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The Impact of Lingual Resistance Training in Two Individuals with

Amyotrophic Lateral Sclerosis: A Case Series

by

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A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science
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Dedication

This manuscript and the work that I have done over the past six years in my journey towards becoming a Speech-Language Pathologist is dedicated to two special women in my life. First, this publication is dedicated to my grandmother, the late Mariah Hicks. I will never forget you or those words I spoke to you back in August of 2009. Thank you for teaching me the most important lesson I will ever learn which is always remember to live, to learn, and to remember that you are absolutely beautiful and to forget about the rest. Keep the vanilla ice cream cold until we meet again.

I would also like to dedicate this work and the research that I will continue to do on this topic to my Floridian grandmother, the late Ruth Johnson Davis Morris. You were my fearless, independent and beautiful grandmother with whom I shared some of the most cherished moments of my life. Although we spent much time apart, the past few years were wonderful and shall not soon be forgotten. Keep Miss Mariah company because I still have many goals left to accomplish and will need both of you guiding me. I will continue to strive for five in all that I do because of who you were to this world.

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First and foremost, I would like to thank my parents who have been so instrumental in helping me to achieve all of the goals I have established for myself. I would not have made it to this point in my career without all of the love and support that you both have given me since that first day you dropped me off at Kindergarten.

Secondly, to the members of my thesis committee, thank you all for the countless hours you spent providing feedback and guidance throughout this process. Especially, thank you to committee member Dr. Catriona Steele and her Swallowing Rehabilitation Research Laboratory for designing the computer program that was an integral part of this study. My gratitude is also extended to Dr. Michael Barker who helped me with data extraction and interpretation. Thank you for always lending your office whiteboard to analyzing data from this study and devoting so much of your time to helping me better understand research concepts.

Finally, I would like to recognize my laboratory mentor, Dr. Emily Plowman, for inducting me into her Neuromotor Speech and Swallowing Restoration Laboratory. You are the reason I ended up at the University of South Florida and I am excited to continue learning from you in the next phase of my educational career. Thank you for the support and mentoring, as I could not have asked for a better person to guide me throughout the past two years. This is just the beginning and we have many more studies to conceptualize, data to analyze and publications to present. Looking forward to all that lies ahead

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Abstract

Introduction: Amyotrophic Lateral Sclerosis (ALS) is a fatal and progressive disease characterized by the deterioration of motor neurons within the body. This degeneration leads to bulbar dysfunction in the form of an impaired ability to communicate and swallow. Currently, bulbar dysfunction is treated via compensatory methods aimed at maximizing comfort and safety that include environmental adaptations, augmentative and assistive communication and gastrostomy tube placement to replace speech and oral feeding. The role of active intervention is controversial in this patient population and no investigations have examined the potential role lingual exercise might play in ALS bulbar management. The purpose of this study was to explore the impact of an eight week lingual resistance training program on lingual strength and lingual endurance, speech, swallowing, global disease progression and patient-reported outcomes in two individuals with ALS.

Methods: Two individuals with ALS (El Escorial criteria) were enrolled across three different time points, each separated by eight weeks (Baseline 1, Baseline 2, Post-Treatment) with a delayed intervention design utilized to benchmark bulbar disease progression. At each evaluation, tongue strength, endurance, swallowing, speech and patient-reported outcomes were collected. Following Baseline 2, participants completed lingual resistance training five days a week for eight weeks (40 sessions). Outcome measures included maximum anterior isometric

tongue pressure (MIP), maximum endurance hold time MHT), speech intelligibility, airway safety and patient-reported outcomes.

Results: On average, MIPs decreased by 2% during the lead in period and increased by 13% across both participants. On average, MHT declined by 25% between baseline 1 and 2 and increased by 144% following lingual resistance training. No improvements were noted for speech intelligibility or airway safety during swallowing. Patient-perceptions of communicative effectiveness, swallowing impairment and quality of life remained relatively stable over the four-month period.

Conclusion: Although no improvements were noted in lingual strength, improvements in lingual endurance hold times were noted in both participants. Further investigation is warranted to validate these preliminary findings in two cases of ALS.

Chapter One

Introduction

Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disease characterized by the rapid and progressive degeneration of motor neurons in the central and peripheral nervous system. ALS is considered a terminal disease with no current cure and represents the most common motor neuron disease. A recent Center for Disease Control registry reported a prevalence of 12,000 in the United States and an incidence of 1.6 per 100,000 individuals (Mehta et al., 2014). More men develop ALS than women (M:F ratio, 1:5:1) and average disease onset is 65 (Mehta et al., 2014). Life expectancy ranges from 2 to 5 years ("About ALS," 2015) and is largely dependent upon disease onset type. Approximately 70% of ALS individuals present with a 'spinal' onset, while 30% a bulbar onset (Kuhnlein et al., 2008). Bulbar-onset ALS is primarily characterized by the development of speech and swallowing deficits, whereas persons with spinal onset will experience initial symptoms in their limb musculature. Nevertheless, regardless of onset type, it is thought that all persons living with ALS will develop problems related to speech, swallowing, respiration, and muscle weakness at some point during the course of the disease (Johnson & Jacobson, 2011).

Given the inevitable fatal outcome of ALS, determining appropriate types of therapeutic interventions can be especially difficult for professionals responsible for their medical care. Further, taking into account the rate at which and the extent that neurons degenerate in persons with ALS, fatigue is a major consideration that must be at the forefront when deciding courses of

possible treatment for these patients (McElhiney, Rabkin, Gordon, Goetz, & Mitsumoto, 2009; Ramirez, Piemonte, Callegaro, & Da Silva, 2008). Given the role that fatigue plays in the development of ALS, recent research indicates that mild to moderate exercise, utilized early during the disease progression may preserve motor neurons and motor function in both animal models of ALS (Deforges et al., 2009; Gerber, Sabourin, Hugnot, & Perrin, 2012; Kaspar, Frost, Christian, Umapathi, & Gage, 2005; Kirkinezos, Hernandez, Bradley, & Moraes, 2003; Veldink et al., 2003)and human clinical trials (Bohannon, 1983; Cheah et al., 2009; Dalbello-Haas, Florence, & Krivickas, 2008; Drory, Goltsman, Reznik, Mosek, & Korczyn, 2001; A. C. Pinto et al., 1999; S. Pinto, Swash, & de Carvalho, 2012; Sanjak, Bravver, Bockenek, Norton, & Brooks, 2010). Although research examining the impact of exercise intervention on bulbar dysfunction in ALS is almost non-existent, a recent pilot study determined that a five-week regime of Expiratory Muscle Strength training (EMST) was feasible, safe and lead to significant gains in subglottic air pressure generating abilities, cough function and airway protection in individuals with ALS (Plowman et al., 2015). The present study was a preliminary effort used to expand this paradigm and examine the potential role of lingual strength and endurance training on lingual strength, lingual endurance, airway safety, communication, and self-reported quality of life outcomes in two individuals with ALS.

This current introductory chapter comprises three substantive parts. First, background information regarding the ALS disease will be described. Second, the role of exercise in the management and treatment of this patient population will be discussed with a particular discussion regarding the potential role of exercise on bulbar dysfunction in ALS. Finally, the methodology of lingual strengthening is introduced as a potential technique in the management of bulbar dysfunction in individuals with ALS.

1.1 Amyotrophic Lateral Sclerosis: The Disease and Its Progression

ALS is classified into a group of diseases known as neurodegenerative disorders, which also include disorders such as Parkinson's disease and Huntingdon's Disease. The term "neurodegenerative" is a combination of "neuro" referring to the nerve cells or neurons and "degenerative" signifying the loss of function of a bodily structure (Przedborski, Vila, & Jackson-Lewis, 2003). In regards to ALS, the matter of neurons is crucial in the understanding of this disease, because one of its hallmark characteristics is that it includes the involvement of both upper motor neurons (UMN) and lower motor neurons (LMN). The human body contains trillions of neurons with the brain alone containing over 100 billion of these nerve cells (Harmon, 2015). There are both sensory and motor neurons within the body; however, regardless of type; these cells are primarily comprised of a cell body and two extending branches known as the axon and the dendrite ("The Life and Death of a Neuron," 2014). Axons are responsible for transmitting messages from a neuron while dendrites receive messages transmitted by other cells ("Neurons and Their Jobs," 2008). In the human body, motor neurons innervate muscle fibers of the body. A single motor neuron can innervate many muscle fibers and the combination of a single neuron with the muscle fibers it innervates is referred to as a motor unit (Knierim, 1997). In the case of ALS, the motor neurons begin to deteriorate impairing their ability to send impulses to the muscle fibers. Thus, without these messages being transmitted, the neuron is no longer able to control its motor unit resulting in denervation (Mitsumoto, 2009). Lacking sufficient impulses from the motor neurons, the brain is unable to initiate and control voluntary muscle movement.
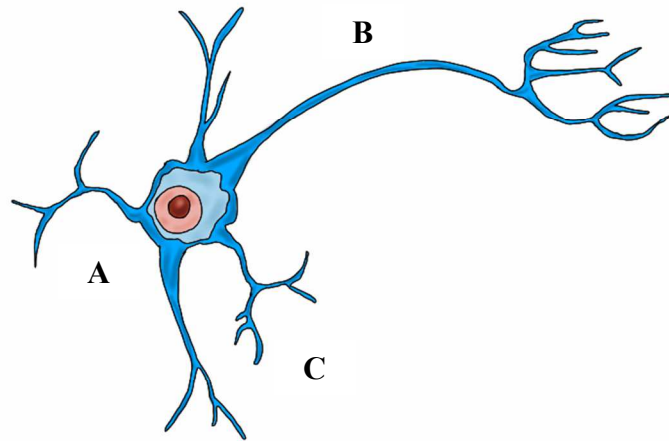
Figure 1. A schematic representation of a typical neuron. Includes (A) cell body, (B) axon, and (C) the dendrite branch. Image courtesy of Kat Stahl, 2015.

This process is adequately captured in the name of the disease as "a" means without, "myo" is the equivalent to muscle and "trophic" translates into nourishment ("What is ALS ", 2010). Indeed, as motor neurons degenerate and communication between the brain and the muscle fibers breaks down, the corresponding muscles will be left without adequate nourishment. Further, "lateral" is used in the name of the disease to capture the location in the spinal cord where the motor nerve tract responsible for control is found whereas "sclerosis" refers to the hardening that occurs as a result of the degeneration to the area ("What is ALS ", 2010). Thus, the name of the disease purports exactly what is happening within the body of people suffering from this disorder.

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Due to the denervation of muscle fibers, weakness is one of the predominant features in the development of ALS. In the initial stages of the disease, this weakness is likely to be restricted to a focal area of the body such as the head, neck, or limb regions. Further, depending on where symptoms first begin to appear, individuals with ALS can be stratified into two different onset types based on the area(s) affected. These divisions are commonly regarded as either a spinal or bulbar-onset ALS and these classifications help discern the pathway of disease progression in a given ALS patient. For persons who do develop ALS, manifestations of the disease are more likely to begin in the limb musculature as 75-80% of these cases can be classified as spinal-onset (C. Armon, 2014b). The remaining individuals will initially experience difficulties involving speech and swallowing and be regarded as bulbar-onset patients. Notwithstanding onset type, the extensive degeneration of upper and lower motor neurons in persons with ALS results in impairments of speech, swallowing, movement, and respiration to develop in these persons. This paper and study are mainly concerned with furthering an understanding of how UMN and LMN damage uniquely affects the function of speech and swallowing throughout disease progression and explore the potential role of lingual strengthening in this unique patient population.

1.2 Bulbar Pathophysiology in ALS

The involvement of both upper and lower motor neurons is central to the diagnosis and development of ALS. This combined UMN and LMN damage is particularly useful for understanding why certain impairments develop in patients with ALS. Inside the human body, there is a network known as the pyramidal motor system that is responsible for voluntary muscle movements. Embedded within the pyramidal system are bundles of nerve fibers referred to as the corticospinal and corticobulbar tracts, which are involved in fine motor control of the muscle

groups in regions such as the head, neck and face by allowing either unilateral and bilateral movements depending on the tract being utilized ("Motor Systems," 2002). The actions of the corticobulbar tract are most relevant for understanding how bulbar dysfunction develops in ALS. Within the corticobulbar tract, upper motor neurons interact with lower motor neurons that oversee the function of various cranial nerves (CN) (Johnson & Jacobson, 2006). The cranial nerves that control facial movements (CN V, the jaw; CN VII, the lip and the face; and CN XII, the tongue) as well as the muscles of swallowing and speech (CN IX and CN X) receive input from the axons of these neurons coursing along the corticobulbar tract (Mitsumoto, 2009). Therefore, as the disease begins or continues its progression in those affected, denervation of upper and lower motor neurons embedded within this tract produces a pathology. UMN and LMN involvement can be manifested anywhere throughout the body; however, when degeneration is leads to impairment of the muscle fibers responsible for controlling swallowing and speech, the person is regarded as having bulbar dysfunction. Consequently, there are certain symptoms that occur as a result of dysfunction to the bulbar region in these persons. UMN degeneration is likely to lead to muscle spasticity as well as overly-sensitive reflexes or, hyperreflexia; while, conversely, LMN damage manifests as muscle weakness, muscle wasting or atrophy, and fasciculations (Howard & Orrell, 2002). Individuals classified as bulbar-onset ALS will initially present with these symptoms immediately in their head and neck regions in the form of a dysarthria and/or dysphagia. However, although this course of ALS progression is not as common as it's spinal counterpart, it is understood that as the disease progresses and upper and lower motor neurons continue to degenerate; atrophy and weakness will spread to other regions (Kinsley & Siddique, 1993). This spread means that all persons diagnosed with ALS will experience bulbar dysfunction either at onset or as the disease continues to progress. Indeed a

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reported 93% of ALS patients will develop dysarthria and 85% dysphagia in their disease course (Carpenter, McDonald, & Howard Jr, 1977; Chen & Garrett, 2005). Given the high prevalence of speech and swallowing dysfunction in ALS and their sequelae on health and pulmonary status, nutrition, and quality of life; proactive education and close monitoring of these symptoms is of paramount importance to the healthcare professional.

1.2.1 Communication Impairments in ALS

The symptoms that result from dysfunction in the bulbar musculature of affected individuals include dysarthria (impairment in speech) and dysphagia (swallowing impairment). With regard to communication disturbances, it is estimated that some 80-95% of persons with ALS will lose their ability to generate functional, natural speech during the progression of the disorder (Beukelman, Fager, & Nordness, 2011). Clinically, symptoms of this communication loss are illustrated by a vocal quality that includes atypical perceptual features described as a mixed spastic-flaccid dysarthria. The "spasticity" is the result of UMN damage and is perceived as a harsh and strained voice quality that is often lower in pitch; by contrast, flaccidity is a result of LMN involvement and is characterized by distortions of speech sounds as well as weakness that manifests itself as slurred speech (Brownlee & Palovcak, 2007). Persons with bulbar-onset ALS display these qualities earlier and, further, they run the risk of completely losing speech (anarthria) very rapidly during the disease course (Leigh et al., 2003). However, even before the progression to anarthria, a person experiencing bulbar dysfunction can be almost unintelligible to those around him or her due to the impaired vocal quality present in these individuals. This notion correlates well with previous research showing that communication effectiveness is reduced across some contexts for persons with ALS resulting in the need to make adaptations to the communication environment (Robison et al., 2014). Accordingly, as bulbar dysfunction leads

to the loss of the ability to communicate functionally and effectively, there is a severe reduction in the quality of life in these persons (Mitsumoto & Del Bene, 2000) thus illustrating the negative impact bulbar involvement has in the progression of this disease.

1.2.2 Dysphagia and ALS

Beyond the changes to speech that occur as a result of bulbar pathology throughout the course of ALS, the development of deficits impacting the capacity of the person to efficiently swallow is even more concerning. Many of the muscles of the face, jaw, mouth, palate, pharynx and larynx that are activated to communicate or, muscles that are activated in order to communicate, are also involved in deglutition. Consequently, regarding bulbar dysfunction in ALS, not only will the perceptual qualities of speech be affected, but also the ability of a person to swallow safely and effectively will be impaired. Typically, in order for a swallow to occur, there are three commonly recognized stages that must be initiated and completed. These stages are regarded as the: a) oral; b) pharyngeal and; c) esophageal stages (Goyal & Mashimo, 2006). It is important to note that the initial stage of swallowing can be further subdivided into the oral preparatory and oral propulsive stages (Matsuo & Palmer, 2008). When one or more of these stages is affected, the individual will experience difficulty completing swallowing tasks, otherwise known as dysphagia. As ALS progresses and further bulbar muscle weakness occurs, the ability of the person to effectively chew, transport food within the oral cavity, maintain appropriate lip closure, and protect the airway will be significantly reduced (Palovcak, Mancinelli, Elman, & McCluskey, 2007).

Figure 2. An illustrative representation of the three stages of swallowing. The swallow
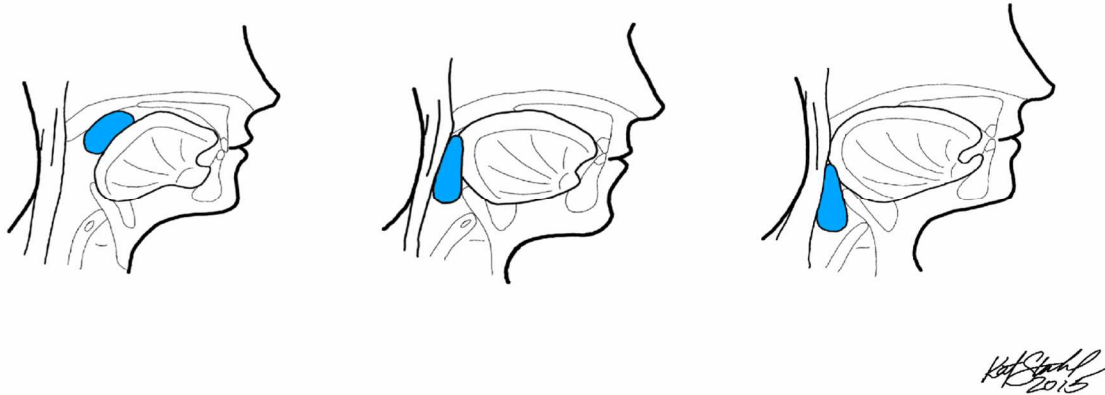
progresses from A) the oral stage to the B) pharyngeal stage before terminating in the C) esophageal stage. During the oral stage, food is prepared within the oral cavity and is then propelled posteriorly back towards the pharynx. Next, food enters the pharynx and as the epiglottis inverts to protect the airway, the bolus is directed through the upper esophageal sphincter (UES). At this time the true and false vocal folds close to achieve laryngeal vestibule closure for airway protection. Lastly, the esophageal stage takes place ensuring that the bolus is sent in a peristaltic wave from the UES to the lower esophageal sphincter (LES) before being emptied into the stomach. Definition adapted from (Matsuo & Palmer, 2008). Image courtesy of Kat Stahl, 2015.

These deficits indicate that patients with ALS primarily experience difficulties related to the oral stage of swallowing. Indeed, research related to ALS and dysphagia has found that the earliest and most common type of dysphagia found in this cohort can be classified as an oral phase dysphagia (Murono et al., 2015; Palovcak et al., 2007; Ruoppolo et al., 2013). Deficits pertaining to this stage can mainly be characterized by the failure to effectively control and transport food and liquid within the mouth. Additionally, oral dysphagia results in difficulty creating the pressure generation necessary to move these boluses into the pharyngeal area. Correspondingly, this lack of control over food and liquid boluses increases the risk for residue to remain in the pockets near the base of the tongue and in the throat, areas known as the valleculae and pyriform sinuses, respectively (Kuhnlein et al., 2008). The remnants of food or

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liquid remaining in these pockets may, in turn, increase the likelihood that these particles will be aspirated, or inhaled into the airway/lungs, during or after subsequent swallows.

Published data show that the presence of aspiration is of utmost importance and relevance in the clinical setting (Daniels, 2006). Within the ALS population, aspiration events are particularly detrimental for a variety of reasons. The cough reflex in this cohort is greatly reduced or absent (Gaziano, Tabor, & Plowman, 2015), indicating that these individuals will have difficulty executing a cough that is effective in clearing the airway. Further, a relationship has been established in other neurologic populations, between difficulty swallowing, aspiration, and the ensuing development of aspiration pneumonia (Pikus et al., 2003) which has been demonstrated to be well correlated with mortality within the ALS population (Corcia et al., 2008).

1.3 Additional Effects of Bulbar Dysfunction in ALS Patients

Another important inter-related factor is nutritional intake in people with ALS (PALS). Indeed, it is known that PALS with dysphagia have a higher likelihood of becoming malnourished and malnutrition and aspiration pneumonia increase the risk of death in this patient population by 7.7 times (Chiò et al., 2009) Particularly, dysphagia in ALS can make it challenging for persons to maintain proper daily nutrition. Muscle wasting is already a concern in these individuals and this factor combined with reduced calorie intake as a result of loss of appetite or swallowing ability can further compromise the nutritional status of these patients (Robert G. Miller, Gelinas, & O'Connor, 2005). In addition to these factors, hyper metabolism exists among persons with ALS and this factor contributes to the decrease of body fat within these patients (Kasarskis & Berryman, 1996). The combination of an inadequate calorie intake

and an over reactive metabolic state translates into the "perfect storm" to induce malnutrition in this population (Plowman, 2014). Malnutrition is alarming in this disease cohort as its presence at the time of diagnosis is correlated with shorter survival time (Limousin et al., 2010). Given that there is neither a cure for this illness nor an effective way to significantly prolong life in this population, examining how the devastating short and long term effects of bulbar dysfunction on the quality of life should be a primary concern of professionals involved in management of this disease. Along with the concurrent limb weakness that develops in these individuals, it is understandable that their quality of life is severely affected in these persons as they become progressively unable to speak, swallow, and ambulate (Leigh & Ray-Chaudhuri, 1994).

1.4 Interventions Intended for the Management of Bulbar Dysfunction

Due to the prognostic trajectory of ALS and the expected outcomes associated with this disorder, many of the interventions utilized by professionals focus on symptom management (C. Armon, 2007; C. Armon, 2014a; R. G. Miller et al., 2009). In regards to managing the bulbar features of this disorder, there are several therapeutic interventions aimed at treating speech and swallowing impairments. Pertaining to improving communication, it has been demonstrated that receiving therapy intervention services from a Speech-Language Pathologist (SLP) can be beneficial at the onset of problems; however, long-term goals should be directed towards finding a suitable assistive communication device for the patient (Körner et al., 2013).

Assistive communication devices, also referred to as augmentative and alternative communication (AAC) devices, are low-to-high technology systems designed to supplement or replace speech (Hess & Plowman, 2014). When changes first begin to affect the perceptual qualities of the voice, lower technology and supplemental options such as handwriting or

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gestures can be used. However, as the disease spreads and the limbs used for writing and gestures are progressively weakened and paralyzed (Birbaumer et al., 1999), the need for higher-level technological devices with eye-tracking software become necessary (Caligari, Godi, Guglielmetti, Franchignoni, & Nardone, 2013). It is recommended that an evaluation for AAC device implementation take place when speaking rate is reduced to 125 words per minute (Mitsumoto, 2009).While AAC devices can help improve quality of life by reducing dependence on others for functional communication, use of these technologies are hampered by the challenges of funding, providing adequate device education, and gaining acceptance of the device by the individual (Ray, 2015). Therefore, the question is whether more can be done to prolong natural speech within this cohort and, additionally, to investigate if behavioral strategies can be employed to target speech deficits in this population (K. Hanson, M. Yorkston, & Britton, 2011).

Expanding treatment options is also an area of interest when it comes to managing the symptoms of dysphagia in an ALS patient. When swallowing difficulties first appear, evidence-based practice suggests that emphasis be placed on postural adjustments, swallow strategies, and texture modifications that can be introduced in order to help improve airway safety and swallowing efficiency during mealtimes (Heffernan et al., 2004). These compensations also help to facilitate the diet consisting of mechanical soft foods and thickened liquids that becomes necessary in this population due to difficulties associated with swallowing both liquids and solids (Walling, 1999). Yet, as the disease progresses and the risk of malnutrition and aspiration rises, alternative means of hydration and nutrition are usually warranted (Golaszewski, 2007) . The preferred method to combat these associated symptoms of dysphagia in the ALS patient is placement of a percutaneous endoscopic gastrostomy (PEG) tube (Bradley et al., 2001). A PEG

tube is inserted directly into the stomach thereby ensuring adequate nutritional needs are met in individuals who have difficulty swallowing or taking food orally ("Percutaneous Endoscopic Gastrostomy (PEG)," 2015). Recent research has indicated that PEG tube placement can prolong survival in spinal-onset patients, but may reduce survival in some cases with bulbar-onset persons (Sterling, Plowman, Dion, Simpson, & Appel, 2015). Still, PEG tube placement is thought to be effective in prolonging survival and improving quality of life in both young and elderly ALS patients with demonstrated bulbar involvement (Mazzini et al., 1995). Effectiveness of PEG tube placement then is perhaps a combination of factors related to recognizing symptoms of dysphagia (dehydration, coughing, and choking), ensuring early/timely placement of the tube, and taking into account additional facets such as body mass index and respiratory status into consideration. (Leigh & Ray-Chaudhuri, 1994; Mazzini et al., 1995; Procaccini & Nemergut, 2008).

Although PEG placement has been demonstrated to be safe in this patient population (Benatar, 2006; Salami, Schiesser, Ditah, Newman, & Alaradi), our study team was concerned with investigating whether an alternative behavioral method of management could be useful in targeting bulbar involvement in ALS. While postural adjustments, texture modifications, and eventual PEG tube placements are demonstrated effective tools in the management of the disease, these techniques, along with the AAC devices used to combat speech deficits, do not directly target the insufficiencies of the bulbar musculature. Indeed, both AAC devices and PEG tubes are bulbar management strategies that altogether bypass the bulbar structures involved in ALS and utilize other regions of the body to compensate for the weaknesses of the bulbar area. Thus, we have undertaken a series of pilot investigations that study the potential application of

treatment modalities aimed at targeting respiratory and bulbar structures that are integral in swallowing and airway protection in these individuals.

1.5 Lingual Intervention: An Alternative Method of Bulbar Management in ALS?

Given the finding that the oral phase impairments were the predominant source of dysphagia in ALS patients (Palovcak et al., 2007), a management protocol involving tongue strengthening and endurance exercises was developed for examination in this population. Lingual strengthening is an intervention method that incorporates the principles of isometric exercise which is, "exercise performed by the exertion of effort against a resistance that strengthens and tones the muscle without changing the length of the muscle fibers" ("Isometric Exercise ", 1995). Regarding lingual strengthening, the "stable resistance" is often accomplished by having the person perform repetitive exercise movements by pressing against a tongue depressor (C. Lazarus et al., 2014; C. Lazarus, Logemann, Huang, & Rademaker, 2003) or squeezing an air-filled pneumatic bulb device known as the *Iowa Oral Performance Instrument (IOPI)* (Malandraki et al., 2012; Robbins et al., 2005; Robbins et al., 2007; Steele et al., 2013; Yeates, Molfenter, & Steele, 2008). Performing lingual movements against the stable resistance provided by these strengthening systems allows individuals to exercise both the anterior and posterior regions of the tongue. Preserving or increasing tongue strength is an important foundation of lingual resistance exercise that relates back to a concept referred to as the functional reserve. The premise of tongue pressure *functional reserve* describes "*the difference in pressures generated in maximum isometric tasks compared to swallowing tasks*" (Steele, 2013). A diminished functional reserve then represents a combination of reduced anterior isometric tongue pressure while the pressure necessary to generate a swallow remains constant, thus, resulting in a disruption to the swallowing process or dysphagia (Robbins, Levine, Wood,

Roecker, & Luschei, 1995). The occurrence of reduced functional reserve implies that strengthening the tongue, then, through isometric exercise can help to normalize maximum tongue pressures and, thereby, eliminate the presence of dysphagia in an individual. It should be noted, however, that the functional reserve has not been extensively investigated; therefore, the implications of a reduced functional reserve are not fully understood. Still, given the degenerative nature of ALS, bulbar dysfunction might signal a reduced functional reserve indicating lingual strengthening is possibly a method of remedying this decreased swallowing capacity.

Potentially improving the strength of the tongue in persons with ALS would likely lead to improved control of food and liquid boluses during deglutition and greater pressurized propulsion of these boluses into the esophagus. Increased performance of the tongue during the initial swallowing stage may help to facilitate less residue in the valleculae and pyriform sinuses. Without these food and liquid remnants remaining in the pockets of the throat, the risk of aspiration would also be decreased. Further, while a relatively small amount of strength is required of the tongue during speech production (Clark, 2003), static exercise of the tongue might assist dysarthric speakers to enunciate more clearly (Tomik & Guiloff, 2010); however, this proposition is controversial (Clark, 2003; Mitsumoto, 2009). Nevertheless, as outlined above, there are currently no behavioral strategies targeting speech and swallowing directly in the ALS population. Thus, further investigations into alternate methods of bulbar management are warranted. Lingual resistance training is a safe rehabilitative strategy that has been utilized in both in animal models as well as in human populations with varying degrees of effectiveness. The following sections summarize findings related to studies involving lingual exercise across these various cohorts.

1.6 Animal Models and Lingual Exercise

Animal models are useful in research related to this disease since the etiology of this disorder is unknown. However, a familial version of this illness is thought to occur due to increased toxicity stemming from a mutant gene product of superoxide dismutase 1 (SOD1) (Boillee, Vande Velde, & Cleveland, 2006). By observing overly expressed mutations of genes such as SOD1 in animal models, researchers are then able to examine this disease *in vitro* at the cellular and molecular level (Tapia, 2014). Table 1 summarizes findings related to lingual resistance training conducted on rats. Common themes observed among the aims of these studies include targeting maximum tongue force generation as well as examining the impact lingual exercise has on finite components of the tongue such as excitatory serotonergic (5HT) input (Behan et al., 2012) and genioglossus cross sectional area (Connor et al., 2009). These highlighted studies demonstrate that generally, training regimes conducted in these rodents for 8-9 weeks resulted in increases in the generated maximum tongue forces generated by the rats (Behan et al., 2012; Ciucci, Schaser, & Russell, 2013; Connor et al., 2009; Schaser, Stang, Connor, & Behan, 2012) with only one of these studies finding age differences in regards to tongue force gains acquired as a result of training (Schaser et al., 2012). Although none of these studies were SOD1 or ALS-specific, the findings of these research efforts indicate that lingual intervention is an effective exercise strategy to induce changes in lingual force with accompanying changes in peripheral mouse fiber composition and central nervous function. The next section details lingual resistance studies that have been examined in various human populations.

Table 1. A Review of Lingual Resistance Training in Animal Models

Author	Aim	Model	Protocol	Results
(Behan et al., 2012)	Examine 1) the effect exercise has on tongue force, 2) if 5HT input to tongue decreases with age; and 3) if tongue exercise augments 5HT input to hypogolossal muscle	Young, Middle, and Old Age Male Fischer 344/BN Rats	Tongue exercise implemented for 8 weeks	-Increase in maximum tongue force for all ages -Significant increase in 5HT immunoreactivity in young rats
(Ciucci et al., 2013)	Determine the impact tongue force generation during licking task has on timing, force, and striatal dopamine sparing.	9-Month old Fischer 344/Brown Norway Rats	16 control rats split into: 1) Exercise group 2) No-Exercise group 14 rats with lesions to the medial forebrain bundle with 6-hydroxydopamine (6-OHDA) split into: 1) Exercise group 2) No-Exercise group	-Animals in exercise group demonstrated better performances in maximum force, average force, and press rate. -6-OHDA animals performed as well as those in control group.
(Connor et al., 2009)	Observe the effects of lingual intervention in rats on measures of protrusive tongue force, and genioglossus muscle fiber areas	Young adult, middle-aged, and old Fischer 344/Brown Norway Rats	-8 weeks of tongue exercise completed -Protrusive tongue forces measured pre and post intervention -genioglossus muscle fibers compared to cross-sectional areas in a no-exercise control group	-Significant increases in maximum tongue force observed across all ages -Significant changes also observed in regards to increases and variability of cross-sectional areas of genioglossus muscle fibers
(Schaser et al., 2012)	Examine the amount of brain derived neurotrophic factor (BDNF) and its receptor, TrkB, in the hypoglossal nucleus of rats. Further, to observe the impact tongue exercise has on BDNF and TrkB and its role in the cranial nucleus utilized in tongue during swallowing.	Young, middle, and old-aged Male Fischer 344/Brown Norway Rats	-8 weeks of lingual exercise training completed. -Training intensity hierarchy: Weeks 1-2: Rats trained at 50% of estimated maximum press (EMP) Weeks 3-4: 60% of EMP Weeks 5-6: 70% of EMP Weeks 7-8: 80% of EMP	-Significantly higher gains in maximum tongue force observed in older than younger rats. -No differences in maximum tongue force observed between middle-aged and old-aged rats.

1.7 Lingual Resistance Training in Human Populations

Lingual resistance training has been studied in human clinical studies. Examining this type of therapeutic intervention at both the cellular level in animal models and from a physiological and functional standpoint in humans allows researchers to gain insight into the molecular changes that occur as a result of training, together with any functional outcomes such as improved swallowing capacity. Table 2 highlights some of the major lingual resistance studies that have been conducted in various human populations. While basic animal science data have provided information regarding the impact of lingual resistance interventions on cellular and molecular changes in the brainstem and motor cortex and peripheral muscle, human clinical trials have examined associated outcomes following lingual resistance training with functional aspects of swallowing including: degree of residue (Robbins et al., 2007; Steele et al., 2013); airway safety status (penetration/aspiration) (Robbins et al., 2005; Steele et al., 2013); and the specific effects of anterior versus posterior tongue regimes (Malandraki et al., 2012; Robbins et al., 2007; Yeates et al., 2008). Although not exhaustive, the available findings from human populations demonstrated that generally, tongue exercise lead to gains in isometric tongue strength. Functional changes in regards to speech and swallowing, however, are not well established by these studies and, further, the potential of this method to rehabilitate tongue weakness in neurodegenerative populations such as ALS has not been examined.

Table 2. Review of lingual resistance training studies conducted in human populations.

Author	Aim	Population	Protocol	Results
(Robbins et al., 2007)	-Observe effects of lingual intervention in post stroke pop	-10 persons with stroke -Age: 51-90 years old	-8 weeks of lingual exercise -Anterior and posterior bulb placement	-Increase in anterior and posterior tongue pressures -Reduced oropharyngeal residue -Greater gains occurred during first 4 weeks of treatment
(Malandraki et al., 2012)	-Case study of 1 patient. -Examine effects of lingual intervention over course of 5 years	-Inclusion body myositis and Sjorgens syndrome -77 years old	-8 weeks of lingual intervention -Completed 3x a year for 5 years	-Observed changes in tongue strength (anterior + posterior) -Anterior pressures overall declined over 5 years with last 2 years occurring more slowly than projected -Posterior pressures stabilized. Decline only occurred during treatment breaks
(C. Lazarus et al., 2003)	Compare the effects of two different tongue exercises in healthy adults	-31 healthy adults -Age: 20-29 years old	-4 weeks of training using IOPI or tongue depressor -4 exercises performed (elevation, protrusion, left, right)	-Those with lower baseline measure made greatest gains -No significant changes regarding endurance across/within groups
(Robbins et al., 2005)	Observe the effects of lingual intervention in older adults	-10 Healthy older adults -Age: 70-89 years old	-8 week lingual intervention program	-Changes to peak pressures during all swallowing conditions except 3 mL -No significant changes related to PAS, residue, bolus flow, or upper aero tract kinematics.

Table 2. (Continued)

Author	Aim	Population	Protocol	Results
(Clark et al., 2009)	-Examine effects of sequential versus concurrent lingual intervention. -Also, observe the effects of directional exercise on the lingual musculature	-39 healthy participants -Age: 18-67 years old	-9 weeks of training -3 exercises included (lateralization, protrusion, elevation) - Sequential group: (30 reps of protrusion, elevation, or lateralization) -Concurrent group: (10 reps each of protrusion, elevation, and lateralization).	-Concurrent group demonstrated higher protrusion measures -Detraining effect observed post treatment - Statistically significant gains were made across all types of training conditions
(Steele et al., 2013)	-Observe effects of a lingual intervention program in persons with acquired brain injury	-6 participants at least 5 months post onset	-24 sessions completed over 11-12 weeks -60 tongue pressure tasks arranged into groups of 6 -Target accuracy and generalization tasks (saliva swallows) completed	-Increased anterior MIPs for 5 participants (2 persons did not maintain these increases) -Gains in posterior MIPs seen in all 6 people for at least 3 consecutive sessions. -Saliva swallowing pressures increased in 3 participants over at least 3 consecutive sessions. -Post-treatment improved safety of swallowing thin liquids for 5 participants. -Improved safety for spoon-thick liquids for about half of participants. -Pharyngeal residues did not improve and actually worsened in some participants.

1.8 Purpose of the Present Study

Bulbar dysfunction is highly prevalent in ALS and leads to reductions in quality of life, malnutrition, aspiration and death. Current treatment strategies for speech and swallowing dysfunction in ALS are lacking and focus on symptom management via environmental support, dietary modification and non-oral feeding. Although there is preliminary evidence to suggest that mild to moderate intensity exercise, applied early in the disease may be beneficial in PALS, to date no group has examined the potential impact of lingual resistance training on bulbar function.

The aims for the current study was to determine the impact of an eight-week lingual resistance program on: 1) lingual strength and endurance; 2) airway safety; 3) speech intelligibility; 4) patient-rated communication effectiveness, swallowing impairment and quality of life; and 5) global disease progression.

We hypothesized that eight-weeks of lingual resistance training would lead to increased maximum anterior isometric lingual pressure and longer anterior lingual hold time durations that would lead to functional improvements in airway safety, speech intelligibility, patient-rated measures of bulbar function and slower global disease progression.

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Chapter Two

Methods

2.1 Participants

Two individuals diagnosed with Amyotrophic Lateral Sclerosis (El Escorial criteria) were included in this study which was approved by the Institutional Review Board at the University of South Florida (IRB# Pro00017453). Inclusion criteria for the study included: 1) a diagnosis of mild to moderate ALS as indicated by an Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) score of 32 or greater 2) cognition within normal limits as determined by the Mini-Mental Status Examination (Rovner & Folstein, 1987); and 3) no allergies to barium or lidocaine. Participants from an ALS multidisciplinary clinic at a local university therefore represented a convenience sample. Participant A was a 50-year old woman with bulbar-onset ALS who, at the time of the study, was 33 months post symptom onset. Participant B was a 59-year-old man with spinal-onset ALS, 23 months since symptom onset. Complete demographic information for each individual is presented in table 3. Both participants were Caucasian and had college level education.

Table 3. Summary demographic information.

Domain	Participant A	Participant B
Age	50	59
Gender	Female	Male
Symptom Onset	November 2011	February 2013
Disease duration (months)	33	23
ALSFRS-R Score	34	41
Forced Vital Capacity	74%	74%

2.2 Experimental Design

This study incorporated a repeated measures design over a four-month period. Given the rapid neurodegenerative nature of ALS, multiple baselines were performed to benchmark bulbar disease progression. Baseline one was performed followed by an 8-week lead-in period at which point a second baseline evaluation was completed. The same tasks that had been administered two months prior at the initial baseline were repeated. The exact same order of testing was performed by each participant to minimize any potential order effects during testing. Immediately following the second baseline, participants underwent eight weeks of lingual resistance training. Following this eight-week treatment period, participants attended a third and final evaluation. A summary of the testing domains covered at each evaluation session is shown in Table 4.

2.3 Testing Procedures and Outcome Measures

Table 4. Outcome measures assessed across study domains.

Domain	Test[1]	Outcome Variable
Lingual Strength	Lingual Pressure Generation	Maximum anterior isometric pressure (kPa)
		Endurance (seconds)
Swallowing	Videofluoroscopy	Penetration-Aspiration Scale
	SWAL-QOL	SWAL-QOL and domain scores
	FOIS	FOIS Score
	EAT-10	EAT-10 Score
Speech	Speech Intelligibility Test	Sentence and word intelligibility ratings
	CES	CES score
Global	ALSFRS-R	ALSFRS-R Total Score

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[1] *SWAL-QOL= The Swallowing Quality of Life Survey; FOIS= Functional Oral Intake Scale; EAT-10=Eating Assessment Tool-10; CES=Communication Effectiveness Survey; ALSFRS-R= Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised

2.3.1 Lingual Pressures

A custom lingual pressure measuring apparatus was utilized to test lingual pressure. This apparatus consisted of the *Iowa Oral Performance Instrument* (IOPI Medical, Redmond, WA) that was connected to a DELL laptop PC (Dell Inspiron; Round Rock, TX), and configured with a data acquisition box (*Dataq systems model DL-155; Akron, OH)*. Additionally, in order to have the lingual pressure measures record in real time, the data acquisition box was connected to the DELL laptop PC using a standard USB cable. The laptop was running a specially designed Excel workbook program in Windows 8 that permitted visual biofeedback during evaluation and training sessions.
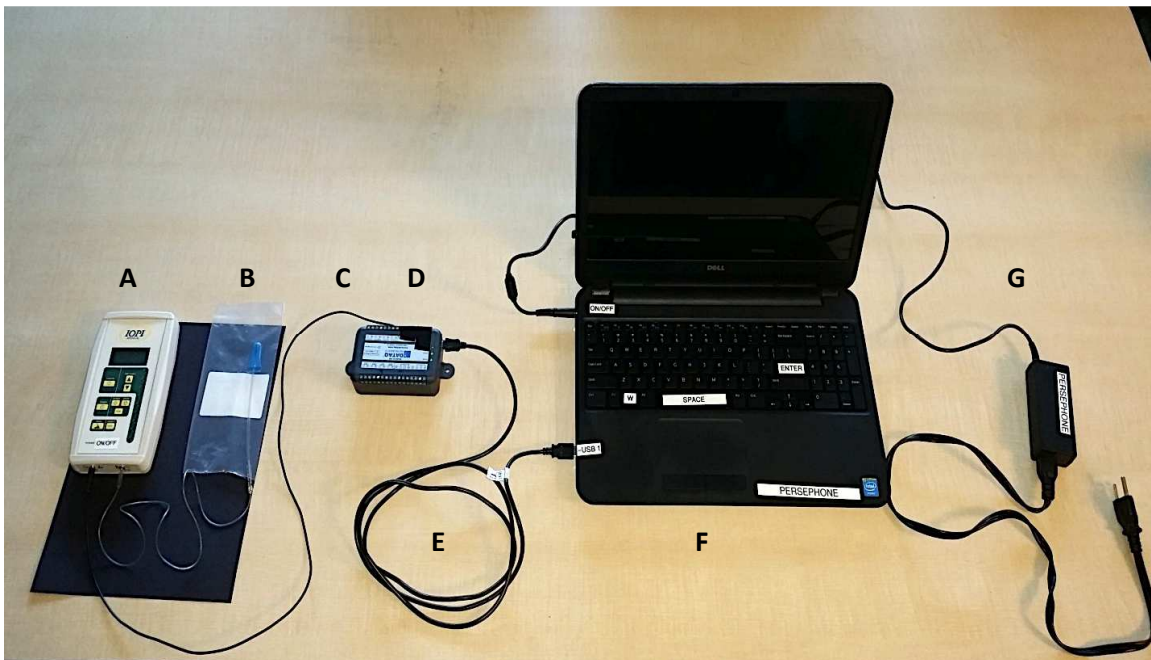
Figure 3. The Iowa Oral Performance Instrument workstation. The setup included A) an IOPI device; B) a tongue bulb; C) a 3.5 mm audio cable; D) a data acquisition box; E) a USB cable; F) a laptop PC and; G) a laptop charger.

As pressure was applied to the tongue bulb of the IOPI for the various lingual pressure tasks, the corresponding value of this pressure (measured in kilopascals) was automatically populated into designated cells of the Excel workbook. During each evaluation participants completed two lingual pressure testing tasks: 1) maximum isometric anterior tongue pressure task and 2) isometric anterior tongue endurance task.

a) Maximum Anterior Isometric Tongue Pressure (MIP) (kPa). To measure MIP during the 3 evaluations, individuals were seated at a table with the Excel workbook program facing them. Instructions were then given for the participant to place the air-filled tongue bulb in their mouth, with the upper surface contacting the alveolar ridge behind their teeth. Next, the individuals were asked by the research clinician to push against the bulb with the front part of the tongue as hard as he or she could for 1-2 seconds before releasing. The two participants were able to identify how well they had approximated the task by viewing the visual biofeedback waveform that appeared on the screen in real time indicating the amount of pressure applied as well as demonstrating how long this pressure was held. This measure was repeated two more times for a total of 3 MIP trials. The highest MIP was used for data analysis purposes and as a target for the subsequent endurance task.

b) Tongue Endurance (seconds). To complete the lingual endurance task, the highest peak pressure obtained during MIP testing was entered into the workbook program. Fifty percent of the MIP was then utilized as the target value for the endurance portion of the evaluation. Once this value was input into the program, a target red line appeared at 50% of the individualized peak MIP and so that the waveform remained at or above the red line for as long as they could with the bulb positioned at the alveolar ridge.

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Participants were instructed to press and hold their tongue for as long as they could with the bulb in place (positioned at the alveolar ridge). A stopwatch was used to record time (in seconds) anterior lingual pressure was held at or greater then 50% of MIP. Endurance time was defined as the total time anterior lingual pressure was held at or above 50% of individualized MIP represented as the red line on the screen. Three endurance trials were completed with a one-minute rest period between trials. The longest endurance time across the three trials was used for data analysis purposes.
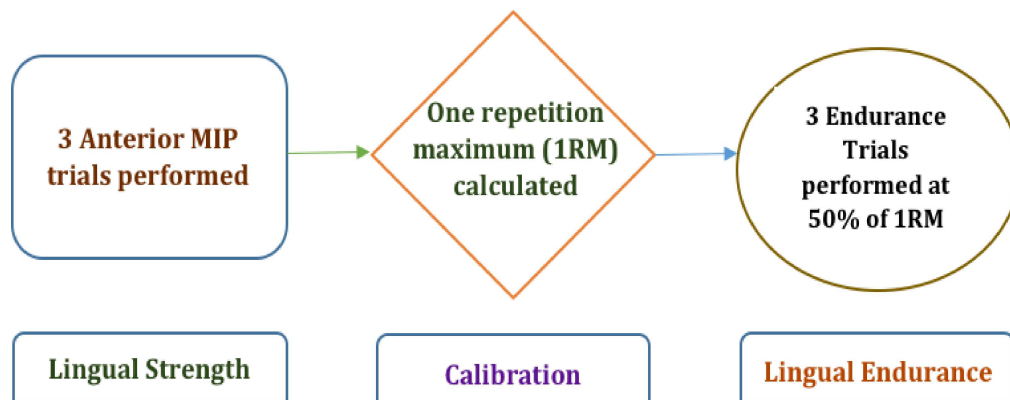
Figure 4. A flow chart representing the lingual pressure-testing regime.

2.3.2 Videofluoroscopic Swallow Study

Radiographic images of both participants' swallowing ability were taken utilizing the gold standard evaluation, the videofluoroscopic swallow study (VFSS). During this exam, participants were seated in an upright position in the videofluoroscopic suite and images of the swallowing were captured at 30 frames per second using a properly collimated Phillips BV Endura fluoroscopic C-arm unit (GE OEC 8800 Digital Mobile C-Arm system type 718074). Participants were initially seated in a position that would allow lateral images of their swallowing mechanism. Subsequently, the participant was moved in order to accommodate an anterior-posterior view of the designated swallowing

task. A standardized protocol was implemented using Varibar™ barium (Bracco Imaging; Milan, Italy) in varying volumes and viscosities. Bolus trials included Varibar ultra thin (diluted to a 40% w/v ratio), thin honey (40% w/v ratio), pudding (40% w/v) and a 13 mm barium tablet. Table 5 details the standardized bolus presentation protocol utilized. This protocol was adhered to, however, if a participant demonstrated episodes of aspiration, he or she would then be advanced to a thicker viscosity. All swallowing images were recorded onto a Kay Pentax workstation (Swallowing Signals Lab, Model 7120; Lincoln Park, NJ) for subsequent viewing and analysis.

Table 5. Standard presentation order of liquid and solid boluses.

Presentation Order	Presentation Type	Volume and consistency
1.	Liquid	5cc ultra-thin
2.	Liquid	5cc ultra-thin
3.	Liquid	5cc ultra-thin
4.	Liquid	Cup sip "comfortable size"
5.	Liquid	Serial Swallow
6.	Liquid	Tablespoon thin honey
7.	Liquid	Tablespoon thin honey
8.	Liquid	Tablespoon thin honey
9.	Soft solid	Tablespoon paste
10.	Pill	13 mm barium tablet
11.[*]	Liquid	20-cc thin honey

[*]Bolus presented in Anterior-Posterior (AP) position.

a) The Penetration Aspiration Scale (PAS). The Penetration-Aspiration scale (Rosenbek, Robbins, Roecker, Coyle, & Wood, 1996) is a validated eight point ordinal scale used to measure airway safety and degree of airway invasion during swallowing. The PAS progresses from safe swallowing events to unsafe (PAS > 3) with the value assigned indicating the deepest point in the laryngo-tracheal airway reached by the bolus, and, additionally, whether or not the material was ejected from this location. Scores of 1 and 2 are considered normal and indicate that no material remains in the airway.

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Penetration, or material entering the airway to the level of the vocal folds or above, is indicated by scores 3, 4, or 5. Aspiration events are designated by the numbers 6, 7, and 8 with the latter number representing "silent aspiration" as the individual making no effort to eject the material. PAS ratings were completed in a blinded fashion by a single rater. Scores were assigned to each swallowing trial individually.

2.3.3 Speech Intelligibility Testing

The *Speech Intelligibility Test for Windows* (SIT) (Yorkston, Beukelman, & Hakel, 1996) was used to evaluate speech intelligibility during the evaluation sessions. Participants were administered the two word intelligibility test and the sentence intelligibility test. For speech testing, participants were seated comfortably facing a DELL laptop PC installed with the SIT program. A microphone headset (ATM73a; Audio-Technica, Machida, Tokyo, Japan) attached to a Tascam DR-40 linear PCM recorder (Tascam, Montebello, CA) was placed on the participant's head with the microphone positioned 1 cm from the bottom right-hand corner of the mouth. First, participants completed the 11-sentence intelligibility test that entailed their reading 11 sentences with gradually increased length and complexity. Next, the participants completed the first word intelligibility test consisting of 57 words in isolation. Finally, the word-in-phrase intelligibility test was administered and this portion of the evaluation involved the individuals reading the same 57 words from the previous test. However, the words were now presented within a pre-selected carrier phrase, "say____again". For example, during the first word intelligibility test, the individual simply would be presented with a word to speak such as, "mane." Then, during the second test, the prompt would change to, "say mane again." The number of sentences, words, and words + carrier

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phrases read by the individuals was recorded and this value varied across evaluation sessions depending on the level of fatigue of the participant. SIT testing was completed at baseline 2 and post-lingual resistance training evaluation sessions only.

2.3.4 Patient-Rated Outcomes

Five patient rated outcomes were administered. These included the: a) *Functional Oral Intake Scale (FOIS); b) Communication Effectiveness Survey (CES); c) Eating Assessment Tool-10 (EAT-10); d) Swallowing quality of life survey; and e) The Amyotrophic Lateral Sclerosis Functional-Rating Scale-Revised (ALSFRS-R).* These items were administered at the end of the evaluation sessions after all other tasks had been completed.

a) Functional Oral Intake Scale. The *Functional Oral Intake Scale* (Crary, Mann, & Groher, 2005) is a 7-point validated ordinal scale that measures food consistencies a patient is consuming in everyday life. The first three items on the scale (numbers 1-3) pertain to individuals who are feeding tube dependent and items 4-7 relate to persons who are taking their diet primarily by mouth. The scale progresses from nothing being passed through the mouth (a score of 1) to a full oral diet with no restrictions (which is indicated by a score of 7). Taken in conjunction with other functional assessments and objective measures, the FOIS is useful in recording how eating and feeding habits change and/or progress over time.

b) Communication Effectiveness Survey (CES). The Communication Effectiveness Survey (Donovan, Kendall, Young, & Rosenbek, 2008) is an eight-question form related to assessing how efficiently an individual perceives their communication abilities across

a variety of personal and functional settings. Responses are ranked on a 4-point ordinal scale with a score of "0" indicating that the person is not effective in that communication area whereas a score of "4" indicates that the individual is effective communicating in the designated context. A total response score is calculated by adding all of the participant's scores together and the resulting number is a score out of 32 possible points. The greater the calculated score, the more effective the individual perceives him or herself at communicating across functional settings. Utilizing this tool was necessary to understand possible communication deficits within these participants and to gauge whether or not lingual strengthening targeted these deficits over time.

c) Eating Assessment Tool-10 (EAT-10). The Eating Assessment Tool-10(Belafsky et al., 2008) is a validated measure used to evaluate how an individual perceives their swallowing ability and to identify any concerns regarding their swallowing performance such as stressful swallowing or coughing when eating. There are 10 questions included as part of the EAT-10 and a 5-point ordinal scale is employed, whereby persons rank their choices with a score of "0" correlating to no problem with the swallowing related item and "4" corresponding to a severe problem regarding the question being asked. A total EAT-10 score was calculated by adding all of the responses together with possible total EAT-10 scores ranging from 0 (normal) to 40 (severe impairment). Total EAT-10 value was recorded and this measure was used for data analysis purposes.

d) Swallowing Quality of Life Survey (SWAL-QOL). The Swallowing Quality of Life Survey (McHorney et al., 2002) is a survey intended to gather information relating to an individual's self-perceived quality of life related to their swallowing function. The

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survey includes 13 questions, 9 of which are broad domain areas that are further subdivided into questions relating to that area. The areas surveyed relate to perceptions of how swallowing impacts the person's mood, attitude, communication, and social roles. Depending on the domain area, respondents are asked to rate their experiences on an ordinal scale with 1 representing "very much true," "almost always," "strongly agree," "always true," or "all of the time;" whereas scores of 5 can indicate "not at all true," "never," "strongly disagree," "never true," and "none of the time." Overall, across the first 9 general areas, the participants rank a total of 44 responses in regards to their perceptions of items relating to eating burden, fatigue, social life, and communication. The remaining 4 questions have responders select one answer each for a total of 48 responses used in data collection. All answers were scored across the domain area and then tallied for a summary SWAL-QOL score value. This resulting number indicated the impact that any swallowing impairment present in these persons had on their perceived quality of life.

e) The Amyotrophic Lateral Sclerosis Rating Scale-Revised (ALSFRS-R). The Amyotrophic Lateral Sclerosis Rating Scale-Revised is a form used by professionals to document global disease progression in individuals with ALS. This 12-item survey includes questions regarding eating, dressing, and functional communication habits. Additionally, questions related to respiration are also included. The individual responds to each question with a scaled score ranging from 4 to 0. A score of 4 indicates that the person demonstrates no impairment within that area whereas a score of 0 represents a significant difficulty with the associated task. Points from each question are then tallied

together to generate a score out of 48 possible points. The lower the number calculated indicates the greater the degree of disease impact for the individual.

2.4 Lingual Resistance Training Protocol

Both participants completed eight weeks of lingual resistance training (LRT) that began immediately following the second baseline evaluation session. A graduate research clinician traveled to each individual's home the day following his or her second scheduled testing session. The clinician worked with the patient and any present caregivers to instruct them how to complete the training exercises included as part of the study. The participants were instructed to complete the training session once a day, five days a week, for the course of the 8-week treatment period. Exercises included four different tasks that targeted the primary outcome variable of the study as well as functional swallowing performance tasks aimed at training efficient swallowing techniques in these individuals.

Each training session began with the participant entering the custom training program designed for use with the IOPI workstation. The Excel workbook program running during the training sessions was similarly designed to the program used throughout the three evaluation sessions; however, the former was a more comprehensive program in order to accommodate the variety of tasks required during training. Upon entering the daily training program, the individual was required to complete baseline measures related to tongue strength and endurance in order to calibrate for the training session. This calibration occurred at the beginning of each training session.

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Following these baseline calibration tasks, the individual was instructed to enter his or her one repetition maximum (1RM) into the corresponding dialogue box. Depending on the exercise being performed, either 50% or 20% of the 1RM was used as a target value for the training practice. Tasks completed during the daily sessions included: a) maximum anterior isometric tongue presses (x5); b) regular saliva swallow (RESS) (x5); c) effortful saliva swallow (ESS) (x5); and d) a tongue endurance hold task (x5). Five repetitions of each exercise were completed during the training session for a total of x20 task repetitions per day and x100 repetitions each week. A description of each of the four therapy tasks is detailed below.

a) Maximum Anterior Isometric Tongue Presses. The first exercise was five sets of maximum anterior isometric tongue presses. On the screen in front of the individual was a screen with a target red line indicating *50% of the IRM*. The prompt on the side of the training screen instructed the participants to place the tongue bulb of the IOPI into their mouth and rest the bulb on the alveolar ridge. Next, they were prompted to lift their tongue to the bulb and apply enough pressure to this bulb with the anterior part of their tongue so that the trace biofeedback waveform appearing on the screen reached or surpassed the red line. Individuals were instructed to apply the appropriate amount of pressure for 1-2 seconds before releasing. Five trials of this task were performed and data from these trials was automatically embedded into an Excel data sheet. The program then advanced the participant onto the next exercise for continuation of the training session.

b) Regular Effort Saliva Swallow (RESS). The regular effort swallow (RESS) was 1 of 2 functional swallowing tasks included as part of the training protocol for this study. During this portion of the session, individuals were prompted to place the tongue bulb on

the alveolar ridge in the same manner as the previous task. Then, with the bulb in place, the individual was asked to swallow the saliva readily available in their mouths. A biofeedback waveform was once again generated as the person completed this swallow; however, no target line was present for this portion of the session. Five repetitions of this task were performed with participants encouraged to rest for 30-60 seconds between trials in order to help prevent fatigue as well as allot time for saliva to re-accumulate. At the conclusion of these five repetitions, the program automatically moved to the next training screen.

   c) Tongue Endurance Holds. As the training program advanced to the tongue endurance exercise, the practice screen generated a horizontal red target line representing *20% of the participant's 1RM* from the daily baseline. Keeping consistent with previous prompts, the participant was asked to place the tongue bulb in their mouth at the same location as previously described. Once in place, the program gave instructions for the participant to press the anterior part of his or her tongue against this bulb with enough pressure so that the biofeedback waveform reached or exceeded the target red line. The training protocol was designed to incorporate a progressive endurance regime within the training sessions. A progressive endurance-training regime was utilized whereby the target lingual hold time was progressively increased by 2-second increments each week. For week one, a 6-second hold time was utilized. Thus, during week one, the participants would hold this endurance position for 6 seconds before releasing the tongue, and then rest for 1 minute before completing an additional 6-second hold. During week 2, the target endurance time would be 8 seconds, and this trend continued until the end of the intervention period. Participants were given the option to hold for 2 seconds less than the

target time for that week if they found that this task was too taxing. Any adaptations to this part of the training session were recorded on a log used by the participants during their sessions and the assigned clinician made note of these deviances while completing the weekly check-in session.
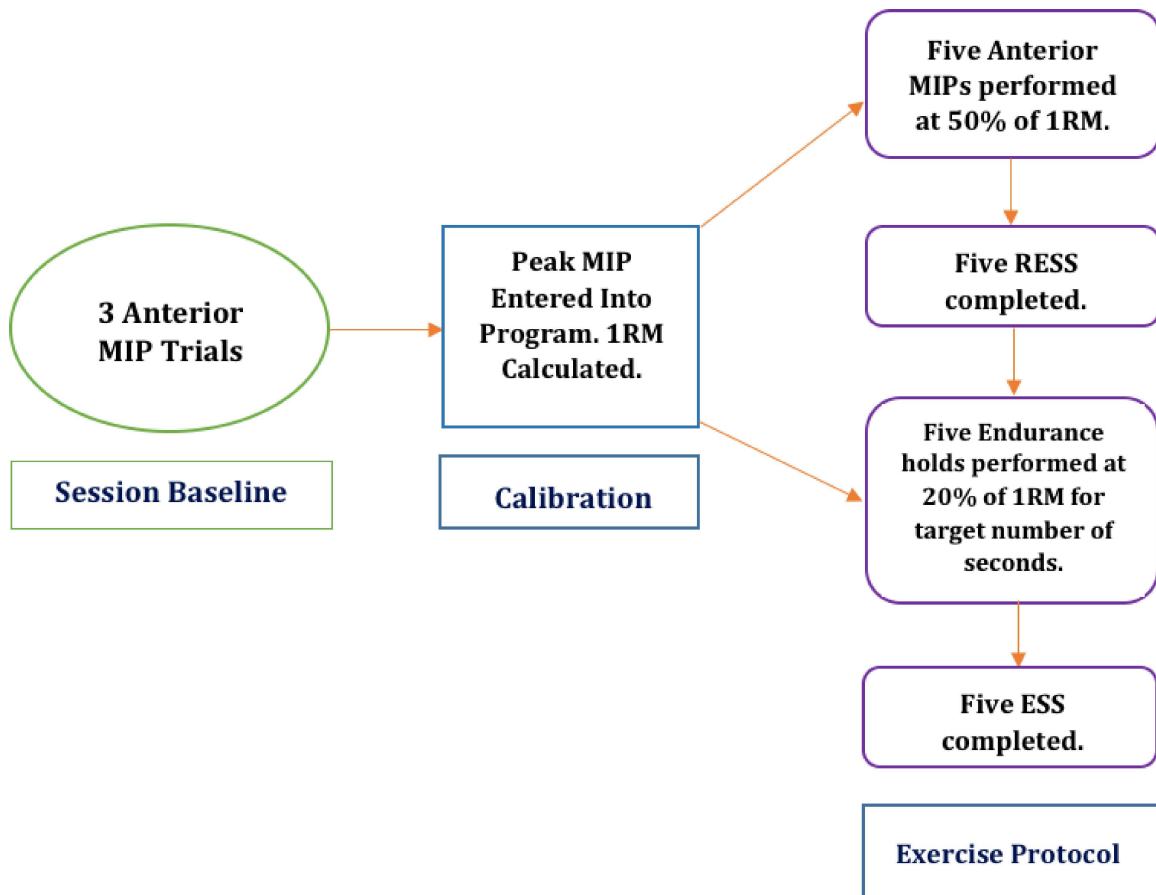
Figure 5. A flow chart representing the daily training session that was completed by participants over the course of the 8-week intervention period.

d) Effortful Saliva Swallow. Following the five endurance trials, participants completed an effortful saliva swallow task that represented a functional swallowing activity. This task rounded out the two functional swallowing activities as included as part of the study. In contrast to the preceding regular effort saliva swallow, participants

were now instructed to "squeeze their swallowing muscles hard" as the tongue bulb remained in position on the alveolar ridge. Similarly to the previous task, however, no target value or red line for this exercise was provided. Nevertheless, as individuals completed this exercise, the biofeedback waveform was still apparent on the screen and allowed the participants to track how effectively they were completing the designated task. Consistent with exercises completed earlier in the session, five repetitions of the endurance task were completed with 1-minute intervals provided between trials in an effort to prevent fatigue.

2.5 Data Collection and Analysis

a) Weekly Clinician-Directed Visits. Participants completed daily LRT in their homes and a clinician performed a weekly home therapy session. These weekly visits to each person were held in order to assess maximum performance tasks in the areas of anterior lingual strength and endurance. The clinician conducted these visits by running the assessment version of the IOPI program (see section 2.3.1 for details) and asked the participant to complete three anterior MIPs as well as 3 endurance repetitions. The MIP and endurance task performed during these visits were designed to assess how well the individual was improving in regards to these measures each week. Understanding task generalization was also important to assess during these visits; thus, for the endurance observations, the participant was asked to position the bulb on the alveolar ridge and push against this bulb for as long as they could without dropping below the target value (50% of 1RM) for more than 2 seconds.

b) Data Analysis. All data regarding the training sessions as well as the clinician-directed weekly visits were captured using the custom IOPI workstation and was extracted for data analysis purposes at the conclusion of the study. Regarding the evaluation sessions, only one evaluation session was attended with a caregiver present; thus, these responses were not included as part of data examination. Moreover, subsequent viewing of the self-populated data workbooks found errors in some of the training sessions relating to equipment issues. Measures obtained from these sessions were also not included in the data extraction component of this study.

Chapter Three

Results

Given that only two cases comprised this research study, descriptive statistics were utilized to document lingual pressure, swallow function, speech intelligibility and patient-reported outcomes. Participant A completed all evaluation sessions and 34/40 training sessions (85%) throughout the study. Participant B completed all evaluation sessions and 35/40 training sessions (87.5%) during the study. Results are presented individually for Participant A and Participant B in this chapter.

3.1 Participant A

3.1.1 Primary Outcome Variable: Lingual Strength and Endurance

a. Maximum Anterior Isometric Tongue Pressure

Maximum anterior isometric pressure remained relatively unchanged across all three-evaluation sessions in Participant A (see Table 6). At the initial baseline, a high degree of bulbar dysfunction was apparent in Participant A whose anterior MIP value was 12 kPa for Baseline 1 and 2. This value is significantly below the normal range (40-80 kPa). During, the eight-week lead in period, MIPs remained stable/unchanged. Following 8-weeks of lingual resistance training (LRT), maximum lingual pressures increased by 8%.

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Table 6. Maximum Lingual Pressures and Endurance Times

	Baseline 1	**Baseline 2**	**Post-LRT**
MIP (kPa)	12	12	13
Endurance (ms)	159	118	250

b. Maximum Anterior Tongue Hold Time (MHT)

Results for maximum anterior tongue hold times (MHT) are displayed in Table 6. MHT for this participant decreased by 35% during the non-intervention period, but increased by 112% from the second baseline to the post-treatment evaluation.

3.1.2 Secondary Outcome Variables: Swallowing and Speech Function

a. Penetration Aspiration Scale

Table 7 presents raw PAS data across all bolus trials and evaluation sessions. As can be seen in this table, the *worst PAS* score for baseline 1, baseline 2, and post-LRT were 5, 5, and 6, respectively. *Average PAS* scores across sessions were 2, 2 and 3. Finally, median PAS scores were 1, 1 and 3 across baseline 1, baseline 2, and post-LRT.

Table 7. PAS scores for each bolus presentation across evaluation sessions.

Bolus	Baseline 1	Baseline 2	Post-LRT
5-cc ultra thin	2	5	1
5-cc ultra thin	3	1	3
5-cc ultra thin	2	1	1
Cup sip challenge	5	1	3
Serial swallow	1	3	6
Tablespoon thin honey	1	1	5
Tablespoon thin honey	1	1	3
Tablespoon thin honey	1	1	3
Tablespoon paste	1	1	1

b. Speech Intelligibility

Overall, speech intelligibility for Participant A was severely impaired with a speech intelligibility rating of 14.55% at the sentence level, 44.00% at the single word level and a speaking rate of 60 wpm [normative range = 150 wpm (Boillee et al., 2006)]. As can be seen in Table 8, overall speech intelligibility as measured by the SIT decreased by 17.09 words per minute at the sentence level pre-vs. post-LRT. Across each SIT variable, speech function deteriorated pre- vs. post-LRT

Speech intelligibility at the single word level (SWL) is shown pre vs. post-LRT in Table 9 and shows no change in intelligibility at the SWL. Initial consonants, affricates and glides were noted to improve following LRT by 110.01%, 50%, and 100%, respectively.

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Table 8. Speech Intelligibility Results for Sentence-Level Production of SIT

Sentence Characteristics	Baseline 2	Post-Treatment	Change
Intelligible Words	16 of 110	11 of 110	-5
Percent Intelligibility	14.55%	10.00%	-4.55%
Timed Intelligible Words	16 of 110	11 of 110	-5
Timed Percent Intelligibility	14.55%	10.00%	-4.55%
Total Composite Duration	1 min 48.50 secs	2 mins, 30.90 secs	+0 min, 42.4 secs
Speaking Rate	60.83 wpm	43.74 wpm	-17.09 wpm
Intelligibility Rate	8.85 wpm	4.37 wpm	-4.48 wpm
Communication Efficiency Ratio	0.05	0.02	-0.03

Table 9. Word Intelligibility at the Single Word Level

Word Characteristics	Baseline 2	Post-Treatment	Change
Word Intelligibility	44.00%	44.00%	N/A
Vowels	54.55%	42.86%	-11.69%
Consonants	35.71%	44.44%	+8.73%
Initial	28.57%	60.00%	+31.43%
Final	35.71%	25.00%	-10.71%
Voiced	25.00%	50.00%	+25.00%
Unvoiced	40.00%	40.00%	N/A
Stops	20.00%	11.11%	-8.89%
Fricatives	42.86%	66.67%	+23.81%
Affricates	0.00%	50.00%	+50.00%
Nasals	100.00%	100.00%	N/A
Glides	0.00%	100.00%	+100.00%
Pressure Consonants	33.33%	28.57%	-4.76%
Nasal Glides	50.00%	100.00%	+50.00%

3.1.3 Tertiary Outcome Variables: Patient Reported Function

a. Functional Oral Intake Scale

At baseline 1 and 2, Participant A reported consuming a regular diet with some food avoidances and a FOIS score of 6. Following LRT, Participant A rated herself as a 5 on the FOIS with her oral diet consisting of food avoidances with multiple consistencies that required special preparation.

b. Eating Assessment Tool-10

EAT-10 scores across testing sessions are shown in Table 10. As can be seen in this table, total EAT-10 scores were 16, 20 and 19 across baseline 1, baseline 2 and post-LRT respectively. Following LRT, Participant A rated item 5 "Swallowing pills takes extra effort" as improving from a 3 to a 2. Overall, these EAT-10 scores are consistent with a self-perceived swallowing impairment.

Table 10. Total Scores for the EAT-10

Stimulus Item	Baseline 1	Baseline 2	Post-LRT
1. My swallowing problem has caused me to lose weight.	2	2	2
2. My swallowing problem interferes with my ability to go out for meals.	1	2	2
3. Swallowing liquid takes extra effort.	2	2	2
4. Swallowing solids takes extra effort.	1	2	2
5. Swallowing pills takes extra effort.	2	3	2
6. Swallowing is painful.	0	0	0
7. The pleasure of eating is affected by my swallowing.	2	2	2
8. When I swallow food sticks in my throat.	2	3	3
9. I cough when I eat.	2	2	2
10. Swallowing is stressful.	2	2	2
Total	**16**	**20**	**19**

c. Communication Effectiveness Survey

Data from the CES are provided in Table 11. Participant A's self-rated communication effectiveness did not change between Baseline 2 and Post-LRT, but a 2 point decrease was reported during the eight-week lead-in period (Baseline 1 vs. Baseline 2).

Table 11. Self-Reported Ratings of Communication Effectiveness

Stimulus Item	Baseline 1	Baseline 2	Post-LRT
1. Having a conversation with a family member or friends at home.	2	1	1
2. Participating in conversation with strangers in a quiet place.	1	1	1
3. Conversing with a familiar person over the telephone.	1	1	1
4. Conversing with a stranger over the telephone.	1	1	1
5. Being part of a conversation in a noisy environment.	1	1	1
6. Speaking to a friend when emotionally upset or angry.	1	1	1
7. Having a conversation while traveling in a car.	2	1	1
8. Having a conversation with someone at a distance.	1	1	1
Total	**10**	**8**	**8**

d. Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised

Table 12 presents ALSFRS-R total and bulbar subscale scores. Global disease progression, as measured by the ALSFRS-R declined for Participant A during the eight-week lead-in period from a total score of 34 to 28 (i.e. a 6-point decrease). Following LRT, the ALSFRS-R score was 29 (i.e. a 1-point increase). When examining the bulbar

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subscale scores (speech, swallowing, and saliva management); Participant A scored 5,4 and 4 across testing sessions.

Table 12. ALSFRS-R Scores Across Functional Domains

Domain	Baseline 1	Baseline 2	Post-LRT
Bulbar function (Speech, Swallowing, Saliva management)	5/12	4/12	4/12
Hand dexterity (Handwriting/Using utensils)	7/8	6/8	6/8
Dressing and Hygiene	8/8	6/8	6/8
Ambulation	6/8	5/8	6/8
Respiration	8/12	7/12	7/12
Total	**34**	**28**	**29**

e. Swallowing-Related Quality of Life

Results from the SWAL-QOL are displayed in Table 13. Total SWAL-QOL scores declined by 11 points between Baseline 1 versus Baseline 2, but remained stable pre versus post-LRT. Overall, self-rated swallowing-related QOL was impaired in this individual.

Table 13. Self-Rated Perceptions of Swallowing Quality of Life.

	Baseline 1	Baseline 2	Post-LRT
Total	68	57	57

3.2 Participant B

3.2.1 Primary Outcome Variable: Lingual Strength and Endurance

a. Maximum Anterior Isometric Tongue Pressure

Maximum anterior isometric pressure decreased by 4.44% for Participant B during the eight-week lead in period and increased by 18.6% following eight weeks of lingual resistance training (see Table 14).

Table 14. Maximum Lingual Pressures and Endurance Times

	Baseline 1	Baseline 2	Post-LRT
MIP (kPa)	45	43	51
Endurance (ms)	999	753	2086

b. Maximum Anterior Tongue Hold Time (MHT)

Results for lingual endurance are displayed in Table 14. MHT for this participant decreased by 25% between Baseline 1 and Baseline 2. Participant B's endurance hold time increased by 177% from 753 ms to 2086 ms pre versus post-LRT.

3.2.2 Secondary Outcome Variables: Swallowing and Speech Function

a. Penetration Aspiration Scale

Table 15 displays raw PAS data across all bolus trials and evaluation sessions. Results demonstrate the *worst PAS* score for baseline 1, baseline 2, and post-LRT were 1, 1 and 7 respectively. *Average PAS* was 1, 1 and 2 across testing sessions. Lastly, *median* PAS scores across baseline 1, baseline 2, and post-LRT were 1, 1 and 1 respectively.

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Table 15. PAS Scores Across Evaluation Sessions.

Bolus	Baseline 1	Baseline 2	Post-LRT
5-cc ultra thin	1	1	1
5-cc ultra thin	1	1	1
5-cc ultra thin	1	1	1
Cup sip challenge	1	2	1
Serial swallow	1	1	7
Tablespoon thin honey	1	1	1
Tablespoon thin honey	1	1	1
Tablespoon thin honey	1	1	1
Tablespoon paste	1	1	1

b. Speech Intelligibility

Sentence intelligibility results for Participant B are presented in Table 16. Overall, speech intelligibility for this participant was minimally impaired with a slower speaking rate of 141.63 words per minute and intelligibility ratings of 94.55%, 98.25% and 94.74%, respectively. Further illustrated in Table 16, overall intelligibility as measured by the SIT increased by 2.72%, however, speaking rate decreased by 21.63 words per minute at the sentence level.

Speech intelligibility at the single word level (SWL) is shown pre versus post-LRT in Table 17. Voiced consonants increased by 4.35% following LRT whereas initial consonants, fricatives, and unvoiced consonants decreased by 2.5%, 7% and 10%, respectively.

Table 16. Speech Intelligibility Results for Sentence Level Production of SIT

Sentence Characteristics	Baseline 2	Post-Treatment	Change
Intelligible Words	104 of 110	107 of 110	+3
Percent Intelligibility	94.55%	97.27%	+2.72%
Timed Intelligible Words	104 of 110	107 of 110	+3
Timed Percent Intelligibility	94.55%	97.27%	+2.72%
Total Composite Duration	0 min 46.60 secs	0 mins, 55.00 secs	+08.40 secs
Speaking Rate	141.63 wpm*	120.00 wpm	-21.63 wpm
Intelligibility Rate	133.91 wpm	116.73 wpm	-17.18 wpm
Communication Efficiency Ratio	0.70	0.61	-0.09

*wpm=words per minute

Table 17. Word Intelligibility at the Single Word Level

Word Characteristics	Baseline 2	Post Treatment	Change
Word Intelligibility	98.25%	96.49%	-1.76%
Vowels	100.00%	100.00%	N/A
Consonants	97.56%	95.56%	-2.00%
Initial	95.83%	93.33%	-2.50%
Final	100.00%	100.00%	N/A
Voiced	95.65%	100.00%	+4.35%
Unvoiced	100.00%	90.00%	-10.00%
Stops	100.00%	100.00%	N/A
Fricatives	95.24%	88.24%	-7.00%
Affricates	100.00%	100.00%	N/A
Nasals	100.00%	100.00%	N/A
Glides	100.00%	100.00%	N/A
Pressure Consonants	96.97%	94.44%	-2.53%
Nasal Glides	100.00%	100.00%	N/A

Results for speech intelligibility at the phrase level are displayed in Table 18. Overall, speech intelligibility at the phrase level increased by 3.51% following eight weeks of LRT. Final consonants, stops and unvoiced consonants increased by 5.26%, 6.67% and 5.88%, respectively, from pre to post-LRT.

Table 18. Word Intelligibility at the Phrase Level

Word Characteristics	Baseline 2	Post-Treatment	Change
Word Intelligibility	94.74%	98.25%	-3.51%
Vowels	93.33%	100.00%	-6.67%
Consonants	95.24%	97.73%	+2.49%
Initial	95.65%	96.15%	+0.50%
Final	94.74%	100.00%	+5.26%
Voiced	96.00%	96.55%	+0.55%
Unvoiced	94.12%	100.00%	+5.88%
Stops	93.33%	100.00%	+6.67%
Fricatives	93.33%	90.91%	-2.42%
Affricates	100.00%	100.00%	N/A
Nasals	100.00%	100.00%	N/A
Glides	100.00%	100.00%	N/A
Pressure Consonants	93.75%	96.67%	+2.92%
Nasal Glides	100.00%	100.00%	N/A

3.2.3 Tertiary Outcome Variables: Patient Reported Function

a. Functional Oral Intake Scale

Participant B reported a full oral diet with no restrictions (FOIS=7) at baseline 1, baseline 2 and post-LRT.

b. Eating Assessment Tool-10

Table 19 displays Participant B's EAT-10 results. Participant B's total EAT-10 scores were 2, 1 and 0 for baseline 1, baseline 2 and post-LRT, respectively.

Table 19. Total Scores for the EAT-10

Stimulus Item	Baseline 1	Baseline 2	Post-LRT
1. My swallowing problem has caused me to lose weight.	0	0	0
2. My swallowing problem interferes with my ability to go out for meals.	0	0	0
3. Swallowing liquid takes extra effort.	0	0	0
4. Swallowing solids takes extra effort.	0	0	0
5. Swallowing pills takes extra effort.	0	0	0
6. Swallowing is painful.	0	0	0
7. The pleasure of eating is affected by my swallowing.	0	0	0
8. When I swallow food sticks in my throat.	0	0	0
9. I cough when I eat.	2	1	0
10. Swallowing is stressful.	0	0	0
Total	**2**	**1**	**0**

c. Communication Effectiveness Survey

Results from the CES are presented in Table 20. Patient-reported values declined by 4 points (i.e. score of 23 to score of 19) during the eight-week lead-in period. Following eight week of LRT, CES scores increased 4 points moving from a total score of 19 to a score of 23.

Table 20. Self-Reported Ratings of Communication Effectiveness

Stimulus Item	Baseline 1	Baseline 2	Post-LRT
1. Having a conversation with a family member or friends at home.	4	3	4
2. Participating in conversation with strangers in a quiet place.	3	2	3
3. Conversing with a familiar person over the telephone.	3	3	3
4. Conversing with a stranger over the telephone.	3	2	2
5. Being part of a conversation in a noisy environment.	2	2	2
6. Speaking to a friend when emotionally upset or angry.	2	1	1
7. Having a conversation while traveling in a car.	3	3	4
8. Having a conversation with someone at a distance.	3	3	4
Total	**23**	**19**	**23**

d. Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised

Total bulbar subscale scores are displayed in Table 21. Global disease progression decreased from a total score of 41 to a score of 40 (i.e. a 1-point decrease) during the eight-week lead-in period. The ALSFRS-R was 39 (i.e. a 1-point decrease) following eight weeks of LRT. Results for the bulbar subscale items demonstrate Participant B consistently scored 10 across testing sessions**.**

Table 21. ALSFRS-R Scores Across Functional Domains

Domain	Baseline 1	Baseline 2	Post-LRT
Bulbar function (Speech, Swallowing, Saliva management)	10/12	10/12	10/12
Hand dexterity (Handwriting/Using utensils)	6/8	5/8	5/8
Dressing and Hygiene	7/8	7/8	6/8
Ambulation	8/8	7/8	7/8
Respiration	10/12	11/12	11/12
Total	**41**	**40**	**39**

e. The Swallowing Quality of Life Survey

Results from the SWAL-QOL are displayed in Table 22. Total SWAL-QOL scores demonstrated a consistent 2-point decline between baseline 1, baseline 2 and post-LRT moving from a total score of 94 to scores of 92 and 90, respectively.

Table 22. Self-Rated Perceptions of Swallowing Quality of Life.

	Baseline 1	**Baseline 2**	**Post-LRT**
Total	94	92	90

3.4. Summary of Results for Participant A and B

a. Primary Outcome: Tongue Strength and Endurance

Table 23 summarizes relative percent change scores for the primary outcome variable (peak MIP and maximum MHT) across participants. On average, peak MIP declined 2% during the lead-in period and increased 13% following LRT. Maximum anterior tongue endurance hold times declined on average 25% during the eight-week lead-in period and increased by 144% post-LRT.

Table 23. Relative Percent Change in Peak Anterior MIP (kPa) and Maximum Endurance Hold Times (ms).

	Peak MIP		**Maximum Endurance**	
	B1-B2	**B2-Post-LRT**	**B1-B2**	**B2-Post-LRT**
Participant A	0%	+8%	-26%	111%
Participant B	-4%	+19%	-25%	177%
Average	**-2%**	**+13%**	**-25%**	**+144%**

b. Secondary and Tertiary Outcome Variables

A summary of relative change across all outcome variables and participants is provided in Tables 24 and 25.

Table 24. Summary of testing results for Participant A

Measure	Baseline 1	Baseline 2	Post-LRT	Change B1-B2	Change B2-Post-LRT
Peak MIP	12	12	13	0%	+8%
Max Endurance	15.9	11.85	25.01	-25%	+111%
FOIS	6	6	5	Diet stable	Downgrade in diet
EAT-10	16	20	19	-4	-1
CES	10	8	8	-2	0
ALSFRS-R	34	28	29	-6	+1
SWAL-QOL	68	57	57	-11	0
PAS	5	6	6	Unsafe-Unsafe	Remained unsafe

Table 25. Summary of testing results for Participant B

Measure	Baseline 1	Baseline 2	Post-LRT	Change B1-B2	Change B2-Post-LRT
Peak MIP	45	43	51	-4%	+18%
Max Endurance	9.99	7.53	20.86	-25%	+177%
FOIS	7	7	7	No change	No change
EAT-10	2	1	0	-1	-1
CES	23	19	23	-4	-4
ALSFRS-R	41	40	39	-1	-1
SWAL-QOL	94	92	90	-2	-2
PAS	1	1	7	Safe-----Safe	Safe-----Aspirator

Chapter Four

Discussion

Bulbar dysfunction is highly prevalent in ALS and leads to malnutrition, aspiration, aspiration pneumonia, and reduced quality of life (Mazzini et al., 1995; Mitsumoto, 2009; Paris et al., 2013). Recommended treatment approaches for dysarthria and dysphagia in this patient population include compensatory strategies, dietary adjustments, percutaneous gastrostomy (PEG) tube placement (Salvioni, Stanich, Almeida, & Oliveira, 2014) and alternative and assistive communication devices (Ball et al., 2010). These treatments, however, do not target the underlying physiology or represent active rehabilitative approaches. The current preliminary investigation examined the impact of an eight-week lingual resistance-training program on lingual strength, lingual endurance, airway safety, speech intelligibility and patient-reported outcomes.

4.1 Impact of Lingual Resistance Training in Two Individuals with ALS

Although the two ALS patients studied had different bulbar profiles, both demonstrated generally similar patterns of response to LRT. Both participants showed no substantial gains in tongue strength; however, improvements in lingual endurance were noted. Indeed, while tongue endurance declined by approximately 25% between baseline 1 and 2, the endurance measure double from 118ms to 250ms and (almost) tripled from 999ms to 2086ms in participants A and B, respectively. Our results of no changes in lingual strength following LRT are not consistent

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with other investigators who documented increases in anterior tongue strength after 8-9 weeks of LRT in a patient with Sjorgen's syndrome and stroke patients (Malandraki et al., 2012; Robbins et al., 2007). Due to the progressive nerve cell degeneration in ALS, a lack of gain in maximum anterior isometric tongue pressures could possibly be attributed to the underlying progressive motor neuron loss and resultant muscle atrophy of the tongue that prevented gains in strength.

One possible explanation to account for the gains in lingual endurance, but not strength is the unique muscle fiber characteristics of the tongue. The tongue is a muscular hydrostat that is comprised of different types of muscle fibers. Primarily, there are type I and type II fibers coursing throughout the tongue muscle (Motoyama, Watanabe, & Ogawa, 2003). Type I fibers contract slowly, are lower in force production and are fatigue resistant whereas Type II fibers are fast-contracting and capable of great force generation and, therefore, more susceptible to fatigue (Sanders, Mu, Amirali, Su, & Sobotka, 2013). Another research study demonstrated that the tongue is predominately composed of Type II fibers although, a further subdivision of the tongue revealed the posterior tongue had a greater proportion of Type I fibers and the anterior portion of the tongue had more Type II fibers (Stal, Marklund, Thornell, De Paul, & Eriksson, 2003). Thus, this finding suggests that the posterior part of the tongue is less prone to fatigue than the anterior portion of this muscle. However, during this study, the anterior portion of the tongue was targeted during lingual resistance training; yet, it was endurance (Type I fibers) that increased while strength (Type II fibers) remained relatively unchanged. Consequently, the exercises of tongue strength and endurance, while seemingly being performed in the same manner are likely affecting the fibers of the tongue differently.

Another explanation that possibly accounts for changes observed in endurance rather than strength is the load (strength) and hold time (endurance) requirements for each of these tasks.

While the strength task load requirement was consistent at 50% of the one repetition maximum, the endurance task requirement (20% of one repetition maximum) had a progressive component whereby the hold time requirement increased (by two seconds every week) throughout the eight-week period. The eight-week training began with a 6-second endurance hold and these time targets increased in length over the course of the eight-week program. Due to these progressive targets being in place, the participants likely became accustomed to applying pressure to the bulb for slightly longer durations as the weeks progressed indicating a potential training effect of the study. The progressive nature of the endurance training thereby may have impacted results and performance in both of these individuals and the endurance measures during the final evaluation might be a manifestation of acclimation to the imposed increasing time target demands.

4.1.1. Measures of Swallowing Function after Lingual Resistance Training.

The observed gains in tongue endurance did not translate into functional outcomes in the area of airway safety during swallowing for both participants. Airway safety during swallowing remained unchanged for Participant A (PAS of 5, 5 and 6 across baseline 1, 2 and post-LRT, respectively) and on average remained relatively stable for Participant B (although they did have a single episode of aspiration with no effective cough reflex produced to expel aspirant material on a 90cc sequential bolus challenge). While the role of tongue strength in the oral phase of swallowing is well established (Shaker, Easterling, Belafsky, & Postma, 2012), the importance of tongue endurance during swallowing is not fully understood. Kays and colleagues (2010) conducted a study examining the relative role of tongue strength vs. endurance during mealtimes in younger and older healthy people. Both young and older persons demonstrated reduced tongue strength and endurance following eating a meal with younger adults displaying a greater decline in anterior tongue endurance than older individuals (Kays, Hind, Gangnon, & Robbins, 2010).

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Thus, the measure of tongue endurance appears to be affected by the act of swallowing and, further, seemingly affects different age groups in different manners. Still, given that transporting the bolus occurs in a "rapid sequence" (Massey, 2006), as demonstrated by this study, being able to sustain the tongue against the hard palate for more than the one second necessary to propel the bolus towards the esophagus (Allen, Prentice, & Caballero, 2005) may be of questionable clinical significance. Accordingly, observing changes only in tongue endurance and not tongue strength perhaps accounts for the lack of improved airway safety observed in these persons. Conversely, literature from sports medicine indicates that strength is a major component of endurance and training regimes should emphasize building strength primarily and then shift the focus to an endurance component (Naclerio, Colado, Rhea, Bunker, & Triplett, 2009). Only one of these variables was increased in both participants, but the possibility exists that augmenting both of these measures would result in improved swallowing in persons affected. However, it is important to note that PAS ratings were the only measure of swallowing and other features of swallowing such as residue and kinematics were not analyzed during this study.

4.1.2. Objective Ratings of Speech Intelligibility.

The results of this study demonstrated that lingual resistance training had no substantial impact on speech intelligibility in either individual. While strength did not improve in either patient, endurance hold times doubled in Participant A and tripled in Participant B. Yet, outcomes such as communication efficiency (a measure of rate of intelligible speech produced divided by rate of typical speech produced on SIT tasks -190 wpm) (Yorkston et al., 1996) decreased in both participants at the sentence level over time and overall intelligibility for the bulbar-onset patient was worse after treatment than before intervention began. Previous research examining repetitive tongue movements in normal speakers has demonstrated that speech in

these persons is altered in perceptibility after the tongue has been fatigued (Solomon, 2000). Findings from this study, then, are perhaps not representative of the lack of gains made in strengthening the lingual musculature; however, they might signal skewed performances due to the fatiguing nature of both the disease as well as repetitive tongue movements across evaluation and training sessions. Indeed, given the knowledge of tongue fiber composition, since strength remained unchanged in these persons, it is reasonable that no changes to the Type II fatigable fibers of the anterior tongue would also not result in any changes to speech that requires fast-contracting and rapid movements.

In combination with external factors such as fatigue potentially contributing to the results displayed here, another possibility is that speech intelligibility was not improved across the treatment period because this modality was not specifically targeted during the protocol. The tongue is one of the primary articulators used in speech (Raphael, Borden, & Harris, 2007) and some perspectives maintain that tongue strength contributes little to producing precise articulation in connected speech (Neel & Palmer, 2012), although reduced tongue strength has been observed in dysarthric speakers (Dworkin & Aronson, 1986). Nevertheless, these results as a whole do not correlate well with recommendations that dysarthria be treated through the use of isometric exercise targeting the articulators used in speech (Murdoch, 1998). However, these findings perhaps coincide with other notions which state that lingual exercise for dysarthria is a valid starting point; however, training should incorporate task specific speech movement in order to be more effective (McNeil, 2009).

4.1.3. Progression in Perceptions of Quality of Life

Generally, perceptions of communication effectiveness swallowing impairment and swallow-related quality of life were not affected by the lingual strengthening regime. Thus, the ways in which the participants observed their strengths and weaknesses across measures appeared to correlate well with objective ratings assessed across the three evaluation sessions. Participant A, who had demonstrated greater bulbar involvement than Participant B, typically rated herself as being less functional in the areas of swallowing and communication than her study counterpart. As the results from VFSS confirmed impaired airway protection over the course of the study for Participant A; food preparation for this individual shifted in order to accommodate safer swallowing habits. Additionally, this study participant identified herself as being highly unintelligible on the CES, a notion that was correlated with findings from speech intelligibility testing. Conversely, Participant B was found to have safe swallowing across the first two evaluations as well as conversational speech that was well understood across baseline 2 and the post-treatment testing session. Hence, his ratings of quality of life were ranked much higher and did not indicate the need for special diet preparations or supplemental speech options. Perceptions of quality of life did not improve for either person throughout the study period, but appeared to steadily decrease for both individuals. This downward trend is likely due to the participants perceiving the progression of ALS and its functional impact on quality of life and bulbar functions and shows that the lingual intervention did not result in improved perceptions of these parameters. Of note for the FOIS and SWAL-QOL in Participant B was the fact that a ceiling effect may have been present whereby his FOIS score of 7 could not improve and his SWAL-QOL score at baseline 1 was a 94. Finally, the fact that large reductions in perceptions of

communication and swallowing function were not observed indicated that although the training program did not improve these ratings, it did not seemingly adversely affect these persons either.

4.2 Strengths and Limitations of Current Study

This study represents the first effort to our knowledge aimed at gathering pilot data related to lingual strengthening in persons with ALS. Therefore, there are several limitations that impacted the findings of this study. The first and most remarkable limitation was the small number of individuals included as participants in this research cohort. Having only two persons in this study altered the way in which we were able to analyze our data, relying purely on descriptive statistics. Therefore, it is difficult to translate these findings from these two participants to the ALS population as a whole. Indeed, it is unknown whether the general trend of no gains in lingual strength, but increases in lingual endurance would have continued, or if these results would be only limited to these two persons. Additionally, with a case series this small, it was impossible to understand the relationships that may or may not have existed between our primary, secondary, and tertiary outcomes and the effect lingual intervention might have had on these relationships.

Another limitation of this study was the lack of data points surrounding the eight-week lead period in prior to the intervention period of the study. Primarily, at the first evaluation, it would have been beneficial to include the measure of speech intelligibility testing instead of limiting this component to only the second and third evaluations. Lacking this initial data point makes it difficult to assess the way in which speech might have changed in these two individuals during the lead in period and whether lingual strengthening played any role in augmenting this trajectory and rate of decline. This is an important point given the neurodegenerative nature of

ALS. Additionally, we recognize that moving forward it is of utmost importance to gather more values regarding lingual pressures during this 8-week non-intervention period. Although no functional gains were observed in these two individuals in the area of lingual strength, it is also not understood whether this measure was changing and/or declining before the intervention period. Therefore, lingual strengthening potentially could have contributed to stabilizing this function by allowing it to plateau in individuals. However, without any direct evidence, we are unable at this time to make any definitive statements about the way in which this protocol may or may not have prevented further decline of lingual strength in these persons.

The third limitation of this study was the inclusion of a training protocol that is less intensive than lingual strengthening regimes that have been used in other populations. Since fatigue is a major factor that must be considered when working with persons with ALS, we decided to incorporate what we viewed as less taxing training session than others found across the literature. However, given that these participants were only performing 5 repetitions of each of the 4 tasks during each training session, it is difficult to understand whether the lack of gains across measures was due to the progressive nature of the disease or if this was due to not incorporating an adequate training load. Interestingly, though, during the daily training sessions, the participants performed the endurance task at 20% of their 1RM at progressively increasing time targets while during the evaluation sessions this task was performed at 50% of the 1RM. Yet, the most significant change observed as a result of this study was the increase in the amount of time each participant held the endurance measure between the second and third evaluations. While this difference does demonstrate that these individuals were able to generalize the task from 20% to 50% of the 1RM, it is also difficult to distinguish whether this gain was due to

persons being more familiar with the task or if completing the daily training sessions helped them increase this measure.

Notwithstanding these limitations, there are also several strengths that can be appreciated in this study. This preliminary effort represents the first report to our knowledge of the investigation into lingual resistance training in individuals with ALS. Utilization of the IOPI workstation equipped with direct data storage helped to ensure that the participants completed all of their training without having to rely upon self-report. Additionally, this workstation provided a way to collect accurate recordings of pressure values across evaluation and training sessions. Further, this setup allowed these individuals to have visual biofeedback thereby allowing them to conceptualize the desired targets and pressure thresholds of the designated task.

Another strength of this study was the inclusion of both lingual and functional swallowing exercises into the daily training protocol. While the theoretical concept of lingual intervention proposes that improving tongue strength can potentially facilitate greater lingual propulsion, base of tongue retraction, and less residue, it is thought that the best rehabilitation for dysphagia is to practice swallowing. Thus, including the functional tasks of a regular effort saliva swallow as well as an effortful saliva swallow added a layer of depth to the training protocol by having these persons continue to use and exercise muscles of the laryngeal musculature.

Finally, we view the incorporation of a repeated measures design as an additional strength of this study. Completing evaluations at the start and conclusion of this period allowed us to understand how bulbar dysfunction as well as the overall disease was progressing in these participants over a given amount of time. While we have previously discussed the changes we

would implement to this non-intervention time of the study in future research efforts, this component still provided us with multiple baseline data sets to use in our analyses.

4.3 Clinical Implications

Due to the fact that only two cases were included in this study, it is difficult to infer any meaningful clinical implications from these data. They do, however, indicate that future studies should be conducted to elucidate the potential role of lingual strength and endurance training in individuals with ALS. Until future research is conducted in individuals with ALS on a larger scale regarding tongue strengthening and bulbar management, the clinical use of this technique is not currently supported.

4.3.1 Tongue Strength as an Independent Predictor of ALS Disease Progression

While lingual intervention did not successfully augment tongue function, swallowing, or speech in these individuals; it is still important to note that their tongue strength values across the study period appeared to correlate well with both objective and subjective measures of bulbar function. A study conducted in 111 patients with ALS found that abnormal tongue strength, or values that fell well below standard norms for age and gender, was indicative of survival time within this population (Weikamp, Schelhaas, Hendriks, de Swart, & Geurts, 2012). The results of that study would signify that based on the observation of tongue pressure generation alone in this cohort, potentially Participant B has a longer survival prognosis than Participant A. Therefore, although this protocol was not particularly useful in possibly prolonging this survival time, the variable of tongue strength is an important observation in persons with ALS. Examining this measure at multidisciplinary clinics or throughout disease progression can serve as way to monitor bulbar dysfunction and also might serve as a marker for when effective management

strategies for swallowing and speech should be implemented. Consequently, tongue strength can become a valuable diagnostic tool to be used in conjunction with other objective and subjective measures to facilitate maximal outcomes for persons with ALS.

4.4 Future Research Directions

Future research is needed to investigate the impact of lingual resistance exercise in ALS on a larger scale to gain a better understanding as to whether or not this type of intervention can be a useful behavioral strategy to manage some aspects of the speech and swallowing decline observed in this challenging patient population. The focus of an expanded study should include a large number of both spinal and bulbar onset ALS patients at different stages of disease progression. By stratifying the data in these various ways, insight can be gathered regarding the way timing, disease duration, and onset type interact with the intervention protocol. Subsequently, it can be determined whether any of these factors have meaningful contribution to the effectiveness of this type of treatment in individuals with ALS. Future work should investigate the impact of lingual resistance training on a greater variety of swallowing outcomes including the degree of residue using the validated Normalized Residue Ratio Scale (Pearson, Molfenter, Smith, & Steele, 2013) and objective kinematic and temporal physiologic measures of swallowing function.

Another factor from this study that should be examined further is the intensity level of the training protocol being utilized. In an effort to discern the maximum amount of training that can be completed without adverse effects such as fatigue, it would be useful to implement this study with a greater number of repetitions of each exercise performed during the daily training session. During the weekly visits directed by the clinician, participants would be asked about the level of

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fatigue they might be experiencing with the training to ensure that the increased number of repetitions is not unnecessarily taxing. However, given that one of the limitations of the study was the inclusion of the least restrictive intervention protocol, moving forward, increasing repetitions across sessions can potentially help researchers understand if this protocol is more effective with a greater training load.

Lastly, the concept of functional reserve and how it relates to neurodegenerative disorders such as ALS should be researched in greater depth. Although the literature states that tongue pressures below 34 kPa will result in dysphagia, it is not well understood which kind of deficits would characterize this swallowing as a result of this reduced pressure. As seen in this study, the bulbar-onset patient did have a significantly low maximum anterior isometric pressure with a baseline value of 11.99 kPa. More research is necessary in order to understand if the functional reserve can be quantified in some way to distinguish the category (normal versus penetrator versus aspirator) and degree (specific PAS score) into which various ranges of lingual pressures would translate.

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Appendix A

Institutional Review Board Approval

6/30/2014

Emily Plowman, Ph.D.
Communication Sciences and Disorders
4202 E. Fowler Ave., PCD 1017
Tampa, FL 33620

RE: **Full Board Approval for Initial Review**
IRB#: Pro00017453
Title: Effects of Lingual Resistance Training in Persons with Amyotrophic Lateral Sclerosis

Study Approval Period: 6/2/2014 to 6/2/2015

Dear Dr. Plowman:

On 6/2/2014, the Institutional Review Board (IRB) reviewed and **APPROVED** the above application and all documents outlined below.

Approved Item(s):
Protocol Document(s):
ALSFRS-R.pdf
El Escorial Criteria.doc
IOPI Manual.pdf
Mini Mental Status Exam.pdf
Research Protocol
Speech Sample Checklist
Speech Sample Protocol
SwalQOL Form.pdf
Therapy Log

Consent/Assent Document(s)*:
ALS-IOPI-ICF.docx.pdf

*Please use only the official IRB stamped informed consent/assent document(s) found under the "Attachments" tab. Please note, these consent/assent document(s) are only valid during the approval period indicated at the top of the form(s).

Appendix B

Permission to Use Images

USF

Raele Robison <rdrobison@mail.usf.edu>

Permission for Illustration
1 message

KatKenobi . <katstahl.horn@gmail.com>   Mon, Aug 3, 2015 at 4:22 PM
To: Raele Robison <rdrobison@mail.usf.edu>

To whom it may concern,

My name is Katherine Stahl and I collaborated with Raele Robison to create images for her thesis. I grant her permission to use these images (a schematic representation of a neuron and swallowing stages) within her thesis document. Any additional permission for use may be given at the discretion of Ms. Robinson or myself.

Best,

Katherine E. Stahl