Respiratory Strength Impacts Speech Pause Patterns in Individuals with Amyotrophic Lateral Sclerosis

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Abstract

Amyotrophic lateral sclerosis (ALS) is a rapid neurodegenerative disease impacting both the central and peripheral nervous systems leading to muscle paralysis of the limbs, axial and bulbar bodily regions (Yunusova, Graham, Shellikeri, & Phuong, 2016). The later leads to functional impairments in speech and the ability to communicate effectively which patients rate as the worst symptom of disease progression (Hecht et al., 2002). Given that the speech subsystem includes the lungs, respiratory dysfunction, known to be prevalent in ALS, further exacerbates speech impairments. Given these findings, emerging evidence suggests that speech pause patterns represents a sensitive marker of bulbar disease progression in ALS.

We aimed to:

1) Delineate speaking rate and pause profiles during connected speech in individuals with ALS.
2) Determine if ALS speaking rate and speech pause patterns differ to established speaking norms.
3) Assess potential relationships between respiratory function (FVC, MIPs, MEPs) and speech pause patterns in individuals with ALS.

Our hypotheses were two-fold:

1) Due to slowness and reduced range of motion caused by underlying weakness and spasticity, individuals with ALS would exhibit decreased speaking rate with increased pause time, duration, and frequency during speech compared to established norms.

2) With respiratory decline, ALS patients will compensate to maintain breath support during connected speech by implementing pauses more frequently and for longer duration.

55 participants with definite diagnoses of ALS read a standardized reading passage, the Bamboo Passage. Recorded were then analyzed with MatLab software to identify speech-pause characteristics (speaking rate, average pause duration, mean pause time, and number of
pauses). Pulmonary function testing included forced vital capacity (FVC), and maximum inspiratory and expiratory pressures (MIP/MEP). The ALS Functional Rating Scale-Revised (ALSFRS-R) was administered to index global disease progression. Spearman’s correlation analyses and descriptive statistics were performed with the data.

Results for aim 1 confirmed our hypothesis and indicated that speaking rate was reduced in ALS patients compared to established norms (143 v. 176 WPM, mean difference = 33). Further, pause frequency and durations were higher in our ALS cohort compared to established normative data (total pause duration: 8.77 vs 5.20 seconds, mean pause duration 0.67 vs 0.62 seconds, total number of pauses 12.77 vs 8.44). Negative correlations were noted between MIP and speaking pause number ($r = -0.27$, $p<.05$), between MEP and mean pause duration ($r = -0.32$, $p<.05$), and between MEP and total pause duration ($r^2 = -0.27$, $p<.05$).

Overall, speech pause patterns in individuals with ALS were longer and more frequent than that of healthy established norms (Yunusova et al., 2016). We believe this is due to the need for individuals with ALS to compensate for their weakening respiratory and bulbar systems. As their inability to both fill their lungs with air with every inspiration and clear their lungs of carbon dioxide with every expiration decreases, they are forced to talk with more laborious and deliberate breath—slowing them down as they need to pause frequently to inspire to power their phonation.
Introduction

Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis (ALS) is a rapidly progressing neurodegenerative disease that attacks entire physiological systems and, ultimately, the entire body (Ingre, Roos, Piehl, Kamel, & Fang, 2015). It is rare—with an incidence of 1/100,000 persons reported annually in the US (Zarei et al., 2015). The average age of onset ranges from 50-60 years, and men are 20% more likely than females to acquire this disease (Zarei et al., 2015). Once diagnosed, life expectancy ranges from 2 years to 5 years, depending on onset severity (Ingre et al., 2015). There are two categories of onsets, each categorized by the musculature and subsystems that they initially impact. Spinal onset is the most common type (~70% of individuals) and adversely affects motor control of the limbs. The remaining 30% of individuals will present with a bulbar onset which is characterized by degeneration of upper and lower motor neurons in the head and neck region, causing problems with speech articulators, swallowing musculature, and respiratory function (Tomik & Guiloff, 2010).

Although only a smaller subset of patients initially present with bulbar symptoms, it is estimated that 85% of ALS patients will experience bulbar dysfunction throughout disease progression (Chen & Garrett 2005). Bulbar dysfunction is a concerning facet of disease progression in individuals with ALS as swallowing impairment can lead to malnutrition, rapid weight loss, and aspiration (Desport, Preux, Truong et al., 1999) while speech difficulties can lead to impaired ability to communicate, isolation from community, and reduced overall quality of life (Plowman et al., 2017). Given the negative impact of bulbar dysfunction in ALS, a need to identify clinical tools that can
effectively monitor disease progression in the bulbar region (Plowman et al., 2017). Research related to these efforts have historically focused on characterizing and observing swallowing deficits caused by bulbar deterioration in ALS (Green et al., 2013). Emerging evidence within the speech system, however, suggests that sensitive clinical biomarkers of speech progression are still needed for these patients to help improve communication outcomes in ALS (Yunusova et al., 2016).

**Speech Impairment in ALS**

Normal speech production is the result of multiple muscles and systems working together. Speech musculature includes the tongue, hard palate, soft palate, jaws, lips, and lungs. Systems involved in the production of speech include the phonatory, resonatory, articulatory, and respiratory systems. Lungs recruit air during inspiration and as the air is forced back up during exhalation, it passes through the vocal folds thus creating movement of the folds. Oral articulators such as the tongue, hard palate, and lips work to form different phonemes from the air as it leaves the mouth. The respiratory aspect of speech is voluntary, as breathing occurs without explicit direction, but we control the abduction and adduction of our vocal folds and articulation of our oral and lingual muscles (Seikel et al., 2016). Taken together, speech is a crucial part of communication that is an integral part of our everyday lives.

In individuals with ALS, the ability to communicate effectively becomes increasingly difficult as the disease progresses. Speech symptoms can exhibit anywhere from 2 years prior to medical diagnosis to 5 years post-diagnosis, depending on the onset-type (Tomik & Guiloff, 2010). Due to deficits in the strength of the oral musculature, speech in individuals with bulbar-onset ALS is often slurred, slow, and
may be unintelligible. As ALS progresses, individuals experience slower speech movements and frequent and prolonged pauses to regain enough breath to sustain connected speech. In extreme cases phonation may not even be possible. Speech in ALS is typically characterized as being dysarthric—that is laborious articulation, slowed rate, and increased hypernasal sound throughout (Tomik & Guiloff, 2010). A review paper by Tomik and colleagues detailed the four primary types of dysarthria that exist in ALS, all with their respective characteristics and markers (Tomki & Guiloff, 2010). Speakers who exhibit flaccid dysarthria have speech characterized by a weak control of articulators, dysphonia, and weak voices. Spastic dysarthria leads to speech that is slurred, slow, and similar weak tongue movement. Mixed flaccid-spastic dysarthria is characterized by speech that combines the clinical signs of both spastic and flaccid, with differing levels of combinations of symptoms included in speech. Lastly, ataxic dysarthria exhibits as poor voice volume control as a result of increased difficulty when it comes to breathing to power speech.

**Respiratory Dysfunction in ALS**

Respiration is the driving force behind speech, as lungs need adequate air to provide ample support for speech. Phonation occurs when air is expelled from the lungs, vibrating the vocal folds, which creates sounds that can be articulated to match the speaker’s intent for communicating (Seikel et al., 2016). The degeneration of neurons that control lung functioning gradually affect the ability of affected persons to generate the breath support necessary for speech. In the body’s natural attempt to preserve systems that sustain life (breathing), other functions (e.g. phonation) are lost first so that the body can focus on living (Seikel et. al., 2016). In such a decompensated
state, speech is merely an accessory and the effects of degeneration can be heard before breathing problems become noticeable. Since speech is so dependent upon respiratory functioning it is our belief that understanding the contribution of the respiratory subsystem to speech production is imperative to track communication decline in ALS.

**Speech Pausing as a Potential Clinical Biomarker:**

Currently, assessments attempting to track communication decline in ALS focus on salient aspects of speech such as volume, quality, intelligibility. While those are aspects affected, the accuracy of such assessment varies (Allison et al., 2017). An individual may notice a perceptual quality change far before a doctor who has never assessed them before does. Furthermore, perceptual characteristics are not able to be objectively measured like other facets of functioning such as respiration. Due to vast variability, characteristics like volume of speech cannot be standardized and used to indicate appropriate speech-system functioning (Rong et al., 2016). Testing quantitative measurements of respiration and lung capacity and comparing to norms required to properly breathe and phonate is far more feasible and accurate (Rong et al., 2016). Research has shown measures of speech subsystems, such as respiration, to be more sensitive to changes in physiologic functioning as a result of disease progression (Green et al., 2013). Specifically, emerging evidence suggests that examining speech pausing in individuals with ALS may be an effective clinical biomarker that provides a more in-depth communication evaluation. Since speech relies upon coordination of structures within the bulbar musculature in conjunction with adequate respiratory control, its characteristics are directly impacted by the decreased functioning of the
respiratory and speech muscles. Pause in connected speech is a crucial underlying factor of effective communication. In normal speech, both the organization and location of pauses impact the message and meaning of what is being communicated. However, in speech affected by ALS, pausing occurs far more frequently and for longer durations, as the individual is required to work harder to breathe and build up adequate respiration for phonation. Due to this, pausing in speech can reveal how well the respiratory system is working in an individual, as it is a speech characteristic reliant on respiration and no other confounding speech subsystem.

**Purpose of the Present Study:**

Speech is an essential foundation to communication, an important component to engage and participate in meaningful life experiences and quality of life (Allison et al., 2017) with the inability to communicate rated as the worst symptom of the disease by ALS patients (Hecht et al., 2002). There are multiple alternative and augmentative methods of communication available to supplement or replace speech as this function diminishes throughout ALS disease progression. However, the practice parameters guiding when to implement use of these devices have not been well established likely due to the lack of clinical tools that can accurately track communication and speech decline, especially in the context of other physiologic speech subsystems. Determining speech pausing in ALS and correlating these characteristics with respiratory functioning may provide a robust metric to track speech progression in ALS and ultimately improve the management of this aspect of the disease.

Therefore, the purposes of this study were to:
1) Delineate speaking rate and speech pausing characteristics in individuals with amyotrophic lateral sclerosis compared to established norms.

   Due to progressive weakening of lower motor neurons and increased spasticity of upper motor neurons, we hypothesized that individuals with ALS would demonstrate reduced speaking rate and increased pause time, duration, and frequency of pauses as compared to established norms.

2) Determine relationships between speech pause patterns in individuals with ALS with: pulmonary function (FVC, MIPs, MEPs)

   Due to respiratory decline, we hypothesized that speech pause patterns would increase in frequency, and duration with worsening / declining respiratory function due to the need to compensate for breath support during speech.

**Methods**

**Participants**

This study included data from 55 individuals with ALS who were enrolled in larger clinical trials ongoing in our laboratory. Table 1 provides a demographic overview for participants. 32 individuals were male, 23 were female and the mean age for this cohort was 62.13 (SD: 10.97). Participants attended a single testing session and were assessed across the physiological domains of respiratory and bulbar function. All participants signed an informed consent upon enrollment.
Table 1. Demographics Overview for the Study Participants.

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Mean (SD)</th>
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<tbody>
<tr>
<td>Gender (M:F)</td>
<td>32 Male (58%) / 23 Female (42%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62.13 years (10.97)</td>
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<tr>
<td>ALSFRS-R</td>
<td>36.76 (6.55)</td>
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</table>

Speech Pause Identification

Speech pause characteristics for each participant were assessed utilizing the standardized Bamboo reading passage. The Bamboo Passage includes 96 words of connected speech written at an elementary reading level. The passage was specifically designed to identify pause in speech by utilizing stop consonants which clearly identify boundaries at which subjects stopped to take a breath. Subjects were fitted with a microphone (TASCAM DR-40X, Teac American Inc., Montebello, CA) on a headset that allowed for placement of the microphone approximately 10cm away from their mouth. Each subject was then instructed to read the passage at their normal speaking rate and volume and a high-quality audio recording was generated for subsequent analysis.

The recordings of the reading of the standardized passage were analyzed in Audacity, according to the methods previously outlined by Green, to ensure audio quality (Green, 2004). The recordings initially underwent a data quality check in which any background noise was identified and removed or muted. Any silence at the beginning or end of the recording was clipped, so as not to be misidentified as pauses. Noise removal was applied if the clip needed enhanced audio quality due to background noise or static within the recording. Any vocal pauses, laughs, coughs, and audible inspirations or expiredins were muted and treated as pauses for analyzing. Partial,
whole-word, or phrase repetitions and/or insertions were deleted from the recording. Mispronounced words were left in the recording, but any pause proceeding the mispronunciation was deleted to accurately portray how an individual would correctly read the passage at their own pace.

The finalized recordings were then saved as a Waveform Audio File (.wav) and imported into Matrix Laboratory (MATLAB; Natick, MA). The files were processed through a custom designed Speech Pause Analysis software program in MATLAB that allowed for the identification of pauses within each subject’s recording. The speech threshold was set at 25 milliseconds (msec) and the pause threshold was set to 300 msec. Any decrease or increase to those numbers to correctly identify pauses was recorded. An excel sheet including data for percent pause, percent speech, mean pause duration, mean speech duration, total duration, pause events, speech events, total pauses, and total speech events were derived from the software for each subject’s recording. Total number of pauses, total pause time, and mean pause duration were recorded and used in subsequent data analysis.

**Words Per Minute**

Utilizing the speech statistics the Matlab derived from the recordings, we calculated the average words per minute (WPM) of an individual during the reading of the Bamboo Passage by multiplying 60 (# of seconds in a minute) by 97 (# of words in the passage) and then dividing the sum by the total time the individual spent reading the passage, which varied by subject.

**Respiratory Function**
Forced Vital Capacity

Forced vital capacity for each participant was measured using a Micro I handheld spirometer (Vyaire Medical, Mettawa, IL) in accordance with the American Thoracic Society (ATS) guidelines. The device was specifically calibrated to every subject’s age, gender, weight, race, and height to calculate percent predicted. A cardboard mouthpiece was inserted into the spirometer. Subjects were instructed to sit upright in a chair, feet flat on the floor and a nose clip was secured on the patient. Each subject was instructed to take in a deep breath and then blow as hard, fast, and long as they could into the device. Two trials were repeated for each participant with the highest value in liters (L) and the associated percent predicted based on established age, height, gender, and race normative values recorded (Hankinson et al, 1999).

Maximum Expiratory Pressure/Maximal Inspiratory Pressure

The participants’ maximum expiratory pressure (MEP) and maximum inspiratory pressure (MIP) were assessed using a handheld manometer in accordance with ATS guidelines. Two pressure valves—inspiratory and expiratory—were fitted on the manometer (Micro RPM Pressure Meter, MDSpiro/Micro Direct, Lewiston, ME) accordingly. The valve of the manometer was fitted with a bacterial filter attached to a rubber flanged mouthpiece (MTH, MDSpiro/Micro Direct, Lewiston, ME) to create an adequate seal and ensure minimal air leakage during the measurement. Each participant was seated and fitted with nose clips during the completion of the three trials.

Global Disease Progression

Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised
The Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) is a global index of disease progression for individuals with ALS (Cedarbaum et al., 1999). The ALSFRS-R assesses function across the domains of speech, swallowing, motor control, and respiration. Questions involve self-reporting of their perceived ability to write, dress, feed, eat, walk, and breathe independently. There are 12 questions with 5 possible ratings per question, ranging from 0 (total loss of function) to 5 (normal functioning). Upon completion of the survey, the sum of all the ratings is taken and total scores range from 0 (complete loss of function) to 48 (normal functioning).

**Statistical Analysis**

Each subject’s data was aggregated into a single Excel file. Analysis of the data was completed using the SPSS statistical package version 25.0 (Armonk, New York). Descriptive statistics were performed to determine the profiles of speech pausing characteristics in the ALS patients. Spearman’s rho correlation analyses were utilized to examine if there were any relationships between the speech pausing characteristics and respiratory function and/or global disease progression.

**Results**

**Overall Pausing Profiles in ALS**

In this cohort of ALS patients, average pause time was 8.77 seconds (SD 4.71) and the mean pause duration was 0.64 seconds (SD: 0.13). Further, ALS patients demonstrated an average of 13.77 pauses (SD: 7.12) during connected speech. Table 2 provides a comparison of these ALS speech pause profiles with established normative data (Yunusova et al., 2016). Compared to normative data, individuals with ALS in this cohort
demonstrated increased pause time (8.77 vs 5.20 sec), mean pause duration (0.64 vs 0.62 sec), and number of pauses (13.77 vs 8.44). When the data was further stratified into spinal versus bulbar groups, it was observed that bulbar onset patients demonstrated increased pausing and duration of pausing as compared to spinal onset patients.

Table 2. Average Speech Pausing Values for ALS Patients Versus Established Normative Data.

<table>
<thead>
<tr>
<th></th>
<th>ALS-Total Mean (SD)</th>
<th>ALS-Bulbar Mean (SD)</th>
<th>ALS-Spinal Mean (SD)</th>
<th>Control Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pause time (seconds)</td>
<td>8.77 (4.71)</td>
<td>0.75 (0.48)</td>
<td>0.63 (0.12)</td>
<td>5.19 (1.50)</td>
</tr>
<tr>
<td>Mean pause duration (seconds)</td>
<td>0.64 (0.13)</td>
<td>10.52 (4.84)</td>
<td>7.94 (4.59)</td>
<td>0.62 (0.12)</td>
</tr>
<tr>
<td>Number of pauses</td>
<td>13.77 (7.12)</td>
<td>16.9 (8.23)</td>
<td>12.06 (6.09)</td>
<td>8.44 (1.98)</td>
</tr>
</tbody>
</table>

Spinal = spinal onset, bulbar = bulbar onset, total = combination of all ALS patients.

Relationships between Respiratory Function and Speech Pausing

Forced Vital Capacity

No significant relationships were noted between FVC percent predicted and total pause time (r=-0.24, p<0.05), mean pause duration (r=-0.10, p<0.05), or number of pauses (r=-0.26, p<0.05) measured in these individuals with ALS.

Maximal Expiratory Pressure

A significant, negative correlation was noted between maximal expiratory pressure and total pause time (Figure 2A) (r = -.27, p<.05). That is, lower MEP was
associated with increased pausing during connected speech. MEP was not significantly correlated with average pause duration or the number of pauses observed.

**Maximum Inspiratory Pressure**

Maximum inspiratory pressure (MIP) was noted to be negatively correlated with total pause time ($r^2 = -.31$, $p<.05$) and number of pauses ($r = -.27$, $p<.05$). No association between MIP and mean pause duration was observed.

**Global Disease Progression**

**Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R)**

Significant, negative correlations were observed between ALSFRS-R total scores and pause time ($r = -.276$, $p<.05$). Thus, individuals with advanced disease progression had to inspire for longer during speech. Similarly, a negative correlation was noted between total ALSFRS-R scores and number of pauses ($r = -.301$, $p<.05$). This relationship suggests that the worse the disease, the slower the rate of speech due to frequent pausing to inspire.
Figure 1. Relationships between forced vital capacity (percent predicted) and pause time (A), mean pause duration (B) and number of pauses (C).
Figure 2. Relationships between maximal expiratory pressure (MEP) and pause time (A), number of pauses (B), and mean pause duration (C).
Figure 3. Relationships between maximal inspiratory pressure (MIP) and pause time (A), number of pauses (B), and mean pause duration (C).
Conclusions

ALS is a fatal and rapidly progressive disease that causes bulbar and respiratory impairment in affected individuals. The combined deficits in respiratory and bulbar function might lead to longer and more frequent pauses during connected speech. The purpose of this study was to characterize speech pausing in ALS and examine relationships between speech pause characteristics and respiration and global disease progression.

In this cohort of patients, overall speaking rate was reduced, on average by XX WPM. ALS patients inserted, an average, 5 additional pauses during connected speech and pause duration was increased by 3.6 seconds as compared to established norms. Normal speech is characterized by pausing to ascribe meaning or emphasis, however, the uncharacteristically frequent and long pausing within speech recordings in this study highlight a specific aberration in ALS speech and suggests that decreased bulbar function requires increased effort to speak, as lungs and expiratory/inspiratory muscles are disadvantaged due to ongoing motor neuron damage.

Negative associations were noted between both respiratory pressure metrics (MEP and MIP) whereby the lower (weaker) the MEP and/or MIP, the longer the pause duration and more frequent the number of pauses during the reading passage. It is likely that expiratory muscle weakness impacts an individuals’ ability to continuously generate subglottic pressure produce connected speech while inspiratory weakness leaves individuals with ALS with the need to take a breath more frequency and with more effort to compensate for inadequate ability to fill lungs to full capacity for air during
speech. Additionally, reduced inspiratory strength leads to connected speech characterized by multiple stops for inspiration in individuals with ALS.

Unlike respiratory pressure derived metrics, we did not observe relationships between speech pause patterns with FVC. It may be that the respiratory subsystem of speech is more dependent on pressure generating components (i.e. MEP or MIP) rather than volume based components (i.e. FVC) during connected speech. Further work will elucidate this observation.

Limitations

While the findings are significant, it is important to include the various limitations this study exhibits. Our study included a small number of participants, thus, this data should be interpreted with caution.

This data also only refers to one time point, and we are unsure how this data would track longitudinally. Further research could gain more insight on the data should it track it over time instead of one specific instance.

Future Directions

In conclusion, studying speech pausing in ALS is an accurate tool for objectively assessing overall communication function in these patients. The strong relationships demonstrated between respiration, disease progression, and pause characteristics provide a template for future research utilizing this specific way of speech analysis in ALS. Since few studies have examined these in-depth characteristics of speech in individuals with ALS, these findings provide support for
further probing in this area. Future studies involving a larger subject sample is warranted to validate these findings.
References


