MITIGATION OF OROPHARYNGEAL SWALLOWING IMPAIRMENTS AND HEALTH SEQUELAE: TWO META-ANALYSES AND AN EXPERIMENT USING SURFACE ELECTROMYOGRAPHIC BIOFEEDBACK

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ABSTRACT

BEHAVIORAL TRAINING FOR OROPHARYNGEAL DYSPHAGIA: TWO META-ANALYSES AND AN EXPERIMENT USING SURFACE ELECTROMYOGRAPHIC BIOFEEDBACK

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Behavioral treatments performed in patients with dysphagia are designed to produce immediate or short-term outcomes that eliminate physiologic or biomechanical impairments of oropharyngeal swallowing. These short-term outcomes are expected to reduce aspiration of swallowed food into the respiratory system, and improve delivery of swallowed material into the digestive system. In the long-term these interventions are justified by expectations that they will reduce patient risk for dysphagia-related consequences such as pneumonia, malnutrition, and death.

Two distinct investigations were performed in this dissertation. The first, a meta-analysis, was performed to evaluate available evidence regarding the efficacy of individually administered dysphagia interventions in neurogenic dysphagia, and the effectiveness of systematic, institutional dysphagia protocols at mitigating public health risks associated with dysphagia. The second investigation, an experimental study, was executed to evaluate whether the addition of surface electromyographic biofeedback to traditional training of the Mendelsohn maneuver, a common individually administered dysphagia intervention, altered the initial (first training session) efficacy of volitional prolongation of muscle activity responsible for upper esophageal sphincter opening during the swallow.

The meta-analysis revealed that well designed investigations of individually administered treatments for short-term elimination of biomechanical impairments demonstrated small to large effect sizes ($r = .13 - .45$) for these treatments, all but one of which were statistically significant, and that overall, their combined effect size was small to medium ($r = .29$) and significant ($p = .03$). However studies of institutionally deployed dysphagia protocols demonstrated moderate effect sizes (Odds Ratio = .44 - .79) which, combined, were not statistically significant ($p = .08$). Overall, few published investigations of sufficiently robust evidence quality were found to justify their inclusion in the meta-analysis, suggesting that more research of this type is needed.

The experiment revealed that training of the Mendelsohn maneuver with and without surface electromyographic biofeedback, produced significantly increased duration ($p < .01$) and average amplitude ($p = .02$) of swallowing myoelectric activity. There were no significant differences between treatment groups in swallow duration or amplitude, however a trend toward increased preparatory myoelectric consistency was observed for the biofeedback trained group ($p = .052$) compared to the non-biofeedback trained group.

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PREFACE

Many individuals have helped me throughout my pursuit of this doctoral degree. Some of that help was genetic, some was verbal, some was enlightening, and much of it came in the form of moral support and tolerance of my pervasive attention to completion of the Ph.D. In the latter category, I must first thank my children, Eli and Lucy, whose recent childhood included an often unavailable father on many weekends and evenings. They have endured my distraction and preoccupation to finish this work. Kids, Daddy can play now. I also thank my partner and wife, Jenny, who has had to learn how to be a single parent of two wonderful children, and sometimes of one additional large, balding child. She is my backbone. I would not have survived this work without her constant tolerance, support and encouragement, relentless and useful editorial suggestions, and mastery of punctuation. Honey, why not go out and have some fun next Saturday; and the next, and the next…

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Friends have also contributed to my completion of this work. I am indebted to Paula Leslie for her friendship and motivational support, and for her example of what a real doctor is. And to Gary Lowery, my training partner from the triathlon days, with whom I learned how to put my head down and keep pushing until the finish line, this one's for you.

I am very appreciative of the most formative scientific learning of my career, gained from my first and continuing mentor, JoAnne Robbins. JoAnne taught me directly and by modeling, how to think like a "swallowology" researcher and clinician. Whatever academic, clinical, and scientific mind I have now was very much shaped by my experiences in Madison developing research methods, recruiting and running subjects, analyzing data, preparing scientific meeting presentations and manuscripts, and troubleshooting clinical trial protocols. Her career's work in the field of "swallowology" is a model that I and others like me can strive to emulate. I am very appreciative of her contributions to the formation of my mind and career, and of her lasting friendship.

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1.0 INTRODUCTION

The human upper aerodigestive tract (UAT) routinely alternates its respiratory functions with those of the individual's digestive needs hundreds of times each day. Oropharyngeal swallowing, the *digestive* function of the UAT, is a complex sequence of physiological actions by which food and liquids are transferred from the oral cavity, propelled through the pharynx, and into the esophagus over a span of about 1 to 2 seconds (Logemann, 1998). The *respiratory* function of the UAT is to provide the conduit for air to flow into the respiratory system where it can interact with the respiratory membrane and contribute to the homeostasis of respiratory blood gases. With few exceptions, alternating access to the UAT for digestive and respiratory functions occurs seamlessly and without consequence.

In disease, the digestive and respiratory functions of the UAT can become asynchronous. Under these circumstances, swallowed material may enter the airway and course into lower respiratory structures and contribute to increases in choking, pneumonia, and atelectasis. Because normal swallowing occurs over such a brief time span, the timing of the necessary biomechanical events which prevent bolus misdirection must remain relatively constant to prevent misdirection of swallowed material. If the larynx is not closed as the food or liquid bolus enters the hypopharynx for delivery into the esophagus, aspiration invariably occurs.

The process of aging introduces physiological changes in performance that mimic mild levels of impairment in the absence of pathology. Some of the age-related changes seen in

healthy individuals are associated with deterioration in neuromuscular functions throughout the human musculoskeletal and neuromuscular systems. The potential effect of these changes to muscle strength, bone mass, and neuromuscular transmission velocity may predispose the normal elderly to a higher risk of injury, or increased morbidity following trauma or disease (Fiatarone & Evans, 1993). Investigators have documented similar kinds of physiological changes with regard to the timing of events and structure of normal swallowing among healthy, non-dysphagic, elderly subjects (Robbins, Hamilton, Lof, & Kempster, 1992; Robbins, Levine, Wood, Roecker, & Luschei, 1995; Shaker et al., 1994). Therefore, age-related changes in swallowing function may enter the realm of pathology (dysphagia) and have greater impact on frail elderly individuals with or without co-occurring disease conditions (Ekberg & Feinberg, 1991).

Oropharyngeal dysphagia is common following a number of disease processes associated with aging, especially stroke. As many as half the adults diagnosed with cerebrovascular accident and other neurological conditions exhibit dysphagia at some point after onset (Dziewas et al., 2004). In addition, dysphagia can result from head and neck cancer and its treatment, and other iatrogenic etiologies, such cranial or peripheral nerve damage secondary to head, neck, or chest surgeries. Dysphagia increases a patient's overall likelihood for developing pneumonia, malnutrition, or other sequelae of impaired swallowing function and airway protection. Rehabilitation literature reports that patients benefit from interventions which compensate for acquired sensorimotor deficits associated with aspiration. Some of these interventions require behavioral training by the speech-language pathologist to teach patients to swallow safely using one or more novel maneuvers (Logemann, 1999). Unfortunately, many published investigations

of dysphagia lack sufficient numbers of subjects to produce robust evidence of anticipated therapeutic success.

1.1 OVERVIEW OF DISSERTATION

1.1.1 Goals

One goal of this dissertation was to conduct a research synthesis to quantify the collective strength of published evidence regarding the effects of dysphagia interventions on various health and biomechanical outcomes. Application of the principles of evidenced based practice (EBP) is an imminent reality for rehabilitative service providers. EBP offers practitioners a powerful tool with which to evaluate published treatment methodologies to enable selection of interventions with the best likelihoods of successful outcomes with individual or groups of patients. This goal was accomplished through the completion of two meta-analyses of the effects of dysphagia interventions for patients with neurogenic dysphagia.

A second goal of this dissertation was to systematically investigate the differences between traditional (i.e., primarily verbal instruction and tactile cuing) and instrumentally-mediated (i.e., traditional training + visual biofeedback) training methods in two groups of normal subjects trained to perform a common therapeutic swallowing maneuver. Instrumentation can be a valuable adjunct to some types of behavioral training because it provides immediate sensory feedback of targeted performance parameters (Crary, Carnaby Mann, Groher, & Helseth, 2004). In the field of speech-language pathology, this is a relevant clinical issue. There are practitioners who allege great success in providing dysphagia treatment

using sEMG biofeedback training from regions of the face and neck (Huckabee & Cannito, 1999). Although biofeedback seems logical and defensible from a biological standpoint, clinical efficacy studies in dysphagia management have not been done in controlled clinical trials or subjected to rigorous single subject design.

1.1.2 Synopsis of Dissertation

Chapter 2 will review relevant background information on the field of dysphagia, surface and intramuscular EMG investigations of swallowing musculature, and biofeedback literature in physical rehabilitation to establish the credibility and potential of biofeedback treatment in swallowing remediation.

Chapter 3 will discuss the anatomy and physiology of normal and abnormal UES function and the biomechanics of the Mendelsohn maneuver. This maneuver is the focus of the experimental portion of this dissertation and also a common treatment strategy used by speech-language pathologists.

The economic and social impact of dysphagia and its consequences will be discussed in Chapter 4. The justification for using statistical evaluation to determine the effectiveness of published dysphagia strategies believed to reduce aspiration will be established.

Chapter 5 will include two rigorously conducted meta-analyses of clinical research reporting the efficacy of individually administered interventions for neurogenic dysphagia impairments, and studies reporting the effectiveness of organized, institutional dysphagia protocols on mitigating global health outcomes such as pneumonia.

Results of the experimental portion of this dissertation will be reported in Chapter 6. Selected parameters of sEMG submental musculature will be analyzed in subjects trained to perform a swallowing maneuver with and without biofeedback.

A comprehensive summary of the major implications of the meta-analyses and the experiment will be presented in Chapter 7.

2.0 BACKGROUND INFORMATION ON EMG AND BIOFEEDBACK

2.1 BACKGROUND: USE OF BIOFEEDBACK IN PHYSICAL REHABILITATION

Surface electromyographic (sEMG) biofeedback programs have been an effective adjunct to rehabilitation designed to restore independence in locomotion, self care, and other daily activities. In patients with disorders affecting neuromuscular functions, sEMG biofeedback can assist patients' neuromuscular reeducation and/or strengthening of limb and trunk function, bladder training, and rehabilitation of other impairments. For example, efforts to rehabilitate urinary incontinence in patients with spinal cord injury, cerebral palsy, and female stress incontinence using electromyographic biofeedback technology have demonstrated moderate success within small subject groups (Dannecker, Wolf, Raab, Hepp, & Anthuber, 2005; Jerkins, Noe, Vaughn, & Roberts, 1987; Yamanishi et al., 2000). Restoration of anal sphincter control in patients with fecal incontinence has also been described both with and without adjunct manometry biofeedback (Mahony et al., 2004). On the whole, these studies support the clinical use of biofeedback with patients.

Physical rehabilitation of gait using electromyographic biofeedback in patients with a variety of neurogenic sensorimotor syndromes has also been investigated (Dursun, Dursun, & Alican, 2004; Jerkins et al., 1987; Jones & Lees, 2003; Mahony et al., 2004; Yamanishi et al., 2000). Dursun et al. (2004) observed significant improvements in ankle joint strength and range

of motion in children with cerebral palsy whose treatment was supplemented with sEMG biofeedback compared to a group treated conventionally. In another study, patients with spinal cord injury who used a full-time portable sEMG biofeedback unit regained near normal gait when compared to patients treated with intermittent biofeedback used only in the clinic (Petrofsky, 2001).

Use of sEMG biofeedback in stroke rehabilitation has received a great deal of attention. One double-blind investigation compared sEMG treated stroke patients to those treated with a placebo sEMG unit (Intiso, Santilli, Grasso, Rossi, & Caruso, 1994). These investigators found that some improvements in strength, ADL independence and mobility were seen in the biofeedback-treated group; however those improvements were not significantly different from the control/placebo group. These investigators also found that overall gait was significantly improved in biofeedback-treated patients when compared to patients treated with conventional physical therapy alone (Intiso et al., 1994).

A meta-analysis performed by Moreland, Thomson, and Fuoco (1998) reviewed and measured the effect of sEMG biofeedback-mediated rehabilitation of lower extremity impairments after stroke. This study indicated that effects of biofeedback-mediated therapy on gait, speed, and ankle angle during gait could be expected to be moderate (with effect sizes between d = .31 to d = .50) to large (d = 1.17) for ankle dorsiflexion during gait.

2.2 BACKGROUND: PHYSIOLOGICAL INVESTIGATIONS OF SWALLOWING

Early investigations of intramuscular oral and pharyngeal myoelectric activity in animals revealed an orderly firing sequence of various floor-of-mouth (FOM) and related musculature

during swallowing (Doty & Bosma, 1955). Many human studies have outlined the roles of individual FOM muscles and the FOM complex during swallowing. Seminal investigations compared concurrent recordings of surface and intramuscular myoelectric activity to verify that sEMG was a valid representation of FOM activation during swallowing. Researchers demonstrated that FOM sEMG signals were reliable correlates to simultaneous intramuscular recordings of individual FOM muscles obtained with needle electrodes without significant influence or crosstalk from adjacent musculature (i.e., platysma and genioglossus), (Palmer, Luschei, Jaffe, & McCulloch, 1999; Spiro, Rendell, & Gay, 1994). These researchers cleared the way for clinical use of less invasive sEMG procedures for measuring myoelectric activity in the FOM or submental musculature.

By using combined methodologies of videofluoroscopy and EMG, researchers began to link patterns of muscular activation to concomitant biomechanical swallowing events. Researchers described the ways in which FOM myoelectric activity correlated with displacement of hyolaryngeal structures throughout the swallow (Dodds, Stewart, & Logemann, 1990; Kahrilas, Logemann, Krugler, & Flanagan, 1991). Additional studies have used simultaneous sEMG recording of FOM musculature and image-tracking of laryngeal displacement to replicate earlier findings. Taken together, all research supports reliable use of the less invasive methodology of sEMG to sample regional myoelectric activity related to swallowing (Ertekin et al., 1995).

Other instrumentation has been piloted in the exploration of swallowing physiology. Investigators have attempted to quantify selected swallowing parameters using electroglottograph, and ultrasound (Litvan, Sastry, & Sonies, 1997; Logemann & Kahrilas, 1990;

Miller & Watkin, 1997; Perlman & Grayhack, 1991). By and large, these methodologies are not user-friendly, nor have they been adapted for use in a routine clinical setting.

2.3 BACKGROUND: USE OF BIOFEEDBACK IN TREATMENT OF DYSPHAGIA

Lingual strengthening programs have generated interest in rehabilitation of dysphagia (Robbins et al., 2005b). Efforts are underway to track changes in lingual strength with biomechanical events of swallowing. Robbins et al. (2005b) reported that fine and gross lingual movements are under significant volitional motor control, whereas other buccopharyngeal musculature is far less amenable to volitional control.

Electromyography enables direct investigation of skeletal muscle electrical activity at rest and during swallowing. With the validation and refinement of surface electrode technology/data processing, sEMG has become a clinically useful, noninvasive approach to the investigation of volitional movements and behavioral training for specific forms of dysphagia. Because studies have shown that sEMG is a valid indicator of swallowing myoelectric activity, and can be used reliably in sampling swallow-related muscle activity, interest in its use as a biofeedback tool in dysphagia rehabilitation has risen dramatically. Clinical reports of case studies of combining sEMG and videofluoroscopic procedures has helped outline the potential clinical applications as well as methods for surface electrode placement.

Crary (1995) reported on a series of brainstem stroke patients trained to increase duration and amplitude of swallow-related myoelectric activity using visual biofeedback to monitor performance. SEMG measurements were obtained from an anatomical site defined as “between the larynx and hyoid” rather than the FOM region. This region contains several layers of

musculature, some of which act to elevate the larynx (i.e., thyrohyoid) and others that depress the larynx (i.e., sternohyoid and sternothyroid) (Ludlow et al., 2007). Unfortunately, this investigator provided only descriptive statistics to characterize the treatment effects of using sEMG biofeedback training.

The same investigators used sEMG in a similar design to compare myoelectric signals of normal subjects and brainstem stroke patients while swallowing (Crary & Baldwin, 1997). Results indicated significant differences in timing and amplitude measures between the disordered and healthy groups. This investigation was useful in its use of videofluoroscopy to match sEMG to swallowing events and in its descriptions of the typical sEMG waveform associated with oropharyngeal swallowing. This, however, was also a descriptive study rather than an investigation of treatment effects.

Huckabee and Cannito (1999) employed FOM sEMG biofeedback methodology as a component of their dysphagia rehabilitation protocol to train patients to execute the Mendelsohn maneuver. Though investigators reported a treatment effect (i.e., prolonged duration of FOM sEMG activity during swallowing), they did not establish which modality of reinforcement (i.e., types of feedback/cues used in conjunction with biofeedback) or how much (i.e., dosage) was responsible for increasing the duration of sEMG activity. In addition, researchers did not indicate whether these measures reflected a change in status of a patient's overall dysphagia severity in terms of meaningful treatment outcomes (i.e., diet advancement, occurrence of aspiration pneumonia, etc.). Though results sounded promising, there were some major flaws in the study design that would preclude replication.

To date, use of physiologic monitoring devices in treating dysphagia has not been the subject of rigorous clinical investigation. Reasons for this include prohibitive equipment costs as

well as availability and environmental considerations of the traditional clinical setting. Recent advances in both software and hardware technology for personal computers have greatly facilitated clinical investigation of physiologic, neuromuscular activities, coordination, and timing of events of the UAT during swallowing. Aggressive marketing of these systems to a variety of rehabilitative settings and clinics on the basis of affordability, trim design, and software programs that make it easy for clinicians to devise objective treatment goals has also contributed to the recent popularity in using therapeutic biofeedback to treat dysphagic patients. Current practice involves speech-language pathologists using biofeedback training with dysphagic patients. However, the evidence base underlying this type of treatment in the head and neck musculature has not been clearly established.

Future research should focus on providing clinicians with useful and sufficiently robust expectations of success and enough clarity to enable replication. Studies should also include a control group to account for the potential placebo effect in studies which provide a single intervention. Careful investigation of reinforcement should be undertaken to determine which type of training (i.e., verbal/traditional, visual, or a combination of the two), and which patterns and schedules of reinforcement and withdrawal, are most efficient in training patients given time pressures inherent in the traditional clinical setting.

3.0 DEGLUTITION: HISTORY, PHYSIOLOGY, AND MANAGEMENT

Oropharyngeal swallowing has been described since the early work of Francois Magendie. He first discussed the role of the epiglottis during deglutition and found that internal laryngeal closure was an important aspect of airway protection (Magendie, 1813). Stevenson and Guthrie (1949) reestablished the importance of Magendie's early investigations of swallowing function. In the 1950's, investigation of oropharyngeal swallowing was of primary interest to researchers involved in pediatrics and dentistry. Doty and Bosma (1955) studied swallowing in children using electromyography and published one of the first descriptions of deglutitive muscle activation in the head and neck. In the 1970's, researchers began probing oropharyngeal swallowing function in postoperative head and neck cancer.

Manofluorography revolutionized the scientific study of swallowing function. McConnel and his colleagues perfected a technique which combined simultaneous recordings of the dynamic events of swallowing using cinefluoroscopy and the pressure changes within the oropharynx using manometry (McConnel, Mendelsohn, & Logemann, 1986; Mendelsohn & McConnel, 1987). Around this time, gastroenterologists became interested in exploring the interrelations between "upper" oropharyngeal and "lower" esophageal transfer of swallowed material employing McConnel's methodology (Dodds et al., 1988; Shaker, Cook, Dodds, & Hogan, 1988). Jerilyn Logemann, a professor of Speech Language Pathology and collaborator in McConnel's research, realized the importance of rehabilitation of disordered swallowing and decided to focus her expertise in anatomy and physiology of the head and neck on dysphagia.

She wrote the first textbook on the evaluation and treatment of swallowing disorders in 1983 (Logemann, 1983). The next twenty years saw dramatic growth in the number of published investigations of swallowing disorders and its management from all three professions and the birth of the Dysphagia Research Society in 1992.

3.1 OROPHARYNGEAL PHYSIOLOGY: UPPER ESOPHAGEAL SPHINCTER (UES) FUNCTION

Oropharyngeal swallowing physiology and biomechanics have been analyzed using a combination of instrumental methods. Historically, imaging studies using real-time videofluoroscopy have been used to track the flow of contrast-enhanced materials through the digestive system. Current descriptions of oropharyngeal deglutitive events focus on the movement of the bolus in relation to structural landmarks from the mouth to the esophagus. Visual imaging studies yield a two-dimensional view of bolus flow and movement of anatomic structures in the UAT. However bolus movement takes place over all three dimensions of space, and is additionally reliant upon development of pressure gradients, maintenance of intrabolus pressure, and intricately timed and coordinated movement of structures toward and past one another. The onset and end of the components of this brief event tend to overlap with other sub-events, thereby rendering any linear discussion of their nature semantically difficult. For discussion purposes, oropharyngeal swallowing is artificially separated into stages which characterize groups of events in terms of timing of structural landmarks and bolus movement. For the purposes of this dissertation, details of this section will focus upon the component of deglutition (i.e., UES opening) modified by the experimental treatment technique (i.e.,

Mendelsohn maneuver) investigated. A detailed discussion of all other stages of normal swallowing can be found in Appendix A. This is included as a reference to the discussions of swallowing abnormalities and treatment strategies which were targeted in some of the articles selected for the meta-analyses portions of this dissertation.

3.1.1 UES Opening during Swallowing

Several forces contribute to UES opening during swallowing. The main source of intrabolus pressure arises from compression of the bolus by the tongue and pharyngeal constrictors. Leakage of material from this pressurized bolus is prevented through a combination of factors including closure of the system's many valves, bolus volume and viscosity, pre-pharyngeal stage inhibition of UES resting tone, and muscular traction forces applied to the sphincter itself. Traction forces contribute to the anterior and superior displacement of the UES (Jacob, Kahrilas, Logemann, Shah, & Ha, 1989; Logemann, 1998). McConnel and his colleagues referred to the cumulative outcome of these co-occurring events as the hypopharyngeal suction pump (McConnel, Cerenko, & Mendelsohn, 1988).

These traction forces arise from suprahyoid musculature that make up the floor of the mouth (FOM) or submental muscle complex: the geniohyoid (GH), anterior belly of the digastric (ABD), and the mylohyoid (MH). Combined concentric forces of this FOM complex are transferred from their fixed origins on the mandible to their insertions on the hyoid bone (Logemann & Kahrilas, 1990). The laryngeal framework is suspended from the hyoid through muscular and connective tissue attachments and is sometimes referred to as the hyolaryngeal complex. Contraction of these muscles generates the traction forces that produce anterior and superior displacement of the hyoid and larynx during swallowing which contributes to UES

opening. The posterior wall of the larynx is shared as the anterior wall of the UES. Studies using electromyography in conjunction with fluorographic and ultrasonic imaging techniques have verified the displacement of the hyoid bone and concurrent distension of the UES resulting from FOM contraction during swallowing (Dodds et al., 1990; Jacob et al., 1989; Kelly, 2000; Miller & Watkin, 1997).

The UES has also been shown to "relax" somewhat from its resting state of tonic closure due to vagal inhibition (Miller, 1986), immediately preceding the onset of hyolaryngeal excursion during the pharyngeal phase of normal swallowing. Some researchers hypothesize that pre-pharyngeal stage vagal inhibition of sphincteric resting tone is responsible for reduction of UES intraluminal pressure during normal deglutition (Cook et al., 1989b). Others have demonstrated reduced UES tone in response to electrical vagal stimulation (Broniatowski, Dessoffy, Shields, & Strome, 1999). This "relaxation" or increased compliance is thought to facilitate sphincteric opening efforts supplied by traction and other forces (Fukushima et al., 2003; Miller, 1997).

3.1.2 Causes of UES Impairment during Swallowing

Dysphagia caused by UES dysfunction is associated with reduced duration and/or diameter of UES opening. Patients who experience incomplete bolus clearance into the esophagus with residual hypopharyngeal residue often report a sensation of food 'sticking in the throat.' Severity can range from minimal separation of the bolus tail to complete absence of esophageal bolus entry. Some research suggests that normal aging causes reductions in the duration and diameter of UES opening (Ekberg & Feinberg, 1991; Frederick, Ott, Grishaw, Gelfand, & Chen,

1996). Thus, the combined effects of age-related UES functional changes and disease processes in the elderly could have negative implications on overall swallow safety and efficiency.

Impaired bolus flow through either the pharynx or the UES has been associated with irradiation treatments to the head and neck for carcinoma, stroke, pathological and iatrogenic sources of injury to vagal peripheral efferents, cricopharyngeal bar, and Zenker's diverticulum (Beutler, Sweeney, & Connolly, 2001; Eisbruch et al., 2002; Fukushima et al., 2003; Jacobs et al., 1999; Robbins & Levine, 1993; Smith-Hammond, Davenport, Hutchison, & Otto, 1997). Among the aforementioned conditions, the majority of patients with central brainstem lesions and specific nuclear and peripheral cranial nerve injuries consistently experience impaired UES opening during deglutition (Kwon, Lee, & Kim, 2005; Robbins & Levine, 1993; Smith-Hammond et al., 1997). Electrophysiologic and videomanometric investigations of swallowing physiology in these populations lend support to one model which centers around a swallowing pattern generator within the medulla and associated reticular formation (Amri, Car, & Jean, 1984; Aydogdu et al., 2001; Ertekin & Aydogdu, 2002; Prosiegel, Holing, Heintze, Wagner-Sonntag, & Wiseman, 2005). Researchers have demonstrated that these "centers" can be influenced by afferent peripheral buccopharyngeal input, and in turn influence motor outflow to structures innervated by efferent branches of the glossopharyngeal, vagus, hypoglossal, facial, and trigeminal nerves emanating from the pons and medulla.

Investigations of swallowing function in postoperative head and neck cancer resections have been invaluable tools for clinicians in terms of predicting the nature of and/or developing treatment models based on the surgical paralysis or ablation of various structures involved in deglutition. One model that clearly illustrates the postoperative impairments to UES traction forces is that of total laryngectomy. Laryngectomy involves removal of the entire larynx

including all inferior attachments to the trachea up to superior and anterior attachments to the suprahyoid musculature and tongue base. Hyoid insertions for the suprahyoid muscle complex are removed anteriorally as well as the rigid anterior wall of the UES upon which suprahyoid traction forces act during swallowing. Additionally, removal of the cricoid cartilage eliminates the site of origins of the cricopharyngeal segment of the inferior constrictor. After complete laryngectomy, the UES can be characterized as a flaccid, tonically closed sphincter with little to no structural foundation for the generation of traction forces (McConnel et al., 1986). The laryngectomy patient must rely upon residual structures above the FOM to generate enough intrabolus pressure to propel the bolus into the esophagus. In many cases, these patients learn to compensate for absent UES function by making adjustments in posture and/or bolus placement which maximize potential for generating oral and pharyngeal intrabolus pressure (McConnel et al., 1986; Nishizawa, Mesuda, Kobashi, Takahashi, & Inuyama, 2001). Findings illustrate that patients can influence UES function during deglutition.

3.2 BEHAVIORAL MANAGEMENT OF IMPAIRED UES OPENING

Mistiming of biomechanical events while swallowing and impaired sensorimotor function of the UAT produce abnormalities in the bolus flow. Traditionally, these abnormalities are detected with videofluoroscopy, or modified barium swallows (MBS). Investigators have described numerous compensatory strategies intended to influence the timing and/or specific properties of swallowing events. These compensatory maneuvers must be used every time food or liquids are swallowed to facilitate bolus clearance and airway protection. Among the many biomechanical abnormalities that could result in aspiration are (a) delayed onset of the pharyngeal response, (b)

impaired clearance of swallowed material into the esophagus, and (c) incomplete airway closure during the swallow. Appendix B contains descriptions of dysphagia interventions used to remediate these specific biomechanical problems. Of particular interest in this dissertation is a behavioral maneuver called the Mendelsohn maneuver, a strategy designed to improve UES opening while swallowing.

3.2.1 Biomechanics of the Mendelsohn Maneuver

The Mendelsohn maneuver requires the individual to consciously prolong the duration of each swallow (Logemann, 1998). This technique was named after the investigator responsible for first describing post-general anesthesia aspiration syndromes spawning an interest in oropharyngeal swallowing physiology and disorders. It is difficult for a clinician to teach patients and more difficult to perform accurately (personal communication, J.A. Logemann, October 24, 2005). Appendix E contains the verbal instructions and cues used by the examiner to train subjects to perform the Mendelsohn Maneuver for the experimental portion of this dissertation.

Volitional prolongation of duration of UES opening was described by Kahrilas et al. (1991) in healthy subjects using simultaneous videofluoroscopy and pharyngoesophageal manometry. The maneuver is selected for individuals with radiographic evidence of incomplete bolus clearance related to (1) UES function or (2) failure of other components of the oropharyngeal pressure pump to completely drive a bolus through the UES into the esophagus (Kahrilas et al., 1991). Some studies investigating behavioral interventions for dysphagia have demonstrated that accurate execution of this maneuver produces prolonged and wider diameter UES opening during the pharyngeal stage, thereby enabling increased hypopharyngeal clearance

(Dodds et al., 1990; Logemann, 1998). Others have identified changes in duration of pharyngeal contraction and intrabolus pressure generation while using this maneuver (Boden, Hallgren, & Witt, 2006).

The Mendelsohn maneuver has been reported as effective in managing dysphagia caused by UES dysfunction in patients with adequate cognition (Logemann, 1998; Robbins & Levine, 1993). The Mendelsohn maneuver is challenging for the average individual to perform and increasingly difficult for individuals with cognitive or language impairments (personal communication, J.A. Logemann, October 24, 2005). Logemann et al. (1990) successfully trained a patient with dysphagia caused by brainstem stroke to prolong UES opening when swallowing. Using sEMG of submental musculature in combination with videofluoroscopy, these researchers were able to verify that prolonged UES opening resulted in less post-swallow pharyngeal residue; thus reducing this patient's risk of postprandial aspiration. Some studies have shown that increased intrabolus pressure a is secondary outcome of performance of the Mendelsohn Maneuver, suggesting greater effort may be applied during its performance by some individuals (Bulow, Olsson, & Ekberg, 1999).

This maneuver is also somewhat difficult for a clinician to demonstrate because the structures involved are located within the neck musculature. Ordinarily, clinicians rely upon palpation of the laryngeal framework to formulate impressions about the relative quality and timing of hyolaryngeal excursion associated with swallowing. They train patients to self-palpate these structures while verbally instructing them to "hold the larynx up" longer. Unfortunately, no studies have demonstrated the accuracy or reliability of clinicians in detection of swallow-related hyolaryngeal motion, or the ability to discriminate between it and hyolaryngeal motion associated with mandible and lingual movements. Data are needed to determine the precision of

the clinicians' subjective impressions of hyolaryngeal movement during swallowing and its relationship to the judgment of the effects of training on swallowing biomechanics.

In summary, accurate performance of the Mendelsohn maneuver causes the subject to lengthen the duration and possibly increase the amplitude of suprahyoid musculature contraction during each swallow. The expected effect of this maneuver is to maintain hyolaryngeal elevation for the purposes of augmenting airway closure and prolonging the duration of UES opening. The desired outcomes include more complete bolus clearance through the UES, and a reduction in post-swallow, hypopharyngeal residue which contributes to an increased risk of postprandial aspiration (Eisenhuber et al., 2002; Logemann, 1998).

4.0 CLINICAL RELEVANCE OF DYSPHAGIA TREATMENT AND ASPIRATION SYNDROMES

4.1 MEDICAL AND ECONOMIC COSTS OF DYSPHAGIA

The most clinically important, health-related outcomes associated with oropharyngeal dysphagia are caused by misdirection of swallowed food or liquids into the upper airway, or aspiration. Aspiration and airway obstructions (choking) occur when any portion of a bolus courses into the airway inlet (or larynx). Aspirated material may progress further into the trachea, smaller airways, and alveoli. Pneumonia is a major consequence of oropharyngeal dysphagia when aspiration is present. Hospitalization rates for aspiration pneumonia (AP) have grown dramatically in the past two decades. Between 1991 and 1998, admissions for AP increased by 94.5% (Baine, Yu, & Summe, 2001). Dozens of diseases trigger some degree of dysphagia in addition to stroke, traumatic brain injury, neurodegenerative diseases, and iatrogenic disruption of sensorimotor substrates of head and neck function. Given the reality of rising medical costs, public healthcare would greatly benefit from research supporting the refinement of non-invasive, therapeutic techniques that would effectively minimize or eliminate deglutitive aspiration.

Studies have estimated that the cost of providing medical care for dysphagic stroke patients ranges between $6,000 for those who successfully regain safe oral intake, and $12,000 for those eventually requiring enteral feeding tubes to ensure safe nutrition and hydration

(Wojner & Alexandrov, 2000). Non-oral management of dysphagia involves surgical placement of an enteral feeding tube, or gastrostomy, presumably to reduce the risk of AP and malnutrition. Ironically, there is little published evidence that non-oral dysphagia management provides measurable benefit in terms of cost or survival. Callahan, Buchanan, and Stump (2001) reported that complications of gastrostomy placement due to either the surgery or the device itself could result in treatment costs in excess of $31,000. Moreover, dysphagic patients undergoing gastrostomy placement may have coexisting esophageal motility disorders (e.g., transient lower esophageal sphincter relaxation or gastroesophageal reflux disease) which put them at greater risk for developing aspiration *with a feeding tube* than without (Ciocon, Silverstone, Graver, & Foley, 1988; Erdil et al., 2005; Finucane & Bynum, 1996). Non-oral dysphagia management does not completely eliminate the risk of patients developing AP, and in fact, can actually cause the problem. Since treatment costs vary with setting, effective dysphagia treatment without hospitalization would be more cost-efficient than inpatient treatment (Kruse, Boles, Mehr, Spalding, & Lave, 2003).

4.1.1 Pneumonia

According to the Centers for Disease Control and Prevention (2006), the seventh leading cause of death in the United States was attributed to influenza and pneumonia, the latter producing the majority of their combined mortalities. In 2003, annual pneumonia-related deaths totaled 63,241 and occurred at a rate of 224 per 10,000 in elderly adults, age 65 and older (National Center for Health Statistics, 2003). Pneumonia is the most frequent cause of death by infectious disease in the United States (Marston et al., 1997).

Community acquired pneumonia (CAP) is caused by microorganisms that thrive in respiratory epithelium. Among bacterial causes of CAP, pneumococcus (streptococcus pneumoniae) is the most common, and results in 40,000 deaths annually (Centers for Disease Control and Prevention, 2006). Other forms of bacterial pneumonia include (a) nosocomial pneumonia, caused by pathogens typical in hospitals and nursing homes, (b) ventilator-associated pneumonia, caused by contamination of mechanical ventilator circuits, (c) Legionella, and (c) mycoplasma pneumonia (Centers for Disease Control and Prevention, 2006). Viral forms of pneumonia include respiratory syncytial virus. A relatively recent category of pneumonia, also classified as CAP, is associated with aspiration of swallowed food or liquids mixed with bacterial pathogens common to saliva.

CAP originates from a number of causative factors and accounts for the majority of pneumonia diagnoses. Seasonal and other cyclic increases in the pool of available pathogens in the community and an increased tendency of indoor activity during winter months raise the infection and cross-infection rates. Additional risk factors shown to be associated with CAP include underlying pulmonary disease, immunocompromise, inactivity, damaged airway mucociliary clearance, and other chronic illnesses including neurological conditions.

Conditions that cause temporary or permanent changes in sensorimotor function often compromise airway protection during swallowing. In elderly patients with stroke, pneumonia increases mortality. In a large, population-based study of 11,286 stroke patients without co-occurring terminal disease or advance directives requiring “do not resuscitate” management, the mortality rate was six times higher (26.9%) in patients who developed pneumonia after onset of stroke compared to those that did not develop pneumonia (4.4%) (Katzan, Cebul, Husak, Dawson, & Baker, 2003). After adjustments for various underlying factors affecting mortality,

the relative risk of death (RRD) of stroke patients who developed pneumonia within 30 days post-onset was 2.99 (i.e., the probability of death was about three times higher) compared to stroke patients without pneumonia.

Many patients survive severe stroke because of aggressive management in intensive care units, however acquiring pneumonia during the post-onset phase significantly reduces both the quality and likelihood of survival. Hilker et al. (2003) prospectively compiled data from the medical records of stroke patients admitted to a neurological intensive care unit. Twenty-one percent of their cohort acquired stroke-associated pneumonia (SAP). Within the SAP group, mortality was three times more likely (both short-term and long-term), and these patients had significantly less rehabilitative success compared to stroke patients without SAP (Hilker et al., 2003).

The incidence of AP has increased dramatically in recent years. In fact, Baine et al. (2001) reported that diagnoses of AP had reached epidemic proportions according to an epidemiological study which sought to estimate the prevalence of aspiration pneumonia from Medicare data. Baine and colleagues (2001) reviewed 5% of all Medicare hospital inpatient bills from 1991 through 1998 to determine the estimated number of hospitalizations for AP in the United States. Their 5% sample revealed that the frequency of hospitalization for all categories of pneumonia grew from 30,292 to 37,153 during that seven year period. Of those admissions, the rate of AP admissions doubled (i.e., from 2974 to 5756 patients) and ranked second only to 'unspecified causes of pneumonia' as coded in hospital discharge summaries (Baine et al., 2001). Extrapolating these data to the population, an estimated 743,000 pneumonia admissions occurred in 1998, with AP constituting 115,120 or 15.5% of Medicare hospital admissions for pneumonia

that year. AP carried the highest case-fatality rate during hospitalization (23.1%) of all pneumonia diagnoses.

In another analysis of Medicare source data, Niederman, McCombs, Unger, Kumar, and Popovian (1998) determined that more than $8 billion was spent treating hospital inpatients for CAP, at an average cost per stay of $6,000 to $7,000. Combining information from both of the aforementioned Medicare review studies, the proportion of CAP inpatient hospital cost for AP was 15.5% of $8.4 billion, or approximately $1.3 billion. Given these figures, the impact of a modest ten percent reduction in either hospital admissions or in length of stay for AP could save the health care system hundreds of millions of dollars each year.

4.2 PREDICTING ASPIRATION SYNDROMES

Treatment of oropharyngeal dysphagia has become common in modern health care institutions. Pneumonia caused by prandial aspiration is the most frequently cited adverse outcome associated with oropharyngeal dysphagia (Doggett et al., 2001). Patients who develop pneumonia because of dysphagia exhibit a 5% mortality rate (Almirall et al., 2000). Recent studies suggest that about half of all stroke patients demonstrate clinically significant dysphagia affecting safe oral intake (Mann, Hankey, & Cameron, 2000). Even when dysphagic stroke patients received temporary enteral nutrition via nasogastric tube, prevalence of pneumonia was as high as 44% (Dziewas et al., 2004).

Among the most likely sequelae of abnormal deglutition is aspiration of swallowed food or liquids which contain colonized bacteria typically present in oropharyngeal secretions (Marik, 2001; Marik & Kaplan, 2003; Tablan, Anderson, Besser, Bridges, & Hajjeh, 2007). Researchers

have shown that aspiration of colonized bacterial contained in saliva is one of the most predictable risk factors for pathogenesis of AP among patients who have a history of aspiration (Langmore et al., 1998; Loeb, Becker, Eady, & Walker-Dilks, 2003; Millns, Gosney, Jack, Martin, & Wright, 2003). Langmore et al. (1998) identified risk factors for pneumonia among a cohort of 189 dysphagic adults from acute care and long-term care settings. Patients dependent upon staff for feeding and oral care, those with dental caries or periodontal disease, and/or those who smoked had significantly higher rates of AP compared to other patients.

The level to which the bolus is aspirated is another factor predictive of pulmonary or airway consequences of dysphagia (Langmore et al., 1998). In a study of 381 hospitalized patients undergoing modified barium swallow (MBS) for suspected dysphagia, pneumonia rates for patients who swallow without material penetrating the airway were only 3% to 4% (Pikus et al., 2003). Conversely, the pneumonia rate for patients exhibiting *laryngeal penetration* (i.e., material penetrated the larynx and remained above the plane of the true vocal folds) on the MBS was 12%. Many patients aspirating at meals are completely unnoticed because their response to aspiration is absent. Of the group reported by Pikus et al. (2003), 27% showed evidence of *tracheal aspiration,* (i.e., below the vocal cords) and almost one-third of these aspirators (31%) did not exhibit any clinical evidence that they had aspirated, such as coughing (i.e., they were asymptomatic or silent aspirators). Interventions that can effectively minimize or reduce the likelihood of aspiration in dysphagic patients and subsequently mitigate pneumonia and other morbidities, are worthy of careful investigation.

Many adverse health sequelae caused by oropharyngeal dysphagia are reversible and transient. Recovery from the acute stages of stroke, for example, results in dramatic improvements in swallowing safety (Johnston et al., 1998; Smithard et al., 1997). The incidence

of pneumonia in stroke patients is estimated at 5% to 20%; therefore, prevention of health sequelae in the acute post-onset stages of stroke is a principal focus of clinical practice in many medical settings.

For more than twenty years, clinical investigators have been interested in strategies and maneuvers that prevent bolus misdirection. Scientists and clinicians worldwide and across disciplines contribute to this body of literature, including Speech-Language Pathology, Gastroenterology, Otolaryngology, Gerontology, Neurology and Neurosurgery, Physiatry, Occupational and Physical Therapy, Nutrition and Dietetics. One of the most significant obstacles to generating this type of research is diminished funding (Logemann, Baum, & Robbins, 2001).

Despite this universal interest in reducing aspiration syndromes related to biomechanical impairments, clinicians continue to seek methods whose published reports provide sufficiently repeatable methods, statistical power, and predictive value. Research synthesis provides consumers of clinical research with the opportunity to carefully assess the value of available research. Studies that represent a common underlying construct can be combined in a met-analysis for the purpose of estimating their overall effectiveness. Ultimately, this will enable clinicians to select more appropriate treatments to maximize the potential therapeutic success for their patients.

4.3 SPECIFIC AIMS

Though empirical evidence of the effectiveness of individually administered interventions for neurogenic dysphagia exists, most studies either lack clear descriptions of

methodology suitable for replication (e.g. Freed, et al., 2001) or have contained serious methodological flaws (e.g. Bulow et al., 2003). Case studies of dysphagic patients offer descriptions of and/or graphic representation of raw data without establishing the patient's pre-intervention abilities (Burke et al., 2000). Without sufficient baseline information, it is difficult to attribute observed changes to the intervention provided (Bryant, 1991; Logemann & Kahrilas, 1990; Robbins & Levine, 1993). Additionally, sEMG biofeedback rehabilitation of disordered swallowing musculature has been investigated in combination with traditional therapy without evidence that it offers a significant benefit to traditional behavioral intervention alone (Crary et al., 2004; Huckabee & Cannito, 1999). Therefore, the purposes of this dissertation are twofold. First, the quality and importance of published evidence describing treatment of oropharyngeal dysphagia and prevention of its associated global health outcomes will be statistically evaluated via modern meta-analytic methods. Secondly, two groups of normal subjects will be trained to use a common compensatory swallowing strategy (i.e., the Mendelsohn maneuver) to determine whether or not the addition of visual biofeedback to traditional training has an effect on post-training submental sEMG activity while swallowing. Both studies will be conducted using standardized protocols, including a priori decision matrices and judgment criteria (in the meta-analyses) and subject randomization (in the experiment) in order to facilitate future replication and to address some of the problems identified in prior meta-analyses and investigations of the effects of sEMG.

4.4 HYPOTHESES

Two independent studies comprise this dissertation: a meta-analytic synthesis of research, and a traditional experiment.

4.4.1 Hypotheses for Meta-Analyses

Based on the trends observed in this literature review and years of clinical experience, it is hypothesized that individual therapeutic interventions for dysphagia will demonstrate measurable and significant beneficial physiologic effects. Furthermore, research will show that implementation of these strategies produces a positive impact on global health outcomes such as pneumonia incidence, nutrition status, and mortality.

4.4.2 Hypotheses for Experimental Investigation

It is hypothesized that a group of healthy normal subjects will demonstrate significantly increased duration and amplitude of submental myoelectric activity while swallowing after they undergo a single training session in the performance of the Mendelsohn maneuver, regardless of which training method is used. Because biofeedback affords the subject the ability to alter muscular physiology "online," it is hypothesized that subjects whose training includes sEMG biofeedback will produce significantly greater duration, mean and peak amplitudes of myoelectric activity while swallowing as compared to subjects having just traditional training. It is also hypothesized that subjects whose training includes biofeedback will exhibit more uniform

patterns and consistent performance of the Mendelsohn maneuver than those with traditional training alone (i.e., no biofeedback).

5.0 TWO META-ANALYSES: EFFICACY OF INDIVIDUALLY ADMINISTERED DYSPHAGIA TREATMENT, AND EFFECTIVENESS OF INSTITUTIONAL DYSPHAGIA PROTOCOLS

Speech language pathologists practicing as swallowing-disorders clinicians are often consulted when patients are suspected of having developed pneumonia, malnutrition, or dehydration due to oropharyngeal dysphagia. After conducting a diagnostic evaluation, dysphagia therapy is subsequently designed to reduce or eliminate biomechanical swallowing impairments that allow the misdirection of swallowed material into the airway, because the therapy is believed to increase the patient's long-term ability to safely eat and drink by mouth. This improved biomechanical function caused by dysphagia therapy is then expected to mitigate the patient's risk of dysphagia related diseases such as aspiration pneumonia. The reduction of swallowing impairments and the prevention of swallowing-related disease are extremely important and interdependent goals of dysphagia therapy.

Specific treatment methods are designed and implemented because they have been shown to modify oropharyngeal biomechanics and physiology, thereby reducing aspiration of swallowed material into the respiratory system, and increasing delivery to the digestive system. The management of bolus misdirection is important. However these interventions are of little value to the individual patient or to the maintenance of public health unless the elimination of

bolus misdirection results in a predictable reduction in the risk of pneumonia, malnutrition, dehydration, or mortality.

Public health consequences of dysphagia include disease, decompensation and death due to aspiration-related respiratory tract infections, airway obstruction, and reduced physiologic reserve caused by malnutrition. Dysphagia also increases the overall cost of medical care due to recurrent hospitalizations for pneumonia, and the need for artificial enteral feeding tube usage. Pneumonia, the most common cause of death by infectious disease in the United States (Marston et al., 1997), occurs at an annual rate of 224 cases per 10,000 persons over age 65 (National Center for Health Statistics, 2003). Among pneumonia diagnoses within acute care hospitals in the United States, aspiration pneumonia, which is caused by the misdirection of swallowed material into the respiratory system (Marik, 2001), ranks second only to "unspecified causes of pneumonia" among coded hospital discharge diagnoses, while carrying the highest case fatality rate among all pneumonia diagnoses (Baine et al., 2001). The actual mortality rate after stroke has been shown to increase as much as six-fold when stroke patients develop pneumonia (Hilker et al., 2003; Katzan et al., 2003).

The economic cost of oropharyngeal dysphagia emphasizes the public health importance of its rehabilitation. In 1998, the cost of treating pneumonia caused by oropharyngeal dysphagia exceeded $1 billion (Niederman, McCombs, Unger, Kumar, & Popovian, 1998). Artificial nutrition is another costly alternative to oral intake in some dysphagic patients. Restoring nutrition safely by rehabilitating oropharyngeal swallowing function, has been shown to be half as costly as implementing non-oral means of nutrition through the use of enteral feeding tubes (Wojner & Alexandrov, 2000).

As illustrated above, modest reductions in the incidence of post-stroke pneumonia and need for enteral feeding could generate a significant decline in morbidity, mortality, and the cost of health care in patients with neurogenic dysphagia. Therefore the overall value of the treatment of individually administered interventions for neurogenic dysphagia must be measured in terms of concomitant reductions in mortality, morbidity, and expense. Individual and public health outcomes, including economic outcomes, must constitute the clinical end points that determine the value of therapeutic intervention for dysphagia as a disorder within the public health domain.

Patients with dysphagia are typically managed with one or more therapeutic interventions because dysphagia-producing neurological diseases such as stroke, amyotrophic lateral sclerosis and Parkinson's disease, cause multiple swallowing impairments. Each individual dysphagia treatment modality should be selected because it has been demonstrated to be effective at eliminating a specific swallowing impairment. When combined to address multiple impairments, properly selected modalities should produce a combination of beneficial physiological changes to swallowing function, such as reductions in aspiration of swallowed food into the respiratory system and increased clearance of food into the digestive system. After implementing these interventions, the clinician should be able to estimate the predictive potential, or prognosis, that the interventions will produce beneficial treatment outcomes such as increased nutrition without artificial support, or reduced likelihood of pneumonia and mortality. When such a prediction can be reliably made, the dysphagia treatments themselves can be justified as clinically valuable (Doggett et al., 2001). Therefore, the effects of individual treatments themselves, as well as the long-term health benefits caused by these treatments, must be ascertained, and reliably predicted, in order for all stakeholders (i.e., clinicians, patients, third

party payers, and policy makers) to make more informed decisions, and ultimately, to determine the value of dysphagia therapy on public health.

The development of individual therapeutic methods begins with stepwise, systematic research into the nature of a target disorder, and evolves into elucidation of tactics that manipulate the patient's disordered physiology in ways that are believed to generate some measurable benefit. When research is properly conducted, the investigators substantiate the validity and reliability of their conclusions through the use and reporting of soundly designed methods. The finest of these experimental investigations employ numerous safeguards to reduce misinterpretation of experimental results. They are designed prospectively, use rigorous methods of subject selection and assignment as well as predefined criteria for instructing subjects and evaluating data before and after treatment.

There are literally hundreds of published studies, available to the clinician and researcher, describing the effects of dysphagia therapy on swallow physiology or health outcomes associated with dysphagia. Researchers observe or assemble cohorts of patients with similar disorders and systematically employ a therapeutic intervention to determine its effects on the impairment of interest. The scientific methods and conduct employed by investigators are published, and can therefore be judged by the research consumer to determine whether the results of the studies themselves confirm that the investigated treatments are worthy of clinical adoption with specific patients with corresponding swallowing impairments. In the same manner that researchers assemble individual patients to generate a group with whom a specific clinical question can be rigorously tested, research articles investigating methods representing a sufficiently similar clinical construct, can be assembled and tested to provide the research consumer with evidence regarding the overall value of the underlying clinical construct they represent.

Meta-analysis, a prospective form of research synthesis whose "participants" are published research studies (vs. groups of patients), enables researchers to gather, sort, evaluate, and when appropriate, combine prior research to determine the collective clinical value and statistical significance of the findings. The studies selected for inclusion in a proper meta-analysis are screened and evaluated using prospective methods to ensure that they meet rigorous eligibility criteria. These studies are ultimately included and analyzed as a group of "participants" because they are sufficiently homogeneous, contain a predetermined level of sufficiently robust design quality and integrity, and they represent a similar, defined, underlying construct (Cooper & Hedges, 1994).

To assess the effects of dysphagia treatments on swallowing impairments, as well as on the global health impact of dysphagia management, two meta-analytic syntheses of published research were conducted. The first was designed to determine the effect of clinical, non-surgical, therapeutic modalities for remediating biomechanical impairments in dysphagic patients with stroke or clearly diagnosed neurological disease. The second meta-analysis investigated the effects of institutional dysphagia protocols on long-term adverse health outcomes such as malnutrition and pneumonia, and mortality.

Figure 1 illustrates the steps performed in the two meta-analyses. Sections 5.2 and 5.3 describe the search strategy and retrieval and the scoring method employed in *both* meta-analyses. Sections 5.4 and 5.5 describe specific procedures that were unique to the first and second meta-analyses, respectively.

5.1 HYPOTHESES

Based on the trends observed in this literature review and years of clinical experience, it is hypothesized that high quality investigations of individually administered interventions for neurogenic dysphagia will demonstrate measurable and significant beneficial effects toward the mitigation of biomechanical impairments of oropharyngeal deglutition. Furthermore, it is hypothesized that high quality research will show that implementation of systematically administered institutional dysphagia protocols produce significantly beneficial global health outcomes such as reduction of pneumonia incidence, improvements in nutrition status, and reduced mortality.

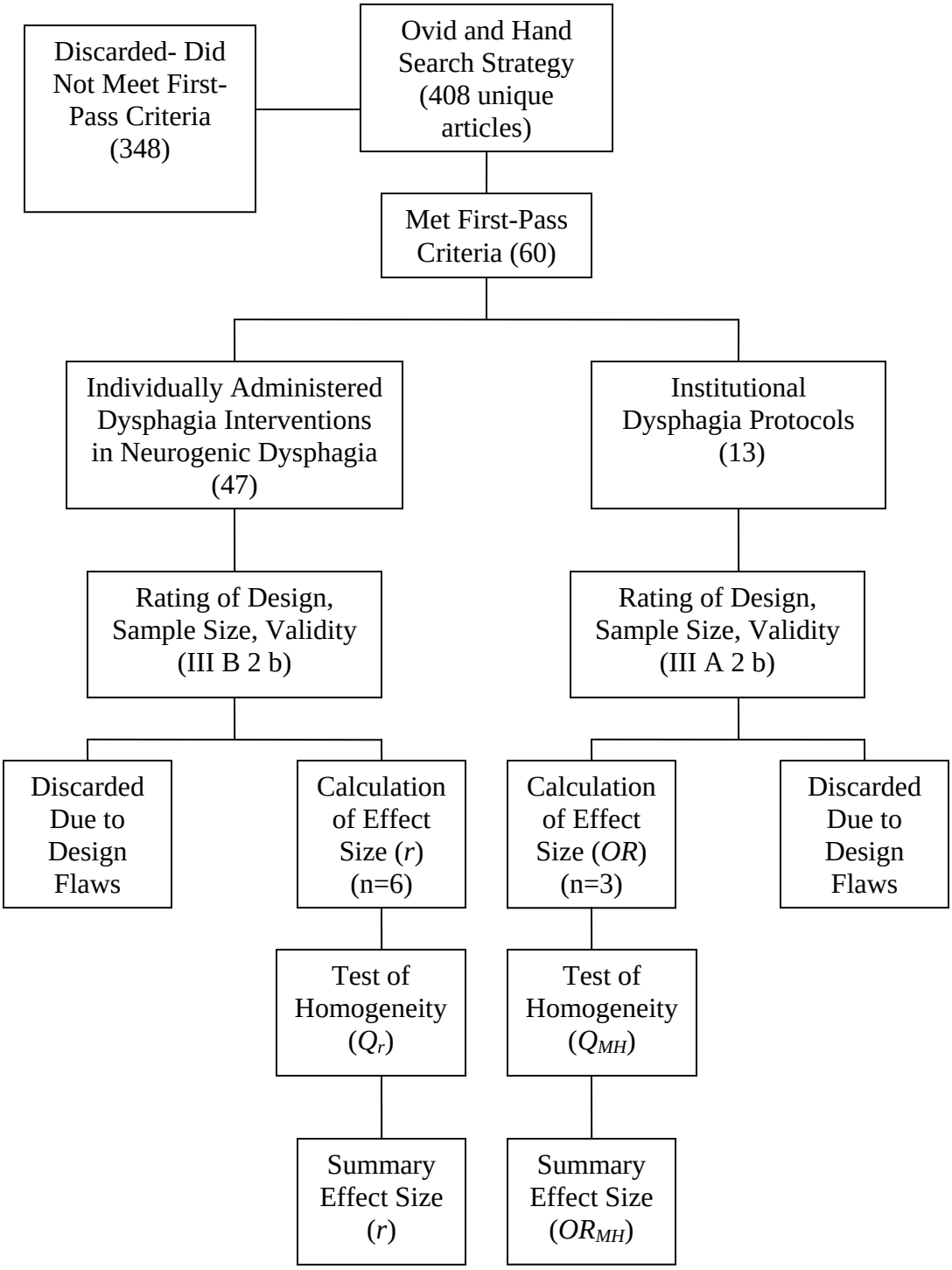

Figure 1. Steps Performed in Meta-Analyses

5.2 LITERATURE SEARCH STRATEGY

For both meta-analyses, a single literature search strategy was developed by the principal investigator, in collaboration with the consultant research librarian for the School of Health and Rehabilitation Sciences of the University of Pittsburgh. The principal investigator is a speech-language pathologist with 19 years clinical experience, who has participated in NIH funded clinical research projects as a regional principal investigator, researcher, judge, manuscript preparer and presenter of results at national and international scientific meetings and conferences. His qualifications include formal coursework in meta-analytic procedures, previous performance and presentation of treatment meta-analysis in peer reviewed, national professional conferences, and recognition as a specialist by the Specialty Recognition Board for Swallowing and Swallowing Disorders.

The search strategy was designed to retrieve published research that would be available to clinicians working with patients with neurogenic dysphagia in health care institutions in the United States. It was developed by creating and combining MeSH terms using the Ovid © search engine (Wolters-Kluwer Health, 2006) and was limited to the time between 1966 and 2006. Ovid © databases used in the search were Medline, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Health and Psychosocial Instruments (HAPI), Database of Abstracts of Reviews of Effects (DARE), Cochrane Database of Systematic Reviews (CDSR), American College of Physicians (ACP) Journal Club, and the Cochrane Central Register of Controlled Trials (CCTR). The search sought all published studies coded with any of the following search terms: randomized controlled trial, controlled clinical trial, random allocation, double-blind method, single-blind method, placebo, random, multicenter studies, prospective studies, intervention studies, cross-over studies, meta-analysis, control, human, deglutition,

deglutition disorders, dysphagia, and swallow. Diagnostic search terms used in the search strategy for meta-analyses were: cerebrovascular accident, amyotrophic lateral sclerosis, muscular diseases, multiple sclerosis, myasthenia gravis, Parkinson's disease, and neurodegenerative diseases. The root word embedded within the various diagnostic labels was included separately to ensure completeness of electronic search. The complete search strategy appears in Appendix C.

The date of initial search was February 14th, 2006. The Medline search generated 351 citations, while the combined search of the remaining databases produced 182 citations. Of the latter group of citations, 166 (92%) were duplicates of articles identified in the Medline search. Therefore, only the 16 unique citations were added to the meta-analysis pool, bringing the total to 367 citations. The search was repeated on December 29th, 2006, yielding 128 new citations. Of those, 25 were unique citations and became part of the final meta-analyses. Three-hundred ninety two unique citations constituted the initial sample of articles retrieved.

Other search strategies were also employed. Hand search and requests to international colleagues were used to cast as wide a search net as possible for articles investigating treatment of oropharyngeal dysphagia. One article was translated from German into English to enable it to be evaluated. Authors of some of the retrieved citations were contacted to clarify their methods when the published methods were insufficiently clear. Unpublished manuscripts and abstracts were not sought as they either did not represent the range of material available to clinicians working with patients (unpublished manuscripts), or contained insufficient methodological and information and data to enable replication or meta-analysis. This search resulted in the addition of 16 articles that had not been electronically identified. A final total of 408 articles was reviewed for the meta-analyses.

5.3 FRAMEWORK OF STEPS FOR THE TWO META-ANALYSES

The aforementioned search strategy was used to cast as wide a net as possible in order to identify all articles that might be eligible for both meta-analyses, and was followed by a "first-pass" screening of retrieved citations.

5.3.1 First-Pass Screening

After the broad search was implemented, the investigator screened the retrieved articles to determine their appropriateness for inclusion into either meta-analysis. A complete bibliography of all retrieved "hits" that included article identification number, abstract, article title, authors, and MeSH terms was printed. The bibliography was used to screen articles for inclusion.

A large number of retrieved articles were considered ineligible for meta-analysis because they did not investigate an individually administered intervention for neurogenic dysphagia. In fact, the majority of citations discarded in the initial screening reported the results of diagnostic comparisons (new clinical tests vs. gold standard instrumental examinations), or were strictly descriptive in nature without systematically maintaining participant assignment to randomized treatments or follow up to outcome. Additional citations were excluded because their investigations involved the treatment of neurological diseases themselves, reduction of stroke risk, or treatment to increase post-stroke survival with surgical and medical interventions, without components addressing the management of post-stroke dysphagia. Specifically, many excluded studies looked at the effects of anticoagulation on cardioembolic stroke risk after first stroke, carotid endarterectomy on stroke risk, effects of intravenous immunoglobulin treatment on exacerbation recovery in multiple sclerosis, and effects of tissue plasminogen activator on

stroke evolution after early presentation of symptoms of stroke. Other studies deemed inappropriate for this meta-analysis addressed surgical or pharmaceutical interventions on some aspect of the underlying disease that caused dysphagia within populations of neurologically impaired patients. It is apparent that this set of excluded articles was retrieved by the search strategy because the presence of neurogenic dysphagia was mentioned in their abstracts.

Some studies were ineligible because they did not contain data or were subjective in nature. Articles which reported results or opinions produced through anecdote, case report, editorial, or letters to editors, and studies that were overtly observational or retrospective in nature, were excluded to ensure adequate evidence quality (Straus, Richardson, Glasziou, & Haynes, 2005). The capture of these citations was unexpected given the meticulously planned search strategies used. However electronic databases captured citations that contained search terms in the publication's title or abstract, or in the key words provided by the authors. As a result studies of individual cases, whose abstracts discussed the need for a randomized controlled trial, were captured by the electronic search.

Several articles did not investigate treatment methods in patients with stroke or other neurogenic dysphagia. Investigations of treatment methods in normal healthy subjects, studies describing the natural history of dysphagia in various diseases, and those in which intervention consisted of diagnosis alone, were also excluded as they did not pertain to the constructs under investigation.

Other studies were excluded because they investigated predictive value of clinical tests (i.e., bedside evaluation), compared two or more types of enteral feeding tube outcomes in patients with and without swallowing disorders, or they evaluated treatments that mitigated or prevented the primary disease (i.e., stroke) without a focus on oropharyngeal dysphagia.

5.3.2 Evaluation of Retrieved Citations

Once inappropriate studies were discarded, a priori inclusion criteria were applied to the remaining citations to detect any articles that did not meet minimum acceptable criteria for research design, sample size, and level of controls used by investigators to ensure adequate internal and external validity. The principal investigator conducted all evaluation of citations and he was not blinded from authors' names.

After the initial first-pass screening procedures, 60 citations remained. These studies fell within two distinct and complementary constructs of oropharyngeal dysphagia treatment and management. Forty-seven of these 60 remaining studies investigated the *efficacy* of individually administered dysphagia interventions for treating discrete, instrumentally measured biomechanical impairments in patients with neurogenic dysphagia in controlled experimental conditions. Thirteen of these 60 studies investigated the *effectiveness* of institutional dysphagia protocols in reducing global health outcomes such as pneumonia and mortality in patients with neurogenic dysphagia. Since these two types of studies were incompatible for combination into a single meta-analysis, it was deemed necessary to conduct two meta-analyses to adequately assess both types of data (i.e., short-term dysphagia treatment effects, and long-term global health outcomes). Ultimately, six studies were entered into the first meta-analysis of the effects of individually administered interventions for neurogenic dysphagia, and three remained in the second meta-analysis of the effects of organized, institutional dysphagia management protocols on public health outcomes.

5.3.2.1 System Used to Rate Evidence Quality

Evaluation of evidence quality for both meta-analyses was performed using methods published by Baker and Tickle-Degnen (2001), which were reduced to a screening form (Appendix D), to evaluate the quality of retrieved studies. This rating system is used to classify studies on the basis of four parameters: investigational design, sample size, experimental controls for internal validity, and experimental controls for external validity. This rating system is clearer and more informative to the consumer of the meta-analysis than other publication ranking systems because it maintains separate scores for each of the four parameters of interest rather than forming a single composite score.

Research design is scored on the basis of the type of investigation. Randomized controlled experimental trials (RCT) and repeated-measures trial with randomized sequence of treatments receiving the highest design ranking ("I") using this system. Non-randomized controlled trials, two-group non-randomized including a treatment and control group, and non-randomized, repeated measures designs with at least two conditions, received a design score of "II". A score of "III" is assigned to non-RCT studies of a single group, and single group pre-post studies. Studies consisting of single subject or one-person pre-post studies, and case studies are scored "IV" and "V", respectively. These latter scores were ineligible for inclusion in either meta-analysis.

Sample size is scored "A" for 20 or more participants or observations per group, and "B" for fewer than 20. In the studies representing the construct of the first meta-analysis of individually administered interventions for neurogenic dysphagia, few studies of 20 or more participants were available, so the minimum sample size score was set at "B". In the final sample of six studies, three had samples of greater than 20 participants. However the studies

representing the construct for the second meta-analysis included large scale investigations of at least 50 participants. For this reason, a sample size score of "B" was considered acceptable for the first meta-analysis, and "A" for the second meta-analysis.

Controls for internal validity judged by this coding system include the rigor in which a) randomized assignment of patients to treatment was conducted, or efforts to create similar groups were carried out, b) judges were blinded to patient assignment, c) judges were masked to measures performed by other judges, d) patients were analyzed in the groups to which they had been randomized and there was no unaccounted for attrition of participants, e) the authors presented justifiable, scientific rationale for the proposed effects of the intervention under investigation. A score of "1" (high internal validity) is assigned to studies in which no alternative explanation for the observed outcome is probable, and in which controls to eliminate internal experimental sources of error and bias were excellent. A score of "2" indicates moderate internal validity, with evidence of reasonable attempts to control for biases imposed by lack of randomization or other errors. A score of "3", low internal validity, indicates that two or more serious alternate explanations for the treatment outcome exist, or in which serious bias is evident. Control for attrition of subjects is an important characteristic of well controlled scientific investigation. For this reason, studies that exhibited attrition of more than 10% of participants were scored "3" in this category. Studies scoring "3" in internal validity were not eligible for either meta-analysis.

Controls for external validity judged by this coding system include the degree to which a) the patients investigated represented the population of interest, b) the sample of patients was sufficiently homogeneous to enable the ability to discern the treatment effects on the target population, c) the treatments represent current practice, or are publicly available and feasible

methods in clinical settings. A score of “a” indicates high external validity, with the participants investigated homogeneously representing the target population and the intervention methods representing current clinical practice. A score of “c” is assigned to studies with heterogeneous samples, the inability to determine whether treatment effects differed by diagnosis, or the interventions do not represent current clinical practice. A score of “b”, moderate external validity, is assigned to studies with characteristics between high and low external validity. Studies scoring “c” in external validity were not eligible for either meta-analysis.

Minimum acceptable inclusion criteria are specified fully in the appropriate subsections of this chapter. The next sections of this chapter describe all procedures performed for the two meta-analyses: section 5.4 discusses the procedures used in the first meta-analysis, and section 5.5 summarizes the procedures used in the second meta-analysis.

5.3.2.2 Measurements Performed on Included Studies

Studies which remained eligible after all evaluative processes were completed, underwent calculation of individual effect size and computation of the summary effect size for all articles included in each meta-analysis. Each meta-analysis underwent testing to determine individual and summary effect sizes, statistical significance, and homogeneity of the sample (as seen in flow-chart diagram-Figure 1). Statistical procedures differed between the two meta-analyses because the types of data in the first meta-analysis produced effect sizes that cannot be combined with those in the second meta-analysis. However each meta-analysis included the same four components: testing of the individual studies to determine their effect sizes, calculation of combined effect sizes for all studies included in the meta-analysis, testing of statistical significance of the results of the combined effect size calculations, and evaluation of the

homogeneity of the sample. The different methods employed in each meta-analysis will be addressed in subsequent sections of this chapter.

5.4 META-ANALYSIS OF INDIVIDUALLY ADMINISTERED INTERVENTIONS FOR NEUROGENIC DYSPHAGIA

5.4.1 Evaluation of Citations: Evidence Quality for Inclusion

5.4.1.1 Acceptable Dependent Variables

To be eligible for inclusion in this meta-analysis of individually administered behavioral and physiologic treatments designed to eliminate biomechanical swallowing impairments, studies were required to objectively measure the intervention's effect on the investigated dependent variables. The dependent variables were required to be objective, and they had to either directly indicate the abnormal flow of swallowed material into the airway (e.g., aspiration, laryngeal penetration-aspiration scores) or incomplete flow of material into the digestive system (e.g., bolus separation by prematurely closing UES). Other dependent variables that were acceptable for this meta-analysis were those that can be observed with instrumental testing (i.e. videofluoroscopic evaluation of swallowing, fiberoptic evaluation of swallowing), and had been previously and established as predictors of the misdirection of swallowed material into the upper airway (e.g., incomplete laryngeal closure, prolonged duration of stage transition), or of incomplete clearance of swallowed material into the digestive system (e.g., reduced diameter or duration of UES opening). Appendix B includes a review of several of these impairments and descriptions of their effects on pulmonary health and nutrition.

Since stroke and neurological disease impair swallowing function and cause patients to aspirate swallowed material, the biomechanical dependent variables influenced by the studies' treatment modalities must have been previously validated as objective risk factors for aspiration or reduced intake of nutrients and fluids into the digestive system.

Biomechanical Impairments Leading to Aspiration

To be considered a validated objective risk factor for aspiration or inadequate oral intake, the dependent variables in eligible studies had to first predispose the patient to aspiration of some or all of the swallowed food or liquid, or result in ineffective transfer of swallowed material into the digestive system. Second, each acceptable dependent variable had to previous show to increased risk of pneumonia, reduced nutritional intake, or dehydration in dysphagic patients.

For example, prandial aspiration is well documented as a primary source of aspiration pneumonia. However unlike aspiration, other swallowing outcomes, such as the need for the patient to swallow more than once to completely deliver a bolus of food into the esophagus, do not directly influence the risk of dysphagia-related pulmonary disease or nutritional compromise. Hence, elimination or reduction of aspiration during swallowing qualified as an acceptable dependent variable for this meta-analysis, while the need to swallow more than once to clear a swallowed bolus did not qualify as an acceptable dependent variable, unless the need to swallow more than once was caused by other impairment such as impaired UES opening during the swallow.

Biomechanical Impairments Affecting Digestive Function

Eligible studies were required to demonstrate the existence of biologically defensible evidence that their investigated treatment methods were protective of the airway during

swallowing and/or were beneficial for the effective transfer of swallowed material into the digestive system. Studies exclusively reporting data relating to outcomes that lacked sufficient evidence of established validity, such as percent of bolus aspirated, percent of bolus retained in pharynx, and subjective swallow function scales without evidence of validation and standardization, were deemed ineligible.

Description of Acceptable Dependent Variables

The biomechanical variables of deglutition qualifying as acceptable dependent variables for included articles in this meta-analysis were those that could be modified by direct treatment. They included a) the duration of specific physiologic events and phases of swallowing, such as the duration of pharyngeal transit, duration of airway closure, and duration of upper esophageal sphincter opening; b) the distance of motion of anatomical structures responsible for safe and efficient swallowing, such as displacement of the hyolaryngeal complex, which is largely responsible for closure of the upper airway and distension of the upper esophageal sphincter; c) closure of the larynx during the swallow. (Please note that the phases of normal swallowing and aspects of swallowing that can be modified were discussed in detail in Appendices A and B, respectively).

Specifically, the duration of specific physiologic events, such as oral to pharyngeal stage transition (also known as pharyngeal delay time), total swallow duration, pharyngeal response duration (duration of pharyngeal activity during the swallow), pharyngeal transit duration (duration of bolus flow through the pharynx), duration of upper esophageal sphincter opening, and duration of laryngeal closure, expressed in standard units of time, were eligible dependent variables for this meta-analysis (Logemann, 1998; Robbins, 1987). Measures expressing distance in standard units of length, including vertical and horizontal hyolaryngeal displacement,

laryngeal closure diameter, lingual to posterior pharyngeal wall contact range, and diameter of opening of the upper esophageal sphincter, were also eligible (Cook et al., 1989b; McConnel et al., 1988; Robbins et al., 1992; Robbins, Levine, Maser, Rosenbek, & Kempster, 1993). Objective observations of aspiration or UES opening, expressed in dichotomous terms, were also acceptable.

For a published study's dependent variable to be considered an objective biomechanical or physiologic measure, it had to have been obtained through an objective instrumental procedure such as videofluoroscopy. By including only studies measuring objective dependent variables, the validity of the observations could be more readily ensured. The use of imaging data enabled the judges in the various studies to continuously observe and quantify the targeted oropharyngeal structures (i.e., their dependent variables) throughout all swallow events. In addition, the dependent variables must have been recorded/measured both before and after treatment in single group studies and in studies with two or more groups.

Qualitative measures of ineffective or inefficient bolus transfer including measures of postprandial, hypopharyngeal residue, were eligible if they had previously been validated as predictive of postprandial aspiration (Eisenhuber et al., 2002; Murray, Langmore, Ginsberg, & Dostie, 1996; Perlman, Booth, & Grayhack, 1994).

Eligible airway compromise dependent variables were required to be dichotomous (aspiration present or absent), or continuous, using validated instruments. For example, the Penetration Aspiration Scale scores airway compromise using an ordinal eight-point scale containing descriptors of anatomic depth of airway compromise and patient response to airway compromise (Rosenbek, Robbins, Roecker, Coyle, & Wood, 1996a).

Data Types Acceptable for Inclusion

Studies were required to have reported either continuous or dichotomous measures from their dependent variables, to be eligible for inclusion in both meta-analyses, though ultimately, studies eligible for the first meta-analysis overwhelmingly reported continuous data, and those eligible for for the second meta-analysis reported dichotomous data.

5.4.2 Acceptable Treatment Methods

The system used to rate the quality of published studies considered for inclusion, has been reviewed in section 5.3.2.1. The overall minimum acceptable score for this meta-analysis was "III, B 2 b" (Baker & Tickle-Degnen, 2001). Interventions that manipulated the dependent variables discussed in the previous section, were eligible for inclusion provided the studies in which they were reported met the criteria for evidence equality outlined in the next section, and had been previously shown to produce the hypothesized physiologic effects.

5.4.2.1 Design and Sample Size

A priori criteria for eligible investigation designs included randomized controlled trials, repeated measures designs with randomized treatment sequences, cohort two-group treatment designs with treatment versus control without random assignment, cohort non-randomized repeated measures designs with two conditions with non-selective assignment of patients to treatment, and cohort one-group pre-post treatment trials. Retrospective designs were ineligible as were post-hoc analyses of secondary outcomes data from investigations of other main hypotheses. Thus, the minimum acceptable design rating score for inclusion into this meta-analysis using the Baker and Tickle-Degnen (2001) rating system was "III."

Few of the retrieved citations representing the construct under investigation in this meta-analysis, investigated groups of 20 subjects per treatment. As a result, the acceptable minimum sample size was 10 or more patients per group, or 10 or more patients examined during both the experimental and control conditions in single group studies. Thus, the minimum acceptable sample size rating score for inclusion into this meta-analysis using the same rating system was "B" (Baker & Tickle-Degnen, 2001).

5.4.2.2 Validity

Studies were required to possess sufficiently robust evidence of controls to maintain internal and external validity, as defined by Baker and Tickle-Degnen (2001) and summarized in the screening form displayed in Appendix D.

Internal Validity

Internal validity was required to be moderately high for inclusion in this meta-analysis. To be eligible for inclusion, studies were required to report or demonstrate 4 of the 5 following criteria: a) effort to control for sources of bias and error caused by lack of randomization; b) evidence of blinding of judges to participant assignment and to other judges' scores; c) masking of participants when appropriate; d) equal treatment outside of experimental and control conditions; and e) reasonably robust methods so as to eliminate alternative explanations for the outcomes. Random assignment to treatment groups and/or random ordering of control and experimental treatments in investigations of two or more treatments were preferable for inclusion. However, since the criteria for inclusion were developed a priori, and since there are few published randomized trials investigating the constructs of interest (Doggett et al., 2001),

studies demonstrating sufficient internal experimental controls as to eliminate bias caused by lack of masking or randomization were also considered eligible.

External Validity

External validity was required to be moderately high for inclusion in this meta-analysis. To be eligible for inclusion, studies were required to report or demonstrate a least 3 of the following 4 criteria: a) both treatment and control groups must represent homogeneous, neurogenic, dysphagic populations that ordinarily receive the interventions of interest; b) all treatments investigated are within the scope of current clinical practice for dysphagic patients with biomechanical swallowing impairments as identified in current dysphagia treatment textbooks and/or practice guidelines published by agencies such as the American Speech Language and Hearing Association; c) studies exhibited no evidence of a possible alternate explanation for the observed outcome; d) studies exhibited no evidence of a potential conflict of interest.

Therefore, using the rating system described by Baker and Tickle-Degnen (2001), the minimum acceptable internal and external validity rating scores for inclusion into this meta-analysis were “2” and “b,” respectively.

5.4.3 Methods

5.4.3.1 Minimum Acceptable Criteria for Eligibility

A priori methods of determining eligibility were employed across the 60 citations remaining eligible after first-pass screening.

Using the rating and coding method described earlier and, the minimum combined score for inclusion into the meta-analysis of investigations of treatments for dysphagia biomechanical impairments, was "III B 2 b". Therefore, minimum eligibility criteria included a non-randomized, controlled trial of one group or one group pre- post trial with at least 10 participants per group or condition and demonstrated moderately high control to maintain internal and external validity. A final set of six articles remained for this meta-analysis, and the results of the evidence quality evaluation are displayed in **Error! Reference source not found.**.

Table 1. Quality Evaluation of Included Studies-Treatment of Biomechanical Impairments

First Author, Rating	Design	Sample Size	Internal Validity	External Validity
Studies of Individually Administered Interventions for Neurogenic Dysphagia (continuous data)				
Shanahan, 1993 III A 1 a	Cohort pre-post	30 Neurogenic, liquid aspirators	High	High
Logemann, 1995 III B 2 b	Cohort pre-post	19 Stroke with pharyngeal delay	Moderate	Moderate
Rosenbek, 1996 III A 2 b	Cohort pre-post	22 Multiple Stroke, dysphagia	Moderate	Moderate
Rosenbek, 1998 III A 1 b	Cohort, random assignment to four dosage groups	43 Stroke with pharyngeal delay	High	Moderate
Shaker, 2002 III B 2 b	Cohort, pre-post	18 Neurogenic dysphagia; tube fed	Moderate	Moderate
Ludlow, 2007 III B 1 b	Cohort pre-post	10 tube fed; chronic neurogenic	High	Moderate

The 6 studies included in the final meta-analysis investigated the effects of individual therapeutic interventions designed to manage oropharyngeal biomechanical impairments that are

expected to cause adverse health sequelae. All 6 studies contained sufficient raw data or results to enable calculation of effect sizes.

5.4.4 Data Extraction

5.4.4.1 Description of Included Studies

A priori criteria for inclusion in the meta-analyses were applied to the 60 remaining citations. Despite casting a broad net to capture studies of treatment of all forms of neurogenic dysphagia, the studies of adequate evidence quality were almost entirely limited to investigations of dysphagia after stroke. As a result, the evidence quality evaluation rendered a final sample of six investigations of treatment investigating the efficacy of individually administered interventions for neurogenic dysphagia caused primarily by stroke (described in the first meta-analysis of this chapter), and three investigations of the effectiveness of institutional dysphagia protocols (described in the second meta-analysis of this chapter).

The 6 studies included in this meta-analysis investigated treatment methods that were designed to eliminate aspiration, increase the flow of swallowed material into the esophagus, increase airway closure, or reduce the delay of the pharyngeal stage onset (Logemann et al., 1995; Ludlow et al., 2007; Rosenbek et al., 1998; Rosenbek, Roecker, Wood, & Robbins, 1996b; Shaker et al., 2002; Shanahan, Logemann, Rademaker, Pauloski, & Kahrilas, 1993). All the impairments observed as dependent variables in these investigations had been demonstrated in prior research to be predictors or direct causes of dysphagia-related pulmonary sequelae of aspiration or of nutritional disability (Eisenhuber et al., 2002; Langmore et al., 1998; Logemann, 1998; Murray et al., 1996; Rosenbek, Robbins, Fishback, & Levine, 1991). The characteristics of these 6 studies are summarized in Table 2 and described below.

Shanahan et al. (1993) investigated the immediate effect of flexion of the head and neck (chin down posture), compared to swallowing in the neutral head position, on changing protective position of the epiglottis over the laryngeal inlet, diameter of the unprotected laryngeal inlet, and on aspiration, in 30 patients with neurogenic dysphagia. This study generated data regarding biomechanical variables of interest as well as dichotomous data regarding aspiration. Fifty percent of aspirating patients did not aspirate while employing the chin-down posture during the swallow. These two data types (continuous vs. dichotomous) were incompatible for combination in the meta-analysis, but the inclusion of this information regarding aspiration must be considered as augmenting the true efficacy of this clinical method.

Logemann et al. (1995) investigated the immediate effects of sensory stimulation, through the addition of sour flavoring to liquid barium during radiographic evaluation, comparing it to unflavored barium, on biomechanical swallowing impairments including duration of stage transition, and oral and pharyngeal transit durations in 27 patients with neurogenic dysphagia, including 19 patients with stroke. The eight patients with non-stroke neurogenic dysphagia were analyzed using different dependent variables that have not been shown to directly influence aspiration or health sequelae. For this reason these data were not included in the meta-analysis. One of the variables reported by the authors in the data for the stroke patients was excluded from analysis (oral pharyngeal swallowing efficiency score) because it has not been validated.

Rosenbek et al. (1996b) investigated the effects of a cold, tactile stimulus (thermal tactile application) to the anterior faucial pillars in 22 patients with dysphagic stroke. Outcome measures of interest were changes in the duration of stage transition, also known as duration of

pharyngeal delay, and total swallow duration, between the stimulated and unstimulated swallows.

Rosenbek et al. (1998) later conducted a larger study using thermal tactile application to the anterior faucial pillars in doses of 150 to 600 stimuli per day over two weeks, in 43 patients with dysphagic stroke. Differences between dosage groups' performance in duration of stage transition and in airway penetration and aspiration were reported.

Shaker et al. (2002) investigated the effects of 6 weeks of an exercise program on upper esophageal sphincter (UES) opening duration and diameter in 18 feeding tube-dependent patients with chronic neurogenic dysphagia. This study initially randomized 11 patients to experimental and 7 patients to "sham" (false) treatments, after which the investigators ceased random assignment of patients. All 18 subjects underwent pre- and post-treatment biomechanical examinations with videofluoroscopy and the authors published complete data from this group of participants. Raw data from patients randomized to the treatment group were published, but raw data from the sham treatment group were not published (only "non-significance" was reported for this group). As a result, the data generated by the cohort of randomized subjects (i.e., the first 11 subjects), who underwent pre- and post-treatment testing, were converted to effect sizes and included in this meta-analysis, as it possessed the required levels of evidence quality described above. Additionally, the result from the original randomized component of the trial that took place before randomization was corrupted, in which 11 treated patients were compared to seven control patients, was included. This component found no significant differences between groups ($p = .40$). This significance level was converted to an effect size and included in the meta-analysis along with the two other effect sizes computed from raw data. Because of the

two types of comparisons included, the lower of the two (pre-post cohort) was used to classify the study.

Ludlow et al. (2007) investigated the effects of neuromuscular electrical stimulation to the anterior neck on laryngeal and hyolaryngeal range of motion during swallowing, in 10 patients with chronic neurogenic dysphagia by collecting baseline unstimulated swallows, treating the patients for two weeks (per the method's proprietary protocol), and then repeating baseline testing. Two levels of electrical stimulation were employed while the patients swallowed during videofluoroscopic swallowing studies. All 10 patients underwent testing with one level of stimulation (sensory) but only eight underwent testing with the higher stimulation intensity (motor). Several physiologic dependent variables were analyzed and reported by the authors, but most have not previously been shown to directly influence aspiration or health sequelae. The only dependent variables qualifying for meta-analysis were airway penetration-aspiration scores. The reason that this study's publication data appears outside of the prospective date range is that the study was made available electronically in December 2006; however its official publication date and print version appeared in January 2007.

Table 2. Studies of Individually Administered Interventions for Neurogenic Dysphagia

First Author, Year	Patients	Treatment Method	Comparison Method	N: Patients, Controls	Dependent variables
Shanahan, 1993	Neurogenic Dysphagia	Chin down posture (head-neck flexion while swallowing)	Neutral posture while swallowing	30 pre/post	Airway diameter, position of epiglottis over airway, aspiration
Logemann, 1995	Dysphagic Stroke	Sour barium bolus	Unflavored barium bolus	19 pre/post	Duration of stage transition; oral and pharyngeal transit durations
Rosenbek, 1996b	Dysphagic Stroke	Thermal tactile application	No stimulation	22 pre/post	Duration of stage transition, total swallow duration
Rosenbek, 1998	Dysphagic Stroke	Thermal tactile application	Varying dosages vs. baseline	43 pre/post	Duration of stage transition, airway penetration or aspiration scores
Shaker, 2002	Tube fed Dysphagic	Exercise of neck flexor group	Sham exercise	18 pre/post *11 Treatment, 7 control.	UES opening duration and diameter
Ludlow, 2007	Neurogenic Dysphagia	Electrical Stimulation (two dosages: sensory, motor)	No stimulation	10 pre/post (sensory stim.) 8 pre/post (motor stim.)	Airway penetration or aspiration scores

*This study violated randomization after 18 (10 treatment, 8 control) patients; and it reported pre-post data for treatment patients only. Statistical significance only, of the randomized trial, was reported. Only these results for these 18 patients were included in the meta-analysis.

5.4.5 Statistical Procedures

Researchers have traditionally reported the results of their studies in terms of statistical significance levels. Significance levels express the results as products of formulae that combine

information about the size of the experimental effect with the size of the study (Rosenthal, 1994). Statistical significance is an essential marker used to indicate whether experimental observations are influenced by experimental manipulations (Straus et al., 2005).

There are two disadvantages of relying solely on statistical significance to quantify treatment effect. First, statistical significance can be influenced by the size of the sample. The significance of a given experimental effect on a dependent variable may appear greater in experiments with very large samples than it appears in the same experiment with a smaller sample even without a corresponding difference in the magnitude of the effect between the large and small samples (Watala, 2007). Second, statistical significance fails to reveal the magnitude of the experimental effect for an individual patient for whom it may be considered a therapeutic option (Sackett, Straus, Richardson, Rosenberg, & Haynes, 2000), because a test statistic is derived by combining information about the effect of the treatment with the size of the sample investigated. As a result the magnitude of the treatment's effect on the average patient in the sample cannot be surmised (Rosenthal, 1994).

Modern published behavioral and biomedical research has begun to supplement statistical significance with additional information about the magnitude of the experimental effects on their dependent variables (Rosenthal & Rubin, 1982). These estimates of magnitude, or effect sizes, express the magnitude of the effect of one variable on another on the average subject within the experiment (Cohen, 1988). The various methods of measuring effect size described in the literature include estimation strategies for variables expressed as continuous, dichotomous, multiple choice, or ranked data. These indices provide the research consumer an indication of the expected effects of a particular treatment method on specific outcomes in the average patient. Rosenthal (1994) discussed two families of parametric effect size measurements that are

interchangeable as well as calculable from a variety of published data and statistics: the *r* family and the *d* family. These have been increasingly common in modern published meta-analytic work.

5.4.5.1 Effect Sizes: Individually Administered Interventions for Neurogenic Dysphagia

The *r* family of effect size statistics expresses the effect size as a relationship between treatment and outcome and includes the familiar Pearson product moment correlation as well as the Fisher transformation of *r*, and various methods using the squared correlation coefficient *r*. Rosenthal and Rosnow (1982) prefer the unsquared *r* because it is directional. Unlike r^2, *r* indicates whether the observed change caused by the experimental treatment is positive or negative. The related *d* family includes Cohen's *d* and Glass's *d* which express effect size as proportions of group raw differences to a measure of variance within the groups.

Cohen's *d* and the effect size correlation *r* are closely related, and express essentially identical information about effect size. Cohen (1988) has translated the scale of *d* scores into verbal ratings of effect size, with a *d* of 0.2 indicating a small effect size, 0.5 medium, and 0.8 large. Aaron et al. (1998) have published calculations for translating *d* to *r* for the purposes of equating Cohen's ratings of effect size, in terms of the numbers of participants in each group (treatment, control). Table 3 displays the qualitative labels *small*, *medium*, and *large*, per Cohen (1988) in the left column, the values for Cohen's d in the center column, and the range of values of the effect size correlation coefficient, *r*, for five subjects per group (the third column) and 100 subjects per group (the fourth column) (Aaron, Kromrey, & Ferron, 1998).

For this meta-analysis, the effect size correlation *r* was selected as the index of summary effect size as it is a widely accepted index of summary effect size for combined studies in meta-analysis.

Table 3. Estimated *r*, from Cohen's *d* (Aaron, et al., 1998).

Size of effect	Cohen's *d*	*r* (n=5)	*r* (n=100)
Small	.2	.1000	.1111
Medium	.5	.2437	.2692
Large	.8	.3730	.4083

5.4.5.2 Effect Size Calculations

A fixed effects model was used to determine the individual effect size for each included study and the summary effect size for the group of included investigations.

The 6 studies included in this meta-analysis reported results using continuous dependent variables, and generated a range of summary results including measures of central tendency, computed p values, and exact values of a statistic, enabling conversion of results into a common index of effect size: the effect size correlation coefficient (*r*). Effect sizes (*r*) were computed for each study.

Three studies reported the results of their experiment on the dependent variables using means and central tendency measures (Rosenbek et al., 1996b; Shaker et al., 2002; Shanahan et al., 1993). For these three studies effect sizes were calculated using means and standard deviations. Cohen's d was calculated using Equation 1, displayed below, where M_2 is the mean score for the experimental or treatment group, M_1 is the mean score for the control group, and SD_{pooled} (Equation 2) is the pooled standard deviation from both group's data (Hassleblad & McCrory, 1995; Rosenthal & Rosnow, 1991). In studies that published standard errors, conversion to standard deviation was first performed using Equation 3 (Streiner, 1996). The effect size *d* was then converted to the effect size correlation coefficient *r* using Equation 4 (Rosenthal & Rosnow, 1991).

Equation 1. Cohen's d

$$d = \frac{M_t - M_c}{SD_{pooled}}$$

Equation 2. Pooled Standard Deviation for Cohen's d

$$SD_{pooled} = \sqrt{(SD_t^2 + SD_c^2)/2}$$

Equation 3. Conversion of Standard Error to Standard Deviation

$$SD = SE(\sqrt{N})$$

Equation 4. Effect Size Correlation Coefficient (*r*) derived from Cohen's d

$$r = \sqrt{\frac{d^2}{d^2 + 4}}$$

Additionally, one variable reported in Shanahan et al. (1993), aspiration, was reported in terms of presence or absence both before and after intervention. All 30 patients aspirated before treatment. While using the intervention during swallowing, 15 of 30 patients aspirated, representing a 50% reduction in aspiration using the intervention.

Two studies reported only *p* values (Logemann et al., 1995; Rosenbek et al., 1998). The *p* values were converted to *Z* scores (one-tailed), using a *Z* score probability table (Rosenthal & Rosnow, 1991). Effect size *r* (Pearson product-moment correlation coefficient) was then computed using Equation 5 (Rosenthal, 1994).

Equation 5. Effect Size Correlation Coefficient (*r*) derived from Z score

$$r = \frac{Z}{\sqrt{N}}$$

One study reported its results in terms of the exact *t* statistic (Ludlow et al., 2007). This result was converted to the effect size (*r*) by using Equation 6 (Rosenthal, 1994). Each effect

size then underwent computation of standard error, 95% confidence intervals, *Z* scores, and statistical significance using Rosenthal's methods (1994), and were plotted (see Figure 2).

Equation 6. Effect Size Correlation Coefficient (*r*) derived from an Exact T statistic

$$r = \sqrt{\frac{t^2}{t^2 + df_e}}$$

5.4.5.3 Combining Effect Sizes for Meta-Analysis

In order to determine the overall effect size for included studies, correlations were first converted by using a Fisher's z transformation of *r* table, which reflects the results of Fisher's variance stabilizing *z* transform (Equation 7), where *ln* is the natural base logarithm (Shadish & Haddock, 1994).

Equation 7. Fisher's *z* transformation of *r*

$$z = .5\{\ln[(1+r)/(1-r)]\}$$

The product of this transformation, referred to as Fisher's transformed *r*, or "T_r", has advantages over the Pearson *r* that render it preferable for use in meta-analysis, including its more rapid convergence to normality than the Pearson *r* (Lipsey & Wilson, 2001). After transforming each effect size *r to* T_r, the variance of each T_r (v_r) was computed using Equation 8, and the standard error for each transformed *r* was computed by taking the square root of the computed variance for each transformed *r* (Shadish & Haddock, 1994).

Equation 8. Variance of Fisher's *r*

$$v_r = \frac{1}{n-3}$$

Upper and lower limits of confidence intervals around each transformed *r* were then computed using Equation 9, where SE_r = the standard error of T_r.

Equation 9. 95% Confidence Interval for Fisher's Transformed *r* (T_r)

$$95\%C.I. = T_r \pm 1.96(SE_r)$$

All mean T_r and the upper and lower limits of their confidence intervals were then transformed back to Pearson *r* using the Fisher's z transformation of r table. Z scores were then computed using Equation 10, and p values were obtained for each study using the *Z* probability table.

Equation 10. Computing Z Score from Effect Size Correlation Coefficient (*r*)

$$Z = r(\sqrt{n})$$

The mean effect size (*r*) with its 95% confidence interval, Z score and p value for the entire sample of studies was then calculated, and a forest plot was generated to display the results (Figure 2).

5.4.5.4 Assessment of Homogeneity of the Sample

Combining effects sizes of several studies to derive an estimate of the effects of their underlying common construct is valid when the combined studies can be shown to cause similar effects within the population of typical patients receiving the treatments. Shadish and Haddock (1994) developed statistical tests to detect the absence of homogeneity within a sample of studies, some of which were used to assess the homogeneity of the 6 qualifying studies. The *Q* statistic, or null test of homogeneity among individual effect sizes, which follows the chi-square distribution, is a measure of significance across several means. The null hypothesis of this test of homogeneity is that the studies are perfectly homogeneous. Thus, a non-significant result of test, indicates that homogeneity of the sample is not rejected and the effect sizes of the studies in the sample are not significantly heterogeneous. Additionally a non-significant result indicates that the effect sizes of the included studies represent the same population effect size (Hedges, 1994; Shadish &

Haddock, 1994). The *Q* statistic is derived from the squared difference between the computed effect sizes from each treatment study in the meta-analysis and the overall computed effect size for the meta-analysis. It is weighted by the inverse of the computed variance of the study's treatment effect. It is calculated using Equation 11, where w_r = the inverse of the variance of the meta-analysis, and T_r is the Fisher's transformed effect size correlation coefficient for the meta-analysis. Computed *Q* is then compared to the critical value of Q, defined as the chi-square statistic at $p \leq 0.05$ with $k - 1$ degrees of freedom, where *k* equals the number of included studies, and where $df = k - 1$. If the computed *Q* does not exceed the critical value of Q, the result of the homogeneity test is non-significant, and the null hypothesis is accepted.

Equation 11. Q Statistic – Continuous Data

$$Q = w_r (T_r)^2 - \frac{(w_r T_r)^2}{w_r}$$

5.4.6 Results

5.4.6.1 Effect Sizes of Individually Administered Interventions for Neurogenic Dysphagia

Individual effect sizes and confidence intervals for the 6 studies were computed. Mean effect size for the construct "individually administered interventions for neurogenic dysphagia" was computed and the homogeneity of the sample was tested. A forest plot was produced to display the results. The effect sizes for all but two of the included citations (Ludlow et al., 2007; Rosenbek et al., 1998) reached statistical significance.

Table 4 displays the effect sizes (*r*) with their respective 95% confidence intervals, *Z* scores, and statistical significance, for each of the individual treatment studies of the effects of individually administered interventions for neurogenic dysphagia, along with a display of the

same parameters for the group of studies as a whole. Figure 2 displays the forest plot of the effect size summary. Effect sizes for the individual studies and the summary effect size (shown on the uppermost line of the figure) are represented by the square points, with their 95% confidence intervals represented by the diamond (lower limit of confidence interval) and triangle (upper end of confidence interval). The dotted vertical line represents the overall effect size (r = .29) to provide context for the individual studies' results.

The overall or summary effect size for the construct "individually administered interventions for neurogenic dysphagia" was r = .29 (95% CI: .17 - .39), which represents a medium to large effect using Cohen's (1988) descriptors of effect size, and after equating effect size correlation coefficients (r) and Cohen's d (Aaron et al., 1998). This result was statistically significant ($Z = 1.87$; p = .03). Individual effect sizes ranged from a "small" low of r = .13 (95% CI: -.33 - .55; Z = 0.56; p = .26) to a "large" high of r = .45 (95% CI: .18 - .66; Z = 2.98; p = <.01).

Table 4. Effect Sizes: Individual Interventions for Neurogenic Dysphagia

Author	Effect size (*r*)	95% C. I.	*Z*	*p*
Summary effect size	**.29**	**.17 - .39**	**1.87**	**.03**
Shanahan, et al., 1993	.25	.00 - .47	1.98	.03
Logemann, et al., 1995	.43	.13 - .66	2.65	<.01
Rosenbek, et al., 1996	.45	.18 - .66	2.98	<.01
Rosenbek, et al., 1998	.14	-.07 - .35	1.30	.10
Shaker, et al., 2002	.30	.01 - .72	1.74	.02
Ludlow, et al., 2007	.13	-.33 - .55	0.56	.26

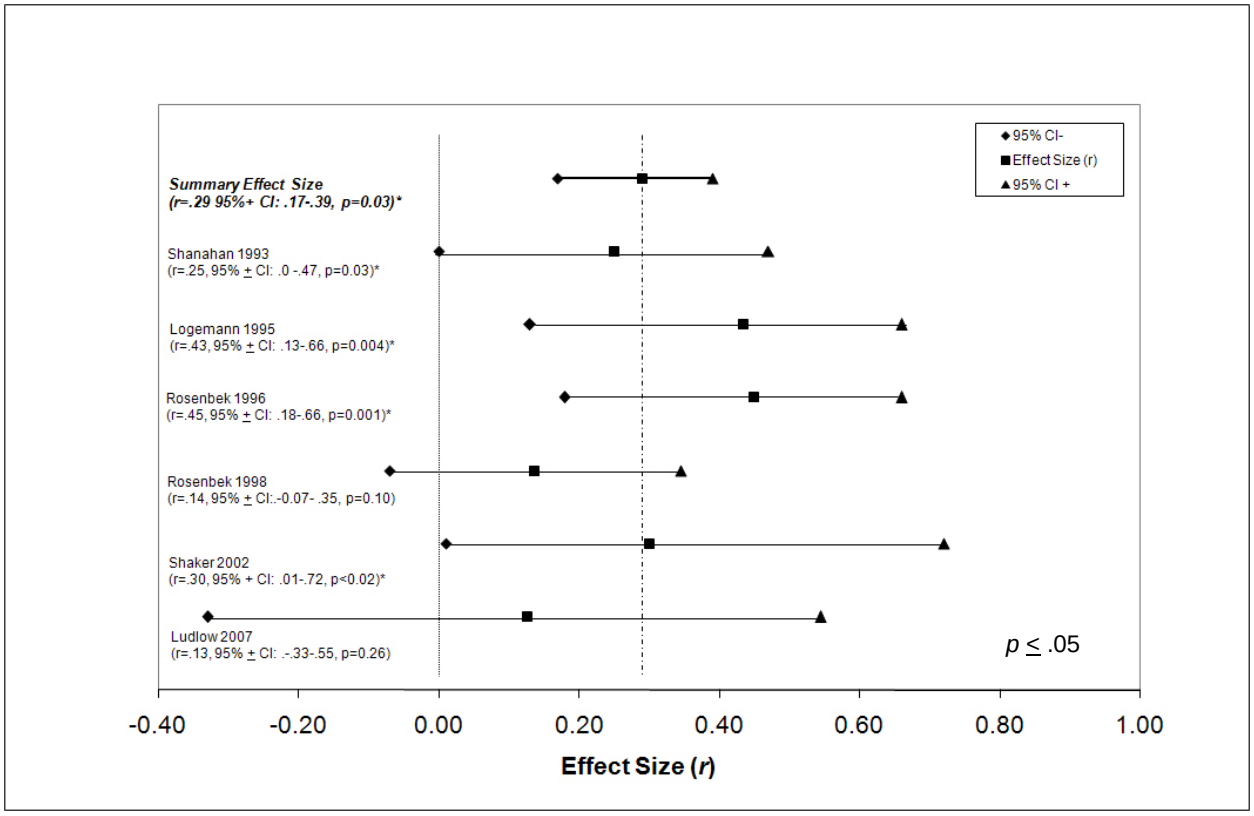

Figure 2. Summary Effect Size: Individual Interventions for Neurogenic Dysphagia

5.4.6.2 Homogeneity of the Sample

The null test of homogeneity, known as Cochrane's X^2 statistic or Q statistic, was used to test the assumption that the variation among effects of the included studies was random (Shadish & Haddock, 1994). This test determines the extent to which the studies included in the meta-analysis actually share a common population effect size. A significant result indicates unacceptable heterogeneity in the sample of studies included in the meta-analysis. The resulting Q statistic for the meta-analysis was $Q = 5.11$, which did not exceed the critical value of Q of 11.07 (X^2, $p = .05$, $df = 5$). This result indicates that the included studies were not significantly heterogeneous.

5.4.6.3 Adapted Analysis of Summary Effect Size

The effect sizes of two of the six studies of individually administered interventions for neurogenic dysphagia did not reach statistical significance. One of these studies is the second study in a series of investigations which examine the effects of a widely used therapeutic intervention for delayed pharyngeal stage onset known as thermal tactile application (Rosenbek et al., 1998). Its very small effect size was in contrast to the medium effect size of the authors' earlier study of the same method, also included in this meta-analysis (Rosenbek et al., 1996b). Therefore, its inclusion in this meta-analysis was considered necessary and appropriate.

However, the other investigation whose effect size did not reach statistical significance in this meta-analysis reported on the effects of electrical stimulation on swallowing physiology and biomechanics in neurogenic dysphagia patients (Ludlow et al., 2007). The clinical methods employed are available only to clinicians who have enrolled in a proprietary training seminar and have purchased equipment from the manufacturer. All other treatment methods included in this

meta-analysis are available to any qualified speech-language pathologist and exist within the public domain.

Electrical stimulation for treatment of dysphagia is a controversial method that has received widespread attention in the media and is a subject of substantial debate within the professional literature. It received FDA approval for use on the basis of a single clinical study (Freed, Freed, Chatburn, & Christian, 2001) that has been widely criticized for substantial flaws in design, investigator bias, selective assignment of patients, unequal treatment of groups, unexplained attrition, and investigator conflicts of interest (Coyle, 2002; Humbert et al., 2006).

The investigator consulted with a second expert judge, whose qualifications include seven peer reviewed experimental publications in the field of oropharyngeal dysphagia, to determine the appropriateness of conducting a second analysis of the effect size data excluding the Ludlow et al. (2007) article because the instrumentation and methods employed are proprietary and unavailable in the public domain, unlike the techniques reported in the other five studies. After reaching a consensus, the meta-analytic calculations were repeated without the Ludlow et al. (2007) citation. Results of the re-analysis appear in Table 5 and Figure 3, and show a very small, insignificant increase in overall effect size, and again, reached statistical significance (r = .31; 95% CI = .12 – .52; $Z = 2.13$, p = .02). The null test of homogeneity was repeated and failed to reject homogeneity of the sample (actual value of Q = 5.81; critical Q = 9.49, (X^2, $p = .05$, $df = 4$).

Table 5. Effect Sizes Excluding Ludlow (2007) Study

Author	Effect size (*r*)	95% C. I.	*Z*	*p*
Summary effect size	**.31**	**.12 - .52**	**2.10**	**.02**
Shanahan, et al., 1993	.25	.00 - .47	1.98	.03
Logemann, et al., 1995	.43	.13 - .66	2.65	<.01
Rosenbek, et al., 1996	.45	.18 - .66	2.98	<.01
Rosenbek, et al., 1998	.14	-.07 - .35	1.30	.10
Shaker, et al., 2002	.30	.01 - .72	1.74	.02

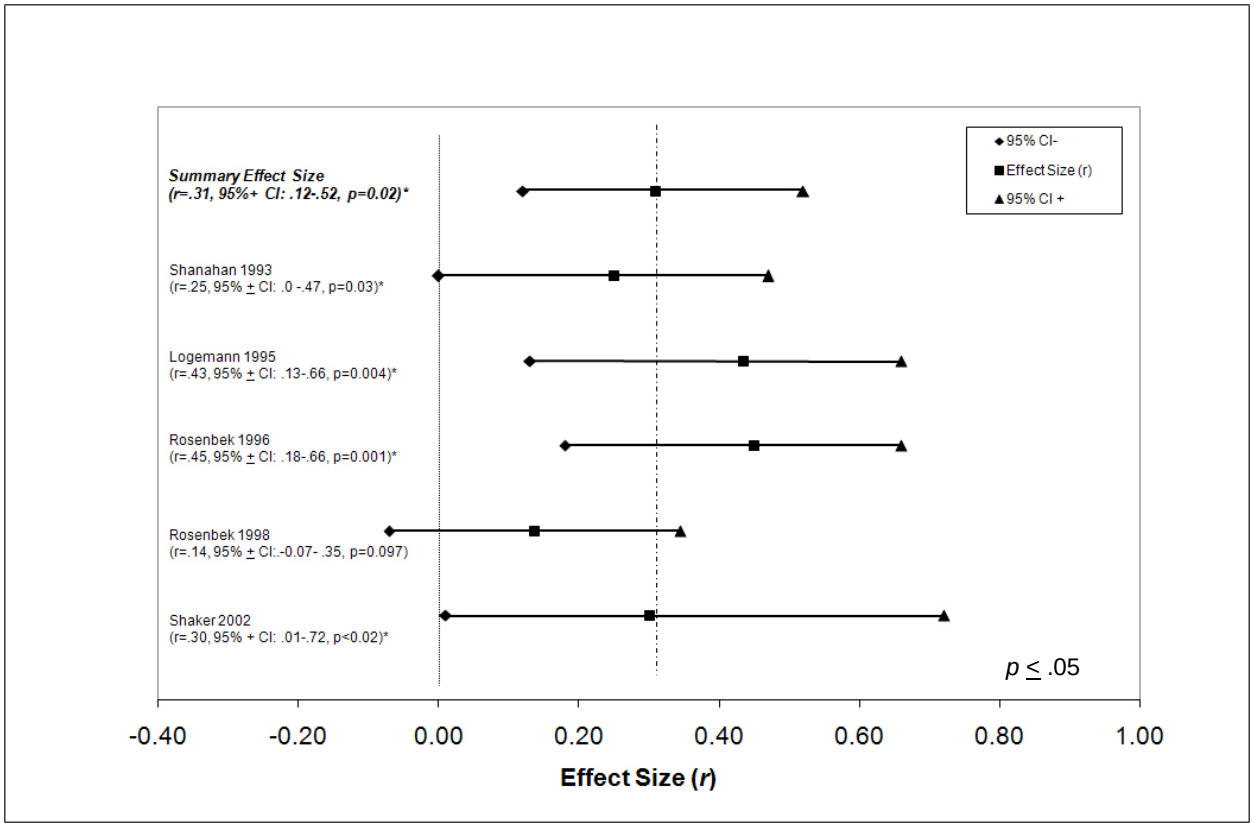

Figure 3. Summary Effect Size Excluding Ludlow (2007) study

5.4.7 Conclusions from Effect Size Summary

The meta-analysis of investigations of individually administered interventions for neurogenic dysphagia demonstrated a medium to large, significant effect, and that the selected investigations were significantly homogeneous. This result indicates that individually administered interventions for neurogenic dysphagia exhibit high efficacy in controlled experimental settings.

5.5 META-ANALYSIS OF ORGANIZED, INSTITUTIONAL DYSPHAGIA PROTOCOLS ON PUBLIC HEALTH OUTCOMES

The search strategy employed in the meta-analysis yielded two complementary sets of studies. The first set, analyzed in the first meta-analysis, included studies that investigated the effect of treatments on altering biomechanical properties of disordered swallowing. The second set consisted of studies that evaluated institutional dysphagia protocols that combined screening, monitoring, and individual treatment of dysphagic patients in networks of health care facilities and institutional health care systems. This second meta-analysis employed the same methods for searching and scoring retrieved articles as described in section 5.3.2.1. All studies were categorized for the second meta-analysis using the previously described Baker and Tickle-Degnen method (2001) which is summarized in the screening form (Appendix D). Minimum inclusion criteria for this meta-analysis were also identical, however the majority of studies in this set were randomized controlled trials with larger samples than retrieved in the first meta-analysis. Acceptable dependent variables differed from the first meta-analysis as the outcomes

of interest of the studies in the second meta-analysis were global public health outcomes such as pneumonia and mortality. Three studies were of sufficient quality to ultimately qualify for inclusion in the second meta-analysis.

5.5.1 Evaluation of Citations: Evidence Quality for Inclusion

To be eligible for inclusion in the second meta-analysis of organized, institutional dysphagia protocols on public health outcomes, each study was required to meet the following criteria related to acceptable treatments and acceptable outcomes.

5.5.1.1 Acceptable Dependent Variables

Accepted clinical end points, also the dependent variables, were a diagnosis of pneumonia or other clinical endpoints such as a diagnosis of malnutrition or mortality.

For studies investigating the effects of organized, institutional dysphagia protocols on the aforementioned dependent variables, the diagnosis of these conditions was required to have been derived using objective, validated standards of care or guidelines such as those published by *The American Academy of Chest Physicians* or *The Centers for Disease Control and Prevention* (Tablan et al., 2007). Patients enrolled in eligible investigations could not display symptoms associated with any of the outcomes of interest at the time of the onset of the disease that caused dysphagia. That is, eligible studies had to demonstrate that they excluded patients if they presented at enrollment pre-existing history of dysphagia or symptoms of pneumonia, or were unequivocally malnourished. Dependent variables were required to be either ordinal or interval continuous measures, or dichotomous outcomes.

5.5.2 Acceptable Treatment Methods

5.5.2.1 Design and Sample Size

Eligibility criteria for the second meta-analysis were identical to the first meta-analysis (please refer to section 5.4.2). Since the scope of this group of studies centered on the effect of institutional protocols on global indices of public health such as pneumonia and mortality, patients in experimental groups were managed using experimental, systematic, institutional dysphagia management protocols, while patients in control groups were subject to routine, traditional management schemes already in place at participating institutions. A minimum sample size of 10 subjects per group was required, though the majority of studies in this set of citations greatly exceeded that number.

5.5.2.2 Validity

Studies were required to possess sufficiently robust evidence of controls to maintain internal and external validity. Identical criteria for internal and external validity were required for inclusion into this meta-analysis (please refer to sections 5.4.2.2).

Internal and external validity were required to be moderately high. Eligible adverse health sequelae of oropharyngeal dysphagia (e.g., pneumonia), were required to be operationalized prospectively according to standard criteria or diagnostic guidelines.

5.5.3 Methods

5.5.3.1 Minimum Acceptable Criteria for Eligibility

The minimum acceptable combined score for inclusion was "III B 2 b" for this meta-analysis of the effectiveness of institutional dysphagia protocols on public health outcomes. The summary of evidence quality evaluations appears in Table 6.

Table 6. Quality Evaluation of Included Studies-Organized Dysphagia Protocols

First Author, Rating	Design	Sample Size	Internal Validity	External Validity
DePippo, 1994 I A 2 b	RCT; treatment/control	77 CVA with radiographic evidence of dysphagia	Moderate	Moderate
Dennis, 2005 II A 2 a	Cohort, two group, non-random assignment, treatment vs. control	859 acute CVA; clinical diagnosis of dysphagia	Moderate	High
Hinchey, 2005 II A 2 a	Cohort, two group, non-random assignment, treatment vs. control	2330 acute CVA; failed dysphagia screen	Moderate	High

5.5.4 Data Extraction

5.5.4.1 Description of Included Studies

Three investigations qualified for this meta-analysis. A summary of study details appears in Table 7 and details are discussed below. All three studies investigated the morbidity or mortality associated with organized, institutional dysphagia management protocols in patients with acute stroke, versus unorganized, traditional, individual management. Articles that were excluded from the meta-analysis, included those that a) failed to use objective outcome measures such as

mortality, pneumonia incidence, or other morbidity directly related to dysphagia, as their dependent variables, or used subjective outcomes such as quality of life or patient satisfaction; b) failed to analyze patients in the groups to which they had been randomized, or c) displayed unacceptable attrition of more than 10% of patients randomized to treatment or control groups or otherwise contained lost data that remained unaccounted for in the published article.

DePippo, Holas, Mandel, and Lesser (1994) investigated the effect of modest and high intensity traditional treatment of post-stroke dysphagia, compared to a control group that received no formal therapy, on pneumonia, dehydration and mortality of patients, during institutionalization and at three, six, and 12 months follow up. All patients were dysphagic, and received treatment for oropharyngeal dysphagia that included an oral diet supplemented by one or more traditional compensatory or rehabilitative maneuvers. Patients were randomized to a control or minimal intensity group (single visit counseling session), or one of two treatment groups (i.e., moderate or high intensity) after videofluoroscopic examination revealed aspiration on at least 50% of all consistencies assessed. The methods employed with the high intensity group (daily therapy and monitoring) and those employed with the control group (a single counseling session following diagnostic examination) were both judged to be sufficiently well-defined and different from one another to enable comparison in the meta-analysis. It was unclear how the moderate-intensity group treatment differed from the high-intensity group; therefore, only the data from the low intensity group (n = 39) and high intensity groups (n = 38) were entered into the meta-analysis.

Dennis et al. (2005) reported the results of a phase of their F.O.O.D. (feed or oral diet) trial in patients with dysphagia following stroke. This study investigated whether the addition of early enteral feeding to traditional, institutional management of dysphagia, reduced mortality

during a median 6.5 months (no enteral supplementation) to 6.8 months (early enteral supplementation) post-randomization follow-up period. Participants in this study consisted of those whose severity of acute dysphagia and other stroke-related impairments were equivocally predictive of a need for enteral supplementation by the attending physician. Patients were screened and otherwise managed by a multidisciplinary care team consisting of speech-language pathologists, dietitians, nurses, and physicians (FOOD Trial Collaboration, 2003), and for whom oral intake was initiated when considered sufficiently safe, using compensatory or other measures to facilitate safest oral feedidng. Patients for whom the attending physician was certain as to the safety or danger of oral intake were excluded from this study. Patients in this study (n = 859) were randomly assigned to receive either early provision of supplemental nutrition via enteral (i.e., feeding tube) means, or to receive no supplemental enteral nutrition for at least seven days post-onset. The dependent variable was mortality.

Hinchey et al. (2005) compared the effectiveness of a formal dysphagia screening protocol that produced increased surveillance and formal dysphagia management to acute stroke patients hospitalized in institutions with formal dysphagia protocols, to patients admitted to facilities without institutional dysphagia protocols. The dependent variable of interest was a diagnosis of pneumonia during the post-stroke onset acute-care hospitalization. This study followed 2532 patients with a diagnosis of acute stroke, admitted to 15 institutions with either formal dysphagia screening and management protocols, or no formal protocol. Their sample of completed and reported and analyzed data sets was slightly smaller at 2330 patients (7.9% attrition). This sample constituted a large cross section of all patients admitted with stroke before dysphagia was formally identified. Follow-up ranged from a median of four days for patients managed in a non-screening institution, to 14 days for patients that developed

pneumonia. This multi-center investigation compared pneumonia rates in facilities without a formal institutional dysphagia protocols to those that used a formal institutional dysphagia protocols for all acute stroke admissions.

Dependent variables in these three studies were dichotomous, categorical observations or endpoints including the presence or absence of mortality, and/or clear-cut adverse health outcomes such as pneumonia in treated and untreated patients. Post hoc analyses of dependent variables that were not included in the stated hypothesis were not included in this meta-analysis.

Table 7. Included Studies of Organized Dysphagia Protocols

First Author	Patients	Treatment	Comparison Method	N: Patients/ Controls	Outcome
DePippo, 1994	Stroke	Intensive Traditional therapy	Low intensity therapy- Single visit	39 / 38	Mortality, dehydration, pneumonia
Dennis, 2005	Stroke	Enteral Feeding plus traditional management	No enteral feeding plus traditional management	430 / 429	Mortality
Hinchey, 2005	Stroke	Formal Screen and management protocol	No formal screening- routine care	704 / 1626	Pneumonia

5.5.5 Statistical Procedures

The most widely published method for estimating risk of dichotomous outcomes, such as the presence or absence of mortality and morbidity associated with experimental pharmaceutical or surgical exposure, is the odds ratio. The odds ratio is also the appropriate index of effect size to employ in investigations reporting the effects of treatment methods in either eliminating mortality or specific adverse outcomes (Fleiss, 1994). Other mathematical indices of predicted

comparative risk of outcomes from treated and control groups include the rate ratio, risk reduction, and numbers needed to treat (Haynes, Sackett, Guyatt, & Tugwell, 2006).

Though it would have been preferable to combine effect sizes from both meta-analyses, the effect size indices used in the first meta-analysis are not directly comparable with those in this meta-analysis which included studies publishing only dichotomous data. Although a method has been developed to calculate an effect size for odds ratios (Chinn, 2000), its relationship to established effect size indices has not been clarified despite efforts to contact the author for explanation.

For this meta-analysis, the investigator calculated odds ratios from the reported frequencies of the various dichotomous outcomes for the experimental and control treatments in each study to determine the odds ratios of their respective end points.

5.5.5.1 Odds Ratios for Organized Dysphagia Protocols

Odds ratios summarize the proportion or odds ratio of the adverse outcome of interest between the treated and untreated groups of patients. This figure has become a standard measure of effect size in studies reporting categorical data (Rosenthal & Rosnow, 1991). The odds ratio is the proportion of the incidence of outcome in the treated group compared to the incidence of outcome in the control group. Odds ratio outcomes are expressed in terms of increased or decreased likelihood of an adverse event such as mortality or morbidity (Straus et al., 2005). An odds ratio of less than one indicates that patients receiving the experimental treatment are less likely to experience the adverse outcome of interest than those treated with the control treatment. An odds ratio of 0.60 is equivalent to a 40% reduced likelihood of experiencing the adverse event, indicating that the treatment is protective from the adverse events supposedly mitigated by the treatment.

Odds ratios of individual studies were computed from the published data using a fourfold table containing raw data indicating the incidence of the outcomes of interest (mortality, pneumonia, malnutrition outcomes) in patients exposed to the experimental and control treatment methods. The odds ratios were computed with Equation 12, where OR = odds ratio, A = experimental patients with adverse outcome of interest, B = experimental patients without adverse outcome of interest, C = control patients with adverse outcome of interest, and D = control patients without adverse outcome of interest (Haynes et al., 2006).

Equation 12. Odds Ratio

$$OR = AD \big/ BC$$

The natural logarithm of the raw odds ratios (*ln*OR) were then used to calculate confidence intervals around the odds ratios because unlike OR, *ln*OR takes on a value of zero when no relationship is present between the two factors, providing a similar interpretation as a zero effect size (*r* or *d*) (Shadish & Haddock, 1994). Log odds ratios and log odds ratio confidence intervals were then antilogged, and the results plotted on a forest plot to display the results.

5.5.5.2 Combining Odds Ratios

To determine the effect size of the studies included in this meta-analysis, odds ratios were combined using the Mantel Haenszel estimate of the odds ratio, displayed in Equation 13, where A, B, C, and D are identical to the variables contained in Equation 12, and T = the total number of subjects in the sample. This method is valid for combining few studies with large samples or many studies with small samples (Shadish & Haddock, 1994).

Equation 13. Mantel Haenszel Combined Odds Ratio

$$OR_{MH} = \frac{\sum AD / T}{\sum BC / T}$$

The confidence interval for the combined Mantel Haenszel estimate of the odds ratio (OR_{MH}) was computed by first estimating the variance of the log OR_{MH} using cell frequencies (Equation 14), where P = A + D, Q = B + C, R = AD / T, and S = BC / T (Shadish & Haddock, 1994).

Equation 14. Variance for Mantel Haenszel Combined Odds Ratio

$$v = \frac{\sum PR}{2\left(\sum R\right)^2} + \frac{\sum\left(PS + QR\right)}{2\left(\sum R\right)\left(\sum S\right)} + \frac{\sum QS}{2\left(\sum S\right)}$$

Significance of the Mantel Haenszel combined odds ratio was evaluated with a Mantel Haenszel chi square statistic (Equation 15), using *df* = 1, where O (observed frequency of outcome in experimental groups) = A; E (number expected to have been observed with outcome in experimental group) = [(A + C)/T](A + B); and V = E[T – (A + C)/T][T – (A + B))/(T – 1)] (Shadish & Haddock, 1994).

Equation 15. Mantel Haenszel Chi Square

$$X^2_{MH} = \frac{\left[\left|\sum(O - E)\right| - 0.5\right]^2}{\sum V}$$

The combined odds ratio confidence interval was computed using the calculated variance among the included studies, along with the individual confidence intervals using the actual published proportions of patients achieving a specific outcome in each study.

5.5.5.3 Homogeneity of the Sample

The null test of homogeneity for the Mantel Haenszel combined odds ratio (the *Q* statistic) was performed on the sample of studies included in the meta-analysis, where, w_i = a weighting factor, the inverse of the variance for each included study, θ_i is the common odds ratio for the each individual included study, and θ_{MH} is the Mantel Haenszel odds ratio for the entire sample (Equation 16) (Strawderman et al., 1998).

Equation 16. Q Statistic for Mantel Haenszel Odds Ratio

$$Q = \sum w_i (\theta_i - \theta_{MH})^2$$

5.5.5.4 Clinical Significance of the Result

Finally, to determine the clinical importance of the individual studies, absolute risk reduction and number needed to treat were calculated. Absolute risk reduction (ARR) describes the difference in the proportions of patients in treated and control groups that achieve the outcome of interest. Number needed to treat (NNT) expresses the approximate number of patients that would need to be treated with the experimental method reported in a study to prevent one adverse outcome (Haynes et al., 2006; Straus et al., 2005). Absolute risk reduction (ARR) and numbers needed to treat (NNT) were computed for each study and for the combined studies, by entering cell frequencies in Equation 17 and Equation 18, where CER = C / (C + D) or the proportion of patients in the control group diagnosed with the adverse outcome of interest, and EER = A / (A + B) or the proportion of patients in the experimental group diagnosed with the adverse outcome of interest.

Equation 17. Absolute Risk Reduction

$$ARR = CER - EER$$

Equation 18. Number Needed to Treat

$$NNT = 1/ARR$$

5.5.6 Results

5.5.6.1 Odds Ratios for Individual Included Studies

Results of computation of odds ratios for the included studies appear in Table 8 .

Odds ratios for the three included studies were .44 (Hinchey et al., 2005), .78 (DePippo, Holas, Reding, Mandel, & Lesser, 1994), and .79 (Dennis, Lewis, & Warlow, 2005), indicating a 21% to 56% reduction in likelihood of adverse outcomes for patients in these studies. DePippo et al. (1994) exhibited a 95% confidence interval that extended beyond an odds ratio of 1.0, indicating poor generalizability of the study, though it is also likely that the small sample contributed substantially to the width of the interval.

5.5.6.2 Combined Odds Ratio for Included Studies

In combination, these three studies showed a small overall advantage in preventing outcomes (i.e., mortality and pneumonia) when organized dysphagia protocols were used ($OR_{MH} = 0.60$; 95 % CI = 0.53 – 1.07). Significance of the combined odds ratio was tested with the Mantel Haenszel chi square statistic (Shadish & Haddock, 1994), and was found to be non-significant ($X^2_{MH} = 3.06$, df = 1; $p = 0.08$). Table 8 summarizes the computed odds ratios for these three studies of organized dysphagia protocols on public health outcomes, and Figure 4 displays the forest plot summary of odds ratios.

Table 8. Effect Size Summary: Organized Dysphagia Protocols

Author	Odds Ratio	95% Confidence Interval
Summary Effect Size	**.60***	**.53 – 1.08**
DePippo et al., (1994)	.78	.25 – 2.41
Dennis et al., (2005)	.79	.68– .93
Hinchey et al. (2005)	.44	.36 – .53

* p = .08

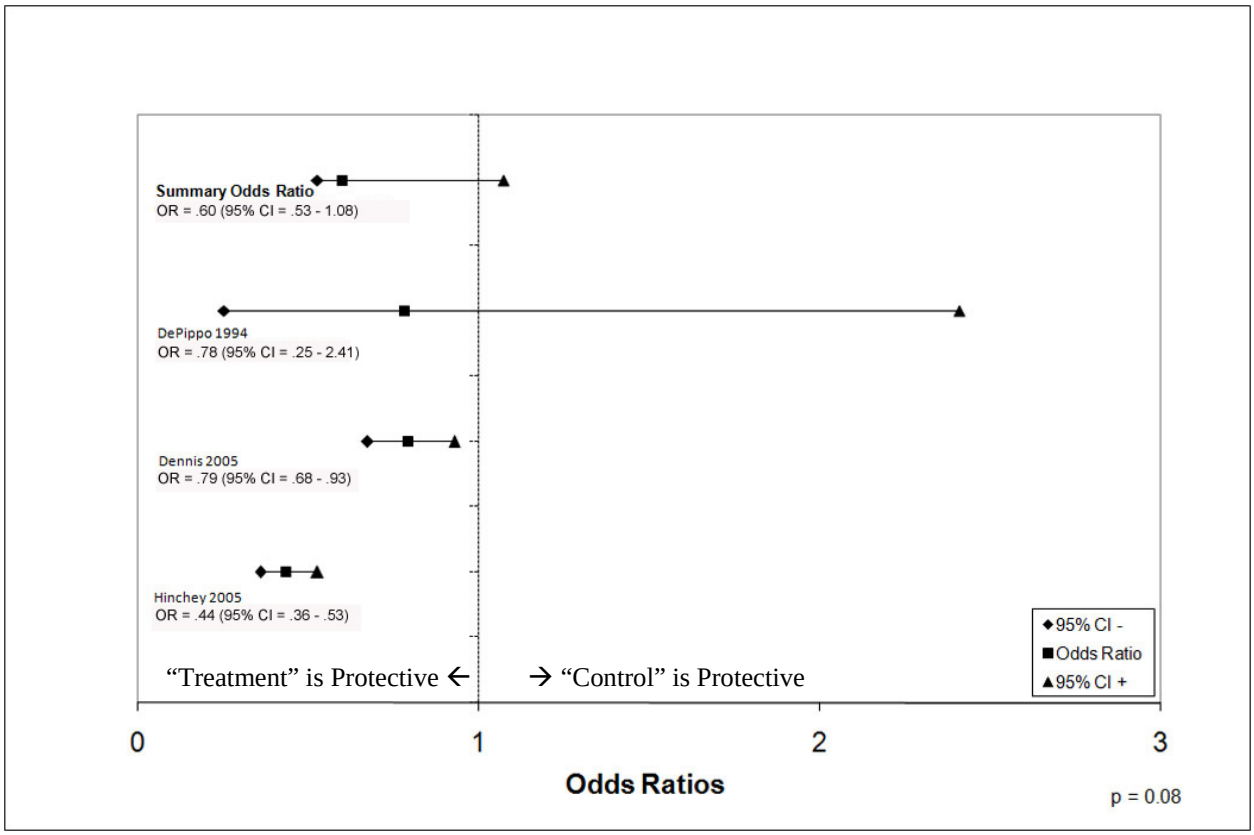

Figure 4. Summary Effect Size: Organized Dysphagia Protocols

As in the effect size forest plot, the calculated odds ratios are represented by the square points on in each row of Figure 4, with the 95% confidence interval represented by the diamonds (lower limit) and triangle (upper limit). Odds ratios below one indicate the percentage reduction in odds of acquiring the adverse outcome of interest compared to the control treatment.

5.5.6.3 Homogeneity of the Sample

The null test of homogeneity failed to reject the homogeneity of the sample, generating a *Q* statistic of 2.39, which is below the critical value of X^2 at *k-1* degrees of freedom of 5.99 ($p \leq .05$). This result indicates that the sample was not significantly heterogeneous.

5.5.6.4 Numbers Needed to Treat

Since NNT expresses numbers of patients, the actual computed value must be rounded up to the nearest whole number. These results are displayed in Table 9. These results suggest that for every 18 to 35 stroke patients treated with organized dysphagia protocols, one stroke patient would be expected to experience mitigated mortality or adverse health outcome.

Table 9. Risk Reduction and Numbers Needed to Treat

First Author	ARR	NNT
DePippo	2.97%	34
Dennis	5.72%	18
Hinchey	2.94%	35

5.5.7 Conclusions from Odds Ratio Summary

A small, non-significant benefit in mortality and public health outcomes appears to be caused by formal dysphagia protocols in institutional settings for patients with stroke, the most common cause of oropharyngeal dysphagia. However a trend toward statistical significance was present ($p = .08$). The small sample size in one study (DePippo et al., 1994), in comparison to the two

larger studies, may explain the width of its confidence interval and subsequently non-significant effect size, and suggests the need for replication on a larger scale.

5.6 DISCUSSION

The purpose of this study was to meta-analytically test two hypotheses that were complementary to one another in addressing the questions, “Are individually administered interventions for neurogenic oropharyngeal dysphagia efficacious in eliminating biomechanical swallowing impairments?”, and “Are institutional dysphagia protocols effective at reducing the global health consequences of oropharyngeal dysphagia?” The first hypothesis, that individually administered treatment of dysphagia would be found to significantly improve biomechanical functions in patients with neurogenic dysphagia, was supported. Under controlled experimental conditions, a significant physiological benefit is produced by the individually administered interventions for neurogenic dysphagia, though the small number of studies meeting eligibility criteria widens the interval of overall confidence in these results. However, the second hypothesis, that institutional dysphagia protocols would be found to produce statistically significant reductions in dysphagia-related morbidity and mortality, was not supported. The second meta-analysis contained only three studies, two of which reached significance. But combined, the three studies did not exhibit an effect size that reached the preselected level of statistical significance. Whether statistical significance is necessary to generate a clinically significant difference in public health outcomes or expenditures remains to be evaluated.

5.6.1 Individually Administered Interventions for Neurogenic Dysphagia

The results of the first meta-analysis of individually administered interventions for neurogenic dysphagia, supported the hypothesis that treatments designed to compensate for, or restore, biomechanical oropharyngeal impairments caused by stroke and neurogenic etiologies, produce clinically significant, beneficial changes in swallow biomechanics and airway protection. The overall effect size for the construct represented by the set of studies in the first meta-analysis was *medium* to *large*, and was statistically significant. This result suggests that overall, such methods do what they purport to do in remediating targeted swallowing abnormalities, increasing the performance of the average neurogenic biomechanical impairment by approximately one-third of one standard deviation from pre-treatment biomechanical performance. The outcome of such interventions, then, reduces the likelihood of aberrant penetration of the upper airway while swallowing, and increases the volume of swallowed material delivered to the digestive system with each single swallow, thereby reducing potential adverse pulmonary and nutritional sequelae.

In the first meta-analysis of individually administered dysphagia interventions, the study by Logemann, et al. and the study by Rosenbek, et al. (1996b) generated robust effect sizes, indicating greater potential for the desired biomechanical outcomes. The two Rosenbek et al. (1996b, 1998) studies of thermal-tactile stimulation generated divergent effect sizes and confidence intervals, one of which included values below zero, despite using the same clinical method of therapy. As discussed above, such a finding indicates that the true results may differ from those observed in the reported research findings. However the earlier of these two studies investigated biomechanical change caused by the treatment rather than to differentiate efficacy among varying levels of dosage as in the later study. This finding may suggest that the true

efficacy of this particular method lies somewhere between the two computed effect sizes, and that thermal-tactile stimulation as a method, produces a moderate immediate effect, while large doses of the same treatment produce no difference in swallow biomechanics, than those produced by small doses. The potential long-term role of this method in producing plasticity of the sensorimotor substrates of swallowing physiology, a subject of increased research demonstrating the facilitative effects of stimulation of the sensory projections to the swallowing cortex on human swallow function, deserves further investigation (Gow, Rothwell, Hobson, Thompson, & Hamdy, 2004)

Another study in this meta-analysis investigated a compensatory posture that places the inlet to the airway in a protected position (Shanahan et al., 1993). This study evaluated two types of outcomes: biomechanical and bolus flow measures using continuous data, and the presence or absence of aspiration with and without the use of the behavioral maneuver while patients swallowed. As discussed earlier, continuous and dichotomous data are incompatible for inclusion into a single statistical meta-analytic model. However the effect size of this intervention of r = .25, a small to medium effect, must be combined with the intervention's resultant reduction of aspiration by 50% in treated patients, when considering the overall value of the method. By considering both the effect size and reduced odds of aspiration, the predicted effects of this method of compensatory swallowing are greater than the calculated effect size alone. Since compensation is limited in its effects only by the patient's failure to perform the maneuver while swallowing, these effects will afford additional protective benefit during early recovery from neurogenic dysphagia, while rehabilitation and recovery ensue. Since compensation is employed while swallowing, and swallowing occurs many hundreds of times

per day, the repeated use of compensatory maneuvers over the long-term, in producing plasticity of the target mechanism, may warrant future research.

Four of the studies in the first meta-analysis investigated the immediate or short-term effects of sensorimotor interventions designed to alter oropharyngeal biomechanics while swallowing, either during or after application of sensory stimuli (Logemann et al., 1995; Ludlow et al., 2007; Rosenbek et al., 1998; Rosenbek et al., 1996b). All of these methods were designed to quicken the onset of pharyngeal activity and closure of the airway in relation to arrival of a swallowed bolus at the inlet to the upper airway. They were not designed to evaluate the lasting, restorative effects of these interventions. The latter of these interventions (electrical stimulation) was found to produce a negligible effect on swallow biomechanics and aspiration and its confidence interval included values below zero, indicating that the method may not produce the intended outcome; it may just as likely produce the opposite effect. It is also possible that its small sample size was partly responsible for the wide confidence interval. Further investigation of this controversial method is encouraged.

Several of the studies in this meta-analysis required either patient or caregiver behavior to perform the intervention. The chin-down posture (Shanahan et al., 1993) and exercise (Shaker et al., 2002) interventions require patient behavior, while thermal stimulation (Rosenbek et al., 1998; Rosenbek et al., 1996b), sour bolus (Logemann et al., 1995), and electrical stimulation (Ludlow et al., 2007) require patient and/or caregiver behavior for implementation. Additionally, all but one of these treatments (exercise) are effective only when performed immediately before (thermal stimulation) or while (electrical stimulation, sour bolus) swallowing. The nature of such compensatory interventions that require patient or caregiver behavioral participation should be considered of varying value in patients with neurogenic

diseases because of altering the ability to actively participate in such behaviors. Fortunately some of these methods (head posturing, flavor enhancement, sensory stimulation) can be implemented by manipulating the patient's environment until he is capable of volitional performance. In either event, their use may be beneficial at preventing adverse sequelae of dysphagia in the earlier stages of recovery from stroke and related conditions, when participation may be more difficult, and may be considered important while patients exhibit more severe impairments after stroke.

The sixth of the studies in this meta-analysis was the only sufficiently well designed investigation evaluating a rehabilitative method designed to augment swallow biomechanics over time with exercise (Shaker et al., 2002). A small improvement in swallow physiology was seen which translates to a reduction in post-swallow hypopharyngeal residue that has been shown to increase the potential for postprandial aspiration (Eisenhuber et al., 2002). Efforts to demonstrate a more robust benefit from this type of intervention, as well as to develop additional rehabilitative interventions with which to combine the results of this study, are highly encouraged and have been emerging in the literature (Kays & Robbins, 2006; Robbins et al., 2007).

All of the included studies investigated methods that caused either immediate change in swallow function, or physiologic change caused by prolonged recruitment of musculature in an exercise regimen. Much interest and research into the potential for behavioral motor therapy (Kays & Robbins, 2006; Sapienza & Wheeler, 2006) and sensory stimulation (Gow et al., 2004) to generate plasticity of the central and peripheral mechanism subserving respirodeglutitive functions, has been emerging in the literature. The studies of individual therapeutic interventions that were included in these meta-analyses are potentially important steps toward elucidating the

effects of long-term implementation of treatment techniques in producing long-term change in the function of the swallowing mechanism.

The studied interventions individually, except Ludlow et al. (2007), and collectively produced clinically and statistically significant, beneficial biomechanical changes in swallow physiology. Since patients with neurogenic dysphagia suffer largely from multiple biomechanical impairments, it is worthwhile to consider that combinations of appropriately implemented therapeutic modalities that are currently employed in every-day clinical practice, may generate a beneficial change in these combinations of biomechanical impairments along with a possible expectation that they may produce additive effects. However the cognitive demands of combined behavioral interventions will need to be considered in patients with neurogenic dysphagia affecting higher level cognitive functions.

The six investigations generating these results constitute a cross section of traditional therapeutic methods available to and in widespread use by speech-language pathologists managing swallowing disorders in patients with stroke and neurogenic dysphagia. But they followed patients to short-term clinical end points only. Since the impairments themselves cause the abnormal flow of swallowed material into the upper airway or away from the digestive system, and since these biomechanical impairments (aspiration, laryngeal penetration, impaired UES opening) predispose to important clinical end points such as pneumonia (Eisenhuber et al., 2002; Langmore et al., 1998; Langmore, Skarupski, Park, & Fries, 2002), this meta-analysis appears to justify the use of properly selected combinations of these treatment modalities to reduce risk of adverse, long-term clinical end points such as pneumonia, malnutrition, dehydration and mortality associated with neurogenic dysphagia. Future investigations should be encouraged to follow both the efficacy of individual treatment methods at remediating

biomechanical impairments, together with the effectiveness of treating patients to these important clinical end points, within the same investigations, to generate more robust evidence for clinical practitioners, future meta-analyses and guidelines.

The effect of individually administered interventions for neurogenic dysphagia in lowering the degree of impairment in the oropharyngeal swallowing mechanism is expected by the clinician to mitigate risks of sequelae of dysphagia such as pneumonia and malnutrition. These small scale studies demonstrate the efficacy of the investigated methods but provide little evidence regarding their effectiveness in lowering morbidity rates because follow up in each of them (and among the majority of studies in this field) was insufficiently long and complete to determine their effects on these health outcomes. For this reason, the second meta-analysis is important it connecting impairment-level therapy to interventions designed to improve global health outcomes.

5.6.2 Institutional Dysphagia Protocols on Health Outcomes

The second meta-analysis investigated the effects of institutional dysphagia protocols on long-term adverse health outcomes and mortality. Its results did not support the hypothesis that formal protocols designed to institutionalize management of dysphagia through standardized surveillance by staff, and timely, aggressive interventions of the types discussed in the first meta-analysis, produce decreased morbidity and mortality associated with dysphagia after stroke. However, too few studies of this type exist, and one of the included studies' odds ratio exhibited a confidence interval that included values greater than 1, indicating that its results may not reflect the actual outcome that may be seen in clinical practice. These overall results are promising, though the research consumer and public health system will need far more such evidence to

justify systematic changes in institutional dysphagia care. Further research is needed in this important area of long-term outcome.

One of the studies in this second meta-analysis (Dennis et al., 2005) compared two institutional protocols for dysphagic stroke patients that differed only by the timing of and use of supplemental enteral nutrition. This study added early enteral (feeding tube) nutrition to traditional interventions by the institutional care team that consisted of speech language pathologists, nurses, dietitians and physicians, in one of the treatment groups, while the second group received traditional management alone. This preemptive use of enteral feeding tubes was shown to produce a small reduction in risk of mortality though the authors stated that the odds of adverse outcomes such as quality of life, and other adverse outcomes, offset these benefits. Early enteral feeding may, in some cases, be a controversial preemptive tactic in stroke given the rapid recovery of neurological function often observed in the initial days following onset of stroke, multiple sclerosis, and some other neurological conditions. In particular, in light of the increased risk of pneumonia imposed by the use of feeding tubes (Marik, 2001; Langmore, et al., 1998), this study may in fact demonstrate no net gain by the addition of early enteral feeding to traditional institutional dysphagia management.

The quality of life and other subjective measures from this study were not included in the meta-analytic calculations because they were not sufficiently clearly operationalized and were not entirely objective and replicable. However the World Health Organization recognizes quality of life as a legitimate clinical end point justifying therapeutic interventions in its International Classification of Functioning, Disability and Health (World Health Organization, 2001). An increase in survival in patients with neurogenic dysphagia may indeed be offset by the use of preemptive enteral supplementation, though quality of life may be adversely affected

by enteral tube usage. The relationship between enteral supplemental feeding and patient satisfaction warrants further investigation using methods reported in Dennis et al. (2005), but they should also include the use of valid, reliable and replicable instruments that evaluate quality of life associated with oropharyngeal dysphagia such as the Swal-QOL (McHorney et al., 2002). Meanwhile, it cannot be ignored that quality of life, one of the adverse outcomes cited as increasing in the early enteral feeding group in this study, is a legitimate therapeutic target. It would be useful to design an investigation comparing the methods used in this study's "early enteral supplementation" group to aggressive, rather than routine, institutional dysphagia management as seen in the second meta-analysis (DePippo et al., 1994), to the same clinical end points of mortality, pneumonia, and quality of life.

Future investigations might consider a larger scale replication of DePippo et al. (1994), which specifically examined the effects of the types of behavioral, physiologic interventions for swallowing impairments assessed in the first meta-analysis on outcomes such as pneumonia, nutritional failure and mortality, while selecting the targeted treatments based on biomechanical analysis rather than clinician preference. Addition of early enteral feeding to mitigate onset of malnutrition, the incidence of which is high during the initial weeks after onset of stroke, with aggressive therapy and surveillance, may indeed be found to ensure optimal short-term recovery and long-term health in stroke survivors, but this requires much more study. Future investigation of this type of question warrants thoughtful development.

Efforts to investigate more global and pragmatic methods to mitigate dysphagia sequelae in routine practice and settings appear to be emerging. This is the motivation behind the performance of the second meta-analysis. It is representative of research trends within institutions and health care systems, and of the priorities of public health funding sources.

Hinchey et al. (2005) and DePippo et al. (1994) in particular, identified modest benefits from direct dysphagia protocols which combined rehabilitative and compensatory therapeutic methods of the types reported in the first meta-analysis, with risk factor management, patient surveillance, staff and patient education and/or training, active management of oral hygiene and diet, and follow up. One of these studies in particular showed a considerable improvement in morbidity and mortality when the institutional protocol was standardized (Hinchey et al., 2005), while the other (DePippo et al., 1994) showed a moderate effect for aggressive dysphagia management, though their sample was too small to generalize to populations. This model of combining treatment for swallowing disorders with risk factor management may offer the best blend of efforts to reduce dysphagia-related morbidity and mortality and deserves further attention in larger studies.

Both types of interventions investigated in these meta-analyses, individually administered treatments and institutional management protocols, are successful at addressing their stated goals of remediating oropharyngeal impairments through behavioral interventions, and reducing morbidity and mortality through institutional protocols that employ behavioral interventions along with additional standardized methods. However the studies in each of the meta-analyses reported in this chapter lacks the strengths of the other. Individually administered interventions for neurogenic dysphagia produce little value to the patient or the health care system, unless a predictable benefit is seen in terms of reduced hospitalizations and longer life expectancies. Likewise, institutional protocols that fail to provide sufficiently aggressive remediation of oropharyngeal biomechanical impairments may produce less positive effects on reduced morbidity and mortality associated with dysphagia.

Both meta-analyses were rigorously conducted to prevent inclusion of studies without high evidence quality. A recently published meta-analyses investigating published evidence regarding electrical stimulation for neurogenic dysphagia (Carnaby-Mann & Crary, 2007), exhibited substantially less rigor than the present meta-analysis, accepting and including studies that did not meet eligibility criteria for the present meta-analyses reported in this chapter. It failed to exclude studies whose controls for sources of bias such as blinding of judges and conflict of interest, measurement error, and other aspects of internal and external validity were of significantly lesser quality that in the meta-analyses. Meta-analysts must maintain diligence and integrity in the rigor of their evidence quality appraisal, to produce meaningful research synthesis. The absence of sufficient numbers of high quality research does not justify meta-analytic inference regarding the effects of treatments that were investigated in poorly designed, biased, or otherwise compromised research.

Strengths of the present meta-analyses include adherence to rigorous and strictly defined inclusion criteria, extensiveness of the search strategy, consultation with a librarian expert in constructing the search, and inclusion of both electronic and hand searches. Weaknesses include the use of a single meta-analyst, and the relative lack of sufficient numbers of high quality literature on the subjects under investigation. Significantly more, high quality evidence is needed to enable health care systems and governmental agencies to formulate guidelines regarding interventions for oropharyngeal dysphagia. These meta-analyses have highlighted the weaknesses in the current body of literature and, hopefully, will provide a road map for the design and evidence quality of future clinical investigation.

The small number of sufficiently good quality published investigations of the constructs evaluated in these meta-analyses points directly to the types of changes necessary in current and

future research into the effects of dysphagia interventions. Unlike pharmaceutical trials in which a single variable, taking one pill or another, is manipulated, large, randomized controlled trials investigating dysphagia interventions are difficult to design and successfully complete. Such studies are complicated by gradients of human compliance, involvement of numerous health care providers in each patient's care, social and ethical dilemmas inherent in age-related disease management, and the shortening length-of-stay of patients in modern health care facilities in the United States.

With increasing demand for this type of information, rigorous studies are beginning to emerge. Large studies of the type recently concluded by the Communication Sciences and Disorders Clinical Trials Research Group (CSDRG), whose publication of results is imminent at the time of this dissertation, which investigated short- and long term effects of dysphagia therapy on aspiration while swallowing, and on morbidity and mortality over a three month follow up, deserve attention by potential investigators and research funding sources. The results of this 10 year randomized controlled treatment study, in which the author of this dissertation participated as a regional principal investigator and member of the central laboratory as a judge for videofluoroscopic data, were presented by the investigators at the American Speech Language and Hearing Association convention in 2006 and have been emerging in the literature (Logemann et al., 2006; Logemann et al., 2001; Logemann & Robbins, 2007). This study examined the effects of postural and textural modifications on aspiration of fluids in groups of patients with neurogenic dysphagia caused by Parkinson's disease or dementia. Its long-term follow up component followed patients to clinical end points of pneumonia and mortality while monitoring secondary variables of hydration and nutrition during a 3-month post-randomization follow up period. This study could not be included in this meta-analysis because it had not

cleared peer review at the time of this meta-analysis; however, it is very likely that findings will be suitable for inclusion into future updates of this research synthesis.

There is little speculation regarding the link between aspiration of swallowed material and pneumonia pathogenesis (Marik, 2001), or between impaired oral intake and malnutrition. As elucidated in this meta-analysis, studies have investigated short-term results of treatment of swallowing impairments, and others have investigated the outcome of dysphagia protocols on health outcomes. To date, no published studies have directly investigated the long-term outcomes associated with individually administered interventions for neurogenic dysphagia on adverse health sequelae. As a result, the more important question concerning the likelihood of disease reduction afforded by specific interventions remains unanswered. These meta-analyses begin to address this important question using available research of sufficiently robust quality and rigor.

5.6.3 Conclusion

Meta-analyses identified small to large and significant therapeutic effects of individually administered interventions for neurogenic dysphagia in mitigating biomechanical swallowing impairments in patients with neurogenic dysphagia, and a small, non-significant effect for institutional dysphagia protocols designed to identify and manage dysphagia through institutional protocols. The studies in the each meta-analysis were not designed to investigate the complementary outcomes studied in its counterpart meta-analysis. That is, the link between remediation of biomechanical impairments and mitigation of adverse health consequences of dysphagia was addressed by neither group of studies. However the medical community, and specifically speech language pathologists, needs to connect individually administered

interventions for neurogenic dysphagia to reasonable predictions of improved health outcomes, to justify treatment at the impairment level.

Though too few studies show the effects of institutional dysphagia protocols in mitigating global health outcomes such as pneumonia and mortality, the findings from the two meta-analyses appear to suggest a need to conduct more research connecting the efficacy of remediation of swallowing impairments to their effectiveness over time, in mitigating the public health effects of oropharyngeal dysphagia in at-risk populations. Such research may produce more robust evidence supporting the need to advocate more strongly for a public health strategy that encourages and provides resources for treatment of biomechanical dysphagia impairments within organized, institutional, surveillance and management protocols for stroke patients. The clinical research community bears much of the responsibility for generating credible, high-quality evidence that points toward methods and combinations of methods to best mitigate the public health and individual burden of disease-produced oropharyngeal dysphagia.

The sheer volume of available published scientific research investigating dysphagia treatment indicates the relative importance of dysphagia in the management of public health. It also reveals two main areas of interest among published investigations of dysphagia therapy and its effects that have garnered funding and attention. These meta-analyses are early steps toward bridging the gap between these two complementary areas of clinical research.

Until investigations of common therapeutic methods include larger numbers of patients randomized to various protocols, sufficient follow up to morbidity or mortality endpoints, provide economic analysis to determine the relative cost-to- benefit ratio of management to health outcomes, and supply the research consumer with adequate information to facilitate further research synthesis, predictions of successful outcome will continue to be weak and

difficult to support. Particularly in the United States where the population is aging and diseases of aging are expected to rise, efforts to clarify the advantages and disadvantages of dysphagia rehabilitation with risk factor mitigation warrant current and future research.

Therapeutic interventions designed to alter oropharyngeal physiology and biomechanics in the short term are prescribed because they are expected to reduce adverse health sequelae. The first meta-analysis gives some support to the notion that similar methods and targeted dependent variables in sensory and motor manipulation should produce a modest benefit in dysphagic patients with stroke. There is also evidence that formal screening and monitoring protocols may reduce the risk of morbidity. The nine included studies in the two meta-analyses contained relatively robust methods and also controlled for experimental errors that cause uncertainty in the clinical marketplace. They are also good examples of research from which clinicians can reasonably estimate likelihood of successful outcomes as necessitated by the codes of ethics of the profession of Speech-Language Pathology among others (American Speech-Language-Hearing Association, 2003). These studies also provide reasonable models for future investigators to emulate. Certainly the cost associated with hospitalization for pneumonia can be considered a potential economic target of dysphagia therapy, and its reduction is measurable in dollars and other tangible and intangible outcomes. This meta-analysis serves as a useful starting point for future research synthesis to further clarify the effects of treatments for dysphagic patients. Future focus on impairments as they relate to both activity and participation, as well as on global indices of nutritional and pulmonary health in relation to oropharyngeal dysphagia, is recommended.

5.7 CHAPTER SUMMARY

In summary, several hundred articles were retrieved on the topic of oropharyngeal dysphagia assessment and treatment which have been published in the past 15 to 20 years. Studies reporting efficacy of individual interventions designed to alter swallowing physiology were "meta-analyzed" alongside studies evaluating the effectiveness of institutional dysphagia protocols designed to reduce adverse sequelae of dysphagia. Robust evidence is shown to exist supporting individual treatment modalities and their benefit to dysphagic patients. However the question of institutional protocols and their effect on reduced morbidity and mortality remains unanswered. The methods of research synthesis demonstrated in this study can begin to address the gap between behavioral treatment strategies and the purported health outcomes claimed to be affected by them. Future efforts at randomized trials should seek to fuse the two ends of this question together.

The next and final chapters describe the implementation of a carefully designed, prospective, experimental research investigation of the effects of a behavioral intervention on swallow physiology in healthy participants. This type of research, when extended to populations of dysphagic patients, will provide a growing body of evidence that future meta-analysts can test to update the research synthesis performed in the present chapter. As that body of high-quality evidence grows, so too will the ability of clinicians to select therapeutic interventions with more confidence.

6.0 INVESTIGATION OF THE IMMEDIATE EFFECTS OF SURFACE ELECTROMYOGRAPHIC BIOFEEDBACK ON BEHAVIORAL TRAINING OF THE MENDELSOHN MANEUVER

6.1 INTRODUCTION

Oropharyngeal dysphagia is a common result of conditions associated with aging, especially stroke. As many as half of stroke patients exhibit dysphagia at some point after onset, which increases their overall likelihood for developing pneumonia, malnutrition, or other sequelae of impaired swallowing function and airway protection (Dziewas et al., 2004). In many cases, patients are reported to benefit from interventions designed to compensate for the acquired sensorimotor abnormalities that cause misdirection of swallowed material. Some of these interventions require behavioral training to teach the patient to swallow safely using one or more novel maneuvers under the guidance of the speech-language pathologist (Logemann, 1999).

The most clinically important outcomes of dysphagia are caused by misdirection of swallowed food or liquids into the upper airway, or aspiration. Pneumonia is a major consequence of oropharyngeal dysphagia when aspiration is present. Hospitalization rates for aspiration pneumonia have increased by 94.5% (Baine et al., 2001) in the past two decades. Mitigation of this important public health problem is a desired outcome of proposed dysphagia treatments.

Surface electromyographic (sEMG) biofeedback-mediated strengthening programs have been validated as an effective adjunct to therapeutic rehabilitative efforts to assist neuromuscular reeducation in limb and trunk rehabilitation, bladder training, and other impairments of locomotion, self care, and activities of daily living, in patients with disorders affecting neuromuscular functions (Bolgla & Uhl, 2005; Dursun et al., 2004; Heymen, Jones, Scarlett, & Whitehead, 2003; Jerkins et al., 1987; Moreland, Thomson, & Fuoco, 1998; Petrofsky, 2001). Recent interest and evidence regarding the value of sEMG as an adjunct to dysphagia rehabilitation has emerged (Crary & Groher, 2000).

A randomized experiment was conducted to compare the effects of traditional training of healthy young participants in performance of the Mendelsohn maneuver to traditional training augmented with visual biofeedback using the sEMG activity in submental/floor of mouth musculature. This musculature is known to contribute to upper esophageal sphincter (UES) opening.

6.2 METHODS

6.2.1 Design

This was a two-group, repeated measures, randomized experiment designed to quantify the effects of an initial, single training session on the duration and amplitude of myoelectric activity of the submental musculature while swallowing, using a trained compensatory swallowing maneuver. All participants were trained to perform the Mendelsohn maneuver while swallowing

5 ml sips of water. Visual biofeedback was added during the training phase for one of the groups.

Participants were randomly assigned to two groups. Submental muscle group sEMG was recorded for all participants. The sEMG waveforms represented the raw data from which dependent variables were measured. All participants were masked from the sEMG waveform and underwent pre-training sEMG sampling to establish baseline deglutitive submental myoelectric activity before they were given any specific information regarding the Mendelsohn maneuver. Both groups received identical written instructions for performance of the Mendelsohn maneuver taken from a textbook in widespread use in academic programs for educating speech-language pathology students (Logemann, 1998). A hierarchy of identical verbal instructions and cues was provided until participants demonstrated they understood the maneuver (See Appendix E for script of instructions and cues). The 'traditional training' (TT) condition included only verbal and tactile cues. The 'biofeedback-mediated training' (BT) included the same verbal/tactile cues and visual cues from the sEMG muscle recordings during the training phase. All participants were masked from the sEMG waveform display during the data collection phases of the experiment. In summary, participants participated in three phases of activity: collection of pre-training baseline data, training in the Mendelsohn maneuver, and collection of post-training data.

6.2.2 Hypotheses

It was hypothesized that both participant groups would produce significantly longer swallow duration of sEMG activity while swallowing, and higher average and peak amplitudes of measured muscle groups when asked to swallow using the Mendelsohn maneuver. It was also

hypothesized that sEMG biofeedback-mediated training (BT) would produce significantly greater increases in the duration, peak and average sEMG swallow amplitudes, and more consistent sEMG duration and amplitudes, than traditional training. No significant group differences were expected with regard to minimum amplitude of submental musculature during either experimental condition.

6.2.3 Subjects

6.2.3.1 Inclusion and Exclusion Criteria

Eligible participants were of either gender, between 20 and 39 years of age, free of pre-existing medical diagnoses or histories of conditions associated with oropharyngeal swallowing disorders (e.g., neurological conditions, head and neck surgery or irradiation, and/or had never sought medical care for difficulty swallowing), and free of known allergies or sensitivity to skin products. Additionally, participants could not have facial hair in the submandibular region which would interfere with reliable performance and adhesion of surface electrodes. Students enrolled in clinical education and training in a speech-language pathology program, and speech language pathologists were not eligible. Of 29 study volunteers, 27 met all eligibility criteria. Two volunteers were excluded - one reported a prior reaction to a skin care product and one was no longer within the eligible age range. The remaining 27 participants (25 females and two males) gave written informed consent, were enrolled, and completed the study.

6.2.3.2 Sample size

Pilot data revealed that a sample size of ten participants per group was necessary to detect an effect size of $d = 0.8$, at $p \leq .05$.

Data collected prior to this investigation was used as pilot data to estimate the necessary sample size for this experiment. Pilot participants were four females who met all study criteria with the exception that they were speech pathology students. SEMG data were recorded from submental muscles for 5 ml water boluses while swallowing normally and while performing the Mendelsohn maneuver. Instrumentation used to collect both the pilot and experimental data allowed for quantification of four dependent variables: sEMG duration, sEMG peak amplitude, sEMG average amplitude, sEMG minimum amplitude. Two of these variables (sEMG duration, sEMG peak amplitude) are directly affected by the Mendelsohn maneuver (Logemann, 1998; Mendelsohn, 1993).

From the pilot data, effect sizes (Cohen's *d*) were computed for each of the four dependent variables of interest. These values are reported in Table 10.

Table 10. Power Analysis: Effect Sizes for Pilot Data

Dependent variable	*d*
Duration of sEMG	1.60
Peak sEMG Amplitude	.98
Average sEMG Amplitude	2.66
Minimum Amplitude	.05

A power analysis using the dependent variables duration, peak sEMG amplitude, average sEMG amplitude, and minimum sEMG amplitude ($p \leq .05$, one-tailed) revealed that a sample size ranging from five to 12 participants, assuming an effect size (*d*) range of 1.6 to 0.8 respectively, would detect a significant difference caused by sEMG biofeedback-mediated Mendelsohn maneuver training Table 11.

Table 11. Power Analysis of Pilot Data

Effect Size (*d*)	Required n	
	2-tailed	1-tailed
1.6	6	5
1.5	6	5
1.4	7	5
1.3	7	6
1.2	8	6
1.1	9	7
1.0	10	8
0.9	12	10
0.8	15	12

A sample size of 10 complete data sets for each participant group (i.e., control and experimental) was selected for the following reasons: (a) the effect sizes for the dependent variables of interest (i.e., sEMG duration and sEMG peak amplitude) were greater than 0.8, (b) the power analysis was obtained from a small sample, and (c) because the planned experiment was expected to produce a larger effect than the method used with pilot participants. To ensure 10 useable data sets in each group, 12 to 15 participants were recruited per group.

Twenty-seven participants were recruited and completed the study, 25 females and two males. The two male participants were randomized into the same group. There is little evidence of between-gender differences in swallow physiology, though some studies have reported differences in swallow apnea between males and females (Hiss, Treole, & Stuart, 2001). Since fewer males were recruited than expected, the proportion of male to female participants was extremely unbalanced. After discussing this with the statistical consultant, a decision was made

to exclude the data generated by the two male participants from the analyses to maintain homogeneity of the sample. The final participant pool was comprised of 25 female participants.

6.2.4 Overview of Procedures

Participants were initially screened for eligibility in person, electronically, or by telephone. After informed consent was obtained, participants were randomized to experimental and control groups, and underwent pre-training testing, training, and post-training testing. Sessions lasted approximately two hours. After data collection ended, participants were given an incentive payment of $20.00. A subject flow diagram appears in Figure 5.

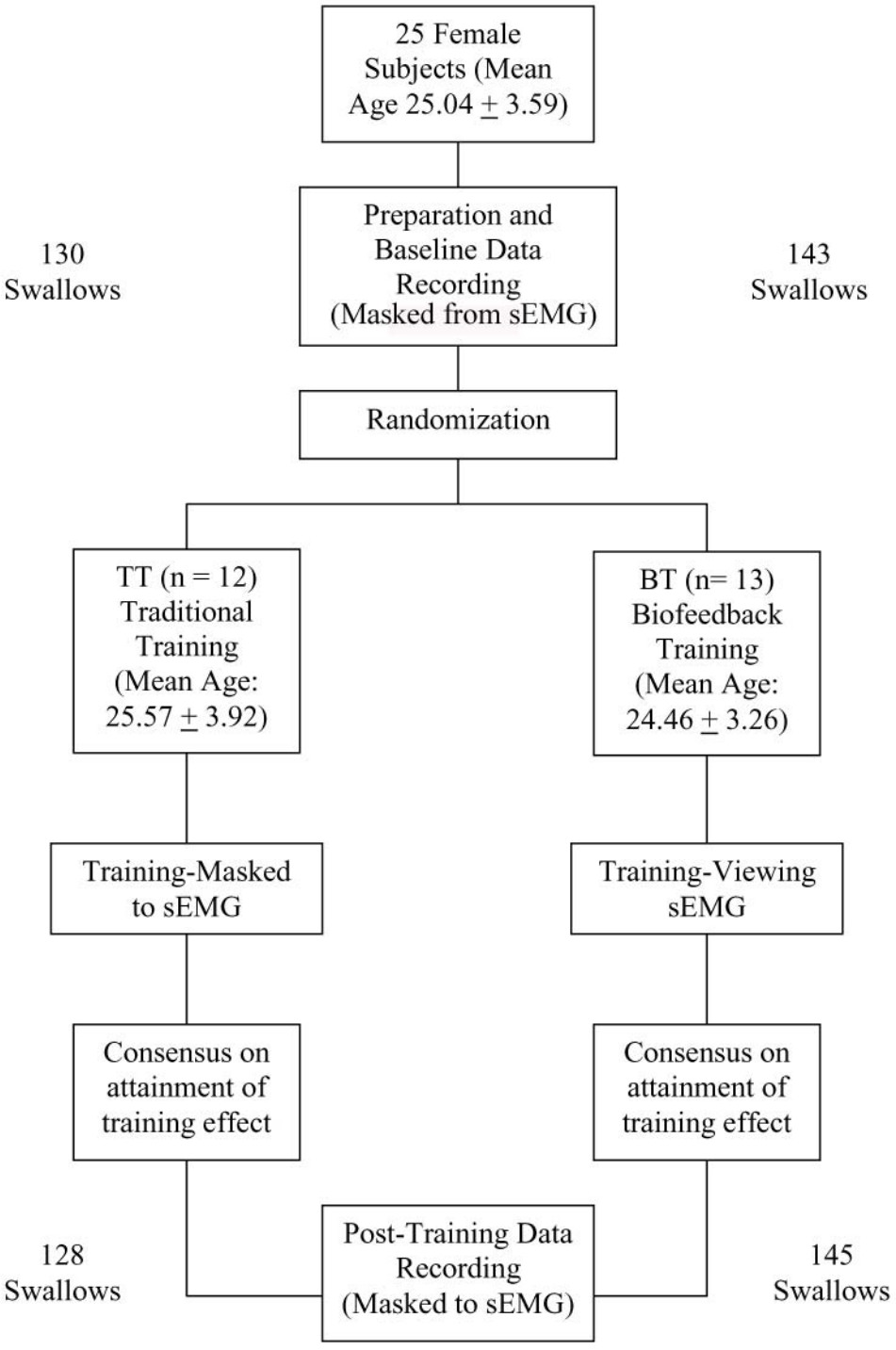

Figure 5. Subject Flow Chart

6.2.4.1 Recruitment

After approval of the experiment by the University of Pittsburgh Institutional Review Board, 29 healthy, young graduate students responded to an IRB approved, posted recruitment advertisement within the School of Health and Rehabilitation Sciences at the University of Pittsburgh. No clinical speech-language pathology students were included in the participant pool for the investigation conducted for this dissertation.

6.2.4.2 Screening

Criteria for inclusion were established a priori to limit sources of variability among participants and were adapted from previous investigations of normal oropharyngeal deglutition (Robbins et al., 1992). All respondents were pre-screened by telephone or in person before inclusion. After they responded to posted recruitment notices, potential participants were informally pre-screened by phone or in person to determine their eligibility, using information contained on a screening form (Appendix F). An appointment was made to participate in the experiment if potential participants met age criteria (between 20 and 39 years of age) and denied a history of swallowing disorders or symptoms. Formal, in-person screening was conducted during the appointment, using the screening form (Appendix F) to document eligibility.

Twenty-nine potential participants passed the pre-screening and visited the laboratory for formal screening. During this final screening, one participant was disqualified because she no longer met age limitations, and one was disqualified because she admitted to skin sensitivity to tape or other products. The final pool of participants consisted of 25 females and two males.

6.2.4.3 Randomization

A single block randomization plan was developed for an expected recruitment pool of 20 participants. The randomization plan was developed a priori using an internet-based program (Dallal, 2003) which employs a previously published pseudo-random number generator (McLeod, 1985; Wichmann & Hill, 1982). This plan randomly assigned participants to either of two groups within a single block while keeping the sizes of the two groups similar (Altman, 1990).

Since recruitment was more successful than anticipated, and the block randomization scheme was developed a priori to ensure equal-sized groups of 10 per group, eligible participants entered into the research after the twentieth participant were assigned by coin toss at the time of their visit. Twelve participants were randomized to the traditional training (i.e., Group 1, TT; the control group), and thirteen were randomized to experimental biofeedback-mediated training (i.e., Group 2, BT; the experimental group).

6.2.4.4 Subject Preparation

After randomization, participants and instrumentation were prepared for the experiment. Participants were not provided with specific explanations of the Mendelsohn maneuver to reduce inadvertent, confounding behavior that could influence baseline swallowing data.

Electrode Placement

Prior to electrode placement, the skin overlying each participant's submental musculature (i.e., anterior and lateral borders are made up of the mandible; posterior border is made up of the body of the hyoid bone) was swabbed with isopropyl alcohol impregnated prep pads (Webcol ® alcohol preps, Tyco Healthcare, Mansfield, MA, USA) to remove skin oil and to ensure adequate

adhesion of the surface electrodes. Bipolar surface electrodes (Bio-Med GS-27 ® saline/adhesive pre-gelled disposable sEMG sensors; 3.175cm. x 1.90 cm. rectangular pads) were applied to skin overlying the submental geniohyoid-mylohyoid-anterior digastric region. There was sufficient separation of electrode pads from the mandible to prevent erroneous signals from the facial musculature originating on the mandible (e.g., platysma) (Ertekin et al., 1998; Ertekin et al., 2001; Ertekin et al., 2002; Ertekin, Yuceyar, & Aydogdu, 1998). This electrode placement has been shown to capture activity from the three submental hyoid elevators (Palmer et al., 1999; Perlman, Palmer, McCulloch, & Vandaele, 1999; Schultz, Perlman, & Vandaele, 1994).

The participant's forehead was similarly prepped prior to placing a third electrode. A reference, or ground electrode was placed on the skin of the forehead (Ding, Larson, Logemann, & Rademaker, 2002; Goodman, Robbins, Wood, Dengel, & Luschei, 1996). Adhesive tape (Micropore ™ Hypo-Allergenic Surgical Tape, 3M™ Corp. St. Paul, MN, USA) was used with some participants to ensure adequate adhesion. Participant preparation took approximately 10 to 15 minutes. Figure 6 and Figure 7 display the instrumentation and electrode placement on a volunteer not included in the experiment.

After electrode placement, each participant was seated comfortably facing the examiner and away from the sEMG display. Participant identification was recorded into a log and anonymous participant numbers were entered into the database to de-identify participants.

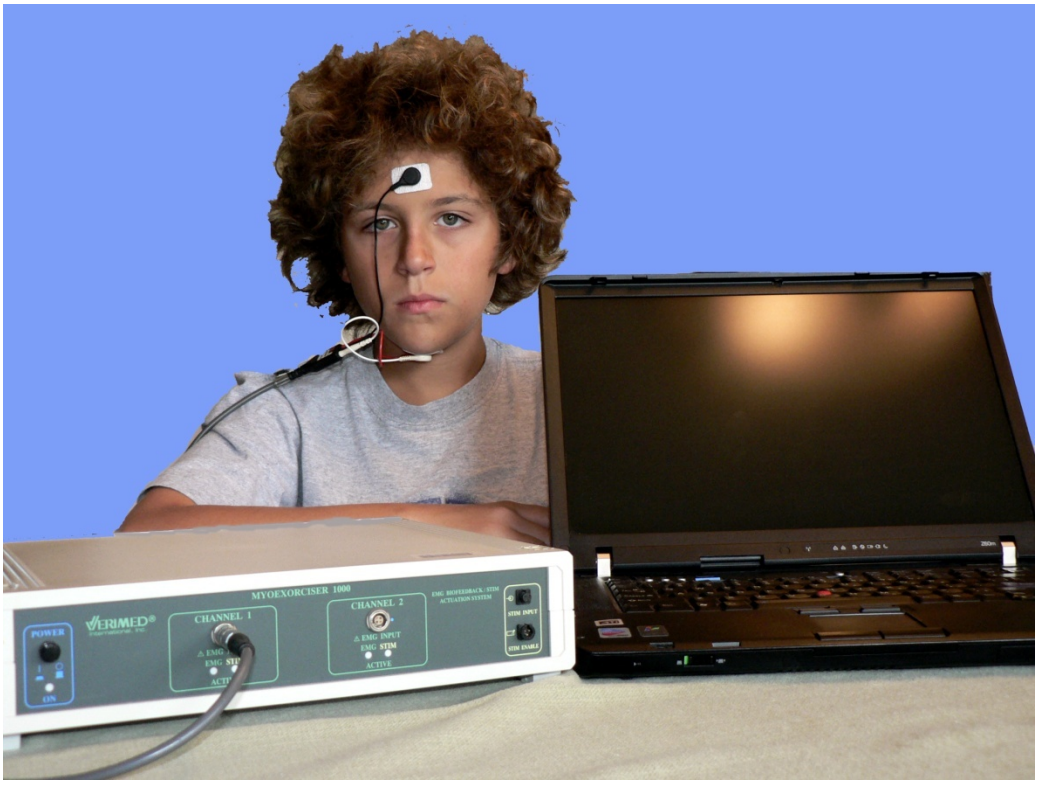

Figure 6. Instrumentation and Electrode Placement

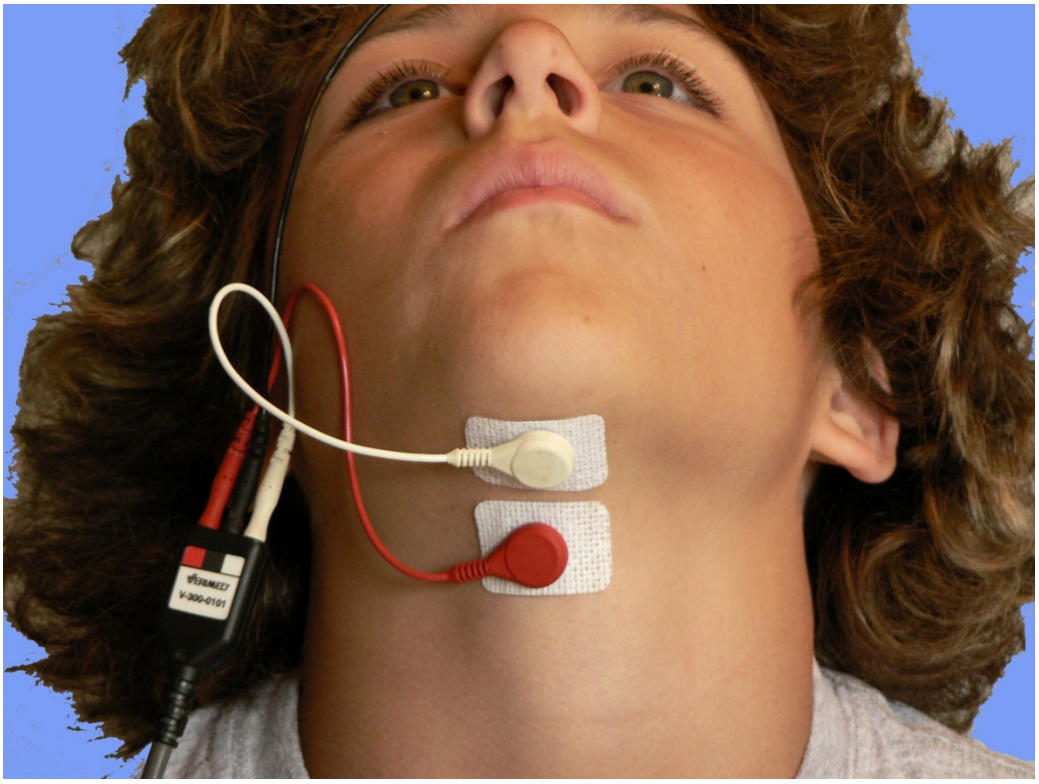

Figure 7. Submental Electrode Placement

6.2.4.5 Training of Participants

Each group of healthy volunteers was trained identically with the exception of the addition of sEMG biofeedback in the experimental group. For both groups, training sessions lasted no more than 20 minutes (range: 7 to 20 minutes) and concluded when both the participant and investigator agreed, using the feedback available for the method of training, that the participant was able to prolong the duration of palpable laryngeal elevation (TT group), or the duration of the submental sEMG waveform (BT group).

Traditional Training (TT)

The control group (TT) received traditional clinical training via investigator instruction to prolong laryngeal elevation during the swallow by using sensory information and tactile cues to "hold" the swallow following Logemann's (1998) instructions. Participants were instructed to palpate the laryngeal framework while swallowing to judge the effect of their efforts to prolong the swallow, while the investigator provided verbal reinforcement. Participants in the TT group were masked to the sEMG display. To ensure standardization, instructions and feedback were scripted (see Appendix E), thus ensuring that all participants were given the same directions and cues.

Biofeedback-Mediated Training (BT)

In addition to the clinical training provided to the control group (TT), the experimental group was unmasked from the sEMG waveform display and was provided with written and verbal instructions for use of the sEMG biofeedback waveform display during their training (refer to script in Appendix E). Therefore, the BT received the control training method plus visualization

of the sEMG waveform and instructions on how to use the visual display to prolong the swallow waveform.

6.2.5 Instrumentation and Variables Measured

6.2.5.1 Instrumentation: sEMG Data Collection

In this experiment, myoelectric waveforms were displayed on a standard LCD video monitor and were represented as an image of continuously captured myoelectric activity from the sampled muscle group. Myoexorciser hardware and software (Myoexorciser 1000, Verimed International, Coral Gables, FL, USA) were used for data collection and analysis in this experiment. This hardware consists of receiving and filtering equipment, input terminals for receiving electromyographic signals from surface electrodes, and a serial interface for connection to a personal computer. Electrode leads were attached to electrode pads at one end and to the electromyographic signal receiver at the other end. This device was connected to the serial port of a laptop computer (Dell Latitude CPt, Dell Inc., Round Rock, TX, USA) running Windows 98© operating system (Microsoft, Redmond, WA, USA), that contained the Myoexorciser software (Verimed International, 1995). The software recorded and displayed sEMG data from the signal receiver in real time.

The Myoexorciser package captures sEMG data with a common mode rejection rate of 100 dB at 60 Hz to filter electrical noise between 25 Hz and 1 kHz from internal or external sources (Verimed International, 1995). Channel cross-talk rejection for this instrument is rated at greater than 80 dB, however only a single channel and a ground electrode were used in this experiment. The hardware device contains pre-set signal processing parameters which provide a clear visual representation of the myoelectric activity for “online monitoring” of data, and also

for later use during data analysis. Signals undergo software filtering and rectification to produce smoothed, positive-going waveforms which represent averaged myoelectric activity across the target event. For data analysis, the software package contains subroutines for signal integration (i.e., the process of calculating the area under the EMG signal curve over a certain interval of time) to produce amplitude values expressed in microvolt*seconds (μV*sec). Microvolt*seconds is an electromyographic correlate to the amount of force exerted by a muscle (De Luca, 1997).

An example of an sEMG waveform from a normal swallow of 5 ml of water appears in Figure 8. The horizontal axis shows elapsed time in seconds within a pre-set time interval (i.e., Figure 8 shows a 10 s time interval). The duration of data displayed per screen can be set at 10, 15, or 30 seconds. The sEMG waveform scrolls continuously from left to right until it reaches the end of the pre-set screen duration, after which the screen refreshes and displays the next interval. The sweep duration (horizontal axis) was set to display 30 s during the training phase and viewed at either the 10 s or 15 s screen interval for data analysis and [text] display.

The vertical axis represents sEMG amplitude. In this figure, the values on the x axis represent percentages of the preset sEMG amplitude range. For example, in Figure 8, the participant's preset sEMG amplitude range was 0 μV*sec to 20 μV*sec. The values displayed in the vertical axis for amplitude (i.e., 25, 50, 75, and 100) represent percentages of the maximum value of the preset amplitude range. Hence, a peak rising to the "50% FS" level in a participant whose amplitude range was preset to 0-20 μV*sec, represents 20μV*sec times 50%, or a peak amplitude of 10μV*sec. The Myoexorciser software requires the investigator to pre-set the upper limit of the vertical (amplitude) axis of the waveform display before data collection. This investigator determined the appropriate setting for each participant's maximum myoelectric

amplitude using a 5 ml water swallow. Thus, settings were specific to each participant's own level of muscle activation while performing the target behavior.

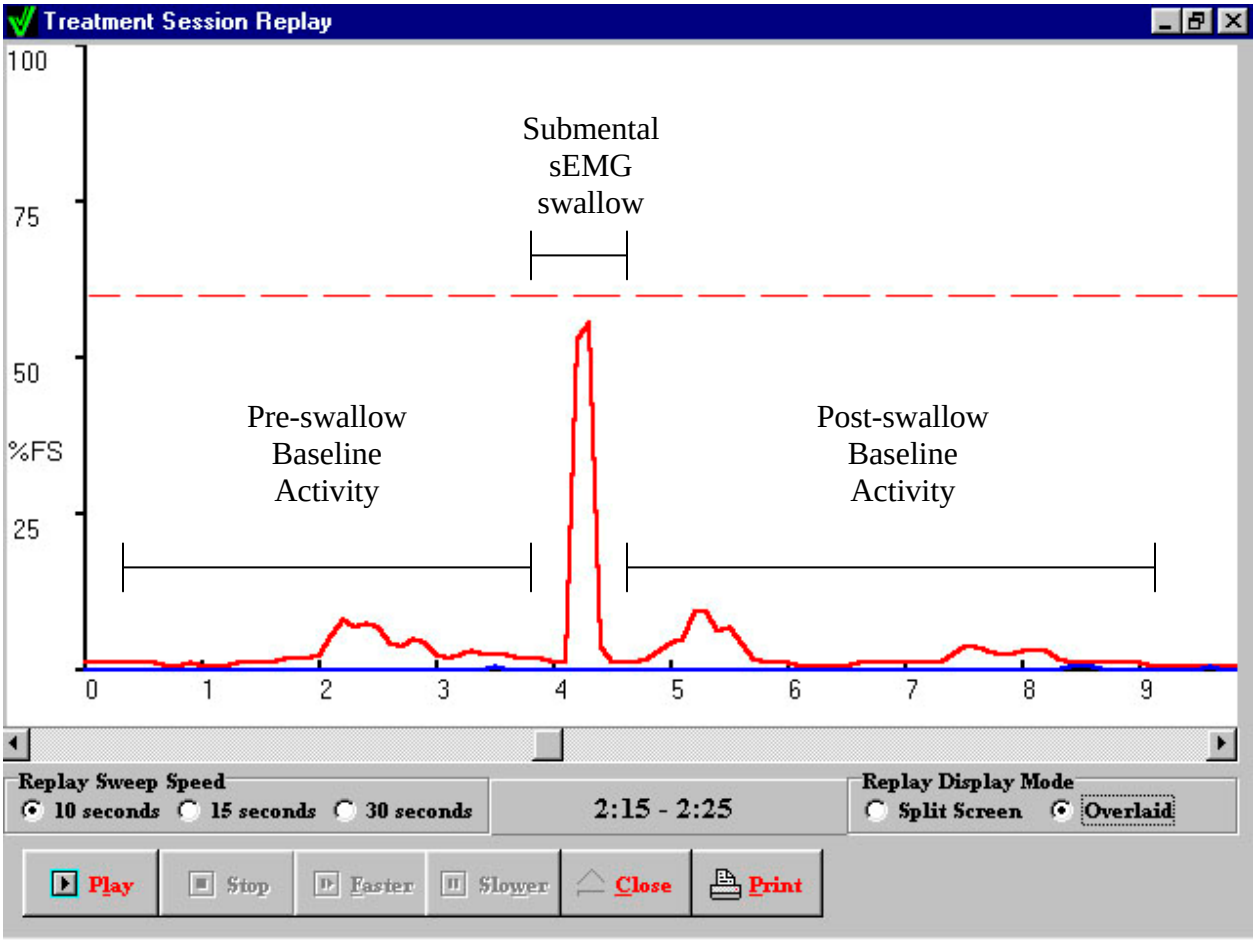

Figure 8. sEMg Waveform from a 5 ml Baseline Swallow

Myoelectric events which generate greater amplitude than the scale's pre-set maximum are truncated in both the visual display and data collection modules by the software. Under these conditions, portions of the EMG signals would appear flat and information about the peak amplitude would be lost. Therefore, it was imperative that the amplitude scale be set with an upper limit that would not truncate the raw data. Also of concern, would be pre-setting the scale to an excessively broad range. For example, a pre-set upper limit of 80 μV*sec would capture absolutely all myoelectric perturbations, but such an extensive scale would yield tiny waveforms

lacking the necessary detail for making precise visually-based measurements and judgments. Therefore, the investigator predetermined the scale for the vertical axis for each participant in order to prevent data loss due to peak attenuation or peak compression, as well as to facilitate judgment accuracy for later data analysis. The investigator's experience with the Myoexorciser hardware and software suggested that some participants would produce peak waveforms that exceeded 10 μV*sec and some would not. For this investigation, the vertical (amplitude) axis was set at either 10 μV*sec or 20 μV*sec depending upon the amount of submental muscle activity exhibited during the masked, 5 ml practice swallow.

As seen in Figure 8, the swallow onset and offset remain visually distinct and are not influenced by small fluctuations in the baseline. Myoexorciser software permits cursor placement of markers onto the image for subsequent measurement. Software generates actual timer (i.e., onset and offset) and amplitude (i.e., minimum, mean, peak amplitude) values between the cursors. The dotted horizontal line that appears in Figure 8 also appears on the video display monitor during data collection. It serves as a visual target for patients on muscle strengthening programs and/or a way to illustrate consistency of muscle activation while performing the target behavior.

6.2.5.2 Measures

Dependent Variables

Based on the pilot data, the primary dependent variables of interest in this experiment were sEMG duration and sEMG peak and average amplitude during the swallow. The secondary dependent variable was minimum amplitude.

The Mendelsohn maneuver is designed to prolong the duration of muscular forces employed while swallowing. Recent studies investigating the Mendelsohn maneuver have suggested that increased myoelectric amplitude from this muscle group may also be caused by training (Ding et al., 2002). Therefore, all three selected dependent variables of interest were expected to exhibit significant changes after training.

Average myoelectric amplitude over an entire swallow is a byproduct of the amplitude of myoelectric activity over the duration of the myoelectric event. It does not appear, on the surface, to be particularly interesting as a dependent variable, as it may be quite high though the swallow duration may fail to be prolonged by the participant. Conversely, average myoelectric amplitude may be quite low over the course of a significantly prolonged swallow, due to the long duration of the swallow itself. For this reason, hypotheses regarding average myoelectric amplitude were not generated, though these data were included in the analysis.

Minimum sEMG amplitude was considered a secondary dependent variable of interest, hypothesized to remain at its pre-training level after training was completed. Since the Mendelsohn maneuver is a compensatory maneuver performed while swallowing a bolus, it is not expected to alter the pre- or post-swallowing myoelectric activity in the target muscle group. For this reason minimum amplitude from the swallow waveforms was included as a secondary dependent variable that would act as a control variable (i.e., minimum amplitude is not expected to exhibit change with training).

Independent Variables

The independent variables for this investigation were group (TT, BT) and time (pre-training, post-training).

6.2.5.3 Data Recording and Processing

Raw sEMG waveforms were recorded and processed in a masked fashion by the investigator and entered into spreadsheets. Pre-training data measurements were performed independent of post-training data measurements.

Pretest / Posttest Data Collection

Pre- and post-training data collection sessions were identical to one another. After preparation and masking from the sEMG waveform display, and before any instruction regarding the training were provided, participants performed ten swallows for each condition (pre- and post-training). The investigator measured 10 to 12 5-ml water boluses with graduated syringes which were dispensed into small cups for each participant. Participants were instructed to self-administer each bolus and then swallow after hearing the verbal command to swallow. The investigator recorded the approximate time (time mark) of each swallowing command on a data collection form to facilitate identification of swallowing waveforms of interest during data reduction and analysis. The recorded data were labeled and saved to a file. The investigator provided no prompts or cues to participants during the data collection. Baseline (pre-) and experimental (post-) data collection took approximately 10 to 20 minutes per participant per condition.

Two data collection logs were used to ensure investigator masking to group assignment. The initial log was used to record the names of participants, their subject identification number, and randomization assignment. The investigator was masked to this log during data analysis. A different log, identifying participants only by number and group, was used during data collection to record approximate time of swallows and any miscellaneous comments (e.g., participant was talking).

To dissociate measurement of post-training data from pre-training data, baseline and experimental swallows were analyzed independently. Measurements were recorded on separate sheets. Additional precautions were taken to reduce investigator bias caused by subject number familiarity. All 25 pre-assigned subject numbers were entered into a random number generator so that measurement of the post-training swallows was done in random order.

The data were transferred by the investigator from data collection logs to a spreadsheet (Excel, Microsoft, Redmond, WA), and later imported into the SPSS © version 14 statistical software package (SPSS Inc., Chicago, IL). Durations of swallow events were calculated by subtracting time of onset from time of offset. Amplitude values were generated by the Myoexorciser software.

6.2.5.4 Examples of Baseline and Experimental sEMG Waveforms

Examples of pre-training swallow sEMG waveforms from a participant appear in Figure 9 and Figure 10. Examples of post-training swallow sEMG waveforms from the same participant appear in Figure 12 and Figure 13. Figure 9 (pre-training) and Figure 12 (post-training) display the participant's raw sEMG waveforms. Figure 10 and Figure 13 display the same swallow events with the cursor markers placed by the investigator to indicate swallow onset and offset. Sample measurements performed on the aforementioned waveforms appear in Figure 11 and Figure 14. The actual timer values used to calculate event durations are shown in the Channel 1 column of the summary, above the amplitude values.

The horizontal axis of the waveforms display reflects time in seconds and indicates the approximation of the time points within the 15 second display-interval rather than the actual timer value. Exact timer values are generated when the waveforms are marked and then displayed in a data summary screen (Figure 11).

The vertical axis of these figures reflects sEMG amplitude as a percentage of the pre-set calibrated maximum amplitude. This axis was set prior to any data recording in accordance with the participant's own baseline level of EMG activity while swallowing. This was done to avoid loss of data due to peak attenuation of sEMG signals.

The vertical lines which appear at the left and right ends of the sEMG waveform peak in Figure 10 and Figure 13 are the cursors placed by the investigator. Markers correspond to the onset (left vertical cursor) and offset (right vertical cursor) of the waveform. Visual comparison of pre- and post-training swallows from the same participant (Figure 9 and Figure 12) shows that differences in the width (duration) and height (peak amplitude) can be observed and measured.

6.2.5.5 Procedures for Swallow Identification on Raw Data

Figure 11 and Figure 14 display data measurements from a marked swallow. Onset and offset of the swallow waveforms were marked by the investigator using Myoexorciser software (Figure 10). Once markers were placed, the software displayed the peak, average, and minimum amplitude for each measured swallow interval (Figure 11). The start (onset) and end (offset) of each marked waveform was recorded onto a data collection log and later converted to 'duration' by subtraction.

The peak of each waveform represented the point at which maximum myoelectric amplitude was generated during the swallow. The ascending and descending phases surrounding this peak indicate the rise from pre-swallow resting and the fall to post-swallow resting, respectively. Onset of deglutitive submental myoelectric activity was defined as the point of onset of a continuous or steep, systematic upward vertical deflection of the sEMG waveform from the pre-swallow baseline, toward the peak. This deflection approximated the time-coded swallow event that had been recorded by the investigator during data collection. Offset was

defined as the end of downward vertical displacement of the waveform corresponding to the end of the time-coded swallow event. Therefore, the typical waveform began when continuous upward deflection from the pre-swallow baseline toward the waveform peak was observed (onset). It lasted until the end of the descending phase from the waveform peak (offset) at which point a stable post-event baseline was observed (Crary & Groher, 2000; Ding et al., 2002). When the post-event baseline was achieved but did not remain stable, the initial return to baseline was selected as the offset. This occurred occasionally when participants spoke or lowered the mandible after the swallow, thus, recruiting the submental musculature. This extraneous movement was noted by the investigator during data collection.

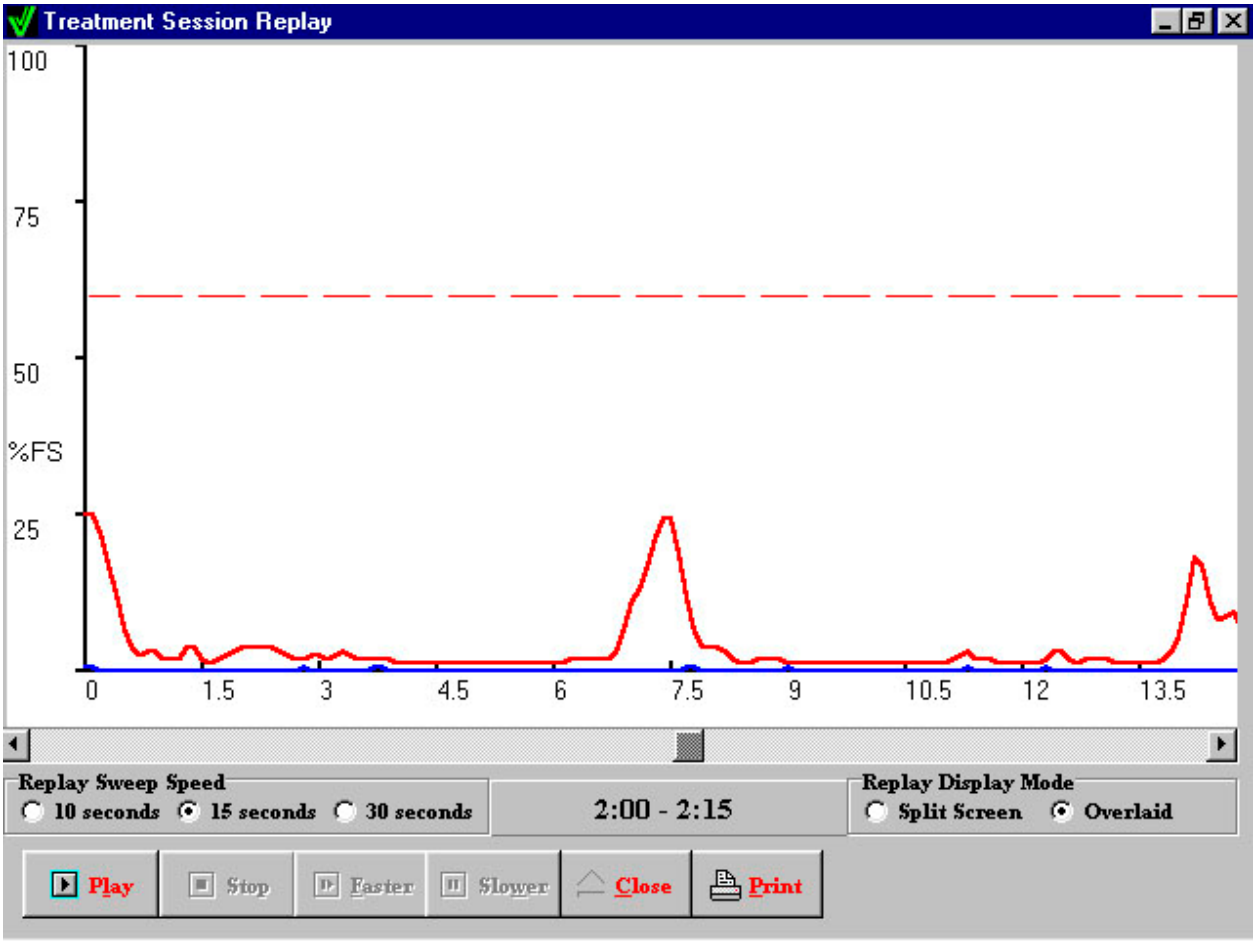

Figure 9. A Pre-Training (Baseline) Swallow Waveform

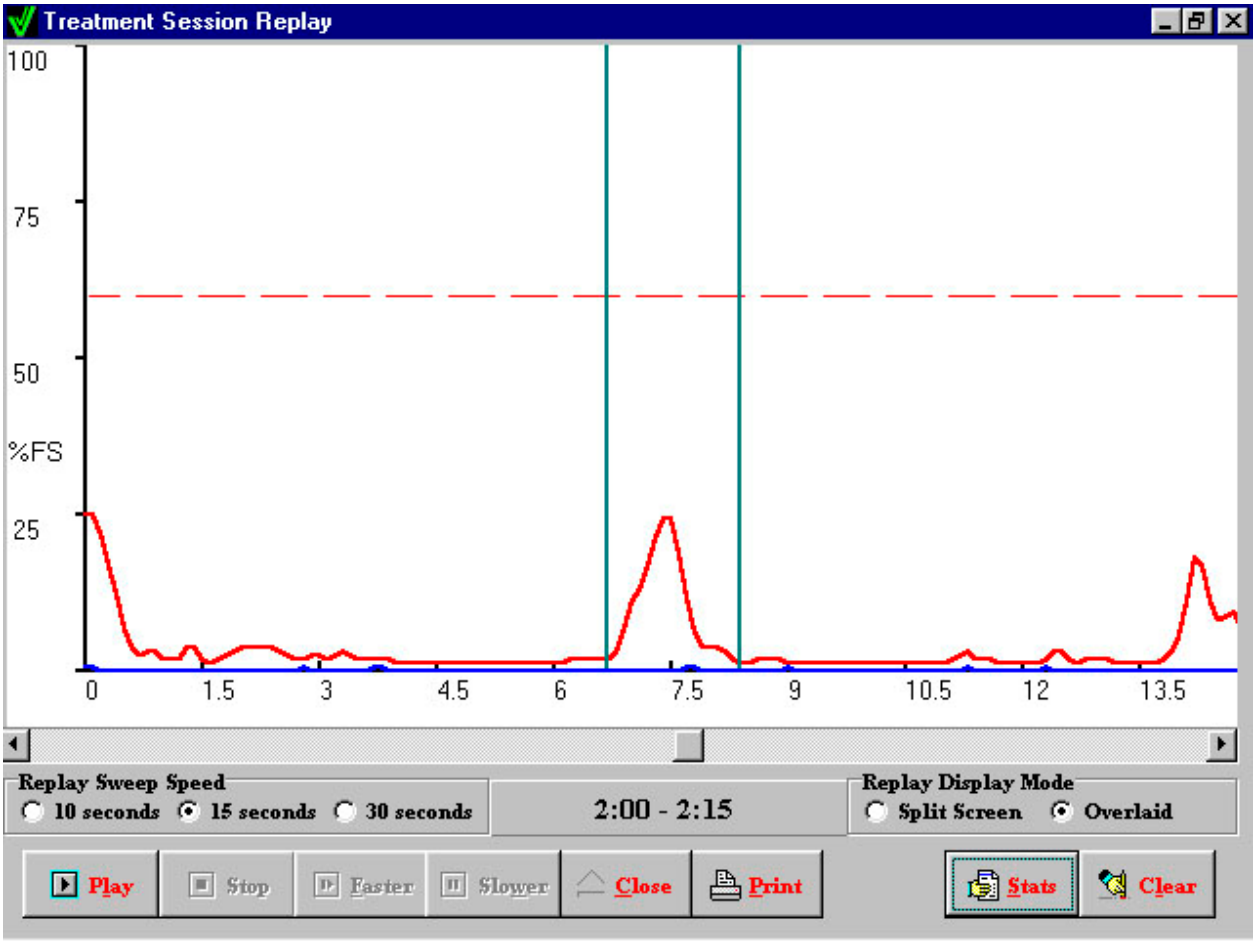

Figure 10. Markers Placed at Onset and Offset of a Baseline Swallow Waveform

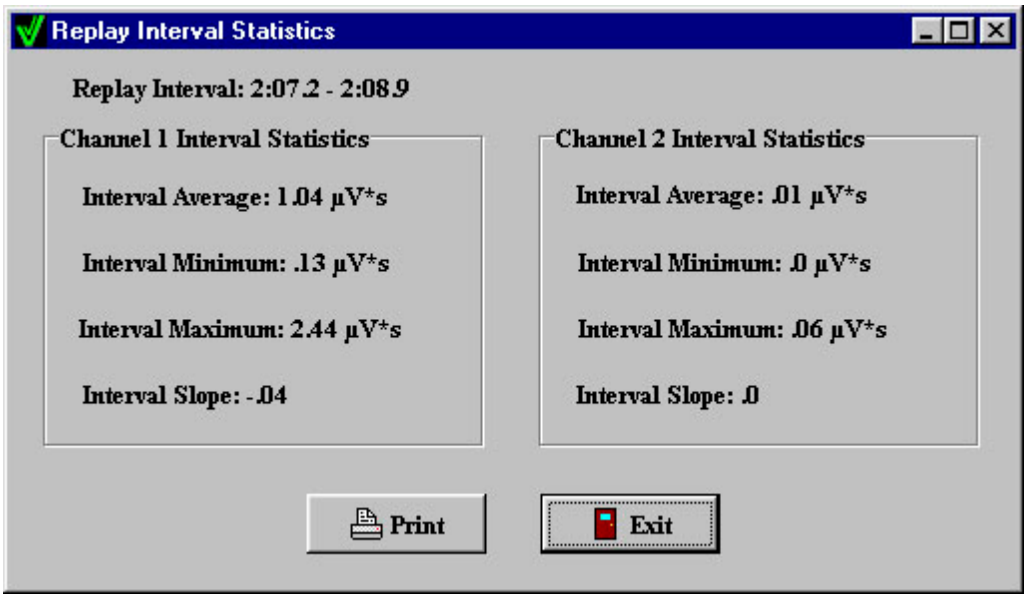

Figure 11. Measurements from Baseline Swallow Displayed in Figure 9 and Figure 10

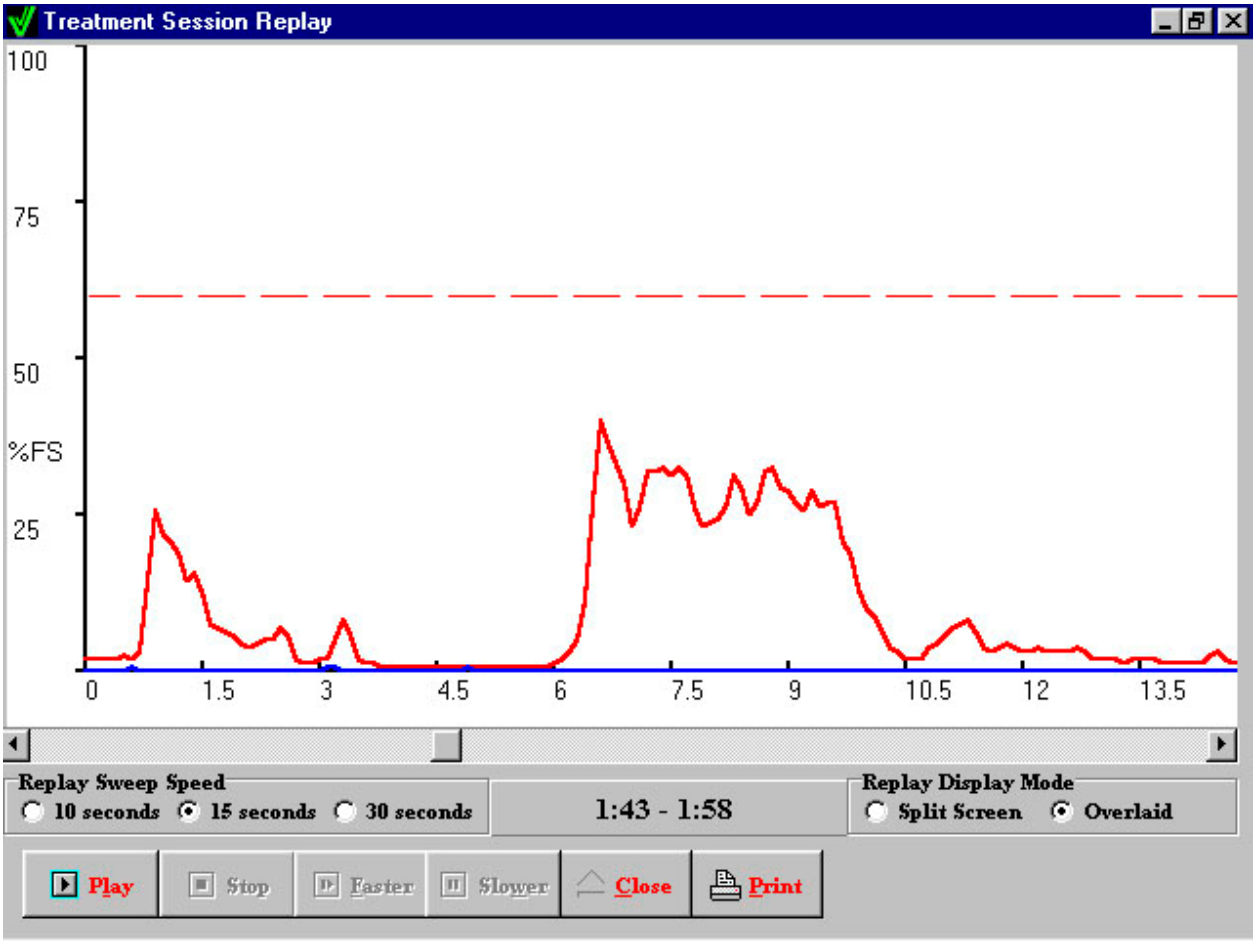

Figure 12. A Post-Training Swallow from Subject Recorded in Figure 9 – Figure 11 .

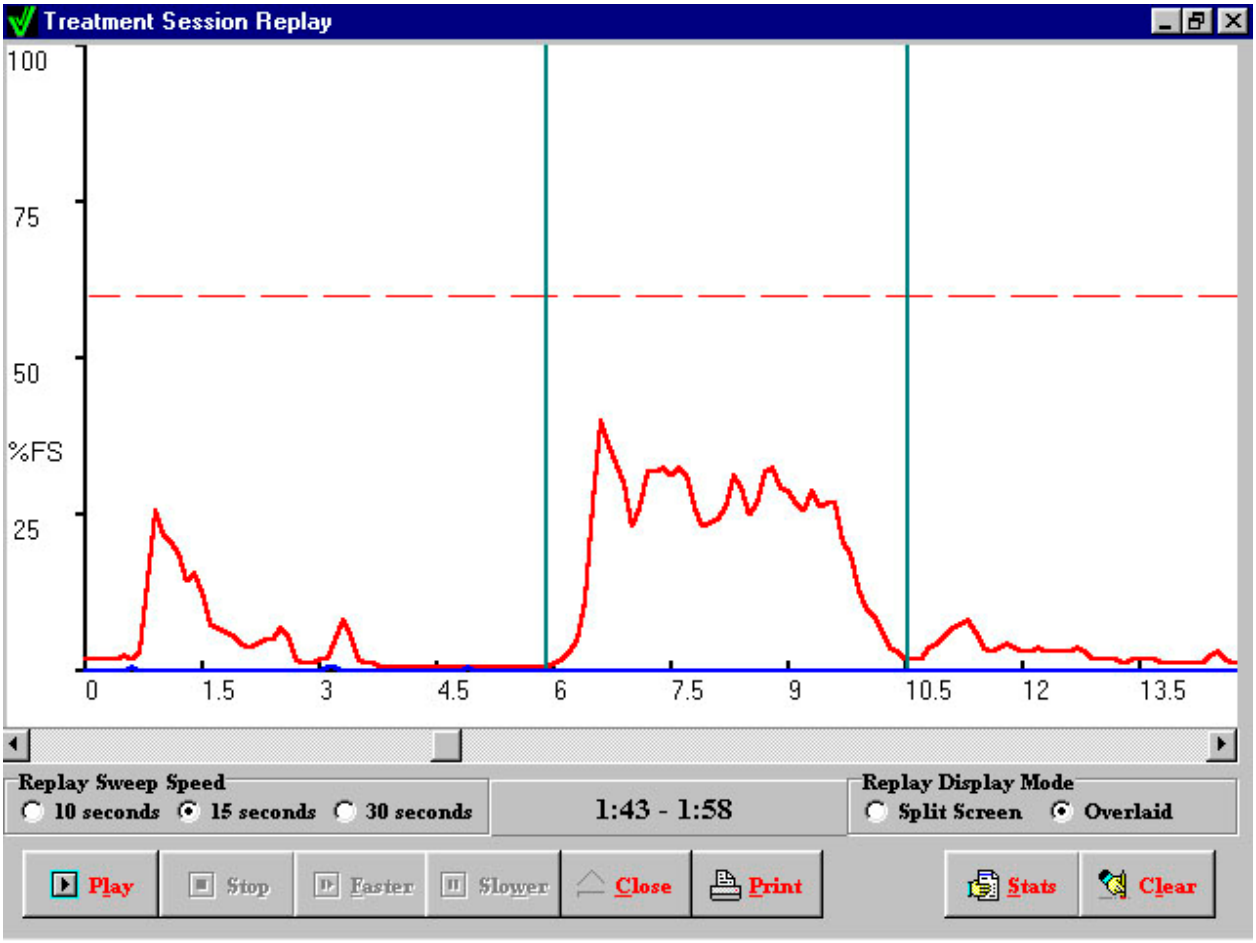

Figure 13. Markers Placed at Onset and Offset of a Post-Training Swallow Waveform

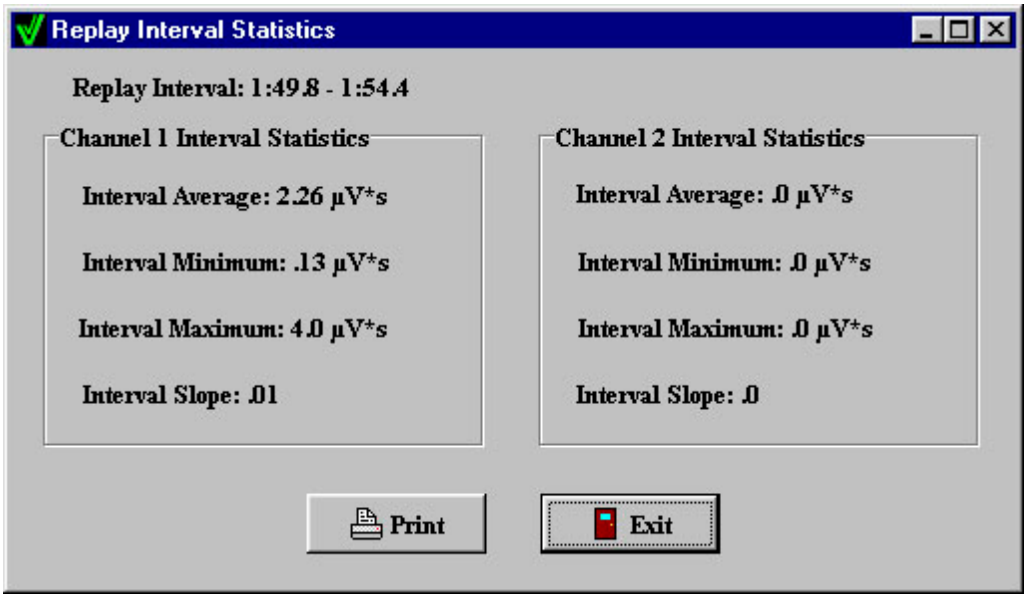

Figure 14. Measurements from Post-training Swallow Displayed in Figure 12

6.2.6 Statistical analysis

This repeated-measures, two-group investigation was designed to investigate the effects of using visual biofeedback as an adjunct to the traditional way that speech-language pathologists train patients to perform the Mendelsohn maneuver. Statistical tests were performed to evaluate the homogeneity of the groups before training, and the effects of the two training methods on the four dependent variables. Additionally, evaluation of the variability of myoelectric performance before and after training was performed, to determine whether the consistency of performance of the Mendelsohn maneuver was differentially influenced by the two training methods.

To test homogeneity of the groups before training, and to assess the effectiveness of the randomization, independent samples t-tests were performed on participant ages, and on pre-training data from each of the four dependent variables (duration, mean amplitude, minimum amplitude, peak amplitude). Additionally, the variability of participant myoelectric activity while swallowing before training was evaluated using an independent t-test of the coefficients of variation from each participant's pre-training raw data, to determine the physiologic homogeneity of the groups before training, and to evaluate the effectiveness of the randomization. All participants were females, so a gender comparison was unnecessary.

To test whether changes in myoelectric activity were caused by either of the two methods of training, a mixed two-way analysis of variance (ANOVA) was performed to determine the main effect of the independent variable time (pre-training to post-training), main effect of the independent variable group (TT, BT), and the interaction of group X time, on the three primary dependent variables (duration of sEMG waveform, average and peak sEMG amplitudes produced during the swallow), and one secondary dependent variable (minimum sEMG amplitude).

To test the hypothesis that sEMG mediated training would produce more consistent performance of the Mendelsohn maneuver than traditional training, the coefficient of variation (CV) was calculated for the each of four dependent variables for each participant, using Equation 19, where $\overline{X}$ represents the mean value for the dependent variable of interest, and *SD* represents the standard deviation of the dependent variable of interest (Munro, 2001). The CV is the ratio of the sample standard deviation to the sample mean, expressed as a percent. It is used when comparing standard deviations (SD) between studies that investigated the same variables or when comparing standard deviations in studies that investigated the same dependent variables in two or more groups receiving different treatments.

Equation 19. Coefficient of Variation

$$CV = 100(SD / \overline{X})$$

Paired samples t-tests were performed on each group's pre- and post-training coefficients of variation to determine whether training produced significant perturbations in participants' variability of myoelectric activity while swallowing, by comparing pre-training CV to post-training CV.

To test whether the two training methods differentially affected the variability of sEMG activity while swallowing using the Mendelsohn maneuver, a mixed methods two-way analysis of variance (ANOVA) was performed to determine the main effect of time (pre-training to post-training), main effect of group (TT, BT), and the interaction of group X time, on the coefficients of variation of the four dependent variables.

Finally, effect sizes (Cohen's *d*), perhaps the most clinically relevant index of the likely effect of a therapeutic technique with a particular patient (Haynes et al., 2006), were calculated for each dependent variable to determine the clinical importance of the results. Cohen's *d* is an

expression of the expected difference between the effects of two treatments (or one treatment versus control treatment) in units of standard deviations. Cohen's *d* is an effect size statistic that uses published research findings to derive the predicted difference a treatment would be expected to produce when compared to the investigated control treatment (Cooper & Hedges, 1994). Since each group in this study contributed a series of pre-training/control swallows and a series of post-training/compensatory swallows, each group has participated in a randomized controlled trial and generated data from which effect sizes for each training method can be computed. Additionally, the effect sizes for the different treatment conditions (TT and BT) can be compared to one another.

Effect sizes (Cohen's *d*) were computed for each of the dependent variables within each group using Equation 1 (see also description in Chapter 5.0 for meta-analysis), where M_2 represents the post-training value and M_1 represents the pre-training values. Raw pre- and post-training means and standard deviations (reported in Table 13) were used to derive the displayed effect sizes.

Equation 1. Cohen's d

$$d = \frac{M_2 - M_1}{SD_{pooled}}$$

6.3 RESULTS

6.3.1 Demographics

Twenty-five female participants, with a mean age of 25.04 $\pm$ 3.59 years were randomly assigned to the two groups. Independent t-test was used to compare groups' age. The demographics data appear in Table 12. There was no significant difference in age between groups (t = 0.79, p = 0.22).

Table 12. Demographics of Groups

	TT (n = 12)	BT (n = 13)
Mean Age (SD)	25.57 (3.92)	24.46 (3.26)

6.3.2 Experimental Results

Twelve participants were randomized into the control group (TT), and 13 into the experimental group (BT). TT produced 130 measurable pre-training swallows (mean 10.83 per participant) and 128 measurable post-training swallows (mean 10.66 per participant). BT produced 143 measurable pre-training swallows (mean 11.0 per participant) and 145 post-training swallows (mean 11.15 per participant). Descriptive statistics for each of the four dependent variables appear in Table 13.

Table 13. Descriptive Statistics

Variable	Pre-Training Mean (SD)	Post-Training Mean (SD)
Traditional Training (TT), n = 12		
Duration (s)	2.03 (0.45)	4.58 (2.32)
Peak Amplitude (μV*sec)	3.16 (1.75)	4.33 (3.53)
Average Amplitude (μV*sec)	1.10 (0.48)	1.51 (0.94)
Minimum Amplitude (μV*sec)	0.20 (0.05)	0.19 (0.07)
Biofeedback-Mediated Training (BT), n = 13		
Duration (s)	2.09 (0.46)	4.21 (1.65)
Peak Amplitude (μV*sec)	3.88 (2.09)	4.41 (2.32)
Average Amplitude (μV*sec)	1.33 (0.65)	1.64 (0.87)
Minimum Amplitude (μV*sec)	0.18 (0.07)	0.19 (0.06)

6.3.3 Homogeneity of Cohort at the Start of the Experiment

Pre-training data were analyzed to determine the physiologic homogeneity of the groups before training.

Independent t-tests were performed for each of the four dependent variables to determine whether there were any between-group differences prior to the training phase of the experiment. There were no significant differences between groups with regard to any of the four dependent variables before training ($p = .32 – .75$). Independent t-tests comparing the groups' pre-training coefficients of variation for the dependent variables were performed. There were no significant differences in the coefficients of variation between groups before training for any of the four dependent variables ($p = .08 – .85$). Thus, the groups were similarly variable before the trial.

6.3.4 Results of Two-Way ANOVA for Effects of Mendelsohn Maneuver

6.3.4.1 Main Effects of Time and Group

A significant main effect for time was detected for two of the three primary dependent variables. Surface EMG myoelectric duration ($p < .01$) and sEMG average amplitude ($p = .02$) were significantly greater after training in both groups. A non-significant increase for peak amplitude was observed though a trend toward significance was present ($p = .07$). No significant change was present for the secondary dependent variable, minimum amplitude ($p = .99$), which remained essentially unchanged. These results are displayed in Table 14.

Table 14. Main Effect of Time

Source	*df*	*MS*	*F*	*p*
Duration	1	68.223	32.29	<.01
Peak Amplitude	1	9.027	3.72	.07
Average Amplitude	1	1.615	5.94	.02
Minimum Amplitude	1	< .001	0.00	.99

No significant main effect for group was present for any of the four dependent variables ($p = 0.34 – 0.75$). These results are displayed in Table 15.

Table 15. Main Effect of Group

Source	*df*	*MS*	*F*	*p*
Duration	1	0.583	0.28	.61
Peak Amplitude	1	1.278	0.53	.47
Average Amplitude	1	0.028	0.10	.75
Minimum Amplitude	1	0.001	0.96	.34

6.3.4.2 Group X Time Interactions

No significant time x group interactions were observed (p = .49 – .71). These results are displayed in Table 16, and in Figure 15 (Duration), Figure 16 (Peak Amplitude), Figure 17 (Average Amplitude), and Figure 18 (Minimum Amplitude).

Table 16. Time X Group Interactions

Source	*df*	*MS*	*F*	*p*
Duration	1	0.314	0.15	.70
Peak Amplitude	1	2.020	0.20	.66
Average Amplitude	1	0.427	0.49	.49
Minimum Amplitude	1	0.001	0.15	.71

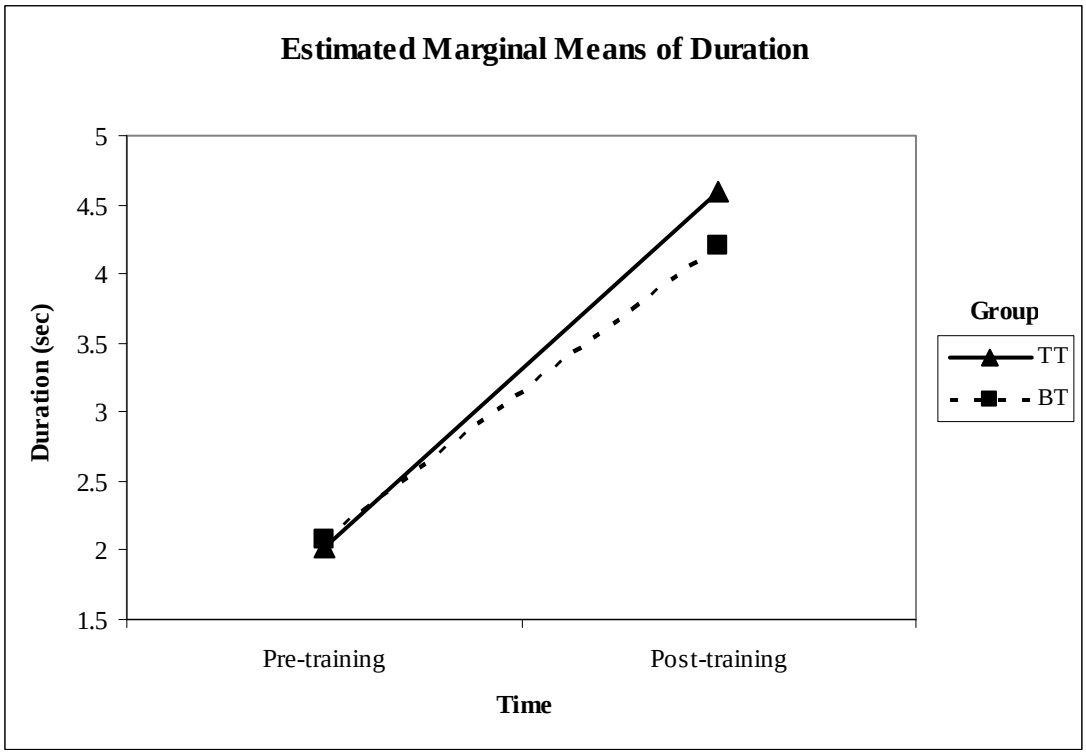

Figure 15. Time X Group ANOVA: Duration

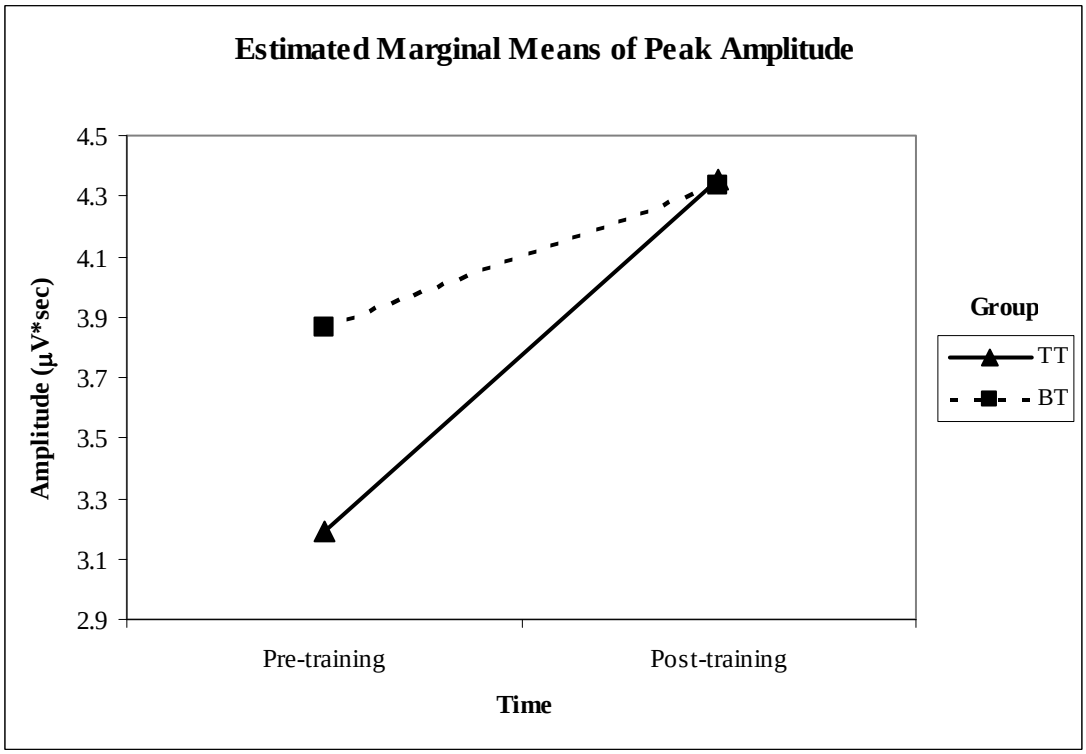

Figure 16. Time X Group ANOVA: Peak Amplitude

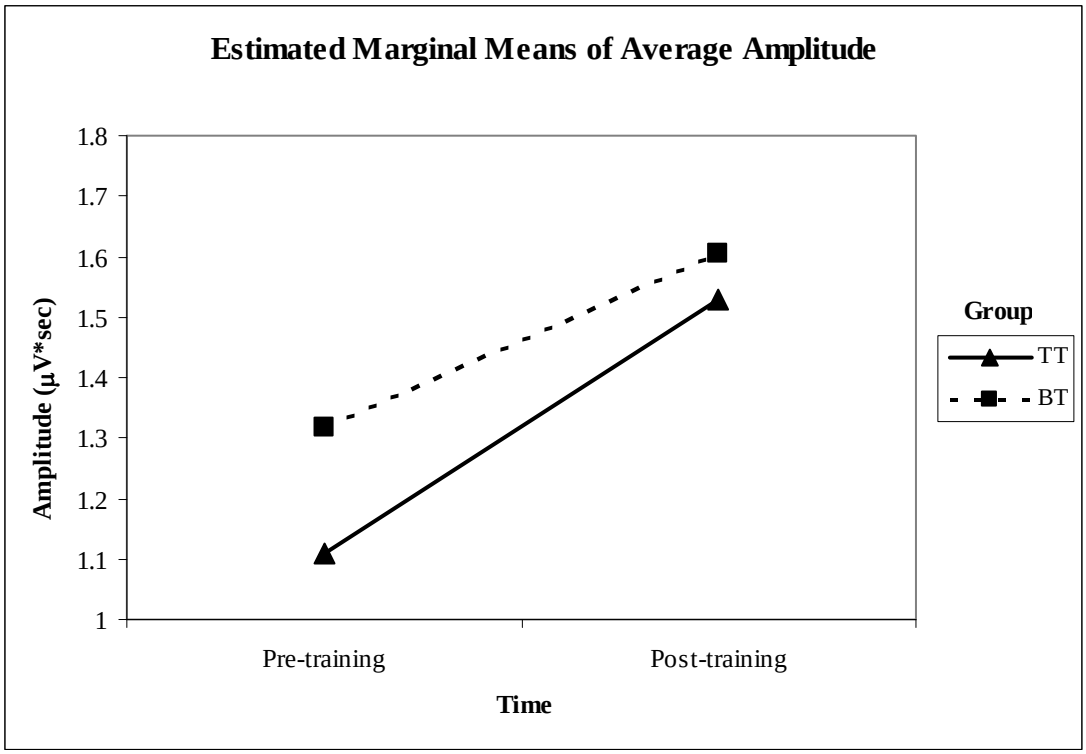

Figure 17. Time X Group ANOVA: Average Amplitude

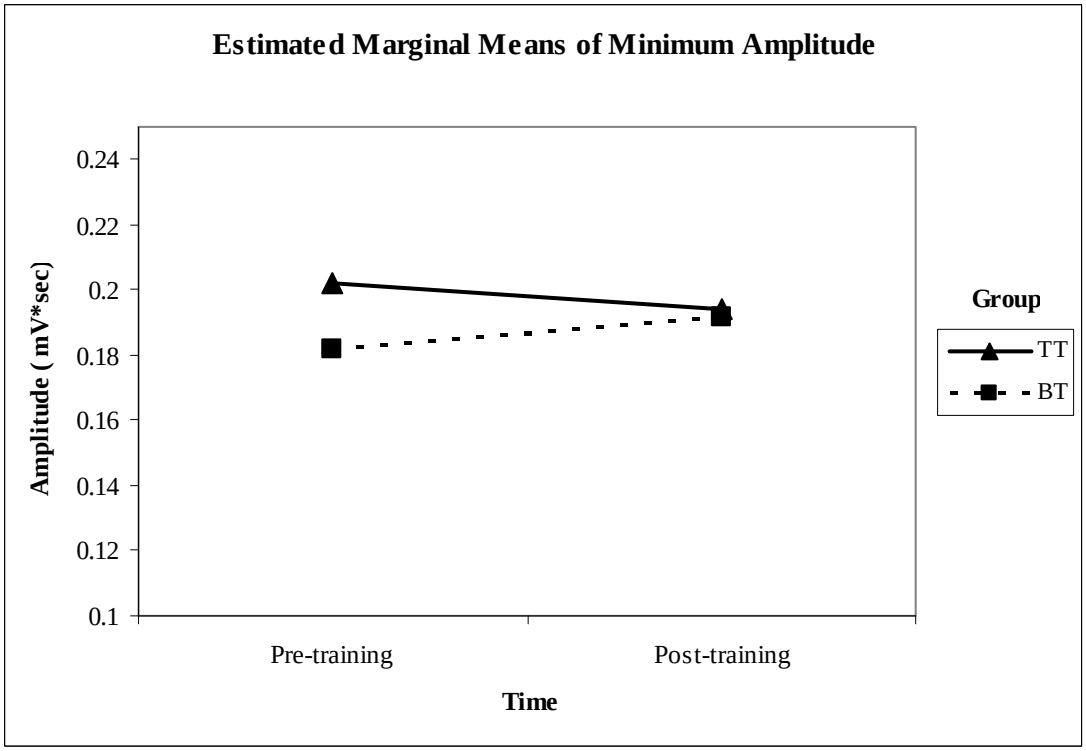

Figure 18. Time X Group ANOVA: Minimum Amplitude

6.3.5 Variability of Performance

The coefficients of variation were computed for each dependent variable by participant, using Equation 19. The coefficient of variation (CV) is the ratio of the sample standard deviation to the sample mean, expressed as a percent. It is used when comparing standard deviations (SD) between studies that investigated the same variables or when comparing standard deviations in studies that investigated the same dependent variables in two or more groups receiving different treatments.

Coefficient of Variation (CV) means for all four dependent variables, separated by group, are displayed in Table 17. Independent t-tests were performed to evaluate pre-training variability in CV data, and a two way analysis of variance (ANOVA) was performed to evaluate the effect of time, group, and time x group interactions, in CV data for the four dependent variables

Table 17. Coefficient of Variation Data by Group

	Group TT			Group BT		
Measure	Mean CV Pretest	Mean CV Posttest	% difference	Mean CV Pretest	Mean CV Posttest	% difference
Duration	22.64	31.81	40.5	22.10	24.50	10.8
Peak Amplitude	17.74	19.52	10.0	16.22	22.44	38.3
Average Amplitude	18.64	18.66	0.0	18.28	23.50	28.6
Minimum Amplitude	18.22	25.54	40.2	32.62	29.82	-9.4

6.3.5.1 Between-Groups Variability Before Training

Independent t-tests were performed on the pre-training CV data for the four dependent variables to evaluate the homogeneity of groups' variability before training, and to further evaluate the effectiveness of the randomization. No significant differences were observed for the pre-training CV for any of the four dependent variables ($p = .08 – .85$). TT displayed a 40.2% increase in CV for minimum amplitude after training while BT exhibited a 9.4% decrease in CV for minimum amplitude (Table 17). This may represent a systematic maintenance or increase in the consistency of preparatory pre-swallow myoelectric activity caused by anticipation of the swallow event in the BT trained group, while the TT trained group exhibited greater variability in assuming a preparatory pre-swallow posture.

6.3.5.2 ANOVA Results for CV Data

The two-way ANOVA revealed no significant main effect of time or group, and no significant interaction effects for CV data for any of the four dependent variables.

Non-significant main effects of time were observed for CV data for all four dependent variables ($p = .10 – .71$) (Table 18).

Table 18. Main Effect of Time (CV)

Source	*df*	*MS*	*F*	*p*
CV Duration	1	417.642	2.100	.16
CV Peak Amplitude	1	199.287	2.186	.15
CV Average Amplitude	1	85.569	2.932	.10
CV Minimum Amplitude	1	63.564	.146	.71

Non-significant main effects of group were observed for CV data for all four dependent variables (p = .10 - .42) (Table 19).

Table 19. Main Effect of Group (CV)

Source	*df*	*MS*	*F*	*p*
CV Duration	1	143.082	.719	.40
CV Peak Amplitude	1	61.625	.676	.42
CV Average Amplitude	1	83.893	2.874	.10
CV Minimum Amplitude	1	319.124	.734	.40

Similarly, no significant group x time interactions were observed (p = .052 - .76) for the CV data for any of the four dependent variables (Table 20), however a trend toward significance was observed for the CV for minimum amplitude (p = 0.052) suggesting greater consistency of minimum amplitude in the BT group after training, while the TT group displayed reduced consistency of minimum amplitude after training (Figure 19).

Table 20. Time X Group Interactions (CV)

Source	*df*	*MS*	*F*	*p*
CV Duration	1	192.406	1.260	.27
CV Peak Amplitude	1	6.178	0.094	.76
CV Average Amplitude	1	62.657	2.180	.15
CV Minimum Amplitude	1	1088.434	4.197	.052

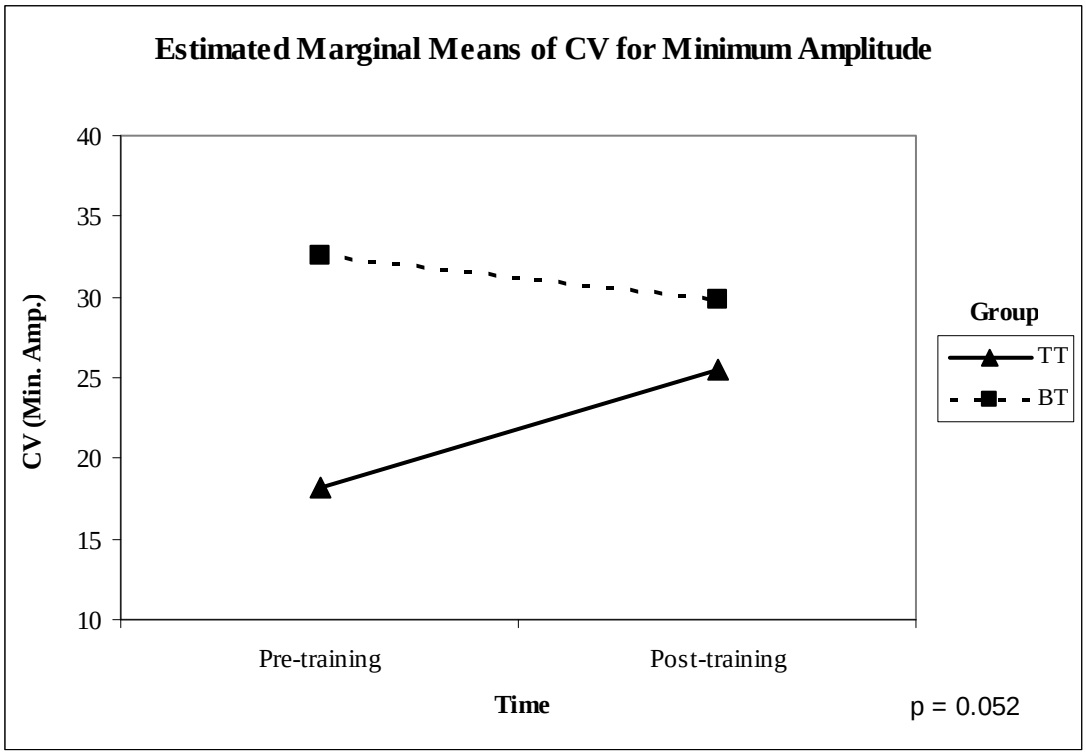

Figure 19. Time X Group Interactions: CV for Minimum Amplitude

6.3.6 Effect Sizes

Cohen's *d* was computed for each of the four dependent variables to determine the magnitude of change produced by each training method in the four dependent variables, and the difference in the magnitude of each training method's effects. Equation 1 was used as discussed in Chapter 5, to compute effect sizes.

To compute the within-groups and between-groups effect sizes of the individual training methods on each dependent variable, the pre-training mean value for each of the four dependent variables was designated as M_1, and the post-training means were designated as M_2, using Equation 1 (Rosnow & Rosenthal, 1996). Table 21 displays the within-groups effect size summary, and Table 22 displays the between-groups effect size summary.

Table 21. Within-Groups Effect Size Summary (Cohen's d)

	Duration	Peak Amplitude	Average Amplitude	Minimum Amplitude
		TT Group		
M_2 (post-training)	4.58	4.33	1.51	.19
M_1 (pre-training)	2.03	3.16	1.10	.20
SD_{pooled}	1.63	2.75	.73	.06
Effect Size (d)	**1.56**	**.04**	**.56**	**-.14**
		BT Group		
M_2 (post-training)	4.21	4.41	1.64	.18
M_1 (pre-training)	2.09	3.88	1.33	.19
SD_{pooled}	1.23	2.21	.77	.07
Effect Size (d)	**1.72**	**.24**	**.40**	**.14**

The within-groups effect size summary indicates that both methods of training produced very large effect sizes for duration, with an advantage apparent for BT. The within-groups effect size for BT (d = 1.72) is slightly larger than the effect size for TT (d = 1.56) despite the relatively similar changes in the two groups' mean durations, because the pooled standard deviation for BT is much smaller. Again, the greater consistency of performance in the BT group, compared to TT, is illustrated by this result.

Small to medium within-groups effect sizes were observed for peak amplitude and average amplitude for both groups with a slight advantage for TT. Minimum amplitude exhibited a negative effect size for TT (d = -0.14) indicating a small decrease in pre-swallow myoelectric activity after training in this method while an increase was seen in the BT group (d = 0.14)

Table 22. Between-Groups Effect Size Summary (Cohen's d)

	Duration	Peak Amplitude	Average Amplitude	Min. Amplitude
M_2 (BT post-training)	4.21	4.41	1.64	0.18
M_1 (TT post-training)	4.58	4.33	1.51	0.19
(SD_{pooled})	2.01	2.99	0.90	0.07
Effect Size (d)	**-0.19**	**0.03**	**0.15**	**0.00**

The between-groups effect size summary (Table 22) indicates that biofeedback assisted training produced a small effect size of d = .15 for average amplitude compared to traditional training. A small effect size of d = -.19 was also identified favoring traditional training for the dependent variable "duration". There was no measurable effect size for peak amplitude or minimum amplitude. This result suggests that a single training session using sEMG biofeedback produces a small increase in myoelectric amplitude over the course of the Mendelsohn maneuver swallow, compared to traditional training. The negative comparative effect size value for duration may be the result of the higher variance in the pre-swallow myoelectric activity seen in the TT group as identified by the ANOVA of the coefficients of variation, or the small size of the sample. Given the larger individual effect size for duration for BT, and the nearly 30% greater pooled standard deviation for TT, the comparative effect size may have been skewed, suggesting that the individual effect sizes may be more reliable predictors of each method's effects than the between-methods effect size. Though the results of the ANOVA did not reach statistical significance, this result warrants further investigation to determine whether a larger sample, longitudinal study, or both, might further elucidate these observed trends.

6.3.7 Measurement Reliability

Intra- and inter-judge reliability for measurement of the sEMG waveforms was calculated. A second judge was trained in selection of both onset and offset of waveforms (i.e., dependent variables). Intraclass correlation coefficients were computed on a random sample of ten percent of swallow waveforms in each of the experimental conditions for these variables. Fifty-nine swallows were independently analyzed yielding a within-judge agreement of 0.978 (95% CI 0.963 – 0.987) and between-judge agreement of 0.873 (95% CI 0.795 – 0.922). This degree of intra- and inter-rater agreement is considered high and indicates that the measures obtained from the raw data were both valid and repeatable. A complete summary of the testing of intra- and inter-judge reliability, including methods and data plots of reliability measures appears in Appendix G.

6.4 DISCUSSION OF EXPERIMENT

This experiment sought to confirm whether training two groups of healthy participants to perform the Mendelsohn maneuver while swallowing, in a single training session, significantly changed swallow-related submental myoelectric activity compared to non-Mendelsohn swallows. It also sought to determine whether the addition of sEMG biofeedback to traditional training, generated significantly more change when compared to traditional training alone. It is the first comparison of its kind in that it has used a strict randomization schedule to assign participants, masking procedures to mitigate bias of examiner familiarity with participant or condition, and controls to eliminate the judges' knowledge of subject group assignment when

performing measurements on the raw data. It is also unique in that it employed standard clinical hardware and software available to ordinary practitioners, and, as is ideal in initial therapy visits, compared the immediate, initial-session training effects of traditional training versus traditional training including sEMG biofeedback. Previous studies have described the use of sEMG to measure training outcomes in groups of healthy participants without comparing biofeedback vs. no biofeedback conditions, used sEMG as an adjunct in the treatment of individual patients, or reported training effects on subjective variables that cannot be verified or replicated with precision. The long-term goals of the research agenda that this investigation has initiated includes pursuit of a model by which patients with impaired UES opening would be identified and treated appropriately toward the clinical endpoints of avoiding surgical or other invasive intervention for impaired UES opening dysphagia, or reversing a pattern of malnutrition or aspiration syndromes.

The results indicate that a single session of training produced similar and significant overall increases in the duration and amplitude of swallow myoelectric activity in groups trained traditionally either with or without sEMG biofeedback, though a greater effect was caused by the addition of sEMG biofeedback. Small differences between the investigated methods were observed. Of particular interest is the unexpected increase in pre-swallow myoelectric consistency in the submental musculature in the group trained with sEMG biofeedback while the traditionally trained group displayed more variability in pre-swallow activity after training. This finding may suggest a potential benefit of increased muscular efficiency resulting from sEMG mediated training. If more stable pre-swallow muscle activity is later shown to translate to increased efficiency of muscular forces during the swallow, the addition of sEMG biofeedback may contribute to increased transsphincteric bolus flow through the UES. Additional study of

the difference between resting myoelectric activity and pre-swallow minimum myoelectric activity before and after training will be beneficial in elucidating whether this observation is an artifact of the small number of participants investigated, or an actual effect of the BT training method.

A slightly larger effect size for sEMG duration was seen for BT than for TT indicating that BT is potentially a more effective method of eliciting a treatment effect for the Mendelsohn maneuver than traditional training, particularly in the initial training session. The effect size data, which demonstrated a greater effect size in the BT group for duration while producing a smaller effect size for peak and average amplitude, may suggest that BT can produce prolonged duration of hyolaryngeal traction forces with less muscular effort. Future investigations could investigate this possible increase in neuromuscular efficiency caused by the BT training, and determine whether an even larger benefit in sEMG duration can be attained if peak amplitude and duration, rather than duration alone, were actively targeted in treatment paradigms.

Given the fact that this maneuver is typically required during every swallow attempted by the dysphagic patient to mitigate postprandial aspiration or ineffective clearance into the esophagus, consistency and efficiency of performance is an enormously important outcome of interest. Higher performance efficiency would indicate that systematically different acquisition of a training effect is present with added sEMG biofeedback, and may add further information to recent research into neuromotor plasticity caused by behavioral training in dysphagia. It is possible that with a larger sample size, the between groups sEMG differences may become clearer.

Strengths of this investigation include rigorous randomization, masking of judges during data reduction and analysis, standardization of experimental methods to enable replication by the

research consumer, use of a clinically common methodology and accessible instrumentation and software in the experiment, the analysis of both changes to the dependent variables themselves as well as changes in variability of performance caused by the investigated training methods, and the measurement of participant homogeneity in demographic and physiologic domains.

There are also several weaknesses of this investigation. First, the small sample may have produced a degree of variance that a larger sample may not exhibit. However the inclusion of only female participants should not have affected the results as there are no reported differences between male and female swallow physiology. The fact that the groups were chronologically homogeneous is important as age-related differences in swallow physiology have been reported in the literature.

Additionally, this study implemented only a single dosage of training in a single visit. Recent studies, including one reported in the first meta-analysis in Chapter 5, have shown the beneficial effects of certain rehabilitative swallowing interventions over time (Kays & Robbins, 2006; Robbins et al., 2007; Shaker et al., 2002). Though the immediate effects of Mendelsohn maneuver training was the focus of this study, the effect of therapeutic repetition and mass training, and the amount and type of reinforcing activity necessary to elicit stable increases in the targeted dependent variables, warrants further investigation. Moreover, establishment of the swallow-specific outcome associated with prolonged hyolaryngeal excursion during swallowing, (i.e., quantifying UES opening diameter and/or duration during videofluoroscopic swallowing examination) will be necessary to enable researchers and clinicians to determine the actual value of this method of training to the dysphagic population.

A longitudinal design that includes a longer duration of follow-up would have more power in detecting differences over time; however this study sought to limit its scope to a single

training session for several reasons. First, patients considered candidates for training in the Mendelsohn maneuver are typically individuals with intractable dysphagia characterized by impairments in UES opening that have chronic diagnoses associated with them, including brainstem stroke (Robbins & Levine, 1993), late effects of radiotherapy for head and neck cancer (Lazarus, Logemann, & Gibbons, 1993; Lazarus, Logemann, Song, Rademaker, & Kahrilas, 2002), and iatrogenic or traumatic peripheral vagal injury (Beutler et al., 2001) to name a few. Individuals with acute etiologies causing dysphagia are most often critically ill for days to weeks, with the overwhelming majority of their health care resources spent in life sustaining efforts. As a result, clinicians appropriately employing the Mendelsohn maneuver in chronic dysphagia are working with outpatients rather than inpatients.

The type and expected success of outpatient intervention is dependent on the training schedule which rarely, in modern medical settings, provides for daily visits. Moreover, the need to predict which patients are appropriate candidates for specific treatment modalities and generate quicker, measurable training effects predictive of longer term success and reduced dysphagia-related morbidity is critical under modern reimbursement limitations and concerns regarding access to care. The effect of sEMG biofeedback mediated-training reflected in the experimental group's more consistent performance after a single training session, may predict more rapid acquisition compared to traditional training, and a need for less therapeutic intervention using this sEMG mediated training, hence, potentially reducing overall cost to final outcome.

Perhaps the nature of the Mendelsohn maneuver, and the need to perform it during each volitional swallow, exposes a potential rehabilitative benefit of the type of training investigated in this study. The Mendelsohn maneuver is designed as a compensatory maneuver rather than a

restorative maneuver. That is, when successfully trained and performed accurately it increases the duration of UES opening, but only when it is performed; it does nothing to augment swallowing when it is not performed. However the Mendelsohn maneuver causes the patient to *prolong* muscular contraction during swallowing, hundreds of times per day (presumably during each volitional swallow), effectively performing prolonged, isometric contractions of the submental musculature during each swallow (Bandy & Hanten, 1993; Kent-Braun, Ng, Doyle, & Towse, 2002; Nicosia et al., 2000; Robbins et al., 2007). Given the nature of isometric exercise, the fact that mass practice is the natural extension of initial training visits of the type investigated in this study, and that mass practice is an essential component of strengthening exercise and motor learning (Judge, Moreau, & Burke, 2003; Kays & Robbins, 2006) such mass repetition of the Mendelsohn maneuver over time, and the influence of mass practice on motor learning and neuromuscular efficiency, may produce not only increased performance efficiency, but also might be found to increase the strength of submental musculature over time. The potential restorative effects of the Mendelsohn maneuver deserve further investigation.

Finally, patients selected for training in the Mendelsohn maneuver traditionally require higher levels of auditory comprehension given the complex nature of instructions eliciting its performance, and patients with stroke and other neurological diseases exhibit varying degrees of impaired language abilities. Visual biofeedback as investigated in this study offers the potential to augment or replace verbal instructions that can confound learning after stroke and other disease. Before investigation of the potential benefit of sEMG-mediated training on patients with stroke or other diseases affecting swallowing and cognitive linguistic functions, treatment effects with healthy individuals must first be elucidated on a larger scale, starting with this dissertation study.

7.0 SUMMARY OF DISSERTATION

This dissertation sought to accomplish two main aims. First, it sought to rigorously evaluate the quality of available published evidence regarding the management and treatment of oropharyngeal dysphagia on patients with neurogenic dysphagia, and to evaluate the size and significance of the effects produced by these interventions on individual patient biomechanics and longer term outcomes such as pneumonia and mortality. Second, it sought to conduct a randomized experiment to determine which of two available methods of training healthy individuals to perform the Mendelsohn maneuver is more effective in producing prolonged myoelectric submental swallowing duration. Additionally the randomized experiment sought to use rigorous design characteristics in the form necessary for inclusion in future, rigorous meta-analyses.

This dissertation represents a practitioner's attempt to bridge the divide between clinical and scientific practice, by distilling a large body of evidence into a concentrated corpus of well supported, rigorously achieved inference, while conducting rigorous experimentation that can be replicated in a clinical setting. Treatment of oropharyngeal dysphagia is shown herein to produce a modest effect toward improved swallow biomechanics and overall global health indices. However, the fact that only nine studies were sufficiently "clean" from over 300 found in the literature is a testament to the need for researchers to cobble together the will to exercise

sufficient care and control over their research in order to generate a body of useful evidence for the "line" clinician to consume.

Therapeutic interventions for dysphagic patients may be described in a textbook, but they must not be selected because they are found in a textbook. They must be selected because the patient exhibits specific impairments shown for which the treatment's efficacy has been established, and there is a reasonable expectation of effectiveness in achieving decreased mortality and medical sequelae of dysphagia. The experiment testing the effects of biofeedback mediated behavioral training versus traditional training in performance of the Mendelsohn maneuver, illustrated strategies for refining treatment using modern techniques. It also showed a potentially important clinical improvement in efficiency over its traditional counterpart, as evidenced by the effect size analysis which showed increased stability of pre-swallow preparatory myoelectric activity in the biofeedback trained group. It has also demonstrated that the rigors of clean research design are suitable for clinical practice.

Once clinicians in the field have selected interventions, they must be applied by the clinical practitioner with the same rigor, operationalized methods, and objective and unbiased data collection and measurement tactics we expect from our researchers. Such an agenda in our clinical settings and research laboratories cannot help but produce the sorts of answers textbooks could only strive to contain.

APPENDIX A

SUMMARY DESCRIPTION OF STAGES OF OROPHARYNGEAL SWALLOWING

Oral Stage

The oral stage described in 1813 by Francois Magendie is subdivided into oral preparatory and oral transit stages, both of which contain sensory and motor events (Magendie, 1813).

Oral Preparatory Stage

When solid foods or liquids are introduced into the oral cavity, humans perform actions designed to contain and prepare the ingested material into a bolus to be propelled into the digestive system. The oral preparation of solid food requires the ingested material to be processed into a semi-fluid bolus through the mechanical destruction of fibrous and other structural connections. In dentate individuals, mastication involves crushing and shearing the solid bolus between the occlusal surfaces of the posterior dentition (or molars) through a series of vertical, axial, and lateral motions (Mishellany, Woda, Labas, & Peyron, 2006). Salivation during the oral preparatory stage contributes to the maintenance of bolus cohesion through its lubricating and softening properties, while salivary enzymes begin the process of starch digestion (Pedersen, Bardow, Jensen, & Nauntofte, 2002). Molars, which are specialized for crushing, are positioned

posteriorly on the opposing mandible and maxillae bilaterally, where maximal occlusal force during mastication is generated by the combined contractions of the masseters and medial pterygoid muscles (Pereira, Duarte Gaviao, & Van Der, 2006). The solid bolus is transferred between left and right molars by combined actions of the tongue and mandible with head lateral flexion.

Oral containment is maintained anteriorly, posteriorly, and laterally. The lips remain relatively closed in relation to the inertia of the bolus and its tendency to flow passively. Contraction of the palatoglossus muscle creates a posterior valve between the velum (or soft palate) and base of tongue; thus, maintains posterior oral containment of the bolus during mastication. Bilateral tension of the lateral walls of the oral cavity produced by buccinators and orbicularis oris opposing one another prevents material from entering the lateral sulci of the mouth during oral preparation. Materials of less viscosity (e.g., liquids and thinner solids) require greater lateral, anterior and posterior valving to maintain containment due to their tendency to flow in the direction favored by gravitational forces, but the pattern of containment is similar. Most solid bolus consistencies are reduced to a condition of granularity before the average healthy individual terminates oral preparation and prepares to swallow the bolus (Pereira et al., 2006).

Oral motor activities are mediated by several motor nerves that originate in motor nuclei in the pons or medulla. Rotary mastication requires alternating and coordinated actions of the bilateral masseter, temporalis, medial and lateral pterygoids, which are innervated by lower motor neurons supplied through the principal motor nucleus of the trigeminal nerves. Labial closure which is partially responsible for anterior oral containment is produced by orbicularis oris and adjacent smaller muscles through the facial motor nerve. Posterior oral containment is

produced by the contact of the velum to the base of tongue, each of which serves as opposing attachments for the palatoglossus and facial musculature which is innervated by vagal motor efferent fibers. There is some evidence that palatoglossus activity at the end of the oral stages is modulated by bolus volume (Tachimura, Ojima, Nohara, & Wada, 2005).

Two general categories of oral sensation are active during oral stages. General sensory information is transmitted from oral mucosa in the entire oral cavity anterior to the velum by branches of the trigeminal nerve. Taste is mediated by special sensory afferents traveling in the facial nerve from the anterior two-thirds of the tongue, and through the glossopharyngeal nerve from the posterior tongue to the rostral solitary nucleus in the medulla oblongata. Remaining afferent, proprioceptive input from the various structures of the oral cavity has been described among some oral skeletal muscles; however such studies with humans are problematic due to the relative size of the musculature in question in relation to total muscle volume, and location. A single post-mortem investigation has identified primitive spindle-like structures in human genioglossus and geniohyoid muscles in human embryos (Mitchenok, 1979). Pathways carrying proprioceptive signals from oral musculature would be expected to lie within the respective peripheral motor nerves innervating the individual muscles.

Oral Transit Stage

The oral transit stage begins when volitional propulsion of the bolus toward the pharynx is observed. During oral transit the tongue and velum reverse their functions. The oral transit stage is momentarily characterized by a brief period of bolus compression during which both anterior labial and posterior linguavelar valves remain tightly closed while the tongue's contact with the hard palate progressively widens in an anterior-to-posterior direction (Tasko, Kent, & Westbury, 2002). This causes an increase in intrabolus pressure that precedes posterior bolus movement

and propulsion as well as a resultant increase in pressure gradient between oral and pharyngeal cavities. Contact of the tongue base and velum which are maintained during oral containment by the palatoglossus muscle is then reversed as each structure is displaced in opposing directions. The velum begins a transition from the role of oral containment to that of intrabolus pressure maintenance and protection of the nasal cavity. Levator veli palatini elevates the velum while tensor veli palatini maintains the velum's stiffness, beginning its transition to the posture it assumes during the pharyngeal stage. The tongue similarly reverses its containment position to that of propulsion of the bolus. The tongue base is depressed by hyoglossus while the anterior tongue continues to widen its palatal surface contact and retract. The bolus is described as having entered the pharyngeal cavity when its leading edge crosses the tonsillar fossa, an anatomical landmark that is represented radiographically by the ramus of the mandible (Robbins et al., 1992).

Oral to Pharyngeal Stage Transition

Transition from the oral to pharyngeal stage contains both oral and pharyngeal events. This "stage transition" is defined as the duration between the moment of bolus head exit from oral cavity and entry into the pharynx, and the onset of pharyngeal deglutitive activity as characterized by the first deglutitive maximal movement of the hyoid (Lof & Robbins, 1990). The identical event has been called "pharyngeal delay time" in earlier studies and texts, and was first described as an important measurement in Jerilyn Logemann's seminal textbook on evaluation and treatment of swallowing disorders (Logemann, 1983).

Stage transition includes release of palatoglossus contraction and its important role of posterior oral containment, to facilitate bolus flow from the posterior oral cavity. The soft palate

then begins its reversal of position from the lingual contact to oppose the posterior pharyngeal wall, thereby occluding the entrance to the nasal cavity. Initiation of hyolaryngeal displacement, responsible for both extrinsic airway protection and a considerable proportion of UES opening, begins during the stage transition.

A critical component of the stage transition and ensuing pharyngeal state is the inhibition of UES resting tone that later facilitates the forces acting to pull the UES open and displace the upper airway out of the bolus pathway (Miller, 1986).

Healthy young subjects tend to initiate pharyngeal deglutitive activity before the head of the oncoming bolus enters the pharynx (Logemann, 1998). Aging has been shown to alter this relationship so that with older individuals the bolus head enters the pharynx before the onset of pharyngeal activity. Since pharyngeal activity onset is marked by the radiographically observed onset of maximal hyoid bone motion, the natural consequence of excessively long stage transition is the arrival of the bolus into the pharynx while the larynx remains open and unprotected (Lof & Robbins, 1990). The implications of normal age-related alterations is the timing of deglutitive events become germane if the aging individual encounters catastrophic illness

Pharyngeal Stage

Once the pharyngeal stage begins, a rapid series of biomechanical events takes place. The exact moment of onset for each event is somewhat stereotyped, though age-associated, progressive changes in timing of the various events are well known (Ekberg & Feinberg, 1991; Robbins et al., 1992). The important protective closure of the upper airway is perhaps the most critical event of the pharyngeal stage from a safety standpoint. As submental musculature apply traction forces to the hyolaryngeal complex, the complex itself is pulled anteriorally and superiorally

toward the mandible. Given the common wall shared between the posterior larynx and anterior UES, these traction forces not only displace the larynx from the path of the oncoming bolus, it pulls the UES open (i.e., assuming the aforementioned inhibition of UES resting tone has occurred beforehand). An additional and fortunate outcome of this hyolaryngeal excursion is the motion of the esophageal inlet toward the oncoming bolus producing an effective increase in the relative speed of the swallowed bolus. Hyolaryngeal excursion, then, is responsible for airway protection, UES opening, and to a degree, bolus transfer toward the UES.

As the tongue continues to propel the bolus the pharyngeal constrictors continue contracting in a semi-circumferential pattern from superior to inferior in conjunction with the descending and propelling tongue base. Toward the end of the pharyngeal stage the tongue of a healthy normal young individual is in contact with the posterior wall of the pharynx. Due to the propulsive forces of the bolus, the free edge of the epiglottis is pushed posteroinferiorally to approximate the laryngeal inlet. At the same time, submental musculature pulls the root of the epiglottis upward and forward. Altogether, this series of events facilitates epiglottic inversion and airway closure. Once the bolus has entered the UES, the pharyngeal structures begin to return to rest. In most healthy individuals, the reopening of the upper airway is immediately followed by the resumption of expiration which has been shown to begin during the onset of the swallow (Hiss, Strauss, Treole, Stuart, & Boutilier, 2003; Hiss et al., 2001; Leslie, Drinnan, Ford, & Wilson, 2005; Perlman, He, Barkmeier, & Van Leer, 2005).

Treatment of Impaired Posterior Oral Containment

Oropharyngeal biomechanical errors are the target of the majority of individually administered dysphagia intervention strategies. These interventions are intended to improve swallowing efficiency and safety by augmenting impaired biomechanical functions. Some of these

remediation techniques were investigated in the treatment studies included in the meta-analysis portion of this dissertation (Chapter 5).

Incomplete, absent, or premature release of any portion of a bolus by the linguapalatal valve results in material flowing toward an unprotected airway. Incomplete laryngeal closure during the swallow can occur due to numerous anatomic and/or physiologic variables, but ultimately results in swallowed material entering the unprotected airway.

Flexion of the head and neck anteriorly, sometimes called the "chin down" posture, places the bolus head slightly forward as compared to its position while swallowing in a head-neutral posture. Researchers have demonstrated that this maneuver can influence several UAT variables related to swallowing including, volume (i.e., widen the valleculae to catch premature spillage), pressure generation, as well as timing relationships among the various anatomic structures (Bulow et al., 1999; Shanahan et al., 1993). This compensatory strategy is relatively easy to perform, can be assessed during the MBS, and has been used successfully by selected patients.

Treatment of Impaired Hyolaryngeal Displacement

Displacement of the hyolaryngeal complex contributes to airway closure and esophageal clearance. This 'complex' is attached anteriorally/superiorally to the mandible and posteriorally/superiorally to the skull base. The result of reflexive contraction of these muscles during the pharyngeal portion of the swallow is a net superior/anterior displacement of the hyolaryngeal complex, inversion of the epiglottis, and distension of the upper esophageal sphincter. Therefore, minimal or reduced hyolaryngeal displacement can result in incomplete laryngeal closure during the swallow and/or partial UES distension causing separation of the

bolus's tail. Hypopharyngeal residue which remains after the swallow is more likely to be aspirated as its volume increases (Eisenhuber et al., 2002)

Anterior/superior displacement of the larynx pulls the inlet to the airway away from the path of an oncoming swallowed bolus. Therefore, the timing of this action must occur prior to the arrival of swallowed material at the laryngeal inlet. Research has shown that the head of a liquid bolus reaches the posterior margin of the larynx several milliseconds after the larynx has been displaced anteriorally and superiorally from the path of the oncoming bolus, and the epiglottis has been securely inverted over the laryngeal vestibule (Dodds et al., 1990). Evidence suggests that normal aging in the absence of pathology may cause slight delays in the onset of hyolaryngeal movement, and that small amounts of the bolus may enter the pharynx prior to initiation of the swallowing (Lof & Robbins, 1990). Research has demonstrated that many elderly adults remain healthy despite the presence of occasional laryngeal penetration and/or premature arrival of the bolus at the laryngeal inlet as the hyolaryngeal complex moves from the bolus path (Robbins, Coyle, Rosenbek, Roecker, & Wood, 1999). The cumulative effects of normal aging and any co-existing health problems involving sensorimotor pathways could pose a significantly greater aspiration risk in the elderly if relative strength or timing of hyolaryngeal excursion is affected.

The epiglottis is attached to the posterior surface of the anterior wall of the thyroid laminae at midline, just superior to the vocal ligament. During deglutition, the epiglottis is pulled anteriorally and superiorally along with the larynx to a horizontal orientation in relation to its free margin, forming a horizontal barrier to oncoming swallowed material. This inversion, together with the forceful lingual propulsion of the bolus, produces a temporary seal between the epiglottis and the roof of the larynx. Incomplete hyolaryngeal excursion is responsible for

incomplete epiglottic inversion and a “leak” into the larynx is possible under these conditions (Kendall, Leonard, & McKenzie, 2004).

Complete hyolaryngeal excursion is also responsible for the majority of UES opening, enabling a swallowed bolus to enter the esophagus completely (Cook et al., 1989a). This phenomenon was discussed in detail in chapter 3, section 3.1. Reduced diameter of UES opening or consequences of mistimed closure of the airway’s uppermost valve enables the pressurized bolus to leak into the larynx and trachea during or after the swallow.

These impairments are addressed therapeutically by attempts to either increase the distance and duration of hyolaryngeal excursion, or to compensate for its delayed or incomplete excursion by volitional, preprandial airway closure, effortful multiple swallowing, and postprandial airway clearance with cough.

Treatment of Impaired Intrinsic Laryngeal Closure

In the event of vocal fold paralysis, the glottic space remains patent during deglutition. This is not problematic in terms of aspiration risk in and of itself because sufficient airway protection is achieved from the combined actions of early and complete hyolaryngeal displacement and adequate intrabolus pressure generation. However, when incomplete laryngeal closure is accompanied by deficits in either one of these events, the airway is vulnerable to aspiration. Some patients have reported limited success using a compensatory maneuver which involves learning to hyperadduct the uninvolved vocal fold, thereby forcing closure. Due to comorbidities and greater health risks, the majority of patients with aspiration due to permanent vocal fold paralysis require surgical intervention in conjunction with behavioral compensatory swallowing treatment (Logemann, 1998).

Treatment of Impaired UES Opening

Impaired UES opening causes a swallowed bolus to fail to enter the esophagus completely. The result is separation and retention of a portion of the swallowed bolus in the hypopharynx. In turn, the patient must swallow consecutively to deliver the bolus remnant remaining in the pharynx, or the bolus residue may enter the airway after the swallow or at the onset of the subsequent swallow (Eisenhuber et al., 2002).

The Mendelsohn maneuver, discussed in Chapter 6, is the primary method used to increase impaired UES opening.

Treatment of Impaired Intrabolus Pressure Generation

Intrabolus pressure is a dominating force contributing to the flow of material from the oral cavity top the esophagus (Cook et al., 1989b; Robbins et al., 2005b). It is generated by the propulsive force imparted by the tongue and pharyngeal constrictors, and it is maintained by closure of the various valves in the oropharyngeal mechanism (e.g., velopharyngeal valve, laryngeal valve).

Intrabolus pressure can be increased in patients with weakness, by augmenting bolus parameters (Dantas et al., 1990; Dodds et al., 1988), by effortful swallowing (Hind, Nicosia, Roecker, Carnes, & Robbins, 2001), or through exercise (Kays & Robbins, 2006; Robbins et al., 2005a).

Pharmacological Management of Dysphagia

Medical professionals have been interested in the pharmacological management of dysphagia. Researchers have investigated the effects of systemic medication regimens that biochemically alter swallow physiology in dysphagic patients (Brandt, 1999; Nakagawa, 1999; Perez, Smithard, Davies, & Kalra, 1998). Pharmaceutical manipulation of swallow function is designed to change

synaptic and tissue physiology of involved structures. Endoscopy is used by physicians to treat dysphagia, especially balloon dilatation in cases of cricopharyngeal dysfunction (Wang, Kadkade, Kahrilas, & Hirano, 2005; Zepeda-Gomez, Loza, Valdovinos, Schmulson, & Valdovinos, 2004). Studies investigating the effectiveness of using botulinum toxin injections into the cricopharyngeal segment of the inferior constrictor muscle to alleviate inadequate upper esophageal sphincter opening are becoming more prevalent for the treatment of chronic dysphagia (Zaninotto et al., 2004).

Surgical Management of Dysphagia

Surgery is sometimes used to reduce the volume of aspiration while swallowing. Cricopharyngeal myotomy has been shown to reduce inertia and flow resistance within the UES in conditions such as medullary stroke and cricopharyngeal achalasia (Cook, 2000). However, patients unable to generate sufficient oropharyngeal pressures and those with esophagopharyngeal reflux are poor candidates for this type of management (Bammer, Salassa, & Klingler, 2002; Cook, 2000). Surgical procedures are also used in cases of intractable dysphagia after failure of conventional interventions. This type of surgery can range in severity from relatively noninvasive/reversible (e.g., tracheostomy), to radical reconstruction of the UAT (i.e., total laryngectomy), to placement of an enteral feeding tube (Bammer et al., 2002; Broniatowski et al., 2001; Kelly, 2000). Tracheostomy, a less invasive and reversible surgical technique, is used to facilitate mechanical ventilation in patients with respiratory failure, however, provides a mechanical barrier to aspiration. A tracheostomy tube with an inflatable cuff effectively increases airway protection and reduces inhalation of aspirated material by partially to completely obstructing the communication between the upper and lower airways (Broniatowski et al., 2001).

Surgical placement of an enteral feeding tube directly into the lower gastro-intestinal tract is performed when a patient is unable to adequately sustain nutrition and hydration by oral means and to reduce the health consequences associated with prandial aspiration (Dennis et al., 2005).

APPENDIX B

META-ANALYSIS SEARCH STRATEGY

1. randomized controlled trial.pt.
2. randomized controlled trials/
3. controlled clinical trial.pt.
4. controlled clinical trials/
5. random allocation/
6. double-blind method/
7. single-blind method/
8. clinical trial.pt.
9. exp clinical trials/
10. (clin$ adj25 trial$).tw.
11. ((singl$ or doubl$ or tripl$ or trebl$) adj25 (blind$ or mask$ or dummy)).tw.
12. placebos/
13. placebo$.tw.
14. random$.tw.
15. research design/
16. (clinical trial phase i or clinical trial phase ii or clinical trial phase iii or clinical trial phase iv).pt.
17. multicenter study.pt.
18. meta-analysis.pt.
19. Prospective Studies/
20. Intervention Studies/
21. Cross-Over Studies/
22. Meta-Analysis/
23. (meta?analys$ or systematic review$).tw.
24. control.tw.
25. or/1-24
26. Animal/
27. Human/
28. 26 and 27
29. 26 not 28

30. 25 not 29
31. exp DEGLUTITION DISORDERS/
32. deglutition/ or deglutition.tw.
33. (dysphagia or swallow).tw.
34. or/31-33
35. exp muscular diseases/
36. ((muscle$ or muscular) adj5 (disease$ or disorder$)).tw.
37. 35 or 36
38. 34 and 37
39. 30 and 38
40. exp Cerebrovascular Accident/
41. (cerebrovas$ adj5 accident).mp.
42. stroke.tw.
43. 40 or 41 or 42
44. 34 and 43
45. 30 and 44
46. exp dementia/
47. 34 and 46
48. 30 and 47
49. exp Amyotrophic Lateral Sclerosis/
50. (amyotro$ adj5 lateral$).tw.
51. 49 or 50
52. 34 and 51
53. 30 and 52
54. exp Multiple Sclerosis/
55. (mult$ adj5 scler$).tw.
56. 54 or 55
57. 34 and 56
58. 30 and 57
59. exp Myasthenia Gravis/
60. (myasth$ adj3 grav$).tw.
61. Myasthenia.tw.
62. 59 or 60 or 61
63. 34 and 62
64. 30 and 63
65. exp Parkinson's Disease/
66. parkinson$.tw.
67. 65 or 66
68. 34 and 67
69. 30 and 68
70. exp Neurodegenerative Diseases/
71. 34 and 70
72. 30 and 71

APPENDIX C

SCREENING FORM FOR META-ANALYSIS

***First Author*_____ *Rater initials* _____**

***Short Title* _____*Year* _____**

***Reference Manager Meta-Analysis Database Number:* _____**

***Investigated treatment:* _____**
_____

***Comparison Treatment:* _____**
_____

***Dependent-Outcome Variables:* _____**
_____

Design (circle one)

I. ☐RCT ☐Repeated measures w/randomized seq. of treatments

II. ☐Non-RCT 2 groups ☐2 group tx vs. ctrl non randomized
☐Repeated design w/o randomization but with ≥2 conditions

III. ☐Non-RCT 1 group ☐One group pre post one intervention

IV. ☐Single Subject Design ☐One person evaluated pre and post intervention

V. ☐Narrative or case study

Sample Size

A. ☐ n≥ 20 subjects or observations per group
B. ☐ n< 20 subjects or observations per group

Internal Validity

1. ☐ High; no alternative explanation for outcome; excellent control for error
2. ☐ Moderate; attempts to control for lack of randomization biases or other errors
3. ☐ Low; two or more serious alternative explanations for outcome; serious bias

External Validity

a. ☐ High; participants/setting represents population/current practice
b. ☐ Moderate; between high and low
c. ☐ Low; heterogeneous sample w/o ability to determine whether effects differed by diagnosis, or treatments do not represent current practice

APPENDIX D

Standard instructions to all subjects, used in traditional training (TT) and biofeedback training (BT)

"Swallow your saliva several times and pay attention to your neck as you swallow. Tell me if you can feel that something (your Adam's apple or voice box) lifts and lowers as you swallow. Now, this time, [water bolus is self-administered by subject] when you swallow and you feel something lift as you swallow, don't let your Adam's apple (or voice box) drop. Hold it up with your muscles for several seconds."

Alternative instructions

"As you swallow can you feel that everything squeezes together in the middle of the swallow? When you can feel this, swallow and hold the squeeze."

Standard permissible prompts and cues for training of TT subjects

a. subject may palpate the laryngeal framework while training.

b. trainer may palpate the subject's laryngeal framework while training.

c. trainer may verbally answer "yes" / "no" questions posed by subject.

d. subject and investigator are blinded to sEMG waveform display

Standard permissible prompts and cues for training of BT subjects

a. as listed for TT.

b. subject and trainer may observe the sEMG waveform display to assist subject with prolongation of the swallow gesture.

c. investigator explains target waveform shape to subjects.

d. “The red line shows what your swallowing muscles are doing when you swallow. Try to make the top or peak of the tracing remain “up” for several seconds longer.”

APPENDIX E

SCREENING FORM FOR SEMG PROJECT

SUBJECT NUMBER_____SUBJECT INITIALS_____

SCREENED BY_____SCREENING DATE_____

SCREENING TIME_____

Investigation of Effects of Surface Electromyographic Biofeedback in the Training of a Compensatory Oropharyngeal Swallowing Maneuver in Normal Healthy Young Adults

University of Pittsburgh IRB# 0604116

James L. Coyle, M.A., Principal Investigator

Screening Questionnaire

1. Are you between the ages of 20 and 39?
    a. YES
    b. NO (ineligible)
2. Have you ever been diagnosed with a swallowing disorder?
    a. YES (ineligible)
    b. NO
3. Do you have any difficulty swallowing food or liquids?
    a. YES (ineligible)
    b. NO
4. Except for routine tonsillectomy, have you ever undergone surgery of the head or neck areas?
    a. YES (ineligible)
    b. NO

5. Have you ever been diagnosed with or treated for head or neck cancer?
    a. YES (ineligible)
    b. NO
6. Have you ever received radiation (or x-ray) therapy in the head or neck areas?
    a. YES (ineligible)
    b. NO
7. Have you ever had a stroke, or been diagnosed with a neurological such as Multiple Sclerosis, Myasthenia Gravis, Amyotrophic Lateral Sclerosis (Lou Gehrig's Disease), or Parkinson's Disease?
    a. YES (ineligible)
    b. NO
8. Do you have an allergy or sensitivity to rubbing alcohol?
    a. YES (ineligible)
    b. NO
9. Do you have an allergy or sensitivity to adhesive tape?
    a. YES (ineligible)
    b. NO

MEASUREMENT OF INTRA- AND INTER-RATER RELIABILITY IN WAVEFORM MEASUREMENTS

Intra- and Inter-Rater Reliability of Measurements

A second judge was trained in the waveform analysis and served as an inter-rater reliability measure. A random number generator was used to renumber all recorded swallow waveforms. Ten percent of swallow waveforms from each of the pre-training and post-training data sets from each group were randomly selected, randomly numbered and de-identified for repeated measurement by the investigator and for a second, trained judge. A blank data sheet with the randomly selected swallow number was prepared for data recording by judges.

The investigator's inter- and intra-rater reliability in measuring fluoroscopic, magnetic resonance, and other physiologic data from swallowing imaging studies has been established in prior peer-reviewed and published work (Coyle, Robbins, Levine, & Roecker, 1999; Coyle, Wood, Robbins, Ford, & Harari, 1994; Dengel, Robbins, Coyle, & Sonies, 1996; Ershler, Coyle, Ford, Harari, & Robbins, 1995; McCullough, Rosenbek, Robbins, Coyle, & Wood, 1998; Robbins, Coyle, Dengel, & Kennell, 1998; Robbins et al., 1999; Rosenbek et al., 1996a). Likewise, the second judge's reliability in measurement of sEMG and other instrumental

videofluoroscopic events has been established in prior published work (Coyle et al., 1994; Goodman et al., 1996; McCullough et al., 1998; Robbins et al., 1995; Robbins et al., 1999; Rosenbek et al., 1996a; Rosenbek et al., 1996b). Thus, both judges have been thoroughly trained and successfully demonstrated sufficient levels in inter- and inter-rater reliability in published investigations associated with normal and disordered swallowing physiology.

Findings-Reliability Measures

Intraclass correlation coefficients were computed to determine the degree of within-judge and between-judge agreement in measures of swallow waveform onset, offset, and duration. Ten percent of swallow waveforms from each of the pre-training and post-training data sets from each group were randomly selected, randomly numbered, and de-identified for repeated measurement.

A second judge was trained in the selection of swallow onset and offset. Both judges conducted onset and offset measurements on fifty-nine swallow waveforms (i.e., 10% of total waveforms). Intra-rater agreement for the investigator, Judge 1, was 0.978 (95% CI 0.963 – 0.987), and is shown in Table 23 and Figure 20. Inter-rater agreement for Judge 1 and Judge 2 was 0.873 (95% CI 0.795 – 0.922) and is shown in Table 24 and Figure 21. This degree of intra- and inter-rater agreement is considered high. Combined with justification for selection of sEMG event onset and offset, this finding indicates that the measures obtained from the raw data were both valid and repeatable.

Table 23. Intraclass Correlation Coefficient -Within Judge 1 Reliability

	Intraclass Correlation	95% Confidence Interval		F Test with True Value 0			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	.978	.963	.987	88.561	58.0	58	.000
Average Measures	.989	.981	.993	88.561	58.0	58	.000

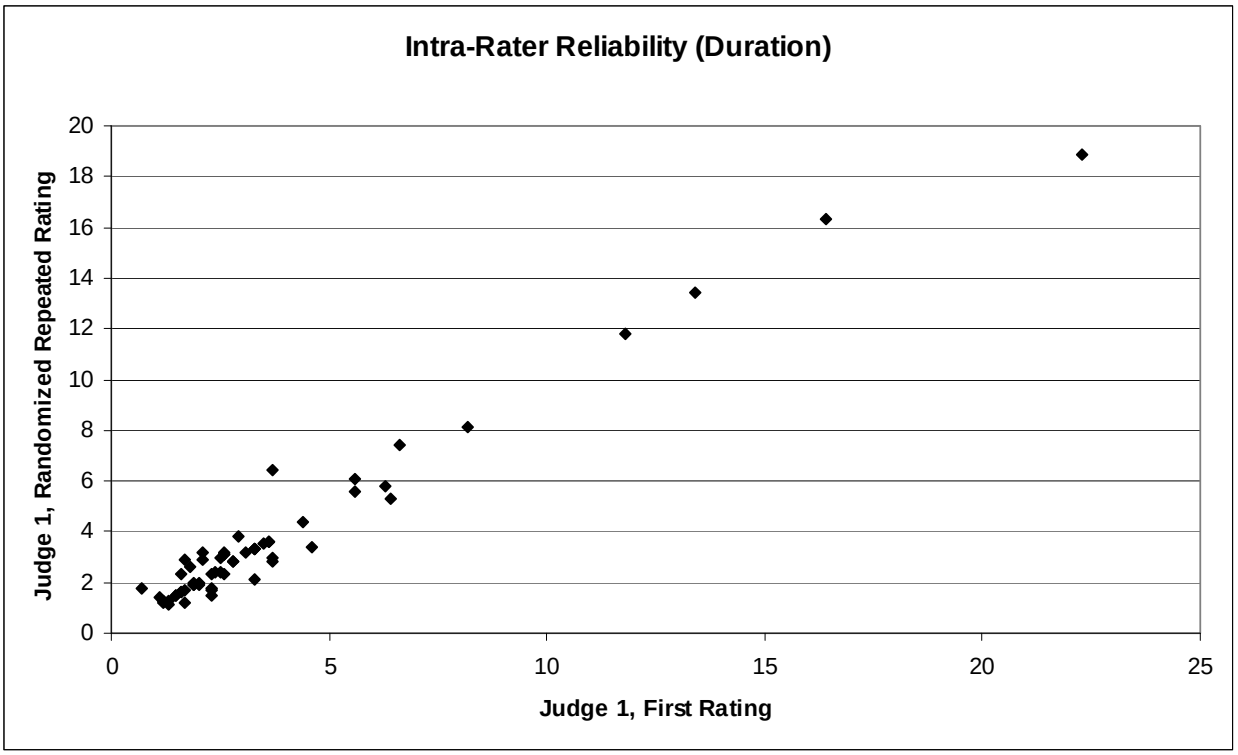

Figure 20. Intra-rater Agreement

Table 24. Intraclass Correlation Coefficient – Between Judges Reliability

	Intraclass Correlation	95% Confidence Interval		F Test with True Value 0			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	.873	.795	.922	14.700	58.0	58	.000
Average Measures	.932	.886	.960	14.700	58.0	58	.000

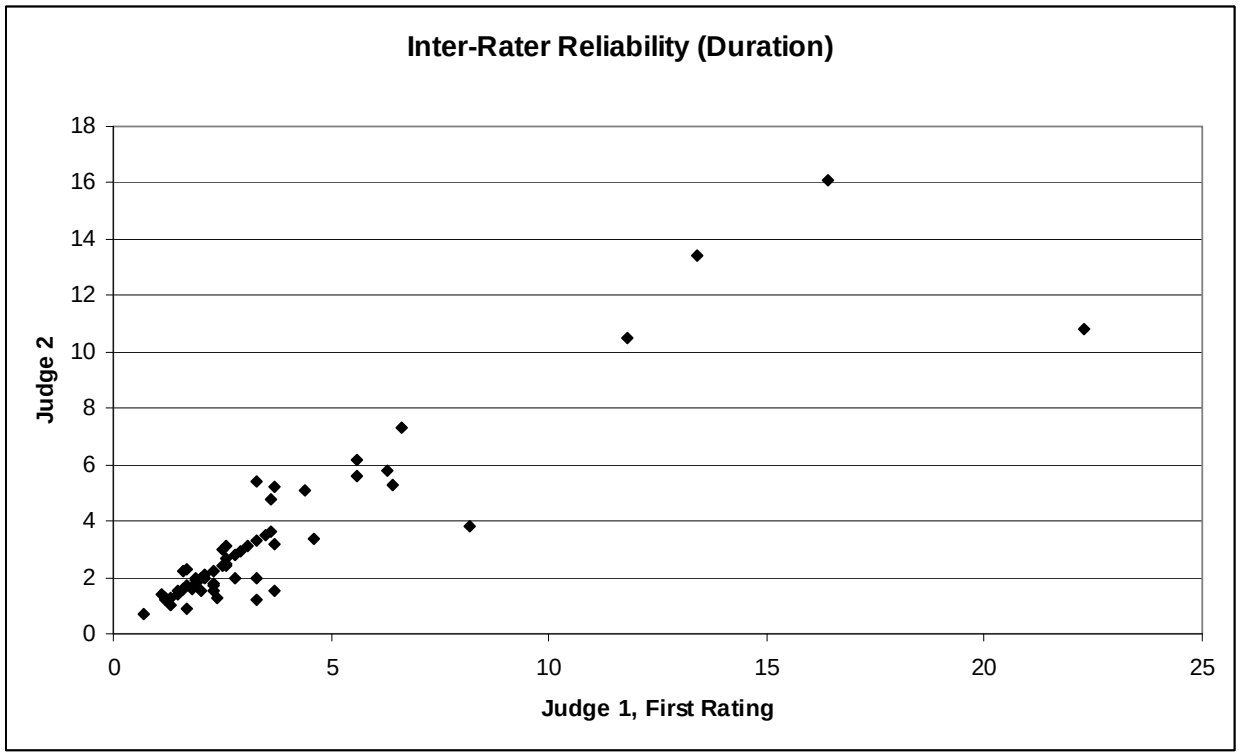

Figure 21. Inter-rater Agreement

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