Perceptual and Physiologic Analysis of Dystussia in Amyotrophic Lateral Sclerosis

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Perceptual and Physiologic Analysis of Dystussia in Amyotrophic Lateral Sclerosis

by

Stephanie Anne Watts

A dissertation submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
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Keywords: Dystussia, Dysphagia, Clinical Swallowing Assessment

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DEDICATION

This work is dedicated to my dad, Charles.
ACKNOWLEDGMENTS

This Ph.D. has been a long journey and there are many important individuals to acknowledge and thank. To my husband, for always being there; I do love you more than you know. To my mom, a role model of strength, resilience, and perseverance. Thank you for telling me when I should breathe and for being so proud. I am especially thankful for my dad, who is no longer physically here. He always encouraged me to keep learning and work hard. Prior to his death he told me to never give up on this Ph.D. and therefore, I did not as there are “no limits” to what I can achieve. To my big brother and sister, I admire you both. To my friends, Anna and Julie, thank you for picking up the phone at any time of day or night.

To my committee, I would like to thank you all for your continued support throughout these series of projects. I have learned so much from each of you and appreciate your time and efforts. Thank you Dr. Eddins for taking me as a student and guiding me to complete this body of work. Thank you Dr. Ozmeral for hours of program writing in MatLab. Dr. Pitts, thank you for being so passionate about your work, your student’s success, and for all the hours of work you put in to help me grow as a scientist. I will always “keep going”. Dr. Plowman, thank you for seeing the potential in me as a Master’s student and providing many opportunities for growth.

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# TABLE OF CONTENTS

List of Tables........................................................................................................iv

List of Figures........................................................................................................v

Chapter One: Introduction.........................................................................................1
  Eupnea/Breathing....................................................................................................4
  Alterations of the Eupneic/Breathing Pattern......................................................7
    Cough.................................................................................................................10
    Swallow.............................................................................................................12
  Cough and Swallow: Shared Neural and Anatomical Space.............................14
    Neuronal Activity...............................................................................................15
    Anatomical Structures.........................................................................................16
    Gating of Airway Protective Behaviors..............................................................18
  Dystussia and Cough Measurement....................................................................20
  Reflexively and Voluntarily Induced Cough .......................................................20
    Airflow Measurement.........................................................................................21
    Sound Characteristics.........................................................................................23
  Dysphagia............................................................................................................24
    Clinical Evaluation of Dysphagia....................................................................25
  Dysphagia, Dystussia, and Airway Protection....................................................26

Chapter Two: To Cough or Not To Cough? Examining the Potential Utility of Cough Testing In the Clinical Evaluation of Swallowing.................................................................29
  Introduction.........................................................................................................29
  Relationship between Cough and Swallow........................................................36
  Clinical Swallowing Evaluation..........................................................................38
  Validated Clinical Swallow Evaluations and Screening Tools..........................39
  Utility of Voluntary Cough Testing in Dysphagia...............................................41
    Stroke.................................................................................................................46
    Parkinson’s disease............................................................................................47
    Amyotrophic Lateral Sclerosis..........................................................................48
    Reflexive or Induced Cough Testing.................................................................51
  Limitations and Future Directions....................................................................57
  Conclusions.........................................................................................................57

Chapter Three Current Practice Patterns...............................................................59
  Introduction.........................................................................................................59
  Methods..............................................................................................................61
Participants…………………………………………………………………………61
Materials and Procedures…………………………………………………………62
Statistical Analysis……………………………………………………………………62
Results……………………………………………………………………………………63
Participant Demographics…………………………………………………………63
Inclusion of Voluntary Cough Assessment…………………………………65
Interaction between Clinical Experience and Certification level……………66
Abnormal Voluntary Cough…………………………………………………………67
Clinical Swallowing Assessment Pattern………………………………………67
Discussion…………………………………………………………………………….68
Limitations and Future Directions………………………………………………71
Conclusions………………………………………………………………………….72

Chapter Four: Perceptual and Clinical Indices of Cough Assessment…………74
Introduction…………………………………………………………………………..74
Methods………………………………………………………………………………..76
Participants……………………………………………………………………………76
Equipment……………………………………………………………………………..77
Testing Protocols……………………………………………………………………77
Data Analysis and Statistics………………………………………………………..81
Results………………………………………………………………………………….81
Presence/Absence of Aberrant Cough Sounds…………………………………84
Reliability of the VAS for Cough Assessment……………………………………85
Discussion……………………………………………………………………………..86
Limitations and Future Directions…………………………………………………87
Conclusions…………………………………………………………………………..87

Chapter Five: Physiologic Assessment of Voluntary Cough in ALS………………89
Introduction……………………………………………………………………………89
Methods………………………………………………………………………………..91
Participants……………………………………………………………………………91
Testing Protocol………………………………………………………………………91
Swallowing……………………………………………………………………………92
Acquisition of Cough Airflow and Acoustic Waveforms………………………92
Data Analysis and Statistics………………………………………………………..93
Results………………………………………………………………………………….98
Discussion……………………………………………………………………………..102
Limitations and Future Directions………………………………………………105
Conclusions………………………………………………………………………….105

Chapter Six: Conclusions and Future Directions…………………………………107

References……………………………………………………………………………109
LIST OF TABLES

Table 2.1: Summary of published clinical swallowing evaluation protocols and screening tools with reference to first author, patient population validated against, protocol items, and test sensitivity and specificity for detecting swallowing impairment and/or aspiration (as specified)…………………… 34

Table 2.2: Definitions of objective voluntary cough airflow measures with reference to illustrative cough waveform depicted in Figure 2.1…………………… 45

Table 2.3: Review of six research studies investigating the significant differences in voluntary cough measures between unsafe (penetrators and/or aspirators) and safe (non-aspirators) swallowers in dysphagic populations including Stroke, Parkinson’s disease, and Amyotrophic Lateral Sclerosis…………… 46

Table 2.4: Summary of published reports investigating the discriminant ability of reflexive cough testing to detect swallowing safety………………………… 54

Table 3.1: Demographic characteristics of survey respondents (N = 605)………………… 65

Table 3.2: Use of voluntary cough assessment by years of experience, practice setting, and level of certification (n = 603)…………………………………… 67

Table 4.1: Definitions of aberrant cough signs including huffing, voicing, wet/gurgled, inspiratory stridor; features were perceptually judged to be present or absent…………………………………………………………………… 83

Table 4.2: Participant demographics (N=44)………………………………………… 84

Table 4.3: Overall and airway safety group distribution for the presence/absence of perceptual cough features including voicing, huffing, inspiratory stridor, and wet/gurgled quality……………………………………………… 87

Table 5.1: ALS participant demographics including global disease rating scale with subscale bulbar and respiratory domain data…………………………… 101
| Table 5.2  | ALS participant respiratory function including forced expiratory volume (FEV1), forced vital capacity (FVC), FEV1/FVC, and peak expiratory flow as measured by a hand held analog peak flow meter. *Average peak flow as calculated from three voluntary cough trials. | 101 |
LIST OF FIGURES

Figure 1.1: Schematic that combines the function of the mechanoreceptors and chemoreceptors with basic input-processing-output systems ............................... 9

Figure 1.2: Same as Figure 2.1 Example of voluntary cough waveform measured with cough spirometry .......................................................... 22

Figure 2.1: Example of voluntary cough waveform measured with cough spirometry .......................................................... 43

Figure 3.1: Color illustrative map of the United States of America representing U.S. participants by state. The darker shaded colors indicate greater number of respondents .......................................................... 63

Figure 3.2: Bar graph representing distribution of respondents who reported assessing voluntary cough during the clinical swallow grouped by years of experience .......................................................... 66

Figure 4.1: Three vertically positioned 100-mm lines were used as a VAS for perceptual ratings of cough strength, loudness, and effectiveness ............. 80

Figure 4.2: A bar graph indicating difference in mean perceptual VAS scores of voluntary cough strength between safe (PAS ≤ 2) vs. unsafe (PAS > 2) swallow groups t(42)=2.08, p < 0.05. ......................................................... 83

Figure 4.3: Scatterplot demonstrating a strong significant positive correlations between disease rating scale, the ALS functional rating scale (ALSFRS-R) scores and perceptual VAS ratings of cough strength ..................... 84

Figure 5.1: Image depicts a sample data collection page rendered using LabChart version7 .......................................................... 97

Figure 5.2: Anthropomorphic features of acoustic cough signals were tagged and recorded. Time and peak amplitude were analyzed to derive final measures: A) onset time of the cough signal to the time of the first peak frequency B) time from the first peak frequency to the time of the second peak frequency, and C) time of the second peak frequency to the end of the acoustic cough signal .......................................................... 98
Figure 5.3: Cough waveform variations were classified for single acoustic cough signals; they were analyzed from the same recording channel for each subject according to the following definitions: A. fast augmenting signal and fast decrementing signal B. slow augmenting and slow decrementing signal C. fast augmenting and slow decrementing signal and D. slow augmenting and fast decrementing acoustic signal.

Figure 5.4: Depicted in three panels, A., B., and C., are airflow, acoustic, and spectral representations of cough in safe (PAS ≤ 2) and unsafe (PAS ≥ 3) swallowers.
CHAPTER ONE:
INTRODUCTION

Swallowing and cough are two vital functions that are reflexive in nature and are related to each other in terms of shared neural and anatomical space. When a disorder impacts normal and effective swallowing and/or cough, the consequences can be life-threatening. Evaluation and treatment of swallowing and cough disorders can fall under the scope of practice of the speech-language pathologist and speech-language pathologists often are leading professionals. Furthermore, much of the current research on swallowing and cough is spearheaded by speech-language pathologists often working with a multi-disciplinary team. The focus of this dissertation is on the clinical evaluation of cough and swallowing, practice patterns of voluntary cough assessment during the evaluation of swallowing, and novel methods of evaluating acoustic voluntary cough waveforms in patients with and without swallowing impairment. The results will provide important information regarding the state of cough assessment tools for clinical swallowing evaluation, clinical practice patterns of voluntary cough assessment, and differences in acoustic cough signals between safe and unsafe swallowers in individuals with Amyotrophic Lateral Sclerosis (ALS).

It is important to understand the basic terminology, physiology, and neurophysiology of swallow and cough in order to frame and interpret the studies included in this dissertation. This introduction is designed to provide the background and motivation for the subsequent investigations. Swallowing is a complex sensory and motor function; it is described by its clinical
characteristics such as coughing and choking while eating or drinking. Dysphagia is the term that denotes disordered swallowing (Logemann, 1984). Unidentified or untreated dysphagia may lead to a pulmonary infection termed, aspiration pneumonia (Ebihara, 2016). Evaluation of swallowing function is performed on a continuum. Swallowing screening implies a pass/fail criteria, clinical swallowing evaluation (CSE) is a more in depth evaluation of swallowing, and finally, the modified barium swallow (MBS) study is considered the gold standard instrumental assessment of swallowing ability. The Penetration Aspiration Scale (PAS) often is used during gold standard swallowing assessment to rate swallowing function and denote level of airway compromise and the patient’s ability to successfully eject material from the airway (Rosenbek, Robbins, Roecker, Coyle, & Wood, 1996).

Cough and swallowing are intricately related. Physiologically, cough consists of “an inspiratory effort (inspiratory phase), followed by a forced expiratory effort against a closed glottis (compressive phase) followed by opening of the glottis and rapid expiratory airflow (expulsive phase)” (Widdicombe & Fontana 2006, p. 10). Clinically, the cough is a respiratory event that serves to maintain ventilation by protecting the lower airways (West 1995). Cough, a vital airway protective mechanism, is particularly important for those with disordered swallowing. Dystussia, or disordered cough is a key clinical feature of dysphagia and described by its clinical features. Physiologically, dystussia reduces a patient’s ability to protect his/her airway. And clinically, dystussia decreases an individual’s ability to protect their airway and thus greatly increases the risk for aspiration, subsequent aspiration pneumonia, and excess hospitalizations (Ebihara, 2016; Hegland, Okun, & Troche, 2014; Pitts, Bolser, Rosenbek, Troche, & Sapienza, 2008; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016; Smith Hammond, 2001).

Although the MBS provides good visualization of a patient’s ability to protect the airway
and direct visualization of cough effectiveness, it is not always performed. The CSE is often implemented in place of, or prior to an MBS and is a critical component of the swallowing evaluation but fails to identify all those with unsafe swallowing especially those who do not respond to deep penetration or aspiration with a cough. Therefore, clinicians rely on clinical signs and symptoms to detect dysphagia or dystussia.

Respiratory, cough, and swallowing impairments are highly prevalent in individuals with neuromuscular diseases such as Amyotrophic Lateral Sclerosis (ALS) and Parkinson’s disease (PD). Dystussia has been described in neurodegenerative disease populations such as PD, Stroke, and ALS (Pitts, Bolser, Rosenbek, Troche, & Sapienza, 2008; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016; Smith Hammond, 2001) by using gold standard physiologic analysis of airflow waveforms called cough spirometry. Although it appears that voluntary cough production is related to airway protection status during swallowing in several patient populations, the gold standard methodology to test cough objectively is costly, the analysis labor intensive and time consuming, and requires extensive training to perform expert evaluation of physiologic cough waveforms. Given the limitations for the application of gold standard cough assessment, clinicians may not have the necessary tools to correctly detect impaired cough. Cough evaluation may therefore be under-utilized while evaluating dysphagia symptoms. While current clinical

evaluation of cough is focused on cough frequency, cough reflex testing (often using tussive agents), voluntary cough measures, and patient subjective ratings of severity, little is known regarding the reliability or validity of clinician perceptions of voluntary cough effectiveness or the acoustic characteristics of cough during the clinical swallow evaluation. A recent study investigated the perceptual features of cough (Laciuga, Brandimore, Troche, & Hegland, 2016), and found that coughs with specific perceptual features also shared airflow characteristics. However, further work is warranted to determine specific disordered features of impaired cough that relate to airway protection in multiple patient populations. Currently, there is little information on the clinical use of perceptual cough ratings and there are no validated screening tools that support clinician rating of cough impairment or that are designed to determine the relation of such ratings to airway protection during swallowing. There remains a clinical need for a cost effective, readily available, low technology, sensitive and specific clinical screening tool of voluntary cough that may aide in determining an individual’s risk for aspiration during swallowing.

**Eupnea/Breathing**

All mammals engage in breathing behaviors. In humans, the transition from a breathing state to swallowing is an essential life sustaining behavior.² The processes of breathing, swallowing, and coughing (airway protection) are interrelated at both neurological and physiological levels (Gestreau, Milano, Bianchi, & Grelot, 1996; Pitts, Rose, Mortensen, Poliacek, Preiksaitis & Mills, 1996; Stanford, Galvin, & Rooholamini, 1988; Terzi, Orlikowski, Aegerter, Lejaille, Ruquet, Zalcman, Fermanian, Raphael, & Lofaso, 2006; Wilson, Thach, Brouillette, & Abu-Osba, 1981)

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² (Feroah, Forster, Fuentes, Lang, Beste, Martino, Pan, & Rice, 2002; Gross, Atwood, Ross, Eichhorn, Olszewski, & Doyle, 2008; Hadjikoutis, Pickersgill, Dawson, & Wiles, 2000; Kelly, Drinnan, & Leslie, 2007; Pitts, Morris, Segers, Poliacek, Rose, Lindsey, Davenport, Howland, & Bolser, 2016; Pitts, Rose, Mortensen, Poliacek, Sapienza, Lindsey, Morris, Davenport, & Bolser, 2013b; Preiksaitis & Mills, 1996; Stanford, Galvin, & Rooholamini, 1988; Terzi, Orlikowski, Aegerter, Lejaille, Ruquet, Zalcman, Fermanian, Raphael, & Lofaso, 2006; Wilson, Thach, Brouillette, & Abu-Osba, 1981)
Sapienza, Lindsey, Morris, Davenport, & Bolser, 2013b; Troche, Brandimore, Godoy, & Hegland, 2014). Quick adaptation from one behavior to another allows for normal airway protection. It is essential to understand the neuroanatomical function of normal breathing including lung function, swallowing, and coughing in order to identify a disordered state. Eupnea (i.e. quiet breathing) is a rhythmic respiratory pattern to move air for ventilation and gas exchange (Bautista, 2014; Bianchi, Denavit-Saubie, & Champagnat, 1995; Bolton, Chen, Wijdicks, & Zifko, 2004; Bonham, 1995; Champagnat, 2003; Clark & Von Euler, 1972; Gray, Janczewski, Mellen, McCrimmon, & Feldman, 2001; Von Euler, 1986; Wang, 1964; West, 1995) Eupnea can be divided into three phases: 1) inspiration; 2) post-inspiration (i.e. early expiration); and 3) expiration (Bianchi, 1995; Richter, 1982; Richter, 1986). The lungs do not have an internal mechanism to produce the rhythmic pattern that characterizes eupnea. As such, eupnea is centrally mediated.

Breathing is controlled via brainstem pathways. The motor neurons that drive respiratory muscles are divided into three groups: 1) sub-nucleus of the nucleus tractus solitaries (NTS) and the dorsal respiratory group (DRG) in caudal dorsomedial medulla; 2) ventral respiratory group in ventrolateral medulla (VRG); and 3) pontine respiratory group (PRG) in dorsolateral pons (Abdala, Rybak, Smith, & Paton, 2009; Ellenberger & Feldman, 1988, 1990). The Raphe and retrotrapezoidal nucleus (RTN/PF) (which overlaps with the para-facial respiratory group) also play a role in the activation of inspiratory and expiratory driven neurons (Connelly, Ellenberger, & Feldman, 1989). Dorsal inspiratory neurons have monosynaptic connection with contralateral phrenic motoneurons (Averill, Cameron, & Berger, 1985; Cohen, 1974). The basic breathing rhythm originates in the ventral reparator group (Smith, Ellenberger, Ballanyi, Richter, & Feldman, 1991).

Inspiration is controlled via the brainstem within the ventral and dorsal respiratory groups,
which activate premotor neurons, and phrenic motoneurons located within the ventral horn of the
cervical spinal cord segments 3-6 (Berger, 1979; Gordon, 1990; Loewy & Burton, 1978). External
intercostal muscles then contract to elevate the anterior rib cage and that contraction draws down
the diaphragm (Troyer, 1985). Simultaneously, the posterior cricoarytenoid (laryngeal abductor)
activation allows for passage of air through the glottis (the space between the vocal folds)
(Berkowitz, Chalmers, Sun, & Pilowsky, 1999). Laryngeal adductors (thyroarytenoid, lateral
cricoarytenoid, and interarytenoids) slightly narrow the glottis during post inspiration (Poliacek,
Stransky, Jakus, Barani, Tomori, & Halasova, 2003). Neurons whos cell bodies are within the
spinal cord termed ‘motoneurons’ supply a method of activation to muscles; the motoneruons that
move muscles within the larynx can be found in the caudal brainstem near the nucleus
retroambiguus (Berkowitz, Chalmers, Sun, & Pilowsky, 1999; Bieger & Hopkins, 1987).

Expiration during quiet breathing occurs as a result of passive recoil from the lungs and
negative atmospheric pressure (relative to thoracic pressure) (Iscoe, 1998), allowing air to be
expelled (Campbell, 1955). Minimal abdominal motor drive occurs during the expiratory phase of
eupnea (Abdala, Rybak, Smith, & Paton, 2009). Attachment of the lungs to the chest wall via the
pleural space allows for movement of the lungs during breathing (Agostoni, 1986).

Essential gases such as oxygen, carbon dioxide, and hydrogen are monitored in the body
by peripheral chemoreceptors within the carotid and aortic bodies; they then project to the NTS
(Donoghue, 1985). These receptors drive neuron activity within the brainstem and sleep-wake
centers, which then moderate interactions with other airway protective pattern generators (cough,
swallow, etc.) (Guyenet, Mulkey, Stornetta, & Bayliss, 2005; Lindsey, Ott, Nuding, Segers,
O'Connor, & Morris, 2011). Their interactions are also termed “reconfiguration.” More
specifically, to describe changes in excitability of eupnea neural network components; these
networks are altered based on evaluation of incoming sensory information into the nucleus tractus solitarius (NTS) (Baekey, Morris, Gestreau, Li, Lindsey, & Shannon, 2001; Lindsey, Hernandez, Morris, Shannon, & Gerstein, 1992; Pitts, Morris, Segers, Poliacek, Rose, Lindsey, Davenport, Howland, & Bolser, 2016; Pitts, Rose, Mortensen, Poliacek, Sapienza, Lindsey, Morris, Davenport, & Bolser, 2013a; Rose, Pitts, Poliacek, Davenport, Morris, & Bolser, 2011; Shannon, 2000).

In vivo translational research studies have elucidated the sensory-neural pathways that regulate breathing/eupnea. Cranial nerve X, the vagus, arises from the inferior and superior vagal ganglia (nodose and jugular respectively) and relays (transports) lung sensory information (Canning, Mazzone, Meeker, Mori, Reynolds, & Undem, 2004; Ootani, Umezaki, Shin, & Murata, 1995). Lung sensory receptors differ in both chemical and mechanical responsiveness, anatomical, embryological, and physiological attributes. They send information to the brainstem respiratory network.

Alterations of the Eupneic/Breathing Pattern

It is theorized that the rhythm of breathing may be altered for many reasons such as sneezing, coughing, exercise, and breath holding. Complicated fine motor behaviors such as speaking and swallowing also may change the basic rhythm of breathing. Essential human functions such as swallowing and respiratory defensive actions such as coughing may be disordered and thus are a specific area of interest to researchers. The primary function of the lungs is to allow for ventilation or the exchange of oxygen and carbon dioxide. Oxygen is moved into the blood stream and carbon dioxide is removed. West (1995) describes a series of fundamental input, processing, and output interactions between pulmonary and cardiac systems to produce breathing and allow for ventilation. The input system is comprised of higher brain activity (cortex
and limbic system) that receives information from mechanoreceptors and chemoreceptors.

Mechanoreceptors are afferent (sensory) receptors that respond to changes in the airway and lungs. Mechanoreceptor subtypes can be classified based on the rate of adaptation. Adaptation refers to how the sensory system changes in terms of the responsiveness to a stimulus after a constant stimulus is presented (Canning, Mori, & Mazzone, 2006). These subtypes include: 1) slowly adapting pulmonary stretch receptors (SARs); 2) rapidly adapting pulmonary irritant receptors (RARs) (Canning, Farmer, & Mori, 2006; Canning, Mori, & Mazzone, 2006); 3) bronchopulmonary C-fibers (afferent) that can be intrapulmonary, extra pulmonary, tracheal, or bronchial (Canning, Farmer, & Mori, 2006); 4) intrapulmonary juxtacapillary or also termed “J-receptors” which react to pulmonary edema or pneumonia (Canning, Farmer, & Mori, 2006; West, 1995); and 5) baroreceptors that come in through the nucleus tractus solitarius (NTS) and excite cells in the aorta in response to the stretch of blood vessels (Ott, Nuding, Segers, Lindsey, & Morris, 2011).

Chemoreceptors sense changes in blood gases including oxygen (O2), carbon dioxide (CO2), pH concentrations, and can be described anatomically in terms of peripheral (airway) and central (neural) loci (Heymans, 1927). They have been described as the most important regulators of breathing (Buchanan, 2013). Peripheral chemoreceptors (aortic and carotid) have many important roles to regulate gas exchange function and are responsible for 25% of chemoreceptor drive of ventilation (Lahiri, 1975). Peripheral chemoreceptors stimulate respiration under the following conditions: 1) during changes in arterial PO2 (decreased oxygen in arteries and tissue) (Green, 1986); 2) during changes in blood pH (non-respiratory problems such as metabolic alkalosis and acidosis); and 3) during depression of central chemoreceptors (Dejours, 1962; Dejours, 1963; Hornbein, 1961). Under the influence from anesthesia or narcotics; peripheral
chemoreceptors may become the primary stimulus for ventilation (Takakura, Moreira, Colombari, West, Stornetta, & Guyenet, 2006). Central chemoreceptors are responsible for 75% of central drive for ventilation and they are sensitive to hydrogen and CO₂ changes in extracellular fluid. When there is a high level of CO₂ in the blood, an inspiration is triggered to promote ventilation (Li & Nattie, 1997; Lindsey, Ott, Nuding, Segers, O’connor, & Morris, 2011).

The ventilation processing system includes respiratory neurons located within the brainstem and spinal cord; they receive mechanical information from the lungs and chemical information from hemoglobin and blood buffers (West, 1995). The incoming pulmonary afferent information is vagally mediated and processed by second order interneurons in the (NTS) (Kubin, Alheid, Zuperku, & McCrimmon 1985, 2006). Motor drive is then provided to the chest

![Figure 1.1](image_url). Schematic that combines the function of the mechanoreceptors and chemoreceptors with basic input-processing-output systems.*

*Input-processing-output schematic generated from material on respiration (Buchanan, 2013).
capillary membrane and hemoglobin and blood buffers (West, 1995).

Ventilation is a complex and carefully orchestrated process involving the coordination of peripheral and central processes; it sustains life. The respiratory musculature also supports and produces other airway protective behaviors including cough and swallow. For a successful cough and swallow to occur, both functioning peripheral and central processes must be coordinated with eupnea. It has been shown that cough and eupnea share similar premotor neuron firing patterns during eupnoea and cough (Baekey, Morris, Gestreau, Li, Lindsey, & Shannon, 2001). Successful coughing and swallowing also require the appropriate functional anatomy and musculature. Understanding the neural and physical alternations of breathing for cough and swallow allow for the proper evaluation and treatment of disordered cough and swallow. The following sections will review the mechanisms of cough and swallow as alterations from the basic breathing rhythm.

Cough

Cough is vital behavior that assists in preserving the gas-exchange function of ventilation by clearing foreign material such as aspirate (any inhaled matter or secretions) (Dicpinigaitis, 2007; Widdicombe & Fontana, 2006); the motor act of a cough can be triggered at multiple locations within the upper aerodigestive and respiratory tracts such as, the larynx, trachea, or bronchi.\(^3\) The European Respiratory Society (ERS) states that cough is a “three-phase motor act” (Morice et al., 2007, p. 1256). An effective cough requires high velocity airflow and that airflow usually results from three phases: 1) inspiration; 2) compression; and 3) expulsion (Castillo & Pitts, 2013; Fontana

\(^3\) (Bolser, 1991; Bolser & Davenport, 2000; Bolser, Degennaro, O'reilly, Chapman, Kreutner, Egan, & Hey, 1994; Forsberg & Karlsson, 1986; Gestreau, Milano, Bianchi, & Grelot, 1996; Jakus, Poliacek, Halasova, Murin, Knockova, Tomori, & Bolser, 2008; Pitts, 2012; Poliacek, Wang, Corrie, Rose, & Bolser, 2010; Rose, Pitts, Poliacek, Davenport, Morris, & Bolser, 2011).
During inspiration the diaphragm and chestwall muscles (parasternal and external intercostals) contract to rapidly increase lung volume (Hanacek, Davies, & Widdicombe, 1984; Langlands, 1967; Lavietes, Smeltzer, Cook, Modak, & Smaldone, 1998; Loudon & Shaw, 1967; McCool, 2006). Next, the vocal folds come together (adduct) and expiratory muscles contract; this is referred to as the “compression phase” and at this time, subglottic pressure increases (McCool, 2006). Abduction of the vocal folds marks the beginning of the expiratory phase. The expiratory muscles continue to contract generating high airflow rates that may reach up to 12 liters per second (L/s) in normal healthy adults (Langlands, 1967). Cough is a vital airway protective behavior and can be initiated via laryngeal and tracheal sensory afferents via a brainstem pattern generator (Morris, Arata, Shannon, & Lindsey, 1996; Mutolo, Cinelli, Bongianni, & Pantaleo, 2014; Poliacek, Corrie, Rose, Wang, & Bolser, 2008; Poliacek, Rose, Corrie, Wang, Jakus, Barani, Stransky, Polacek, Halasova, & Bolser, 2008).

The production of cough may appear rudimentary to novel observers, however it is a very complex motor act involving the coordination of multiple physiological systems as well as neurological networks. Understanding of the neural bases of cough and motor output drive is necessary in order to effectively target pharmacological treatment and/or to manage impaired cough (Mutolo, Bongianni, Cinelli, Fontana, & Pantaleo, 2008; Poliacek, Plevkova, Pitts, Kotmanova, Jakus, & Simera, 2016; Shannon, Baek, Morris, Nuding, Segers, & Lindsey, 2004).
Cough is a vagally mediated behavior, which can be activated by myelinated and non-myelinated vagal afferent nerves; it is diminished by anesthesia and eliminated by vagotomy (Canning, Mazzone, Meeker, Mori, Reynolds, & Undem, 2004; Canning, Mori, & Mazzone, 2006).

Peripheral afferent fibers detect stimuli in the laryngeal and pulmonary mucosa. Data based on in vivo cat, rabbit and guinea pig models indicate that non-myelinated C-fibers (specifically in the carina) respond to chemical irritants (Sant'ambrogio, Sant'ambrogio, & Davies, 1984). Messages are sent ascending through the dorsal root ganglion to second-order neurons in the nucleus tractus solitarius (NTS) (Kubin, Alheid, Zuperku, & Mccrimmon, 2006; Kubin, 1985). Central pattern generators (CPGs), or groups of neurons in the brainstem and medulla, respond to incoming sensory information and regulate descending neural drives. Pontine and medullary respiratory neurons send descending motor drives to muscles of inspiration and expiration for production of the cough. The neurophysiology of cough requires precise temporal activation and suppression of neural networks (Bolser, Poliacek, Jakus, Fuller, & Davenport, 2006).

Two distinct types of defensive reflexes of the respiratory tract are described throughout the literature: 1) cough (Leith, 1977), and the 2) expiration reflex (Williams, 1841). Although both reflexes can be induced by mechanical and chemical irritation to the aerodigestive and respiratory tracts, they differ in the sensory pathway that are activated within the brain and also the central nervous system circuits which control the behaviors (Widdicome & Fontana, 2006). Cough and expiration reflex also differ in terms of the presence of a pre-explosive inspiratory phase. Expiratory reflex does not have the inspiratory effort prior to the expulsion of air.

Swallow

Swallowing encompasses the integration of a complex sensory and motor system that is under both reflexive and voluntary control. Normal swallowing is a continuous series of events
that scientists and clinicians conceptually divide into “phases”; these three phases are: oral prepatory, oral, pharyngeal, and esophageal (Doty, 1968; Logemann, 1984; Miller, 1982). Some literature report a pre-oral prepatory phase prior to mastication, where neural activity begins and the body anticipates bolus (material swallowed) delivery (Leopold, 1997). Single and consecutive swallow events require precise temporal integration of neural activity and muscle movements; with this, muscle movements within the throat are coordinated and permit food and liquid to flow through the pharynx and into the esophagus (food pipe). The process of swallow and the associated motor movement of the oral structures and larynx have been well defined in the literature (Doty, 1956) as a series of chambers and valves that participate to allow for safe passage of a bolus through the oral cavity and pharynx and then safely into the esophagus (Dodds W.J, 1990; Kahrilas & Logemann, 1993; Logemann, 1998; Olthoff, Zhang, Schweizer, & Frahm, 2014).

During the pharyngeal stage of swallow, the soft palate elevates to meet the pharyngeal wall; this velopharyngeal valve closes off the passageway to the nasal cavity and allows for buildup of pressure within the pharynx (Kahrilas, 1993; Logemann, 2007). Following elevation of the pharynx, the larynx elevates through contraction of submental muscles which move the hyoid bone superiorly and anteriorly; subsequently, three levels of laryngeal airway protection ensue (Logemann, 1984). Multiple valves begin to close off the passage to the airway as food or liquid passes through the pharynx (Logemann, 2007). The pharyngeal phase of swallow is described as the following behavioral sequence: 1) the epiglottis inverts; 2) the ventricular folds and arytenoid cartilages move to a medial position; 3) the vocal folds adduct, sealing the passage to the to the airway within the larynx (Logemann, 2007); and 4) the superior portion of the esophageal sphincter (UES) relaxes (Kahrilas P.J., 1988; Logemann, 1984, 2007). These actions result in the bolus passing through the UES into the esophagus completing the pharyngeal phase.
A single swallow takes less than 2 seconds to complete and within that time, twenty-six pairs of muscles and five cranial nerves coordinate sensory and motor actions. The neurologic network underpinnings of swallow are not completely understood; however, brainstem control of the swallowing process has been investigated in vivo (Gestreau, 1996; Mogoseanu, 1993; Jean, 2001). The neural network for swallowing is sophisticated and involves carefully organized connections between respiratory and cough neural networks (Gestreau, 1996; Pitts, 2012).

Mechanisms of a swallow central pattern generator (CPG) are discussed in the literature as an organization of central control of swallowing (Ertekin & Aydogdu, 2003). The swallow CPG is located in the brainstem and is comprised of two distinct areas, dorsal and ventral. The dorsal population is within nucleus tractus solitaries (NTS) and while the ventral swallow group is a group of pre-motor neurons within the nucleus ambiguous (NA) (Ertekin & Aydogdu, 2003). This extensive network provides control and regulation of over the swallow process (Ertekin & Aydogdu, 2003) both augmenting and decrementing-descending motor drives to muscles. Pre-motor neurons relay information to motor neurons, which in turn send drives to muscles. “Behavior control assemblies” or BCAs represent additional networks within the system that are theorized to regulate processes of respiration, cough, and swallow by overriding CPGs (Bolser, Poliacek, Jakus, Fuller, & Davenport, 2006). It is suggested that, if there is a disruption to the peripheral-sensory, central-neural motor, anatomical-structural mechanisms, or a combination of each, then the swallow behavior will be disordered.

**Cough and Swallow: Shared Neural and Anatomical Space**

Cough and swallow are remarkably coordinated behaviors both in terms of neuronal activity and shared anatomical structures. As aforementioned, afferent (sensory) information is
being processed in the NTS which activates the central generators. The CPG then drives the pre-motor and motor neurons-activate muscles stimulating the superior laryngeal nerve to produce both cough and swallowing. Evidence shows that there are both shared neural and anatomical substrings; a shared NTS (Gestreau, 1996); shared pre-motor neurons (Shiba K., 2007) and muscle activity (Pitts, Rose, Mortensen, Poliacek, Sapienza, Lindsey, Morris, Davenport, & Bolser, 2013b). Below is a review of these interconnectivities.

**Neuronal Activity**

Neural networks and activation patterns for breathing, cough, and swallow have both shared and distinct properties (Dick, Oku, Romaniuk, & Cherniack, 1993; Gestreau, 1996). As previously discussed, CPGs in the brainstem regulate the process of eupnea. CPGs must be flexible in their connectivity to allow for rapid change between behaviors of breathing, swallowing, and coughing. Coordination and/or presence of both cough and swallow has been proposed as being a “meta-behavior” (Pitts, Rose, Mortensen, Poliacek, Sapienza, Lindsey, Morris, Davenport, & Bolser, 2013b) in that a central control system coordinates the motor output of the distinct CPGs for either a cough behavior or swallow. Jean (2001) proposed that the shared CPG for swallow and breathing is located within the brainstem in the area of the nucleus ambiguus (NA), dorsal respiratory group (DRG), and ventral respiratory group (VRG). Evidence of a flexible neural system was discovered as Gestreau and colleagues (1996) examined the intracellular response of 33 neurons in the DRG during fictive swallowing. In the experiment by Dr. Gestreau and colleagues, superior laryngeal nerve (SLN) afferent fibers were stimulated to produce a fictive swallow. DRG neurons exhibited swallow-related burst activity in response to SLN stimulation (Gestreau et al., 1996). Results indicated that neurons in this region might be “flexible” in their functions and adapt to incoming stimuli. Rapid timing between changes from swallow to cough
behavior offer further evidence of shared and flexible underpinnings (Bolser, 2002). Authors describe the multi-synaptic connections within respiratory neural networks that allow for the prompt behavior selection; coughing immediately in response to tracheal irritants such as aspiration.

Neurons that are firing during respiration have also been shown to fire during swallow. Bulbospinal inspiratory modulated neurons in the nucleus tractus solitaries (NTS) are depolarized (making the cell positively charged) and exhibit burst activity during swallowing (Bautista, 2014; Jean, 2001). Propriobulbar inspiratory modulated neurons also are activated during swallow (Gestreau et al., 1996). This inspiratory neuronal activity may be responsible for the “shluckatmung” (Spearman, 2014). The “shluckatmung” is a term for the “swallow breath,” which is a burst of phrenic activity during swallow (Spearman, 2014). Evidence of the shluckatmung was shown by EMG recordings of increased parasternal activity and neuroanatomical connectivity related to the behaviors of cough and swallow in the feline model (Pitts, Rose, Mortensen, Poliacek, Sapienza, Lindsey, Morris, Davenport, & Bolser, 2013b). This has also been shown in humans and goats (Feroah, Forster, Fuentes, Lang, Beste, Martino, Pan, & Rice, 2002; Hardemark Cedborg, Sundman, Boden, Hedstrom, Kuylenstierna, Ekberg, & Eriksson, 2009).

Higher order cortical processing may also be a part of the shared coordination of the neural systems. Computational modeling incorporating shared cortical networking components has derived motor activity outputs resembling in vivo studies (Olthoff, Zhang, Schweizer, & Frahm, 2014). The models elucidate additional shared networks participating in the coordination of swallow and cough behaviors.

Anatomical Structures

Breathing, swallowing, and cough share common anatomy. As the central pattern generator
within the brain evaluates information regarding the quality of the swallow (i.e., if the swallow is safe or unsafe), motor activation within respiratory muscles change (Pitts et al., 2013). Peripheral afferent fibers lining the mucosa of the larynx and trachea detect aspiration by informing the swallow CPG (Pitts, Morris, Lindsey, Davenport, Poliacek, & Bolser, 2012). The pharyngeal muscles have been described as having a dual role including as a passive participant in the movement of food through the pharynx as well as functioning as a sensory feedback system for cough production (Pitts et al., 2013). Pitts (2013) described suppression of the thyropharyngeus muscle activity during cough in an animal model and proposed that this activity is meant to protect the airway by collecting food and liquid that has not been completely expelled.

The “dual valve hypothesis” proposed by Pitts and colleagues (2013) is based on a mechanism within the brainstem control network that prepares the pharynx (swallow modulated muscles) for cough behavior. These researchers suggest that the upper esophageal sphincter (UES) and larynx act together to coordinate thyropharyngeus suppression. During a swallow the glottis is closed and the UES is open allowing passage of bolus material (Logemann, 1985, 2007; Pitts, 2013); this seals the trachea for airway protection and maintains pressures for passage of bolus material. During the compression phase of cough, both the larynx and UES are maximally closed and this closure maintains intrathoracic pressure to promote the effectiveness of a cough (Pitts, et al., 2013).

Examination of temporal musculature relationships between cough and swallow behaviors has been studied in vivo (Pitts et al, 2013). Bipolar fine-wire electrodes were used to obtain electromyograms (EMGs) in conjunction with esophageal pressures; wires were placed in seven muscles to assess the presence of cough and swallow behaviors (Pitts et al., 2013). Mechanical stimulation to the trachea induced cough and injection of water into the pharynx induced swallow;
Tracheal aspiration was induced with a water bolus presentation (Pitts et al., 2013). Results of this study showed that, after introduction of water to the oropharynx, cough EMG recordings had significantly greater amplitudes from parasternal, rectus abdominis, and thyropharyngeus muscles as well as positive esophageal pressure (Pitts et al., 2013). Abdominal muscle activation during a swallow activity provided evidence of shared physiological processes. This study was the first to show alteration of the posterior pharyngeal constrictor during cough, exhibiting the physiological coordination of mechanisms between cough and swallow.

“Behavior selection” is the concept that airway protective decision making, which occurs via afferent feedback, occurs on a moment-by-moment basis (Bolser, Pitts, & Morris, 2011). It is suggested that actions that require little central processing take “precedence” over centrally-mediated processes and can block centrally-mediated behaviors until the brainstem-controlled behaviors are completed. Thus, the brainstem-controlled swallow action may take precedence over centrally-mediated breathing. The apneic period (moment of not inhaling/exhaling during a swallow) is evidence of pattern selection.

Foundational knowledge of the neural and physiological underpinnings of breathing, swallowing, and coughing is essential to understand dystussia in patient populations. Even in the absence of brainstem impairment, neurogenic populations that have both upper and lower motor neuron dysfunction may exhibit concurrently impaired cough and swallowing (Hegland, Okun, & Troche, 2014; Pitts, Bolser, Rosenbek, Troche, & Sapienza, 2008; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016; Smith Hammond, 2001).

**Gating of Airway Protective Behaviors**

Central processing of afferent stimuli can significantly modify cough and swallow excitability. This action is termed “gaiting” (Bolser, Poliacek, Jakus, Fuller, & Davenport, 2006),
and can result in hyper- and hypo-excitability of the cough (Morice, Jakes, Faruqi, Birring, Mcgarvey, Canning, Smith, Parker, Chung, Lai, P avord, Van Den Berg, Song, Millqvist, Farrell, Mazzone, & Dicpinigaitis, 2014). Although gaiting is often considered to be under automatic control, we are beginning to understand that the cortex can significantly modulate cough excitability (Vertigan, 2008). Davenport and colleagues (2008) demonstrated that in response to a reflexive cough challenge all subjects first experience a sensation. The authors then went on to measure this sensation termed the “Urge to Cough”. They ultimately proposed that supramedullary (cortical) input to the brainstem cough CPG is intimately involved in the ultimate magnitude of the cough motor response.

The conclusions of many animal-model studies are consistent with the premise that motor control of cough is under automatic control from brainstem CPGs. However, the “Urge-to-Cough” model (Davenport, 2008) presents a representation of a feedback loop, which supports the presence of a cortical component of the cough system.

“There are six stages to the cough ‘motivation-to-action’ model: 1) stimulus - trigger for neural event; 2) urge - the physical need to respond; 3) desire - translation of urge to a central neural targeted goal; 4) action - physical response that satisfies the urge-desire; 5) evidence - feedback to the neural system on the action; and 6) reward - sensory system that determines if the urge was satisfied (Davenport, 2008, p. 107)”.

Taking into account the motivation-to-action model, researchers have studied higher-level cortical involvement, or the conscious decision making during the production of a cough. Hegland et al. (2012) administered capsaicin to 20 healthy adults; they were asked to modify their cough response including shorter/softer and longer/louder coughs. Results showed that individuals could voluntarily modify the reflexive behavior even under exposure to irritants (Hegland et al., 2012).
Additional evidence to support a cortical component to cough regulation includes a blunted afferent C-fiber response to stimulation in an anesthetized, in vivo preparation (Moreno-Lopez, Perez-Sanchez, Martinez-Lorenzana, Condes-Lara, Rojas-Piloni, 2013). The ability to voluntarily gate a response to sensory stimuli implies cortical processing of the cough response in humans.

Descending motor drive signals are activated in a graded manner (Davenport, 2008). Depending on the strength of the stimulus, either a high concentration of an irritant or verbal instruction to produce a “strong cough,” the resulting cough behavior will be related to the stimulus (Davenport, 2008). Therefore, it is essential to note that the specific directions given to human subjects when eliciting a voluntarily induced cough may be related to the strength of voluntary cough production.

**Dystussia and Cough Measurement**

The presence of dystussia has multiple negative health implications in a variety of patient populations (Nakajoh K., 2000). Understanding cough as it is related to airway safety in a variety of clinical populations will have major health care implications as we can possibly detect early signs of swallowing impairment or rehabilitate cough for improved airway protection. It is an advancing area of research in both the basic science and clinical science research realms. Cough production is a measurable physiologic phenomenon. Objective measures of cough can be obtained using different elicitation methods such as inducing a reflexive cough or prompting a voluntarily induced cough. Cough evaluation tools include cough monitors, perceptual assessment, evaluating acoustic characteristics, and physiologic measurement. Each evaluation tool and cough elicitation method provides unique and valuable objective information about cough function.

**Reflexively and Voluntarily Induced Cough**

Elicited or induced cough is frequently tested with flow dosimeters or nebulizers to
administer irritant gases; these irritants may include but are not limited to capsaicin, citric acid aerosols, and fog (Fontana & Widdicombe, 2007). This methodology directly evaluates responsiveness of the afferent system. Induced cough is often associated with an expiratory reflex as there may be an absent or reduced inspiratory effort. Binary outcomes (present/absent) of cough production are typically recorded as well as quantifying the number of coughs produced, and time to cough production. Recording airflow waveforms produced during a cough effort may also be coupled with the administration of irritants.

Voluntary cough is acquired by having the patient cough upon command to a verbal stimulus. It consists of a multistage event including an inspiration, closure of the vocal folds during a compression phase, and a forced expiration. Possible outcome measures include objective airflow measures, subjective ratings, and acoustic properties.

**Airflow Measurement**

Both induced and voluntary cough assessment methods allow for the acquisition of cough airflow data. Airflow data allows the clinician/researcher to gather information regarding the function of the respiratory system. Airflow values are dependent upon a number of variables including stimulus, laryngeal closure (build-up of subglottic pressure), expiratory muscle activity (Widdicombe, 2006) and in some cases inspiratory effort. Airflow waveforms are recorded by using an oral pneumotachograph, a device that measures rate of airflow, connected to a spirometer (pressure transducer) that then sends signals to a recording system to display waveforms on the computer (Pitts, Bolser, Rosenbek, Troche, & Sapienza, 2008; Smith Hammond, 2001). Cough production is recorded as a measure of airflow in liters (L) over time in seconds (L/s). Typical measures derived from the waveforms include temporal aspects of the cough, amplitude in L/s, and volume of expired airflow.
As illustrated in Figure 1.2, common objective measures of cough production that have been reported in previous research studies include, but are not limited to, inspiratory phase duration (IPD), inspiratory peak flow (IPPF), compression phase duration (CPD), expiratory peak flow (EPPF), expiratory rise time (EPRT), and cough volume acceleration (CVA); these terms are well described throughout the cough literature. CVA is described in the literature as a measure that is thought to be indicative of cough effectiveness (Bolser, 2002; Fontana & Lavorini, 2006; Smith Hammond C.A., 2001). To obtain outcome measures, waveforms are analyzed by identifying physical landmarks on the cough waveform. Data points are recorded and a series of calculations are made to obtain the final value for each objective measure.

**Figure 1.2** Same as Figure 2.1 which has been previously published in Watts et al, 2016, p. 268, “Example of voluntary cough waveform measured with cough spirometry. Select derived objective measures are delineated on the waveform including: A) inspiratory phase duration; B) inspiratory peak flow; C) compression phase duration; D) peak expiratory flow rate; and E)
cough expired volume. Expiratory rise time is calculated by subtracting time at end of compression from peak expiratory flow time. Cough volume acceleration is not depicted but is calculated by dividing peak expiratory flow rate by the expiratory rise time.”

Although testing methodology differs between elicited and voluntary cough, researchers suggest that airflow patterns of voluntary cough are similar to reflexive cough (Widdicombe & Fontana, 2006). When a cough is elicited by either an irritant or verbal command, there is a cognitive awareness of a need to cough; this is termed, “Urge-to-Cough” (Davenport, 2009). Authors suggest that this implies that cough has been activated via cortical neural pathways; specifically, the super pontine pathways have activated and the cognitive aspect of awareness and the urge precedes the behavior response in both elicited and voluntary cough (Hegland, Bolser, & Davenport, 2012).

Sound Characteristics

As cough is an audible physiologic event, acoustic and auditory perceptual characteristics of cough have also been investigated. Current methods that have been employed in current practice include a sound level meter to measure the sound pressure level (dB SPL) associated with a cough. In addition, cough has been characterized by having a rater listen to a cough and make subjective ratings (Laciuga, Brandimore, Troche, & Hegland, 2016). Subjective ratings of auditory perceptual characteristics of cough include but are not limited to: bovine, inadequate, weak, strong, wet, dry, productive, barking, hacking, present or absent. There is little consensus as to what these sound characteristic imply about the physiologic mechanism producing the cough. Furthermore, perceptual ratings are limited by the arbitrary and or ordinal nature of the ratings and can be strongly biased by context while lacking desirably high inter- and intra-rater reliability (Shrivastav, 2005).
Cough monitors vary in design and employ the use of a microphone in an attempt to objectively measure how many times the subject coughs in a given period of time. The recordings acquire an acoustic cough waveform. The European Respiratory Society (ERS) guidelines state that, for the assessment of acoustic recordings, cough is defined as “a forced expulsive maneuver or maneuvers against a closed glottis that are associated with a characteristic sound or sounds” Acoustic recordings of cough are quantified in a number of ways: 1) explosive cough sound (counting the explosive sounds waves); 2) cough seconds (time spent coughing); 3) cough breaths (how many coughs occur within breath group); and 4) cough epochs (cough sound that continues without a 2-s pause) (Morice et al., 2007). cough epochs (cough sound that continues without a 2-s pause) (Morice et al., 2007).

Dysphagia

*Dysphagia* refers to difficulty swallowing and results as a symptom of a medical diagnosis rather than an etiology. Medical diagnoses that may lead to dysphagia include: neurologic diagnosis, connective tissue or rheumatoid disorders, structural diagnosis (e.g., tumors), iatrogenic diagnoses, respiratory compromised conditions, esophageal disorders, and psychogenic conditions (Groher & Puntil-Sheltman, 2010). There is a reportedly wide range of patients (52-82%) with neurodegenerative diseases that are affected by oropharyngeal dysphagia (Clavé, 2004).

Symptomology of dysphagia may include a combination of prandial (i.e., during swallowing) and post prandial coughing or choking, nasal or oral regurgitation of food or liquid, odynophagia (painful swallowing), labial spillage, unexplained weight loss, nutritional deficiencies (Groher & Puntil-Sheltman, 2010), halitosis, or sensation of food/pills getting “stuck” within the throat.

Dysphagia impacts health, quality-of-life, and increases a patient’s financial burden (Da Costa
Subsequent aspiration pneumonia (lung infection) from severe untreated or unmanaged dysphagia constitutes a serious health concern (Delegge, 2002). Aspiration in already medically compromised patients may lead to decreased hospital outcome and may cause death (DeLegge, 2002). In fact, dysphagia is associated with pulmonary sequelae and a leading cause of death in Parkinson’s disease (PD) (Hoehn & Yahr, 1967) and attributes to mortality in Amyotrophic Lateral Sclerosis (ALS) (Czaplinski A., 2006).

Clinical Evaluation of Dysphagia

Dysphagia assessment involves a variety of health professionals (Groher M.E., 2010). There are both clinical and instrumental (using high-tech instrumentation) approaches to dysphagia assessment. The “gold standard” instrumental assessment involves performing the Modified Barium Swallow Study (MBS) (Logemann, 1984). The MBS is a fluoroscopic imaging study in which the patient is given barium, an inert radiographic substance, to swallow and bolus flow through the oral cavity and pharynx are visualized. Other instrumental evaluation includes the Fiberoptic Endoscopic Evaluation of Swallowing (FEES). This methodology requires the clinician to pass a scope trans-nasally to view the laryngeal vestibule during swallowing tasks.

Instrumental swallow evaluation affords direct visualization of the swallow process and thus, in the hands of a skilled clinician, can lead to an accurate diagnosis of oropharyngeal impairment. Assessment that does not require the use of instrumentation or radiography includes various non-instrumental clinical evaluations. The terms clinical swallow examination (CSE), or bedside swallow examination (C/B E) is used to describe this type of assessment (McCullough, 2001, Logemann, 1984).
The CSE can be performed at the patient’s bedside but is not restricted to the bedside (Groher M.E., 2010) and does not include internal visualization of the swallow mechanism. CSE are widely used by SLPs to assess patients who are suspect of having oral or oropharyngeal dysphagia. During a CSE, clinicians carefully examine the structure and function of the oral mechanism and evaluate the oral phase of swallowing. Patients are commonly asked to complete a series of both swallowing and non-swallowing tasks; based on the patient’s performance, clinicians make determinations regarding swallow safety and the pharyngeal phase of the swallow.

There are three main components to the CSE: 1) the medical history 2) physical inspection of swallow anatomy and musculature 3) swallow trials (Logmann 1984, Groher M.E., 2010). The purpose of the CSE is to accurately detect the presence or absence of a disordered pharyngeal stage of swallow without direct internal visualization of the anatomy. Instead, “clinical signs” are used to detect the presence of penetration or aspiration. The clinical assessment of swallow may consist of variations of these three main components. Several studies outline the predictive values of these measures in specific patient populations.

**Dysphagia, Dystussia, and Airway Protection**

Cough is a vital airway protection mechanism during swallowing; it acts as a sweeping mechanism to clear the lower airways of aspirant material (Bolser, 2002; Pitts, 2012; Smith Hammond C.A., 2001). Dystussia decreases an individual’s ability to protect their airway and thus, in certain neurogenic populations, can increase the risk for aspiration, dysphagia, subsequent aspiration pneumonia, and morbidity (Smith-Hammond 2009; Pitts, 2010). Normally, the cough reflex is an audible clinical indicator of aspiration. Therefore, the absence of a cough reflex in the event of aspiration may be an indicator of impairment (Pitts, 2013) as this may indicate poor sensory feedback response. Clinically, dystussia has been described in neurodegenerative disease
populations such as Parkinson’s disease (PD) (Pitts, Bolser, Rosenbek, Troche, & Sapienza, 2008, 2010), stroke (Smith-Hammond et al., 2001; Smith-Hammond et al., 2009), and Amyotrophic Lateral Sclerosis (ALS) (Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016). Both respiratory and swallowing impairments are highly prevalent in individuals with Parkinson’s disease (PD) and Amyotrophic Lateral Sclerosis (ALS).

Although it appears that voluntary cough production is related to airway protection status during swallowing in neurodegenerative disease populations, the methodology to test cough objectively is costly and the analysis labor intensive, time consuming, and requires intensive training to perform expert evaluation of physiologic cough waveforms. The current voluntary cough testing methodology is not a feasible method to utilize in busy clinic environments.

Methods available to assess cough during a clinical swallowing evaluation without the use of airflow recordings include evaluating the strength of a cough (Daniels, 1998; Laciuga, Brandimore, Troche, & Hegland, 2016; Mccullough, 2001). This relies on the perception of “strength” and there is a lack evidence to support the reliability and validity of perceptual evaluation of voluntary cough (i.e., strength) for the purpose of clinically assessing swallowing function and airway protection mechanisms. While current clinical evaluation of cough is focused on cough frequency (how many times a person coughs), cough reflex testing (often using tussive agents), voluntary cough measures, and patient subjective ratings of severity, little is known regarding the reliability or validity of clinician perceptions of voluntary cough effectiveness or auditory characteristics of cough. Therefore, clinicians may not have the necessary tools to describe impaired cough, and its role in dysphagia screening may be currently underutilized.

Critical research questions to address include: 1) what clinical swallowing assessments are available to assess cough; 2) what voluntary cough assessment methods are speech language
pathologists using in their clinical practices; 3) what physiologic features of cough are useful in determining the presence of a swallowing disorder; 4) what, if any, novel, objective, acoustic parameters of voluntary cough are useful in detecting the presence of a swallowing disorder?

The relevance of such work is paramount for professionals who serve populations with impaired swallow ability as traditional methods of clinical swallowing assessment often fail to identify those with impaired swallowing who silently aspirate (i.e., no reflexive cough). Current binary subjective measures (i.e., strong/weak) used during clinical swallow assessments fail to provide quantitative data or describe deviant auditory features of cough. There remains a need to investigate novel methodologies to assess voluntary cough in humans for the purposes of evaluating swallowing dysfunction. The results of such studies may lead to more sensitive and specific means of speech-language pathologist’s clinically assessing swallow function and may provide better health outcomes for patients. Although there are studies that focus on the relationship between cough and swallow, there is a paucity of data on clinician reliability of assessing cough function, or deviant audible features of dystussia which may inform clinicians of decreased airway protection.
CHAPTER TWO:

TO COUGH OR NOT TO COUGH? EXAMINING THE POTENTIAL UTILITY OF COUGH TESTING IN THE CLINICAL EVALUATION OF SWALLOWING

Note to Reader

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Introduction

Dysphagia (impaired swallowing) impacts the ability of an individual to consume oral intake safely and efficiently. Dysphagia accounts for approximately 7% of hospital admissions in the United States (Altman, 2011; Altman, 2010) and is estimated to have a total economic burden of approximately $547 million dollars per year (Cichero, 2012). Impairments in swallowing efficiency refer to difficulties transporting foods and liquids from the oral cavity into the stomach that result in residue in the oral cavity, pharynx, and esophagus, and that are linked to malnutrition (Moreira, 2016). Impairments in airway safety occur when ingested foods or liquids enter the airway (i.e., penetration or aspiration) and are linked to increased pneumonia risk (Cabre, Serra-Prat, Force, Almirall, Palomera, & Clave, 2014). The inability to eat or drink by mouth is associated with reductions in mental well-being, quality of life, and increased caregiver burden (Cichero, 2012; Leow, Huckabee, Anderson, & Beckert, 2010; Maclean, Cotton, & Perry, 2009; Paris, Martinaud, Hannequin, Petit, Cuvelier, Guedon, Ropenneck, & Verin, 2012; Plowman-

Evaluation of swallowing begins with a “bedside” or clinical swallow examination (CSE). The CSE typically includes a review of patient history, patient-reported symptoms, assessment of the oral mechanism, and observation of liquid and food swallowing trials (Suiter, 2012). Subsequent instrumental evaluation may be performed at the clinician’s discretion, if clinical signs or symptoms warrant further evaluation, and pending the availability of resources. The Videofluoroscopic Swallow Study (VFSS) represents the gold standard instrumental swallowing assessment. It constitutes the only type of assessment with direct visualization of both the oral and pharyngeal phases of swallowing to confirm specific impairments in swallowing that maybe suspected during the CSE, and affords the ability to determine specific contributing mechanisms of oral, pharyngeal and often esophageal stage impairments (Logemann, 1984). Although VFSS represents the gold standard instrument, many clinicians may rely solely on the CSE given limited or no access to VFSS (Association, 2000). Another instrumental evaluation technique, the fiberoptic endoscopic evaluation of swallowing (FEES), is a useful tool in providing a 3-dimensional visualization of the pharyngeal stage of swallowing. FEES is noted to provide superior and direct imaging of pharyngeal anatomy, secretions, and vocal fold movement, however is limited in its application in many settings due to access to equipment and skill level of the clinician.

Since the CSE does not permit direct visualization of the swallowing process, its ability to accurately identify individuals who ‘silently’ aspirate (i.e., no cough in response to material
entering airway) has been identified as a major limitation (Miles, Moore, Mcfarlane, Lee, Allen, & Huckabee, 2013; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016; Smith Hammond, 2008). For example, one study documented that the CSE identified only 30% of radiographically confirmed aspirators in 107 hospitalized patients (Splaingard MI, 1988). Considering this limitation, research has focused on determining the sensitivity and specificity of various validated clinical tools, screeners and clinical signs to identify dysphagia or aspiration in order to improve the utility of the CSE (Mccullough & Martino, 2013; Mccullough, 2005, 2001; Rosenbek, Mccullough, & Wertz, 2004). For example, can tasks identifying poor lingual movement discriminate safe versus unsafe swallowing? Determining components of the CSE that accurately detect swallowing safety and efficiency during swallowing is a significant research initiative and may reduce error during CESs.

Although the American Speech Language Hearing Association (ASHA) provides guidelines for performing an instrumental evaluation of swallowing (Karen Dikeman, 2003), only practice recommendations (and no published guidelines) exist for the CSE (Association, 2000). As a result, current CSE protocols vary widely, and might constitute use of a validated CSE tool (see Table 2.1) or combinations of various standardized assessments. Further, procedural policies for conducting a standardized CSE are limited and, given the variability in clinical practice patterns, dysphagia recommendations and management strategies also vary (Mathers-Schmidt & Kurlinski, 2003). suggests that cough airflow measures may serve as a useful physiologic metric to index airway defense capabilities in at-risk individuals (Anna Miles 2013; Hegland, Okun, & Troche, 2014; Pitts, Bolser, Rosenbek, Troche, & Sapienza, 2008; Pitts, Troche, Mann, Rosenbek, Okun, & Sapienza, 2010; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016; Sato, Tohara, Iida, Wada, Inoue, & Ueda, 2012; Smith Hammond C.A. , 2001; Smith Hammond,
Goldstein, Horner, Ying, Gray, Gonzalez-Rothi, & Bolser, 2009). Cough function has been an area of increasing interest in the evaluation, management, and treatment of dysphagia (Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016). This is not surprising given the crucial role cough serves in defending the airway during swallowing. Indeed, recent research highlights a close relationship between voluntary and reflexive cough airflow measures and airway safety status during swallowing; emerging data The purpose of this narrative review is to examine the relationship between cough and swallow, summarize current validated CSE’s, and review the discriminant capacity of both voluntary, and reflexive, cough testing to detect unsafe swallowing.
Table 2.1 Summary of published clinical swallowing evaluation protocols and screening tools with reference to first author, patient population validated against, protocol items, and test sensitivity and specificity for detecting swallowing impairment and/or aspiration (as specified).*Acute stroke defined as: patients admitted to hospital immediately following a stroke; **Rehabilitation stroke is defined as: Patients in a sub-acute rehabilitation facility following stroke; ***Heterogeneous population by author includes: Logemann (1999): single stroke, multiple strokes, head and neck cancer, spinal cord injury, other; Suieter (2008): cardiothoracic surgery, esophageal surgery, head and neck surgery, neurosurgery, medical, pulmonary, cancer, other, left stroke, right stroke, brainstem stroke, Parkinson’s disease, dementia, other neurological; Suieter (2014): esophageal surgery, head and neck cancer, neurosurgery, medical, neurological (stroke, multiple sclerosis, traumatic brain injury); Clave (2008): cerebrovascular disease, chronic neuropathy, diabetes, geriatric diseases, neurodegenerative diseases (amyotrophic lateral sclerosis, multiple sclerosis, Parkinson’s disease, Alzheimer’s disease, Huntington’s disease, Duchenne muscular dystrophy, and other), Zenker’s diverticulum, cricopharyngeal bar, post surgical, and tracheotomy. Abbreviations: cc: cubic centimeter; FEES: Fiberoptic Endoscopic Evaluation of Swallowing; mL: Milliliter; oz.: Ounce; VFSS: Videofluoroscopic Swallow Study.

§ Swallow Safety: Sensitivity and specify outcome measures in reference to swallow safety status and the presence of penetration or aspiration.

♀ Dysphagia: Outcome measures in reference to presence or absence of general swallowing impairment (dysphagia).

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<tbody>
<tr>
<td>Martino (2008)</td>
<td>The Toronto Bedside Swallowing Screening Test (TOR-BSSST)</td>
<td>Nurse Speech-Language Pathologist</td>
<td>Inpatient Stroke: Acute; Rehabilitation** (N = 311) VFSS</td>
<td>Kidd 50cc water swallow test; tongue movement; general dysphonia; voice quality before and after 50ml. liquid trial.</td>
<td>Dysphagia 91.5%</td>
<td>Dysphagia 66.7%</td>
<td>No</td>
</tr>
<tr>
<td>Mann (2002)</td>
<td>Mann Assessment of Swallowing Ability (MASA)</td>
<td>Speech-Language Pathologist</td>
<td>Acute Stroke VFSS</td>
<td>Ratings across the following items: Alertness; cooperation; auditory comprehension; respiration; respiratory rate during swallowing; dysphasia, dysarthria, dysphonia, saliva, lip seal; tongue movement/strength; coordination; gag; palate; voluntary cough; reflexive cough during</td>
<td>§Aspiration 53%</td>
<td>§Aspiration 63%</td>
<td>Yes</td>
</tr>
<tr>
<td>Author</td>
<td>Study Title</td>
<td>Participants</td>
<td>Methods</td>
<td>Notes</td>
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<tr>
<td>Antonios</td>
<td>Modified Mann Assessment of Swallowing Ability</td>
<td>Physician</td>
<td>Acute Stroke* (N = 150) Comprehensive Clinical Assessment based on MASA</td>
<td>Dysphagia (N 1) 82% Dysphagia (N 1) 87% Yes</td>
<td></td>
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<tr>
<td>Trapl</td>
<td>Gugging Swallowing Screen</td>
<td>Speech-Language Pathologist (Gp 1) Nurse (Gp 2)</td>
<td>Acute Stroke* (N=50) Group 1 n = 20 Group 2 n = 30 FEES</td>
<td>Dysphagia 4/5 Group 1: 100% Group 2: 100%</td>
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<tr>
<td>Edmiaston</td>
<td>Acute Stroke Dysphagia Screen</td>
<td>Nurse</td>
<td>Acute Stroke* (N = 300) MASA</td>
<td>Dysphagia 95% Aspiration 68% No</td>
<td></td>
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</tr>
<tr>
<td>Edmiaston</td>
<td>Bames-Jewish Hospital Stroke Dysphagia Screen</td>
<td>Nurse</td>
<td>Acute Stroke* (N = 225) VFSS</td>
<td>Dysphagia 95% Aspiration 50% Dysphagia 91</td>
<td></td>
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<tr>
<td>Hinds</td>
<td>Timed Swallow Test</td>
<td>Physician</td>
<td>Acute Stroke* (N = 93)</td>
<td>Not Assessed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Logsmann</td>
<td>Northwestern Dysphagia Patient Check Sheet</td>
<td>Not specified</td>
<td>Heterogeneous*** (N = 200) VFSS</td>
<td>Dysphagia &amp; Reported for 28 individual items</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Suiter</td>
<td>3-oz. Water Swallow Test (WST)</td>
<td>Speech-Language Pathologist</td>
<td>Heterogeneous*** (N = 3,000) FEES</td>
<td>Dysphagia 96.5% Aspiration 48.7% No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Test Name</td>
<td>Researcher(s)</td>
<td>Methodology</td>
<td>Results</td>
<td></td>
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<tr>
<td>Suiter (2014)</td>
<td>Yale Swallow Protocol</td>
<td>Speech-Language Pathologist</td>
<td>Heterogeneous*** (N = 25) VFSS</td>
<td>Cognitive screen; brief oral mechanism examination and liquid swallow trial of 90cc of water. Patient instructed to drink continuously without stopping. Swallow trials including 5, 10, and 20cc of nectar thick liquid, thin liquid and pudding.</td>
<td>§ Aspiration 100%</td>
<td>§ Aspiration 64%</td>
<td>No</td>
</tr>
<tr>
<td>Clave (2008)</td>
<td>Volume-Viscosity Swallow Test (V-VST)</td>
<td>Speech Swallow Therapist</td>
<td>Heterogeneous*** Control N = 12 Patients N = 85 VFSS</td>
<td>Penetration 83.7% Aspiration 100% Penetration 64.7% Aspiration 28.8%</td>
<td>No</td>
<td></td>
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</tr>
</tbody>
</table>
**Relationship between Cough and Swallow**

Cough is a sensorimotor behavior involved in airway protection to forcefully eject foreign material from the laryngeal vestibule and lower airways (Bolser, 2002; Pitts, 2012; Ross, 1955; Smith Hammond C.A., 2001). An effective cough is therefore critical in removing aspirate material from the airway during swallowing, particularly in patients with additional co-morbidities who are more susceptible to developing pulmonary sequelae. In many neurogenic populations, dystussia (impaired cough) and dysphagia present in parallel (Hegland, Okun, & Troche, 2014; Pitts, Bolser, Rosenbek, Troche, & Sapienza, 2008; Pitts, Troche, Mann, Rosenbek, Okun, & Sapienza, 2010; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016; Smith Hammond, 2001), a finding that is not surprising given the shared neural and anatomical substrates of respiration, cough, and swallowing function (Gestreau, 1996; Pitts, 2012; Troche, Brandimore, Godoy, & Hegland, 2014).

Central pattern generators (CPGs) in the brainstem regulate the processes of eupnea (unlabored respiration), swallow, and cough (Davenport, Bolser, & Morris, 2011). The nucleus ambiguus, dorsal respiratory group, and ventral respiratory group located within the brainstem are associated with the neural control of the behaviors of respiration, cough, and swallow (Bolser, 2002; Gestreau, 1996; Jean, 2001). Vagal afferent nerves that are both chemically and mechanically sensitive and non-myelinated c-fibers across multiple afferent beds (J.G., 1998) provide sensory feedback during swallowing (e.g. bolus volume consistency and volume, presence of aspirate material in the airway) which then informs the swallow central CPG (Pitts, 2012). The CPGs are inherently flexible in their connectivity to allow for rapid, on-line modification between the behaviors of cough, breathing, and swallowing such as, increasing apnea duration due to a larger swallowed bolus or the execution of a rapid and protective cough in response to aspirated
material during swallowing (Bianchi & Gestreau, 2009). Changes in respiratory muscle activation occur as the swallow CPG is informed about characteristics of the swallow (i.e., safe vs. unsafe, sequential vs. single sip) (Pitts, Rose, Mortensen, Poliacek, Sapienza, Lindsey, Morris, Davenport, & Bolser, 2013b). Higher order cortical processing or supramedullary input such as sensory integration and motor planning also provides vital input modulating both cough and swallowing behaviors. Computational modeling studies performed to determine neural networks of both cough and swallowing have elucidated shared efferent and afferent pathways involved for breathing, swallowing and cough (Davenport, Bolser, & Morris, 2011; Pitts, 2012).

Evidence from human studies suggests that supramedullary input is involved in both voluntary and reflexive cough, with neural processing of stimuli prior to the act of cough resulting in what Davenport and colleagues (2008) have termed the “Urge to Cough” (Davenport, 2008; Davenport, Vovk, Duke, Bolser, & Robertson, 2009; Hegland K.W., 2011; Widdicombe, Eccles, & Fontana, 2006). This cortical regulatory component in humans is supported by the voluntary suppression of a reflexive cough response (Hegland K.W., 2011). In addition to the established shared central neurologic substrates, functions of respiration, swallow, and cough also peripherally share anatomical structures of the upper airway, pharynx, and oral and nasal cavities. Troche and colleagues (2014) conceptualized a framework for understanding the shared neural and anatomical substrates of cough and swallow in a comprehensive review on this topic (Troche, Brandimore, Godoy, & Hegland, 2014). This conceptual framework presents swallowing and cough along a ‘spectrum of airway protective behaviors’, with swallowing at one end of the spectrum (protective function) and cough at the opposite end (defensive function) (Troche, Brandimore, Godoy, & Hegland, 2014). Thus, these two sensorimotor acts have highly coordinated and reciprocal functions with shared anatomical and neurologic underpinnings that provide a mechanistic,
anatomical and neurologic foundation for considering the role of cough during a clinical swallow examination.

**Clinical Swallowing Evaluation**

The main components of the CSE include a thorough medical history review; patient and caregiver interview of symptoms; physical inspection of the integrity of swallow anatomy at rest and during movement; and observation of performance on food and liquid swallowing trials (Logemann, 1984). The CSE is typically completed by a certified Speech-Language Pathologist (SLP) and performed across a variety of healthcare settings that include, but are not limited to: acute, sub-acute, and rehabilitation hospitals; specialized outpatient clinics’ skilled nursing homes; home health care; and assisted living facilities. The objective of the CSE is to obtain information from the patient’s history, self-reported symptoms and presenting clinical signs to make best clinical judgments regarding swallowing safety and efficiency and to provide dietary and treatment recommendations. The CSE plays an important role in patient care and it is critical to accurately identify patients who may have compromised swallow efficiency and airway safety. Dysphagia screening is typically implemented more broadly to asymptomatic patients in order to detect a possible condition (Suiter, 2012). At-risk patient groups (e.g. stroke) are often targeted for dysphagia screening.

Given the previously identified limitations of the CSE to identify all individuals with dysphagia, and barriers to use, there exists a critical need for sensitive screening tools to be incorporated during the CSE (McCullough, 2001; Plowman, Tabor, Robison, Gaziano, Dion, Watts, Vu, & Gooch, 2016; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016). Given the shared neurologic, anatomic and mechanic roles of cough and swallow, the potential utility of cough testing in the CSE has been a recent topic of interest to provide
information regarding mechanisms of airway safety and the physiologic ability of an individual to defend their airway (Pitts, Bolser, Rosenbek, Troche, & Sapienza, 2008; Pitts, Troche, Mann, Rosenbek, Okun, & Sapienza, 2010; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016; Smith Hammond C.A., 2001; Smith Hammond, Goldstein, Horner, Ying, Gray, Gonzalez-Rothi, & Bolser, 2009; Wheeler Hegland, Troche, Brandimore, Davenport, & Okun, 2014). Currently, however, cough testing is not routinely incorporated in the CSE across all settings. There is substantial variability in current practice patterns in the evaluation of swallowing function (Mcallister, Kruger, Doeltgen, & Tyler-Boltrek, 2016).

**Validated Clinical Swallow Evaluations and Screening Tools**

Commonly utilized validated clinical swallow protocols include the: Barnes-Jewish Hospital Stroke Dysphagia Screen (BJH-SDS) (Edmiaston, Connor, Loehr, & Nassief, 2010; Edmiaston, Connor, Steger-May, & Ford, 2014); Mann Assessment of Swallowing Ability (Mann, 2002); Modified Mann Assessment of Swallowing Ability (MMASA) (Antonios, Carnaby-Mann, Crary, Miller, Hubbard, Hood, Sambandam, Xavier, & Silliman, 2010); Toronto Bedside Swallowing Test (TOR-BSST) (Martino, Silver, Teasell, Bayley, Nicholson, Streiner, & Diamant, 2009); Timed Swallow Test (Hinds, 1998); Acute Stroke Dysphagia Screen (ASDS) (Edmiaston, Connor, Loehr, & Nassief, 2010; Edmiaston, Connor, Steger-May, & Ford, 2014); Gugging Swallow Screen (GUSS) (Trapl, Enderle, Nowotny, Teuschl, Matz, Dachenhausen, & Brainin, 2007); Yale Swallow Protocol (Suiter, Sloggy, & Leder, 2014); Volume Viscosity Test (Clave, Arreola, Romea, Medina, Palomera, & Serra-Prat, 2008); Northwestern Dysphagia Patient Check Sheet (Logemann, 1999); and the 3 oz. Water Swallow (Suiter & Leder, 2008). Table 1 provides a summary of these published, validated CSEs, with reference to the patient population the tool was validated for, tool administration, inclusion of cough testing, and any published statistical data.
regarding its discriminant ability to identify dysphagia or unsafe swallowing.

Of the 11 validated CSEs commonly used, 6 were designed to be administered specifically by Speech-Language Pathologists, 3 to be administered by trained nursing staff, and 1 by physicians (Logemann et al. did not specify). Review of published reports indicates that the highest levels of sensitivity (>85%) for detecting aspiration is provided by the BJH-SDS (Edmiaston, Connor, Loehr, & Nassief, 2010; Edmiaston, Connor, Steger-May, & Ford, 2014), Acute Stroke Dysphagia Screen (ASDS) (Edmiaston, Connor, Loehr, & Nassief, 2010; Edmiaston, Connor, Steger-May, & Ford, 2014), Yale Swallow Protocol (Suiter, Sloggy, & Leder, 2014), Volume Viscosity Test (Clave, Arreola, Romea, Medina, Palomera, & Serra-Prat, 2008), Northwestern Dysphagia Patient Check Sheet (Logemann, 1999), and the 3 oz. Water Swallow Test (Suiter & Leder, 2008). However, none of the protocols reach the highest level (>85%) of reported overall specificity for detecting aspiration. The Modified Mann Assessment of Swallowing Ability, a physician-administered protocol, provides the highest levels of sensitivity and specificity for detecting global swallowing impairment (i.e., 92% and 87% respectively).

Of the 11 validated CSEs, 4 (36%) incorporate some form of cough testing. Description of cough testing methodology varies within the context of each examination. Upon careful inspection of the published protocols that include cough assessment, specific instructions for eliciting the cough task are vague, and the subjective perceptual measures of cough vary between protocols. The MMASA (same tasks as the MASA for cough testing) contains the most detailed instruction for cough elicitation and perceptual cough judgment. Per protocol, the physician or administrator asks the patient to ‘cough as strong as possible’ (Antonios, Carnaby-Mann, Crary, Miller, Hubbard, Hood, Sambandam, Xavier, & Silliman, 2010). Judgments of cough strength and clarity are rated, with an outcome score is assigned corresponding to one of the following: no abnormality,
cough attempted but is hoarse in quality, attempt inadequate, no attempt, or unable to perform. Logemann et al. (1999) described a subjective cough assessment in the Northwestern Dysphagia Patient Check Sheet, in which administrators judge either a voluntary cough, or throat-clearing maneuver, and perceptually rated the strength of the behavior. A strong cough/throat clear was judged as ‘safe’, and weak cough/throat clear was judged as ‘unsafe’ (Logemann, 1999). The GUSS includes an assessment of ‘voluntary cough’ without reference to specific cough task instruction; the cough task is rated based on a weak or absent response (Trapl, Enderle, Nowotny, Teuschl, Matz, Dachenhausen, & Brainin, 2007).

Laciuga and colleagues recently investigated relationships between perceptual ratings of cough and objective airflow measures of cough (Laciuga, Brandimore, Troche, & Hegland, 2016). Thirty clinicians (speech-language pathologists, otolaryngologists and neurologists) rated the subjective parameters of strength, duration, quality, quantity, and overall ‘effectiveness’ of ten audio recordings of cough containing specific airflow characteristics. Objective physiological aerodynamic parameters of cough airflow were associated with the clinical perception of cough strength and effectiveness. The specific parameters that were clinically perceived as strong and effective included: compression phase duration, peak expiratory flow rate, peak expiratory flow rise time, cough volume acceleration and total expired volume. Interestingly, only 4 CSE protocols reviewed here currently utilize perceptual judgment of cough as part of the swallowing examination, and none include physiologic measures of cough airflow.

Utility of Voluntary Cough Testing in Dysphagia

Voluntary or volitional cough testing involves asking a patient to cough (typical instructions are: “as hard as you can” or “like have something stuck in their throat”). The resulting motor output can then be assessed either subjectively by listening, or objectively with specialized
equipment. For a complete review of the physiologic components of cough, we refer readers to Smith-Hammond et al. (ref number). Briefly, cough is characterized of three distinct phases:

1) **Inspiratory phase:** composed of contraction of the external intercostal muscles elevating the anterior rib cage and drawing down the diaphragm as it contracts (West, 1995) while laryngeal muscle activation allows for passage of air through the glottis resulting negative pressure drawing air into the lungs (Bautista, Sun, & Pilowsky, 2012; West, 1995).

2) **Compression Phase:** during which adduction of the vocal folds builds and maintains subglottic pressure generation.

3) **Expiratory Phase:** composed of a forceful and rapid abduction of the vocal folds. Physiologic cough testing using the gold standard pneumotachograph measures airflow signals across all three phases that can be subsequently analyzed using specialized software. Objective cough flow measures can be derived and are illustrated in Figure 2.1 with definitions provided in Table 2.2.

Several investigators have examined relationships between voluntary cough airflow measures and swallow safety status to elucidate the clinical utility of voluntary cough spirometry testing in several patient populations (Pitts, Bolser, Rosenbek, Troche, & Sapienza, 2008; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016; Smith Hammond C. A., 2001; Smith Hammond, Goldstein, Horner, Ying, Gray, Gonzalez-Rothi, & Bolser, 2009). These are summarized in Table 2.3 and reviewed below.
**Stroke**

Smith-Hammond and colleagues (2001) first examined the relationship between objective
Table 2.2. Definitions of objective voluntary cough airflow measures with reference to illustrative cough waveform depicted in Figure 2.1. Specific references of published studies utilizing each measure are also provided.

<table>
<thead>
<tr>
<th>Phase:</th>
<th>Measure:</th>
<th>Description:</th>
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<tbody>
<tr>
<td>Inspiratory Phase:</td>
<td></td>
<td>Time from onset of inspiration at 0 L/s to the beginning of glottic closure (Pitts, Bolser, Rosenbek, Troche, &amp; Sapienza, 2008; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, &amp; Gooch, 2016; Smith Hammond, 2001) or the start of the expiration onset if there is no appreciable compression phase (Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, &amp; Gooch, 2016).</td>
</tr>
<tr>
<td>A</td>
<td>Inspiratory Phase Duration (s)</td>
<td>Peak inspiratory flow during the inspiratory phase (Pitts, Bolser, Rosenbek, Troche, &amp; Sapienza, 2008; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, &amp; Gooch, 2016; Smith Hammond, 2001).</td>
</tr>
<tr>
<td>Compression Phase:</td>
<td></td>
<td>Time to glottic opening measured from the end of the inspiratory phase to the beginning of the expiratory phase (Hegland, Okun, &amp; Troche, 2014; Pitts, Bolser, Rosenbek, Troche, &amp; Sapienza, 2008; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, &amp; Gooch, 2016; Smith Hammond, 2001).</td>
</tr>
<tr>
<td>C</td>
<td>Compression Phase Duration (s)</td>
<td></td>
</tr>
<tr>
<td>Expiratory Phase:</td>
<td></td>
<td>Peak expiratory airflow during the expiratory phase of the cough (Hegland, Okun, &amp; Troche, 2014; Pitts, Bolser, Rosenbek, Troche, &amp; Sapienza, 2008; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, &amp; Gooch, 2016; Smith Hammond, 2001).</td>
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<tr>
<td>D</td>
<td>Peak Expiratory Flow Rate (L/s)</td>
<td>Percent of total expired volume of air expired during a cough epoch (Hegland, Okun, &amp; Troche, 2014)</td>
</tr>
<tr>
<td>E</td>
<td>Cough Expired Volume (%)</td>
<td>Time from the beginning of the expiratory phase to the peak of the expiratory flow (Pitts, Bolser, Rosenbek, Troche, &amp; Sapienza, 2008; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, &amp; Gooch, 2016; Smith Hammond, 2001).</td>
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<td></td>
<td>Expiratory Rise Time (s)</td>
<td>A ratio measure derived by dividing expiratory peak flow by expiratory rise time. Proposed to be a measure of cough effectiveness (Hegland, Okun, &amp; Troche, 2014; Pitts, Bolser, Rosenbek, Troche, &amp; Sapienza, 2008; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, &amp; Gooch, 2016; Smith Hammond, 2001).</td>
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<tr>
<td></td>
<td>Cough Volume Acceleration (L/s/s)</td>
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Table 2.3 Review of six research studies investigating the significant differences in voluntary cough measures between unsafe (penetrators and/or aspirators) and safe (non-aspirators) swallowers in dysphagic populations including Stroke, Parkinson’s disease, and Amyotrophic Lateral Sclerosis.

<table>
<thead>
<tr>
<th>First Author Year</th>
<th>Patient Population Number (N) Studied</th>
<th>Swallowing Assessment Method and Testing Stimuli</th>
<th>Significant Outcomes: Summary of Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smith-Hammond (2001)</td>
<td>Stroke N = 43 Stroke; 18 control Three airway safety groups Severe aspirators (asp' on all bolus trials) Mild aspirators (asp' on one or two bolus consistencies) Non-Aspirators (no asp across trials)</td>
<td>VFSS or FEES (group n is not specified), 5mL, 15 mL, and unregulated cup sips of thin liquid, Ensure Plus, and ‘thickened liquid’ (250-300 cP). (Liquid prepared to match available driniks to impatient). Between groups comparison (severe aspirators vs. non-aspirators)</td>
<td>Severe aspirators (vs. non-aspirators) demonstrated: Lower peak inspiratory flow rate (770.60 vs. 1.120 mL/s) Lower peak expiratory flow rate (-875.13 vs -1.884.14 mL/s) Higher expiratory rise times (0.34 vs. 0.09 sec) Lower cough volume acceleration (5.49 vs. 27.84 mL/s)</td>
</tr>
<tr>
<td>Pitts (2008)</td>
<td>Parkinson’s disease N = 20 Safe: PAS score 1 Unsafe: PAS score 2-8</td>
<td>VFSS 30mL liquid Between groups comparison (safe vs. unsafe)</td>
<td>PD patients with unsafe PD swallowing demonstrated: Longer compression phase durations (0.36 vs. 0.16 sec) Higher expiratory rise times (0.41 vs. 0.21 sec) Lower peak expiratory flow rate (6.17 vs. 8.94 L/s) Lower cough volume acceleration (17.02 vs. 45.24 L/s)</td>
</tr>
<tr>
<td>Smith-Hammond (2009)</td>
<td>Stroke N = 96 Non-aspirators: PAS score 1-4 Aspirators: PAS score 5-8 Parkinson’s disease N = 58 Safe: PAS score 1 Unsafe: PAS score 2-8</td>
<td>VFSS (n = 91) or FEES (n = 5) Pearson correlation coefficient to determine associations between aspiration risk (PAS ≥ 5) and objective cough measures</td>
<td>Stroke patients who aspirated demonstrated: Lower inspiration phase volume (0.45 vs. 0.69 L) Lower inspiration peak flow (-0.82 vs. -1.44 L/s) Lower peak expiratory flow rate (1.98 vs. 5.62 L/s) Higher expiratory rise times (161.50 vs. 14.05 ms) Lower cough volume acceleration (23.49 vs. 136.15 L/s)</td>
</tr>
<tr>
<td>Pitts (2000)</td>
<td>Parkinson’s disease N = 40 Safe: PAS score 1-2 Unsafe: PAS score 3-8</td>
<td>VFSS ≤5mL thin liquid; cup sip thin liquid; two sequential sips thin liquid; spoon-sized pudding bolus; cookie coated in barium Between groups comparison among cough parameters and penetrator/aspirator vs. non-PAS</td>
<td>Discriminant ability of voluntary cough airflow measures to detect penetration/aspiration: Compression phase duration: CP: 0.2 s, sensitivity: 95.8%, specificity: 64.7%, LR: 2.7, AUC: 0.83 Expiratory phase rise time: CP: 70.8 ms, sensitivity: 70.8%, specificity: 64.7%, LR: 2.7, AUC: 0.71 Expiratory phase peak flow: CP: 7.5 L/s, sensitivity: 87.5%, specificity: 50%, LR: 1.8, AUC: 0.69 Cough volume acceleration: CP: 84.5 m/s, sensitivity: 54.5%, specificity: 97.1%, LR: 18.4, AUC: 0.72</td>
</tr>
<tr>
<td>Hegland (2014)</td>
<td>Parkinson’s disease N = 70 Safe: PAS score 1-2 Unsafe: PAS score 3-8</td>
<td>VFSS ≤5mL thin liquid; cup sip thin liquid; two sequential sips thin liquid; spoon-sized pudding bolus; cookie coated in barium Between groups comparison among cough parameters and penetrator/aspirator vs. non-PAS</td>
<td>On the first cough of the epoch, PD patients with safe swallow (PAS&lt;4) swallowing demonstrated: Longer compression phase durations (0.45 vs. 0.22 s) Lower peak expiratory flow rates (5.51 vs. 4.19 L/s) Lower amount of air expired during the sequential cough (49 vs. 42%)</td>
</tr>
<tr>
<td>Plowman (2016)</td>
<td>Amyotrophic Lateral Sclerosis N = 70 Safe: PAS score 1-2 Unsafe: PAS score 3-8</td>
<td>VFSS 20mL liquid Between group comparisons and receiver operator characteristic analysis.</td>
<td>Unsafe ALS patients demonstrated: Lower cough volume acceleration (33.21 vs. 103.71 L/s) Longer peak expiratory rise times (159.20 vs. 78.80 ms) Lower peak expiratory flow rate (2.88 vs. 5.31 L/s) Discriminant ability of voluntary cough airflow measures to detect penetration/aspiration: Cough volume acceleration: CP: 45.83 m/s, sensitivity: 91.3%, specificity: 82.2%, LR: 5.1, AUC: 0.85 Expiratory rise time: CP: 80 ms, sensitivity: 82.6%,</td>
</tr>
</tbody>
</table>

Abbreviations: FEES: Fiberoptic Endoscopic Evaluation of Swallowing; PAS: Penetration-Aspiration Scale; VFSS: Videofluoroscopic Swallow Study; CP: cut point; AUC: area under the curve value; PPV: Positive predictive value, LR: Likelihood ratios

voluntary cough airflow measures and swallowing and noted significant relationships between expulsive rise times and aspiration status (p < 0.001) in 43 stroke patients (Smith Hammond,
Subsequently Smith-Hammond et al. (Smith Hammond, Goldstein, Horner, Ying, Gray, Gonzalez-Rothi, & Bolser, 2009) expanded these preliminary findings in a larger cohort of 96 stroke patients who underwent cognitive testing, a CSE, voluntary cough spirometry testing, cough sound pressure level testing (dB SPL), and an instrumental swallow evaluation (either FEES or VFSS). Swallow safety status was objectively defined using the Penetration-Aspiration Scale (PAS) score (Smith Hammond, Goldstein, Horner, Ying, Gray, Gonzalez-Rothi, & Bolser, 2009), with participant groups delineated into non-aspirators (PAS ≥ 4) vs. aspirators (PAS ≥ 5). Clinical indications such as absent swallow initiation, difficulty with secretions, and elicitation of post-prandial reflexive cough had an overall sensitivity of 53% and specificity of 83%, indicating poor sensitivity and moderate specificity in relation to the clinical assessment measures. Acoustic cough testing demonstrated clinical utility, with mean cough sound-pressure levels significantly lower in aspirators compared to non-aspirators (83.7 vs. 96.4 dB SPL; \( p < 0.0001 \)). There were significant differences in several cough airflow measures between the groups. Specifically, non-aspirators demonstrated lower inspiration phase volume (0.45 vs. 0.69 L; \( p < 0.05 \)), inspiration peak flow (0.82 vs. 1.44 L/s; \( p < 0.0001 \)), peak expiratory flow rate (1.98 vs. 5.62 L/s; \( p < 0.0001 \)), higher expiratory rise times (161.50 vs. 14.05 ms; \( p < 0.0001 \)), and lower cough volume acceleration (23.49 vs. 136.15 L/s/s; \( p < 0.0001 \)). These authors concluded that, in addition to instrumental swallowing assessment techniques, objective measures of voluntary cough spirometry may be useful in identifying airway safety status in individuals post stroke (Smith Hammond, Goldstein, Horner, Ying, Gray, Gonzalez-Rothi, & Bolser, 2009).

**Parkinson’s disease**

Pitts et al. (2008) first documented relationships between voluntary cough airflow measures and swallowing airway safety status in 20 individuals with Parkinson’s disease (PD).
Unsafe PD swallowers (PAS ≥ 2) demonstrated longer compression phase durations (0.36 vs. 0.16s; p < 0.001), longer peak expiratory rise times (0.41 vs. 0.21s; p < 0.001), lower peak expiratory flow rates (6.17 vs. 8.94 L/s; p < 0.001), and lower cough volume accelerations (17.02 vs. 45.24 L/s/s; p < 0.001).

In a larger follow-up investigation, Pitts and colleagues (Pitts, Troche, Mann, Rosenbek, Okun, & Sapienza, 2010) evaluated the discriminant ability of voluntary cough airflow measures for detecting unsafe swallowing in 58 individuals with PD. Results of this work indicated that the same four cough measures reported to be different in their earlier study demonstrated good discriminant ability to detect unsafe PD swallowers (Pitts, Troche, Mann, Rosenbek, Okun, & Sapienza, 2010).

Hegland et al. (2014) most recently demonstrated that sequential voluntary cough is associated with airway safety status in individuals with PD (Hegland, Okun, & Troche, 2014). Airflow measures were recorded and objective cough spirometry measures, including percent cough expired volume (%CEV), were obtained across two trials of sequential voluntary coughs. Significant differences between safe (PAS ≤ 2) vs. unsafe (PAS ≥ 3) swallowing groups were noted for: compression phase duration, expiratory peak flow, and percent cough expired volume (p < 0.05). PD patients with safe swallowing demonstrated coughs with higher peak expiratory flow rates, cough volume acceleration, and percent cough expired volume (i.e. significantly different in the first and third expiratory effort). Further, Hegland and colleagues noted that differences in cough-expired volumes between safe and unsafe swallow groups provided evidence of uncoordinated sequential cough patterns in the unsafe swallow PD subjects (Hegland, Okun, & Troche, 2014).

*Amyotrophic Lateral Sclerosis*
Plowman et al. (Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016) studied voluntary cough spirometry airflow measures and airway safety status in 70 individuals with amyotrophic lateral sclerosis (ALS). Participants completed both voluntary cough airflow testing and a VFSS and were grouped into safe (PAS ≤ 2) or unsafe (PAS ≥ 3) ALS swallowers. Similar to findings in stroke and PD patient populations, significant differences were observed across a number of measures. ALS patients with unsafe swallowing demonstrated lower cough volume acceleration (33.21 vs. 103.71 L/s/s, \( p = 0.00001 \)), longer peak expiratory rise times (159.20 vs. 78.80 ms, \( p = 0.003 \)), and lower peak expiratory flow rates (2.88 vs. 5.31 L/s, \( p = 0.00005 \)). Further, these three expiratory phase measures showed a good discriminant ability to detect the presence of penetration and/or aspiration (see Table 2.3 for full results) (Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016). Sensitivity and specificity were highest for cough volume acceleration (91.3 and 82.2% respectively) and ALS patients whose cough volume acceleration was below 45.28L/s/s were 5.12 times more likely to penetrate/aspirate. These authors concluded that impairment in the expiratory phase of voluntary cough may be related to degeneration of laryngeal, respiratory, and upper aerodigestive tract musculature, which compromises the ability to build ballistic force generation needed for an effective expiration phase (Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016). Recommendations were made for the consideration of cough-flow testing in the clinical screening of individuals with ALS and the use of their published cut points as references when considering airway safety risk status (Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016).
Table 2.3 Review of six research studies investigating the significant differences in voluntary cough measures between unsafe (penetrators and/or aspirators) and safe (non-aspirators) swallowers in dysphagic populations including Stroke, Parkinson’s disease, and Amyotrophic Lateral Sclerosis.

<table>
<thead>
<tr>
<th>First Author (Year)</th>
<th>Patient Population Number (N) Studied Swallowing Safety Groups</th>
<th>Swallowing Assessment Method and Testing Stimuli Statistical Comparison</th>
<th>Significant Outcomes: Summary of Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smith-Hammond (2001)</td>
<td>Stroke N = 43 Stroke; 18 control Three airway safety groups: Severe aspirators (asp’ on all bolus trials) Mild aspirators (asp’ on one or two bolus consistencies) Non-Aspirators (no asp’ across trials)</td>
<td>VFSS or FEES (group n is not specified) 5mL, 15 mL, and unregulated cup sips of thin liquid, Ensure Plus, and “thickened liquid” (250-300 cP). (Liquid prepared to match available drinks to inpatients) Between groups comparison (severe aspirators vs. non-aspirators)</td>
<td>Severe aspirators (vs. non-aspirators) demonstrated: Lower peak inspiratory flow rate (770.60 vs. 1.120 mL/s) Lower peak expiratory flow rate (:875.13 vs. -.1884.14 mL/s) Higher expiratory rise times (0.34 vs. 0.09 sec) Lower cough volume acceleration (5.49 vs. 27.84 mL/s)</td>
</tr>
<tr>
<td>Pitts (2008)</td>
<td>Parkinson’s disease N = 20 Safe: PAS score 1 Unsafe: PAS score 2-8</td>
<td>VFSS 30mL liquid Between groups comparison (safe vs. unsafe)</td>
<td>PD patients with unsafe PD swallowing demonstrated: Longer compression phase durations (0.36 vs. 0.16 sec) Higher expiratory rise times (0.41 vs. 0.21 sec) Lower peak expiratory flow rate (6.17 vs. 8.94 L/s) Lower cough volume acceleration (17.02 vs. 45.24 L/s)</td>
</tr>
<tr>
<td>Smith-Hammond (2009)</td>
<td>Stroke N = 96 Non-aspirators: PAS score 1-4 Aspirators: PAS score 5-8</td>
<td>VFSS (n = 91) or FEES (n = 5) Pearson correlation coefficient to determine associations between aspiration risk (PAS ≥ 5) and objective cough measures</td>
<td>Stroke patients who aspirated demonstrated: Lower inspiration phase volume (0.45 vs. 0.69 L) Lower inspiration peak flow (0.82 vs. 1.44 L/s) Lower peak expiratory flow rate (1.98 vs. 3.62 L/s) Higher expiratory rise times (161.50 vs. 14.05 ms) Lower cough volume acceleration (23.49 vs. 136.15 L/s)</td>
</tr>
<tr>
<td>Pitts (2010)</td>
<td>Parkinson’s disease N = 58 Safe: PAS score 1 Unsafe: PAS score 2-8</td>
<td>VFSS 30mL liquid Receiver operator characteristic analysis</td>
<td>Discriminant ability of voluntary cough airflow measures to detect penetration/aspiration: Compression phase duration: CP: 0.2 s, sensitivity: 95.8%, specificity: 64.7%, LR: 2.7, AUC: 0.83 Expiratory phase rise time: CP: 70.8 ms, sensitivity: 70.8%, specificity: 64.7%, LR: 2.7, AUC: 0.71 Expiratory phase peak flow: CP: 7.5 L/s, sensitivity: 87.5%, specificity: 50%, LR: 1.8, AUC: 0.69 Cough volume acceleration: CP: 84.5 s/i, sensitivity: 54.5%, specificity: 97.1%, LR: 18.4, AUC: 0.72</td>
</tr>
<tr>
<td>Hegland (2014)</td>
<td>Parkinson’s disease N = 40 Safe: PAS score 1-2 Unsafe: PAS score 3-8</td>
<td>VFSS 5mL thin liquid; cup sip thin liquid; two sequential sips thin liquid; spoon-sized pudding bolus; cookie coated in barium Between groups comparison among cough parameters and penetrator/aspirator vs. non-P/A</td>
<td>On the first cough of the epoch, PD patients with safe vs. unsafe (PAS=4) swallowing demonstrated: Longer compression phase durations (0.45 vs. 0.22 s) Lower peak expiratory flow rates (5.31 vs. 4.19 L/s) Lower amount of air expired during the sequential cough (49 vs. 42%)</td>
</tr>
</tbody>
</table>

Abbreviations: FEES: Fiberoptic Endoscopic Evaluation of Swallowing; PAS: Penetration-Aspiration Scale; VFSS: Videofluoroscopic Swallow Study; CP: cut point; AUC: area under the curve value; PPV: Positive predictive value, LR: Likelihood ratios

These studies, across three different neurogenic patient populations, highlight the potential utility of voluntary cough assessment during the clinical evaluation of swallowing. Several
limitations exist, however, regarding the practical implementation of such testing protocols. First, the equipment required to perform such testing is expensive and likely cost-prohibitive in most clinical settings. Second, specialized software and training of personnel is required to analyze cough waveforms and the analyses are labor and time intensive. Finally, this equipment is not easily portable, posing a barrier to access in certain patient populations. A potential alternative to the gold standard pneumotachograph airflow testing techniques utilized in the aforementioned studies is the use of a hand-held digital, or analogue, peak cough flow meter capable of measuring peak cough flow (L/s) and forced expiratory volume (FEV1, L) in real time without the need for waveform analysis or cost-prohibitive equipment. Indeed, Silverman et al. (Silverman, Carnaby-Mann, Pitts, Davenport, Okun, & Sapienza, 2014) recognized this need and studied the concordance of several handheld digital and analog peak cough flow devices to quantify peak cough airflows compared to the gold-standard pneumotachograph method. Silverman et al (Silverman, Carnaby-Mann, Pitts, Davenport, Okun, & Sapienza) indicated that both digital and analog devices (the Mini Wright peak flow meter, and Mini Wright digital peak flow meter) demonstrated good concordance with the gold standard method for measuring peak cough flow in healthy males and older female PD patients. The analog peak airflow device was reported to demonstrate a higher level of concordance for cough strength in both healthy and disease states (Silverman, Carnaby-Mann, Pitts, Davenport, Okun, & Sapienza, 2014). It is important to note, however, that these devices do not provide the detailed measurement parameters offered by cough spirometry testing. Additionally, there is contraindicating evidence that documents poor agreement between portable peak flow meter readings and the peak cough flow as measured by the gold standard physiologic assessment (i.e., pneumotachograph) (Kulnik, Macbean, Birring, Moxham, Rafferty, & Kalra, 2015). Further research is necessary to determine the validity of voluntary
cough testing using such handheld devices in several patient populations and healthy controls.

An additional consideration regarding the utility of voluntary cough testing in the evaluation of swallowing function is the fact that evaluating a *volitional* cough (i.e. asking a patient to cough) does not provide direct information on the nature of a *protective cough response* to aspirated material during swallowing (i.e. triggered by afferent stimuli in the airway). Additionally, voluntary cough production is *highly* dependent on instruction. That is, airflow patterns and perceived “strength” of a cough has been noted to change in a graded manner based upon the instruction provided (Davenport, 2008). A testing method that more closely models an airway protective cough response is the reflexive cough testing method, and will be discussed next.

**Reflexive or Induced Cough Testing**

Another method of testing cough is to perform reflexive cough testing to induce or elicit a cough response and measure response profiles. Using this method, an individual inhales an aerosolized irritant such as capsaicin, citric acid aerosols, fog, tartaric acid, acetic acid, or hypertonic solutions (Fontana & Widdicombe, 2007) that can be delivered at different concentrations through a nebulizer or facemask. A patient’s response profile can then be measured and their cough threshold determined and compared to normative values. Outcomes can be as simple as a binary measure (present / absent cough response) or airflow parameters can be measured using the cough spirometry techniques previously discussed. In addition to measuring the motor output of the cough response, the afferent aspect of this sensorimotor behavior can be probed by asking the patient their perceived ‘Urge to Cough’ using a modified Borg scale across each cough trial (Davenport, 2008). Cough output is affected by irritant type, concentration, volume and duration of exposure, order of presentation, placebo trials, nasal afferent stimulation, and lung volume at the start of cough initiation (Troche, Brandimore, Godoy, & Hegland, 2014).
These variables impact cough flow rates, number of coughs produced, urge to cough (self-report), amplitude and duration of expiratory muscle activation, and time to initiation of a cough response (Troche, Brandimore, Godoy, & Hegland, 2014). Similar to voluntary cough testing, several investigators have examined the potential discriminant ability of reflexive cough testing in determining swallowing safety status, which will now be highlighted. A summary of these studies is provided in Table 2.4.

**Table 2.4** Summary of published reports investigating the discriminant ability of reflexive cough testing to detect swallowing safety.

<table>
<thead>
<tr>
<th>First Author Year</th>
<th>Patient Population</th>
<th>Swallowing Assessment Method</th>
<th>Reflex Cough Testing Protocol</th>
<th>Summary of Results and Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sato (2012)</td>
<td>Heterogeneous*</td>
<td>FEES</td>
<td>Oral inhalation of citric acid (1% w/v) via nebulizer delivered for 1 minute or until first cough.</td>
<td>Discriminant ability of reflex cough testing to distinguish: - Silent aspirators vs. non-silent aspirators: A cut value of 30 seconds to elicit first cough to distinguish silent aspirators vs. aspirators (sensitivity: 92%, specificity: 94%, PPV: 97%, NVP: 83%) - Silent aspirators vs. non-silent and safe swallowers: A cut value of 60 seconds to elicit first cough to distinguish silent aspirators vs. non-silent and safe swallowers. (sensitivity: 81%, specificity: 65%, PPV: 45%, NVP: 91%) - Conclusions: The ability to detect silent aspiration (true positive) in this heterogeneous patient population was high (0.81) however, there were a high number of false positives (0.65); therefore this methodology may over identify individuals with unsafe swallowing.</td>
</tr>
</tbody>
</table>
Abbreviations: FEES: Fiberoptic Endoscopic Evaluation of Swallowing; NPV: Negative predictive value; OR: Odds ratio; PAS: Penetration Aspiration Scale; PPV: Positive predictive value; SCT: Simplified Cough Test (reflexive cough test); VFSS: Videofluoroscopic Swallow Study.

*Heterogeneous sample Sato (2012) included 141 consecutive patients; 89 individuals post stroke, 22 disuse syndrome, 8 neuromuscular, 14 respiratory, 3 cancer, 2 cervical spine injury, 3 miscellaneous. Neuromuscular disease included Parkinson’s disease, corticobasal degeneration, multiple systems atrophy, and spinocerebellar degeneration. Miles (2013) included Stroke, Head and neck cancer, respiratory, progressive neurological, other neurological, and other.

∞Binary classification based on total number of coughs produced was as follows: “responders” were defined as those who produced at least 2 coughs on 2/3 trials for each irritant type independently (fog and capsaicin).

** Positive cough response defined as two or more consecutive coughs triggered.

Sato et al. (2012) evaluated 141 consecutively referred patients with non-specific complaints of dysphagia. Primary medical diagnoses included stroke, neuromuscular disease,
deconditioning, respiratory disease, cancer, cervical spinal injury, and ‘miscellaneous.’ FEES was used to determine airway safety status, yielding 53 unsafe swallwers (aspirators) and 88 safe swallwers (no aspiration). Reflex cough testing was performed using a citric acid-saline solution [1% weight/volume (w/v)] to induce a reflexive cough with time from citric-acid administration to elicitation of the first cough the primary metric of interest. Results indicated that time to first cough demonstrated excellent discriminant ability for identifying silent aspirators in this cohort. Specifically, a value of 30 seconds post-irritant administration to the first cough demonstrated a sensitivity and specificity for detection of silent aspiration of 92% and 94%, respectively. When including all aspirators, however, a cutoff of 60 seconds for cough reaction time yielded a sensitivity and specificity for detection of aspiration at 81% and 65%. These results suggest that subtle differences in cough reaction time affects the accuracy of detecting silent aspiration.

Miles at al. (2013) examined the utility of reflexive cough testing for identification of silent aspiration in 181 consecutively referred inpatients with diagnoses including stroke, head and neck cancer, ‘respiratory disease,’ progressive neurologic disease, and ‘other.’ All individuals were evaluated with reflexive cough testing and an instrumental swallowing evaluation (either FEES or VFSS). Swallowing safety status was determined by a blinded SLP who rated either the FEES or VFSS using the PAS scale and patients were grouped by: no aspiration, aspiration with cough (not specified if it was an effective cough), trace silent aspiration, and silent aspiration.

Cough thresholds were evaluated using randomly administered citric acid solutions (0.4 mol/L, 0.6 mol/L, 0.8 mol/L, and placebo) via facemask nebulizer on a continuous flow. The primary outcome measure was presence or absence of cough following each 15-second interval. The trial was considered a “positive” response and if the patient coughed two or more times at a
given concentration. Additionally, researchers perceptually rated subjective cough response strength (weak or strong). The concentration of 0.6 mol/L was shown to have the highest level of accuracy for discriminating between safe and unsafe swallowers on the VFSS (sensitivity of 71%, specificity of 60%). However, these values are considered below ideal for a good screening tool.

More recently, Hegland et al. (2016) investigated cough response profiles to varied irritant types in both healthy controls and individuals with PD. Patients underwent VFSS and were categorized into safe (non-aspirators, PAS ≤ 4) vs. unsafe (aspirators, PAS ≥ 5) swallowing groups. Irritant stimuli included diluted capsaicin (200μM dissolved in vehicle solution of 80% physiologic saline and 20% ethanol) and aerosolized water (fog). Both irritants were delivered through a nebulizer (Omron Micro-Air NE U22 V, Tokyo, Japan) for 60 seconds and the mean number of coughs produced within a 30 second time-frame and categorical ‘responders’ and ‘non-responder’ data was collected. For binary responder/non-responder outcomes, there were differences in response to irritant type with regards to the sensitivity and specificity for detecting laryngeal penetration and/or aspiration. Specifically, capsaicin yielded a sensitivity of 44.4% and specificity of 100% and fog a sensitivity of 77.8% and specificity of 90.9%. Additionally, there were significant differences in the number of coughs produced between safe and unsafe swallowers, with unsafe swallowers producing fewer coughs to both fog and capsaicin.

Hegland and colleagues reported poor sensitivity (20%) but good specificity (95.9%) for detecting unsafe swallowing with reflexive cough testing (using capsaicin) in PD (Hegland, Troche, Brandimore, Okun, & Davenport, 2016) and concluded that the high false negative (not detecting an impairment) may indicate that the single inhalation may not be the correct methodology to implement to rule out aspiration in this population. The authors also reported that a difference in response to fog vs. capsaicin suggests possible differences in neural control of
cough regulation.

Kallesen et al. (Kallesen, Psirides, & Huckabee, 2016) investigated the clinical utility of reflexive cough testing for assessment of swallowing impairment in 106 recently extubated intensive care unit patients (Kallesen, Psirides, & Huckabee, 2016). Patients underwent FEES evaluation and reflexive cough testing with concentrations of 0.4, 0.6, and 0.8 mL/L nebulized citric acid mixed with 0.9% sodium within 24 hours of extubation. The PAS was used to differentiate penetrators (PAS ≤ 5) vs. aspirators (PAS ≥ 6), yielding 13 aspirators, 9 of which were identified as silent aspirators (69%). Concentrations of 0.4, 0.6, and 0.8 mL/L demonstrated sensitivity values of 100%, 100%, and 88% and a specificity of 42%, 49%, and 58% for detecting aspiration, respectively. Kallesen and colleagues concluded that reflex cough testing over-identified aspiration in this patient population.

Multiple variables can be manipulated when performing reflexive cough testing and thus, may result in drastically different patient responses. These studies highlight the potential utility of reflexive cough evaluation for the assessment of aspiration status and also provide complimentary literature to the voluntary cough testing. Cough reflex testing methodology may be more practical as part of a screening assessment as the methodology is inexpensive, quick to administer, and objective outcomes relatively simple to interpret. However, the lack of consensus for testing protocols and scarce data in multiple patient populations highlight an important gap in the literature. This leads to the inability to provide cohesive practice recommendations in regards to the optimal irritant type and strength of solution, length of delivery, and outcome measures. Although these articles provide an excellent foundation, more research is warranted to provide guidelines to practicing clinicians.

**Limitations and Future Directions**
Although an emerging and promising dataset supports the use of cough testing in the clinical evaluation of swallowing, current data is limited and restricted to only a few patient populations with a critical need for more data to validate these promising findings in other patient populations. Practical limitations of objective voluntary cough testing procedures necessitate the need for further studies to examine the discriminant ability of simple and inexpensive cough testing using handheld peak-flow meters, similar to the work of Silverman and colleagues (Silverman, Carnaby-Mann, Pitts, Davenport, Okun, & Sapienza, 2014). Reflexive cough testing represents a relatively simple, inexpensive and relatively quick method of testing that is currently being utilized clinically by Dr. Karen Hegland in a busy clinic for individuals with Parkinson’s disease, with binary cough threshold testing and urge to cough screens performed routinely at every patient visit (Hegland, personal communications).

**Conclusions**

This narrative review highlights the shared neural and anatomical substrates mediating cough and swallowing, as well as the co-occurring presence of dystussia and dysphagia. Additionally, the role of cough in defending the airway and rationale for providing a physiologic index of airway defense in patients at risk for dysphagia has been delineated. A small but growing body of literature supports the inclusion of cough testing in the CSE to provide an index of overall function and capacity of airway defense mechanisms to aide in clinical and diagnostic decision-making and assessment of potential risk of impairments in swallowing safety. Clearly more data are needed to validate these findings, in addition to using practical, inexpensive and efficient methods that can be easily implemented in busy clinical settings to provide valid and reliable results across practice settings.
CHAPTER THREE
CURRENT PRACTICE PATTERNS

Introduction

Dysphagia is a symptom of underlying disease and unfortunately, associated with a variety of medical diagnoses. Dysphagia adversely impacts health status, quality-of-life (QOL), and creates financial burden for patients and their caregivers (Cichero, 2012; Leow, Huckabee, Anderson, & Beckert, 2010; Maclean, Cotton, & Perry, 2009). When evaluating the swallowing process, it is critical to incorporate assessment of airway safety status, bolus efficiency, and airway protective ability (i.e., cough). Impairments in these domains often lead to pulmonary sequela, and undernourishment (Guest, Panca, Baeyens, De Man, Ljungqvist, Pichard, Wait, & Wilson, 2011). Pulmonary infection also termed, aspiration pneumonia, has been identified as the leading cause of death Parkinson’s disease (PD) and the elderly (Fernandez & Lapane, 2002; Gorell, Johnson, & Rybicki, 1994; Hely, Reid, Adena, Halliday, & Morris, 2008; Marik & Kaplan, 2003; Shill & Stacy, 1998). Further, malnutrition has been associated with oropharyngeal dysphagia in the geriatric population, (Cabre, Serra-Prat, Force, Almirall, Palomera, & Clave, 2014; Chapman, 2006; Namasivayam-Macdonald, Morrison, Steele, & Keller, 2017) and increases the risk of death in individuals with amyotrophic lateral sclerosis (ALS) (Chio, Logroscino, Hardiman, Swingler, Mitchell, Beghi, Traynor, & Eurals, 2009; Serra-Prat, Palomera, Gomez, Sar-Shalom, Saiz, Montoya, Navajas, Palomera, & Clave, 2012). Timely identification of swallowing impairment and reduced ability to protect the airway is vital to ensure implementation of management strategies to optimize oral intake and maintain pulmonary health and patient QOL.
Physicians, nurses, and speech-language pathologists (SLP) who hold a certificate of clinical competency (CCC-SLP) perform clinical swallow assessments (CSE) across a variety of health care settings hospitals and skilled nursing facilities (Association, 2000; Logemann, 1998). Regardless of the practitioner, an individual may only have five to fifteen minutes to determine a patient’s swallow safety status. The accuracy of clinical swallow evaluation techniques and assessment capabilities of airway protective behaviors vary widely (Daniels, Anderson, & Willson, 2012; Leder, Suiter, Murray, & Rademaker, 2013; Mathers-Schmidt & Kurlinski, 2003). CSE components may include: review of case history, cranial nerve assessment, clinical feeding trials of various bolus consistencies, and a voice quality assessment (McCullough, Wert, Rosenbek 2001, McCullough, Rosenbek, Wertz, McCoy, Mann, McCullough, 2005, Daniels, Anderson, Willson, 2012). However, a recent study has shown that SLPs prioritize clinical skills and reasoning above following an outlined checklist assessment method such as item-based protocols (Mcallister, Kruger, Doeltgen, & Tyler-Boltrek, 2016).

Of late, there is increasing evidence indicating the usefulness of gold standard voluntary cough using spirometry to determine airway safety status (Pitts, Bolser, Rosenbek, Troche, & Sapienza, 2008; Pitts, Troche, Mann, Rosenbek, Okun, & Sapienza, 2010; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016; Smith Hammond, Goldstein, Horner, Ying, Gray, Gonzalez-Rothi, & Bolser, 2009; Smith Hammond, 2001; Troche, Okun, Rosenbek, Musson, Fernandez, Rodriguez, Romrell, Pitts, Wheeler-Hegland, & Sapienza, 2010). However, instrumental voluntary cough testing methods remain outside of current CSE published guidelines. With the addition of quality literature over the past decade regarding relationships between cough and swallow, it remains is unclear if subjective assessment of voluntary cough sound is widely used in clinical practice, and/or what aspects of cough are being considered as clinically useful.
The lack of insight into current practice patterns of voluntary cough assessment limits the usefulness of research on optimization of cough techniques that are easily implemented in the clinical settings. Consequently, the aim of the current investigation is to define current practices for subjective voluntary cough assessment during the CSE. Based on limited clinical practice guidelines for cough testing and limited inclusion of cough testing methods included in CSE’s, it is hypothesized that across a variety of medical settings that subjective assessment of cough sound is not routinely implemented despite years of training or clinical experience.

Methods

Participants

SLPs and other medical professionals who currently assess swallowing were targeted to complete an online survey via forum post on two professional organization sites: American Speech Language Hearing Association (ASHA) special interest group 13 (swallowing and swallowing disorders) and Dysphagia Café. A total of 781 individuals responded to the survey. This study received approval by the University of South Florida Institutional Review Board (#00017474) (see Appendix B) and all participants provided consent via an online questionnaire prior to the initiation of the survey.

Materials and Procedures

Qualtrics online survey software was used to construct, disseminate, and store acquired survey data (Qualtrics; Provo, UT). The pilot survey included 22 questions divided into two sections: 1) demographic information; and 2) bedside swallow evaluation practices with specific reference to cough testing. Questions regarding perceptual cough assessments allowed for free text answers for trend analysis. In addition, survey construction was designed to reduce participant bias. Field-testing of the pilot survey included review of each item for relevance, mutually
exclusivity, and clinical significance. There were a total of 18 remaining questions following field-testing (please see Appendix C to view the final constructed survey questions).

The electronic survey format, Qualtrics, allowed for the use of “skip logic.” Certain questions were revealed to the participant based on response to a prior question. For example, if the participant answered “no” to the question, “Are you a Speech Language Pathologist (SLP)?” the question, “What is your SLP certification level?” was skipped. Mandatory responses (14 in total) were deemed as responses that must be completed despite skip logic. These are denoted in Appendix C.

Participants had access to the survey for a total of three months. A two-tier elimination process was utilized to evaluate for completed and appropriate responses. First, given that the survey was related to CSE practice patterns, participants who responded “no” to “do you conduct clinical swallow examinations?” or left the response blank were excluded. This exclusion resulted in 722 valid responses. Lastly, mandatory responses (items displayed regardless of skip logic) were tabulated; participants who completed <85% of mandatory responses were excluded, this resulted a total of 605 survey responses used for analysis.

Statistical Analysis

Survey responses were analyzed using descriptive and associiative methods. A Chi-square test statistic was used to determine if there was a significant difference in voluntary cough assessment patterns between certification level and years of experience. This was chosen because the nominal data was derived from a random sample, the sample groups were independent of one another and observations within the sample groups were independent of one another (i.e., respondents were in one category or another). Binary and categorical data were summarized as frequencies. Open question responses were analyzed based on thematic content and grouped according to theme. Data
is presented as mean ± standard deviation (SD), and significance was set at \( p < 0.05 \).

**Results**

*Participant Demographics*

Following the two-tier elimination process to include appropriate and complete responses, 605 out of 781 (77%) survey responses were analyzed for this study, representing 48 states and 1 United States territory represented (see Figure 3.1). Of the 605 participants, 505 were from the United States of America, 24 were from Canada, and 76 were from outside of North America. Table 3.1 contains full respondent demographics. The total mean time to complete the survey was 11.7 ± 59 minutes.

![Figure 3.1](image)

**Figure 3.1** Color illustrative map of the United States of America representing U.S. participants by state. The darker shaded colors indicate greater number of respondents.
Table 3.1 Demographic characteristics of survey respondents (N = 605).

<table>
<thead>
<tr>
<th>Variable</th>
<th>(n)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speech Pathologist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>597</td>
<td>98.7</td>
</tr>
<tr>
<td>No</td>
<td>8</td>
<td>1.3</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Masters</td>
<td>468</td>
<td>77.3</td>
</tr>
<tr>
<td>Doctorate</td>
<td>41</td>
<td>6.8</td>
</tr>
<tr>
<td>Student</td>
<td>82</td>
<td>13.6</td>
</tr>
<tr>
<td>No response</td>
<td>14</td>
<td>2.3</td>
</tr>
<tr>
<td>Advanced Certification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Board registered swallowing specialist</td>
<td>18</td>
<td>2.9</td>
</tr>
<tr>
<td>Experience in medical practice (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1</td>
<td>65</td>
<td>11.0</td>
</tr>
<tr>
<td>1 - 2</td>
<td>94</td>
<td>15.5</td>
</tr>
<tr>
<td>3 - 5</td>
<td>139</td>
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</tr>
<tr>
<td>6 - 10</td>
<td>122</td>
<td>20.1</td>
</tr>
<tr>
<td>11 - 20</td>
<td>92</td>
<td>15.2</td>
</tr>
<tr>
<td>20 +</td>
<td>84</td>
<td>13.8</td>
</tr>
<tr>
<td>No response</td>
<td>9</td>
<td>1.48</td>
</tr>
<tr>
<td>Country of Practice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>505</td>
<td>83.5</td>
</tr>
<tr>
<td>Canada</td>
<td>24</td>
<td>4.0</td>
</tr>
<tr>
<td>Other</td>
<td>76</td>
<td>12.5</td>
</tr>
<tr>
<td>Work Environment**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital</td>
<td>213</td>
<td>35.2</td>
</tr>
<tr>
<td>Skilled nursing facility</td>
<td>204</td>
<td>34.7</td>
</tr>
<tr>
<td>Outpatient rehabilitation</td>
<td>70</td>
<td>11.6</td>
</tr>
<tr>
<td>Multiple practice locations</td>
<td>49</td>
<td>8.1</td>
</tr>
<tr>
<td>Voice and swallow center</td>
<td>18</td>
<td>3.0</td>
</tr>
<tr>
<td>Private Practice</td>
<td>14</td>
<td>2.3</td>
</tr>
<tr>
<td>Home Health</td>
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<td>2.3</td>
</tr>
<tr>
<td>Graduate training clinic</td>
<td>12</td>
<td>2.0</td>
</tr>
<tr>
<td>Other</td>
<td>11</td>
<td>1.8</td>
</tr>
</tbody>
</table>

*Final survey responses were selected using a 2-tier validation process; 1) participants complete CSEs and 2) answered 85% or greater of the mandatory questions (i.e., not skip logic) and conduct clinical swallowing evaluations at their setting.
Inclusion of Voluntary Cough Assessment

Eighty-seven percent (529 of 605) of respondents reported they do assess voluntary cough during a CSE. Two participants (< 0.5%) did not respond, however they did note specific qualities that they look for in cough in response to a later question. See Table 3.2 for full detail of voluntary cough assessment by workplace, years of experience, and certification status.

Table 3.2 Use of voluntary cough assessment by years of experience, practice setting, and level of certification (n = 603).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Voluntary cough Assessment (n)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Experience (Years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1</td>
<td>52</td>
<td>13</td>
</tr>
<tr>
<td>1 - 2</td>
<td>81</td>
<td>13</td>
</tr>
<tr>
<td>3 - 5</td>
<td>125</td>
<td>13</td>
</tr>
<tr>
<td>6 - 10</td>
<td>106</td>
<td>16</td>
</tr>
<tr>
<td>11 - 20</td>
<td>80</td>
<td>11</td>
</tr>
<tr>
<td>20 +</td>
<td>76</td>
<td>8</td>
</tr>
<tr>
<td>No response</td>
<td>9</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>529</td>
<td>74</td>
</tr>
<tr>
<td>Practice Setting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home Health</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Hospital</td>
<td>183</td>
<td>29</td>
</tr>
<tr>
<td>Multiple Locations</td>
<td>46</td>
<td>3</td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Outpatient</td>
<td>62</td>
<td>8</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private Practice</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Skilled Nursing</td>
<td>178</td>
<td>25</td>
</tr>
<tr>
<td>Graduate Clinic</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Voice/Swallow Center</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>No Response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>529</td>
<td>74</td>
</tr>
<tr>
<td>Certification Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Student/Training</td>
<td>67</td>
<td>15</td>
</tr>
<tr>
<td>Masters</td>
<td>411</td>
<td>55</td>
</tr>
<tr>
<td>Advanced Training</td>
<td>37</td>
<td>4</td>
</tr>
<tr>
<td>No Response</td>
<td>14</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>529</td>
<td>74</td>
</tr>
</tbody>
</table>

* Of the 605 participants who responded to years of experience, 2 did not rate whether or not they assess voluntary cough. Description of working environment as follows: Hospital
includes individuals identified as working in a hospital setting including inpatient rehabilitation, multiple practice locations include individuals who identified working in multiple settings (i.e., hospital and skilled nursing facility). “Other” category included varied community based facilities for adults or medically fragile children.

Interaction between clinical experience and certification level

No significant difference was found between the years of clinical experience (ordinal rank groups) and use of voluntary cough (\(X^2 (2) = 5.893, p = 0.43\)). Level of certification was categorized into three groups: 1) training status including SLP-assistant; student clinician (currently in a master’s program); or clinical fellow (has obtained a master’s degree but has not received professional certification), 2) professional level (CCC-SLP) and 3) advanced training (BRS-S or Ph.D.). There was no significant difference between certification level and use of voluntary cough (\(X^2 (5) = 2.99, p = 0.22\)). Figure 3.2 depicts ranked frequencies for years of experience.

![Figure 3.2 Bar graph representing distribution of respondents who reported assessing voluntary cough during the clinical swallow grouped by years of experience.](image)

Figure 3.2 Bar graph representing distribution of respondents who reported assessing voluntary cough during the clinical swallow grouped by years of experience.
Abnormal voluntary cough

For the open format question, “What aspects of voluntary cough do you listen for to indicate abnormality (e.g., strength)?” 523 responses were analyzed (523/605 responded to this question). The number of descriptive terminologies used to describe disordered cough varied greatly. The minimum number of descriptors = 1, maximum = 7, the average number of descriptor to describe disordered cough was 2.7 ± 1.2. Trends in the use of the terms strength, loudness, effectiveness, and productive to describe aberrant voluntary cough sounds were analyzed. The most prevalent individual term was “strength.” This term was used by 458/523 respondents (87.5%) to evaluate voluntary cough for the purpose of assessing airway protection. When combing this term with “weak,” the number increased to 470/523 (89.9%) respondents. The second most commonly used term was “productive” with 91/523 (17.4%) respondents using this to assess ability to protect the airway. The third most commonly used term was “volume/loudness,” used by 34/523 (6.5%) respondents. The fourth most commonly used term was “effective/ineffective,” used by 19/523 (3.6%) respondents. Respondents also listed a variety of terms outside of the aforementioned categories including: “acoustics,” “respiratory strength,” “pharyngeal residue,” and “strength of exhalation.”

Clinical Swallowing Assessment Pattern

Participants reported having knowledge of one or all of the following clinical swallow protocols: Gugging Swallowing Screen (Trapl, Enderle, Nowotny, Teuschl, Matz, Dachenhausen, & Brainin, 2007); Modified Mann Assessment of Swallowing Ability (MASA) (Mann, 2002); The Toronto Bedside Swallowing Screening Test (TOR-BSST) (Martino, Silver, Teasell, Bayley, Nicholson, Streiner, & Diamant, 2009); and Yale 3 ounce water swallow test (Suiter, Sloggy, & Leder, 2014). Fifty-three percent of individuals use one of the validated clinical swallowing
protocols listed above. The option for open typed responses was provided in order facilitate insight as to why a validated protocol was not followed during a clinical swallowing evaluation. Responses were grouped thematically. The following reasons were provided for not following a validated CSE protocol: 1) “not part of policy at the hospital”; 2) “not a common practice in the particular country”; 3) “lack of training/education/access/familiarity”; 4) “learned a specific way of informal swallow clinical protocol”; 5) “a specific non-standardized protocol is the standard practice at the place of employment”; 6) “the evidence based practice for the protocol is not proven”; and/or 7) “the assessments are not personalized”.

The most common assessment components that were reportedly used during a CSE included: 1) cranial nerve assessments; 2) oral feeding trials; 3) medical chart review; and 4) cognition/orientation testing.

**Discussion**

This is the first study to demonstrate that a majority of clinicians are using voluntary cough assessment during their CSE examinations, regardless of the clinician’s level of experience or relevant certification. While one may view this as positive trend in the SLP field; discouragingly, a large percentage of clinicians are still not using standardized/validated CSE protocols which use similar terminology such as “weak and strong” to denote cough impairment. Given, this lack of standardization, there also remains a discrepancy in the language/terminology used by clinicians to perceptually describe aberrant cough.

According to survey responders, terms related to cough “strength” are most commonly used to define abnormality. However, rating a parameter such as strength with a binary outcome (weak or strong) has been found to show poor ability to detect abnormality. Smith-Hammond and colleagues (2001) demonstrated that CSE examinations of cough using terms of strength and
quality had very low sensitivity (42 and 26 respectively). The authors further noted that almost 40% of patients who might have benefited from swallow therapy would not have been identified based on these cough metrics. Lack of agreement on descriptive terms of cough within speech language pathology practice and related fields studying cough may contribute to these findings as there is a lack of consistency and understanding of perceptual cough metrics to apply to our clinical populations. Objective cough rating using a scale indices or physiologic measurement of cough may provide a platform for a more cohesive and systematic measurement of cough impairment in the clinical setting.

Our data demonstrate that that the majority of survey participants (87%) are attending to the cough process as they indicated that they do assess voluntary cough during a clinical swallowing evaluation. When examining literature from our rehabilitation colleagues in physical and occupational therapies, we see that “strength” can measurable within an interval rating scale (Price, 2012). Physiologically, a person’s strength can be measured by force against and object. Objectively, strength also is a measurable phenomenon. Therefore, clinically, we may be using an incorrect method of measurement by categorically defining perceptual cough features into “weak” or “strong”.

A promising alternative may be the use of a peak cough flow meter to evaluate cough. For example, Silverman et al., (2014) investigated cough measurement devices in healthy controls and persons with PD. Thirty-five healthy controls and thirty-five participants with PD were recruited; all participants were instructed to cough into three types of cough measurement devises: 1) an analog peak flow meter; 2) digital peak flow meter; and 3) a pneumotacograph (gold standard cough measurement). The participants were asked to produce three types of cough including a “weak, moderate, and strong” cough. Authors reported that average peak cough flow outcomes
were significantly different for both analog and digital peak flow meters and the pneumotacograph for the presence of disease (PD) and between genders; in addition, all of the devices produced similar normative outcome values (Silverman et al., 2014). Conversely, a study investigating the accuracy of portable devices measuring peak cough flow indicated poor agreement between gold standard pneumotactograph recordings and portable peak cough flow meters (Kulnik, MacBean, Birring, Moxham, Rafferty, Kalra, 2015). Those authors highlighted the potential for inaccuracy when using this methodology to assess peak cough flow as authors reported poor agreement between the gold standard of airflow measurement and portable cough airflow devises (Kulnik, S.T., MacBean, V., Birring, S.S., Moxham, J., Rafferty, G.F, Kalra, L, 2015). As within clinical voice practice, clinicians are listening to voluntary cough and perceptually evaluating its characteristics. Given the current discrepancy in the use of objective means of cough assessment such as the peak flow meter and in the use of perceptual evaluation of cough, there is a need to investigate these properties in both healthy controls and a variety of patient populations.

In many fields, agreement on, and consistent use of terminology is lacking and often there are overlapping and poorly defined terms to describe abnormality. Within the field of speech-language pathology, we can look within the voice literature and see that many terms have been used to describe voice quality based on an auditory-perceptual assessment of voice (Hirano, 1981). Even among expert listeners, there can be discrepancies in reliability of voice ratings (Kreiman, 1996). Though it should be noted that inter- and intra-rater reliability can be very high if the measurement methods are suitable for perceptual measurements (Shrivastav et al., 2005; Patel et al., 2010). Reliability is especially an issue for rating scale methods, which in clinical evaluations, typically involves a single judge and single trial listening.

The auditory-perceptual evaluation most common in current clinical practice is the
Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V) (Kempster, 2009) that relies on a series of rating scales and other perceptual judgments. This method is similar to the grade, roughness, breathiness, asthenia, and strain (GRABAS) scale described by (Hirano, 1981). Under controlled laboratory conditions with expert judges, the inter- and intra-rater reliability of such measures can be quite high (Nemr, Simoes-Zenari, Cordeiro, Tsuji, Ogawa, Ubrig, & Menezes, 2012) though other investigations have not shown such high reliability within a clinical setting (Kreiman, 1993). The voice quality literature has created a path to assess vocal quality using subjective perceptual rating scales as well as objective acoustic measures to inform the listener of abnormality, even though the most widely used measures (e.g., CAPE-V) are still considered inadequate by many professionals. Klein and colleagues (2000) examined the relationship between objective and subjective measures of voice quality and this contribution in the description of voice using a multichannel input for simultaneous assessment of acoustic and physiologic parameters. The authors concluded that the subjective voice ratings indeed provided useful information regarding the voice that the objective data alone did not convey. In the case of cough, we need to pick terminology, clearly define this terminology, and understand what it means physiologically.

**Limitations and Future Directions**

There are several limitations of this study associated with the phrasing of specific questions and those limitations make interpretation of some of the results less clear than originally planned. For example, in the question “What aspects of cough do you listen to when assessing voluntary cough?” the term “strength” was listed as an example of a voluntary cough feature. This potentially biased the responders to include strength or terms related to strength in their responses and may have led to over estimation of the use of such terms relative to terms that were not provided as examples. Similarly, in the question “Do you assess voluntary cough (e.g., ask the patient to
perform a cough)?” the inclusion of the example in the parenthetical clause may have biased participants to include responses such as “perform a cough” leading to overestimation of such responses relative to other objectives measures such as objective peak cough flow meters to test voluntary cough function or nebulizers to assess reflexive cough function. Future work focusing on survey analysis of the variety of clinical cough testing methodologies that are currently being used and also clinicians feeling towards to use of new cough testing methodologies may help shape future research aims.

Conclusion

The aim of the investigation was to define current practices for subjective voluntary cough assessment during the CSE. It was hypothesized that across a variety of medical settings, that subjective assessment of voluntary cough sound is not routinely implemented despite years of training or clinical experience. The results of this study did not support that hypothesis as 89% of survey respondents replied that they do assess voluntary cough (e.g. ask the patient to perform a cough) during the CSE, and the use of voluntary cough testing did not differ between years of clinical experience or certification type (i.e., advanced clinical training).

Cough evaluation within the clinical setting is gaining attention. Researchers are reporting the utility of hand held meters to evaluate cough function in select patient populations (Silverman et al., 2014), there are reports of perceptual variants of cough and how this relates to airflow measures (Laciuga et al., 2016), and several authors have published data on the use of cough airflow flow testing using a pneumotacograph to determine airway safety status. The current survey completed by 605 participants’ shows that a majority of survey respondents across practice settings, levels of experience, and certification are clinically assessing voluntary cough function as part of their practice. With a growing body of basic and clinical literature demonstrating
relationships between swallowing the airway protective behavior of cough, there is an urgent need for standardization of cough assessment protocols and understanding terminology used to describe aberrant cough.

Expert clinicians and scientists agree that cough is a behavior that is essential to one’s health and wellbeing especially those who are at risk for penetration or aspiration events. Standardization of cough assessment and common language used to describe aberrant cough may help improve dystussia evaluation as well as direct future research aims.
CHAPTER FOUR

PERCEPTUAL AND CLINICAL INDICES OF COUGH ASSESSMENT

Introduction

Voluntary cough measures are predictive of airway safety status during swallowing in several patient populations including stroke (Smith Hammond C.A. , 2001; Smith Hammond, Goldstein, Horner, Ying, Gray, Gonzalez-Rothi, & Bolser, 2009), Parkinson’s disease (PD) (Pitts, Bolser, Rosenbek, Troche, & Sapienza, 2008; Pitts, Troche, Mann, Rosenbek, Okun, & Sapienza, 2010) and Amyotrophic Lateral Sclerosis (ALS) (Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016). Voluntary cough testing methodology has varied across these studies; however, all have utilized cough airflow testing (the current gold-standard cough evaluation method). This methodology requires costly equipment and the analysis is labor intensive, time consuming, and requires intensive training to perform expert evaluation of the cough airflow waveforms. The modified barium swallow study (MBS) (the current gold-standard swallowing evaluation method) affords visualization of airway protection safety status in real time (Logemann, 1984). The Penetration Aspiration Scale (PAS) (Rosenbek, Robbins, Roecker, Coyle, & Wood, 1996) is an 8-point rating scale used to quantify and categorize level of airway protection based off of results from the MBS. A rating of 1 indicates that nothing has entered the laryngeal vestibule and a rating of 8 indicates that swallowed material has gone below the level of the true vocal folds and a cough response was not elicited. The PAS scale does contain information regarding a patient’s ability to protect the airway during a swallowing task (i.e., the attempt to “eject” the material or cough was successful or not) and therefore is efficient in understanding if a
cough is effective or not. Unfortunately, the MBS may be costly and not readily available to all clinicians such as those in skilled nursing facilities, home-health practitioners, or those who provide clinical assessment via telehealth. Many clinicians utilize swallowing screening and clinical swallowing evaluations to determine both airway safety status and assess a patient’s ability to effectively protect the airway.

Although there are data to support the relationship between cough and swallowing, not all available clinical swallowing assessment protocols contain a cough-testing component (Watts, Tabor, & Plowman, 2016). Cough effectiveness is a term used to describe cough in terms of the ability of the force of that cough to expel material from the airway. Current clinical evaluation of cough is focused on cough frequency, peak expiratory airflow rate collected via a hand-held peak flow meter, and subjective ratings of cough “effectiveness” in a binary manner (i.e., weak or strong). To this point, little is known regarding the reliability or validity of clinician perceptions of voluntary cough effectiveness during the clinical swallow evaluation (Laciuga, Brandimore, Troche, & Hegland, 2016).

There is a paucity of data on the ways in which audible perceptual features of dystussia (disordered cough) may differ from audible features of normal cough. Additionally, there is limited knowledge on whether perceptual parameters of cough can inform clinicians of decreased airway protection during swallowing, or if perceptual measures of cough are a reliable means to judge such differences in disordered vs. functional cough. There is currently no standardized tool to assess subjective ratings of cough impairment by healthcare professionals. There remains a great clinical need for a cost-effective, readily available, low-tech, sensitive and specific clinical tools to evaluate voluntary cough function. A visual analog scale (VAS) is often used to characterize the intensity of a biological function across a simple numeric continuum (Gould et al., 2001).
However, there is some debate throughout the literature as to whether the use of a VAS is credible measure of certain functions (Price, Staud, & Robinson, 2012). The VAS, in the context of quantifying the perception of pain, has been reported to demonstrate ratio-scale properties and be sensitive to small changes in the perception of pain (Myles & Urquhart, 2005; Price, McGrath, Rafii, & Buckingham, 1983; Price, Bush, Long, Harkins, 1994; Price & Harkins, 1987). The goals of this study were to determine if there were differences between airway safety groups in individuals with ALS for in perceptual measures of cough strength, loudness, and effectiveness as measured by a VAS, and for the presence/absence of aberrant cough features. We hypothesized that measures of cough strength, loudness, and effectiveness would be reduced in individuals with unsafe swallowing relative to those with safe swallowing. Further, we hypothesized that individuals with unsafe swallowing would demonstrate one or more identifiable aberrant cough features.

**Methods**

**Participants**

Retrospective data were collected from participants who were previously enrolled in a pilot study and a grant-funded (R21) research study run by principle investigator Dr. Emily K. Plowman. Patients were enrolled in a treatment study assessing the effects of expiratory muscle strength training (EMST) on swallow and respiratory function in individuals with ALS. Study data was collected from baseline study assessment prior to participation in respiratory training. Participants included 44 individuals with a diagnosis of probable/definite Amyotrophic Lateral Sclerosis (ALS) in accordance with the Revised El-Escorial Criteria (Brooks Br, 2000). According to the study protocol designed by Dr. Plowman, all patients were screened with specific inclusion and exclusion criteria including: 1) diagnosis of probable or definite ALS; 2) Amyotrophic Lateral
Sclerosis Rating Scale Revised score (ALSFRS-R) (Cedarbaum, 1999) greater than 32; 3) reduced maximum expiratory pressure compared to published normative data for gender and age (Wilson, 1984); 4) forced vital capacity greater than 65%; 5) cognition within normal limits as determined by > 24 points on the Mini Mental Status Exam (Folstein, 1975); 6) no reported allergies to barium; 7) no current tracheotomy or mechanical ventilation; 8) absence of diaphragmatic pacer; and 9) no significant concurrent respiratory disease (e.g., COPD) (Plowman, Watts, Tabor, Robison, Gaziano, Domer, Richter, Vu T, Gooch C, 2016)

Equipment

Two testing procedures were included for analysis: 1) videofluoroscopic evaluation of swallowing and 2) standardized voluntary cough spirometry testing. For the videofluoroscopic swallow diagnostic study, a Phillips BV Endura fluoroscopic C-arm unit (GE OEC 8800 Digital Mobile C-Arm system type 718074) was used to acquire the radiographic images at 30 frames per second. Cough spirometry testing was recorded on each patient using the following methodology. An oral pneumotachograph (MLT 1000, ADInstruments, Inc; Colorado Springs, CO) was connected to a spirometer filter (MQ 304 Spirometer Filter, Vacumed; Ventura, CA) which recorded airflow measures via a transducer (Powerlab (8/35, ADInstruments, Inc Vacumed; Ventura, CA) during voluntary cough production. The pneumotachograph, fitted with a sanitary filter, was held in place by the examiner.

Testing Protocols

1) Swallow function: Patients were evaluated using a videofluoroscopic evaluation. Videofluoroscopy is considered the “gold standard” to assess airway compromise across multiple patient populations. Participants were seated in an upright position and both lateral and anterior
images were obtained during the consumption of the following barium contrast boluses via syringe: thin liquid contrast in volumes of, 1 cc, 5 cc, and 20 cc, and 5 cc of barium paste. The 20-cc thin liquid trial was utilized for evaluation of airway compromise. If the patient was unable to swallow 20 cc of the liquid contrast, the largest bolus challenge that the patient completed was assessed. A blinded rater evaluated the level of airway compromise live and then a second blinded rater provided reliability using the recorded video. Airway compromise was assessed using the standardized PAS. The PAS is an 8-point scale that assesses penetration and aspiration where 1 equals no penetration or aspiration and 8 equals aspiration without a cough response (i.e., silent aspiration). Using the PAS scale, participants were stratified into one of two swallowing safety groups. A PAS score of 1 or 2 was classified as “safe” swallowing and a PAS score of 3 (penetration above the level of the folds with residue) to 8 was classified as “unsafe” swallowing.

2) Cough function: Patients were seated upright in a chair or wheelchair with their feet on the floor and their arms placed on the armrests. A respiratory filter in line with a pneumotachograph was placed in the participant’s mouth. He or she was instructed to breathe normally for at least three tidal breaths to acclimate to the filter. According the protocol outlined in the EMST study designed by Dr. Plowman, they were then instructed to take a deep breath and, “cough hard like there is something stuck in your throat”. The patient completed this activity three times. Collection of this airflow data was also audio-recorded using a Sony HD HandyCam video recorder positioned directly in line with the pneumotachograph. This audio recording provided a means to re-assess subjective ratings of cough effectiveness, loudness, and volume after primary data collection.

All data was video and audio recorded. Two raters assessed perceptual cough features using audiovisual recordings after the cough airflow data was collected. Raters evaluated perceived
cough strength, loudness, and effectiveness using a 100-mm, visual-analog scale (VAS) (see Figure 4.1). More specifically, the perceived quality (weak, moderate, and strong) for cough strength, loudness, and effectiveness were judged by marking a horizontal tic mark on a 100-mm vertical VAS. The total possible rating for each perceptual measure was out of a 100 with 0 being a poor rating, and 100 being a (perceptually) excellent rating. Scores for each measure were derived by using a ruler to measure distance (in millimeters) from the “0” end point on the line to where the horizontal tic marks were made. Additionally, raters determined the presence or absence of binary cough quality ratings (huffing, voicing, wet, inspiratory stridor) based on operational definitions (see Table 4.1).

Rater 1 reviewed all 44-recorded assessments and made judgments of cough strength, loudness, and effectiveness as well as determined the presence/absence of aberrant cough features. Using a random number generator, 20% of the 44 auditory cough epochs sampled (9) were randomly selected to be re-analyzed by a second blinded rater. Rater 2 utilized the recorded audio/video files to assess all perceptual parameters at a time point after data collection.

**Table 4.1** Definitions of aberrant cough signs; perceptually judged to be present/absent by a blinded rater.
Figure 4.1 Three vertically positioned 100-mm lines were used as a VAS for perceptual ratings of cough strength, loudness, and effectiveness. Next to the lines were references for each perceptual VAS measure. As such, for the perceptual measure of cough strength, a horizontal tic mark made along the lower end of the line indicated a “weak” cough, a horizontal tic mark within the mid-range of the line indicated a “moderately strong” cough and a horizontal tic along the top of the vertical indicated a very strong cough. Precise numerical measurements were derived by using a ruler to measure the distance from bottom of the vertical line (0) to the horizontal tic mark provided by the rater. Each perceptual measure was out of a total score of 100.
Data Analysis and Statistics

Because of uncertainty about whether the measurement properties of the VAS scale should be as ordinal or interval data, and uncertainty about the underlying distributions (i.e., normal or not) of scores given the limited size of the data set, non-parametric Mann Whitney U tests as well as T tests were used to evaluate the hypotheses that safe and unsafe swallowing groups were associated with statistically significant different perceptual VAS scores. These tests were performed for the individual VAS ratings of

Results

A total of 44 individuals (30 male, 14 female) were included in the analysis. See Table 4.2 for description of participants. A blinded rater reviewed the modified barium swallow studies and identified 26 safe swallowers (PAS ≤ 2) and 18 unsafe swallowers (PAS ≥ 3) within the ALS participant sample.

<table>
<thead>
<tr>
<th>Quality Parameter:</th>
<th>Operational Definition:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huffing:</td>
<td>Blowing or puffing with force during the cough attempt.</td>
</tr>
<tr>
<td>Voicing:</td>
<td>Vocalization during the cough attempt.</td>
</tr>
<tr>
<td>Wet / Gurgled:</td>
<td>Cough sounds broken, irregular, or noisy.</td>
</tr>
<tr>
<td>Inspiratory Stridor:</td>
<td>Harsh, grading, or creaking sound while breath is taken in during first phase of voluntary cough.</td>
</tr>
</tbody>
</table>
Table 4.2 Participant demographics (N = 44). Sample included 26 participants with unsafe swallowing as defined by a PAS score \( \leq 2 \), and 18 unsafe swallowers as defined by a PAS score of > 3.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall</th>
<th>Safe Swallowers</th>
<th>Unsafe Swallowers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD) Range</td>
<td>Mean (SD) Range</td>
<td>Mean (SD) Range</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62 (+/- 10.3)</td>
<td>59 (+/- 11) 30 - 75</td>
<td>66 (+/- 7.6) 57 - 83</td>
</tr>
<tr>
<td>ALSFRS-R Disease Duration (months)*</td>
<td>33 (+/- 7.9) 16 - 47</td>
<td>34 (+/- 7.4) 16 - 47</td>
<td>30 (+/- 8.3) 16 - 47</td>
</tr>
</tbody>
</table>

*Disease duration as measured from time of symptom onset to clinical study assessment.

Visual Analog Scale

Using a non-parametric statistical approach, a significant group difference was revealed between mean VAS scores in safe (50.88/100) vs. unsafe (33.56/100) swallow groups for the perceptual measure of cough effectiveness \( (U = 148, p = 0.04) \) while the group difference was just above our 0.05 significance criteria for the perceptual measure of cough strength \( (U = 152.5, p = 0.052) \). Using a parametric approach, a significant difference was revealed between mean VAS scores in the safe (43.3/100) vs. unsafe (28/100) swallow groups for the perceptual measure of cough strength \( (t (42) = 2.08, p < 0.05; (Figure 4.2) \) and for cough effectiveness \( (t (42) = 2.10, p < 0.005) \).
Figure 4.2 A bar graph indicating difference in mean perceptual VAS scores of voluntary cough strength between safe (PAS ≤ 2) vs. unsafe (PAS > 2) swallow groups $t(42)=2.08$, $p < 0.05$.

Moderate positive correlations were revealed between perceptual VAS indices and global disease rating scores. Low perceptual VAS clinical ratings of cough “strength” were associated with global disease progression ($\rho = 0.67$, $p = 0.001$). Likewise, low perceptual ratings of cough “loudness” were associated with global disease progression ($\rho = 0.68$, $p = 0.000$). Similarly, low perceptual ratings of cough “effectiveness” were associated with global disease progression ($\rho = 0.64$, $p = 0.000$). Additionally, perceptual measures of cough strength and effectiveness with strongly positively correlated ($\rho = 0.94$, $p = 0.00$) See Figure 4.3 for scatterplots representing these correlations.
Figure 4.3 Scatterplots demonstrating: A) a moderate positive correlation between disease rating scale score, (the ALS functional rating scale ALSFRS-R) and perceptual VAS ratings of cough strength; B) a moderate positive correlation between the ALSFRS-R score and loudness score; C) a moderate positive correlation between the ALSFRS-R score and cough effectiveness score; and D) a strong correlation between the perceptual rating scores for cough strength and effectiveness.

**Presence/absence of Aberrant Cough Sounds**

Voicing was identified as the most aberrant cough sound feature overall as determined by a frequency count of cough sounds. Huffing was present in a greater number of ALS individuals who penetrated/aspirated (38.88%) vs. those who did not (3.84%), ($\chi^2 (1) = 8.78, p = 0.003$). The presence of huffing was also associated with swallowing safety status and 10 times more prevalent in ALS patients with unsafe swallowing (see Table 4.3).
Table 4.3 Distribution for the presence/absence of perceptual cough features including voicing, huffing, inspiratory stridor, and wet/gurgled quality. The distribution is represented for the over group (all 44 participants) and by airway safety group. The presence of “huffing” was revealed as statistically significant and found in a higher portion on unsafe vs. safe swallowers. Table 4.3 also displays the inter-rater Kappa values as determined between rater 1 and rater 2.

<table>
<thead>
<tr>
<th>Cough Sign</th>
<th>Overall (N = 44) (%)</th>
<th>Safe Swallowers (n = 26) (%)</th>
<th>Unsafe Swallowers (n = 18) (%)</th>
<th>p-value</th>
<th>Interrater Kappa</th>
<th>Level Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voicing</td>
<td>22/44 (50%)</td>
<td>12/26 (46%)</td>
<td>10/18 (55.5%)</td>
<td>0.540</td>
<td>.500</td>
<td>Weak</td>
</tr>
<tr>
<td>Huffing</td>
<td>8/44 (18%)</td>
<td>1/26 (4%)</td>
<td>7/18 (39%)</td>
<td>0.003*</td>
<td>.353</td>
<td>Minimal</td>
</tr>
<tr>
<td>Inspiratory Stridor</td>
<td>3/44 (7%)</td>
<td>1/26 (4%)</td>
<td>2/18* (11%)</td>
<td>0.347</td>
<td>.482</td>
<td>Weak</td>
</tr>
<tr>
<td>Wet/Gurgled</td>
<td>2/44 (4.5%)</td>
<td>1/26 (4%)</td>
<td>1/18 (5.5%)</td>
<td>0.789</td>
<td>.645</td>
<td>Moderate</td>
</tr>
<tr>
<td>No Features</td>
<td>9/44 (20.5%)</td>
<td>11/26 (42%)</td>
<td>0/18 (0%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*Participant counted two times in tally for displaying more than one aberrant feature.

Reliability of the VAS for Cough Assessment

Good inter-rater reliability (between rater 1 and rater 2) was revealed for all VAS measures. ICC values for strength were 0.79 (CI = 95%, 0.615 – 0.885, p = 0.000), ICC values for volume were 0.79 (CI = 95%, 0.627 – 0.889, p = 0.000), and ICC values for effectiveness were 0.77 (CI = 95%, 0.592 – 0.879, p = 0.000). Excellent intra-rater reliability was shown for all VAS measures as assessed by rater 1 at two different time periods (though note that this is based only on 8 sample points). ICC value for strength was 0.899, volume was 0.945, and effectiveness was 0.906.
Reliability Binary outcomes

Weak and minimal inter-rater reliability was shown between rater 1 and rater 2 for the identification (presence or absence) of binary cough quality ratings of huffing, voicing, and inspiratory stridor, moderate reliability was shown for the detection of the sound wet/gurgles (see table 4.3). Fair intra-reliability was found between rater 1 assessments of binary measures.

Discussion

This study represents the first attempt to investigate perceptual ratings of cough using a visual analog scale (VAS) and defined binary ratings of aberrant cough for the assessment of dysphagia in ALS. Conservatively, the VAS outcome measures were considered ordinal data and non-parametric statistics were used to assess differences in mean scores between airway safety groups. There were significant differences in the perceptual measures of cough “effectiveness” between airway safety groups and this rating was also found to have good inter reliability (between rater 1 and rater 2 when assessed at different time points).

Visual analog scales are quick methods of obtaining quantifiable information. The continuous 100 mm line version of the VAS has shown improved sensitivity for measurement of subjective assessments of pain and mood (Pfennings, Cohen, & Van der Ploeg, 1995). Anchors on the scale are may represent a point of reference for the rater using the scale and may indicate opposite descriptors such as “cold and hot”. There are ways to consider improvement of the VAS scale rating system to evaluate perceptual indices of cough used within this study. The anchor reference for cough measurement could be changed by using anchors that represent a more universal point of reference for raters such as color (i.e., bright blue and pale blue). Changing the reference points to a relatable reference other than extremes of cough may provide more accurate measurement of what the perceived cough “strength” is.
Although the use of VAS scores for the subjective assessment of cough impairment may only represent incremental improvements in clinical cough measurement and there is debate on the use of such rating scales in perceptual rating, there remains a dire need to move beyond binary ratings of clinical cough assessment. As demonstrated in our data, the presence of “huffing” was present in more patients with unsafe swallowing than safe swallowing, however, this measure was not shown to be reliable between raters. Clinically, the use of more objective cough measurements have the potential to: 1) more accurately identify patients with cough impairments who are at high risk for aspiration; 2) provide a quantifiable, objective measure of cough impairment to identify pre/post intervention change; and 3) provide a universal system of cough measurement that is easily accessible to and understood by clinicians.

Limitations and Future Direction

In this investigation, the perceptual judgments of cough strength, loudness, and effectiveness were assessed via recordings of the cough process. Placement of the recording devices was not standardized for optimal audiovisual data collection and subsequent analyses. Future work should include standardization of cough recording during the data collection process; in addition, both online (during the collection of cough data) and recorded cough sounds should be assessed. Further work is needed to understand VAS measurements of cough in several patient populations and to study this measurement in a more controlled manner to limit contextual biases. Additionally, there remains a need for objective quantification of cough sound patterns to improve the assessment of patients who are at risk for having undetected dysphagia and/or dystussia.

Conclusions

The goals of this study were to determine if individuals with ALS who were classified by airway safety groups (safe vs. unsafe swallowing) differed in terms of perceptual measures of
cough strength, loudness, and effectiveness or in the presence/absence of aberrant cough features. We hypothesized that measures of cough strength, loudness, and effectiveness would be reduced in individuals with unsafe swallowing relative to individuals with safe swallowing. Further, we hypothesized that individuals with unsafe swallowing would demonstrate one or more aberrant cough features. The results of the study partially supported the hypothesis. Visual analog scale measurement of cough “effectiveness” was significantly lower in the unsafe swallowing group and the measurement of “strength” reached near significance and was lower in the unsafe swallowing group. Additionally, the aberrant cough feature of “huffing” was associated with the unsafe swallowing group.

This study attempted to identify the perceptual differences within cough features in a way that could be easily conducted in a clinical setting and quickly interpreted. Although differences were found for perceptual ratings, the judgments were made retrospectively and further work is warranted to determine feasibility of use in a clinical setting.
CHAPTER FIVE

PHYSIOLOGIC ASSESSMENT OF VOLUNTARY COUGH IN ALS

Introduction

Amyotrophic Lateral Sclerosis (ALS) is a progressive and debilitating neurodegenerative disease resulting in diffuse and progressive muscle wasting and death (Wijesekera, 2009). Dysphagia, or swallowing impairment, is prevalent in this patient population (Ertekin, 2000). Presenting symptoms and disease onset are heterogeneous; thus, dysphagia symptoms manifest differently across patients and can be difficult to assess clinically. Individuals with ALS may present with bulbar onset of the disease in which case lingual and masticatory deficits are prominent features of dysphagia. In the spinal onset variant of ALS, limb motor impairment is the first salient feature identified (Ruoppolo, 2013). Recent evidence indicates that, although patients with bulbar onset have more prevalent oromotor features; in patients with spinal onset dysarthria is significantly correlated with presence of dysphagia (Da Costa Franceschini, 2015).

In addition to sensorimotor dysfunction of the swallowing mechanism, ALS simultaneously results in motor cough deficits, (Plowman et al., 2016) and presumably sensory cough deficits. Thus, despite onset type, patients are likely to develop pervasive airway protective dysfunction characterized by both dysphagia and impaired reflexive cough (Ruoppolo, 2013). There are relationships between cough and swallow at a neural (Gestreau, Grelot, & Bianchi, 2000; Gestreau, 1996; Oku, Tanaka, & Ezure, 1994) and anatomical/functional level (Pitts, Bolser, Rosenbek, Troche, & Sapienza, 2008; Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016; Smith Hammond, 2001). Recent work by Plowman and colleagues (2016) has shown...
that impaired voluntary cough function identifies patients with ALS who are at risk for penetration/aspiration. The authors postulated that there might be clinical utility for the use of voluntary cough testing to detect presence of dysphagia in this patient population. Although cough may be a clinically useful tool to determine compromised swallowing function or the ability to clear aspirant material, cough evaluation methodology and implementation is widely varied throughout the literature (Watts, Tabor, & Plowman, 2016).

Methodology for common clinical cough testing includes subjective assessments of strength and/or weakness (as presented in Chapter 3). This is regardless of clinician demographics such as years of experience, certification status, and/or practice setting. Unfortunately, it has been shown that subjective assessments of cough are unreliable and are not able to detect swallowing impairment. For example, McCullough et al. (2005) reported high sensitivities (<79%) but low specificities (<42%) for detection of aspiration using perceptual ratings. The authors reported that almost half of the at-risk patients were wrongly categorized based on a “weak” cough rating.

Acoustic measurements of voluntary cough sounds have been investigated in healthy adults. Olia et al. (2000) studied 234 cough patterns in healthy male and female adults. The authors subdivided cough patterns into distinct anthropomorphic features consisting of three components 1) explosive phase (phase timing and amplitude), 2) continuous phase (phase timing), and 3) the variable phase (timing). Authors reported that there were significant differences found between gender for the length of the expulsive phase, frequency of the first phase, and highest continuous frequency of the continuous phase. Although there are limitations in acoustic cough analysis, these studies are necessary to provide objective qualification of a subjective physiologic event. Objective quantification of cough may help to determine change in airway protection in specific diseases over time or monitor improvement in airway protection following therapeutic intervention.
Therefore, the aim of this study was to determine anthropomorphic characteristics of voluntary cough acoustic signals in individuals with ALS and healthy controls. Given differences in anthropomorphic features of cough previously found in participants with and without lung disease, it is hypothesized that there will be anthropomorphic differences between healthy controls and patients with ALS and between patients with ALS who are safe swallowers and those who are not safe swallowers.

Methods

Participants

Participants included 10 patients diagnosed with ALS according the El Escorial Criteria (Brooks et al., 2000); 5 males and 5 females with bulbar, spinal, and mixed disease onsets, and 10 healthy aged-matched controls; 5 males and 5 females with no known history of pulmonary disease. ALS patients were recruited from the Morsani Medical Center’s ALS neurology clinic, and the Center for Swallowing Disorders. This study received approval by the University of South Florida Institutional Review Board (#00023151) (see Appendix D) In addition to the diagnoses above, specific inclusion criteria included: 1) cognition within normal limits as determined by > 24 points on the Mini Mental Status Exam (Reisberg, 1982). Specific exclusion criteria include: 1) presence of tracheotomy or mechanical ventilation; 2) presence of diaphragmatic pacer; 3) diagnosis of significant concurrent respiratory disease (e.g. COPD); or 4) allergies to barium.

Testing Protocol

Once enrolled, participants were assigned a study number and underwent all testing procedures on the same day. Data collection was counterbalanced in order to account for fatigue in this patient population. Assessments included: 1) swallowing evaluation using
videofluoroscopy; 2) physiologic cough spirometry testing coupled with acoustic recording; 3) voluntary peak expiratory flow rate cough testing; 4) spirometry testing; and 5) completion of disease-specific rating scales including the ALS functional rating scale revised (ALSFRS-R) (Cedarbaum, et al., 1999).

Swallowing

Swallowing was assessed using the modified barium swallow study (MBSS). The MBSS is the gold standard evaluation for swallowing function. Participants were seated in an upright position. A Phillips BV Endura fluoroscopic C-arm unit (GE OEC 8800 Digital Mobile C-Arm system type 718074) was used to collect radiographic images of the swallow (30 frames/second); images were collected in both a lateral and anterior-posterior viewing plane. A Kay Pentax Swallowing Signals Lab unit (Kay Pentax, Lincoln Park, NJ) digitally recorded the fluoroscopic images that were stored for subsequent analysis. The standardized protocol consistent of the following bolus challenges: 1) 1-cc, 5-cc, 10-cc and cup sips of ultra-thin liquid contrast, 2) 5-cc of barium paste, and 3) ¼ of graham cracker coated with 5 cc barium paste in the lateral view; and 4) cup sips of ultra-thin barium liquid, 5) ¼ of graham cracker coated with 5 cc barium paste, and 6) 13-mm barium tablet in the anterior/posterior view. To ensure patient safety, the sequence of bolus presentations may have been altered. The MBS study was discontinued if the patient silently aspirated and could not tolerate further swallow testing procedures.

Acquisition of Cough Airflow and Acoustic Waveforms

Cough airflow during voluntary cough was assessed for each patient using spirometry. Patients were asked to “cough as if something were stuck in your throat.” Prior to airflow data collection, the airflow signal was calibrated using a 3-liter syringe. The patient was placed in a seated position; a spirometer filter (MQ 304 Spirometer Filter, Vacumed; Ventura, CA) was
coupled to an oral pneumotachograph (MLT 1000, ADInstruments, Inc; Colorado Springs, CO). The airflow signal was measured via a spirometer (ADInstruments, Inc, Colorado Springs, CO), which was attached to data acquisition hardware (PowerLab System 16/35, ADInstruments, Inc).

Acoustic cough recordings were collected in conjunction with airflow measures and independent of airflow measures (Figure 5.1). An Audio-technica microphone (ATM73a) with the mouthpiece placed at a standardized distance from the patient’s oral cavity. Prior to collection of acoustic cough data, the acoustic signal was calibrated using a 90 dB pure tone. The microphone was routed to a preamplifier unit and the signal split into two A/D channels. Via software control, the sensitivity of each channel was set to allow simultaneous low and high-sensitivity recordings. This allowed for very high cough sound pressure levels to be recorded without clipping on the low-sensitivity channel and very low sound pressure levels to be recorded with an adequate signal-to-noise ratio. Audiovisual recording of the cough assessment was obtained using a Sony HD HandyCam video recorder positioned directly in line with the patient at a three-foot distance.

Data Analysis and Statistics

Cough Airflow

Offline analysis of the airflow and acoustic waveforms were completed using separate software utilities consisting of a series of MATLAB scripts. Each of the MATLAB utilities included several automatic assessment features to reduce measurement error (Appendix E). For the airflow waveform, physiologic aspects of the cough airflow signal were measured as in previous investigations of voluntary cough production, (Smith Hammond C.A., 2001). As previously described in publications of cough airflow analysis, the following measures of cough airflow were derived with MATLAB software scripts: 1) inspiratory phase duration: this is defined in the literature as the time from the start of the inspiratory event (airflow crossing 0 L/s) to the
beginning the compression phase of cough (airflow reaches 0 L/s and remains relatively stable); 2) inspiratory peak flow: this is determined as the lowest peak measurement during the inspiration (-L/s); 3) compression phase duration: commonly defined within the literature as time total time of glottis closure measured from the end of the inspiration to the start of the expiratory phase; 4) expiratory rise time: this time measurement is referred to as the time it takes from the opening of the glottis to reach peak expiratory flow. It is measured from the start of the expiratory phase to the time the peak expiratory flow occurs; 5) expiratory peak airflow: this is referred to as the highest peak point during a cough expiration. It is measured by identifying the highest peak in an expiration (L/s); and 6) cough volume acceleration: this measurement is a calculation of expiratory peak flow/expiratory rise time often described within the literature as the effectiveness of the cough. These samples were analyzed separately from the acoustic analysis and were derived at separate intervals during the cough testing procedure.

Cough Acoustics

Analysis of acoustic cough waveforms were processed and measured using the LabChart (version 7) software and subsequently exported to MATLAB (Mathworks, Inc.). Anthropomorphic features of cough sound included the following measures: (see figure 5.2). 1) expulsive cough phase time: onset time of the cough signal to the time of the first peak frequency; 2) continuous cough phase time: time from the first peak frequency to the time of the second peak frequency; 3) variable cough phase time: time of the second peak frequency to the end of the acoustic cough signal; 4) total length of acoustic cough signal: time from the onset of the acoustic cough signal to the end of the acoustic cough signal; and 5) augmenting and decrementing cough pattern: acoustic cough recording in microvolts (mV) was analyzed for the cough signal pattern (see Figure 5.3).
Figure 5.1 Image depicts a sample data collection page rendered using LabChart version 7. Time is along the x-axis. There are 4 panels displayed along the y-axis. The first panel represents the raw cough waveform, second panel represents the filtered cough waveform, third panel is a high sensitivity data capture of acoustic recording and the fourth panel is a low sensitivity data capture of acoustic signal. Acoustic data were collected in two ways, simultaneously with airflow (pictured) and independently (not pictured) without airflow. Acoustic recordings without airflow were used for analysis.
Figure 5.2 Anthropomorphic features of acoustic cough signals were tagged and recorded. Time and peak amplitude were analyzed to derive final measures: A) onset time of the cough signal to the time of the first peak frequency B) time from the first peak frequency to the time of the second peak frequency, and C) time of the second peak frequency to the end of the acoustic cough signal.
Figure 5.3 Cough waveform variations were classified for single acoustic cough signals; they were analyzed from the same recording channel for each subject according to the following definitions: A) fast augmenting signal and fast decrementing signal; B) slow augmenting and slow decrementing signal; C) fast augmenting and slow decrementing signal; and D) slow augmenting and fast decrementing acoustic signal.

Handheld Peak Flow Meter Testing

Voluntary peak cough airflow was measured for each patient using a portable, hand-held flow meter. The patient remained in a seated position. A Mini Wright Peak Flow Meter (KW Med, Inc., Antioch, IL) was placed in the patient’s mouth. The clinician helped to create a tight lip seal around mouthpiece. If needed, the nose was occluded with nose clips for the cough task. The patient was asked to cough “as if something were stuck in their throat.” Standard-range (60 to 850 liters per minute) and low-range (30 to 400 liters per minute) peak flow meters were available for testing depending on the patients’ typical airflow. Each patient performed three trials of the peak cough flow test; an average of the three trials was used for subsequent analysis.
Respiratory function

Forced vital capacity (FVC) was assessed with a Micro 1 Handheld Spirometer (CareFusion, Vyaire Medical, Mettawa, IL). The patient was instructed to sit fully upright and performed a maximal inhalation and exhalation effort with cueing from the experimenter.

Statistical Analysis

Descriptive statistics including mean, standard deviation, and range were used to describe demographic characteristics of the sample. Given the largely heterogeneous presentation of the sample population, normal distribution was not assumed. Therefore, the non-parametric Mann Whitney U Test was used to compare sample means between cough airflow measures in safe (PAS \( \leq 2 \)) and unsafe swallowing groups (PAS \( > 3 \)); and anthropomorphic acoustic cough measures between healthy controls and patients with ALS and across airway safety groups in ALS. Spearman’s Rho Correlation analysis with alpha set at 0.05 was utilized to determine associations between continuous spirometry data and voluntary cough airflow and acoustic measures.

Results

Patient Demographics

Ten patients with ALS underwent evaluation. Mean age of the sample was 63 years (range 39-73 years), and 50% of the sample was female. All subjects scored \( > 26 \) on the MMSE and were deemed appropriate to participate in the cough and swallow evaluation protocols. Table 5.1 summarizes the demographic and disease data for each subject. Of the ten ALS patients evaluated, 5 patients were judged to have unsafe swallowing (PAS score \( \geq 3 \)) as evaluated during any swallow task completed during the swallow study protocol (see Table 5.1, second column). Peak cough flow testing and respiratory function information for each patient can be found in table 5.2. In
addition, 10 healthy control subjects underwent acoustic cough evaluation. Mean age of the control sample was 59.2 years (range 42 to 75 years), and 50% of the sample was female.

Table 5.1 ALS participant demographics including global disease rating scale with subscale bulbar and respiratory domain data. *Disease duration is reported as time (in months) from reported symptom onset to study assessment date.

<table>
<thead>
<tr>
<th>Participant ID</th>
<th>Gender</th>
<th>PAS Score</th>
<th>ALSFRS-R Bulbar</th>
<th>ALSFRS-R Respiratory</th>
<th>Disease Onset</th>
<th>Disease Duration (mo.)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>7</td>
<td>26</td>
<td>3</td>
<td>5</td>
<td>Bulbar 37</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>8</td>
<td>29</td>
<td>0</td>
<td>9</td>
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<td>3</td>
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<td>11</td>
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<td>3</td>
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<td>9</td>
<td>10</td>
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<tr>
<td>5</td>
<td>M</td>
<td>7</td>
<td>24</td>
<td>7</td>
<td>7</td>
<td>Spinal 24</td>
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<td>2</td>
<td>26</td>
<td>9</td>
<td>8</td>
<td>Spinal 17</td>
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Table 5.2 ALS participants respiratory function including forced expiratory volume (FEV1), forced vital capacity (FVC), FEV1/FVC, and peak expiratory flow as measured by a hand held analog peak flow meter. *Average peak flow as calculated from three voluntary cough trials.

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<th>Gender</th>
<th>Predicted (%)</th>
<th>PEF Average* (hand held meter) L/m</th>
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Voluntary Cough Airflow in Patients with ALS

The modified barium swallow study identified 5 safe swallowers (PAS ≤ 2) and 5 unsafe swallowers (PAS > 2) within the ALS participant sample.

Cough Airflow Data

Based on cough airflow data, no significant differences were revealed between airway safety groups for average cough airflow characteristics. There was a significant difference between compression phase duration (CPD) for epoch 1, cough 1 between airway safety groups (U = 8, \( p = 0.032 \)). The unsafe swallowing group exhibited a slightly longer compression phase duration than the unsafe swallowing group. The air-flow characteristics inspiratory phase duration, expiratory rise time, peak expiratory flow, and cough volume acceleration were not significantly different between the safe and unsafe groups.

Anthropomorphic Features of Cough

Anthropomorphic acoustic cough features were analyzed based on acoustic cough waveforms collected without coupled airflow data. Healthy controls (n = 10) and ALS participants (n = 10) were compared. Significant differences were detected between healthy controls and patients with ALS for continuous cough phase time (U = 69, \( p = 0.02 \)). In healthy participants, the mean continuous phase length was longer than individuals with ALS (12.4 ms vs. 8.6 ms). No other anthropomorphic features such as expulsive phase time, variable phase time, or expulsive phase peak amplitude were significantly different between healthy controls and ALS participants.

Additional analysis was performed to determine if there were differences in anthropomorphic features between safe and unsafe swallowers. There were significant differences identified for expulsion phase time (U = 2, \( p = 0.03 \)). The unsafe swallowing group exhibited longer expulsive phase time \( (M = 3.4 \text{ seconds } +/- 4.7) \) than the unsafe swallowers \( (M = 7.60 \)
Although the measure of total acoustic cough length did not meet the 0.05 significance criteria, total cough length was found to be longer in unsafe swallowers (M = 7.4 ms) compared to safe swallowers (M = 3.6 ms) (U = 3, p = 0.056). No differences were determined for group means for the variable or continuous phases or peak expulsive amplitude.

Further analysis was performed between ALS participants; in this analysis, groups were stratified based on aspiration status. PAS ≥ 6 versus safe swallowers with penetrators were compared. In participants who aspirated, there was a significant difference in total cough duration, (U = 0, p = 0.01). Total cough length was longer in participants who-aspirated (M = 0.99 ms) versus those who did not (M = 0.36 ms). Significant difference between mean expulsive phase rise time was identified between groups (U = 0, p = 0.01). The expulsive phase time was longer in individuals who-aspirated (M = 0.3 ms) verses those who did not (M = 0.02 ms). There was also a significant difference for the measure, variable phase time between groups (U = 1, p = 0.01). The mean variable phase time was longer in the aspiration group (M = 0.42 ms) versus the non-aspiration group (M = 0.18). Lastly, peak expulsive phase amplitude was lower in participants who aspirated versus those who did not (U = 1, p = 0.01). Mean amplitude for the aspiration group = 117.7 mV and the non-aspiration group mean amplitude = 318.5 mV.

*Augmenting and decrementing cough pattern*

Based on the cough acoustic waveform signal patterns collected independently from airflow signals results showed that all healthy controls (10/10 or 100%) presented with fast onset cough pattern. Of the ten ALS participants, seven participants displayed a fast cough onset, and of those 7 individuals, all were safe swallowers who did not aspirate. No healthy controls exhibited a slow augmenting acoustic cough pattern whereas 40% (4/10) of ALS participants had a slow augmenting cough pattern. Four of ten healthy individuals presented with a slow decrementing
cough pattern and 7 of 10 ALS participants presented with a slow decrementing cough pattern.

![Figure 5.4](image)

**Figure 5.4** Depicted in three panels, A., B., and C. are airflow, acoustic, and spectral representations of cough in safe (PAS ≤ 2) and unsafe (PAS ≥ 3) swallowers. Figure 5.4 panel B. depicts a fast augmenting and fast decrementing cough pattern found in a safe swallower and a slow augmenting slow decrementing cough pattern as found and unsafe swallower.

**Discussion**

This is the first study to evaluate anthropomorphic features of cough in healthy controls and ALS participants. The results of this study showed that there are salient features of acoustic voluntary cough signals that are different when comparing aspirators to non-aspirators. However,
no significant differences were found between anthropomorphic features of cough in healthy controls and ALS participants, or voluntary airflow measures between safe and unsafe ALS participants. This data does not confirm what has been previously published (Plowman, Watts, Robison, Tabor, Dion, Gaziano, Vu, & Gooch, 2016), and may be due to our small sample size.

The present study included a mixed sample of both spinal and bulbar onset ALS in the advanced stages of the disease, and thus, both bulbar and spinal features were present in all participants. Not surprising, the unsafe group had patients of both bulbar and spinal onset, reflecting a global degeneration of cardinal motor symptoms and corticobulbar degeneration. It is likely that insidious motor dysfunction across the neural axis contributed to these findings as lesions anywhere along the neuraxis may impact cough motor and subsequently acoustic function.

Physiological impairment leading to dystussia may have origins in airway afferent impairment, respiratory muscle weakness, or a combination of both. In terms of motor impairment, chest wall rigidity in patients with PD decreases their ability to inflate the lungs (Pitts, 2008). The work of Ebihara and colleagues (2003) indicated that involvement of motor and sensory impairment might depend on the stage of PD progression. In contrast, the ALS patient population presents in a heterogeneous manner and it is difficult to evaluate and benchmark impairment especially using clinical indices such as perception via rating scales and even with more objective measures. Results suggest that the cough and swallow relationship in ALS may be a much less linear relationship between the physiologic parameters as has previously postulated. These results may also be reflective of a small sample size.

Voluntary cough sound patterns have been shown to detect abnormality in pulmonary lung function in human models (Abaza, 2009). Abaza and colleagues (2009) investigated simultaneous voluntary cough airflow and sound pressure waves (time in seconds over amplitude) using a high
fidelity recording system composed of a mouthpiece attached to a metal tube with a microphone. The participants (52 health adults and 60 individuals with lung disorders, both male and female) watched a short video on how to perform a voluntary cough test. They then were instructed to, “keep their glottis open” as they, “coughed vigorously” (Abaza, p. 2) in order to prevent sound due to glottal closure. Authors used novel methodology to classify cough sound and airflow patterns. They reported that this methodology yielded a 94% rate of identifying abnormal lung function in female subjects and 97% rate for identifying abnormal lung function in male subjects.

As professionals, speech language pathologists have evaluated voice quality in both subjective (often with visual analog scales) and objective (vocal acoustic signal) manners as well as with models that invoke auditory-processing front-ends to capture the non-linear transformation of sound into perceptual constructs (Eddins, 2016; Shrivastav, 2011, 2003). Specifically, there have been robust studies of acoustic parameters of subjective quality in voice. However, subjective ratings of breathy voice quality have been found unreliable (Kreiman et al., 1993, Dejonckere, Obbens, De Moor, Wieneke, 1993) in some studies while very reliable in other studies (Bassich & Ludlow, 1986). Thus acoustic measures are often used provide objective quantification of voice quality (Bhuta, 2004). However, there is a clear disconnect between acoustic and perceptual indices of voice due to the non-linear nature of the perception of sound. Thus, it is not surprising that perceptual and acoustic correlates of voice quality are often in poor agreement. Cough creates a distinct sound pattern during the transition from a compression phase, or closure of the glottis, to expiration is completed (Korpas, 1996). Given the presence of a perceptual sound pattern, it is assumed that there are also unique acoustic characteristics that determine and aberrant cough. Additionally, Laciuga et al. (2016) identified that physiologic characteristics are associated with certain perceptual aspects of cough. Nevertheless, assessment of perceptual strength and
effectiveness of cough was less consistent using ratings such as scales and the authors suggested that there should be a more uniform way of judging the perceptual attributes of cough (Laciuga, Brandimore, Troche, & Hegland, 2016).

Our study revealed swallowing safety group differences for cough airflow measurements but did reveal group-dependent differences in measures within the acoustic cough signal. Additionally, when comparing aspirators to non-aspirators, there were multiple differences in anthropomorphic cough features. This disparity in results may represent that laryngeal structures participating the production of cough and resulting the cough sound pattern are a salient feature of cough impairment. The structure of the laryngeal and pharynx responsible for the sound of a cough may be an important feature of aberrant cough to investigate beyond cough airflow data.

Limitations and Future Directions

One limitation of the current study is that, the data were recorded and analyzed by the same researcher. This presents a potential confound as the results may be analyzed and interpreted with bias. A second limitation is that the study represented a small sample of patients. Finally, the analyses were somewhat simplistic. Future work should include a more sophisticated set of analyses, blind analyses, and a larger group of samples.

Conclusions

The aim of this study was to determine anthropomorphic characteristics of voluntary cough acoustic signals in individuals with ALS and healthy controls. We hypothesized that there would be anthropomorphic differences between healthy controls and patients with ALS and between patients with ALS who are safe swallowers and those who are not safe swallowers. Our results did partially supported hypothesis. Significant differences in the continuous cough phase were identified; healthy participants demonstrated longer continuous cough phase times than
individuals with ALS. This may reflect ability to reach peak flows.
CHAPTER SIX
CONCLUSIONS AND FUTURE DIRECTIONS

Results from the studies reported in this dissertation represent several additions to the current literature on cough and swallowing. There are well-established relationships between cough and swallowing in clinical populations. The relevance of such work is paramount for professionals who serve populations with impaired swallow ability as traditional methods of clinical swallowing assessment often fail to identify those with impaired swallowing who silently aspirate (i.e., no reflexive cough). In addition, dystussia promotes poor airway protection and must be a target of evaluation and intervention. Review of current literature indicates that there are several novel testing options for cough evaluation within both the voluntary and reflexive methodologies. However, these are not readily available for clinical use and have varied measures of sensitivity and specificity, which are not suitable for clinical use (Watts, Tabor & Plowman, 2016). Additionally, current binary subjective measures (i.e., strong/weak) used during clinical swallow assessments fail to provide quantitative data or describe deviant auditory features of cough.

Cough evaluation within the clinical setting is gaining attention. The survey study completed by 605 participants’ revealed that a majority of individuals across practice settings, levels of experience, and certification are assessing coughing in their clinical practice. The measure of “strength” is used most constantly. However, strength is a continuum of performance and not a binary outcome. With a growing body of basic and clinical literature demonstrating strong relationships between swallowing and airway protective behaviors; there is an urgent need for
standardization of cough assessment protocols and terminology.

Although there are studies that focus on the relationship between cough and swallow, there is a paucity of data on clinician reliability of assessing cough function, or deviant audible features of dystussia which may inform clinicians of decreased airway protection. The third study investigated perceptual ratings of cough using a visual analog scale (VAS) and defined binary ratings of aberrant cough. The study showed promising results for revealing differences between airway safety groups for perceptual measures of effectiveness and binary measures of “huffing”. However, in line with literature concerning the use of VAS scales in perceptual analysis, the measures were largely unreliable between different raters.

The fourth study aimed to investigate a novel method of cough evaluation for the purpose of identifying safe versus unsafe swallowers and differentiating cough patterns between healthy controls and ALS participants. Differences in anthropomorphic features of cough based on (airflow, acoustics, both?) between aspirators and non-aspirators indicate that there are salient features between airway safety groups that differ and may help identify those at risk for aspiration. Unfortunately, the evaluation method failed to differentiate healthy controls versus ALS participants suggesting this methodology may not yield favorable sensitivity and specificity results.

The systematic studies presented inherent limitations such as having non-standardized acoustic recordings of cough for VAS analysis, non-standardization of blinding methods for anthropomorphic analysis, and small number of participants. However, given several significant findings across the body of work, further investigation is required in order to continue to identify salient features of aberrant cough that differentiate patients who are at risk for poor airway protection and potentially help decrease morbidity and mortality due to pulmonary injury.
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126


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Apr 17, 2017

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SURVEY IRB

June 5, 2015
Stephanie Watts (Randall)
Communication Sciences and Disorders
Tampa, FL  33604

RE: Exempt Certification
IRB#: Pro00017474
Title: Survey of Clinical Swallow Evaluation Practices

Dear Ms. Watts (Randall):
On 6/5/2015, the Institutional Review Board (IRB) determined that your research meets criteria for exemption from the federal regulations as outlined by 45CFR46.101(b):

(2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
(i) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

Approved Items:
 Protocol _5.22.15
 Informed Consent

As the principal investigator for this study, it is your responsibility to ensure that this research is conducted as outlined in your application and consistent with the ethical principles outlined
in the Belmont Report and with USF IRB policies and procedures. Please note, as per USF IRB Policy 303, "Once the Exempt determination is made, the application is closed in eIRB. Any proposed or anticipated changes to the study design that was previously declared exempt from IRB review must be submitted to the IRB as a new study prior to initiation of the change."

If alterations are made to the study design that change the review category from Exempt (i.e., adding a focus group, access to identifying information, adding a vulnerable population, or an intervention), these changes require a new application. However, administrative changes, including changes in research personnel, do not warrant an amendment or new application. Given the determination of exemption, this application is being closed in ARC. This does not limit your ability to conduct your research project. Again, your research may continue as planned; only a change in the study design that would affect the exempt determination requires a new submission to the IRB.

We appreciate your dedication to the ethical conduct of human subject research at the University of South Florida and your continued commitment to human research protections. If you have any questions regarding this matter, please call 813-974-5638.

Sincerely,

Kristen Salomon, Ph.D.,
Vice Chairperson USF Institutional Review Board
**APPENDIX C:**

**SURVEY OF CLINICAL SWALLOW EVALUATION PRACTICES**

*Mandatory questions are denoted with an asterisk*

*1) Are you a Speech Language Pathologist (SLP) or SLP student?
1. Yes
2. No

2) What is your professional title?
1. Medical Doctor (MD)
2. Registered Nurse (RN)
3. Licensed Practical Nurse (LPN)
4. Other: Please type in title:

3) What is your speech language certification? Please select all that apply.
1. Ph.D.
2. BRS-S
3. CCC-SLP
4. CF-SLP
5. SLPA
6. Student

*4) Years of experience in medical SLP practice.
1. <1 year
2. 1-2 years
3. 3-5 years
4. 6-10 years
5. 11-20 years
6. 20+ years

*5) Country where you practice
1. United States
2. Canada
3. None of the above

*6) State where you practice

1-50. Select drop down of U.S. states

*7) Which type of facility do you work in? Pick all that apply.

1. Skilled nursing facility (SNF)
2. Hospital
3. Private practice
4. Voice center
5. Swallow center
6. Voice and swallow center
7. University medical clinic
8. SLP graduate training clinic
9. Outpatient rehabilitation
10. Other

*8) Please select all that apply in regards to your main caseload.

1. Outpatient rehabilitation
2. Inpatient rehabilitation
3. Acute
4. Sub-acute
5. ICU
6. SICU
7. Other

*9) Do you conduct clinical (bedside) swallow examinations?

1. Yes
2. No

*10) What populations do you assess with a clinical swallow evaluation? Select all that apply.

1. Neurogenic
2. Head and Neck
3. Trauma
4. Cardiac Care
5. Long-term care
6. Post surgical
7. Other
11) Why do you not perform clinical swallow evaluations? Select all that apply.

1. I am not trained in conducting clinical swallow evaluations
2. I only perform instrumental examinations
3. Clinical swallow does not provide adequate diagnostic information
4. In none of the above, please provide other reason(s)

*12) Do you perform an oral mechanism examination during your clinical swallow evaluation?

1. Yes
2. No

*13) Do you assess voluntary cough (e.g., ask the patient to perform a cough)?

1. Yes
2. No

*14) What aspects of voluntary cough do you listen for to indicate abnormality (e.g., strength)?

1. Open typed response

*15) Please list all of the components of your clinical swallowing evaluation.

1. Open typed response

*16) Please select the validated swallow protocols you are familiar with (you may select more than one).

1. Yale 3 oz. water swallow test
2. The Toronto Bedside Swallow Screening Test (TOR-BSST)
3. Gugging Swallowing Screen
4. Modified Mann Assessment of Swallowing Ability (MMASA)
5. Other

*17) Of the previous validated swallow protocols you selected, do you implement and of these in clinical practice?

1. Yes
2. No

18) If you do not implement validated clinical swallow protocols, please briefly indicate why. 1. Open typed response
10/5/2015
Stephanie Watts (Randall)
Communication Sciences and Disorders
1017 E Crenshaw Street
Tampa, FL 33604

RE: Full Board Approval for Initial Review
IRB#: Pro00023151
Title: Perceptual and Physiologic Analysis of Dystussia for the Assessment of Dysphagia

STUDY APPROVAL PERIOD: 10/5/2015 TO 10/5/2016

Dear Ms. Watts:
On 10/5/2015, the Institutional Review Board (IRB) reviewed and APPROVED the above application and all documents contained within, including those outlined below.

Approved Item(s):
Protocol
Document(s):
Protocol V2 CLEAN

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

As the principal investigator of this study, it is your responsibility to conduct this study in accordance with IRB policies and procedures and as approved by the IRB. Any changes to the approved research must be submitted to the IRB for review and approval via an amendment. Additionally, all unanticipated problems must be reported to the USF IRB within five (5) calendar days.

We appreciate your dedication to the ethical conduct of human subject research at the University of South Florida and your continued commitment to human research protections. If you have any questions regarding this matter, please call 813-974-5638.

Sincerely,

[Vjorgensen, MD]

E. Verena Jorgensen, M.D., Chairperson

USF Institutional Review Board
APPENDIX E:
MATLAB CODING

%run data analysis
clear all; clc; close all;
rootdir = pwd;
addpath(genpath(rootdir));
[filename,path] = uigetfile();
data.fullname = fullfile(path,filename);
data.filepath = path;
data.filename = filename;

[alldata,time] = importData(data.fullname);

chansegexp = inputdlg({'Enter Channel Number','Enter Segment Number','Enter Master File for Export'},'Select Data',1,{'2','4','masterfile.xlsx'});
chan = str2double(chansegexp{1});
seg = str2double(chansegexp{2});
data.exportFN = chansegexp{3};
data.x = time{chan,seg}';
data.y = alldata{chan,seg};
data.finish = 0;

%begin analysis of this file

idx = 1;  %keep track all files/segments

%get data points
while ~data.finish
    [handles.brushPage,data] = brushPage(data);
    %set(handles.brushPage,'Visible','off');

    [handles.analysisPage,data] = analysisPage(data);
    % set(handles.analysisPage,'Visible','off');

    allData{idx} = data;
    idx = idx + 1;
end

%calculate all derived measures
for ii = 1:length(allData)
%IPD (B-A) in time
allData{ii}.IPD = allData{ii}.B(1)-allData{ii}.A(1);

%IPFF (E)
allData{ii}.IPPF = allData{ii}.E(2);

%CPD (C-B) in time
allData{ii}.CPD = allData{ii}.C(1)-allData{ii}.B(1);

%EPRT (D-C) in time
allData{ii}.EPRT = allData{ii}.D(1)-allData{ii}.C(1);

%EP (D - C) in amplitude
allData{ii}.EP = allData{ii}.D(2) - allData{ii}.C(2);

%CVA (D/(D-C)) in amplitude/time
allData{ii}.CVA = allData{ii}.EP/allData{ii}.EPRT;

end

[pth,name,ext] = fileparts(data.filename);
datafile = fullfile(rootdir,'export',[name,'_export',ext]);
%save to files
save(datafile,'allData');  %mat file

exportData(allData);  %xlsx file