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Evaluating The Relationship Between Diadochokinesis And Severity Of Dysphagia As It Relates To Forced Vital Capacity In Individuals With Amyotrophic Lateral Sclerosis

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EVALUATING THE RELATIONSHIP BETWEEN DIADOCHOKINESIS AND SEVERITY OF DYSPHAGIA AS IT RELATES TO FORCED VITAL CAPACITY IN INDIVIDUALS WITH AMYOTROPHIC LATERAL SCLEROSIS

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DEDICATION

This research project is dedicated to the individuals with Amyotrophic Lateral Sclerosis and the control participants who so graciously participated in this study.

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CHAPTER 1

INTRODUCTION

"Amyotrophic Lateral Sclerosis (ALS) is one of the most common neuromuscular diseases worldwide, and people of all races and ethnic backgrounds are affected" (NINDS, 2013). ALS is a rapidly progressive neuromuscular disease characterized by degeneration of the upper motor neurons (UMN) in the cortex, and lower motor neurons (LMN) in the brainstem and spinal cord (Francis, Bach, & Delisa, 1999; Giordana, 2011; Kiernan et al.; Kumar, Aslinia, Yale, & Mazza, 2011). Increased muscle tone and spasticity are a result of deterioration of UMN tracts. Muscle flaccidity, atrophy and fascicule are due to deterioration of LMN tracts (Baumann et al., 2010; Giordana, 2011; Kiernan et al.; Misulis & Head, 2007; Yorkston, Miller, & Strand, 1995). Disease presentation, both onset and progression, is unique to each individual. Functional decline is independent of age of onset or initial clinical presentation (Kawai et al., 2003; Yorkston et al., 1995). The average life span after diagnosis is approximately two to five years (Bradley et al., 2001; Giordana, 2011).

Progressive deterioration in speech, swallowing and respiratory function has been well documented (Hillel, 1999; Kawai et al., 2003; Kuhnlein et al., 2008; Ruoppolo et al., 2013; Sathyaprabha, Pradhan, Nalini, Thennarasu, & Raju, 2010; Tjaden & Turner, 2000). A decline in speech function often precedes changes in swallowing (Ball, Willis, Beukelman, & Pattee, 2001; Devine, 2013). Furthermore repeated assessments of swallowing function to determine the severity of dysphagia, disordered swallowing ability, and to reduce the risk of aspiration are vital. Aspiration, the passage of food, liquid or saliva into the lungs, may result in pneumonia (Hadjikoutis & Wiles, 2001; Scannapieco, 2014; Smith Hammond, 2008). Respiratory failure in ALS, is frequently the result of bronchopneumonia, a lung infection of

fungal, viral or bacterial (including aspiration) origin (Corcia et al., 2008). Mortality in ALS is most commonly a result of respiratory failure (Czaplinski, Yen, & Appel, 2006; Fitting, Paillex, Hirt, Aebischer, & Schluep, 1999; Hardiman, 2011b; Kiernan et al.; Mathus-Vliegen, Louwerse, Merkus, Tytgat, & Vianney de Jong, 1994; Morgan et al., 2005; Similowski et al., 2000; Vender, Mauger, Walsh, Alam, & Simmons, 2007). In a study by Corcia et al. (2008), post-mortem autopsy found that pneumonia was the cause of death in approximately 75% of individuals with ALS.

Compensatory strategies and diet modification are often recommended to address issues of dysphagia in individuals with ALS. Recommendations are generally reactive, based on an individual's complaints. Experienced Speech-Language Pathologists attempt to predict the likely progression of dysphagia based on clinical assessment of components of the articulatory, respiratory and swallowing systems. Although a relationship between deglutition, articulatory, and respiratory functions is known to exist, very little research has been conducted to attempt to identify measures that are predictive of decline in swallowing function in ALS. There is an absence of foundational evidence on which to base any predictive measures regarding the severity of dysphagia. The purpose of this study is to determine if the severity of dysphagia, as determine by Penetration Aspiration Scale (PAS) ratings (Rosenbek, Robbins, Roecker, Coyle, & Wood, 1996) and pharyngeal residue scale ratings (Kelly, Macfarlane, Ghufoor, Drinnan, & Lew-Gor, 2008) in individuals with ALS, can be predicted through performance on diadochokinesis (DDK) and force vital capacity (FVC) measures. Additional aims of this study include the investigation of potential predictive relationships between dysphagia ratings and other commonly utilized measures in the evaluation and treatment of ALS including duration of disease, type of onset (axial,

bulbar, mixed), current Amyotrophic Lateral Sclerosis Function Rating Score – Revised (ALS-FRS-R) score (Cedarbaum et al., 1999), body mass index, and the Dysphagia Handicap Index (DHI) patient-reported outcomes based dysphagia tool (Silbergleit, Schultz, Jacobson, Beardsley, & Johnson, 2012).

Based on existing literature describing the process of normal swallowing and the known deficits attributed to ALS, the following is hypothesized: 1) There will be significant negative correlations between rate of production of diadochokinetic tasks with PAS ratings, pharyngeal residue ratings, and number of swallows per bolus; 2) There will be significant negative correlations between FVC performance with PAS ratings, pharyngeal residue ratings and, number of swallows per bolus; and 3) There will be significant positive correlations between DHI total score and PAS rating, pharyngeal residue ratings, and number of swallows per bolus.

CHAPTER 2

REVIEW OF LITERATURE

The existence of a degenerative process resulting in muscle weakness and spasticity including changes in speech, swallowing and respiratory function has been documented since the early 1800's. Charles Bell was credited as the first Neurologist to describe cases of ALS (Rowland, 2001) while Aran, Duchenne and Cruveilher contributed to early understanding of the syndrome (Gubbay, 1985; Wijesekera, 2009). In 1869, Dr. Jean Martin-Charcot was the first to provide a complete description of symptoms and neurogenic impairments associated with motor neuron involvement, and in 1874 he established Amyotrophic Lateral Sclerosis (ALS) as a unique disease (Rowland, 2001). During the 19th century, multiple physicians conducted research to investigate the etiologies of various disorders with similar muscle involvement that would be classified as Motor Neuron Disease (MND) (Mitsumoto, Chad, & Pioro, 1998; Rowland, 2001)

Motor Neuron Physiology

In order to understand MND, it is important to examine the motor system and function of motor neurons. Motor neurons are composed of three regions, UMN, LMN and bulbar region of the brainstem (Kiernan et al.; Wijesekera, 2009). Together these three regions are responsible for relaying impulses necessary for voluntary motor activity from the motor cortex in the cerebrum through descending motor pathways to the desired muscles. The motor cortex is composed of the premotor cortex, the supplemental motor cortex and the primary motor cortex (Mitsumoto et al., 1998). The premotor cortex is involved in processing and planning the initiation of movement and the supplemental motor cortex is responsible for programming complex muscle sequences (Mitsumoto et al., 1998). Finally, the primary

motor cortex is responsible for initiation and strength of muscle contractions (Carrow, Rivera, Mauldin, & Shamblin, 1974; Mitsumoto et al., 1998; Teismann, 2011).

According to Mitsumoto et al. (1998), upper motor neurons originate in one of the areas of the motor cortex and relay neural impulses to LMNs through the pyramidal tract. The pyramidal tract controls volitional movement and is composed of the corticobulbar and corticospinal tracts. Corticobulbar tract fibers synapse with cranial nerves in the brainstem and are responsible for voluntary control of muscles involved in speech and swallowing including the larynx, pharynx, palate, face and jaw (Kiernan et al.). Corticospinal tract fibers synapse with LMN in the spine and govern voluntary fine muscle movements of the extremities. Impairments to the corticobulbar and corticospinal tracts are characterized by muscle spasticity.

Motor Neuron Diseases

Motor Neuron Disease (MND) is a category of progressive neurogenic disorders characterized by degeneration in one, two or all three regions of the motor pathway. The category of MND is composed of six disorders whose etiologies are either hereditary, sporadic or both (Mitsumoto et al., 1998). Amyotrophic Lateral Sclerosis is largely sporadic, but approximately 10% of documented cases are hereditary in nature (Haverkamp, 1995; Kiernan et al.; Wijesekera, 2009). ALS is defined by degeneration in both UMN and LMN tracts with impairments in axial and bulbar functions (Chen, 2005; Kiernan et al.). Mitsumoto et al. (1998) summarized the motor system impairments for each of the MNDs. Primary lateral sclerosis (PLS) is a sporadic disease characterized by UMN impairments of the face and extremities. Adult onset Progressive Bulbar Palsy (PBP) is a sporadic disease, defined by initial degeneration of LMNs at the brainstem level affecting speech, swallowing and

mastication. Progressive Muscular Atrophy (PMA) is a sporadic disease, described by degeneration of LMNs resulting in progressive axial weakness and atrophy without UMN degeneration. It is highly likely that PLS, PBP and PMA will eventually become ALS (Carrow et al., 1974). There is a chance, however, that each of those diseases will remain a pure disease process without transformation to ALS. The other two diseases included in the MND category are pure diseases. Spinal muscular atrophy (SMA) is a hereditary autosomal recessive disorder resulting in lower motor neuron impairments with axial weakness. Lastly, pseudobulbar palsy is a sporadic disorder with deterioration of UMN impairment affecting speech and swallowing function without LMN involvement or degeneration.

Diagnostic Testing

Diagnosis of MNDs require a thorough assessment utilizing several diagnostic tools. Often confirmation of ALS is generally a diagnosis of exclusion. There are many disorders that may result in motor neuron impairment. The most common differential diagnoses include stroke, brain or spinal cancer, and spinal stenosis (Mitsumoto et al., 1998). The most important diagnostic tool is clinical presentation and a thorough history and physical examination. Supportive information is necessary from additional testing including neuroimaging of the head and spine to assess for potential cerebral infarcts, tumor and nerve impingement in the spinal column; electromyography (EMG) to evaluate nerve conduction of UMNs and LMNs; blood tests to evaluate creatine phosphokinase (CPK) levels, an enzyme found in the heart, brain and skeletal muscle that is secreted into the blood when muscle stress or damage occurs; and on rare occasion a muscle biopsy is completed (Brooks, 1994; Mitsumoto et al., 1998). A diagnosis of ALS may take up to fifteen months from initial symptom onset (Hardiman, 2011b).

EMG assessments are crucial to diagnose ALS and other MNDs. The requirements for World Federation of Neurology Criteria for the Diagnosis of ALS include 1) presence of LMN degeneration in one or more of the four regions (bulbar, cervical, thoracic, lumbrosacral); 2) presence of UMN degeneration in one or more of the four regions; and 3) determined progression of symptoms and spreading of impairment across regions. The diagnosis is further classified as definite, probable, possible, or suspected ALS based upon the EMG findings. Definite ALS is defined through clinical presence of both UMN and LMN signs in the bulbar region and two or more spinal regions, or the presence of UMN and LMN in three spinal regions. Probable ALS is defined clinically with UMN and LMN in at least two regions, but the regions may be different. Possible ALS is defined as UMN and LMN present in only one region, or UMN signs present in two regions without signs of LMN involvement. Primary lateral sclerosis and progressive bulbar palsy are a few of the disorders that fall in this category. Suspected ALS is defined as presence of only LMN involvement in two or more regions (Brooks, 1994; de Carvalho et al., 2008).

Amyotrophic Lateral Sclerosis

Amyotrophic Lateral Sclerosis is a complicated disease that remains difficult to diagnose due to the variation of symptoms at onset and varied rate of progression (Hardiman, 2011a). Approximately 70% of the individuals diagnosed with ALS present with axial involvement, while 25% experience initial changes in bulbar function, speech or swallowing function (Hardiman, 2011a; Kuhnlein et al., 2008). A small percentage initially experience a combination of bulbar and axial impairment (Kiernan et al.; Paris et al., 2013; Teismann, 2011; Yorkston et al., 1995). Less than five percent of all patients with ALS experience respiratory impairments as the initial symptom (Hardiman, 2011a; Lo Coco et al., 2006;

Similowski et al., 2000; Vender et al., 2007). Disease progression eventually affects all extremities, speech production, respiration and swallowing function (Hillel, 1999; Kawai et al., 2003; Kuhnlein et al., 2008; Ruoppolo et al., 2013; Sathyaprabha et al., 2010; Tjaden & Turner, 2000). The disease course and rate of decline varies from individual to individual. When presenting symptoms are bulbar in nature, a rapid rate of decline with reduced length of survival is likely.

ALS – Early Speech and Swallowing Signs

Subtle changes in speech production usually precede changes in swallowing function (Haverkamp, 1995; Kuhnlein et al., 2008). Speech changes are largely due to lingual weakness resulting in imprecise movement generally when tired and then becoming more consistent throughout the day (Dworkin, Aronson, & Mulder, 1980; Weismer, Yunusova, & Westbury, 2003). Hypernasality also becomes apparent due to palatal weakness (Kuhnlein et al., 2008). As oral muscle strength declines, people with ALS will experience a decrease in rate of speech and vowel production will become centralized (Hillel, 1999; Turner & Tjaden, 2000). Throat clearing and coughing with liquids is generally the first reported sign of swallowing difficulty (Strand, Miller, Yorkston, & Hillel, 1996). Swallowing impairments generally occur with liquids first due to the increased transit speed of liquids which requires more precise and timely coordination of oral pharyngeal muscle movements for airway protection and bolus propulsion. Oral preparation of food is affected by lingual weakness and masseter weakness (Chen, 2005). As muscle strength declines, meal time increases due to inefficient mastication and bolus propulsion resulting in residue in the oral cavity and the pharynx requiring additional dry swallows to clear the oral-pharyngeal region.

Respiratory Function in ALS

The pulmonary system is a complex system involving structures, muscles and nerves originating in the brainstem and traveling inferiorly to the diaphragm and abdominal muscles (Similowski et al., 2000). Impairment in diaphragm movement and the phrenic nerve has been implicated in the decline of pulmonary function and presence of dyspnea, shortness of breath. There is a strong correlation between patients with reported dyspnea and increased respiratory rate, discoordinated abdominal movement with respiration, and decreased lung vital capacity (Similowski et al., 2000). Dyspnea is quite common in the middle to late stages of the disease process (Lo Coco et al., 2006).

Respiratory compromise in ALS is due to a combination of denervation of upper and lower motor neurons resulting in impairment of all three muscle groups of respiration, inhalation, exhalation and the upper airway including the palate and larynx, (Lyall, Donaldson, Polkey, Leigh, & Moxham, 2001). Patients with the bulbar type of ALS have a higher likelihood of respiratory involvement in comparison to ALS patients with strictly limb involvement. A study by Lyall et al. (2001) revealed that respiratory involvement in bulbar ALS was correlated specifically with lower maximum expiratory pressures, lower maximum inspiratory pressures, and increased rate of respiratory decline. Respiratory decline is often accompanied by a slow generalized decline in overall strength (Magnus et al., 2002; Schmidt et al., 2006; Similowski et al., 2000). Frequent assessment of pulmonary function is a critical determinant in predicting the rate of progression and length of survival in ALS (Lechtzin, Rothstein, Clawson, Diette, & Wiener, 2002; Lechtzin, Shade, Clawson, & Wiener, 2006; Schmidt et al., 2006).

Pulmonary function measurements are conducted through invasive and non-invasive methods. Invasive measurements are more accurate and able to detect changes in muscle function, however, they also require internal placement of balloon catheters in the mid-esophagus or at the level of the diaphragm. Non-invasive measurements involve either a mouth piece or a nasal catheter. There are several volitional non-invasive methods to assess respiratory function. Some of these non-invasive assessments have high sensitivity and specificity similar to that of invasive measures (Lechtzin, Wiener, Shade, Clawson, & Diette, 2002). All volitional measurements of respiratory function are vulnerable, to some degree, to submaximal effort and poor lip seal (Fitting, 2006; Hadjikoutis & Wiles, 2001; Héritier, Rahm, Pasche, & Fitting, 1994; Lechtzin, Rothstein, et al., 2002; Lyall et al., 2001). The most common methods of respiratory assessment include forced vital capacity (FVC), maximum inspiratory pressure (MIP), and maximum expiratory pressure (MEP). Of these assessments, the most researched and commonly used method is forced vital capacity (FVC) in the upright position (Schmidt et al., 2006).

Longitudinal research has established the importance of continued assessment of FVC throughout ALS disease progression (Hadjikoutis & Wiles, 2001; Vender et al., 2007). Assessment of respiratory function in patients with ALS through measurement of FVC has been conducted as a standard of assessment for many years (Lechtzin, Rothstein, et al., 2002). An average decline in FVC of approximately 3.5% per month is common in ALS (Lechtzin, Wiener, et al., 2002). To measure FVC, a subject is asked to take a deep breath and exhale as quickly and forcefully as possible for as long as possible through a mouthpiece. Normative data has been established for age, height, weight and gender. Measurements are generally reported in liters and as a percentage of predicted value (Lo Coco et al., 2006). FVC has been

highly correlated with scores obtained on the Norris ALS Scale of thirty-four parameters of function (Lechtzin, Rothstein, et al., 2002; Lechtzin, Wiener, et al., 2002). The forced vital capacity measure is able to identify changes in respiratory function with 53% sensitivity and 89% specificity (Lechtzin, Rothstein, et al., 2002; Lyall et al., 2001).

Predictive Ability of Respiratory Measures

Respiratory measures are currently used to predict the likelihood of mortality once respiratory function falls below a certain degree of impairment in individuals with ALS. A study by Morgan et al (2005) reported that in the ALS population, the FVC measure was 58% sensitive for predicting mortality in six months when the measurement was below 50% of the predicted value; however, when FVC was greater than 50% of the predicted value the measure was 96% specific. Respiratory assessment through FVC is effective in documenting profound respiratory involvement. Upright FVC has a 70% predictive value for ALS survival at one year when scores were within normal range (Schmidt et al., 2006).

Normal Swallowing

Normal swallowing function is dependent on coordinated, precise controlled movements of the articulators (Groher, 1992). The movements and timing of swallowing function has been studied in normal healthy adults throughout adulthood (Butler et al., 2010; Ding, Logemann, Larson, & Rademaker, 2003). The oral pharyngeal muscles involved in executing swallowing movements send and receive sensory and motor impulses through cranial nerves V, VII, IX, X and XII which synapse in the bulbar region of the brainstem with UMNs (Groher & Crary, 2010). Impulses are then routed though different regions of the cerebrum and cerebellum.

Cerebral Involvement in Swallowing

Swallowing function was once thought to be a "reflex". Recent research describes the act of swallowing as a "complex but stereotyped motor sequence" (Jean, 2001. p 929). A brain stem driven operation (Martin, Goodyear, Gati, & Menon, 2001; Martin et al., 2004; Yorkston et al., 1995) controlled by a central pattern generator in the medulla oblongata that produces sequential and rhythmic patterns for swallowing (Jean, 2001). Further research provided conflicting information identifying five major components involved in neural control of swallowing including sensory and motor features of the cranial nerves, cerebral and midbrain connections with the brainstem, bilateral swallowing centers within the brainstem, and the muscles and organs that are controlled by the other components (Robbins et al., 2008).

A study by Martin et al (2001) examined regions of cerebral activation using functional magnetic resonance imaging (fMRI) during various types of swallows including: naïve saliva swallow, voluntary saliva swallow and water bolus swallow. Common areas of activation for all types of swallows included the bilateral premotor, primary motor and association motor cortices, as well as the insula and primary somatosensory cortices bilaterally. Activation of these cortical areas was significant because it contradicted the previous belief that swallowing function was managed solely by the brainstem. Volitional swallows resulted in activation of the anterior cingulate gyrus where as naïve secretion management swallows did not activate the cingulate region. Activation of the sensory cortex was likely due to the need to integrate information regarding mastication, lingual position, secretion accumulation and sensory feedback from the oropharynx. The motor cortex

controlled bolus manipulation and propulsion. The insula was implicated in mediation of motor and sensory impulses to various cortical areas to govern functioning of the oropharynx, esophagus and gastrointestinal tract. Anterior cingulate cortex activation was thought to be due to attention and premotor processing crucial in initiating a volitional swallow.

Structures and Phases of Swallowing

The swallowing mechanism is very complex. It contains many structures and muscles responsible for bolus deformation, cohesion, and propulsion as well as airway protection. Swallowing function is typically divided into three main regions, the oral cavity, pharynx (nasopharynx and hypopharynx) and esophagus. These three regions contain four phases of swallowing, the oral preparatory phase, the oral phase, the pharyngeal phase and the esophageal phase (Dodds, 1990).

The oral preparatory phase is responsible for grinding and pulverizing solid foods as well as the creation of a cohesive bolus, of all material placed in the oral cavity, to prepare it for ingestion. During this phase, saliva is introduced to aid in pre-digestion, improved bolus cohesion and transit through the rest of the swallowing phases. The main structures involved in this phase of swallowing include the lips, teeth, tongue, velum and muscles of the lower face and jaw. Labial movements are important to remove food from a utensil, cup or straw and create a seal to prevent drooling or anterior leakage of the bolus. Appropriate tone of the facial muscles prevents pocketing of food in the buccal cavities. Mastication is composed of coordinated movements of the lips, mandible, tongue and cheeks (Kikutani et al., 2009). Mastication and swallowing pattern in healthy individuals varies from that of people with swallow impairments in that healthy individuals thoroughly chew an entire bolus prior to swallowing. Healthy individual also tend to swallow fewer times to ingest a bolus (Stachler

et al., 1994). Food that requires additional deformation may be moved anteriorly, depending on sensory feedback, to be further broken down (Hiiemae & Palmer, 1999). Tongue movements are crucial in the oral preparatory, oral and pharyngeal phases of swallowing. During the oral preparatory phase, the tongue is responsible for movement of food laterally for mastication by the molars, and to collect food on the surface of the tongue to prepare boluses for transit into the pharynx (Hiiemae & Palmer, 1999; Wilson, 2007). Oral preparation duration varies greatly depending on the texture and density of the bolus (Stachler et al., 1994). Oral preparation for liquids is very short, where as preparatory needs for solid foods is much more extensive (Hiiemae & Palmer, 1999; Stachler et al., 1994).

Once food has been appropriately masticated, the bolus is collected on the lingual surface and the oral phase is initiated and carried out (Groher & Crary, 2010). The primary objective of the oral phase is movement of bolus material into the pharynx. Several events occur in sequence to provide coordinated and efficient bolus transportation. The tongue tip and lateral borders elevate to contact the alveolar ridge and hard palate respectively to contain the bolus on the center of the tongue and form a groove extending the length of the tongue. Timely sequential movements and appropriate strength from elevation of the tip, blade and finally the dorsal segment of the tongue propel food and liquid from the anterior two-thirds of the oral cavity posteriorly to the base of the tongue, which is responsible for bolus propulsion through the pharynx (Robbins, Levine, Wood, Roecker, & Luschei, 1995; Wilson, 2007; Yoshida et al., 2006). Simultaneously, the soft palate elevates and lateral and posterior walls of the nasopharynx contract to protect against nasopharyngeal regurgitation (Dodds, 1990).

As the bolus enters the oral pharynx, the pharyngeal phase is initiated. The main functions of the pharyngeal phase are to protect the airway while transporting bolus material

through the pharynx. In preparation for bolus transit through the pharynx, several airway protective acts are set in motion instantaneously with initiation of the oral phase. The arytenoid cartilages adduct and angle anteriorly, to compress the laryngeal vestibule, followed by near vocal fold closure (Groher & Crary, 2010). Respiration is inhibited, generally after slight expiration to increase pressure in the trachea. Base of tongue retraction, during the oral phase, results in elevation and anterior movement of the hyolaryngeal complex and epiglottic retroflexion completing the steps for airway protection as the bolus passes through the pharynx. The pharynx widens to allow bolus passage as a result of pharyngeal constrictor relaxation. Bolus material is propelled through the pharynx by a combination of base of tongue retraction with contact on the posterior pharyngeal wall and contraction of the pharyngeal constrictors (Dodds, 1990). Relaxation of the pharyngeal esophageal segment is achieved through anterior movement of the hyoid, creating a forward pulling affect, in addition to sensory relaxation of the segment to allow appropriate bolus passage into the esophagus (Dodds, 1990)

The esophageal phase begins as the head of the bolus passes through the cricopharyngeal segment and continues to travel inferiorly through the esophagus and eventually into the stomach. Passage into the esophagus is dependent on relaxation of the cricopharyngeal segment which occurs as a result of hyolaryngeal elevation and anterior movement. Normal transit time through the esophagus averages from 6-20 seconds depending on the composition of the bolus. Liquids may actually travel through the esophagus and into the stomach in as little as 3 seconds(Groher & Crary, 2010).

Swallowing and Respiratory Function

Respiratory function and swallowing function are intertwined. Breathing and swallowing are physiologically connected to provide protection from aspiration (Hiss, Strauss, Treole, Stuart, & Boutilier, 2003; Martin-Harris et al., 2005; Martin, Logemann, Shaker, & Dodds, 1994). Extensive research has been conducted in the area of breathing and swallowing dynamics to identify the impact of reduced subglottic pressure and the effect of respiratory support on breath phase patterns surrounding swallowing. "Swallowing apnea is the cessation of respiration that occurs with swallowing" (Hiss, Strauss, Treole, Stuart, & Boutilier, 2004). A period of apnea is crucial for every swallow, food, liquid or saliva, to close and protect the airway from aspiration, the entry of a foreign substance (food, liquid or saliva) into the trachea. Apnea for swallowing in healthy individuals is generally initiated at the onset of the oral phase and ceases as the bolus passes through the pharyngeal esophageal segment. A study by Martin-Harris et. al (2005) studied healthy controls to determine if differences in apnea duration and respiratory phases surrounding swallowing were dependent on subject age. This study revealed that older subjects, 65 years of age or older, were more likely to extend the duration of apnea and vary the phase of breathing by either inhaling immediately before or after swallowing. This inhalation pattern may increase the risk of aspiration (Martin-Harris et al., 2005). Increased periods of apnea with earlier onset occur with increased bolus size (Hiss et al., 2004). Aging also affects the onset of apnea related to swallowing. Older healthy individuals are likely to initiate apnea prior to lingual retraction (Hiss et al., 2004)

Lung capacity and respiratory support are very important to facilitate safe swallowing (Martin et al., 1994). The severity of dysphagia may be exacerbated by compromised lung

volumes. As lung volume approaches residual lung volume bolus transit time and pharyngeal activation duration are prolonged and subglottic pressure is reduced which can increase the risk of aspiration (Gross, Atwood, Grayhack, & Shaiman, 2003).

Dysphagia

Dysphagia, impaired swallowing ability, is not a primary diagnosis, rather a symptom of underlying disease. Dysphagia is associated with many medical conditions and affects more than 22% of people over the age of 50 (Howden, 2004). That percentage increases up to 60% in the elderly and neurologically impaired populations such as Parkinson's, Multiple Sclerosis, stroke, and Amyotrophic Lateral Sclerosis. (Howden, 2004). As many as 87% of nursing home residents may suffer from dysphagia (Groher & Crary, 2010). Disorders of the peripheral and central nervous system as well as cancer of the alimentary tract are likely to result in long term changes to swallowing function. The most common causes of dysphagia are neurogenic disorders including stroke, Parkinson's disease, Multiple Sclerosis and Amyotrophic Lateral Sclerosis (Groher & Crary, 2010).

Dysphagia in ALS – Oral Pharyngeal Decline

The progression of bulbar ALS can cause dysphagia, even in the early stages of the disease (Kawai et al., 2003). During the course of ALS, bulbar degeneration affects lingual elevation and coordination as well as the timeliness of laryngeal elevation resulting in aspiration and piecemeal deglutition (Kawai et al., 2003). The most common patterns of oral motor impairment include decreased anterior lingual coordination and posterior oral holding. Swallowing safety is not affected by impaired anterior lingual coordination; however, posterior oral holding increases the risk of aspiration (Kawai et al., 2003).

Impaired base of tongue movement will also result in increased pharyngeal transit duration, oral and pharyngeal residue, which are risk factors for dehydration, weight loss and aspiration pneumonia (Holaas, DePippo, & Reding, 1996; Kawai et al., 2003; Robbins et al., 1995). Base of tongue function has been evaluated through various methods including pressure testing using oral manometry and diadochokinesis. Lingual pressures were significantly reduced in subjects who complained of dysphagia compared to subjects who did not complain of swallowing difficulty (Nicosia et al., 2000; Yoshida et al., 2006).

Reduced bolus size and piecemeal swallowing movements has been associated with individuals with all forms of ALS (Goeleven, Robberecht, Sonies, Carbonez, & Dejaeger, 2006). These movements are most often attributed to impaired base of tongue retraction resulting from prolonged bolus propulsion in to the pharynx as well as increased pharyngeal residue, fatigue (ClavÉ et al., 2006). It is common to witness a reduction in meal size with an increase in meal duration (Tanasescu et al., 2007). Fatigue and muscle weakness resulting in a greater number of swallows per bolus often leads to reduced appetite and weight loss.

Dysphagia in ALS - Effects of Respiratory Compromise

In addition to decline in oral motor coordination and strength, individuals with ALS commonly experience a decline in swallowing function as a result of disease progression associated with respiratory decline. The effect of decline in respiratory function on swallowing ability, as it relates to ALS, introduces several obstacles including reduced glottic abduction potentially resulting in upper airway obstruction, reduced diaphragmatic innervation, reduced coordination of apnea and swallowing timing as well as general fatigue (Hadjikoutis & Wiles, 2001). This relationship was examined more closely in a study by Strand, Miller, Yorkston and Hillel (1996) that examined the correlation between the ALS

severity scale score for speech and swallowing (Yorkston et al., 1995) with clinical or objective swallowing assessments and with FVC scores. There was a strong relationship between decline in speech, swallowing and respiratory function (Strand et al., 1996). Decline in FVC can indicate impairments in other areas. For example, when FVC was less than 1.5 liters, fatigue was frequently reported. Impairment in cough and secretion management were reported when FVC was less than one liter (Hillel, 1999; Yorkston et al., 1995). Respiratory decline results in an increased likelihood of feeding tube placement (Bradley et al., 2001). Feeding tubes were placed frequently after forced vital capacity declined below 50% of the predicted value (Bradley et al., 2001; Sarfaty, 2013). Respiratory function may be preserved, yet swallowing function may be severely impaired to the point that a feeding tube is required if oral motor function is severely affected.

Dysphagia Assessment Tools

Dysphagia is a major cause of morbidity and mortality in hospitalized patients. The identification of dysphagia and aspiration has to become increasingly important in order to improve; patient health and safety and reduce length of hospitalization (Langmore et al., 1998). The two most common objective assessment tools to date are the modified barium swallow study (MBSS) and the fiberoptic endoscopic evaluation of swallowing (FEES). The MBSS has been the gold standard in the identification of impairment throughout the upper aerodigestive tract for decades (Langmore & Logemann, 1991). There is an appropriate place for each assessment tool in the medical settings. Both interventions have their advantages and disadvantages. Advantages to MBSS evaluations include unobstructed view of all phases of swallowing, given adequate positioning, proper weight constraints, and the patient's ability to sit upright and sit still (Langmore & Logemann, 1991; Spinelli, Easterling, & Shaker, 2002).

An objective assessment examining the overall application of the MBSS was beneficial in identifying its many functions. In addition to the evaluation of aspiration, the MBSS is used to modify diet recommendations, generate referrals for further assessment to Otolaryngologists or Gastroenterologists and Dietitians, and assess swallowing strategies and techniques to maintain safe oral intake (Martin-Harris, Logemann, McMahon, Schleicher, & Sandidge, 2000). Martin-Harris et al. (2000) examined MBSS results of 608 patients with various medical diagnoses of which, only ten percent were determined to have normal swallowing function. The remaining ninety percent benefited in various ways from the MBSS. In another study that evaluated swallowing function through MBSS, pharyngeal residue was found to be a predictive marker for aspiration (Eisenhuber et al., 2002). Laryngeal penetration and/or aspiration were significantly more common in the presence of pharyngeal residue then in its absence, 93% to 33% respectively (Eisenhuber et al., 2002).

On the other hand, the FEES provides visualization of pharyngeal and laryngeal anatomy and physiology for speech and swallowing (Hafner, Neuhuber, Hirtenfelder, Schmedler, & Eckel, 2008; Langmore & Logemann, 1991). FEES can be completed in the patient's room and repeated without the adverse effects of radiation exposure. A study by Hafner et al. (2008) provided excellent results for assessment of nearly one thousand patients using FEES in the intensive care setting. Medically fragile patient's swallowing function was assessed; aspiration and pharyngeal dysphagia was also assessed at bedside. FEES examination allows for flexible and frequent assessment of swallowing function in addition to evaluation of pharyngeal and laryngeal sensation in high risk aspiration patients.

According to Aviv et al. (2001), disadvantages to the FEES examination include mild discomfort as a result of passage of the nasendoscope through the inferior nasal meatus and

through the nasopharynx to rest in the region of the oral pharynx during bolus trials. The most remarkable disadvantage of the FEES examination is the brief obstructed view of the larynx, at the height of the swallow, due to posterior pharyngeal wall contraction in coordination with base of tongue retraction and epiglottic inversion. The laryngeal vestibule, true vocal folds and trachea are able to be visualized prior to and immediately after the swallow. There potential complications of the endoscopic evaluation include epistaxis, nose bleed, a vasovagal syncope or loss of consciousness and reflex syncope resulting in temporary decreased cardiac function due to stimulation of the vagus nerve.

Self-Reported Severity of Dysphagia

While objective assessment measures such as the MBSS and the FEES are the most objective and complete method of swallowing evaluation, individual awareness and complaints of swallowing difficulty frequently are the source of the dysphagia evaluation consult referral. Dysphagia can result in anxiety and panic during meal times causing individuals to avoid social situations during meals, resulting in isolated meal behaviors (Elmståhl, Bülow, Ekberg, Petersson, & Tegner, 1999; Gustafsson & Tibbling, 1991). Dysphagia was also reported to reduce perceived quality of life (Ekberg, Hamdy, Woisard, Wuttge–Hannig, & Ortega, 2002). There area several patient self-reported outcome based tools available. Most of them are disease specific such as the MD Anderson Dysphagia Inventory (Chen et al., 2001) for patients with head and neck cancer, and the health-related quality of life instrument (Carrau et al., 2004) to examine the effects of laryngopharyngeal reflux. A few outcomes based patient reported dysphagia inventories do exist. Two of the most common are the SWAL-QOL (McHorney et al., 2002) and the Dysphagia Handicap Index (DHI) (Silbergleit et al., 2012). Both patient report tools examine the physical,

emotional and functional components of swallowing. The DHI is composed of 25 questions whereas the SWAL-QOL is a 44 question assessment (McHorney et al., 2000). Test-retest reliability was the same for both tools with a Pearson's correlation coefficient of 0.83 overall.

Dysarthria in ALS

Impairments in speech, dysarthria, are a result of abnormalities in muscle function and structures that affect voice quality, rate of speech, articulatory precision, intelligibility, pitch, volume, phrase length, velopharyngeal function and weakness of articulators (Ball et al., 2001). Dworkin and Aronson (1986) found that dysarthria was attributed to decreased lingual strength and range of motion, as well as changes in tongue size, shape and position. The type of dysarthria associated with ALS is generally classified as a mixed spastic-flaccid type of speech impairment (Yorkston, 2007; Yorkston et al., 1995). Speech impairments include: slowed rate, increase effort to enunciate words, decreased intelligibility, and imprecise articulation (Carrow et al., 1974; Chen, 2005; Duffy, 1995; Hillel, 1999). Voice impairments include: hypernasality, voice quality may sound breathy, harsh, hoarse or strained (Hillel, 1999). Oral motor impairments in the ALS population include: weakness of the tongue, palate and facial muscles, and fasciculations of the tongue at rest (Chen, 2005; Hillel, 1999). Appearance of dysarthria characteristics from the time of symptom onset is variable dependent on the initial symptom onset type and individual rate of disease progression.

Throughout the years, dysarthria has been evaluated through a variety of methods including the assessment of intelligibility, rate of speech and diadochokinesis. Assessment tool selection is up to the discretion of the Speech-Language Pathologist, Neurologist or other specialist evaluating speech production. Formal tests for intelligibility and dysarthria include the Assessment of Intelligibility of Dysarthric Speech (AIDS) (Yorkston & Beukelman,

1981b), Frenchay Dysarthria Assessment (Enderby, 1983) and Sentence Intelligibility Test (Yorkston, Beukelman, & Tice, 1991) among others. Each test has varying degrees of completeness. For example, the Assessment of Intelligibility of Dysarthric Speakers is an evaluation of intelligibility of single words and sentences from five to 15 words in length. The Frenchay Dysarthria Assessment is the most complete assessment tool; however, special training is required for a Speech-Language Pathologist to administer the tool. The Frenchay Dysarthria Assessment has 11 sections: reflex, respiration, lips, jaw, palate, laryngeal, tongue, intelligibility, rate, sensation, and associated factors. Informal speech and voice assessment tools are frequently used in clinical settings. Assessments include sustained phonation; diadochokinetic rate, conversational speech production, and examination of the oral mechanism..

Decline in rate of speech is an early indicator of bulbar involvement (Ball et al., 2001; Nishio & Niimi, 2006). Normal rate of speech for healthy subjects is approximately 150 words per minute; however, intelligibility was not a statistically significant predictor of true level of speech impairment in individuals with ALS (Ball et al., 2001). Other non-statistically significant changes in speech ability include decreased velopharyngeal closure that results in hypernasality and in more severe cases, nasal emission, during conversation. There were statistically significant correlations between rate of speech decline, below 100 words per minute or less, and vocal quality change and rate of tongue movement in ALS (Ball et al., 2001). Statistical significance was also found between a decline in tongue strength and dysarthria in ALS (Dworkin et al., 1980).

Several studies have investigated factors contributing to decreased rate of speech in ALS including segmental timing (Tjaden & Turner, 2000), acoustic differences in content and

function words (Tjaden & Turner, 2000), phonetic contrast errors and laryngeal involvement (Riddel & McCauley, 1995), vowel space and temporal distinctiveness (Riddel & McCauley, 1995; Tjaden & Turner, 1997, 2000). Tjaden and Turner (2000) analyzed habitual and slow rate of speech in healthy control subjects and subjects with ALS. Slow exaggerated speech rate was similar between groups; however, habitual rate was significantly decreased in the ALS population. Interestingly, at the exaggerated rate of speech, ALS subjects produced inconsistently lengthened vowels more than consonants (Tjaden & Turner, 1997, 2000). Exaggerated speech characteristics differed from healthy controls even though the rate of speech was very similar. In addition, subjects with ALS produced more centralized vowel sounds (Tjaden & Turner, 2000) that were likely a result of decreased lingual strength and range of movement (Dworkin et al., 1980).

Intelligibility

Previous research has determined that intelligibility measures were not effective for early identification of bulbar symptoms (Ball et al., 2001; Nishio & Niimi, 2006). In fact, intelligibility tended to remain relatively normal until the middle stages of disease progression. Decline in intelligibility is preserved despite a reduction in articulatory precision, rate of speech and slowed diadochokinesis (Nishio & Niimi, 2006; Yorkston & Beukelman, 1981a). Each intelligibility measure has a floor and ceiling effect and is only appropriate to changes in speech within a specific range (Yorkston & Beukelman, 1981a). The severity of dysarthria dictates the type and complexity of task necessary to accurately assess intelligibility. Speech intelligibility in single words or sentences may remain relatively normal despite significant impairments in articulatory agility and rate of production (Yorkston & Beukelman, 1981a).

Rate of Speech

As rate of speech declines there are definite ranges where all other variables become impaired. A study by Ball et al. (2001) revealed that strength of volitional cough and lingual movements were the first to become impaired at approximately 150 words per minute (wpm). At approximately 125wpm voice quality was significantly affected. There was rapid decline in speech intelligibility, velopharyngeal closure and the communication effectiveness index at 100wpm (Ball et al., 2001; Yorkston & Beukelman, 1981a; Yorkston & Beukelman, 1978).

Researchers hypothesized that vowel spacing is crucial for speech intelligibility, due to the consistent findings regarding vowel space and duration (Turner, Tjaden, & Weismer, 1995). In addition to vowel duration, Riddel and McCauley (1995) also assessed phonetic contrast errors. Significant findings included delayed initiation of voice onset, and imprecise articulation that resulted in difficulty distinguishing fricatives from affricates specifically alveolar phonemes from palatal fricatives.

While rate of speech can be directly measured, it must be combined with an intelligibility rating as well. In healthy adults, rate of speech can be affected by many factors. Language and linguistic factors including reading level, comfort reading aloud, syntactic structure, lexical selection, eye sight and length of utterance with longer utterance characteristically producing a more rapid rate of speech (Yuan, Liberman, & Cieri, 2006). Other factors known to affect rate of speech include demographic, cultural, physiological, psychological differences and natural aging (Amerman & Parnell, 1992; Verhoeven, De Pauw, & Kloots, 2004; Yuan et al., 2006). Diadochokinesis (DDK) is an effective method of assessing basic motor speech capabilities for various levels of impairment (Darley, Aronson, & Brown, 1975; Duffy, 1995; Kent, Kent, & Rosenbek, 1987; Wang, Kent, Duffy, Thomas,

& Weismer, 2004; Ziegler, 2002). DDK is sensitive to mild, even subtle neuromuscular impairments often overlooked in conversational tasks (Fletcher, 1972; Gadesmann & Miller, 2008; Nishio & Niimi, 2006; Ziegler, 2002) and in structured reading tasks (Nishio & Niimi, 2006).

Diadochokinesis

Diadochokinesis is composed of two tasks: alternating motion rates (AMRs) and sequential motion rates (SMRs). AMRs include rapid repetition of monosyllabic targets such as /pʌ/, /tʌ/ or /kʌ/ while SMRs include repetition of a multi-syllable target such as /pʌtʌkʌ/. Each sound production assesses a different articulation point. Labial movements are assessed with /pʌ/, tongue tip movement is assessed with /tʌ/, and movement of the dorsum of the tongue is assessed with /kʌ/ (Kikutani et al., 2009). AMRs are often affected before rate of speech is impaired (Nishio & Niimi, 2006). There is minimal linguistic burden, simple syntactic structure in this task which allows subjects of most levels of cognitive functioning to complete the assessment (Wang, Kent, Duffy, & Thomas, 2005). Diadochokinesis utilizes the simplest form, consonant-vowel, of speech and language sequence for the AMR portion of the assessment (Wang et al., 2005) and only a slightly more difficult 3 syllable combination for the SMR portion. The simplicity of this task allows assessment of even severely dysarthric subjects who are unable to produce multiple word utterances (Duffy, 1995). Correct production of DDK requires intact, balanced, rapid movement of the oral structures as well as adequate oral muscle integrity. Any impairment in coordination or muscle strength will result in a slowed rate of production and/or imprecise articulation (Dworkin et al., 1980; Fletcher, 1972). In addition, inter-rater and intra-rater judgments are good for rate precision with inter-rater agreement only varying by plus or minus one syllable (Gadesmann & Miller, 2008).

Order of presentation of stimuli does not significantly affect performance (Fletcher, 1972; Pierce, Cotton, & Perry, 2013)

Previous research has examined DDK in many ways from measuring the length of time it took for twenty productions of a target AMR (Fletcher, 1972), to measuring the number of productions in a set amount of time usually between 4 and 10 seconds (Dworkin et al., 1980; Gadesmann & Miller, 2008; Kikutani et al., 2009; Louzada, Beraldinelle, Berretin-Felix, & Brasolotto, 2011; Neel & Palmer, 2012; Nishio & Niimi, 2006; Ozawa, Shiromoto, Ishizaki, & Watamori, 2001; Padovani, Gielow, & Behlau, 2009; Pierce et al., 2013; Portnoy & Aronson, 1982; Wang et al., 2004). The average number of productions per second is approximately 6 to 6.5 productions of each AMR per second and approximately 1.3 productions of SMR per second.

Subjects with ALS produce abnormalities in diadochokinesis due to lingual weakness that results in slower AMR and SMR productions (Dworkin et al., 1980). Rate of production of AMR and SMR was significantly reduced in one study during repeated trials as a result of lingual fatigue (Dworkin et al., 1980). Subjects with ALS and dysarthria were found to have significantly slowed rate of DDK, approximately 66% of the rate of ALS subjects without dysarthria (Mulligan et al., 1994). Significantly slowed DDK rates have been found in stroke, ALS, myasthenia gravis and head trauma when compared to control subject groups (Nishio & Niimi, 2006; Portnoy & Aronson, 1982; Strong et al., 1999; Wang et al., 2004). Subjects with spastic dysarthria tend to exhibit a DDK pattern with a slow rate of production and normal rhythm (Portnoy & Aronson, 1982).

Predictive Measures

The impending decline of respiratory function combined with deterioration in function of lingual, pharyngeal and laryngeal musculature throughout the course of ALS, create a critical role for the Speech-Language Pathologist (SLP) in the continued assessment and treatment of speech and swallowing function throughout the disease progression. It is imperative to accurately evaluate the swallowing function of each patient with ALS to reduce their risk of aspiration and minimize any controllable pulmonary infection when possible. The role of the SLP, when working with patients with ALS, requires not only accurate assessment of current level of speech and swallowing function, but also the ability to predict the rate of decline of function that is likely in the near future. Prediction of rate of decline is important to determine the appropriate time to discuss diet consistency modification, nutrition supplementation and alternative methods of nutrition including long term feeding tube placement. Patients frequently require professional intervention when it is necessary to modify liquid consistency or discuss feeding tube placement. To date, the fundamental data necessary, on which a predictive model may be based, does not exist.

Predictive measures have been adopted in health care with the goal of prevention of adverse conditions or medical problems. Predictive measures have been implemented to predict certain disorders, recurrent medical problems or even frailty. Predictive measures have been developed to determine frailty of older adults through simple questionnaires to assist in identifying people at higher risk for medical problems (Dayhoff, Suhrheinrich, Wigglesworth, Topp, & Moore, 1998). Previously, (Arena, Humphrey, & Peberdy, 2003) created an algorithm to predict future hospitalizations in patients with congestive heart failure through the assessment of pulmonary function tests. Prediction of function exercise capacity in patients with Multiple Sclerosis was determined by examining walking distance in six

minutes (Savci et al., 2005). A previous study (Gerdhem, Ringsberg, Åkesson, & Obrant, 2005), found that function tests were not as accurate in predicting future falls as was a history of previous falls, conditions affecting the balance, tendency to fall, intake of psychoactive medication, inability to stand on one leg, of increased age. Prediction tools are very useful for patient safety in addition to aiding healthcare professionals in planning and providing appropriate levels of care and medical recommendations.

The ability to predict the severity of dysphagia in people with ALS would be a very useful tool to assist in planning for feeding tube placement, and reducing hospitalizations for aspiration pneumonia and possible associated breathing issues. The most notable benefit from prediction of dysphagia severity in ALS through clinical measures is that clinical assessments could be provided in many clinical or private practice settings, especially in geographic locations were large hospitals or advanced medical care is not readily accessible.

The Goal of this Study

The progressive decline and impairment of even basic functions have been well studied in ALS. Previous research has investigated the effects of ALS on speech, swallowing and respiratory function. Limited research has been completed examining the relationship between decline in speech, swallowing and respiratory function in ALS (Strand et al., 1996) and individual self-assessment of dysphagia severity (Silbergleit et al., 2012). Predictive measures are more abundant in healthcare and have proved beneficial in predicting length of survival based on FVC scores, future hospitalizations in congestive heart failure patients and exercise capacity in multiple sclerosis patients to name a few. There is an absence of foundational evidence on which to base any predictive measures regarding the severity of dysphagia in ALS. The goal of this investigation is to determine if the severity of dysphagia

in ALS can be predicted through common clinical tasks including DDK, FVC, number of swallows per bolus and patient dysphagia ratings on the DHI.

Research Questions

In order to better understand the correlation between speech and swallowing functions and the severity of dysphagia in individuals with ALS with bulbar involvement, the following research questions were examined in this study: 1) Do individuals diagnosed with ALS with bulbar involvement perform significantly different on clinical measures (DDK, FVC, DHI, and tired level) and on objective swallowing measures (PAS, pharyngeal residue and number of swallows per bolus) when compared to a control group? 2) Are there significant correlations between clinical measures and objective swallowing measures which would support the theory that swallowing function could be predicted in individuals with ALS? 3) In the ALS group, is there a significant correlation between type of symptom onset, duration of disease, and body mass index with the clinical assessment measures and objective swallowing measures?

Working Hypotheses

Hypotheses for this dissertation are summarized as follows.

Research Hypothesis #1

H_0: There will not be a significant difference in performance on DDK, FVC, PAS pharyngeal residue, DHI, or number of swallows between the ALS group in comparison to the control group.

H_1: There will be a significant difference in performance on DDK, FVC, PAS pharyngeal residue, DHI, and number of swallows per bolus trial between the ALS group in comparison to the control group.

It is expected that the ALS group will demonstrate impairments in all assessment areas resulting in rejection of the null hypothesis.

Research Hypothesis #2

H_0: There will not be significant correlations between DDK with PAS and pharyngeal residue scale results.

H_1: There will be significant correlations between DDK with PAS and pharyngeal residue scale results.

It is expected that subjects who present with greater impairments in DDK will have more severe impairments on both swallowing function measures as a result of weakness and reduced oral motor movements resulting in rejection of the null hypothesis.

Research Hypothesis # 3

H_0: There will not be significant correlations between number of swallows per bolus with PAS, pharyngeal residue scale, DDK and FVC results.

H_1: There will be significant correlations between number of swallows per bolus with PAS, pharyngeal residue scale, DDK and FVC results.

It is expected that there will be a relationship between number of swallows and PAS, pharyngeal residue scale, DDK, and FVC performance resulting in rejection of the null hypothesis.

Research Hypothesis # 4

H_0: There will not be significant correlations between FVC with PAS and pharyngeal residue scale results.

H_1: There will be significant correlations between FVC with PAS and pharyngeal residue scale results.

It is expected that subjects who present with impaired FVC will exhibit more significant impairments on both swallowing function measures resulting in rejection of the null hypothesis.

Research Hypothesis # 5

H_0: There will not be significant correlations between DHI with PAS, pharyngeal residue scale, DDK and FVC results.

H_1: There will be significant correlations between DHI with PAS, pharyngeal residue scale, DDK and FVC results.

It is expected that the scores on a patient reported outcomes tool for swallowing function will be positively related to impairments on both swallowing measures resulting in rejection of the null hypothesis.

Research Hypothesis #6

H_0: There will not be a significant correlation, in the ALS group, between duration of disease, type of symptom onset, ALS-FRSR score or body mass index with performance on DDK, FVC, PAS, pharyngeal residue scale, number of swallows per bolus, or DHI.

H_1: There will be a significant correlation, in the ALS group, between duration of disease, type of symptom onset, ALS-FRSR score or body mass index with performance on DDK, FVC, PAS, pharyngeal residue scale, number of swallows per bolus, or DHI.

Based on previous research it is likely that ALS-FRSR, symptom duration and type of onset will be significantly correlated to clinical and objective swallowing measures

resulting in rejection of the null hypothesis. It is questionable if there will be a significant correlation with BMI.

Research Hypothesis # 7

H_0: There will not be significant interactions of DDK and FVC with PAS and pharyngeal residue scale results.

H_1: There will be significant associations of DDK and FVC with PAS and pharyngeal residue scale results.

It is expected that the combination of impairment in both FVC and DDK will result in abnormal results on the swallowing function measures. Impairments in diadochokinesis will likely have the greatest effect on overall swallowing function and result in more severe ratings on the PAS and pharyngeal residue scale. Impairment in FVC will affect swallowing function but not to the same degree as impaired DDK resulting in rejection of the null hypothesis.

Expected Outcomes

Based upon previous research, it is expected that performance on clinical assessment measures will significantly correlate with severity of dysphagia documented during the FEES assessment through PAS, pharyngeal residue and number of swallows per bolus. Previous studies have identified that impairment in oral motor movements and respiratory function increase the risk of dysphagia and aspiration in individuals with ALS. This study may provide foundational data for a protocol to predict the severity of dysphagia in patients with ALS.

It is also expected that the ALS group will be significantly more impaired on all measures in comparison with the control group. It is expected that certain historical data (duration of symptoms, type of onset, ALS-FRSR and potentially BMI) will significantly

correlate with impairments in DDK, FVC, PAS, pharyngeal residue, number of swallows per bolus or the DHI.

CHAPTER 3

METHODS

Subject Characteristics and Selection

A total of 33 participants (18 subjects with ALS and 15 controls) were included in this study. All participants with ALS had an El Escorial World Federation of Neurology (Brooks, 1994) criteria diagnosis of probable or definite ALS, as determined by a Neurologist, and presence of oral motor or speech symptoms consistent with bulbar dysfunction, as determined by a Speech-Language Pathologist. Bulbar dysfunction was defined as impairments in oral motor, speech/voice or swallowing function (Carrow et al., 1974; Chen, 2005; Hillel, 1999).

Subject recruitment was conducted from October 2012 thru May 2014 in the Harry J. Hoenselaar ALS Multidisciplinary Clinic in the Neurology Department at Henry Ford Hospital, Detroit, Michigan. Subjects were recruited during a regularly scheduled clinic visit. All subjects were between 40 and 85 years of age. Inclusion and exclusion criteria were developed in an effort to obtain speech, swallowing and respiratory deficits solely attributed to ALS. All subjects and controls spoke Standard American English as their first language, and did not have a previous history of neurological or speech disorders. Tobacco use was documented and subjects with current use or history of use were included. Subjects were excluded if they had a documented history of emphysema, chronic obstructive pulmonary disease or other remarkable respiratory impairment unassociated with ALS. Individuals with any history of head and neck cancer or radiation or surgical intervention to the oral pharyngeal region were also excluded.

Patient subjects were divided into three groups based upon respiratory function (normal, mildly impaired, and moderately impaired). Respiratory function was determine by

performance on forced vital capacity assessment where groups were defined as: 1) normal function as determined by FVC performance of greater than 80% predicted capacity; 2) mildly impaired as determined by FVC performance between 65-79% predicted capacity and 3) moderately impaired as determined by FVC performance between 50-64% predicted capacity (Schmidt et al., 2006). Group A consisted of 9 subjects (4 males and 5 females) diagnosed with ALS and presented with oral motor or speech abnormalities and normal respiratory function (greater than 80% predicted). Group B was composed of 4 subjects (4 females) diagnosed with ALS and presented with oral motor or speech abnormalities and mild respiratory impairment (between 65-79% predicted). Group C included 5 subjects (2 males and 3 females) diagnosed with ALS and presented with oral motor or speech abnormalities and moderate respiratory impairment.

There were 148 ALS patients screened over 339 clinic visits. Of these, 87 (59%) were male and 61 (41%) female. Forty patients met the inclusion criteria on at least one visit and 18 (45%) were enrolled. Of the 22 patients who refused enrollment, 15 stated they were too tired and 9 declined to due the necessity of having a nasopharyngeal scoping procedure as part of the swallowing examination. Of the 108 patients excluded, the most common reasons were presence or history of another neurologic condition (n=28, 26%) including stroke, seizure or a dementing process, total nutritional dependence by feeding tube (n=21, 19%) and FVC below 50% predicted (n=21, 19%).

The ALS participant group was composed of 6 males and 12 females with an age range of 54-82 years of age, with a mean age of 67.9 years. The age range for male participants was 55-78 years of age, with a mean age of 68.7 years. The age range of female participants was 54-82 years of age, with a mean age of 67.6 years.

The control group was composed of 4 males and 11 females with an age distribution similar to that of the ALS subject group. The age range for all control subjects was 58-84 years of age, with a mean age of 65.4 years. The age range for male controls was 59-69 years of age, with a mean age of 64.3 years. The age range of female controls was 58-84 years of age, with a mean age of 65.8 years.

All participant data were coded for privacy. Participants in the ALS group were coded with ALS, a number and then a gender indicator. Control group participants were coded with CON, a number and a gender indicator.

Testing Procedures and Instrumentation

In this study, standardized clinical assessment batteries and self-report questionnaires were used to evaluate the speech, respiratory and swallowing function of the all participants in the ALS and control groups. Assessment measurements included: 1) Oral motor and speech examination for symptoms consistent with bulbar dysfunction; 2) Questionnaire for inclusion and tiredness scale; 3) Dysphagia Handicap Index (DHI) (Silbergleit et al., 2012); 4) Forced Vital Capacity; 5) Diadochokinesis; 6) Swallowing function assessment with Fiberoptic Endoscopic Evaluation of Swallowing (FEES) (Langmore, Schatz, & Olsen, 1988) with impairment ratings using the Penetration-Aspiration Scale (Rosenbek et al., 1996) and a pharyngeal residue scale (Kelly et al., 2008); and 7) Documentation of the number of independent swallows generated for each bolus trial. Additional information was collected for all subjects with ALS including: Amyotrophic Lateral Sclerosis-Functional Rating Scale-Revised (ALS-FRSR) (Appendix A), date of diagnosis, and height and weight on the date of study participation (Appendix B), reported onset date, area of weakness complaint (bulbar, axial or mixed) and ALS-FRSR scores (Appendix C). All assessments were completed

during one clinic visit. Instrumentation was calibrated by the principle investigator or a member of the research team. A testing effect was not a concern since each subject was only assessed one time.

Oral Motor Examination

Oral motor assessments included an evaluation of labial appearance, retraction, protrusion and seal; lingual appearance and range of motion; palatal appearance and elevation.

Questionnaire:

All subjects were asked a series of questions to verify their appropriateness for this study (Appendix D). The questionnaire included standard questions to identify possible impairments in speech, swallowing and/or breathing which could be attributed to a disorder other than ALS. In addition to inclusion/exclusionary questions, age and tobacco use was also documented. A history of tobacco use was reported for three females in both the ALS and control groups and two male in both ALS and control groups.

Dysphagia Handicap Index

The Dysphagia Handicap Index is a patient reported outcomes tool that assesses the handicapping effects of dysphagia and allows subjects to rank their own swallowing ability in a series of 25 questions that cover physical, emotional and functional aspects of swallowing (Appendix E). There were nine questions for both the function and physical sections and seven questions for the emotional section. One of the emotional questions was excluded as a result of a typographical error. The statement read “I feel depressed because I can’t eat when I want” instead of “I feel depressed because I can’t eat what I want.” Subjects were asked to respond to each question regarding their swallowing difficulty as occurring always (4 points), sometimes (2 points), or never (0 points). In addition, each subject provided a self-reported

severity of dysphagia on a 7-point scale with 1 being normal and 7 being a severe problem. Results were recorded based on categorical aspects of swallowing (physical, emotional and functional), overall score and self-reported severity of dysphagia (Appendix F).

Tired Rating

All subjects were asked to rate how tired they were on a 7-point scale from 1 (normal baseline) to 7 (severely tired) at the time of this study (Appendix G). This information was obtained to determine if general fatigue or level of tiredness contributed to swallowing function.

Forced Vital Capacity (FVC)

Forced vital capacity (FVC) is a measurement of maximal inhalation to total lung capacity, followed by immediate forced rapid exhalation for as long as possible, then completed with immediate maximal inhalation back to total lung capacity (Gold, 2000). FVC measurement is calculated in terms of percent predicted capacity based upon standardized data for gender, age, height and weight. The median percent predicted value based on gender, height, weight and age is considered 100% (Stanojevic et al., 2008). As a result, it is possible for a person to have an FVC of greater than 100% predicted.

FVC measurements were collected using a handheld SpiroPro+ from Jaeger with mouth piece. A nasal closure was assured with a nasal occlusive device. The SpiroPro+ Version V2.32 04.05.2006 had a calibration of 0.99%. Subjects were instructed to place the mouth piece between the lips and teeth and to "close lips firmly around the mouthpiece creating a seal; slowly inhale to take a full deep breath and then forcefully exhale as hard, fast and long as possible." During exhalation, encouragement was provided by the examiner to

"blow hard" and "keep going". FVC measurement was performed one time per subject and recorded first manually and then transferred to an Excel Spreadsheet (Appendix G).

Diadochokinesis

Each subject performed one trial of each of the diadochokinetic tasks /pʌ/, /tʌ/, /kʌ/ and /pʌtʌkʌ/ in the same order following the examiners instructions and demonstration.

The subjects were instructed to "take a deep breath and say the syllable /pʌ/ as quickly and evenly as possible for approximately 7 seconds, until requested to stop" by the investigator. Then the examiner demonstrated the task, taking a deep breath and repeating /pʌpʌpʌ.../. The examiner repeated these instructions for each additional syllable target, /tʌ/, /kʌ/ and /pʌtʌkʌ/. All productions were monitored and redirection was provided as necessary. The consonant-vowel combinations were selected due to their frequent use in clinical speech assessments for the evaluation of three major articulatory organs: lung, tongue tip and tongue dorsum, in addition to relatively low cognitive burden.

Recording

All diadochokinesis speech productions were digitally recorded using an Olympus WS-300M digital voice recorder and a Shure headset microphone placed 5 centimeters from the subjects mouth (Svec & Granqvist, 2010). The recording of all speech productions for each subject was transferred from the Olympus WS-300M digital recorder to a computer with Praat software for speech analysis. Praat software displayed a speech waveform for every speech production as well as a time stamp. During the Praat assessment, a 5 second voice production segment was analyzed. Data analysis was initiated after approximately one second of speech production for each task. Speech productions were calculated for total productions during continuous production of five seconds. The total number of speech productions over a

5 second period was then averaged to determine average productions per second (Appendix H).

Fiberoptic Endoscopic Evaluation of Swallowing (FEES)

The basic FEES protocol as outlined in Langmore, Schatz & Olsen (1988) was used as a guideline for placement of nasendoscope with the subject sitting comfortably upright in a chair. A flexible nasendoscope was passed through the most patent nostril as determined by patient report and visual observation by the primary investigator. This procedure was performed without administration of topical anesthetics or vasoconstrictor application to the nasal passage to eliminate the potential for adverse anesthetic reactions (Aviv, Kaplan, & Langmore, 2001). FEES equipment consisted of a 3.6 millimeter diameter flexible fiberoptic rhinolaryngoscope (Olympus, ENF-P3P4), light source (Olympus CLK-4), camera (ELMO), an ACER color monitor and hard drive. All data for subjects and controls was recorded on the system hard drive and backed up on DVD. The FEES assessment provided visualization of the oral-pharyngeal and pharyngeal phases of swallowing except for a brief period when base of tongue retraction and inversion of the epiglottis obstructed the view of the larynx at the height of the swallow. Liquid bolus amounts were measured using a 60mL syringe. The desired amount was placed in a 6 ounce Styrofoam cup. All thin liquid and pudding boluses were dyed blue with food coloring for improved visualization and given in the following order: 1) 10mL thin liquid bolus by straw, 2) 30mL thin liquid bolus by straw, 3) 3 ounce thin liquid bolus by straw, 4) 5mL puree bolus (leveled teaspoon), 5) 5mL puree bolus (leveled teaspoon), and 6) one inch by one inch piece of graham cracker. The monitor was shielded from the subject. No visual or verbal feedback was provided during the assessment.

Bolus trials were provided in the same order for all participants. Participants were handed the premeasured amount of liquid in 6 ounce Styrofoam cup with a straw. The instructions were to drink all the liquid in the cup and swallow as many times as necessary. All participants swallowed the entire measured amount for each trial, except for one female ALS subject she frank aspiration resulted in early termination (after 46mL) of the 3 ounce thin liquid trial.

Swallowing Measures

After a subject completed the FEES, the swallow evaluation was reviewed in real-time and slow motion to collect the following data for each trial: counting the initial swallow and number of successive swallows per bolus trial, and rating swallowing function with the Penetration-Aspiration Scale (PAS) (Rosenbek et al., 1996), and the Pharyngeal Residue Scale (Kelly et al., 2008). The PAS is an 8-point ordinal scale of swallowing severity dependent on the depth of events of laryngeal airway penetration and tracheal aspiration as well as patient reaction to those events (Appendix I). PAS analysis occurred throughout all swallows for each bolus. The most severe rating, at any point during each trial was documented for that trial. The pharyngeal residue scale (Kelly et al., 2008) was also utilized for each bolus trial. Approximately 10 seconds after all oral pharyngeal movements ceased, the subject was asked, "Are you done swallowing?" At that time the pharyngeal residue was rated on a 5 point ordinal scale (Appendix I).

All data were recorded on the FEES Rater Sheet (Appendix I) and then transferred to the Electronic Data Sheets. All data was organized by group and task in the following order: 1) PAS ratings: female ALS group, male ALS group, and control group (Appendix J); 2) Pharyngeal residue ratings: female ALS group, male ALS group, and control group

(Appendix K); and 3) Number of swallows per bolus: female ALS group, male ALS group, and control group (Appendix L).

Data Processing and Statistical Analysis Procedures

When comparing the ALS patients to the control subjects, chi-squared tests were used for the categorical variables. For the continuous variables, a two sample t-test was used for age and Wilcoxon two sample tests were used for FVC and the DHI, DDK and FEES measurements. For assessing associations among the FVC, DHI, DDK and FEES measurements, Spearman's correlation coefficients were used. These nonparametric methods of Wilcoxon tests and Spearman's correlations were done because the variables did not always follow a normal distribution or were measured on an ordinal scale. Similar tests were used when assessing the association of ALS characteristics with the FVC, DHI, DDK and FEES measurements. All testing was done at the 0.05 level. Statistical analyses were performed using SAS version 9.4 (SAS, 2014). Agreement between readers for the FEES measurements was assessed using kappa statistics for the ordinal responses of aspiration and residue and intraclass correlation coefficients for number of swallows.

Interrater Reliability

Preliminary interrater reliability was established between two experienced Speech-Language Pathologists who ranked the swallowing function of 15 individual (91 individual swallows) FEES examinations selected randomly from a clinical database. The SLPs independently rated each swallow and compared severity rankings on the PAS and residue scales. Cohen's Kappa analysis for interpreter reliability revealed very good to excellent agreement between the two raters with kappa values of 0.75 for PAS and 0.72 for pharyngeal residue scale.

Interrater reliability was conducted all recorded swallow trials for this study. Each of the two Speech-Language Pathologists, the Primary Investigator and one other SLP trained in the FEES procedure, individually ranked the swallowing function of all 32 participants (169 unique swallowing trials). Swallowing rankings included the number of swallows per bolus trial, a Penetration-Aspiration Scale rating for each bolus trial, and a residue severity rating for each bolus trial.

CHAPTER 4

RESULTS

The primary purpose of this investigation was to examine potential correlations between commonly utilized clinical measures to assess speech and respiratory function with swallowing ability in individuals with ALS. ALS group performance was compared to performance of a control group of similar age and gender composition.

Interrater Reliability Rating

All FEES measurements were rated independently by two reviewers. Their results were assessed for agreement. All individuals of the ALS group and control group were included in the following analyses. For the measurements of PAS and pharyngeal residue, regular Kappa statistics and weighted Kappa statistics were computed, along with their 95% confidence intervals. Regular Kappa statistics do not distinguish between different levels of agreement where as weighted Kappa statistics account for disagreement between adjacent levels in a different weight compared to discordances of more than one level. Due to the ordinal nature of the measurements, weighted kappa statistics were utilized for interpretation of the analysis. For the measurement of number of swallows, the intra-class correlations coefficients (ICC) were computed, along with their 95% confidence intervals. Landis and Koch (1977) provided interpretation for levels of agreement using these statistics. Proposed values of agreement were as follows: <0 as poor, 0 to .2 as slight, 0.21 to 0.4 as fair, 0.41 to 0.6 as moderate, 0.61 to 0.8 as substantial and >0.8 as almost perfect agreement.

Measures of agreement for PAS and residue were determined for six different bolus trials per individual (Table 1). Levels of agreement for the PAS ranged from moderate to almost perfect for the weighted Kappa analysis. The range of agreement for the pharyngeal residue

measure varied from substantial to almost perfect for the weighted Kappa results. The level of agreement was almost perfect for measurement of the number of swallows (Table 2).

Comparison of ALS and Control Group Performance

Performance on all tasks was assessed for significance between individuals in the ALS group and the control group. Various analyses were utilized to determine significance including two sample t-test, chi-square test and Wilcoxon two sample test. The Wilcoxon two sample test was selected, over the two sample t-test to compare scores between the ALS and control group because of unequal variability between the groups and/or measurements using an ordinal scale.

Demographics and FVC

Analysis of the demographic composition did not reveal significant differences in age, gender or history of tobacco use. Significant differences were present with FVC %, a continuous measure ($p=<0.001$), and FVC categories ($p=0.004$). FVC performance for all control group participants was above the 80% predicted threshold for the within normal limits (WNL) category, while ALS participant performance was dispersed throughout all three categories, WNL, mild and moderate (Table 3).

DHI and Tired Rating

Performance on the DHI and tired rating measures were assessed with Wilcoxon two sample tests. Significant differences were present between ALS subjects and controls on all measures of the DHI (Physical, Functional, Emotional, Overall rating and Self-reported Severity of Dysphagia) as well as self-reported tired rating at the time of the study (Table 4). The lowest level of significance on these measures was $p=0.018$. ALS subjects consistently reported higher ratings in all categories of the DHI and on the tired rating.

DDK, Number of Swallows, PAS and Pharyngeal Residue

Individuals in the control group produced significantly more target repetitions per second than ALS subjects across all variables (p=0.001 or p=<0.001) (Table 5). Controls achieved 2 more productions of /pʌ/, /tʌ/ and /kʌ/ per second in comparison to subjects with ALS. The repetition rate for /pʌtʌkʌ/ was also significantly reduced in the ALS group at a rate of 1.3 repetitions per second in comparison to 2 repetitions per second in the control group.

Significant differences were present between the ALS group and the control group for number of swallows for both the thin liquid 30mL (p=0.009) and thin liquid 3 ounce (p= 0.002) boluses. No significant differences were present for number of swallows with thin liquid 10mL, puree or solid bolus trials (Table 6). There was a significant difference for PAS measure ratings for all consistencies and trials with the exception of thin liquid 10mL (Table 7).

Significant differences were discovered in severity of pharyngeal residue after both the initial swallow and after the final swallow of various consistencies (Tables 8 and 9). Significantly increased pharyngeal residue severity, after the initial swallow, was present in the ALS group with thin liquid 30mL, thin liquid 3 ounces and puree #2 boluses. The control group severity was most often rated as coated, whereas the ALS group was frequently rated as mild with a few in the moderate range. Individuals in the ALS group had significantly higher, more severe, pharyngeal residue scale ratings after the final swallow for puree and solid boluses. There was not a significant difference in pharyngeal residue ratings after the final swallow for thin liquid bolus trials despite increased pharyngeal residue severity ratings for ALS subjects.

ALS Group Correlations for Speech, Respiration and Swallowing Measures

Correlations between DDK and FVC with Swallowing Measures

Within the ALS group, correlations between speech, respiration and swallowing measures were assessed. Correlations between PAS severity ratings for all 6 bolus trials with the four DDK measures and FVC were examined (Table 10). Significant negative correlations between PAS and /kʌ/ per second with thin liquid 10mL ($r = -0.504$, $p = 0.046$), and between PAS and /pʌtʌkʌ/ per second for thin liquid 10mL ($r = -0.556$, $p = .025$). There were also significant negative correlations between PAS ratings for thin liquid 3oz and FVC ($r = -0.540$, $p = 0.046$). The ratings of swallowing impairment increased as FVC performance and DDK productions per second decreased.

Pharyngeal residue severity ratings for all 6 bolus trials were examined for significant correlations at two discrete periods (after the initial swallow and after the final swallow) during each trial with the four DDK measures and FVC performance (Table 11). Significant negative correlations were found between pharyngeal residue ratings for the second puree 5mL bolus and solid bolus with DDK production /kʌ/ per second. A significant negative correlation was also present with pharyngeal residue rating for thin liquid 10mL and DDK production of /pʌtʌkʌ/ per second ($r = -0.560$, $p = 0.024$). The volume of pharyngeal residue increased as DDK production decreased. There were no significant correlations between FVC performance with either period of pharyngeal residue severity analysis. There were no significant correlations between pharyngeal residue after the first swallow of a bolus and DDK (Table 12)

Correlations between Number of Swallows with Swallowing Measures, DDK and FVC

Number of swallows per bolus was also analyzed for potential correlations with the PAS, the pharyngeal residue scale, DDK, FVC and DHI (Tables 13, 14 and 15). Significant positive correlations were determined between the number of swallows per bolus and the severity of PAS rating and pharyngeal residue severity rating after the final swallow with thin liquid 10mL bolus trials (Table 14). The severity of the PAS rating for puree bolus #1 and solid bolus were also positively associated with number of swallows per bolus trial. No significant correlations were revealed between DDK and FVC with number of swallows per bolus trial (Table 13).

Correlations between the DHI with Swallowing Measures, DDK and FVC

Significant correlations were present between the DHI with the PAS, the pharyngeal residue scale, DDK and FVC. Significant positive correlations were found between the PAS rating for thin liquid 30mL and the Functional, Emotional and Dysphagia Self-rating subscales of the DHI. Significant positive correlations were present between the PAS severity rating for thin liquid 3 ounce bolus trial and all of the DHI scales except the physical subscale. Levels of significance for both 30mL and 3 ounce thin liquid boluses were between $p = 0.001$ and $p = 0.039$ (Table 16).

Significant positive correlations were present for all DHI scales with pharyngeal residue severity (after the final swallow) for at least one bolus trial (Table 17). The puree bolus trial number two had a significant positive correlation with the Physical and Overall scales of the DHI. Pharyngeal residue severity for thin liquid 10mL has a significant positive correlation with the Functional, Overall, and Dysphagia Self-Rating scales of the DHI. There was a significant positive correlation between the Emotional, Overall and Dysphagia Self-Rating scales of the DHI and pharyngeal residue severity, after the final swallow, with solid boluses.

Pharyngeal residue rating severity for 30mL was also significantly positively correlated with Functional scale severity on the DHI.

No significant correlations were present with DHI and pharyngeal residue after the initial swallow with any bolus trial (Table 18). Significant negative correlations existed between the Functional scale of the DHI and the FVC percentage ($r = -0.517$, $p = 0.028$), and between the Emotion scale of the DHI and the Ka/second DDK measure ($r = -0.502$, $p = 0.034$) (Table 19).

Analysis of ALS Aspiration/Non-Aspiration Groups with Clinical Assessments and Swallowing Measures.

Swallowing ability was assessed categorically within the ALS group to evaluate for significant correlations between aspirators and non-aspirators. This analysis combined PAS ratings 1-5 (no aspiration) and 6-8 (aspiration) (Tables 20-22). Significant correlations were found between aspiration and non-aspiration groups with the thin liquid 10mL trial (Table 20) and ka/second, $p = 0.024$. The non-aspiration group produced twice as many targets per second on average as the aspiration group.

Significant correlations were present between aspirators and non-aspirators with the thin liquid 30mL bolus (Table 21) and the Functional DHI scale ($p = 0.049$), Emotional ($p=0.04$) and Self-Rating of Swallowing ($p = 0.029$). Functional DHI scores on average were 2.87 times greater for the aspiration group (14.75) than the non-aspiration group (5.14). For the mean Emotional DHI score, the aspiration group was 5.42 times higher than the non-aspiration group. Self-Reported Severity of Dysphagia scores were 2.59 times greater (i.e., indicating more severe impairments in swallowing ability) for the aspiration group (4.06) in comparison to the no aspiration group (1.57). Significant differences were also present between PAS severity rating of thin liquid 3 ounces trials (Table 22) with the following DHI

severity scales: Functional (p = 0.030), Emotional (p = 0.016), Overall (0.034) and Self-Rating of Swallowing (p = 0.043). On average, the aspiration group reported a severity level that was more than twice as much compared to the non-aspiration group. PAS categories were not assessed with puree #1, puree #2 or solid boluses due to the limited number of aspiration events.

Analysis of Duration of Disease, Onset, ALS-FRSR and BMI with Clinical and Swallowing Measures in the ALS Group

During the course of the study, several additional factors were identified for analysis. These factors included: type of ALS symptom onset, duration of ALS disease at time of study completion, body mass index (BMI) at the time of study completion and total ALS-FRSR score. These factors were analyzed to determine if any correlations existed with the primary assessment measures (FVC, PAS, pharyngeal residue, DDK and DHI).

There were no significant correlations between FVC categories (WNL, Mild, Moderate impairment) and DHI measures, DDK performance, PAS severity, pharyngeal residue severity or number of swallows per bolus (Table 23-27). Analysis between type of onset (bulbar, axial and mixed) and DHI scores revealed significant correlations with the Physical and the Self-Reported Severity of Dysphagia Rating (Table 28). In both DHI measures the bulbar onset group reported the most severe ratings, the mixed onset group second most severe and the axial onset group with the least impairments. The bulbar onset group scored more than twice as high (more severe) as the other two groups. Significant differences were present between type of onset and PAS severity with thin liquid 10mL (Table 29) and with pharyngeal residue severity with thin liquid 30mL (Table 30). The bulbar onset group demonstrated the greatest impairments on both the PAS and pharyngeal residue scales. Eighty percent of the bulbar onset group, 13% of the axial group and 0% of the mixed

group received the most severe PAS rating score for thin liquid 10mL. There were no significant correlations between type of onset and DDK or FVC (Table 31).

Seventeen of the ALS participants had duration of symptoms less than four years, while one patient has had symptoms for over 15 years. Analyses for duration of ALS symptoms were done for all ALS participants, as well as only those with duration within the last four years. Significant positive correlations between duration of ALS symptoms (including all participants) with PAS score for puree #2 ($r = 0.517$, $p = 0.040$) and with number of swallows for thin liquid 3oz and puree #1 (Tables 32 and 33) were noted. No significant associations were found between duration of ALS symptoms (all participants) and DDK, FVC, DHI or pharyngeal residue measures (Tables 34-36). Significant positive correlation was present between duration of ALS symptoms (within 4 years) and number of swallows for thin liquid 3oz and puree#1 (Table 37). No significant correlations were present between duration of ALS symptoms (within 4 years) and DDK, FVC, DHI, pharyngeal residue or PAS ratings (Tables 38-41).

A significant positive correlation was present between total ALS-FRSR score and number of swallows for thin liquid 10mL and solid boluses ($r = 0.569$, 0.574 and $p = 0.021$, 0.016 respectively) (Table 42). There were no significant correlations between total ALS-FRSR and DDK, FVC, DHI, PAS or pharyngeal residue (Tables 43-46).

Analyses were completed to examine the correlation between body mass index (BMI) rating of normal or overweight/obese and with FVC, DDK, DHI, PAS severity, pharyngeal residue severity and number of swallows per bolus. There was a significant difference in pharyngeal residue of thin liquid 30mL between the normal or overweight/obese BMI groups (Table 47). Eighty-eight percent of the ALS participants in the overweight/obese BMI

category had mild residue compared to only 29% of the subjects with normal BMI category. There were no significant correlations between BMI and DDK, FVC, DHI or PAS measures (Tables 48-51).

Table 1: Measurements of Interrater Agreement for PAS and Pharyngeal Residue				
	PAS		Residue	
Bolus	Kappa w/ 95%CI	Weighted Kappa w/ 95%CI	Kappa w/ 95%CI	Weighted Kappa w/ 95%CI
Thin liquid 10ml	0.54 (0.34,0.74)	0.72 (0.56, 0.89)	0.83 (0.64, 1.00)	0.85 (0.70, 1.00)
Thin liquid 30ml	0.67 (0.48, 0.86)	0.81 (0.68, 0.95)	0.70 (0.45, 0.94)	0.73 (0.50, 0.96)
Thin liquid 3oz	0.54 (0.33, 0.75)	0.77 (0.65, 0.90)	0.72 (0.50, 0.94)	0.76 (0.56, 0.96)
Puree 1	0.70 (0.48, 0.93)	0.83 (0.67, 0.98)	0.63 (0.37, 0.89)	0.69 (0.47, 0.92)
Puree 2	0.65 (0.44, 0.87)	0.86 (0.74, 0.98)	0.72 (0.51, 0.94)	0.77 (0.59, 0.95)
Solid	0.44 (0.20, 0.67)	0.58 (0.30, 0.85)	0.59 (0.38, 0.81)	0.74 (0.59, 0.88)

Table 2: Measurements of Interrater Agreement for Number of Swallows	
Bolus	ICC w/ 95% CI
Thin liquid 10ml	0.98 (0.96, 0.99)
Thin liquid 30ml	0.98 (0.96, 0.99)
Thin liquid 3oz	0.81 (0.65, 0.90)
Puree 1	0.89 (0.79, 0.94)
Puree 2	0.95 (0.90, 0.97)
Solid	0.91 (0.83, 0.95)

Table 3: Demographic and FVC for ALS and Control subjects				
Variable	Response	ALS patients (N= 18)	Controls (N= 15)	p-value
Age	Mean ± S.D	67.9 ± 8.7	65.5 ± 8.2	0.409[a]
	Median (Range)	66 (54 to 82)	63 (58 to 84)	
Gender	F	12 (67%)	11 (73%)	0.678[b]
	M	6 (33%)	4 (27%)	
Tobacco History	N	13 (72%)	10 (67%)	0.730[b]
	Y	5 (28%)	5 (33%)	
FVC, %	Mean ± S.D	76.2 ± 16.7	110.7 ± 16.8	<.001[a]
	Median (Range)	79 (51 to 107)	112 (87 to 150)	
FVC categories	WNL	9 (50%)	15 (100%)	0.004[c]
	Mild	4 (22%)	0 (0%)	
	Moderate	5 (28%)	0 (0%)	

a -- p-value from two sample t-test.

b -- p-value from chi-square test.

c – p-value from Wilcoxon two sample test.

Table 4: DHI response and tired rating for ALS and Control subjects				
Variable		ALS patients (N= 18)	Controls (N= 15)	p-value[a]
Physical	Mean ± S.D	9.9 ± 6.5	3.9 ± 2.7	0.004
	Median (Range)	6 (2 to 22)	4 (0 t 10)	
Functional	Mean ± S.D	11.2 ± 9.6	0.1 ± 0.5	<.001
	Median (Range)	8 (0 to 30)	0.2 0 (0 to 2)	
Emotional	Mean ± S.D	4.9 ±5.8	0	0.001
	Median (Range)	2 (0 to 16)	All 0's	
Overall	Mean ± S.D	26.0 ± 19.8	4.0 ± 3.0	<.001
	Median (Range)	18 (6 to 68)	4 (0 to 12)	
Self-report	Mean ± S.D	3.0 ± 1.9	1.3 ± 0.6	0.006
swallowing difficulty	Median (Range)	2.5 (1 to 6)	1 (1 to 3)	
Tired Rating	Mean ± S.D	3.2 ± 2.0	1.5 ± 0.7	0.018
	Median (Range)	3.5 (1 to 7)	1 (1 to 3)	
a – p-value from Wilcoxon two sample test.				

Table 5: DDK information for ALS and control subjects				
Variable		ALS patients (N= 18)	Controls (N= 15)	p-value[a]
pʌ /sec	Mean ± S.D	3.6 ± 1.6	5.7 ± 0.6	<.001
	Median (Range)	3.3 (1.4 to 6.4)	5.6 (4.6 to 6.8)	
tʌ/sec	Mean ± S.D	3.2 ± 1.6	5.3 ± 0.7	0.001
	Median (Range)	3.1 (1 to 6.4)	5.2 (4.4 to 6.8)	
kʌ/ sec	Mean ± S.D	2.8 ± 1.3	5.1 ± 0.7	<.001
	Median (Range)	2.7 (1 to 5.8)	5.3 (4.2 to 6)	
pʌtʌkʌ/sec	Mean ± S.D	1.3 ± 0.6	2.0 ± 0.3	0.001
	Median (Range)	1.2 (0.4 to 2.066)	2 (1.6 to 2.6)	
a – p-value from Wilcoxon two sample test.				

Table 6: Number of swallows for ALS and control subjects				
Bolus	Response	ALS patients (N= 18)	Controls (N= 15)	p-value[a]
Thin liquid 10mL	Mean ± S.D	5.8 ± 5.2	3.4 ± 1.5	0.104
	Median (Range)	4 (2 to 22)	3 (2 to 7)	
Thin liquid 30 mL	Mean ± S.D	7.1 ± 4.9	3.9 ± 1.2	0.009
	Median (Range)	6 (1 to 22)	4 (2 to 6)	
Thin liquid 3 oz	Mean ± S.D	11.5 ± 4.6	6.3 ± 3.0	0.002
	Median (Range)	10 (6 to 23)	5 (4 to 13)	
Puree 5mL #1	Mean ± S.D	3.4 ± 1.9	2.9 ± 1.0	0.829
	Median (Range)	3 (1 to 8)	3 (2 to 5)	
Puree 5mL #2	Mean ± S.D	3.4 ± 2.2	2.9 ± 1.1	0.798
	Median (Range)	3 (1 to 10)	3 (2 to 5)	
Solid	Mean ± S.D	3.9 ± 2.1	3.1 ± 1.2	0.248
	Median (Range)	4 (1 to 9)	3 (1 to 5)	
a – p-value from Wilcoxon two sample test.				

Table 7: Penetration Aspiration Scale for ALS and control subjects				
Bolus	Response	ALS patients (N= 18)	Controls (N= 15)	p-value[a]
Thin Liquid 10 mL	Does not enter airway	5 (31%)	8 (53%)	0.158
	Enters airway, above VF, ejected from airway	2 (13%)	2 (13%)	
	Enters airway, above VF, not ejected from airway	2 (13%)	0 (0%)	
	Enters airway, contacts VF, ejected from airway	1 (6%)	0 (0%)	
	Enters airway, contacts VF, not ejected from airway	1 (6%)	5 (33%)	
	Enters airway, below VF, no effort made to eject	5 (31%)	0 (0%)	
Thin Liquid 30 mL	Does not enter airway	3 (20%)	10 (67%)	0.005
	Enters airway, above VF, ejected from airway	2 (13%)	1 (7%)	
	Enters airway, above VF, not ejected from airway	1 (7%)	1 (7%)	
	Enters airway, contacts VF, ejected from airway	0 (0%)	1 (7%)	
	Enters airway, contacts VF, not ejected from airway	1 (7%)	2 (13%)	
	Enters airway, below VF, not ejected from trachea despite effort	1 (7%)	0 (0%)	
	Enters airway, below VF, no effort made to eject	7 (47%)	0 (0%)	
Thin Liquid 3 oz	Does not enter airway	1 (7%)	9 (60%)	0.003
	Enters airway, above VF, ejected from airway	3 (21%)	3 (20%)	
	Enters airway, contacts VF, not ejected from airway	3 (21%)	0 (0%)	
	Enters airway, below VF, ejected into larynx or out of airway	0 (0%)	2 (3%)	
	Enters airway, below VF, not ejected from trachea despite effort	1 (7%)	1 (7%)	
	Enters airway, below VF, no effort made to eject	6 (43%)	0 (0%)	
Puree 5mL #1	Does not enter airway	8 (50%)	14 (93%)	0.014
	Enters airway, above VF, ejected from airway	1 (6%)	0 (0%)	
	Enters airway, above VF, not ejected from airway	4 (25%)	1 (7%)	
	Enters airway, contacts VF, not ejected from airway	2 (13%)	0 (0%)	
	Enters airway, below VF, no effort made to eject	1 (6%)	0 (0%)	
Puree	Does not enter airway	7 (44%)	12 (80%)	0.026

Table 7: Penetration Aspiration Scale for ALS and control subjects				
Bolus	Response	ALS patients (N= 18)	Controls (N= 15)	p-value[a]
5mL #2	Enters airway, above VF, ejected from airway	0 (0%)	1 (7%)	
	Enters airway, above VF, not ejected from airway	5 (31%)	2 (13%)	
	Enters airway, contacts VF, not ejected from airway	1 (6%)	0 (0%)	
	Enters airway, below VF, no effort made to eject	3 (19%)	0 (0%)	
Solid	Does not enter airway	7 (44%)	11 (73%)	0.037
	Enters airway, above VF, ejected from airway	2 (13%)	4 (27%)	
	Enters airway, above VF, not ejected from airway	2 (13%)	0 (0%)	
	Enters airway, contacts VF, not ejected from airway	4 (25%)	0 (0%)	
	Enters airway, below VF, no effort made to eject	1 (6%)	0 (0%)	
a – p-value from Wilcoxon two sample test.				

Table 8: Comparing Pharyngeal Residue after the Initial Swallow for ALS and Control subjects

Variable	Response	ALS patients (N= 18)	Controls (N= 15)	p-value[a]
Thin liquid 10ml	None	1 (6%)	2 (13%)	0.911
	Coating	6 (38%)	3 (20%)	
	Mild	8 (50%)	10 (67%)	
	Severe	1 (6%)	0 (0%)	
Thin liquid 30ml	Coating	3 (19%)	10 (67%)	0.004
	Mild	10 (63%)	5 (33%)	
	Moderate	3 (19%)	0 (0%)	
Thin liquid 3oz	None	0 (0%)	1 (7%)	0.010
	Coating	3 (19%)	9 (60%)	
	Mild	12 (75%)	5 (33%)	
	Moderate	1 (6%)	0 (0%)	
Puree 1	None	0 (0%)	1 (7%)	0.826
	Coating	6 (35%)	4 (27%)	
	Mild	10 (59%)	10 (67%)	
	Moderate	1 (6%)	0 (0%)	
Puree 2	Coating	1 (6%)	5 (33%)	0.038
	Mild	13 (81%)	10 (67%)	
	Moderate	2 (13%)	0 (0%)	
Solid	None	5 (29%)	6 (40%)	0.287
	Coating	3 (18%)	4 (27%)	
	Mild	6 (35%)	4 (27%)	
	Moderate	1 (6%)	1 (7%)	
	Severe	2 (12%)	0 (0%)	

[a]P-value from Wilcoxon two sample test.

Table 9: Pharyngeal Residue Scale after the Final Swallow for ALS and Control subjects

Variable	Response	ALS patients (N= 18)	Controls (N= 15)	p-value[a]
Thin liquid, 10mL	None	0 (0%)	2 (13%)	0.09
	Coating	5 (31%)	7 (47%)	
	Mild	11 (69%)	6 (40%)	
Thin liquid, 30 mL	None	0 (0%)	2 (13%)	0.054
	Coating	6 (40%)	9 (60%)	
	Mild	9 (60%)	4 (27%)	
Thin liquid, 3 oz	None	0 (0%)	3 (20%)	0.061
	Coating	8 (53%)	9 (60%)	
	Mild	7 (47%)	3 (20%)	
Puree, 5mL #1	None	0 (0%)	2 (13%)	0.015
	Coating	3 (18%)	7 (47%)	
	Mild	13 (76%)	6 (40%)	
	Moderate	1 (6%)	0 (0%)	
Puree, 5mL #2	None	0 (0%)	1 (7%)	0.006
	Coating	3 (18%)	9 (60%)	
	Mild	12 (71%)	5 (33%)	
	Moderate	2 (12%)	0 (0%)	
Solid	None	1 (6%)	9 (60%)	0.002
	Coating	4 (24%)	3 (20%)	
	Mild	10 (59%)	3 (20%)	
	Moderate	2 (12%)	0 (0%)	

a – p-value from Wilcoxon two sample test.

Table 10: Associations for PAS with DDK and FVC				
DDK	Bolus	N	Spearman's Correlation Coefficient	p-value
pʌ/sec	Thin liquid 10mL	16	-0.267	0.317
	Thin liquid 30 mL	15	-0.023	0.936
	Thin liquid 3 oz	14	-0.307	0.286
	Puree 5mL #1	16	0.088	0.747
	Puree 5 mL #2	16	-0.189	0.484
	Solid	16	0.036	0.895
tʌ/ sec	Thin liquid 10mL	16	-0.251	0.348
	Thin liquid 30 mL	15	-0.102	0.717
	Thin liquid 3 oz	14	-0.366	0.198
	Puree 5mL #1	16	0.209	0.437
	Puree 5 mL #2	16	-0.091	0.737
	Solid	16	0.174	0.519
kʌ/sec	Thin liquid 10mL	16	-0.504	0.046
	Thin liquid 30 mL	15	-0.261	0.348
	Thin liquid 3 oz	14	-0.509	0.063
	Puree 5mL #1	16	0.124	0.646
	Puree 5 mL #2	16	-0.087	0.750
	Solid	16	-0.032	0.907
pʌtʌkʌ/sec	Thin liquid 10mL	16	-0.556	0.025
	Thin liquid 30 mL	15	-0.092	0.746
	Thin liquid 3 oz	14	-0.236	0.417
	Puree 5mL #1	16	0.199	0.460
	Puree 5 mL #2	16	0.125	0.646
	Solid	16	0.084	0.756
FVC	Thin liquid 10mL	16	-0.366	0.164
	Thin liquid 30 mL	15	-0.314	0.255
	Thin liquid 3 oz	14	-0.540	0.046

Table 10: Associations for PAS with DDK and FVC				
DDK	Bolus	N	Spearman's Correlation Coefficient	p-value
	Puree 5mL #1	16	0.024	0.930
	Puree 5 mL #2	16	-0.295	0.268
	Solid	16	-0.340	0.198

Table 11: Associations for Pharyngeal Residue Scale (after final swallow) with DDK and FVC				
DDK	Bolus	N	Spearman's Correlation ~~Coefficient~~Coefficient	p-value
pʌ/sec	Thin liquid 10mL	16	-0.308	0.245
	Thin liquid 30 mL	15	0.174	0.535
	Thin liquid 3 oz	15	0.232	0.405
	Puree 5mL #1	17	0.385	0.127
	Puree 5 mL #2	17	-0.441	0.076
	Solid	17	-0.211	0.416
tʌ/sec	Thin liquid 10mL	16	-0.278	0.296
	Thin liquid 30 mL	15	0.158	0.574
	Thin liquid 3 oz	15	0.186	0.507
	Puree 5mL #1	17	0.424	0.089
	Puree 5 mL #2	17	-0.455	0.067
	Solid	17	-0.258	0.317
kʌ/sec	Thin liquid 10mL	16	-0.397	0.128
	Thin liquid 30 mL	15	-0.079	0.779
	Thin liquid 3 oz	15	0.171	0.542
	Puree 5mL #1	17	0.317	0.215
	Puree 5 mL #2	17	-0.512	0.036
	Solid	17	-0.484	0.049
pʌtʌkʌ/sec	Thin liquid 10mL	16	-0.560	0.024
	Thin liquid 30 mL	15	-0.159	0.572
	Thin liquid 3 oz	15	0.109	0.698
	Puree 5mL #1	17	0.296	0.248
	Puree 5 mL #2	17	-0.350	0.169
	Solid	17	-0.293	0.253
FVC	Thin liquid 10mL	16	-0.337	0.202
	Thin liquid 30 mL	15	-0.095	0.737
	Thin liquid 3 oz	15	-0.449	0.093
	Puree 5mL #1	17	0.344	0.176
	Puree 5 mL #2	17	0.060	0.818
	Solid	17	-0.139	0.594

Table 12: Associations of Pharyngeal Residue Scale (after first swallow) with DDK and FVC with residue after first swallow				
DDK	Bolus	N	Spearman's Correlation Coefficient	p-value
pʌ/sec	Thin liquid 10ml	16	-0.020	0.943
	Thin liquid 30ml	16	0.067	0.806
	Thin liquid 3oz	16	0.147	0.587
	Puree 1	17	0.170	0.515
	Puree 2	16	0.069	0.798
	Solid	17	-0.077	0.770
tʌ/sec	Thin liquid 10ml	16	0.060	0.825
	Thin liquid 30ml	16	0.067	0.806
	Thin liquid 3oz	16	0.145	0.592
	Puree 1	17	0.182	0.485
	Puree 2	16	0.179	0.508
	Solid	17	-0.047	0.857
kʌ/sec	Thin liquid 10ml	16	-0.205	0.446
	Thin liquid 30ml	16	-0.134	0.622
	Thin liquid 3oz	16	-0.098	0.717
	Puree 1	17	0.136	0.603
	Puree 2	16	-0.108	0.692
	Solid	17	-0.209	0.421
pʌtʌkʌ/sec	Thin liquid 10ml	16	-0.263	0.326
	Thin liquid 30ml	16	-0.067	0.806
	Thin liquid 3oz	16	-0.068	0.801
	Puree 1	17	0.303	0.237
	Puree 2	16	0.053	0.844
	Solid	17	-0.226	0.383
FVC, %	Thin liquid 10ml	16	-0.242	0.367
	Thin liquid 30ml	16	-0.399	0.126
	Thin liquid 3oz	16	0.049	0.858
	Puree 1	17	0.415	0.097

Table 12: Associations of Pharyngeal Residue Scale (after first swallow) with DDK and FVC with residue after first swallow				
DDK	Bolus	N	Spearman's Correlation Coefficient	p-value
	Puree 2	16	-0.128	0.638
	Solid	17	-0.033	0.901

Table 13: Associations for DDK and FVC with number of swallows				
Swallows	Bolus	N	Spearman's Correlation Coefficient	p-value
Thin liquid 10ml	pʌ/sec	16	0.039	0.886
	tʌ/sec	16	0.040	0.884
	kʌ/sec	16	-0.194	0.471
	pʌtʌkʌ/sec	16	-0.276	0.300
	FVC, %	16	-0.029	0.917
Thin liquid 30ml	pʌ/sec	15	0.316	0.252
	tʌ/sec	15	0.311	0.259
	kʌ/sec	15	0.000	1.000
	pʌtʌkʌ/sec	15	0.015	0.959
	FVC, %	15	0.097	0.730
Thin liquid 3oz	pʌ/sec	15	-0.178	0.526
	tʌ/sec	15	-0.163	0.563
	kʌ/sec	15	-0.312	0.257
	pʌtʌkʌ/sec	15	-0.190	0.497
	FVC, %	15	-0.139	0.622
Puree 5 mL #1	pʌ/sec	17	0.215	0.407
	tʌ/sec	17	0.323	0.206
	kʌ/sec	17	0.240	0.353
	pʌtʌkʌ/sec	17	0.161	0.537

Table 13: Associations for DDK and FVC with number of swallows				
Swallows	Bolus	N	Spearman's Correlation Coefficient	p-value
	FVC, %	17	-0.265	0.305
Puree 5 mL #2	pʌ/sec	17	-0.018	0.945
	tʌ/sec	17	0.101	0.701
	kʌ/sec	17	0.008	0.977
	pʌtʌkʌ//sec	17	0.017	0.949
	FVC, %	17	-0.156	0.551
Solid	pʌ/sec	17	0.257	0.320
	tʌ/sec	17	0.330	0.196
	kʌ/sec	17	0.095	0.717
	pʌtʌkʌ/sec	17	-0.024	0.928
	FVC, %	17	-0.264	0.305

Table 14: Association of PAS and residue with number of swallows					
		PAS		Residue	
Swallows	N	Spearman's Correlation Coefficient	p-value	Spearman's Correlation Coefficient	p-value
Thin liquid 10ml	16	0.689	0.003	0.522	0.038
Thin liquid 30ml	15	0.188	0.503	0.460	0.084
Thin liquid 3oz	14	0.329	0.251	0.158	0.574
Puree 5 mL #1	16	0.532	0.034	0.100	0.704
Puree 5 mL #2	16	0.440	0.088	0.034	0.896
Solid	16	0.631	0.009	-0.077	0.768

Table 15: Associations of DHI with Number of Swallows

Swallows	DHI	N	Spearman's Correlation Coefficient	p-value
Thin liquid 10ml	Physical	16	0.316	0.233
	Functional	16	0.435	0.092
	Emotional	16	0.205	0.446
	Overall	16	0.464	0.070
	Self-rating swallowing	16	0.293	0.271
	Tired Rating	16	-0.231	0.389
Thin liquid 30ml	Physical	15	0.269	0.331
	Functional	15	0.183	0.514
	Emotional	15	0.005	0.987
	Overall	15	0.194	0.488
	Self-rating swallowing	15	0.118	0.675
	Tired Rating	15	-0.344	0.209
Thin liquid 3oz	Physical	15	0.368	0.177
	Functional	15	0.364	0.182

Table 15: Associations of DHI with Number of Swallows				
Swallows	DHI	N	Spearman's Correlation Coefficient	p-value
	Emotional	15	0.113	0.689
	Overall	15	0.266	0.338
	Self-rating swallowing	15	0.150	0.593
	Tired Rating	15	-0.185	0.508
Puree #1	Physical	17	0.140	0.592
	Functional	17	0.235	0.365
	Emotional	17	0.095	0.717
	Overall	17	0.186	0.475
	Self-rating swallowing	17	-0.080	0.761
	Tired Rating	17	-0.143	0.583
Puree #2	Physical	17	0.225	0.386
	Functional	17	0.123	0.639
	Emotional	17	-0.097	0.710
	Overall	17	0.112	0.668

Table 15: Associations of DHI with Number of Swallows				
Swallows	DHI	N	Spearman's Correlation Coefficient	p-value
	Self-rating swallowing	17	-0.137	0.599
	Tired Rating	17	-0.446	0.073
Solid	Physical	17	0.166	0.524
	Functional	17	0.242	0.349
	Emotional	17	-0.041	0.876
	Overall	17	0.174	0.505
	Self-rating swallowing	17	0.030	0.908
	Tired Rating	17	-0.356	0.161

Table 16: Associations for Penetration-Aspiration Scale (PAS) with DHI				
DHI	Bolus	N	Spearman's Correlation Coefficient	p-value
Physical	Thin liquid 10mL	16	0.099	0.714
	Thin liquid 30 mL	15	0.059	0.835
	Thin liquid 3 oz	14	0.347	0.224
	Puree 5mL #1	16	-0.122	0.652
	Puree 5mL #2	16	-0.043	0.875
	Solid	16	0.002	0.993
Functional	Thin liquid 10mL	16	0.446	0.083
	Thin liquid 30 mL	15	0.545	0.035
	Thin liquid 3 oz	14	0.653	0.011
	Puree 5mL #1	16	-0.102	0.707
	Puree 5mL #2	16	0.049	0.858
	Solid	16	0.286	0.283
Emotional	Thin liquid 10mL	16	0.256	0.339
	Thin liquid 30 mL	15	0.538	0.039
	Thin liquid 3 oz	14	0.771	0.001
	Puree 5mL #1	16	-0.079	0.770
	Puree 5mL #2	16	0.306	0.250
	Solid	16	0.328	0.215
Overall	Thin liquid 10mL	16	0.399	0.126
	Thin liquid 30 mL	15	0.410	0.129
	Thin liquid 3 oz	14	0.679	0.008
	Puree 5mL #1	16	-0.154	0.568
	Puree 5mL #2	16	0.066	0.808
	Solid	16	0.250	0.351
Self-rating swallowing	Thin liquid 10mL	16	0.435	0.092
	Thin liquid 30 mL	15	0.558	0.031

Table 16: Associations for Penetration-Aspiration Scale (PAS) with DHI				
DHI	Bolus	N	Spearman's Correlation Coefficient	p-value
	Thin liquid 3 oz	14	0.601	0.023
	Puree 5mL #1	16	-0.391	0.135
	Puree 5mL #2	16	-0.061	0.823
	Solid	16	-0.027	0.921

Table 17: Associations for Pharyngeal Residue Scale (after final swallow) with DHI				
DHI	Bolus	N	Spearman's Correlation Coefficient	p-value
Physical	Thin liquid 10mL	16	0.163	0.545
	Thin liquid 30 mL	15	0.321	0.244
	Thin liquid 3 oz	15	0.266	0.337
	Puree 5mL #1	17	0.322	0.208
	Puree 5mL #2	17	0.554	0.021
	Solid	17	0.366	0.149
Functional	Thin liquid 10mL	16	0.529	0.035
	Thin liquid 30 mL	15	0.174	0.534
	Thin liquid 3 oz	15	0.450	0.092
	Puree 5mL #1	17	0.012	0.965
	Puree 5mL #2	17	0.246	0.341
	Solid	17	0.438	0.079
Emotional	Thin liquid 10mL	16	0.374	0.154
	Thin liquid 30 mL	15	0.049	0.864
	Thin liquid 3 oz	15	0.225	0.420
	Puree 5mL #1	17	0.003	0.990
	Puree 5mL #2	17	0.437	0.080
	Solid	17	0.668	0.003
Overall	Thin liquid 10mL	16	0.528	0.036

Table 17: Associations for Pharyngeal Residue Scale (after final swallow) with DHI				
DHI	Bolus	N	Spearman's Correlation Coefficient	p-value
	Thin liquid 30 mL	15	0.237	0.395
	Thin liquid 3 oz	15	0.341	0.213
	Puree 5mL #1	17	0.206	0.429
	Puree 5mL #2	17	0.513	0.035
	Solid	17	0.583	0.014
Self-rating swallowing	Thin liquid 10mL	16	0.507	0.045
	Thin liquid 30 mL	15	0.274	0.323
	Thin liquid 3 oz	15	0.476	0.073
	Puree 5mL #1	17	0.040	0.878
	Puree 5mL #2	17	0.436	0.080
	Solid	17	0.491	0.046

Table 18: Associations of Pharyngeal Residue (after first swallow) with DHI				
DHI	Bolus	N	Spearman's Correlation Coefficient	p-value
Physical	Thin liquid 10ml	16	0.040	0.882
	Thin liquid 30ml	16	0.045	0.869
	Thin liquid 3oz	16	0.241	0.370
	Puree 1	17	0.407	0.105
	Puree 2	16	0.343	0.193
	Solid	17	0.322	0.207
Functional	Thin liquid 10ml	16	0.369	0.159
	Thin liquid 30ml	16	0.523	0.038
	Thin liquid 3oz	16	0.243	0.364
	Puree 1	17	0.023	0.931
	Puree 2	16	0.362	0.169
	Solid	17	0.334	0.190
Emotional	Thin liquid 10ml	16	0.220	0.413
	Thin liquid 30ml	16	0.407	0.117
	Thin liquid 3oz	16	0.016	0.953
	Puree 1	17	0.081	0.757
	Puree 2	16	0.349	0.185
	Solid	17	0.036	0.891
Overall	Thin liquid 10ml	16	0.339	0.200
	Thin liquid 30ml	16	0.333	0.207
	Thin liquid 3oz	16	0.201	0.454
	Puree 1	17	0.170	0.515
	Puree 2	16	0.345	0.191
	Solid	17	0.393	0.119
Self-reported Severity of Self-reported	Thin liquid 10ml	16	0.278	0.296

Table 18: Associations of Pharyngeal Residue (after first swallow) with DHI				
DHI	Bolus	N	Spearman's Correlation Coefficient	p-value
Severity of Dysphagia	Thin liquid 30ml	16	0.474	0.063
	Thin liquid 3oz	16	0.126	0.642
	Puree 1	17	0.033	0.900

Table 19: Associations for DDK and FVC with DHI (n=17 for all)			
DHI	Bolus	Spearman's Correlation Coefficient	p-value
Physical	pʌ/sec	-0.124	0.624
	tʌ/sec	-0.202	0.422
	kʌ/sec	-0.302	0.223
	pʌtʌkʌ/sec	-0.059	0.816
	FVC, %	0.035	0.891
Functional	pʌ/sec	-0.191	0.447
	tʌ/sec	-0.183	0.466
	kʌ/sec	-0.304	0.219
	pʌtʌkʌ/sec	-0.287	0.247
	FVC, %	-0.517	0.028
Emotional	pʌ/sec	-0.404	0.096
	tʌ/ /sec	-0.408	0.092
	kʌ/sec	-0.502	0.034
	pʌtʌkʌ/sec	-0.365	0.136
	FVC, %	-0.412	0.090
Overall	pʌ/sec	-0.272	0.275
	tʌ/sec	-0.2685	0.252
	kʌ/sec	-0.378	0.122

Table 19: Associations for DDK and FVC with DHI (n=17 for all)			
DHI	Bolus	Spearman's Correlation Coefficient	p-value
	pʌtʌkʌ/sec	-0.297	0.232
	FVC, %	-0.364	0.137
Self-rating swallowing	pʌ/sec	-0.238	0.342
	tʌ/sec	-0.297	0.231
	kʌ/sec	-0.372	0.129
	pʌtʌkʌ/sec	-0.306	0.218
	FVC, %	-0.465	0.052

Table 20: PAS (Asp/no Asp) of Thin liquid 10mL with DHI, DDK and FVC			
Variable	No Aspiration (N= 11)	Aspiration (N= 5)	p-value[a]
DHI			
Physical	7.27 ± 5.08	14.00 ± 5.83	0.116
Functional	8.18 ± 7.24	18.80 ± 11.01	0.108
Emotional	4.18 ± 5.40	8.40 ± 6.54	0.153
Overall	19.64 ± 16.19	41.20 ± 21.57	0.073
Self-rating of swallowing	2.36 ± 1.80	4.50 ± 1.12	0.061
Tired rating	3.36 ± 2.06	2.60 ± 1.14	0.426
DDK and FVC			
pʌ/sec	3.75 ± 1.51	2.64 ± 1.38	0.211
tʌ/ sec	3.38 ± 1.62	2.33 ± 1.34	0.211
kʌ/sec	3.22 ± 1.33	1.64 ± 0.61	0.024
pʌtʌkʌ/sec	1.33 ± 0.47	0.79 ± 0.42	0.058
FVC, %	80.27 ± 16.79	67.60 ± 17.94	0.231
[a]P-values from Wilcoxon two sample tests			

Table 21: PAS (Asp/no Asp) of Thin liquid 30mL with DHI, DDK and FVC			
Variable	No Aspiration (N= 7)	Aspiration (N= 8)	p-value[a]
DHI			
Physical	6.86 ± 4.74	10.50 ± 6.39	0.282
Functional	5.14 ± 4.30	14.75 ± 9.07	0.049
Emotional	1.43 ± 2.23	7.75 ± 5.70	0.040
Overall	13.43 ± 6.60	33.00 ± 20.28	0.076
Self-rating of swallowing	1.57 ± 0.79	4.06 ± 1.78	0.029
Tired rating	3.43 ± 2.07	2.88 ± 1.81	0.859
DDK and FVC			
pʌ/sec	3.83 ± 1.82	3.28 ± 1.15	0.570
tʌ/sec	3.72 ± 1.84	2.70 ± 1.15	0.341
kʌ/sec	3.49 ± 1.61	2.28 ± 0.70	0.152
pʌtʌkʌ/sec	1.35 ± 0.50	1.08 ± 0.47	0.428
FVC, %	82.57 ± 18.46	73.50 ± 16.13	0.341
[a]P-values from Wilcoxon two sample tests			

Table 22: PAS (Asp/no Asp) of Thin liquid 3oz with DHI, DDK and FVC			
Variable	No Aspiration (N= 7)	Aspiration (N= 7)	p-value[a]
DHI			
Physical	6.86 ± 4.74	11.43 ± 6.29	0.177
Functional	4.57 ± 4.43	16.29 ± 8.44	0.030
Emotional	1.14 ± 2.23	8.86 ± 5.15	0.016
Overall	12.57 ± 6.90	36.57 ± 19.00	0.034
Self-rating of swallowing	1.57 ± 0.79	4.00 ± 1.91	0.043
Tired rating	3.00 ± 2.24	3.57 ± 1.51	0.405
DDK and FVC			
pʌ/sec	3.94 ± 1.69	3.37 ± 1.21	0.574
tʌ/sec	3.87 ± 1.66	2.77 ± 1.20	0.386
kʌ/sec	3.57 ± 1.52	2.31 ± 0.69	0.181
pʌtʌkʌ/sec	1.35 ± 0.50	1.18 ± 0.41	0.659
FVC, %	86.57 ± 17.80	72.71 ± 11.80	0.096
[a]P-values from Wilcoxon two sample tests			

Table 23: Association of FVC categories with DHI					
Variable	Response	WNL (N=9)	Mild (N=4)	Moderate (N=5)	p-value[a]
Physical	Mean (SD)	11.33 (7.00)	5.00 (1.15)	11.20 (7.01)	0.257
Functional	Mean (SD)	9.78 (9.82)	5.50 (3.79)	18.40 (9.32)	0.088
Emotional	Mean (SD)	3.11 (4.91)	3.50 (3.00)	9.20 (7.56)	0.245
Overall	Mean (SD)	24.2 (19.40)	14.00 (5.66)	38.80 (23.18)	0.250
Self-rating for swallowing	Mean (SD)	2.89 (1.96)	1.50 (0.58)	4.50 (1.50)	0.065
Tired rating	Mean (SD)	3.00 (1.58)	4.75 (2.87)	2.40 (1.67)	0.338
[a] P-value from Kruskal-Wallis test.					

Table 24: Association of FVC categories with DDK

Variable	Response	WNL (N=9)	Mild (N=4)	Moderate (N=5)	p-value[a]
pʌ/sec	Mean (SD)	3.80 (1.64)	3.70 (1.60)	3.20 (1.63)	0.727
tʌ/sec	Mean (SD)	3.47 (1.66)	3.30 (1.48)	2.76 (1.73)	0.737
kʌ/sec	Mean (SD)	3.09 (1.34)	2.70 (0.60)	2.40 (1.74)	0.486
pʌtʌkʌ/sec	Mean (SD)	1.36 (0.57)	1.42 (0.35)	0.91 (0.57)	0.179

[a] P-value from Kruskal-Wallis test.

Table 25: Association of FVC categories with Number of swallows

Bolus	Response	WNL (N=9)	Mild (N=4)	Moderate (N=5)	p-value[a]
Thin liquid10ml	Mean (SD)	5.75 (3.73)	3.00 (1.00)	7.40 (8.26)	0.284
Thin liquid 30ml	Mean (SD)	8.13 (5.84)	4.33 (3.06)	7.25 (4.19)	0.551
Thin liquid 3oz	Mean (SD)	11.78 (5.36)	12.00 (5.29)	10.00 (1.73)	0.971
Puree 1	Mean (SD)	2.67 (1.00)	3.33 (0.58)	4.60 (3.13)	0.500
Puree 2	Mean (SD)	2.89 (1.27)	4.00 (2.00)	4.00 (3.46)	0.678
Solid	Mean (SD)	3.44 (1.59)	3.33 (0.58)	5.20 (3.19)	0.528

[a] P-value from Kruskal-Wallis test.

Table 26: Association of FVC categories with PAS

Variable	Response	WNL (N=9)	Mild (N=4)	Moderate (N=5)	p-value[a]
Thin liquid 10ml	Does not enter airway	3 (38%)	1 (33%)	1 (20%)	0.286
	Enters airway, above VF, ejected from airway	1 (13%)	1 (33%)	0 (0%)	
	Enters airway, above VF, not ejected from airway	1 (13%)	1 (33%)	0 (0%)	
	Enters airway, contacts VF, ejected from airway	0 (0%)	0 (0%)	1 (20%)	
	Enters airway, contacts VF, not ejected from airway	1 (13%)	0 (0%)	0 (0%)	
	Enters airway, below VF, no effort made to eject	2 (25%)	0 (0%)	3 (60%)	
Thin liquid 30ml	Does not enter airway	2 (25%)	1 (33%)	0 (0%)	0.498
	Enters airway, above VF, ejected from airway	1 (13%)	0 (0%)	1 (25%)	
	Enters airway, above VF, not ejected from airway	1 (13%)	0 (0%)	0 (0%)	
	Enters airway, contacts VF, not ejected from airway	0 (0%)	1 (33%)	0 (0%)	
	Enters airway, below VF, not ejected from trachea despite effort	1 (13%)	0 (0%)	0 (0%)	
	Enters airway, below VF, no effort made to eject	3 (38%)	1 (33%)	3 (75%)	
Thin liquid 3oz	Does not enter airway	1 (13%)	0 (0%)	0 (0%)	0.380
	Enters airway, above VF, ejected from airway	2 (25%)	0 (0%)	1 (33%)	
	Enters airway, contacts VF, not ejected from airway	2 (25%)	1 (33%)	0 (0%)	
	Enters airway, below VF, not ejected from trachea despite effort	1 (13%)	0 (0%)	0 (0%)	
	Enters airway, below VF, no effort made to eject	2 (25%)	2 (67%)	2 (67%)	

Table 26: Association of FVC categories with PAS

Variable	Response	WNL (N=9)	Mild (N=4)	Moderate (N=5)	p-value[a]
Puree 1	Does not enter airway	4 (50%)	1 (33%)	3 (60%)	0.506
	Enters airway, above VF, ejected from airway	0 (0%)	0 (0%)	1 (20%)	
	Enters airway, above VF, not ejected from airway	4 (50%)	0 (0%)	0 (0%)	
	Enters airway, contacts VF, not ejected from airway	0 (0%)	2 (67%)	0 (0%)	
	Enters airway, below VF, no effort made to eject	0 (0%)	0 (0%)	1 (20%)	
Puree 2	Does not enter airway	5 (63%)	0 (0%)	2 (40%)	0.059
	Enters airway, above VF, not ejected from airway	3 (38%)	1 (33%)	1 (20%)	
	Enters airway, contacts VF, not ejected from airway	0 (0%)	0 (0%)	1 (20%)	
	Enters airway, below VF, no effort made to eject	0 (0%)	2 (67%)	1 (20%)	
Solid	Does not enter airway	5 (63%)	0 (0%)	2 (40%)	0.052
	Enters airway, above VF, ejected from airway	1 (13%)	0 (0%)	1 (20%)	
	Enters airway, above VF, not ejected from airway	2 (25%)	0 (0%)	0 (0%)	
	Enters airway, contacts VF, not ejected from airway	0 (0%)	3 (100%)	1 (20%)	
	Enters airway, below VF, no effort made to eject	0 (0%)	0 (0%)	1 (20%)	

[a] P-value from Kruskal-Wallis test.

Table 27: Association of FVC categories with Pharyngeal Residue

Variable	Response	WNL (N=9)	Mild (N=4)	Moderate (N=5)	p-value[a]
Thin liquid10ml	Coating	3 (38%)	1 (33%)	1 (20%)	0.811
	Mild	5 (63%)	2 (67%)	4 (80%)	
Thin liquid 30ml	Coating	3 (38%)	2 (67%)	1 (25%)	0.549
	Mild	5 (63%)	1 (33%)	3 (75%)	
Thin liquid 30oz	Coating	6 (67%)	2 (7%)	0 (0%)	0.135
	Mild	3 (33%)	1 (33%)	3 (100%)	
Puree 1	Coating	1 (11%)	1 (33%)	1 (20%)	0.540
	Mild	7 (78%)	2 (67%)	4 (80%)	
	Moderate	1 (11%)	0 (0%)	0 (0%)	
Puree 2	Coating	1 (11%)	1 (33%)	1 (20%)	0.641
	Mild	7 (78%)	2 (67%)	3 (60%)	
	Moderate	1 (11%)	0 (0%)	1 (20%)	
Solid	None	1 (11%)	0 (0%)	0 (0%)	0.735
	Coating	2 (22%)	1 (33%)	1 (20%)	
	Mild	5 (56%)	2 (67%)	3 (60%)	
	Moderate	1 (11%)	0 (0%)	1 (20%)	

[a] P-value from Kruskal-Wallis test.

Table 28: Association of type of onset with DHI

Variable	Response	bulbar (N=6)	axial (N=9)	Mixed (N=3)	p-value[a]
Physical	Mean (SD)	16.33 (6.38)	6.22 (3.67)	8.00 (3.46)	0.030
Functional	Mean (SD)	18.67 (9.85)	7.33 (7.75)	8.00 (7.21)	0.095
Emotional	Mean (SD)	8.00 (7.38)	2.67 (3.32)	5.33 (7.57)	0.298
Overall	Mean (SD)	43.00 (20.50)	16.22 (12.55)	21.33 (18.15)	0.054
Self-rating swallowing	Mean (SD)	4.92 (1.11)	2.00 (1.22)	2.33 (2.31)	0.011
Tired Rating	Mean (SD)	2.50 (1.52)	3.67 (2.35)	3.33 (2.08)	0.597

[a]P-values from Kruskal-Wallis test.

Table 29: Association of type of onset with PAS

Bolus	Response	bulbar (N=6)	axial (N=9)	Mixed (N=3)	p-value[a]
Thin liquid 10 mL	Does no enter airway	1 (20%)	1 (13%)	3 (100%)	0.032
	Above VF, ejected	0 (0%)	2 (25%)	0 (0%)	
	Above VF, not ejected	0 (0%)	2 (25%)	0 (0%)	
	Contacts VF, ejected	0 (0%)	1 (13%)	0 (0%)	
	Contacts VF, not ejected	0 (0%)	1 (13%)	0 (0%)	
	Below VF, no effort	4 (80%)	1 (13%)	0 (0%)	
Thin liquid 30mL	Does no enter airway	1 (25%)	1 (13%)	1 (33%)	0.885
	Above VF, ejected	0 (0%)	2 (25%)	0 (0%)	
	Above VF, not ejected	0 (0%)	1 (13%)	0 (0%)	
	Contacts VF, not ejected	0 (0%)	1 (13%)	0 (0%)	
	Below VF, not ejected with effort	1 (25%)	0 (0%)	0 (0%)	
	Below VF, no effort	2 (50%)	3 (38%)	2 (67%)	
Thin	Does no enter airway	0 (0%)	1 (13%)	0 (0%)	0.408

Table 29: Association of type of onset with PAS

Bolus	Response	bulbar (N=6)	axial (N=9)	Mixed (N=3)	p-value[a]
liquid 3 oz	Above VF, ejected	0 (0%)	3 (38%)	0 (0%)	
	Contacts VF, not ejected	1 (33%)	1 (13%)	1 (33%)	
	Below VF, not ejected with effort	1 (33%)	0 (0%)	0 (0%)	
	Below VF, no effort	1 (33%)	3 (38%)	2 (67%)	
Puree 5mL #1	Does no enter airway	4 (80%)	2 (25%)	2 (67%)	0.468
	Above VF, ejected	0 (0%)	1 (13%)	0 (0%)	
	Above VF, not ejected	0 (0%)	4 (50%)	0 (0%)	
	Contacts VF, not ejected	0 (0%)	1 (13%)	1 (33%)	
	Below VF, no effort	1 (20%)	0 (0%)	0 (0%)	
Puree 5mL #2	Does no enter airway	3 (60%)	3 (38%)	1 (33%)	0.602
	Above VF, not ejected	1 (20%)	4 (50%)	0 (0%)	
	Contacts VF, not ejected	0 (0%)	0 (0%)	1 (33%)	
	Below VF, no effort	1 (20%)	1 (13%)	1 (33%)	
Solid	Does no enter airway	3 (60%)	2 (25%)	2 (67%)	0.808
	Above VF, ejected	0 (0%)	2 (25%)	0 (0%)	
	Above VF, not ejected	0 (0%)	2 (25%)	0 (0%)	
	Contacts VF, not ejected	1 (20%)	2 (25%)	1 (33%)	
	Below VF, no effort	1 (20%)	0 (0%)	0 (0%)	

[a]P-values from Kruskal-Wallis test.

Table 30: Association of type of onset with Pharyngeal Residue

Bolus	Response	bulbar (N=6)	axial (N=9)	mixed (N=3)	p-value[a]
Thin liquid 10 mL	Coating	0 (0%)	3 (38%)	2 (67%)	0.141
	Mild	5 (100%)	5 (63%)	1 (33%)	
Thin liquid 30 mL	Coating	0 (0%)	3 (38%)	3 (100%)	0.034
	Mild	4 (100%)	5 (63%)	0 (0%)	
Thin liquid 3 oz	Coating	1 (25%)	5 (63%)	2 (67%)	0.436
	Mild	3 (75%)	3 (38%)	1 (33%)	
Puree 5mL #1	Coating	1 (17%)	1 (13%)	1 (33%)	0.639
	Mild	4 (67%)	7 (88%)	2 (67%)	
	Moderate	1 (17%)	0 (0%)	0 (0%)	
Puree 5mL #2	Coating	0 (0%)	2 (25%)	1 (33%)	0.100
	Mild	4 (67%)	6 (75%)	2 (67%)	
	Moderate	2 (33%)	0 (0%)	0 (0%)	
Solid	None	0 (0%)	1 (13%)	0 (0%)	0.661
	Coating	1 (17%)	2 (25%)	1 (33%)	
	Mild	4 (67%)	4 (50%)	2 (67%)	
	Moderate	1 (17%)	1 (13%)	0 (0%)	

[a]P-values from Kruskal-Wallis test.

Table 31: Association of type of onset with DDK and FVC					
Variable	Response	bulbar (N=6)	axial (N=9)	mixed (N=3)	p-value[a]
pʌ/sec	Mean (SD)	2.80 (1.34)	4.38 (1.50)	2.93 (1.33)	0.125
tʌ/sec	Mean (SD)	2.44 (1.22)	4.07 (1.61)	2.33 (0.90)	0.086
kʌ/sec	Mean (SD)	2.07 (1.13)	3.44 (1.35)	2.40 (0.60)	0.085
pʌtʌkʌ/sec	Mean (SD)	0.97 (0.62)	1.43 (0.50)	1.27 (0.46)	0.195
FVC	Mean (SD)	69.83 (16.92)	81.11 (16.20)	74.33 (19.30)	0.399

[a]P-values from Kruskal-Wallis test.

Table 32: Associations for Duration of symptoms (all participants) with PAS			
Bolus	N	Spearman's Correlation Coefficient	p-value
Thin liquid 10ml	16	0.000	1.000
Thin liquid 30ml	15	-0.011	0.968
Thin liquid 3oz	14	0.284	0.325
Puree #1	16	0.374	0.153
Puree #2	16	0.517	0.040
Solid	16	0.246	0.357

Table 33: Associations for Duration of symptoms (all participants) with number of swallows			
Bolus	N	Spearman's Correlation Coefficient	p-value
Thin liquid 10ml	16	-0.112	0.679
Thin liquid 30ml	15	-0.115	0.683
Thin liquid 3oz	15	0.654	0.008
Puree #1	17	0.560	0.019
Puree #2	17	0.482	0.050
Solid	17	0.066	0.802

Table 34 Associations for Duration of symptoms (all participants) with DDK and FVC N=18		
DDK	Spearman's Correlation Coefficient	p-value
pʌ/sec	-0.184	0.464
tʌ/sec	-0.109	0.668
kʌ/sec	-0.137	0.587
pʌtʌkʌ/sec	-0.110	0.664
FVC	-0.382	0.117

Table 35: Associations for Duration of symptoms (all participants) with DHI N=18		
DHI	Spearman's Correlation Coefficient	p-value
Physical	0.184	0.466
Functional	0.387	0.113
Emotional	0.249	0.319
Overall	0.296	0.233
Self-rating swallowing	0.227	0.365

Table 36: Associations for Duration of symptoms (all participants) with Pharyngeal Residue			
Bolus	N	Spearman's Correlation Coefficient	p-value
Thin liquid 10ml	16	0.190	0.481
Thin liquid 30ml	15	0.189	0.500
Thin liquid 3oz	15	0.186	0.508
Puree #1	17	-0.377	0.136
Puree #2	17	-0.067	0.798
Solid	17	-0.042	0.874

Table 37: Associations for Duration of symptoms (onset within 4 yrs) with number of swallows			
Bolus	N	Spearman's Correlation Coefficient	p-value
Thin liquid 10ml	15	0.049	0.862
Thin liquid 30ml	14	0.091	0.757
Thin liquid 3oz	14	0.577	0.031
Puree #1	16	0.515	0.041
Puree #2	16	0.383	0.144
Solid	16	0.060	0.827

Table 38: Associations for Duration of symptoms (onset within 4 yrs) with DDK and FVC N=17		
DDK	Spearman's Correlation Coefficient	p-value
pʌ/sec	-0.058	0.826
tʌ/sec	0.012	0.963
kʌ/sec	-0.079	0.763
pʌtʌkʌ/sec	-0.090	0.731
FVC	-0.369	0.145

Table 39: Associations for Duration of symptoms (onset within 4 yrs) with DHI N=17		
DHI	Spearman's Correlation Coefficient	p-value
Physical	0.245	0.344
Functional	0.477	0.053
Emotional	0.283	0.271
Overall	0.381	0.131
Self-rating swallowing	0.382	0.130

Table 40: Associations for Duration of symptoms (onset within 4 yrs) with Pharyngeal Residue			
Bolus	N	Spearman's Correlation Coefficient	p-value
Thin liquid 10ml	15	0.419	0.120
Thin liquid 30ml	14	0.388	0.170
Thin liquid 3oz	14	0.337	0.239
Puree #1	16	-0.231	0.389
Puree #2	16	0.136	0.617
Solid	16	0.093	0.731

Table 41: Associations for Duration of symptoms (onset within 4 yrs) with PAS			
Bolus	N	Spearman's Correlation Coefficient	p-value
Thin liquid 10ml	15	0.156	0.578
Thin liquid 30ml	14	0.188	0.519
Thin liquid 3oz	13	0.183	0.550
Puree #1	15	0.251	0.368
Puree #2	15	0.421	0.118
Solid	15	0.136	0.628

Table 42: Associations for Total ALS FRSR with number of swallows			
Bolus	N	Spearman's Correlation Coefficient	p-value
Thin liquid 10ml	16	0.569	0.021
Thin liquid 30ml	15	0.330	0.230
Thin liquid 3oz	15	0.308	0.263
Puree #1	17	0.067	0.798
Puree #2	17	0.396	0.115
Solid	17	0.574	0.016

Table 43: Associations for Total ALS FRSR with DDK and FVC N=18		
DDK	Spearman's Correlation Coefficient	p-value
PΛ/sec	0.087	0.731
tΛ/sec	0.138	0.586
kΛ/sec	-0.022	0.931
pΛtΛkΛ/sec	-0.096	0.704
FVC	-0.099	0.696

Table 44: Associations for Total ALS FRSR with DHI N=18		
DHI	Spearman's Correlation Coefficient	p-value
Physical	0.366	0.135
Functional	0.371	0.129
Emotional	-0.031	0.903
Overall	0.314	0.204
Self-rating swallowing	0.301	0.225

Table 45: Associations for Total ALS FRSR with PAS			
Bolus	N	Spearman's Correlation Coefficient	p-value
Thin liquid 10ml	16	0.427	0.099
Thin liquid 30ml	15	-0.184	0.512
Thin liquid 3oz	14	-0.119	0.685
Puree #1	16	0.009	0.974
Puree #2	16	-0.430	0.097
Solid	16	0.126	0.642

Table 46: Associations for Total ALS FRSR with Pharyngeal Residue			
Bolus	N	Spearman's Correlation Coefficient	p-value
Thin liquid 10ml	16	0.337	0.202
Thin liquid 30ml	15	0.331	0.228
Thin liquid 3oz	15	0.232	0.405
Puree #1	17	0.479	0.052
Puree #2	17	0.031	0.907
Solid	17	-0.143	0.584

Table 47: Association of BMI with Pharyngeal Residue

Variable	Response	Normal (N=9)	Overweight/ Obese (N=9)	p-value[a]
Thin liquid10ml	Coating	3 (38%)	2 (25%)	0.654
	Mild	5 (63%)	6 (75%)	
Thin liquid 30ml	Coating	5 (71%)	1 (13%)	0.047
	Mild	2 (29%)	7 (88%)	
Thin liquid 30oz	Coating	5 (63%)	3 (43%)	0.514
	Mild	3 (38%)	4 (57%)	
Puree 1	Coating	2 (22%)	1 (13%)	0.411
	Mild	7 (78%)	6 (75%)	
	Moderate	0 (0%)	1 (13%)	
Puree 2	Coating	2 (22%)	1 (13%)	0.723
	Mild	6 (67%)	6 (75%)	
	Moderate	1 (11%)	1 (13%)	
Solid	None	1 (11%)	0 (0%)	0.708
	Coating	2 (22%)	2 (25%)	
	Mild	5 (56%)	5 (63%)	
	Moderate	1 (11%)	1 (13%)	

[a]P-value from Wilcoxon two sample test.

Table 48: BMI and DDK and FVC

Variable	Response	Normal (N=9)	Overweight/ Obese (N=9)	p-value[a]
pʌ/sec	Mean (SD)	3.58 (1.71)	3.64 (1.49)	0.827
Tʌ/sec	Mean (SD)	3.13 (1.77)	3.34 (1.45)	0.827
kʌ/sec	Mean (SD)	2.84 (1.42)	2.78 (1.27)	0.930
pʌtʌkʌ/sec	Mean (SD)	1.32 (0.61)	1.18 (0.51)	0.487
FVC, %	Mean (SD)	76.22 (12.88)	76.22 (20.67)	0.965

[a]P-value from Wilcoxon two sample test.

Table 49: Association of BMI with DHI

Variable	Response	Normal (N=9)	Overweight/ Obese (N=9)	p-value[a]
Physical	Mean (SD)	11.56 (7.40)	8.22 (5.33)	0.382
Functional	Mean (SD)	15.56 (9.15)	6.89 (8.37)	0.073
Emotional	Mean (SD)	7.11 (6.25)	2.67 (4.69)	0.109
Overall	Mean (SD)	34.22 (20.48)	17.78 (16.23)	0.102
Self-rating for swallowing	Mean (SD)	3.67 (1.87)	2.39 (1.80)	0.207
Tired rating	Mean (SD)	4.11 (1.62)	2.33 (2.06)	0.056

[a]P-value from Wilcoxon two sample test.

Table 50: Association of BMI with PAS

Variable	Response	Normal (N=9)	Overweight/ Obese (N=9)	p-value[a]
Thin liquid 10ml	Does not enter airway	3 (38%)	2 (25%)	0.632
	Enters airway, above VF, ejected from airway	1 (13%)	1 (13%)	
	Enters airway, above VF, not ejected from airway	1 (13%)	1 (13%)	
	Enters airway, contacts VF, ejected from airway	0 (0%)	1 (13%)	
	Enters airway, contacts VF, not ejected from airway	1 (13%)	0 (0%)	
	Enters airway, below VF, no effort made to eject	2 (25%)	3 (38%)	

Table 50: Association of BMI with PAS

Variable	Response	Normal (N=9)	Overweight/ Obese (N=9)	p-value[a]
Thin liquid 30ml	Does not enter airway	1 (14%)	2 (25%)	0.763
	Enters airway, above VF, ejected from airway	0 (0%)	2 (25%)	
	Enters airway, above VF, not ejected from airway	1 (14%)	0 (0%)	
	Enters airway, contacts VF, not ejected from airway	1 (14%)	0 (0%)	
	Enters airway, below VF, not ejected from trachea despite effort	1 (14%)	0 (0%)	
	Enters airway, below VF, no effort made to eject	3 (43%)	4 (50%)	
Thin liquid 3oz	Does not enter airway	0 (0%)	1 (14%)	0.202
	Enters airway, above VF, ejected from airway	1 (14%)	2 (29%)	
	Enters airway, contacts VF, not ejected from airway	1 (14%)	2 (29%)	
	Enters airway, below VF, not ejected from trachea despite effort	1 (14%)	0 (0%)	
	Enters airway, below VF, no effort made to eject	4 (57%)	2 (29%)	
Puree 1	Does not enter airway	4 (50%)	4 (50%)	0.738
	Enters airway, above VF, ejected from airway	0 (0%)	1 (13%)	
	Enters airway, above VF, not ejected from airway	2 (25%)	2 (25%)	
	Enters airway, contacts VF, not ejected from airway	1 (13%)	1 (13%)	
	Enters airway, below VF, no effort made to eject	1 (13%)	0 (0%)	

Table 50: Association of BMI with PAS

Variable	Response	Normal (N=9)	Overweight/ Obese (N=9)	p-value[a]
Puree 2	Does not enter airway	3 (38%)	4 (50%)	0.478
	Enters airway, above VF, not ejected from airway	2 (25%)	3 (38%)	
	Enters airway, contacts VF, not ejected from airway	1 (13%)	0 (0%)	
	Enters airway, below VF, no effort made to eject	2 (25%)	1 (13%)	
Solid	Does not enter airway	3 (38%)	4 (50%)	0.551
	Enters airway, above VF, ejected from airway	1 (13%)	1 (13%)	
	Enters airway, above VF, not ejected from airway	1 (13%)	1 (13%)	
	Enters airway, contacts VF, not ejected from airway	2 (25%)	2 (25%)	
	Enters airway, below VF, no effort made to eject	1 (13%)	0 (0%)	

[a]P-value from Wilcoxon two sample test.

Table 51: Association of BMI with Number of swallows

Variable	Response	Normal (N=9)	Overweight/ Obese (N=9)	p-value[a]
Thin liquid10ml	Mean (SD)	7.13 (7.14)	4.38 (1.77)	0.874
Thin liquid 30ml	Mean (SD)	6.86 (6.96)	7.38 (2.67)	0.220
Thin liquid 3oz	Mean (SD)	12.25 (5.92)	10.57 (2.70)	0.953
Puree 1	Mean (SD)	3.44 (1.94)	3.25 (2.05)	0.557
Puree 2	Mean (SD)	3.78 (2.86)	3.00 (0.93)	>0.99
Solid	Mean (SD)	3.78 (2.39)	4.13 (1.96)	0.773

[a]P-value from Wilcoxon two sample test.

CHAPTER 5

DISCUSSION

The primary objective of this study was to determine if there was a correlation between speech, respiratory and swallowing functions in individuals with ALS with bulbar involvement. This study examined three research questions. In the investigation of the first research question, do individuals diagnosed with ALS with bulbar involvement perform significantly different on clinical measures (DDK, FVC, DHI, and tired level) and on objective swallowing measures (PAS, pharyngeal residue and number of swallows per bolus) when compared to a control group? Between-group differences were evaluated for ALS and control groups, performance on measures of speech, swallowing and respiratory function were compared between individuals with ALS with bulbar impairment and a control group of similar age. In this study, significant differences were found in the performance between the ALS group and the control group on all clinical measures for speech production, respiratory function and patient reported outcomes for swallowing function. ALS group performance was consistent with decline in muscle strength and degeneration of motor neurons resulting in impairments of FVC and a 40% reduction in rate of DDK production ($p = 0.001$) for all targets, compared to the control group. Reduced rate of DDK production is strongly suggestive of articulatory impairment, specifically reduced rate of lingual movement. Diadochokinetic tasks are frequently utilized for identification of early speech changes in neurogenic diseases (Enderby, 1983; Gadesmann & Miller, 2008; Kent et al., 1987; Nishio & Niimi, 2006). The results from the control group are consistent with previous normative DDK literature.(Nishio & Niimi, 2006; Portnoy & Aronson, 1982; Ptacek, Sander, Maloney, & Jackson, 1966; Wang et al., 2004) As expected, the ALS group showed significant

impairments in FVC and speech productions, compared to the control group. This finding is consistent with previous research by Lechtzin et al. (2002). They found that forced vital capacity is likely to decline by 3.5% per month as a result of ALS.

In the investigation of the second research question, are there significant correlations between clinical measures and objective swallowing measures which would support the theory that swallowing function could be predicted in individuals with ALS? This study examined the correlations between clinical measures and objective swallowing measures. One of the focuses of this study was to investigate if the hypothesis that swallowing function can be predicted in individuals with ALS by clinical measures, such as DDK, FVC, DHI and tired level would be supported. In motor speech research, DDK is a common method to assess articulatory precision and agility (Nishio & Niimi, 2006; Portnoy & Aronson, 1982). It is commonly accepted that alterations in speech production in ALS are associated with decreased range, rate and strength of the tongue and oral pharyngeal musculature (Mulligan et al., 1994) and that decreased lingual coordination and impaired base of tongue movement increases the risk of pharyngeal residue and aspiration (Kawai et al., 2003). This study investigated the ability of DDK tasks to assess lingual movements that may predict swallowing impairments in ALS subjects. The results of this study supported the hypothesis that testing /kʌ/ is important because of the finding of a negative correlation between reduced /kʌ/ productions per second and severity of dysphagia. Individuals with ALS who aspirated 10mL liquid boluses produced, on average, half the number of /kʌ/ repetitions per second as the ALS non-aspiration subjects. This may indicate that highly timed movements are more important in the management of small bolus volumes. The idea of the importance of highly coordinated movements for safe swallowing of small volumes is further supported by the

significant negative correlation between /pʌtʌkʌ/ productions per second and pharyngeal residue and aspiration ratings in the ALS group. Rate of /kʌ/ productions per second was also negatively correlated with severity of residue with the second puree and solid bolus trials within the ALS group. Base of tongue movements for formation of velar sounds such as /kʌ/ during speech production as well as bolus propulsion through the pharynx during swallowing, require similar posterior lingual movements. The negative correlation between pharyngeal residue with rate of /kʌ/ productions supports the hypothesis that impairment in production of velar sounds can indicate impairments in base of tongue movements affecting swallowing function. Anterior lingual movements are important in bolus manipulation and initiation of transport to the posterior oral cavity; however, posterior lingual movement, responsible for production of /kʌ/, is important for bolus holding and propulsion through the pharynx. Impairment in base of tongue movement is more likely to result in aspiration and pharyngeal residue (Kawai et al., 2003; Takahiro Ono, 2007).

ALS subjects with more impaired respiratory function demonstrated increased risk of aspiration with large, 3 ounce, liquid trials. Increased PAS scores for a larger bolus may be a result of dis-coordination of the swallow apnea period. The onset of swallow apnea occurs earlier in the oral phase with larger boluses (Hiss et al., 2004). This earlier onset of swallow apnea may place increased stress on the respiratory system due to lack of respiratory reserve resulting in early opening of the larynx after swallowing or alteration of the exhale-swallow-exhale typical motor pattern (Gross et al., 2003). The FVC assessment is part of the gold standard assessment for determining progression of ALS. It is often necessary to anticipate feeding tube placement for supplemental and eventually total nutrition, as FVC approaches 50% predicted function (Miller, 1999). For this reason, ALS patients with an FVC below

50% were excluded from this study. This study showed that the ALS group declined in both speech rate production and respiratory function which is consistent with previous research. This study also showed that the significant correlation between DDK with risk of aspiration and pharyngeal residue is supportive of the hypothesis to predict swallowing impairments through DDK and FVC assessment in individuals with ALS.

Compared to the control group, the ALS group exhibited impairments in swallowing function characterized by greater pharyngeal residue with food versus liquids and increased aspiration risk with all bolus trials, except the 10mL liquid trial. The thin liquid 10mL bolus trial is representative of a small sip. An average liquid bolus size taken by an adult over the age of 55 is 11 to 17mL for a female and 20 to 23mL for a male (Ertekin, 2000; Hughes & Wiles, 1996). Multiple investigations have documented the decline in bolus size as a function of decline in swallowing ability (Ertekin, 2000; Kawai et al., 2003). This may explain why there was not a significant difference in PAS for the 10mL liquid trial. PAS scores were greater for larger thin liquid bolus trials, 30mL and 3 ounces, and for puree and solid boluses in the ALS group as a result of this group's inability to manage larger volumes of liquid and food. In this study, a higher rate of aspiration occurred during the second puree bolus compared to the first puree bolus, 19% and 6% respectively, in the ALS group. Additionally, the ALS group demonstrated significant correlations in pharyngeal residue only for the second puree bolus compared to DDK and the DHI. It is also possible that fatigue played a role in the significant finding of increased pharyngeal residue and aspiration with larger liquid boluses and during the second puree bolus in comparison to the first puree bolus. ALS subjects swallowed between 15 and 50 times during the four boluses preceding the second puree bolus. In comparison, subjects in the control group swallowed on average between 10-

25 times during the initial four boluses. The need for frequent and repetitive swallows to manage boluses could be fatiguing which would explain the correlation with the final two bolus trials in this study. In addition, texture and order of presentation may have also contributed to increased residue on these two trials. All liquid trials were completed at the beginning of the study so subjects were provided with three food boluses sequentially.

The severity of swallowing impairment demonstrated by increased ratings on the PAS and pharyngeal residue tool likely affected the ratings on the DHI for the ALS group. ALS subjects reported higher scores for all categories of the DHI and severity of dysphagia potentially indicating awareness of decline in swallowing function compared to the control group. The concept of awareness of swallowing difficulty in the ALS group was supported by a significant difference on all sections of the DHI (Physical, Functional, Emotional, Overall and Self-reported Severity of Dysphagia). These significant differences in DHI scores indicate that the participants in the ALS group are aware of their swallowing impairments and that these impairments affect their quality life. For example, reported physical impairments included symptoms such as coughing when eating or drinking. Emotional stressors included concerns of anxiety, depression and fear of eating in public. Functional modifications of oral intake were also reported, including small bites and sips, modification of diet, and smaller meal portions.

The significant group differences between ALS, as compared to the control group, vividly describe the challenges associated with progressive dysphagia. Physical deterioration in swallowing function is associated with declining oral pharyngeal muscle strength and fatigue which consequently results in increased risk for laryngeal penetration and aspiration as well as increased pharyngeal residue. These physical impairments are likely to cause

necessary functional modifications to oral intake in the form of eliminating challenging foods, smaller bolus size and smaller portions. Meal times may be prolonged as a result of fatigue and reduced respiratory support affecting rate of oral intake due to the need for additional time to recover from obligatory periods of swallowing apnea. The emotional stress and anxiety due to concerns of swallowing difficulty could alter the perception of eating from an enjoyable, social experience to an activity completed in isolation.

Awareness of decline in swallowing function and implementation of compensatory strategies may contribute to significant differences in the number of swallows per bolus for larger, 30mL and 3 ounce, thin liquid volumes in the ALS group as compared to the control group. It is possible that the ALS subjects intentionally partitioned larger bolus amounts into several swallows of smaller volumes to compensate for lingual weakness and decreased bolus control in an attempt to avoid an aspiration event. The theory of the ALS subjects utilizing multiple swallows as a compensatory strategy is further supported by the absence of significant differences of pharyngeal residue after the final swallow of liquid boluses. Even though the ALS group demonstrated significantly increased pharyngeal residue with food boluses, there was not a significant difference in the number of swallows compared to the control group. These findings may suggest that an intact motor response to sensory feedback could initially lead to a greater number of swallows to reduce bolus retention. However, as muscle fatigue progresses during a meal, motor responses may be too impaired to generate a swallow despite appropriate sensation, or there may be reduced sensory function which results in fewer swallows. Alternately, it is entirely possible that there may be an increased demand in motor movement and sensory-motor coordination in order to prevent aspiration events with thin liquids, more so than to reduce pharyngeal residue with solid foods. This hypothesis

requires further study. Piecemeal deglutition is common in the swallowing impaired population (Ertekin, 2000; Hiss et al., 2004; Kawai et al., 2003). Within the ALS group, high correlations between DHI scores with higher PAS ratings for large thin liquid volumes and greater pharyngeal residue scores with puree and solid boluses support the hypothesis that the DHI may be beneficial in predicting swallowing decline in individuals with ALS. Surprisingly, number of swallows was not significantly correlated with DDK production, pharyngeal residue or FVC performance. It was expected that the /kʌ/ production of DDK would be associated with number of swallows. DHI scores for emotion were highly correlated with DDK /kʌ/ production indicating that the swallowing problems associated with base of tongue impairments result in feeling of anger, depression, stress and lack of enjoyment of eating. FVC performance was correlated with the DHI functional scale ratings likely indicating that ALS subjects with respiratory impairments implement compensatory strategies to alter foods or methods of intake in order to accommodate for longer periods of apnea.

When examining PAS ratings for the ALS group, a large percentage demonstrated silent aspiration across bolus consistencies in this study. In the ALS group, 30% of all bolus trials were aspirated. Of the total number of aspiration events, only 8% were followed by an attempt to protect the airway (cough or throat clear). Silent aspiration occurred in 31%, 47% and 43% of thin liquid boluses of 10mL, 30mL and 3 ounces respectively. The frequency of silent aspiration was greatest with liquids, but also occurred in puree #2 trials. This finding is concerning because by definition, ALS is strictly a motor disease without sensory deterioration. If laryngeal and tracheal sensations are not impaired as a result of ALS, an alternative possibility is that the laryngeal and tracheal sensory receptors no longer perceive

the bolus material as foreign due to a history of prolonged duration of aspiration events. In previous ALS research, silent aspiration rates are generally between 0% (Chen et al., 1992; Leder, Novella, & Patwa, 2004; Ruoppolo et al., 2013) and 15% (Briani et al., 1998). In the study by Leder, Novella and Patwa (2004), aspiration was documented in 17% of subjects. In a study by Ruoppolo et al. (2013), no aspiration occurred during the assessment of swallowing function, despite a diagnosis of impaired cough reflex during laryngeal sensitivity testing in 20% of the ALS subjects tested. It is noteworthy that the current study used larger bolus volumes (30mL and 3 ounces) whereas previous research evaluated swallowing function with 3-20mL bolus trials of thin liquid, nectar thick liquid and puree consistencies (Briani et al., 1998; Leder et al., 2004; Ruoppolo et al., 2013). It is possible that aspiration, especially silent aspiration, has been under diagnosed in ALS as a result of assessments with limited bolus size.

Laryngeal penetration with vocal fold contact or aspiration occurred within a few subjects in the control group. In the control group, laryngeal penetration contacting the vocal folds, without aspiration occurred during the smaller thin liquid bolus trials of 10mL and 30mL. During the 3 ounce thin liquid trial, 20% of the control group aspirated followed by an immediate attempt to clear the material from the trachea with a cough. Control subjects who aspirated were 59, 65 and 84 years of age and female. The findings of this study were consistent with previous research from Daggett (2007) and Butler et al. (2009). Natural changes in swallowing function of the healthy aging population resulted in occasional episodes of laryngeal penetration and aspiration (Butler, 2009; Daggett, 2007; Todd, 2013). Decline in swallowing function in healthy adults has been attributed to prolonged oral

pharyngeal phase duration and a delay in bolus transit and delayed airway protection (Daggett, 2007)

The third research question examined the correlations between patient history and the development of the disease, individual and disease course information including symptom onset, duration of symptoms, BMI and ALS-FRSR scores. All of these analyses showed significant correlations with clinical assessments and objective swallowing ratings. Subjects with bulbar onset were found to have the greatest impairment in swallowing function with 80% of participants with bulbar onset silently aspirating the 10mL liquid bolus and demonstrated pharyngeal residue of thin liquid 30mL boluses. Swallowing function was distributed across the 8 levels of the PAS rating for axial and mixed type of onset. This data supports the findings that individuals with bulbar onset ALS have a more significant decline in swallowing function than non-bulbar onset individuals (Ruoppolo et al., 2013).

The duration of ALS symptoms was significantly positively correlated to the number of swallows for the liquid 3 ounce and first puree bolus trial as well as aspiration risk (PAS) for the second puree bolus. These correlations are likely due to changes in timing of muscle movements to contain and propel bolus material safely and efficiently through the pharynx. Onset type was also significantly correlated to DHI ratings for the physical category and the Self-Reported Severity of Dysphagia. Bulbar onset ALS individuals appear to experience more symptoms of dysphagia including coughing, choking, and weight loss than non-bulbar patients with ALS. The finding of swallowing decline as a result of bulbar onset and prolonged duration of symptoms is consistent with deterioration of the corticobulbar tract. Subsequently, the decline in the corticobulbar tract certainly affects the functions of cranial

nerves essential for appropriate swallowing movements such as the trigeminal, facial, glossopharyngeal, vagus and hypoglossal nerves.

Findings associated with BMI and ALS-FRSR was limited. Body mass index was not significantly associated with any other measure or bolus trial with the exception of pharyngeal residue with a thin liquid 30mL bolus. It was expected that low BMI would be positively correlated with decline in swallowing function due to the known association between decreased BMI and reduced caloric intake (Clavelou, Blanquet, Peyrol, Ouchchane, & Gerbaud, 2013). However, ALS-FRSR scores were significantly positively correlated with the number of swallows required for thin liquid 10mL and solid boluses only. This positive correlation suggests that ALS subjects with more severe swallowing impairments will swallow fewer times per bolus. This finding may also support the theory that muscle fatigue will override sensory feedback which dictates the frequency of swallows per bolus. This study integrated the number of swallows per bolus measure to assess effort required for bolus propulsion. This measure also appears to be an indicator of fatigue.

In this study, the ALS-FRSR scores were not significantly correlated with PAS or pharyngeal residue scales. This finding directly contradicts previous research by Ruoppolo (2013), which found that the risk for dysphagia increased by 9% for every point variation from normal function on the ALS-FRS scale. Inconsistencies in findings between the two studies may be a result of a different version of the ALS-FRS used. In the current study the ALS-FRSR was used compared to the ALS-FRS in the Ruoppolo (2013) study. In the current study, most subjects with ALS were rated as having either normal or mildly impaired function on most sections of the ALS-FRSR which may have accounted for the differences in findings. In the study by Ruoppolo (2013), individuals with ALS were examined in an

attempt to establish clinical indicators of dysphagia though evaluation of demographic data including duration of disease, type of onset (bulbar or axial), ALS-FRS score and completion of a clinical swallowing assessment and FEES examination. The current study supplements the findings of Ruoppolo (2013) by adding findings of significant correlations between dysphagia with diadochokinesis, number of swallows and the Dysphagia Handicap Index. Overall, in this study, foundational data have been established for future investigation to determine if swallowing function in ALS patients could be predicted though common clinical assessments.

Limitations of the Current Study

In this study, enrollment included 18 subjects with ALS and 15 controls similar in age. While the enrollment criteria ensured that participating members would most likely only present with impairments secondary to the ALS disease process, it also resulted in challenges with subject recruitment. A large number of the potential ALS subjects (108) were excluded due to the stringent exclusionary criteria. The small sample size prohibited assessment of potential interactions between PAS and pharyngeal residue ratings with combinations of DDK, FVC, number of swallows per bolus and DHI scores. In addition, the small sample size reduced the power to detect some clinically meaningful findings. Correlations between 0.4 and 0.5 may provide useful information. However, with a sample size of 18 the power to detect associations at this level is very low, between 10 to 53%, assuming alpha of 0.05 and two sided testing.

Furthermore, subject recruitment was limited to the Harry J. Hoenselaar ALS clinic schedule. Subject enrollment and study completion was convenient for ALS subjects since patients were already in clinic for an appointment; however, several patients declined

participation due to fatigue from a long clinic appointment. Testing time and duration for ALS subjects were not controlled. Thus, the study occurred anywhere from 30 minutes to 4 hours into the appointment. The duration of the clinic appointment may have also contributed to the increased tiredness rating or other findings within the study in the ALS group in comparison to the control group.

There were several measures that were approaching but did not achieve significance in this study, for example differences in pharyngeal residue ratings with liquid boluses between the ALS group and the control group. Additional studies with larger sample sizes may further verify results of this study.

Summary:

Early identification of dysphagia in individuals with ALS can facilitate appropriate planning and discussions regarding proper nutritional goals and a long term nutritional plan while reducing the risk of complications from aspiration pneumonia. This study revealed statistical significance between objective swallowing measures of the PAS and pharyngeal residue rating with clinical assessments of the DHI, DDK, FVC and number of swallows per bolus, along with common disease assessment information, ALS-FRSR, type of onset, duration of disease and BMI. The battery of clinical measures included in this study provides a foundational step toward the development of a predictive dysphagia assessment that could be conducted to determine the risk of dysphagia in an individual with ALS.

Additional findings indicate that individuals with ALS demonstrated significant impairment of all clinical assessment and objective swallowing measures in comparison to healthy controls. Unexpected but clinically relevant findings included a high rate of silent aspiration in the ALS group with all consistencies. This important finding suggests that

dysphagia and aspiration may have been overlooked in the clinical setting. Additionally there were findings of aspiration with cough in the control group during the 3 ounce liquid trial which is consistent with previous research (Butler, 2009; Daggett, 2007).

Future research should focus on the incidence of silent aspiration in ALS patients as well as attempt to replicate the results of this study on a larger scale. If silent aspiration is more prevalent than previously thought, implementation of periodic objective swallowing evaluations through MBSS or FEES will be beneficial. In addition, future studies should include the examination of whether or not dysphagia occurs prior to the presence of bulbar impairment for all patients with ALS. Based upon the results of this study, it may be beneficial to assess the relationship between number of swallows, DHI, FVC and DDK as predictive measures of dysphagia in other neurological populations.

APPENDIX A: ALSFRS-R The ALS Functional Rating Scale, Revised

Total Score:

I. Comparisons are made with the patient's status prior to the onset of the disease, not with the status at the last visit

II. Patient's response (on a 5-point scale is recorded in relation to the question "How are you doing at (…)?" for each of the 12 functions listed.

1. Speech

[ ] 4 Normal speech processes
[ ] 3 Detectable speech disturbance
[ ] 2 Intelligible with repeating
[ ] 1 Speech combined with non-vocal communication
[ ] 0 Loss of useful speech

2. Salivation

[ ] 4 Normal
[ ] 3 Slight but definite excess of saliva in mouth; may have nighttime drooling
[ ] 2 Moderately excessive saliva; may have minimal drooling
[ ] 1 Marked excess of saliva with some drooling
[ ] 0 Marked drooling; requires constant tissue or handkerchief

3. Swallowing

[ ] 4 Normal eating habits
[ ] 3 Early eating problems-occasional choking
[ ] 2 Dietary consistency changes
[ ] 1 Needs supplemental tube feeding
[ ] 0 NPO (exclusively parenteral or enteral feeding)

4. Handwriting

[ ] 4 Normal
[ ] 3 Slow or sloppy; all words are legible
[ ] 2 Not all words are legible
[ ] 1 Able to grip pen but unable to write
[ ] 0 Unable to grip pen

5a. Cutting Food and Handling Utensils *(patients without gastrostomy)*

[ ] 4 Normal
[ ] 3 Somewhat slow and clumsy, but no help needed
[ ] 2 Can cut most foods, although clumsy and slow; some help needed

[ ] 1 Food must be cut by someone, but can still feed slowly
[ ] 0 Needs to be fed

5b. Cutting Food and Handling Utensils ***(alternate scale for patients <u>with</u> gastrostomy)***

[ ] 4 Normal
[ ] 3 Clumsy but able to perform all manipulations
[ ] 2 Some help needed with closures and fastners
[ ] 1 Provides minimal assistance to caregiver
[ ] 0 Unable to perform any aspect of task

6. Dressing and Hygiene

[ ] 4 Normal function
[ ] 3 Independent and complete self-care with effort or decreased efficiency
[ ] 2 Intermittent assistance or substitute methods
[ ] 1 Needs attendant for self-care
[ ] 0 Total dependence

7. Turning in Bed and Adjusting Bed Clothes

[ ] 4 Normal
[ ] 3 Somewhat slow and clumsy but no help needed
[ ] 2 Can turn alone or adjust sheets, but with great difficulty
[ ] 1 Can initiate, but not turn or adjust sheets alone
[ ] 0 Helpless

8. Walking

[ ] 4 Normal
[ ] 3 Early ambulation difficulties
[ ] 2 Walks with assistance
[ ] 1 Non-ambulatory, functional movement only.
[ ] 0 No purposeful leg movement

9. Climbing Stairs

[ ] 4 Normal
[ ] 3 Slow
[ ] 2 Mild unsteadiness or fatigue
[ ] 1 Needs assistance
[ ] 0 Cannot do

10. Dyspnea

[ ] 4 None

[ ] 3 Occurs when walking
[ ] 2 Occurs with one or more of the following: eating, bathing, dressing (ADL)
[ ] 1 Occurs at rest, difficult breathing when either sitting or lying
[ ] 0 Significant difficulty, considering using mechanical respiratory support

11. Orthopnea

[ ] 4 None
[ ] 3 Some difficult sleeping at night due to shortness of breath.
Does not routinely use more than two pillows
[ ] 2 Needs extra pillow in order to sleep (more than two pillows)
[ ] 1 Can only sleep sitting up
[ ] 0 Unable to sleep

12. Respiratory Insufficiency

[ ] 4 None
[ ] 3 Intermittent use of BiPaP
[ ] 2 Continuous use of BiPaP
[ ] 1 Continuous use of BiPaP during the night and day
[ ] 0 Invasive mechanical ventilation by intubation or tracheostomy

APPENDIX B: ALS Group - History of Disease, Weight and Height

Subject ID #	Symptom onset	Date of Diagnosis	Study Enrollment Date	Weight (kg)	Height (cm)
Female:					
ALS_001F	1997	1997	10/22/2012	59	160
ALS_002F	1/1/2010	12/14/2011	10/29/2012	45	152
ALS_003F	3/1/2011	4/1/2011	10/29/2012	62	154
ALS_004F	5/1/2011	6/1/2012	11/19/2012	80	160
ALS_005F	12/1/2010	6/1/2012	12/3/2012	62	167
ALS_006F	2/1/2011	7/6/2012	1/14/2013	93	167
ALS_007F	1/1/2011	11/1/2012	1/14/2013	60	170
ALS_008F	12/1/2011	10/15/2012	2/4/2013	83	161
ALS_009F	5/1/2012	7/1/2013	8/26/2013	61	165
ALS_010F	9/1/2012	6/4/2013	2/3/2014	45	152
ALS_011F	8/15/2013	2/12/2014	3/17/2014	81	164
ALS_012F	7/1/2013	3/24/2014	5/5/2014	79	168
Male:					
ALS_001M	5/1/2011	3/18/2013	4/15/2013	77	178
ALS_002M	1/1/2012	7/12/2012	4/29/2013	102	180
ALS_003M	2/13/2013	3/28/2013	7/1/2013	62	170
ALS_004M	spring 2012	7/19/2013	7/22/2013	61	172
ALS_005M	1/1/2012	6/29/2012	9/9/2013	100	170
ALS_006M	11/1/2012	11/1/2013	12/16/2013	108	178

APPENDIX C: ALS Group - Region of Onset and ALS-FRS Revised Scores

Subject ID #	Onset Bulbar, Axial or Mixed	ALS-FRSR Scores Speech	Saliva	Swallow	Dyspnea	Resp.	Overall ALS-FRSr Score
Female:							
ALS_001F	Mixed	2	4	4	4	4	33
ALS_002F	Axial	3	4	3	2	4	34
ALS_003F	Axial	3	3	2	3	4	31
ALS_004F	Axial	4	4	4	2	4	31
ALS_005F	Bulbar	1	4	1	4	4	36
ALS_006F	Bulbar	2	2	3	3	3	31
ALS_007F	Bulbar	3	3	3	1	4	36
ALS_008F	Axial	4	4	4	4	4	21
ALS_009F	Axial	3	3	3	3	4	19
ALS_010F	Axial	2	4	3	4	4	26
ALS_011F	Bulbar	2	3	3	3	4	43
ALS_012F	Bulbar	3	4	2	4	4	45
Male:							
ALS_001M	Bulbar	3	3	3	4	4	45
ALS_002M	Axial	2	3	4	4	4	28
ALS_003M	Axial	4	4	4	4	4	37
ALS_004M	Mixed	3	2	3	3	4	25
ALS_005M	Axial	4	4	4	4	4	39
ALS_006M	Mixed	2	4	4	4	4	34

- The ALS-FRSR is a patient reporting tool composed of 12 functions (Speech, Salivation, Swallowing, Handwriting, Cutting Food and Handling Utensils, Dressing and Hygiene, Turning in Bed and Adjusting Bed Clothes, Walking, Climbing Stairs, Dyspnea, Orthopnea and Respiratory insufficiency.
- Rating for each function uses a 5 point scale: 4=normal function and 0=severe dysfunction.
- Maximum Overall Score is 48 points

APPENDIX D: Questionnaire for DDK and dysphagia assessment in ALS.

		Y/N	
	If any **bold** response is reported the subject does not meet criteria for this study.		
1	Do you have a history of tobacco use?	Y	N
2	Do you currently use tobacco?	Y	N
3	What is your current age? Birthdate?		
4	History of stroke or other neurologic event other than ALS?	**Y**	N
5	History of speech difficulties unrelated to ALS?	**Y**	N
6	History of swallowing difficulties unrelated to ALS?	**Y**	N
7	History of respiratory disease unrelated to ALS (emphysema, COPD, Lung CA)?	**Y**	N
8	History of head/neck cancer?	**Y**	N
9	History of radiation or surgery to the head/neck?	**Y**	N
10	Is English the first language you learned?	Y	**N**
11	Have you noticed changes in your speech?	Y	N
12	Have you noticed changes in your swallowing?	Y	N
13	Compared to your baseline, on a scale from 1-7, how tired are you right now? 1 = normal 7 = severely tired		

APPENDIX E: DYSPHAGIA HANDICAP INDEX (DHI)

Silbergleit, A.K., Schultz, L., Jacobson, B., Beardsley, T. and Johnson, A. (*Dysphagia*, 2011)

Please place a check in the box that describes your swallowing difficulty

	NEVER	SOMETIMES	ALWAYS
1P. I cough when I drink liquids.			
2P. I cough when I eat solid food.			
3P. My mouth is dry.			
4P. I need to drink fluids to wash food down.			
5P. I've lost weight because of my swallowing problem.			
1F. I avoid some foods because of my swallowing problem			
2F. I have changed the way I swallow to make it easier to eat.			
1E. I'm embarrassed to eat in public.			
3F. It takes me longer to eat a meal that it used to.			

	NEVER	SOMETIMES	ALWAYS
4F. I eat smaller meals more often due to my swallowing problem			
6P. I have to swallow again before food will go down.			
2E. I feel depressed because I can't eat what I want.*			
3E. I don't enjoy eating as much as I used to.			
5F. I don't socialize as much due to my swallowing problem.			
6F. I avoid eating because of my swallowing problem.			
7F. I eat less because of my swallowing problem.			
4E. I am nervous because of my swallowing problem.			

* This question was excluded from data analysis due to a typographical error. The word "what" was accidentally replaced with the word "when".

	NEVER	SOMETIMES	ALWAYS
5E. I feel handicapped because of my swallowing problem.			
6E. I get angry at myself because of my swallowing problem.			
7P. I choke when I take my medication.			
7E. I'm afraid that I'll choke and stop breathing because of my swallowing problem.			
8F. I must eat another way (e.g. feeding tube) because of my swallowing problem.			

	NEVER	SOMETIMES	ALWAYS
9F. I've changed my diet due to my swallowing problem.			
8P. I feel a strangling sensation when I swallow.			
9P. I cough up food after I swallow.			

Please circle the number that matches the severity of your swallowing difficulty
(1 = no difficulty as all; 4 = somewhat of a problem; 7 = the worst problem you could have):

1 2 3 4 5 6 7

normal moderate problem severe problem

APPENDIX F: Demographic Information and Dysphagia Handicap Index (DHI) Scores

Table F1: ALS Female Group - Demographic Information and Dysphagia Handicap Index (DHI) Ratings

Subject ID #	Age	Tobacco Use		DHI				
		Past	Current	Physical	Functional	Emotional	Over-all	Self-Report
ALS_001 F	58	N	N	6	6	2	14	1
ALS_002 F	75	N	N	14	24	8	46	4
ALS_003 F	79	N	N	4	8	6	18	2
ALS_004 F	67	N	N	6	0	0	6	1
ALS_005 F	62	N	N	18	30	20	68	5
ALS_006 F	65	N	N	4	8	2	14	4.5
ALS_007 F	69	N	N	20	24	16	60	6
ALS_008 F	64	Y	N	10	0	0	10	1
ALS_009 F	82	Y	N	6	10	4	20	4
ALS_010 F	63	N	N	4	8	10	22	2
ALS_011 F	73	N	N	18	26	16	60	6
ALS_012 F	54	Y	N	16	6	2	24	3

- The DHI is composed of 24 statements (one was excluded due to a typographical error) that require the patient to respond with Never (0 points), Sometimes (2 points) or Always (4 points) to each.
- Statements are separated into 3 categories: Physical (9 statements with maximum 36 possible points), Emotional (6 statements with maximum 24 possible points) and Functional (9 statements with maximum 36 possible points).
- Additionally an Overall score and a Self Reported Severity of Dysphagia rating (7 points scale where 1 is normal and 7 is severely impaired).

Table F2: ALS Male Group - Demographic Information and Dysphagia Handicap Index (DHI) Ratings

Subject ID #	Age	Tobacco Use		DHI				
		Past	Current	Physical	Functional	Emotional	Over-all	Self-Report
ALS_001 M	60	Y	N	22	18	0	40	5
ALS_002 M	55	Y	N	6	0	0	6	1
ALS_003 M	78	N	N	2	4	0	6	1
ALS_004 M	77	N	N	12	16	14	42	5
ALS_005 M	77	N	N	4	12	0	16	2
ALS_006 M	65	N	N	6	2	0	8	1

- The DHI is composed of 24 statements (one was excluded due to a typographical error) that require the patient to respond with Never (0 points), Sometimes (2 points) or Always (4 points) to each.
- Statements are separated into 3 categories: Physical (9 statements with maximum 36 possible points), Emotional (6 statements with maximum 24 possible points) and Functional (9 statements with maximum 36 possible points).
- Additionally an Overall score and a Self Reported Severity of Dysphagia rating (7 points scale where 1 is normal and 7 is severely impaired).

Table F3: Control Group - Demographic Information and Dysphagia Handicap Index (DHI) Ratings								
Subject ID #	**Age**	**Tobacco Use**		**DHI**				
		Past	**Current**	**Physical**	**Functional**	**Emotional**	**Over -all**	**Self-Report**
CON_001 F	60	N	N	2	0	0	2	1
CON_002 M	66	Y	N	2	0	0	2	2
CON_003 F	65	N	N	2	0	0	2	1
CON_004 F	61	N	N	2	0	0	2	1
CON_005 M	69	Y	N	2	0	0	2	1
CON_006 F	66	Y	N	2	0	0	2	1
CON_007 M	63	N	N	0	0	0	0	1
CON_008 F	59	N	N	6	0	0	6	2
CON_009 F	69	N	N	4	0	0	4	1
CON_010 F	62	Y	N	6	0	0	6	3
CON_011 F	84	N	N	10	2	0	12	1
CON_012 F	58	Y	N	4	0	0	4	1
CON_013 F	58	N	N	4	0	0	4	1
CON_014 M	59	N	N	8	0	0	8	1
CON_015 F	83	N	N	4	0	0	4	1

- The DHI is composed of 24 statements (one was excluded due to a typographical error) that require the patient to respond with Never (0 points), Sometimes (2 points) or Always (4 points) to each.
- Statements are separated into 3 categories: Physical (9 statements with maximum 36 possible points), Emotional (6 statements with maximum 24 possible points) and Functional (9 statements with maximum 36 possible points).
- Additionally an Overall score and a Self Reported Severity of Dysphagia rating (7 points scale where 1 is normal and 7 is severely impaired).

APPENDIX G: Tired Rating and Forced Vital Capacity Performance

Table G1: ALS Female Group - Tired Rating and Forced Vital Capacity Performance

Subject ID #	Tired Rating	Forced Vital Capacity		
		Within Normal Limit (+80%)	Mild Impairment (79-65%)	Moderate Impairment (64-50%)
ALS_001F	4		68%	
ALS_002F	4	85%		
ALS_003F	1		71%	
ALS_004F	7		69%	
ALS_005F	3			55%
ALS_006F	1			51%
ALS_007F	5	84%		
ALS_008F	1	93%		
ALS_009F	4	84%		
ALS_010F	7		76%	
ALS_011F	2			58%
ALS_012F	3	89%		

- Tired rating on a seven point scale where a normal = 1 and severely tired = 7.
- FVC scores are documented as percent predicted performance based on height, weight, age and gender.
- An FVC score of 100% predicted capacity is the median predicted value (based on height, weight, age and gender), as such it is possible to achieve a percent predicted FVC that is greater than 100%.

Table G2: ALS Male Group - Tired Rating and Forced Vital Capacity Performance

Subject ID #	Tired Rating	Forced Vital Capacity		
		Within Normal Limit (+80%)	Mild Impairment (79-65%)	Moderate Impairment (64-50%)
ALS_001M	1	82%		
ALS_002M	4	107%		
ALS_003M	4	93%		
ALS_004M	5			59%
ALS_005M	1			52%
ALS_006M	1	96%		

- Tired rating on a seven point scale where a normal = 1 and severely tired = 7.
- FVC scores are documented as percent predicted performance based on height, weight, age and gender.
- An FVC score of 100% predicted capacity is the median predicted value (based on height, weight, age and gender), as such it is possible to achieve a percent predicted FVC that is greater than 100%.

Table G3: Control Group - Tired Rating and Forced Vital Capacity Performance				
Subject ID #	**Tired Rating**	**Forced Vital Capacity**		
		Within Normal Limit (+80%)	**Mild Impairment (79-65%)**	**Moderate Impairment (64-50%)**
CON_001F	1	128%		
CON_002M	2	115%		
CON_003F	1	88%		
CON_004F	2	94%		
CON_005M	1	113%		
CON_006F	1	125%		
CON_007M	1	104%		
CON_008F	3	150%		
CON_009F	1	112%		
CON_010F	1	125%		
CON_011F	1	87%		
CON_012F	3	114%		
CON_013F	2	101%		
CON_014M	2	101%		
CON_015F	1	103%		

- Tired rating on a seven point scale where a normal = 1 and severely tired = 7.
- FVC scores are documented as percent predicted performance based on height, weight, age and gender.
- An FVC score of 100% predicted capacity is the median predicted value (based on height, weight, age and gender), as such it is possible to achieve a percent predicted FVC that is greater than 100%.

APPENDIX H: Diadochokinesis Results

Table H1: ALS Female Group - Diadochokinesis Results

Subject ID #	Alternating Motion Rate (AMR)						Sequential Motion Rate (SMR)	
	/ pʌ/		/ tʌ/		/ kʌ/		/ pʌtʌkʌ/	
	# in 5sec	x̄/sec	# in 5sec	x̄/sec	# in 5sec	x̄/sec	# in 5sec	x̄/sec
ALS_001F	9.00	1.80	7.00	1.40	9.00	1.80	5.00	1.00
ALS_002F	24.00	4.80	22.00	4.40	13.00	2.60	7.00	1.40
ALS_003F	21.00	4.20	18.00	3.60	15.00	3.00	7.00	1.40
ALS_004F	28.00	5.60	25.00	5.00	15.00	3.00	9.30	1.86
ALS_005F	7.00	1.40	6.00	1.20	5.00	1.00	2.00	0.40
ALS_006F	9.00	1.80	6.00	1.20	7.00	1.40	2.00	0.40
ALS_007F	17.00	3.40	15.00	3.00	14.00	2.80	6.00	1.20
ALS_008F	27.00	5.40	24.00	4.80	21.00	4.20	10.00	2.00
ALS_009F	9.00	1.80	5.00	1.00	8.00	1.60	2.66	0.53
ALS_010F	16.00	3.20	16.00	3.20	15.00	3.00	7.00	1.40
ALS_011F	16.00	3.20	14.00	2.80	7.00	1.40	4.66	0.93
ALS_012F	10	2.00	10.33	2.07	9.00	1.80	4.00	0.80

- x̄/sec = Average number of productions per second; sec = seconds

Table H2: ALS Male Group - Diadochokinesis Results

Subject ID #	Alternating Motion Rate (AMR)						Sequential Motion Rate (SMR)	
	/ pʌ/		/ tʌ/		/ kʌ/		/ pʌtʌkʌ/	
	# in 5sec	x̄/sec	# in 5sec	x̄/sec	# in 5sec	x̄/sec	# in 5sec	x̄/sec
ALS_001M	25.00	5.00	22.00	4.40	20.00	4.00	10.33	2.07
ALS_002M	14.00	2.80	14.00	2.80	13.00	2.60	6.00	1.20
ALS_003M	32.00	6.40	32.00	6.40	29.00	5.80	10.33	2.07
ALS_004M	22.00	4.40	16.00	3.20	15.00	3.00	9.00	1.80
ALS_005M	26.00	5.20	27.00	5.40	26.00	5.20	5.00	1.00
ALS_006M	13.00	2.60	12.00	2.40	12.00	2.40	5.00	1.00

- x̄/sec = Average number of productions per second; sec = seconds

Table H3: Control Group - Diadochokinesis Results								
Subject ID #	**Alternating Motion Rate (AMR)**						**Seq. Motion Rate (SMR)**	
	/ pʌ/		**/ tʌ/**		**/ kʌ/**		**/ pʌtʌkʌ/**	
	# in 5sec	**x̄/sec**	**# in 5sec**	**x̄/sec**	**# in 5sec**	**x̄/sec**	**# in 5sec**	**x̄/sec**
CON_001F	34.00	6.80	34.00	6.80	30.00	6.00	13.00	2.60
CON_002M	26.00	5.20	24.00	4.80	21.00	4.20	9.00	1.80
CON_003F	28.00	5.60	28.00	5.60	27.00	5.40	9.00	1.80
CON_004F	30.00	6.00	28.00	5.60	27.00	5.40	8.00	1.60
CON_005M	32.00	6.40	29.00	5.80	29.00	5.80	11.33	2.27
CON_006F	27.00	5.40	24.00	4.80	24.00	4.80	9.00	1.80
CON_007M	24.00	4.80	22.00	4.40	21.00	4.20	10.00	2.00
CON_008F	30.00	6.00	30.00	6.00	29.00	5.80	11.00	2.20
CON_009F	28.5	5.70	24.00	4.80	23.00	4.60	9.00	1.80
CON_010F	23.00	4.60	22.00	4.40	22.00	4.40	9.00	1.87
CON_011F	27.00	5.40	23.00	4.60	21.00	4.20	9.00	1.80
CON_012F	31.00	6.20	31.00	6.20	30.00	6.00	12.00	2.40
CON_013F	28.00	5.60	29.00	5.80	29.00	5.80	11.00	2.20
CON_014M	26.00	5.20	25.00	5.00	23.2	4.64	10.00	2.00
CON_015F	29.00	5.80	26.00	5.20	26.5	5.30	10.00	2.00

- x̄/sec = Average number of productions per second; sec = seconds

APPENDIX I: FEES Rater Sheet with PAS and Pharyngeal Residue Scale Ratings

Subject ID _____ **Date**

Investigator _____

Bolus	Number of Swallows	PAS Rating	Pharyngeal Residue Rating	Comments
10mL Thin Liquid by spoon				
30mL Thin Liquid by straw				
3 oz Thin Liquid by straw				
5mL Puree				
5mL Puree				
Cookie bite				

Penetration - Aspiration Scale

Rating	Definition
1	material does not enter the airway
2	material enters the airway, remains above the vocal folds, and is ejected from the airway
3	material enters the airway, remains above the vocal folds, and is not ejected from the airway
4	material enters the airway, contacts the vocal folds, and is ejected from the airway
5	material enters the airway, contacts the vocal folds, and is not ejected from the airway
6	material enters the airway, passes below the vocal folds and is ejected into the larynx or out of the airway
7	material enters the airway, passes below the vocal folds, and is not ejected from the trachea despite effort
8	material enters the airway, passes below the vocal folds, and no effort is made to eject

Rosenbek, J. C., Robbins, J., Roecker, E. B., Coyle, J. L., & Wood, J. L. (1996). A penetration-aspiration scale. *Dysphagia, 11*, 93 - 98.

Pharyngeal Residue Scale

Rating	Definition	
0	None	No coating/residue in pharynx
1	Coating	coating of pharyngeal mucosa, no pooling
2	Mild	mild pooling/residue
3	Moderate	moderate pooling/residue
4	Severe	severe pooling/residue

Kelly, A. M., Macfarlane, K., Ghufoor, K., Drinnan, M. J., & Lew-Gor, S. (2008). Pharyngeal residue across the lifespan: a first look at what's normal. *Clinical Otolaryngology, 33*(4), 348-351.

APPENDIX J: Penetration Aspiration Scale (PAS) Ratings

Table J1: ALS Female Group - Penetration Aspiration Scale (PAS) Ratings

Subject ID#		FEES results					
		Thin Liquid 10mL Straw	Thin Liquid 30mL Straw	Thin Liquid 3oz straw	Puree (5mL)	Puree (5mL)	Solid
ALS_001F	Rater 1	1	1	8	5	8	5
	Rater 2	1	1	8	5	8	5
ALS_002F	Rater 1	8	8	8	3	3	3
	Rater 2	8	8	6	3	2	2
ALS_003F	Rater 1	3	8	8	5	8	5
	Rater 2	5	5	5	8	8	3
ALS_004F		Terminated at Subject Request No bolus trials					
ALS_005F	Rater 1	8	n/a	n/a	8	8	8
	Rater 2	8	n/a	n/a	8	8	8
ALS_006F	Rater 1	8	8	n/a	1	3	1
	Rater 2	8	8	n/a	2	3	1
ALS_007F	Rater 1	1	7	7	1	1	1
	Rater 2	1	7	7	1	1	1
ALS_008F	Rater 1	1	2	2	3	3	3
	Rater 2	2	2	2	3	3	2
ALS_009F	Rater 1	5	8	8	1	1	1
	Rater 2	8	4	8	1	1	4
ALS_010F	Rater 1	2	5	5	1	3	5
	Rater 2	5	5	5	1	3	3
ALS_011F	Rater 1	8	8	8	1	1	5
	Rater 2	5	5	5	2	2	2
ALS_012F	Rater 1	8	1	5	1	1	1
	Rater 2	8	3	8	1	1	3

- PAS ratings are based on an 8 point scale were one is the least severe and 8 is the most severe.
- n/a = Not administered due to severity of impairment on smaller bolus trial.

Table J2: ALS Male Group - Penetration Aspiration Scale (PAS) Ratings							
Subject ID#		**FEES results**					
		Thin Liquid 10mL Straw	**Thin Liquid 30mL Straw**	**Thin Liquid 3oz straw**	**Puree (5mL)**	**Puree (5mL)**	**Solid**
ALS_001M	Rater 1	UTV	UTV	UTV	UTV	UTV	UTV
	Rater 2	UTV	UTV	UTV	UTV	UTV	UTV
ALS_002M	Rater 1	2	1	1	3	3	1
	Rater 2	3	1	1	3	3	3
ALS_003M	Rater 1	3	3	2	3	1	2
	Rater 2	1	1	1	3	1	1
ALS_004M	Rater 1	1	8	8	1	5	1
	Rater 2	1	8	8	1	5	1
ALS_005M	Rater 1	4	2	2	2	1	2
	Rater 2	2	2	2	2	2	2
ALS_006M	Rater 1	1	8	5	1	1	1
	Rater 2	1	8	5	1	3	1

- PAS ratings are based on an 8 point scale were one is the least severe and 8 is the most severe.
- UTV = Unable to visualize

Table J3: Control Group - Penetration Aspiration Scale (PAS) Ratings							
Subject ID#		**FEES results**					
		Thin Liquid 10mL Straw	**Thin Liquid 30mL Straw**	**Thin Liquid 3oz straw**	**Puree (5mL)**	**Puree (5mL)**	**Solid**
CON_001F	Rater 1	1	1	1	1	1	2
	Rater 2	1	1	1	1	1	2
CON_002M	Rater 1	1	1	1	1	3	1
	Rater 2	1	1	1	1	3	1
CON_003F	Rater 1	5	5	6	1	1	1
	Rater 2	5	5	8	3	UTV	1
CON_004F	Rater 1	2	2	2	1	1	1
	Rater 2	2	UTV	2	2	1	1
CON_005M	Rater 1	5	3	2	1	1	1
	Rater 2	2	2	2	1	2	2
CON_006F	Rater 1	1	1	1	1	1	1
	Rater 2	1	1	1	1	1	1
CON_007M	Rater 1	1	1	1	3	3	2
	Rater 2	1	1	1	3	3	1
CON_008F	Rater 1	1	1	6	1	1	1
	Rater 2	1	1	7	1	1	1
CON_009F	Rater 1	1	1	1	1	1	2
	Rater 2	1	1	1	1	2	2
CON_010F	Rater 1	1	1	1	1	1	1
	Rater 2	1	1	1	2	1	1
CON_011F	Rater 1	5	5	7	1	1	1
	Rater 2	5	5	8	1	1	1
CON_012F	Rater 1	1	1	1	1	1	2
	Rater 2	1	1	1	1	1	2
CON_013F	Rater 1	2	1	1	1	1	1
	Rater 2	2	1	1	1	1	1
CON_014M	Rater 1	5	4	2	1	2	1
	Rater 2	5	5	5	1	2	1
CON_015F	Rater 1	5	1	1	1	1	1
	Rater 2	2	1	2	1	2	1

- PAS ratings are based on an 8 point scale were one is the least severe and 8 is the most severe.
- UTV = Unable to visualize

APPENDIX K: Pharyngeal Residue Ratings

Table K1: ALS Female Group - Pharyngeal Residue Ratings							
Subject ID#		**FEES results**					
		Thin Liquid 10mL Straw	**Thin Liquid 30mL Straw**	**Thin Liquid 3oz straw**	**Puree (5mL)**	**Puree (5mL)**	**Solid**
ALS_001F	Rater 1	1	1	1	1	1	1
	Rater 2	1	1	1	2	1	2
ALS_002F	Rater 1	2	2	1	2	2	3
	Rater 2	3	2	2	3	3	3
ALS_003F	Rater 1	2	2	2	2	2	2
	Rater 2	2	2	2	2	2	1
ALS_004F		Terminated at Subject Request No bolus trials administered					
ALS_005F	Rater 1	2	n/a	n/a	2	3	2
	Rater 2	2	n/a	n/a	2	3	3
ALS_006F	Rater 1	2	2	n/a	1	2	2
	Rater 2	2	2	n/a	1	2	2
ALS_007F	Rater 1	2	2	2	2	2	2
	Rater 2	2	2	2	2	2	2
ALS_008F	Rater 1	1	2	1	2	2	2
	Rater 2	1	2	1	2	2	2
ALS_009F	Rater 1	2	1	1	1	2	2
	Rater 2	2	2	2	1	1	3
ALS_010F	Rater 1	2	1	1	2	2	2
	Rater 2	2	2	2	2	3	2
ALS_011F	Rater 1	2	2	2	2	2	3
	Rater 2	3	2	2	2	3	4
ALS_012F	Rater 1	2	2	1	3	3	2
	Rater 2	2	2	2	3	2	2

- Pharyngeal residue ratings were based on a 5 point scale where 0 = no residues or coating and 4= severe residue
- n/a = Not administered due to severity of impairment on smaller bolus trial.

Table K2: ALS Male Group - Pharyngeal Residue Ratings							
Subject ID#		**FEES results**					
		Thin Liquid 10mL Straw	**Thin Liquid 30mL Straw**	**Thin Liquid 3oz straw**	**Puree (5mL)**	**Puree (5mL)**	**Solid**
ALS_001M	Rater 1	UTV	UTV	2	2	2	1
	Rater 2	UTV	UTV	2	2	2	1
ALS_002M	Rater 1	1	2	2	2	2	1
	Rater 2	1	2	2	2	2	2
ALS_003M	Rater 1	1	1	1	2	1	0
	Rater 2	1	1	1	2	1	0
ALS_004M	Rater 1	1	1	2	2	2	2
	Rater 2	1	1	2	2	2	1
ALS_005M	Rater 1	2	2	2	2	1	1
	Rater 2	2	2	2	2	1	1
ALS_006M	Rater 1	2	1	1	2	2	2
	Rater 2	2	1	1	2	2	2

- Pharyngeal residue ratings were based on a 5 point scale where 0 = no residues or coating and 4= severe residue
- UTV = Unable to visualize

Table K3: Control Group - Pharyngeal Residue Ratings							
Subject ID#		**FEES results**					
		Thin Liquid 10mL Straw	**Thin Liquid 30mL Straw**	**Thin Liquid 3oz straw**	**Puree (5mL)**	**Puree (5mL)**	**Solid**
CON_001F	Rater 1	2	1	1	2	2	0
	Rater 2	2	1	1	2	2	1
CON_002M	Rater 1	1	1	1	2	2	0
	Rater 2	1	1	1	1	2	0
CON_003F	Rater 1	2	2	0	1	1	2
	Rater 2	2	1	0	2	UTV	2
CON_004F	Rater 1	1	1	1	1	1	0
	Rater 2	1	1	1	1	1	0
CON_005M	Rater 1	2	1	2	2	2	2
	Rater 2	2	2	2	2	2	2
CON_006F	Rater 1	1	1	1	1	1	0
	Rater 2	1	1	0	1	1	0
CON_007M	Rater 1	1	2	1	2	2	0
	Rater 2	1	2	1	2	2	0
CON_008F	Rater 1	1	1	1	1	1	0
	Rater 2	1	2	1	1	1	0
CON_009F	Rater 1	2	2	1	1	1	0
	Rater 2	2	2	1	1	1	0
CON_010F	Rater 1	1	1	2	1	1	1
	Rater 2	1	1	2	2	1	1
CON_011F	Rater 1	1	1	1	0	1	1
	Rater 2	2	1	1	1	1	1
CON_012F	Rater 1	0	0	0	1	1	1
	Rater 2	0	0	0	1	1	1
CON_013F	Rater 1	0	0	0	0	0	0
	Rater 2	0	0	0	0	0	0
CON_014M	Rater 1	2	2	2	2	2	2
	Rater 2	2	2	2	2	2	2
CON_015F	Rater 1	2	1	1	2	1	0
	Rater 2	2	1	1	2	1	1

- Pharyngeal residue ratings were based on a 5 point scale where 0 = no residues or coating and 4= severe residue
- UTV = Unable to visualize

APPENDIX L: Number of Swallows per Bolus Trial

Table L1: ALS Female Group - Number of Swallows per Bolus Trial							
Subject ID#		**FEES results**					
		Thin Liquid 10mL Straw	**Thin Liquid 30mL Straw**	**Thin Liquid 3oz Straw**	**Puree (5mL)**	**Puree (5mL)**	**Solid**
ALS_001F	Rater 1	2	1	18	4	6	4
	Rater 2	2	2	5	4	6	4
ALS_002F	Rater 1	14	22	23	4	4	4
	Rater 2	13	22	21	3	5	4
ALS_003F	Rater 1	4	5	10	3	4	3
	Rater 2	4	4	9	4	4	3
ALS_004F		Terminated at Subject Request No bolus trials/No interrater necessary					
ALS_005F	Rater 1	22	n/a	n/a	8	10	9
	Rater 2	20	n/a	n/a	8	11	9
ALS_006F	Rater 1	3	6	n/a	2	2	3
	Rater 2	3	6	n/a	2	2	4
ALS_007F	Rater 1	4	6	14	3	2	3
	Rater 2	3	6	12	3	3	3
ALS_008F	Rater 1	4	9	8	4	3	6
	Rater 2	6	6	8	4	3	5
ALS_009F	Rater 1	5	4	8	1	1	1
	Rater 2	4	4	6	1	1	2
ALS_010F	Rater 1	3	7	8	3	2	3
	Rater 2	3	7	9	2	2	3
ALS_011F	Rater 1	5	13	11	2	2	6
	Rater 2	4	13	11	2	3	8
ALS_012F	Rater 1	8	6	8	2	3	4
	Rater 2	8	5	6	2	3	3

- The number of discrete swallows per bolus were counted during each trial
- n/a = Not administered due to severity of impairment on smaller bolus trial.

Table L2: ALS Male Group - Number of Swallows per Bolus Trial							
Subject ID#		**FEES results**					
		Thin Liquid 10mL Straw	**Thin Liquid 30mL Straw**	**Thin Liquid 3oz Straw**	**Puree (5mL)**	**Puree (5mL)**	**Solid**
ALS_001M	Rater 1	UTV	UTV	13	3	5	4
	Rater 2	UTV	UTV	13	3	4	4
ALS_002M	Rater 1	2	5	10	2	2	2
	Rater 2	2	5	10	2	2	2
ALS_003M	Rater 1	5	5	6	2	2	5
	Rater 2	4	5	6	2	2	4
ALS_004M	Rater 1	2	3	8	3	2	1
	Rater 2	2	3	8	3	3	1
ALS_005M	Rater 1	5	7	11	8	4	7
	Rater 2	5	8	5	8	5	6
ALS_006M	Rater 1	4	8	16	3	4	2
	Rater 2	5	8	15	3	4	2

- The number of discrete swallows per bolus were counted during each trial
- UTV = Unable to visualize

Table L3: Control Group - Number of Swallows per Bolus Trial							
Subject ID#		**FEES results**					
		Thin Liquid 10mL Straw	**Thin Liquid 30mL Straw**	**Thin Liquid 3oz Straw**	**Puree (5mL)**	**Puree (5mL)**	**Solid**
CON_001F	Rater 1	2	5	7	3	2	3
	Rater 2	2	5	7	3	2	3
CON_002M	Rater 1	3	4	4	2	2	2
	Rater 2	3	4	4	2	2	2
CON_003F	Rater 1	3	5	13	3	3	4
	Rater 2	3	5	8	3	2	3
CON_004F	Rater 1	2	4	4	2	3	1
	Rater 2	2	2	3	2	2	1
CON_005M	Rater 1	3	4	7	3	3	3
	Rater 2	3	4	7	2	3	2
CON_006F	Rater 1	5	6	8	4	4	5
	Rater 2	4	4	7	4	3	4
CON_007M	Rater 1	2	3	4	3	3	3
	Rater 2	2	3	4	2	3	3
CON_008F	Rater 1	3	4	11	4	5	5
	Rater 2	3	4	8	4	5	3
CON_009F	Rater 1	3	4	4	3	2	3
	Rater 2	3	2	3	2	2	3
CON_010F	Rater 1	6	6	4	2	2	3
	Rater 2	6	6	4	3	2	3
CON_011F	Rater 1	3	3	10	5	5	5
	Rater 2	3	3	7	2	5	4
CON_012F	Rater 1	7	3	5	4	4	3
	Rater 2	5	3	4	3	3	2
CON_013F	Rater 1	3	2	6	2	2	2
	Rater 2	3	2	4	2	2	2
CON_014M	Rater 1	4	3	4	2	2	2
	Rater 2	4	3	4	2	2	2
CON_015F	Rater 1	2	3	4	2	2	2
	Rater 2	2	3	3	2	2	2
- The number of discrete swallows per bolus were counted during each trial							

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ABSTRACT

EVALUATING THE RELATIONSHIP BETWEEN DIADOCHOKINESIS AND SEVERITY OF DYSPHAGIA AS IT RELATES TO FORCED VITAL CAPACITY IN INDIVIDUALS WITH AMYOTROPHIC LATERAL SCLEROSIS

by

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Major: Speech-Language Pathology

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Purpose: To determine if the severity of dysphagia, as determined by Penetration Aspiration Scale (PAS) ratings and pharyngeal residue scale ratings in individuals with ALS, can be predicted through performance on diadochokinesis (DDK) and force vital capacity (FVC) measures.

This study was designed to evaluate differences in performance of clinical measures and objective swallowing severity ratings between individuals with ALS and a Control group of similar age. The goal of this study was to attempt to develop a clinical assessment battery that can predict swallowing impairment in ALS patients. In addition, potential predictive relationships between dysphagia ratings and other commonly utilized measures in the evaluation and treatment of ALS including duration of disease, type of onset (axial, bulbar, mixed), current Amyotrophic Lateral Sclerosis Function Rating Score – Revised (ALS-FRS-R) score, body mass index, and the Dysphagia Handicap Index (DHI) patient-reported outcome based dysphagia tool were also investigated.

Swallowing function was assessed with three thin liquid boluses of increased volume, two 5mL pudding boluses and one piece of graham cracker. Pharyngeal residue, PAS and number of swallows per bolus were rated by two independent investigators. Between-group findings included significant impairment in function in the ALS group on all clinical measures and all swallowing severity ratings with the exception of the smallest liquid bolus trial, compared to the performance of the control group. Within the ALS group, significant correlations were present to support the hypothesis that swallowing function can be predicted by various clinical measures including DDK, FVC the DHI and number of swallows per bolus. Duration of disease and type of onset were significantly correlated with severity of dysphagia in ALS.

In conclusion, clinical measures can be beneficial in predicting severity of dysphagia in individuals with ALS. There is a significant correlation between DDK, FVC, DHI, number of swallows per bolus with decline in swallowing function in ALS.

AUTOBIOGRAPHICAL STATEMENT

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Arthur Knack is a Staff Speech-Language Pathologist at the Veteran's Affairs Medical Center in Detroit, Michigan. He received his Bachelor of Health Science from the University of Kentucky and Master of Science from the University of North Carolina at Chapel Hill. His clinical and research interests are in the area of dysphagia. Arthur was the Inpatient Speech-Language Pathology Coordinator at Henry Ford Hospital – Detroit for 8 years in addition to his role as the primary Speech-Language Pathologist for nine years in the Harry J. Hoenselaar ALS clinic He has presented at various conferences in Michigan. He is married to Adrienne Knack and is the proud father of Lily Knack. He resides in Brighton, Michigan.