you would like to participate, one $25 gift card will be awarded to each participant.

The information you provide will allow us to continue to improve voice care for children at Cincinnati Children's Hospital. Your participation is greatly appreciated. Please contact Delaney Hurst to schedule date and time for an appointment via phone call/text message or email using the contact information listed below. Appointment dates are also listed below and can be accommodated to your schedule if possible.

Thank you for your consideration,

Delaney Hurst
Pediatric Voice Center
Cincinnati Children's Hospital Medical Center

(269) 967-1636
hurstdel@msu.edu

*Appointments will be available Fridays and Saturdays in February 2018.

Appendix C: PHONE CALL SCRIPT

“Hello, is Mr./Mrs. ________ available?

Hi Mr./Mrs. _______. My name is Delaney Hurst; I’m calling on behalf of follow-up care for the Pediatric Voice Center at Cincinnati Children’s Hospital. How are you today?

One of your children was identified as being previously seen at Cincinnati Children’s Hospital for complaints of a hoarse voice. You may have received a letter in the mail recently with information about a study we are currently conducting. I would like to invite you and your child to participate in our study. If you choose to participate, you will receive a $25 gift card. If you are interested or have any questions regarding this study, please call give me a call back….

I am calling today to invite you and your child to participate further in our research by coming into our clinic. There, your child’s voice will be analyzed using the same tests that they have previously been given upon one of their first visits to the clinic. We plan to use this new information about your child’s voice to compare it to the previous measurements taken when they were younger.

If you and your child decide that you are interested in participating, you will be awarded a $25 visa gift card, one per child.

If you are interested in signing up now, I can take your information and schedule a date and time for you and your child to come in within the next few weeks.

If you would like time to consider your options, we look forward to hearing from you soon. Thank you for your time and have a nice day.”

Appendix D: APPROVED BUDGET

A. Senior/Key Personnel				Year 1- 7/1/17-6/30/18										
	Prefix	First	M.I.	Last	Suffix	Role, Affiliation & Support	Base Salary	% Effort	Cal Months	Acad Months	Sum Months	Requested Salary	Fringe Benefit	Funds Requested
	Ms.	Delaney		Hurst	BA	PI, MSU, scholarship	$0	50%	6			$ -	$ -	$ -
	Dr.	Alessandro		DeAlarcon	MD	Mentor, CCHMC, in-kind	$0	5%	0.6			$ -	$ -	$ -
	Dr.	Stephanie		Zacharias	PhD	Mentor, CCHMC, in-kind	$0	10%	1.2			$ -	$ -	$ -
	Dr.	Dimitar		Deliyiski	PhD	Mentor, MSU, in-kind	$0	5%	0.6			$ -	$ -	$ -
	Dr.	Maryam		Naghibolhosseini	PhD	Mentor, MSU, in-kind	$0	5%	0.6			$ -	$ -	$ -
							$0	0%	0			$ -	$ -	$ -
										A. TOTAL		$ -	$ -	$ -
B. Other Personnel														
		TBD					$0	0%	0			$ -	$ -	$ -
										B. TOTAL		$ -	$ -	$ -
C. Equipment														
												$ -		
												$ -		
												$ -	$ -	
Patient Care Costs														
												$ -		
										$ -				
													C. Total	$ -
D. Travel														
	PI project-related travel between MSU and CCHMC											$ 1,000.00		
	(travel will be supported by MSU, Voice and Speech Lab)													
													D. Total	$ 1,000
E. Participant/Trainee Support Costs														
	Tuition/Fees/Health Insurance													
	Stipends													
	Travel													
	Subsistence													
	Other													
													E. Total	$ -
F. Other Direct Costs														
	Materials and Supplies											$ -		
		Study Subjects Incentives				30	$ 25.00			support by CCHMC		$ 750.00		
		Subjects' Travel Expenses										$250		
												$ -		
	Publication Costs											$ -		
	Data Storage											$ -		
	Consultants					$ -						$ -		
	Subaward/Consortium/Contractual Costs					0	0					$ -		
	Equipment or Facility Rental/User Fees											$ -		
	Alterantions/Renovations											$ -		
													F. Total	$ 1,000
G. Total Direct Costs														
													G. Total	$ 2,000
H. Indirect Costs														
													H. Total	$ -
													Total Project Period	$ 2,000

Appendix E: PEDIATRIC VOICE HANDICAP INDEX

Instructions: These are statements that many people have used to describe their voices and the effects of their voices on their lives. Circle the response that indicates how frequently you (your child) have the same experience.

<table>
<tr><td colspan="2">Patient Number:</td><td>Date:</td></tr>
<tr><td rowspan="2">Please describe your child’s current voice quality:
Check all that apply.

_____ Hoarse
_____ Raspy
_____ Low-pitched
_____ Breathy
_____ None
_____ Other
_________________________.</td><td rowspan="2">Has your child undergone the start of puberty (voice change)?

_____ Yes
_____ No
_____ Unsure</td><td>Have your child’s voice problems resolved?
_____ Yes
_____ No
At what age? _____________.</td></tr>
<tr><td>This form was completed by:
_____ Parent
_____ Patient (child)
_____ Other:
_________________.</td></tr>
<tr><td colspan="3">Please indicate any type of treatment or surgery your child has received to treat his/her voice disorder:
Please circle any that apply:
• Surgery
• Voice Therapy
• None</td></tr>
<tr><td colspan="3">I would rate my child’s talkativeness as the following (circle response):

Quiet listener (0)   1   Average talker (2)   3   Extremely talkative (4)</td></tr>
</table>

	Never	Almost Never	Sometimes	Almost Always	Always
Part I - F					
My child's voice makes it difficult for people to hear him/her.	0	1	2	3	4
People have difficulty understanding my child in a noisy room.	0	1	2	3	4
At home, we have difficulty hearing my child when he/she calls through the house.	0	1	2	3	4
My child tends to avoid communicating because of his/her voice.	0	1	2	3	4
My child speaks with friends, neighbors, or relatives less often because of his/her voice.	0	1	2	3	4
People ask my child to repeat him/herself when speaking face-to-face	0	1	2	3	4
My child's voice difficulties restrict personal, educational, and social activities.	0	1	2	3	4

Continue to Page 2

Part II - P

	Never	Almost Never	Sometimes	Almost Always	Always
My child runs out of air when talking.	0	1	2	3	4
The sound of my child's voice changes throughout the day.	0	1	2	3	4
People ask, "what is wrong with your child's voice?"	0	1	2	3	4
My child's voice sounds dry, raspy, and/or hoarse.	0	1	2	3	4
The quality of my child's voice is unpredictable.	0	1	2	3	4
My child uses a great deal of effort to speak (e.g. straining)	0	1	2	3	4
My child's voice is worse in the evening.	0	1	2	3	4
My child's voice "gives out" when speaking.	0	1	2	3	4

My child has to yell in order for others to hear him/her.	0	1	2	3	4
Part III - E					
My child appears tense when talking to others because of his/her voice.	0	1	2	3	4
People seem irritated with my child's voice.	0	1	2	3	4
I find other people don't understand my child's voice problem.	0	1	2	3	4
My child is frustrated with his/her voice problem.	0	1	2	3	4
My child is less outgoing because of his/her voice problem.	0	1	2	3	4
My child is annoyed when people ask him/her to repeat.	0	1	2	3	4
My child is embarrassed when people ask him/her to repeat.	0	1	2	3	4

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