Critical Review: Effectiveness of the Acoustic Analysis of Voice in the Detection of Early Bulbar Signs in Patients with Amyotrophic Lateral Sclerosis

Remika Gautam
M.Cl.Sc (SLP) Candidate
University of Western Ontario: School of Communication Sciences and Disorders

The purpose of this critical review was to evaluate the effectiveness of using instrumental analysis of voice to detect early bulbar signs in patients with amyotrophic lateral sclerosis (ALS). Included in this review are study designs such as quasi-experimental designs (case control), retrospective series, and longitudinal case studies. There is support for the use of acoustic analysis of voice as a possible clinical indicator of bulbar signs in patients with ALS. Further research is necessary to determine which acoustic measures are most sensitive in the early detection of laryngeal dysfunction.

Introduction

Amyotrophic lateral sclerosis (ALS) is a degenerative disease that can affect both upper and lower motor neurons (Duffy, 1995). Assessment and diagnosis of ALS are crucial in maintaining quality of life. This is especially true for patients with bulbar involvement who experience a more rapid progression of the disease (Duffy, 1995). Perceptual measures have traditionally been used to evaluate changes in voice quality which indicate bulbar involvement. However, with ongoing advances in the acoustic analysis of voice, it is possible that more sensitive and reliable quantitative measures will enhance the early detection of laryngeal dysfunction. Such measures could indicate early bulbar signs well before those signs manifest themselves perceptually.
Hence, early detection through the acoustic analysis of voice could have implications for patient treatment including the possibility of augmentative and alternative communication devices.

Objectives

The primary objectives of this critical review were to determine if (1) the literature contains evidence for the effectiveness of the acoustic analysis of voice for early detection of laryngeal abnormality in patients with ALS and (2) if sensitivity of acoustic parameters for such early detection can be established.

Methods

Search Strategy
Computerized databases including SCOPUS, PubMed, ProQuest Education and CINAHL were used along with the keywords ((ALS)) AND ((speech)) or ((ALS)) AND ((voice)) OR ((bulbar)). The search was limited to articles from 1990 to 2003.

Selection Criteria
For this critical review, studies that were included primarily contained instrumental analysis of voice. All patients diagnosed with ALS either demonstrated symptoms of bulbar involvement or no symptoms. Studies that contained perceptual and pulmonary measures in addition to acoustic measures were also selected. No other limits were set in terms of demographic information of the patients or acoustic measures.

Data Collection
Search results from the literature, in accordance with the selection criteria, yielded the following studies: (5) quasi-experimental - case control studies, (3) longitudinal case studies and (1) retrospective series.

Results

Quantifying Tremor in ALS

Aronson, Ramig, Winholtz, and Silber conducted a study where they quantified the frequency of perceived tremor[1] by the use of a fast Fourier transformation in 8 patients (4 men and 4 women) with ALS. A control group age and sex matched was also included. The authors hypothesized that determining the frequency band of tremor might explain the physiology of the dysfunction causing it. Results indicated much more prominent modulations in patients with ALS as compared to the control group and spanned the entire analysis range from 0 to 25 Hz. Their research indicated that intermittent firing of motor units within the laryngeal musculature produces a perceived tremor (Aronson, 1992).

The methodology of this paper contains relative strengths such as detailed case history on each patient including onset of general symptoms and onset of speech symptoms. Other strengths include analysis of

both amplitude and frequency measures. Seventy-five percent of the data were also reanalyzed to ensure reliability using the Pearson product-moment correlation coefficients for repeated measures (Aronson, 1992).

Along with its strengths, however, this paper is a quasi-experimental study and contains a moderate level of evidence. The sample size was also very small and the possible effects of gender were not discussed. In addition, the authors do not make a distinction between tremor and flutter and use these terms interchangeably. This study was included because it discusses flutter and addresses the question of laryngeal dysfunction however; its importance is mitigated because it does not directly address the analysis of specific acoustic parameters of phonation.

[1] The distinction between tremor and flutter are as follows: tremor has frequencies between 2-10Hz while flutter is a higher frequency tremor – between 10 and 20 Hz. (Budder, 2003). However, since the authors of this study have used these terms interchangeably, for the purposes of this review, this term will be referred as 'tremor' throughout.

Acoustic Measures in Women

Strand, Buder, Yorkston, and Ramig (1994) acoustically analyzed the voices of four women with ALS ranging from 41 to 70 years old. One age matched control subject was also included. Using CSpeech (version 4.0) acoustic analysis software, they looked at fundamental frequency, pitch and intensity contours, and acoustic measures such shimmer, jitter and signal to noise ratio during sustained phonation and phrase production (Strand, 1994). Results of their study showed that all four patients varied greatly in their fundamental frequencies for sustained phonation and were 2 standard deviations (SD) from the normal distribution for their age range. They also showed a reduction in fundamental frequency variation for stressed words in a phrase production – "Say top again." (Strand, 1994).

Acoustic measures demonstrated that all four patients exhibited greater shimmer and jitter values than that of their one control subject in sustained phonation and for the word 'top' in the carrier phrase "Say top again" (Strand, 1994). In three 500ms samples of sustained phonation, one subject had jitter values that were >2SD above the mean percent jitter for the control subject (0.42%) while all four patients with ALS had shimmer values that were ≥2SD above the control mean percent (2.6%). For signal-to-noise ratio values, two patients were >3 SD below the control mean (21.30dB). In a 200 ms sample of phonation for the word 'top' in the carrier phrase "say top again", three out of the four patients demonstrated both jitter and shimmer values either within range or lower as compared to the control subject's mean while one patient exhibited higher values for both measures. Signal-to-noise ratios were much lower compared to the mean of the control subject (27.60) for all patients (Strand, 1994).

Methodological strengths that were demonstrated in this study included using both sustained phonation as well as connected speech to determine any similarities or differences between the two samples. The authors also accounted for each patient's history, onset of the disease, onset of bulbar symptoms, and conducted motor speech exams to determine tongue strength and movement. Intelligibility, vital capacity, velopharyngeal port function, and voice quality was also taken into account which aided in interpreting results. The authors also ensured each sample was taken at different intervals to reduce amounts of error.

Although this study demonstrated some relative strengths, there were elements which would suggest that one should be cautious with regard to their conclusions. Only one control subject was used for this study which the authors claim yielded similar results to control group data of another study. A more effective method would have been to use a control group matched for gender and age. Another inconsistency noted was the lack of statistical testing in this study. Without a control group or applicable normative values tests of statistical significance were not possible. The sample size used in this study is very low. Each patient demonstrated very different speech profiles hence the acoustic data that was obtained may be a reflection of those individual differences. In addition, two out of the four patients demonstrated audible tremor which could have introduce artifacts in most of the acoustic measures. All of these factors suggest the use of caution with regard to the interpretation of this study's results.

Robert, Pouget, Giovanni, Azulay and Triglia also studied acoustic and aerodynamic measures in patients with ALS. They incorporated a control group gender and age matched, and 63 patients with ALS; 40 with at least one symptom of bulbar involvement and 23 with no bulbar involvement. They focused on women in order to enhance sensitivity in comparing both the control and experimental groups (Robert,

1999). Results indicated that five of the eight measures analyzed (jitter, coefficient of variation for frequency, shimmer, number of harmonics and maximum phonatory frequency range) were abnormal in both groups with bulbar and no bulbar involvement. When the group with bulbar involvement was compared to the control group, increases in jitter, coefficient of variation for frequency (CVF), and shimmer, were found. A decrease in the number of harmonics and maximum phonatory frequency range were found ($p<0.001$). The group without bulbar involvement indicated similar results but demonstrated an increase in CVF. When both groups were compared with each other, an increase was found in jitter, CVF, and shimmer ($p<0.001$). In predicting bulbar involvement, they found that 73% of patients in the bulbar group were identified, but only 52% were identified in the non-bulbar group.

This study demonstrates strengths such as a larger sample size, control for gender effects, and the inclusion of patients without bulbar symptoms. However, as in the other studies, this is a case-control study therefore the evidence is considered moderate. Other weaknesses include patient inclusion: for patients to be considered asymptomatic only two speech–language pathologists were used and no tests of intelligibility were done. Despite some weaknesses, this study demonstrated relative strengths in both its design and sample size selection.

Kent et.al conducted a study with 10 women with ALS and 15 female controls. In addition to studying acoustic measures (phonatory function and formant analysis), they studied intelligibility and pulmonary measures. Results for the phonatory acoustic measures, which included fundamental frequency, jitter, shimmer and signal-to-noise ratio, indicated that 5 out of 10 patients were 2 standard deviations above the control means for jitter. In addition, 6 out of 10 patients were 2 standard deviations above the control mean for shimmer. Signal to noise ratio values were found to be typically lower than that of the control group ($p=0.05$). There was no significant difference found for fundamental frequency because the values were distributed either too high or too low compared to the values of the control group.

This study demonstrated several strengths. The authors studied and compared intelligibility data obtained to the acoustic data which allowed them to assess whether any acoustic abnormalities could be detected even when intelligibility was not affected. Having done voice analysis on a group of men with ALS, they were able to compare and contrast between this study and the previous one to determine any differences of gender in this disease. They also reported all intelligibility scores, phonetic contrasts and graphs of all formant analyses. Along with these strengths are some critical weaknesses such as the statistical analysis of the phonation measurements. The statistical (t-test) results were not clearly reported. This study was a quasi-experimental case control design and therefore provides only moderate evidence.

Acoustic Measures in Men and Women

Silbergleit, Johnson and Jacobson, conducted an acoustic study in which they included 20 patients with ALS who were judged to have perceptually normal vocal quality, (5 female and 15 male, mean ages 63.2 and 57.2) and 26 control subjects (13 male and female, mean ages 56.1 and 56.5). Of the 4 acoustic parameters measured (jitter, shimmer, signal-to-noise ratio and maximum phonation frequency range) results showed a significant group difference in jitter values ($p = 0.005$) and in maximum phonation frequency range (MPFR) ($p = 0.0025$). Smoking was also taken into consideration as three women and six men in the ALS group smoked and two men and two women in the control group smoked. For MPFR, smoking was a significant main effect for the group ($p=0.041$) and was treated separately from non-smokers in the group. Shimmer values varied across trials when compared to the control group but demonstrated no overall group differences ($p=0.113$). Signal-to-noise ratios also did not demonstrate any group differences ($p=0.703$).
Some methodological strengths in this study include incorporating a larger sample size, having both men and women in the study, and an age matched control group. The statistical analyses (ANOVA and t-tests) used in this study accounted for many factors that could have influenced results such as individual differences, gender differences and smoking influence. They also collected data on not only a comfortable pitch with the sound /a/ but incorporated glides to the highest and lowest pitch. Although this study demonstrated many positive aspects, it is a quasi-experimental case-control study; therefore it contains a moderate level of evidence.

In three longitudinal case studies by Watts et. al. (2001), Kent et. al. (1991), and Ramig et. al. (1990), acoustic measures studied in three patients (2 women, 1 man) over time indicated variability and was deemed to be an unreliable measure as the disease progressed in all three studies. Despite these results, when values of initial trials in each study were compared to normative data collected by Kent,

Vorperian, Kent and Duffy (2003), all three studies demonstrate abnormalities in jitter, shimmer, and signal-to-noise ratio values. Although changes over time may not have yielded consistent results for these acoustic measures, they did demonstrate abnormal phonatory acoustic measures that were present early in the patients' disease progression.

However, these are longitudinal case studies and they represent a lower level of evidence. In the study by Watts et. Al. (2001), the authors do not represent their data with appropriate statistical testing. In addition two of the three subjects across all three studies had bulbar symptoms at the beginning of the studies hence abnormal phonatory acoustics might be expected. Therefore, the results of all three studies should be treated conservatively.

A Protocol for Acoustic Analysis of Voice

In a retrospective series by Kent, Vorperian, Kent and Duffy (2003), they recommended procedures and standards for acoustic analysis of voice and they also presented preliminary data that was collected from a new assessment tool – the Multi-Dimensional Voice Program (MDVP) (Kent, 2003). Normative data from this tool was gathered from six large samples of adult males and females. Pediatric values were obtained from a sample size of 100 children. The authors reviewed the results of several phonatory acoustic studies of ALS that were reported between 1974 and 1999. Their review of this phonatory acoustic literature raised concerns about the sensitivity and reliability of these measures in the detection of laryngeal abnormality in ALS. In general, they highlighted the need for large sample sizes, adequate controls for variables that affect the voice and careful consideration of the effects of inter-trial variability.

This retrospective study demonstrates considerable strength. The paper is divided into two parts. The first part discusses the assessment tool itself (MDVP) and gives a protocol for using this type of tool to analyze phonation measures in a reliable way. The second part discusses research done using acoustic measures for different types of dysarthria in different neurological diseases and trauma. This was important to highlight because acoustic analysis has the potential to be applied to dysarthria found in all different types of neurological disease. Although this study is a retrospective series which contains a lower level of evidence, it can certainly be referred to as a potential guideline for using such instruments in the analysis of voice.

Discussion

Some caution should be given to the evidence found in these studies as sample sizes were generally small and specific factors, such as gender, were not always accounted for. In addition, the possible effects of tremor in patients with ALS could potentially confound the results. Only one study, Ramig's (1990) longitudinal study, out of the seven made provisions to ensure that tremor would not influence results by removing the linear trend from their analysis of shimmer. These corrections should be made to ensure that acoustic measures are not influenced by the presences of tremor in patients with ALS.

Some trends emerged from the four quasi-experimental studies. They demonstrated abnormalities with regard to three acoustic parameters: jitter, shimmer, and signal-to-noise ratio. The three longitudinal studies showed some variance among which acoustic parameters demonstrated abnormality. These results should be taken conservatively as the level of evidence is quite low. Although in this review the 7 studies found acoustic parameters of phonation abnormal in patients with ALS, there was not a clear consensus with regard to which parameters were consistently abnormal. It is recommended that future studies involving the acoustic analysis of voice in patients with ALS consider including the following: patients with no bulbar signs and early diagnosis of ALS, male patients with ALS as there were many studies done on female patients only, using a larger sample size, the use of standard assessment protocols such as those mentioned in the retrospective study by Kent (2003), and an analysis of one or two specific acoustic parameters to verify reliability using detailed statistical analysis.

Conclusion

The overall conclusion of this review is that acoustic parameters of phonation may be used as possible clinical indicators of early laryngeal dysfunction in patients with ALS but further testing and analysis must be done in order to determine the reliability and sensitivity of these parameters. As well there is a need for larger sample sizes in order to verify consistency of sensitivity and reliability within groups. Early detection of speech deterioration may provide better predictions about future communication needs and allow patients and their families to make appropriate plans and decisions regarding the use of augmentative and alternative communication devices.

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