ACOUSTIC MEASURES OF PHONATORY FUNCTION IN INDIVIDUALS WITH WILLIAMS SYNDROME

by

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CHAPTER 1

INTRODUCTION

The human vocal folds are organized in layers, the epithelial layer, three layers of the lamina propria, and the vocalis muscle. Each layer of the lamina propria contains different amounts and forms of elastin, and it has been suggested that an alteration in the elasticity of the vocal folds may cause dysynchronous vibration (Kahane, 1987). The elastin gene codes (ELN) for all the elastin present in all elastic fibers of the connective tissues in the body. It has been found that individuals with ELN deletion have perceptually and acoustically different voices than the general population. However, no researchers to date have measured the acoustic properties of individuals with ELN deletion who exhibit the neurobehavioral characteristics of WS. The purpose of this study was to determine if the acoustic properties of voices in individuals with WS were measurably different than those of normal individuals.

LITERATURE REVIEW

Vocal Folds

The human vocal folds are organized as a layered structure composed of an epithelial surface, three layers of lamina propria (superficial, intermediate, and deep), and the vocalis division of the thyroartyenoid muscle (Stemple, Glaze, & Kaben, 2000). Vibration of the vocal folds is necessary for sound production, and each of these layers plays an important role in the process of vibration. The epithelial layer is a mucosal covering made up of stratified squamous cells that cover the outer surface of the vocal folds. The lamina propria is composed of a small amount of cells, mostly fibroblasts, and matrix substances produced by the following cells: glycosaminoglycans (GAGs), proteoglycans, and fibrous proteins, including collagen and elastin (Hammond, Gray, Butler, Zhou, & Hammond, 1997). Each layer of the lamina propria is uniquely arranged. The superficial layer contains a minimal amount of elastic and collagen fibers as well as a large amount of amorphous ground material, and so this layer is often described as "gelatinlike" (Stemple, Glaze, & Kaben, 2000). The area between the epithelium and the superficial layer is the basement membrane zone (BMZ) and serves as a means of attachment for the two layers because it contains a complex arrangement of fibers and proteins, including collagen (Gray, Hirano, Sato, 1993). The intermediate layer of the vocal folds contains an increased amount of elastic fibers, and the deep layer contains a larger concentration of collagen (Gray, Titze, Alipour, & Hammond, 2000).

In the cover-body theory of phonation, the epithelium and the superficial layer of the lamina propria are considered the cover, the intermediate and deep layers of the lamina propria are considered the transition, and the vocalis muscle is considered the body (Hirano,

1981; Hirano, 1996; Hirano, Matuso, Kakita, Kawasaki, Kurita, 1983). This theory, presented by Hirano, is based on the knowledge that each layer of the vocal folds contributes a different mass and amount of compliance needed for vocal fold vibration. The cover is a loose, fluid layer and the body is stiff, providing a stabile core for the cover to move over. The transition, or vocal ligament, attaches the two and the layers increase in stiffness from the superficial layer to the vocalis muscle (Stemple et al., 2000). Thus, the deep layer of the lamina propria is considered to be stiffer than the intermediate layer of the lamina propria. The elastic and collagen fibers that make up this ligament are positioned so that they are oriented in the same direction as the vocalis muscle, which allows the ligament to balance the tensions in the surrounding layers (Gray et al., 2000). This histologic composition is necessary for normal vibratory biomechanics and voice quality during sound production.

Elastin

The concentration of elastin and collagen varies throughout the three layers of the lamina propria and this variance is what allows for differentiation between the layers. Elastin and collagen are fibrous proteins that make up the extracellular tissue of the vocal folds. These fibrous proteins are necessary for the shape and form of the vocal folds and are meant to handle the stress that is put on the vocal folds during vibration (Gray et al., 2000). Elastic fibers are present in three forms within the vocal folds: oxytalan, elaunin, and mature elastic fibers. All three contain microfibrils; however, elaunin and elastic fibers contain amorphous material in addition to the microfibrils, and elastic fibers contain more amorphous material than elaunin (Gray et al., 2000). Elaunin and oxytalan are less “elastic” than mature elastic fibers and so are “found in tissue in which stress is much higher” (Gray et al., 2000). In the vocal folds, elaunin and oxytalan are found in the superficial layer of the lamina propria

whereas a small amount of elastic fibers are present in this layer. In addition, the largest concentration of elastic fibers is found in the intermediate layer (Hammond, Zhou, Hammond, Pawlak, & Gray, 1996). Elastic fibers are important for normal voice production and are believed to influence the ability to alter pitch by allowing the vocal folds to stretch. It has been suggested that an alteration in the elasticity of the vocal folds may cause dysnychronous vibration (Kahane, 1987).

All three forms of elastic fibers are produced by a single gene, ELN, which has been mapped to the long arm of chromosome 7 in humans, specifically to 7q11.2 (Fazio et al., 1990). ELN not only enables the production of the elastin protein in the vocal folds, but also is responsible for the production of elastin present in all elastic fibers of the connective tissues in the body, from the cardiovascular system to the skin (Tassabehji et al., 1997). ELN first produces tropoelastin, a polypeptide that gives the protein its resilience. Once produced, each tropoelastin chain undergoes a process of cross-linkage forming a network of elastic fibers (Tassabehji et al., 1997). Since elastin is found throughout the body, it is expected that disruption of the elastin gene would cause problems in all connective tissues containing elastin.

Genetic Conditions with Elastin Disruption

One condition in which the disruption of the elastin gene plays a threatening role is supravalvular aortic stenosis (SVAS), which is characterized by a congenital narrowing of the ascending aorta and is usually progressive (Eisenberg, Young, Jacobson, & Boito, 1964). SVAS may occur alone (nonsyndromic SVAS) or along with another disorder, such as Williams syndrome (WS) (Christiano & Uitto, 1997). WS is characterized by cardiovascular complications, facial dysmorphology, cognitive impairments usually within the range of

moderate mental retardation, and hypersociability (Marens, Wilson, & Reutens, 2008; Jones et al., 2000). Disturbances in ELN do not result in identical genetic expression, which is evident by the fact that SVAS and WS do not always coexist (Christiano & Uitto, 1997). In addition, SVAS may vary from slight cardiac irregularities to severe stenosis of several arteries just as the various problems seen in patients with WS can vary in severity depending on the amount of expressivity and penetrance (Tassabehji et al., 1997). Thus, the exact location and amount of ELN disturbance is important when determining the effects the disturbance will have on an individual.

Through the use of fluorescent in situ hybridization (FISH) it has been found that one elastin allele is deleted in individuals who have been diagnosed with WS (Ewart et al., 1993). This hemizygosity of the elastin gene may account for all of the connective tissue abnormalities seen in WS (Ewart et al., 1993). In contrast, the extent of connective tissue abnormality may not be as great in SVAS (Christiano & Uitto, 1997). The cause of this could lie in the fact that point mutations of specific exons have been found to be the cause of SVAS (Tassabehji et al., 1997), whereas deletion of one allele has been found to be the cause of WS (Ewart et al., 1993). However, the wider range of connective tissue disturbances seen in patients with WS may be caused by the deletion or silencing of other genes (Tasabehji et al., 1997). Dridi et al. (1999) looked at skin elastic fibers in WS and nonsyndromic SVAS and found a "decrease in pre-elastic and mature elastic fibers in agreement with the decreased amount of elastin in the skin" in those diagnosed with WS. However, when looking at the skin elastic fibers in SVAS, mature elastic fibers were not significantly reduced, whereas pre-elastic fibers were significantly reduced (Dridi et al., 1999). The results found by Dridi et al.

supplies further evidence of the phenotypic differences seen in those with WS versus those with SVAS.

Genetics and Voice

It is clear that genetic factors influence voice qualities because of the many genetic disorders that have been documented to co-occur with voice disorders. For example, a study conducted by Wold and Montague (1979) found that adults with Down syndrome had voices that were rated as "breathy" in addition to lower and higher pitch levels as compared to normals matched on age and gender. In addition, it is assumed that function is related to structure in all parts of the body, including the laryngeal cartilages, vocal fold length and structure, and size and shape of the supraglottic vocal tract (Sataloff, 1993). Since these physical characteristics are genetically determined and are related to the quality of voice that is produced, it is believed that voice quality is also genetically determined, at least in part (Sataloff, 1993). Moran studied whether special educators (graduate students and faculty) and speech pathologists (graduate students and faculty) could distinguish between adults with Down syndrome and those with hoarse voices by listening to prolonged vowel samples. The study found that both groups were able to differentiate speakers with Down syndrome from speakers with hoarse voices with a moderate degree of accuracy. However, when comparing the acoustic measures of formant frequencies of the two populations it was found that the difference between the two groups was nonsignificant. (Moran, 1986)

Akefeldt, Akefeldt, and Gillberg (1997) studied the voice, speech, and language characteristics of children with Prader-Willi syndrome compared to a group matched for age, IQ, sex, and body mass index (BMI). The study found that, "resonance was more often hypernasal and pitch level abnormally high" in the children with Prader-Willi syndrome as

measured on a rating scale of 0 (normal) to 2 (abnormal) by a speech pathologist (Akefeldt, Akefeldt, & Gillberg, 1997). Van Borsel, 2004 completed a meta-analysis of the occurrence of voice and resonance disorders in genetic syndromes and found that "when a syndrome is associated with voice problems (118/299 syndromes), voice quality is the most frequently affected parameter (74/118)." Pitch problems were found to be present in about one fourth of the syndromes and resonance disorders were reported in 162 of the 299 syndromes. However, many disorders have no information regarding association with communication disorders and so further research in this area is needed (Van Borsel, 2004). Likewise, even though a voice disturbance may be expected in a particular genetic disorder, the understanding of how the voice is different acoustically and why the voice is perceived differently is incomplete.

Though there are consistent reports of hoarseness in populations with ELN abnormalities, few studies have examined the perceptual and acoustic vocal qualities in these populations. Vaux, Wojtczak, Benirschke, & Jones (2003) looked at autopsy tissue of the vocal cords from a patient with ELN deletion and documented WS and the vocal cords of a similarly aged patient. This study found a distinct lack of elastic fibrillar components in the vocal cords of the patient with WS compared to the control. Based on these results, the authors hypothesized that the paucity of vocal cord elastin may account for the hoarseness noted in the majority of patients with WS. Watts, Marler, and Urban (2007) measured the acoustic characteristics of fundamental frequency (F_o), jitter, shimmer, noise-to-harmonic ratio, average speaking F_o, physiological frequency range, and spectral tilt of six individuals with confirmed ELN mutations, but none of the neurobehavioral characteristics of WS compared to age-matched controls. The study found that the acoustic measures of speaking

F_o were below normal ranges, corresponding to a perceptually low pitch, for both males and females in the SVAS group (Watts, Marler & Urban, 2007). In addition, it was found that the degree of difference was greater for the males in the experimental group compared to the controls than for the females. A greater degree of spectral tilt in the SVAS group was also found. This suggests that the degree of vocal fold closure was reduced in this group, which the authors hypothesize is due to the "reduced amounts and/or disorganization of elastic fibers in the vocal folds of the participants in the SVAS group." Watts, Awan, and Marler (2008) investigated the voice quality in individuals with genetically diagnosed ELN mutations or deletions who presented with either WS or SVAS compared to age and gender matched controls. The acoustic characteristics of F_o, pitch sigma, jitter, harmonics-to-noise ratio, shimmer, discrete fourier transformation ratio, and spectral peak prominence/ expected peak amplitude were examined. The authors found significant group differences in pitch sigma and jitter. Perceptual characteristics were examined and it was found that the SVAS/WS subjects had a significantly greater frequency of occurrence for "Hoarse" and "Rough" versus the controls (Watts, Awan, & Marler, 2008).

It has been found that individuals with ELN deletion have perceptually and acoustically different voices than the general population. However, no researchers to date have measured the acoustic properties of individuals with ELN deletion who exhibit the neurobehavioral characteristics of WS.

CHAPTER II

STATEMENT OF PURPOSE

The purpose of this study was to examine the acoustic voice quality of individuals with WS compared to normal controls so that a better understanding of the phenotypic differences between individuals with ELN abnormalities and the general population could be attained. This study also provided additional information regarding the role of the elastin gene on measures of voice quality since the genotype of the population being studied is different than the population at large with ELN abnormalities, and the combined population of SVAS/WS that has been previously studied. The specific research questions this study addressed are as follows:

1. Do individuals with WS exhibit different levels of habitual F_o than unimpaired controls?
2. Do individuals with WS exhibit different levels of jitter than unimpaired controls?
3. Do individuals with WS exhibit different levels of shimmer than unimpaired controls?
4. Do individuals with WS exhibit different noise to harmonic ratios than unimpaired controls?

CHAPTER III

METHODOLOGY

Participants

Two groups of speaking participants were recruited for this study. An experimental group consisting of 16 individuals with WS (8 male, 8 female) were recruited and recorded prior to the initiation of this study. Inclusion criteria for these participants consisted of genetically confirmed WS genotype (deletion of multiple genes at the 7q11.2 location, including ELN) via fluorescence in situ hybridization (FISH) testing and confirmation of the WS behavioral phenotype by a medical professional. A convenience sample of 16 normal controls was recruited through class announcements, word of mouth, and phone calls from the investigator's acquaintances in the Houston area as well as the Dallas/Fort-Worth area. The controls were matched to WS participants on two variables: (1) gender and (2) age. The mean chronological age of participants in the WS group was 28.6 for males and 24.6 for females. The range of chronological age for participants in the WS group was 16-56 for males and 18-34 for females.

Prior to recruiting control participants, the following criteria were set: participants in the control group were gender-matched equally (8 normal males and 8 normal females). For age, the control group as a whole fell within the range, +/- 2 years of ages recruited for the WS group, and within 6 months of the group's mean age. In addition, each participant was matched within 6 months for children below 18 years of age (and within 3 years for adults). No participants were under the age of 16 and all were required to report that they are able to read. Inclusion criteria for the normal controls were as follows: negative history for voice

disorder, genetic disorder, and neurological disorder, non-smoker, and no current voice complaints.

Sixteen control participants (8 male, 8 female) were recruited. The mean age for the control males was 28.6 with a range of 16-55. The mean age for the control females was 24.1 with a range of 19-34. None of the normal participants reported having a history of voice disorders, smoking, neurological disorders, or genetic disorders. Each of the voices of the normal participants were recorded and analyzed using the protocol stated in the methods section of this report. The age and gender of all participants is listed in Table 1.

Table 1: Age and gender of all participants

Group	Gender	Age (years)	Group Mean/Range
WS			
L	M	47	
B	M	22	
S	M	31	
D	M	16	
G	M	17	
J	M	56	
J	M	18	*WS Male Mean: 28.6*
B	M	22	*WS Male Range: 16-56*
B	F	19	
K	F	19	
K	F	18	
H	F	20	
D	F	28	
M	F	31	
T	F	28	*WS Female Mean: 24.6*
K	F	34	*WS Female Range: 18-34*
Normal			
RA	M	55	
BA	M	23	
PM	M	50	
AA	M	20	
AA	M	16	
SA	M	27	
CP	M	16	*Normal Male Mean: 28.6*
JF	M	22	*Normal Male Range: 16-55*
KW	F	19	
KG	F	34	
JB	F	27	
JS	F	19	
BG	F	28	
CC	F	27	
DG	F	19	*Normal Female Mean: 24.1*
AK	F	20	*Normal Female Range: 19-34*

Procedure

All speaking participants (WS & control) were recorded in the local community using a digital recording device (for WS participants, a marantz digital tape recorder was used; for normal participants, a marantz digital memory recorder was used). The same microphone was utilized for all sites, in a quiet location with background noise below 45dBSPL (as tested via a portable sound level meter). Each participant was recorded using a head-mounted microphone, which was connected to the recording device with a mouth-to-mouth distance of no greater than 3cm. Testing began after an explanation of the study procedures and associated risks were given to the participants and caregivers (if accompanied the participant and the participant was under 18 – individuals under 18 were not allowed to participate without the caregiver present), and the consent form was signed. Demographic and history information was collected. Some of this information was used to either include or exclude the participant's data in the study (see Appendix A for participant questionnaire).

For acoustic analyses, participants produced five types of vocalizations, which included: (1) reading a standard passage (the Grandfather Passage), (2) sustained vowel production for 5 seconds, (3) maximum phonation duration, (4) maximum and minimum phonation frequency attempts, and (5) sustained high pitch vowel prolongation (See Appendix B for participant instructions). Only steady state portions of the sustained vowel production (task 2) were analyzed for the purposes of this study. Participation in the study required no more than 20 minutes from each participant.

Instrumentation

Digital hardware/software equipment (for acoustic measurements) was utilized for this study. A portable digital audio tape recorder (DAT) was used to initially record voices. These were then digitally transferred to the Computerized Speech Lab (CSL - Kay Elemetrics, Lincoln Park, NJ), which was used both as a signal capture and as a signal analysis device. An AKG Acoustics head-mounted microphone was connected to the DAT for direct analog-to-digital conversion of vocal productions at 44.1 KHz sampling rate.

Analyses

For the acoustic productions, measurements from the sustained vowel productions were as follows: fundamental frequency (F_o), jitter percent, shimmer percent, and N/H (noise to harmonic) ratio. These measurements were chosen as they are the most commonly reported acoustic measures in the research literature and have known applicability to aspects of voice quality. Voice samples were analyzed by the CSL one vowel at a time. The CSL automatically calculated the four independent variables being studied. The F_o represents the average rate of vocal fold vibration, in Hertz. Jitter and shimmer are time-based measures of cycle-to-cycle variability in frequency and intensity, respectively. N/H ratio represents the ratio of harmonic noise energy in the acoustic signal to non-harmonic noise energy.

Data from the three vowel productions were averaged for each participant and displayed in table and graphical form for preliminary analyses. SPSS was utilized for all statistical analyses. A MANOVA was first applied to the data with group and gender as the independent variables, and was followed by eight separate one-way ANOVAs, with the

independent variable being group assignment (WS vs. Control) for four ANOVAs and gender (male vs. female) for the remaining four. A significance level of .05 was used as the basis for judgments of statistical significance in the first omnibus MANOVA, although a modified Bonferroni adjustment was used to correct the individual comparisons (the eight separate ANOVA's) alpha levels to .025 each, in order to better protect against type 1 errors.

The primary investigator reanalyzed 20% of the signals in order to assess intra-rater reliability. A 2nd investigator reanalyzed 20% of the signals in order to assess inter-rater reliability. Inter-rater and intra-rater reliability were calculated by re-analyzing 20% (21 total) of the acoustic files. All files were randomly selected for re-analysis. Each dependent variable (jitter, shimmer, F_o, N/H ratio) was reanalyzed in each file, so that a total of 84 (21 files x 4 measurements) measurements were recalculated for both inter-rater and intra-rater reliability. Pooled across all measurements, inter- and intra-rater reliability was calculated at 98% agreement, respectively, which was considered very high.

CHAPTER IV

RESULTS

The design of this study utilized two independent variables (group & gender) and four dependent variables (acoustic measures of Fo, jitter, shimmer, & N/H ratio). For the omnibus MANOVA, an alpha level of .05 was used as the criterion for statistical significance. For the eight one-way ANOVAs, an alpha level of .025 was used as the criterion for statistical significance. Data is summarized in Table 2.

Table 2: Means of Acoustic Measurements for group (Normal, Williams Syndrome) and Gender (male, female).

Measurement	Group	Gender	N	Mean	Standard Deviation
Fundamental Frequency	Normal	Male	8	113.75	8.51
		Female	8	233.63	35.24
		Total	**16**	**173.69**	**66.67**
	WS	Male	8	121.88	19.2
		Female	8	222.5	33.69
		Total	**16**	**172.19**	**58.32**
	Normal + WS	Male	16	117.81	14.95
		Female	16	228.06	33.8
		Total	**32**	**172.94**	**61.62**
Jitter Percent	Normal	Male	8	.73	.19
		Female	8	1.56	.89
		Total	**16**	**1.15**	**.76**
	WS	Male	8	.67	.49
		Female	8	.91	.62
		Total	**16**	**.79**	**.55**
	Normal +WS	Male	16	.70	.36
		Female	16	.91	.62
		Total	**32**	**.97**	**.68**
Shimmer Percent	Normal	Male	8	2.96	.9
		Female	8	3.84	2.43
		Total	**16**	**3.4**	**1.82**
	WS	Male	8	1.28	1.25
		Female	8	1.57	1.25
		Total	**16**	**1.43**	**1.22**
	Normal +WS	Male	16	2.12	1.37
		Female	16	2.7	2.2
		Total	**32**	**2.4**	**1.83**
Noise/Harmonic Ratio	Normal	Male	8	.15	.02
		Female	8	.14	.05
		Total	**16**	**.14**	**.04**
	WS	Male	8	.13	.02
		Female	8	.13	.03
		Total	**16**	**.13**	**.02**
	Normal +WS	Male	16	.14	.02
		Female	16	.14	.04
		Total	**32**	**.14**	**.03**

Trends in this data were as follows:

Fundamental Frequency (F_o): Both groups (WS and Normals) manifested similar measures of F_o (see Figure1). The WS group had an average F_o of 172Hz with a standard deviation of 58Hz and the Normal group had an average F_o of 174Hz with a standard deviation of 67Hz. For both groups, the females were measured to have a higher F_o than males, which is expected considering the normative data for males and females. The female participants had an average F_o of 228Hz with a standard deviation of 34Hz, and the males had an average F_o of 118Hz with a standard deviation of 15Hz.

Jitter: The normal group was measured to have a higher jitter percentage than the WS group (see Figure 2). The normal group had an average jitter percentage of 1.15% with a standard deviation of .76% and the WS group had an average jitter percentage of .79% with a standard deviation of .55%. When comparing the jitter percentage of all males to all females, it was found the females had a slightly higher jitter percentage. The males had an average jitter percentage of 2.12% with a standard deviation of 1.3% and the females had an average jitter percentage of 2.7% with a standard deviation of 2.2%.

Shimmer: The normal group was measured to have a higher shimmer percentage than the WS group, with a mean of 3.4% and a standard deviation of 1.8% for the former and a mean of 1.4% and a standard deviation of 1.2% for the latter (see Figure 3). The females of both groups were measured to have a slightly higher jitter percentage than the males of both groups. The females received a mean of 2.7% and standard deviation of 2.2% and the males received a mean of 2.1% and a standard deviation of 1.4%.

N/H ratio: Both groups of participants received similar ratings of N/H ratio, with the normal group's mean being .14 with a standard deviation of .04 and the WS group's mean being .13 with a standard deviation of .02 (See Figure 4). Likewise, the males and females received similar ratings of N/H ratio, with the females' mean being .14 with a standard deviation of .04 and the males' mean being .14 with a standard deviation of .02.

Figure 1: Mean fundamental frequency for all Subjects (In Hz)

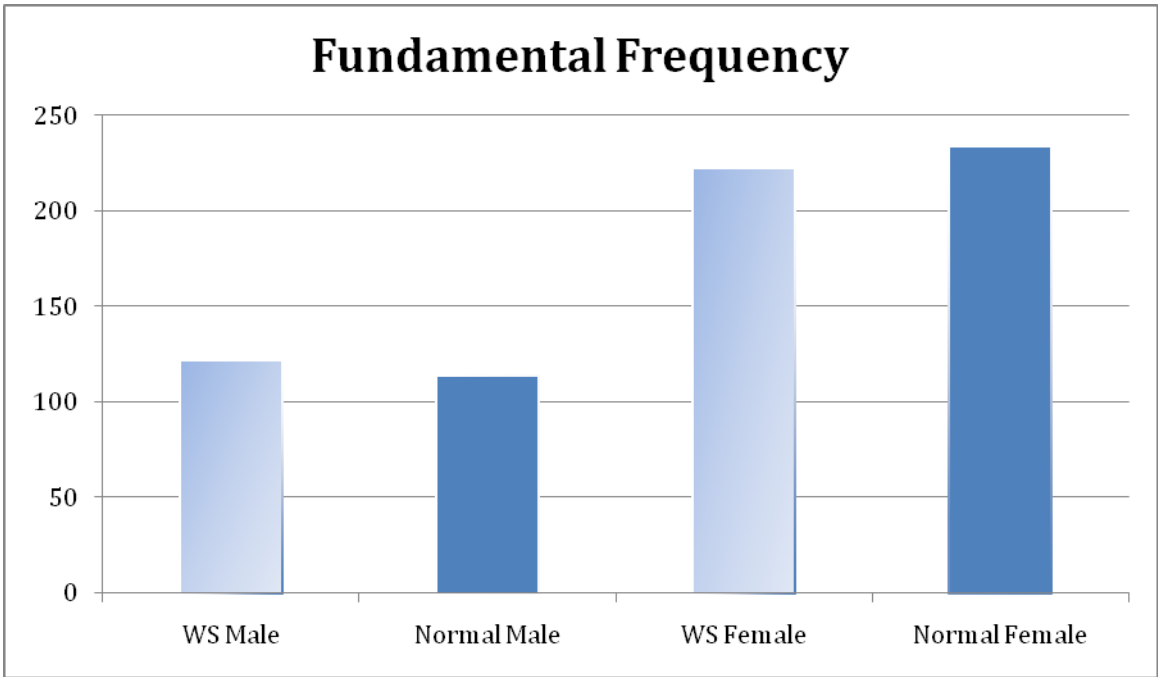


Figure 2: Mean jitter Percent (%) for all groups

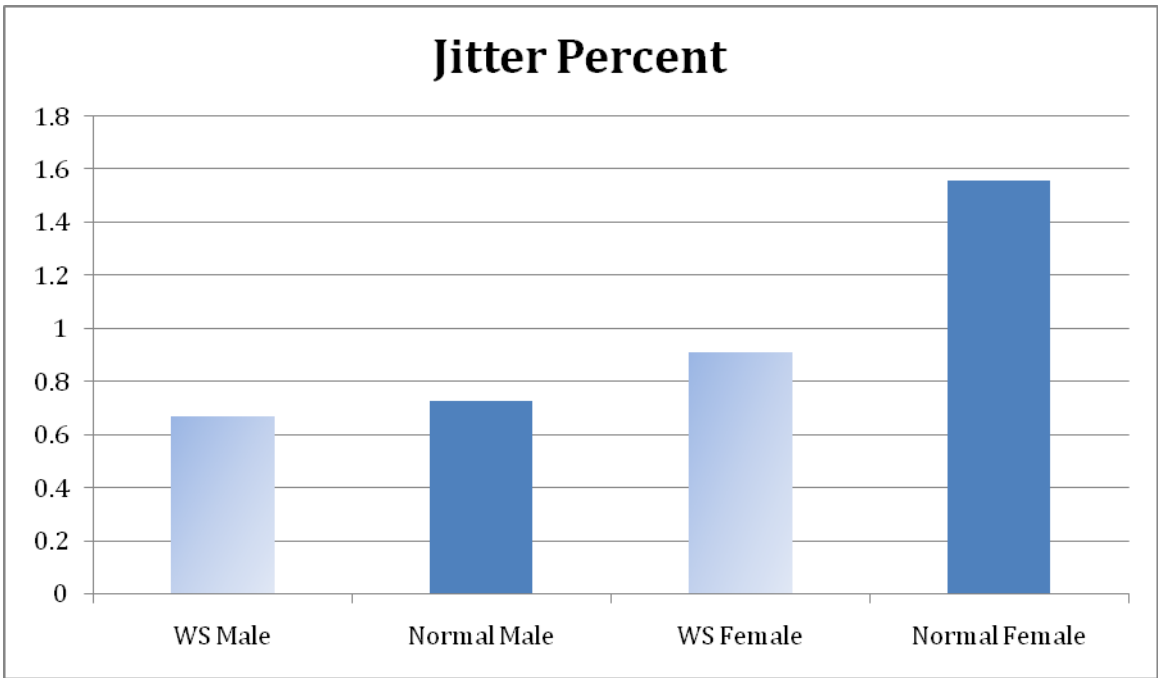


Figure 3: Mean shimmer percent for all groups

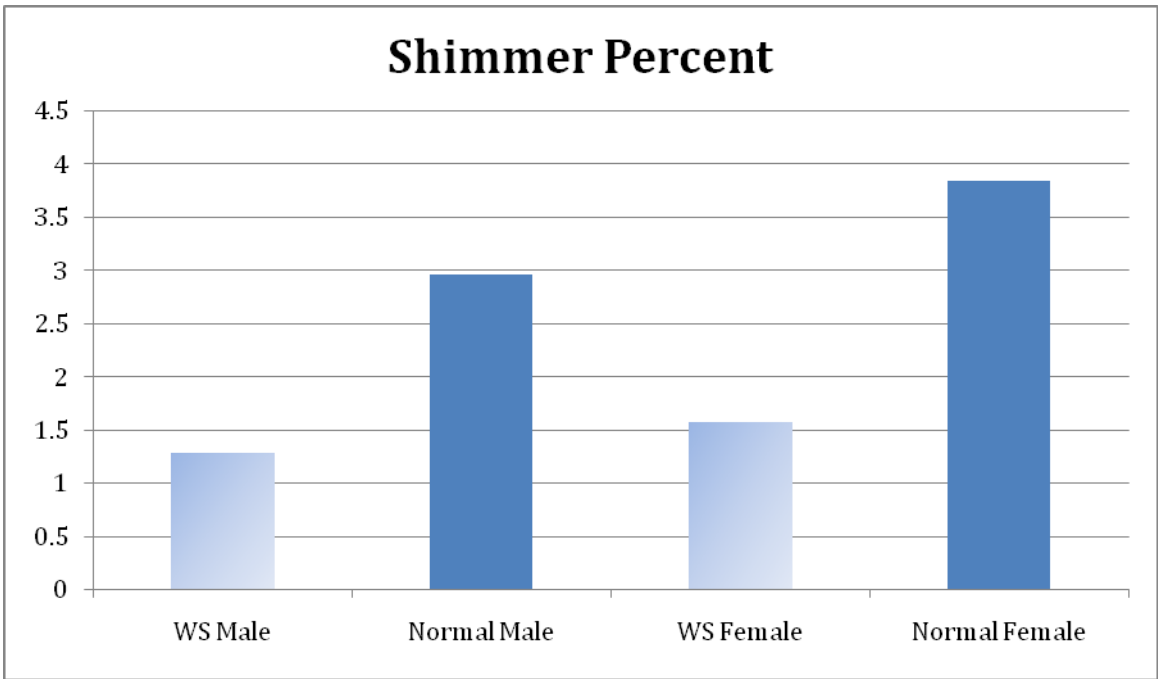
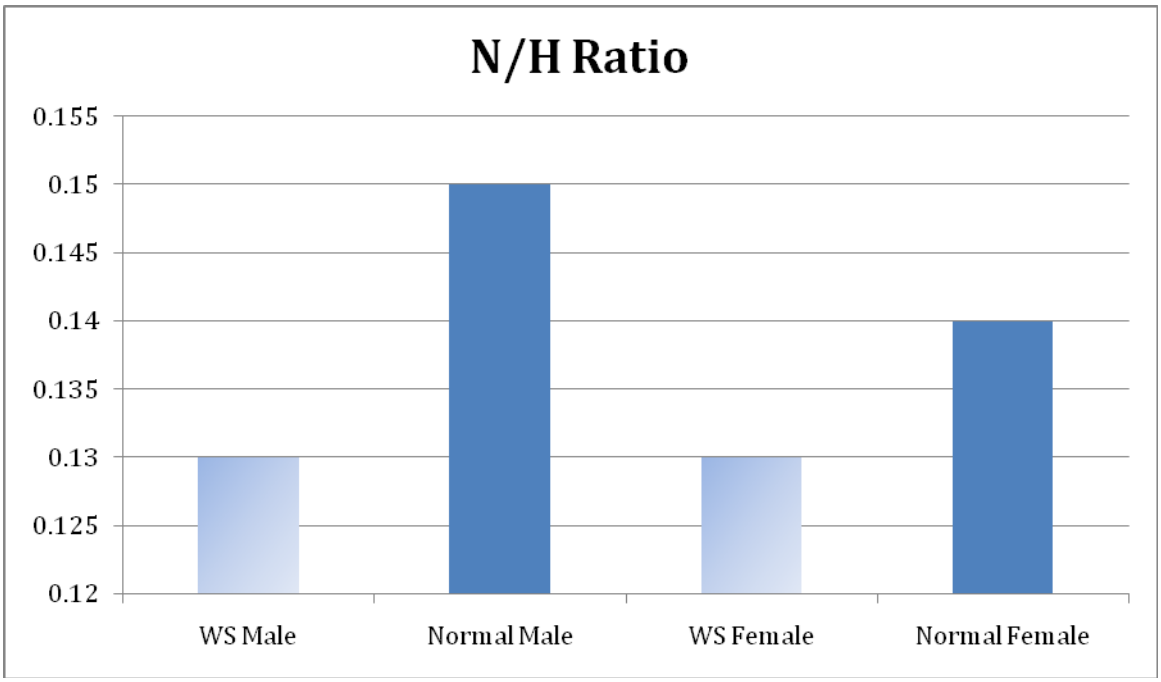


Figure 4: Mean N/H ratio for all groups



A Multivariate Analysis of Variance (MANOVA) was completed in order to determine whether each independent variable, group (WS or normal) and gender (male or female), or the interaction of these variables had an effect on the dependent variables (acoustic measurements) as a whole. The results of a MANOVA revealed significant effects for group (Pillai's Trace = .444, $F[4, 25] = 4.99$, $p = .004$) and gender (Pillai's Trace = .897, $F[4, 25] = 54.59$, $p < .000$). However, the interaction of group and gender was not statistically significant (Pillai's Trace = .167, $F[4, 25] = 1.25$, $p = .315$).

Because the MANOVA does not indicate where significance occurs within the levels of an independent variable, four separate one-way Analyses of Variance (ANOVA) were completed for each independent variable. The results of the ANOVAs for the group independent variable are listed in Table 3 and the results of the ANOVAs for the gender independent variable are listed in Table 4.

Table 3: Analyses of Variance for Group

ANOVA

		Sum of Squares	Df	Mean Square	F	Sig.
Fundamental Frequency	Between Groups	18.000	1	18.000	.005	.946
	Within Groups	117707.875	30	3923.596		
	Total	117725.875	31			
Jitter Percent	Between Groups	1.022	1	1.022	2.332	.137
	Within Groups	13.153	30	.438		
	Total	14.176	31			
Shimmer Percent	Between Groups	31.166	1	31.166	12.932	.001
	Within Groups	72.298	30	2.410		
	Total	103.463	31			
Noise/Harmonic Ratio	Between Groups	.002	1	.002	1.605	.215
	Within Groups	.029	30	.001		
	Total	.030	31			

Table 4: Analyses of Variance for Gender

ANOVA

		Sum of Squares	Df	Mean Square	F	Sig.
Fundamental Frequency	Between Groups	97240.500	1	97240.500	142.405	.000
	Within Groups	20485.375	30	682.846		
	Total	117725.875	31			
Jitter Percent	Between Groups	2.301	1	2.301	5.812	.022
	Within Groups	11.875	30	.396		
	Total	14.176	31			
Shimmer Percent	Between Groups	2.714	1	2.714	.808	.376
	Within Groups	100.749	30	3.358		
	Total	103.463	31			
Noise/Harmonic Ratio	Between Groups	.000	1	.000	.011	.916
	Within Groups	.030	30	.001		
	Total	.030	31			

These results indicate that between groups (Normal and WS) the acoustic measurement of shimmer was statistically significant ($F[1,30] = 12.665$, $p = .001$). In addition, statistically significant effects were found for F_o ($F[1, 30] = 138.026$, $p < .000$) and jitter ($F[1,30] = 6.328$, $p = .018$) between gender. There were no other comparisons that reached statistical significance.

CHAPTER V

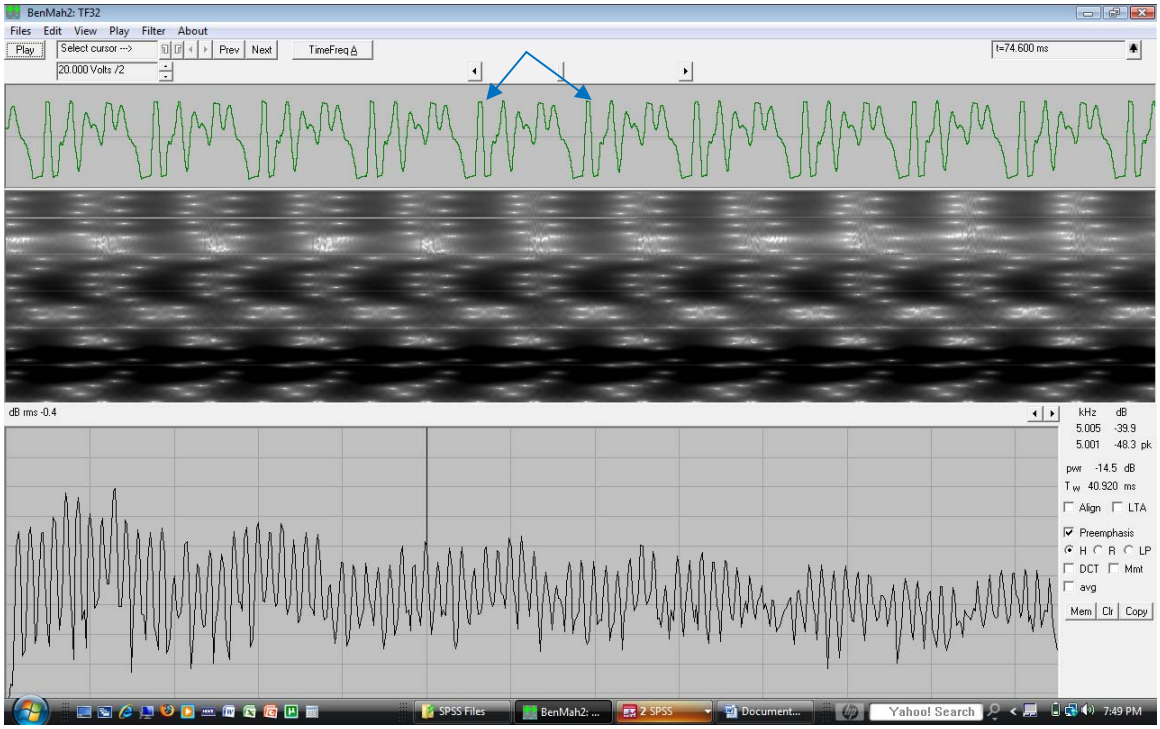
DISCUSSION

The purpose of this study was to determine if there is a difference in acoustic voice characteristics of individuals with WS compared to normal controls. The results showed that the WS and control groups were different on the measurement of shimmer, with the control group manifesting a higher percentage of shimmer than the WS group. In addition, males and females differed on the measurements of jitter and F_o. The females had a higher percentage of jitter than the males while the males had a lower F_o than the females. Both of these latter findings were expected considering the norms for acoustic measurements for males and females. All subjects were measured to have a Fo within the normal range, which is 106Hz for males and 193Hz for females (Stemple, Glaze, & Kaben, 2000). In addition, Gelfer, Andrews, & Schmidt (1991) and Orlikoff (1990) found normal females to have a higher percentage of jitter than normal males.

The finding that normal controls were measured to have a higher percentage of shimmer than the individuals with WS was not expected and prompted the researchers to look at the original files with spectral analyses. When doing this it was found that some segments within the WS files were clipped (e.g., some of the amplitude information was lost during the recording process due to the sound pressure level of the signal being too great), which created an artificial amplitude stability. This translated into lower shimmer measurements for the WS voices. Thus, the finding of lower shimmer percentages for the individuals with WS compared the normal controls is believed to be an artifact of recording rather than a

characteristic of the WS voices. An example of clipping and its effects on the amplitude of the signal are illustrated in Figure 5, below.

Figure 5: Amplitude clipping in one WS signal (notice the horizontal peaks on some of the vertical bars [indicated by blue line], indicating the loss of some amplitude information from the signal).



Unlike the study by Watts, Marler, & Urban (2007), which found individuals with SVAS to have a Fo below the normal ranges, the present study found individuals with WS to have F_o within the normal range. In addition, the study by Watts, Awan, & Marler (2008) found differences in pitch sigma and jitter between individuals with ELN mutations or deletions and normal controls, but this was not found in the present study. One explanation for possible vocal differences in WS and SVAS may be as follows: it has been found that one elastin allele is deleted in individuals diagnosed with WS and it has been suggested that the

hemizygosity of the elastin gene may account for all of the connective tissue abnormalities seen in WS (Ewart et al., 1993). In contrast, the extent of connective tissue abnormalities may not be as great in SVAS (Christiano & Uitto, 1997). This phenotypic difference could have accounted for the lack of statistical significance in jitter values between normals and WS participants in this study.

The differences in location and amount of deletion or mutation of elastin between individuals with SVAS and WS may account for the discrepancy in F_o measures between the Watts, Marler, & Urban, 2007 study and the present study. A lower F_o was found in individuals with SVAS compared to normal controls (Watts, Marler, & Urban, 2007) whereas in the present study no difference in F_o was found in individuals with WS compared to normal controls. This suggests that individuals with SVAS and individuals with WS may have different amounts of elastin in the vocal folds. This claim may be supported by Dridi et al. (1999), who looked at skin elastic fibers in WS and nonsyndromic SVAS and found a decrease in pre-elastic ad mature elastic fibers in those diagnosed with WS and a decreases in only pre-elastic fibers in individuals with nonsyndromic SVAS.

CHAPTER VI

CONCLUSION

In conclusion, this study found no differences in acoustic measures of voice quality between individuals with WS and normal controls. These findings are in disagreement with the results from previous studies that investigated individuals with ELN abnormalities. It should be noted, however, that this study is the first to compare individuals with WS alone to normal controls and even though previous studies have found differences between individuals with SVAS and normal controls (Watts, Marler, & Urban, 2007) and individuals with ELN mutations or deletions (SVAS/WS) and normal controls (Watts, Awan, & Marler, 2008) those findings may have occurred because individuals with SVAS were included in the data pool. Although, it has been found that individuals with SVAS have point mutations of specific exons (Tassabehji et al., 1997) and individuals with WS have deletion of one elastin allele (Ewart et al., 1993), thus the extent of connective tissue abnormality may not be as great in SVAS (Christiano & Uitto, 1997), the amount and organization of elastin in the vocal folds of individuals with SVAS may be an exception.

Although none of the normal controls had a history of smoking, neurological disorder, or voice disorder, the time of day of the recording, amount of water consumed as well as other variables may have affected the results. In addition, a different recording device was used to record the voices of the WS individuals than was used to record the voices of the normal controls. Further studies comparing WS to normal controls should be completed in order to clarify the relationship between the two groups. It is recommended that identical

recording equipment be used for both groups and that more detailed history information regarding vocal hygiene be obtained.

APPENDIX A

Participant Questionnaire

Name:_____ Date of Birth (MM/DD/YY): _____

Please check the box that applies to you:

Gender: ☐ MALE ☐FEMALE

Do you have a problem with your voice? ☐ YES ☐NO

Have you ever smoked cigarettes on a daily basis? ☐ YES ☐NO

Do you currently smoke cigarettes? ☐ YES ☐NO

Have you ever been diagnosed with a voice disorder? ☐ YES ☐NO

Have you ever been diagnosed with a neurological disorder? ☐ YES ☐NO

Have you ever been diagnosed with a genetic disorder? ☐ YES ☐NO

APPENDIX B

Voice Production Tasks

1. Take a good breath, and say the vowel /a/ at a comfortable pitch and loudness, a steady as you can until I say stop. (Have participant hold for approximately 5 seconds. Repeat 3 times.)
2. Read Grandfather Passage
3. Take a good breath, and starting at a comfortable pitch glide up on the vowel /i/ until you get to your highest pitch. (Repeat 3 times.)
4. Take a good breath, and starting at a comfortable pitch glide down on /i/ until you get to your lowest pitch (Repeat 3 times.)
5. Take a good breath, and sustain your highest pitch on the /i/ vowel, until I tell you to stop. (Repeat 3 times.)

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ABSTRACT

ACOUSTIC MEASURES OF PHONATORY FUNCTION IN INDIVIDUALS WITH WILLIAMS SYNDROME

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The human vocal folds are organized in layers, the epithelial layer, three layers of the lamina propria, and the vocalis muscle. Each layer of the lamina propria contains different amounts and forms of elastin, and it has been suggested that an alteration in the elasticity of the vocal folds may cause dysynchronous vibration. The elastin gene (ELN) acts as the instruction manual for the cellular production of elastic fibers throughout the body, including those within the vocal folds. It has been found that individuals with Williams Syndrome (WS) and individuals with Supravalvular Aortic Stenosis (SVAS) have irregularities in ELN. The purpose of this study was to examine the acoustic voice quality of individuals with WS compared to normal controls so that a better understanding of the phenotypic differences, with respect to vocal production, between WS and the general population can be attained.

In this study, 16 individuals with WS (8 male, 8 female) and 16 normal controls produced sustained vowels to which acoustic measures were applied. Acoustic measurements included fundamental frequency (F_o), jitter, shimmer, and noise-to-harmonic ratio. The results indicated that individuals with WS did not manifest significantly different acoustic measures of voice quality compared to normal controls. With regard to gender effects, the male participants as a whole were found to have a lower F_o than the female participants and the female participants were found to have a higher percentage of jitter than the males, irrespective of group. These results will be discussed in context with previous studies that have focused on disorders affecting ELN and the effects on voice production abilities.