

EFFECTS OF EMST ON RESPIRATORY EVENTS DURING SWALLOW IN PARKINSON'S
DISEASE

By

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To my parents and future patients

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The purpose of this study was to determine if individuals with Parkinson's disease (PD) demonstrate abnormal respiratory events surrounding swallows of thin liquid. Additionally, this study sought to identify relationships between respiratory events, swallow apnea duration (SAD), and penetration-aspiration (PA) scale scores. Finally, this study investigated the effects of expiratory muscle strength training (EMST) intervention on respiratory-swallow events, SAD, and P-A scores. Thirty nine individuals with PD were given 10 trials of a 5 mL thin bolus. Swallows were evaluated before and after 4 weeks of EMST using videofluoroscopy coupled with a nasal cannula to record respiratory signals. Findings indicated that expiration was the predominant respiratory event following the swallow and did not seem to differ from percentages of post-swallow events reported in healthy adults. Additionally, individuals with decreased swallow safety, as measured by the P-A scale, were more likely to inspire after swallows and have shorter SAD. Individuals who inspired pre-swallow also had longer SAD. Finally, EMST intervention did not significantly alter respiratory events before or after the swallow. It is likely that EMST did not produce a change in respiratory events because there was a ceiling effect, where in respiratory patterns associated with swallowing were mostly normal, thus minimizing the opportunity to measure change. Additionally, it may be that EMST intervention is more

appropriate in individuals with reduced strength, and intervention targeting respiratory-swallow dis-coordination, should be more swallow-specific.

CHAPTER 1 INTRODUCTION

Introduction of Parkinson's Disease

James Parkinson [1] first described symptoms of Parkinson's disease (PD) in *An Essay on the Shaking Palsy* in 1817. In his Essay, Parkinson described the Shaking Palsy as a progressive disease beginning as a unilateral tremor, but eventually impairing all systems including speech, respiration, swallowing, and digestion. For this reason, he proposed that the origin of this multisystem disease was in the medulla spinalis. Today, PD is described as a neurodegenerative disease resulting from the progressive deterioration of the dopamine producing cells in the substantia nigra and other subcortical structures, such as the brainstem [2-5]. Extraparamidal symptoms associated with PD include rigidity [6, 7], tremor, bradykinesia [8, 9], and postural instability [10, 11]. The symptoms can be of variable degree affecting muscular function of both the corticospinal and corticobulbar systems [2, 7, 12, 13]. Consequently, various functional difficulties in speech, breathing, cough, and swallow are present in those with PD [14-38]. The literature classically defines the speech disorder in PD as hypokinetic dysarthria [35, 39-41]. In comparison, breathing impairment in PD is less well defined, and reported prevalence rates vary from 5 to 90% [15-20]. The swallowing literature states individuals with PD demonstrate a predominant impairment in the voluntary oral-preparatory and oral swallowing phases [30-32, 35, 42]; however, disturbances of the reflexive pharyngeal and esophageal phases have also been reported [29-33, 36]. Cough, which is one physiologic mechanism for airway protection, has only come under study over the past ten years [21, 22, 43], but has been reported to be reduced in magnitude PD.

Respiration in PD

With regard to the breathing impairment, individuals with PD do not frequently report respiratory related symptoms, despite decreased performance in physiological measures of pulmonary function [14, 20]. The symptoms may be multifactorial, due to motor impairment and often the sedentary life-style led by persons with PD [8, 9, 44-46] which ultimately reduces demands on respiration, yet decreasing the perception of respiratory difficulty. This coupled with the known decrease in Parkinson patients' perception of their disease state, often contributes to a general lack of awareness of their symptoms [47].

Upper airway obstruction (UAO) and restrictive lung disease are the two most frequently reported respiratory impairments [15-20]. Restrictive ventilatory pattern is associated with reduced compliance of the lung or chest wall, as well as weak inspiratory muscles. Obstructive airway disease is characterized by a large total lung capacity (TLC), with decreased expiratory flow [48]. Reports of restrictive ventilatory impairment in those with PD range from 28-85%, with UAO between 5-65%, and mixed obstructive-restrictive impairment reported as 24% in one study [16]. This data was derived from sample sizes ranging from 58 to 63 for the restrictive impairments, from 21 to 63 for the ranges reported for the UAO and 58 persons for the study that reported obstructive-restrictive impairment. The variance in findings among studies may be a product of the criteria for defining respiratory disease, the time of administration of antiparkinsonian medication, or participant benefit from antiparkinsonian medication. Izquierdo-Alonso, Jiménez Jiménez, Cabrera-Valdivia, and Mansilla-Lesmes [15] investigated airway dysfunction in 63 persons with PD, 59 of whom were on antiparkinsonian medication. They identified restrictive ventilatory pattern when the ratio of forced expiratory volume in 1 second (FEV_1) to forced vital capacity (FVC) was equal to or greater than 80% ($FEV_1/FVC \geq 80\%$). The presence of UAO required a combination of at least two of three spirometric indices: FEV_1/PEF

(peak expiratory flow), $FEV_1/FEV_{0.5}$, and the ratio of forced inspiratory flow to forced expiratory flow at 50% vital capacity (FIF_{50}/FEF_{50}). Eighty five percent of the participants had a restrictive ventilatory pattern and 4.76% had UAO [15]. The reported percentage of UAO in this study was lower than previously published reports, but this was attributed to the discrepancy in selective criteria used to define UAO. Izquierdo-Alonso et al. attributed the presence of restrictive lung disease to impaired coordination of expiratory effort or low chest wall compliance secondary to rigidity [15]. Further study by Sabaté, González, Ruperez, and Rodríguez [16] examined pulmonary function tests of 64 participants with PD when “off” antiparkinsonian medications (no medication 8 hours prior to the test) and reported a lower occurrence of restrictive ventilatory pattern (28%) and higher percentage of UAO (65%) compared to the previously mentioned study. Sabaté et al. observed a higher degree of bradykinesia in the participants with UAO. Upper airway obstruction is associated with decreased forced inspiratory and expiratory flow rates. The researchers suggested that the more severe bradykinesia might have contributed to the decreased forced inspiratory and expiratory flow rates. Bradykinesia is slow movement resulting from impaired recruitment of motor units which activate agonist muscles for movement [9] and may prevent sufficient voluntary muscle recruitment necessary to generate normal airflow rates.

Levodopa is a pharmacological therapy widely prescribed to treat symptoms of PD including bradykinesia and rigidity [49-52]. Several studies have investigated L-Dopa's affect on pulmonary function in persons with PD [14, 18, 20]. In a study conducted by Pal, Sathyaprabha, Tuhina, and Thennarasu [20], 22.6% of 53 participants presented with significantly impaired pulmonary function of the restrictive type when “off” medication. Of those with a restrictive ventilatory pattern in the “off” state, 75% of the 12 improved after taking L-Dopa as determined by increases in FVC and FEV_1 . Additionally, FVC, FEV_1 , maximum voluntary ventilation

(MVV), maximum expiratory (MEP) and inspiratory pressures (MIP) were all significantly lower in persons with PD compared to healthy controls in both “on” and “off” states. These investigators concluded that L-Dopa therapy may reduce symptoms of respiratory complications, including both UAO and restrictive lung disease. In contrast, Weiner et al. [14] reported no significant improvement of pulmonary function measures, including FVC and FEV₁ or respiratory strength (MIP and MEP) after L-Dopa administration. Despite inconsistent improvement in subclinical measures of pulmonary function following L-Dopa, participants reported a decrease in perception of dyspnea an hour after taking antiparkinsonian medications as rated on a visual analogue scale [14, 18]. Vercuei, Linard, Wuyam, Pollak, and Benchetrit [18] reported that all 11 participants, with moderately-advanced PD (Hoehn & Yahr stages III-V), experienced significant akinesia and rigidity without medication, but decreased breathing discomfort following L-Dopa administration (as rated on a visual analogue scale). Additionally, they described breathing patterns at rest, rather than respiratory disease, in the 11 participants, in both “on” and “off” L-Dopa conditions. Following L-Dopa administration, minute ventilation decreased significantly in 7 participants (63%), inspiratory phase duration increased in 9 participants (81.8%) and expiratory phase duration increased in 4 participants (36.3%). Mechanisms for the drug related changes included enhanced external intercostals function, the muscles responsible for postural support, although change to intercostal muscle function was not directly tested [18].

Respiratory muscles are also involved in other behaviors which serve minor or no ventilatory function such as coughing, sneezing, vomiting, swallowing, and speaking [53-63]. Both MEP and MIP measures, known indices of expiratory and inspiratory muscle strength, are reduced in persons with PD when compared to healthy reference values [14, 64-68]. The reduced

respiratory muscle strength in PD might cause some serious consequences to these non-ventilatory functions. Therefore, the activities of the respiratory muscles amid performing these behaviors as well as the possible effects of their rehabilitation are worth exploring. Thus, improving the strength of the respiratory muscles has the potential to improve ventilatory and non-ventilatory functions.

Cough in PD

Cough, which is ultimately a respiratory driven act, is impaired in PD [21, 22, 69]. Specifically, muscle and motor unit activation is impaired and impacts the recruitment for ballistic acts. Fontana et al. [21] found decreased integrated electromyographic activity in the abdominal muscles during volitional and reflexive cough, as well as in MEP, and indicated that this was due, in part, to decreased recruitment or frequency of motor unit discharge. Cough serves as one protective mechanism to aid in airway clearance [70], relying on shearing forces generated by its ballistic nature to expel foreign material. Ability to clear the airway with cough is important, particularly if penetration/aspiration of foreign material during swallow occurs [22, 70-72]. Pitts, Bolser, Rosenbek, Troche, and Sapienza [22] reported significantly longer compression phase duration (CPD), expiratory phase rise time (EPRT), decreased cough volume acceleration (CVA) and reduced expiratory peak flow (EP) as measured from voluntary cough flow waveforms in individuals with PD who penetrated-aspirated compared to those who did not. It was suggested that persons with decreased swallow safety, as determined by the P-A score, also had impaired cough, characterized by slowed actions of cough related events (longer CPD and EPRT) and a reduction in the final ballistic action of cough (decreased EP), [22]. Impaired cough may put these individuals at greater risk because they have a reduced ability to effectively expel penetrated or aspirated material. In a study of individuals who had suffered stroke, those with significant aspiration had a more impaired voluntary cough compared to those who did not

aspirate [72]. This is of particular importance because persons with PD commonly suffer from dysphagia [29-34]. Some individuals with PD have a significantly impaired swallow and are unable to sufficiently protect the airway, leading to aspiration of foreign material [30-34]. This may lead to aspiration pneumonia, a leading cause of mortality in persons with PD [73, 74]. Thus, decreased cough strength when coupled with an impaired swallow leaves individuals with PD vulnerable to poor pulmonary health.

Dysphagia in PD

Similar to respiration, in the early stages of PD, individuals do not recognize dysphagia symptoms despite their clinical presence [29, 30]. Persons with PD present with a myriad of swallow-related impairments, often due to the disruption of both volitional and autonomic control of oral and pharyngeal motility and timing. These disturbances occur across all phases of swallowing. Oral phase abnormalities include oral residue, piece-meal swallows, lingual pumping, lingual tremor, pre-swallow spill and prolonged oral transit times [30-32]. Deviances in the pharyngeal phase include vallecular residue after the swallow, residue in the pyriform sinuses, delayed onset of laryngeal elevation, abnormal pharyngeal wall motion, coating of the pharyngeal wall, aspiration [29-33] and decreased duration and opening of the upper esophageal sphincter (UES) [32, 33]. Additionally, individuals with PD, when compared to both young and healthy older adults, have impaired esophageal function most frequently reported as increased esophageal transit time and increased transit time in the lower esophagus [29]. Treatment of dysphagia with L-Dopa has produced inconsistent results, with limited improvements reported in the oral-preparatory and oral phases [31, 33, 34]. Fuh et al. [31] reported 12 of 19 persons with PD showed signs of dysphagia and 50% showed improvement 60 minutes after L-dopa administration. Although Fuh et al. [31] used a variety of bolus sizes and types, 3-7 mL, thin, paste, and cookie; they did not distinguish post L-Dopa improvements by bolus size or type. Six

individuals exhibited oral phase abnormalities including prolonged oral transit time, tongue elevation preventing bolus passage into the pharynx, reduced anterior-posterior motion of the tongue, and oral tremor. Oral tremor and tongue elevation improved in three participants after L-Dopa. Pharyngeal phase abnormalities were evident in 11 of 12 participants with dysphagia, with symptoms of delayed swallow reflex, decreased laryngeal elevation, residue in the valleculae and pyriform sinuses, laryngeal penetration and aspiration. All but one participant showed a reduction of pharyngeal dysphagia after L-Dopa, with valleculae and pyriform sinus residue being the most responsive [31]. While the majority of participants with PD showed improvements in pharyngeal phase abnormalities, only 50% showed oral phase improvements. Monte et al. [33] suggested differences in swallowing improvements may be L-Dopa dose-dependent. Higher doses of L-Dopa may result in excess movement, or dyskinesia [75]. Monte et al. [33] reported that persons who showed signs of dyskinesia had greater oropharyngeal swallowing efficiency for 10 mL liquid boluses as compared to persons with PD who showed little or no symptoms of dyskinesia. The researchers attributed the greater swallowing efficiency in the dyskinetic group to higher doses of L-Dopa. In an earlier study by Hunter, Crameri, Austin, Woodward, and Hughes [34], improvements in the oral-preparatory phase were described, but only with thin liquids and semi-solids. In fact, a decline in oral phase efficiency was observed with solid boluses, 60 minutes after L-Dopa, as demonstrated by an increase in oral phase time and swallow initiation time. Robbins, Logemann, and Kirshner [35] suggested dysphagia in oral-preparatory and oral phases, which are under volitional control, resulted from rigidity and bradykinesia in the oral musculature, and therefore improved with L-Dopa. Hunter et al. [34] were less confident in this hypothesis because they failed to see improvements in other swallow actions under volitional control, such as the length of the oral phase and the number of

tongue elevations that occurred during a single bolus transport. Because of this, it is possible that dopaminergic depletion is not the only reason for abnormalities in the phases of swallowing. Improvements of motor function after L-Dopa are widely recognized, but are not as extensive in swallowing. Moreover, early swallowing impairment does not correlate with disease severity [33, 34, 36]. Hunter et al. [34] suggested that dysphagia in PD may have an additional, non-dopamine dependent disturbance originating from impairments of the central pattern generator in the pedunculopontine nucleus or other medullary structures.

Coordination of Respiration and Swallowing

Respiration and swallowing are centrally controlled acts, mediated by the brainstem via central pattern generators, [76], and whose neural signals originate in close anatomical proximity [77-79]. In addition to sharing neuronal pathways, functions associated with respiration and swallowing also share anatomical space in the pharynx. Coordinated respiratory and swallow function is elucidated during swallow initiation whereby respiratory activity ceases momentarily (swallow apnea). Swallow apnea is under bulbar control [76] and can occur in the absence of glottal closure [80]. The onset of swallow apnea is variable among healthy adults and may occur well before laryngeal closure [81, 82]; however, timing of swallow apnea offset is more consistent among healthy individuals and generally occurs when the hyoid bone returns to rest [82]. The duration of swallow apnea is relatively unchanged across boluses less than 20 mL [81-86], but may increase with larger boluses (100-200 mL), directly relating to duration of laryngeal elevation [83, 87]. Once apnea occurs the vocal folds close, sealing off the glottal space, the ventricular (false) vocal folds approximate to mid-line to ensure further laryngeal airway penetration, the laryngeal vestibule rises up and forward, and the epiglottis inverts to protect the airway.

Dominant respiratory-swallow pattern has also been defined for healthy adults. Several researchers have reported that expiration precedes and follows 72-100% of swallows [81, 82, 84-89]. Expiration after a swallow may serve as a final protective mechanism to expel any penetrant that may have fallen into the airway as the laryngeal vestibule descends to rest. This pattern is stable across bolus consistencies [86, 88] and thin liquid boluses from 3-20 mL [81-83, 85-87]. As bolus size increases, the respiratory pattern varies and inspiration surrounds more swallow events [86, 87, 89]. Dozier, Brodsky, Michel, Walters, and Martin-Harris [89] found that inspiration occurred 56% of the time before a 50 mL swallow however, expiration continued to be the dominant post-swallow pattern as 78.6% of swallows were followed by expiration. Results from another study which used a 100 mL bolus reported that most swallows were initiated in expiration, but were followed by inspiration [87]. Likewise, participants involved in a study conducted by Preiksaitis and Mills [86] also produced more swallows ending in inspiration after drinking a 200 mL bolus from a straw. It is possible that a 100-200 mL sequential swallow is an inherently different task compared to 50 mL, with the larger bolus placing an increased respiratory demand on participants, and thus requiring more inspiratory events to follow the swallow.

Coordination of Respiration and Swallowing in PD

The combination of respiratory compromise and disrupted swallow timing associated with PD in particular may leave these individuals susceptible to a disrupted respiratory-swallow pattern [37, 38]. Pinnington, Muhiddin, Ellis, and Playford [37] non-invasively investigated swallowing by studying the respiratory patterns associated with a 5 mL thin liquid bolus in 12 persons with PD (H & Y II-V) and 14 healthy controls using the Exeter Dysphagia Assessment Technique (EDAT) [90-92]. The EDAT method is a non-invasive way of simultaneously recording respiratory signals and swallow function. This method uses a bi-directional nasal

cannula to record nasal airflow and a microphone attached to the neck to simultaneously record swallow sounds. An electrode is placed on the spoon handle and the person's leg or hand. When the spoon contacts the lips or tongue the circuit is completed and swallow initiation is recorded. Using this method, Pinnington, Muhiddin, Ellis, and Playford [37], found a significant difference in the percent of swallows followed by expiration with 99% of swallows followed by expiration in control subjects and 80% of swallows followed by expiration in those with PD. For those with PD, 18% of swallows were followed by inspiration and 2% of swallows were followed by a brief period of apnea [37]. More recently, Gross, Atwood, Ross, Eichhorn, and Olszweski [38] investigated the swallow patterns associated with pudding and cookie boluses in 25 individuals with PD and 25 healthy controls using a nasal cannula, respiratory inductance plethysmography, and surface electromyographic electrodes (sEMG). Participants with PD inhaled before and after swallows, regardless of bolus type, significantly more than healthy subjects. With the cookie bolus, individuals with PD initiated 29/211 (13.7%) of swallows in inspiration and followed 52/210 (24.7%) of swallows with inspiration, while healthy controls initiated 4/214 (1.8%) of swallows in inspiration and followed 22/230 (9.3%) of swallows in inspiration [38]. Similar differences were reported in the presence of a pudding bolus with inspiration preceding 29/211 (13.7%) of swallows and following 60/235 (25.5%) of swallows in persons with PD, compared to 22/230 (9.5%) of swallows beginning in inspiration and 17/230 (7.3%) ending in inspiration in the healthy controls. Moreover, unlike the healthy controls, individuals with PD did not demonstrate an increase in swallow apnea duration (SAD) during swallows initiated on inspiration. This may be due to the disease-related respiratory compromise [38]. It is also possible that this is not only the result of a peripheral abnormality, but rather a disruption in the signal from the brainstem which modifies respiratory pattern based on sensory input [93]. Both

abovementioned studies reported aberrant respiratory-swallow patterns in persons with PD compared to healthy adults using non-invasive techniques and also relying on patient report for presence or symptoms of dysphagia [37, 38].

In order to examine swallow, videofluoroscopy is one method for observing swallow function in real time, allowing description of swallowing events, while also providing a mean for identifying anatomic and physiologic differences responsible for patient symptoms [94, 95]. To date, there are no known studies which have used videofluoroscopy coupled with a respiratory signal from a nasal cannula to describe respiratory-swallow events in those with PD.

Videofluoroscopy has been used to define temporal measures of swallow [81, 95-99] and describe the coordination of these temporal events with respiration [81, 82, 89, 100-102] in healthy individuals. These studies provide a foundation for comparison of swallowing abnormalities associated with PD, including timing and motility disturbances in the oral and pharyngeal phases of swallow and occurrence of penetration or aspiration [30-36, 103]. The increased risk of penetration-aspiration with post-swallow inspiration event warrants the use of videofluoroscopy [95] because it allows the clinician to make observations of oral and pharyngeal dysfunction, penetration-aspiration, and associated respiratory events. The present study sought to investigate respiratory-swallow events in persons with PD and associated swallow safety measures (P-A score) using videofluoroscopy and a nasal cannula in order to contribute to existing literature which has used this technique to describe dysphagia in PD and respiratory-swallow events in healthy older adults [82].

Treating Respiratory-Swallow Dis-coordination

Past treatment attempts to alleviate symptoms of dysphagia were based on postural changes and compensatory techniques [104-108]. Treatment also focused on increasing swallow ability through increased physiological effort such as an effortful swallow coupled with

biofeedback or through exercise such as lingual strengthening [109-111]. To date, there have been few studies to define parameters, such as exercise amount or intensity, of these rehabilitative approaches for dysphagia. The Lee Silverman Voice Treatment® (LSVT®), with extensive results supporting its improvements in speech intelligibility, projection and voice quality in individuals with Parkinson's disease [26, 112-114], demonstrated preliminary improvements in swallow function in a pilot study of 8 persons with PD [115]. Sharkawi et al. [115] reported swallowing improvements after LSVT® which included decreased “rocking-like” tongue motion resulting in decreased oral transit time, decreased residue after liquid, paste and cookie boluses, eliminating the delayed triggering of swallow, and improved base of tongue retraction and subsequently less residue on base of tongue and valleculae. Although some changes were observed, LSVT® did not improve the occurrence of laryngeal penetration in persons with PD.

Expiratory muscle strength training (EMST) is an intervention program founded on the principles of exercise physiology [116]. Strength can be defined as the ability to apply force [117] (references). The more immediate effects of strength training are due almost entirely to improvements in neuro-muscular coordination [117-119] with later effects of strength training affecting muscle size [117, 118, 120-122]. In recent years EMST has been studied in several populations including PD [67, 69, 123], multiple sclerosis [124, 125], elderly [126, 127], professional voice users [128], instrumentalists [129], and young healthy adults [130, 131]. In each of these studies, EMST has been shown to increase MEP, an important measure of expiratory muscle strength [67, 69, 123-129, 131], which is decreased in persons with PD [14, 64-66, 68]. Increasing MEP with EMST is not a new finding as this was also demonstrated by Weiner, Magadle, Beckerman, Weiner, Berar-Yanay [132], Gozal and Thiriet [133], Weiner, et

al. [134], Smeltzer, Lavietes, and Cook [135], Suzuki, Masamichi, and Okubo [136], and Okroy and Coast [137].

Evidence also supports using EMST in rehabilitative efforts to improve both cough and swallow function in PD [69, 116, 124, 130]. Pitts, Bolser, Rosenbek, Troche, Okun, and Sapienza [69] examined the effects of EMST in 10 male participants with PD who evidenced penetration or aspiration during a 3 oz swallowing task under videofluoroscopic evaluation. The participants demonstrated a significant increase in MEP, and a change in cough airflow patterns characterized by decreased compression phase duration and expiratory phase rise time, and increased cough volume acceleration (VA) after 4 weeks of training with EMST. The researchers stated that EMST increased cough effectiveness, as measured by cough VA, which is a measure related to the ability of the cough to create shearing forces to expel foreign material [69]. Four weeks of EMST also resulted in an increase in swallow safety, as determined by lower P-A scores [138, 139]. In addition to increased respiratory muscle strength, there is preliminary evidence suggesting EMST also targets muscles involved in swallowing. The improvements of respiratory muscle strength and improved swallow safety may decrease the physiologic demands associated with respiratory-swallow coordination [69, 140].

Wheeler, Chiara, and Sapienza [140] measured submental muscle activation in 20 healthy adults with sEMG during dry swallow, wet swallow, and EMST tasks. Compared to both swallow tasks, EMST resulted in greater duration, peak amplitude and average amplitude of activity in the submental muscles [140]. Submental muscles are specifically important during the pharyngeal stage of swallowing, as their contraction allows for hyolaryngeal elevation and excursion, which ultimately leads to airway protection and UES opening [98, 141]. This objective measurement of submental muscle activation compliments the study conducted by Pitts

et al. [69], which found a decrease of P-A scores after EMST use in persons with PD, who previously penetrated/aspirated. Activation of the submental muscles during EMST may result in positive training effects [118, 121, 122, 142] which increase submental muscle strength and in turn, swallow efficiency. Submental muscle activation is important for hyoid bone elevation because it results in laryngeal elevation and excursion [130], essential acts that contribute to the passage of the bolus into the esophagus during swallowing. The combination of improvements in respiratory strength and swallow safety may suggest a reduced demand on the mechanisms involved in respiratory and swallowing coordination.

There are only a few published studies on respiratory-swallow pattern in PD [37, 38] and they have suggested that this population is susceptible to using an abnormal respiratory pattern, characterized by post-swallow inspiration. As discussed above, breathing and swallowing coordination is a complex physiologic integration that is mediated by the respiratory and swallowing central pattern generators [78]. Swallows followed by inspiration may render the individual susceptible to aspirating post-swallow residue, due to the negative pressure below the glottis. Improvements in respiratory strength, increased cough effectiveness, and increased submental muscle activation as seen in EMST may reduce confounding factors that increase post-swallow inspiration events.

Aims and Hypotheses

There were three aims of this study.

- The first aim was to determine the predominant respiratory events that accompany the swallow of a 5 mL thin bolus in individuals with PD as compared to healthy older adults. It was hypothesized that the respiratory events in those with PD would show a greater predominance of abnormality as compared to healthy older adults.
- The second aim was to determine the relationship between the identified respiratory events and penetration/aspiration scores and SAD for the 5 mL thin bolus. It was hypothesized that swallows followed by expiration would be statistically significant and positively correlated with P-A scores that reflect a safe swallow (P-A score ≤ 2) and would be related

to longer SAD. Furthermore, swallows followed by inspiration would be significantly and positively correlated with unsafe swallow (P-A score ≥ 3) and shorter SAD in persons with PD.

- The final aim was to determine if the identified respiratory events would be altered after 4 weeks of expiratory muscle strength training (EMST). It was hypothesized that individuals with PD who present with abnormal post-swallow respiratory events, swallows followed by inspiration, would change the post-swallow respiratory event to expiration, following 4 weeks of EMST.

CHAPTER 2 METHODS

Thirty nine participants (29 males and 10 females; mean age of 67.8 years, SD=9.28 years) with Parkinson's disease (PD), referred from the University of Florida (UF) and Malcom Randall Veteran's Affairs (VA) Movement Disorders Centers in Gainesville, FL were included in this study. All participants signed an informed consent prior to enrollment. The UF and VA Institutional Review Boards (154-2003 and 195-2005) approved the study. Following informed consent, a UF Movement Disorders neurologist completed a clinical assessment of each individual's PD disease severity, making the diagnosis of PD based on UK Brain Bank Criteria [143]. Severity was determined based on guidelines presented by Hoehn and Yahr (H&Y), [144]. Participants with H & Y scores of II-IV were included (mean H&Y score of 2.73). All participants were receiving benefit from an antiparkinsonian medication (i.e., Carbidopa/Levodopa, a dopamine agonist, an MAO-B inhibitor, and/or Amantadine) and reported a degree of swallowing disturbances (i.e. reports of coughing/choking with meals, increased eating duration, etc) prior to enrollment.

Participant criteria

Additional inclusion criteria for participation included: 35 to 85 years old and a score of at least 24 on the Mini-Mental State Examination [145]. Exclusionary criteria were: history of other neurologic disorders, head and neck cancer, gastrointestinal disease, gastro-esophageal surgery, chronic and acute cardiac disease, untreated hypertension, heart disease, smoking in the past five years, history of breathing disorder or disease, failure to pass a screening test of pulmonary functioning (e.g., $FEV_1/FVC < 75\%$), or difficulty complying due to neuropsychological disturbance such as severe depression or dementia.

Design

Participants were randomized into an experimental or sham (placebo) group. All participants took part in a baseline swallow assessment which included 10 trials of 5 mL thin barium contrast. The baseline assessment was followed by 4 weeks of either the active or sham treatment. After the 4 weeks of training, participants returned for a post treatment swallow assessment. Speech pathologists with significant clinical experience evaluating patients with PD analyzed the barium swallow studies for expiratory or inspiratory events related to a swallow cycle, swallow apnea duration (SAD), and penetration-aspiration (P-A) score and were blinded to the participants' identity and treatment randomization.

Instrumentation

Videofluoroscopy was used to examine swallowing function. The Kay Elemetrics Swallowing Signals Lab unit (Kay Elemetrics, Lincoln Park, NJ) coupled with a nasal cannula, digitally recorded the fluoroscopic images at 29.97 frames per second using a scan converter. Nasal respiratory flow was captured using a standard, 7-foot nasal cannula coupled to the *Workstation* using the Swallow Signals Lab hardware and software to create a digital display of the respiratory phase and swallow apnea duration. The nasal cannula was calibrated between each participant to ensure accurate measures. The sampling rate for the respiratory tracing was 250Hz. Videofluoroscopic recordings were made with a resolution of 60 fields (30 frames) per second. Therefore, the resolution for determining measurements using digital video recordings was approximately 17 ms per digital field. The recordings were conducted in a standard fluoroscopic suite. Participants sat upright and their swallow function was recorded in the lateral viewing plane using a properly collimated Phillips Radiographic/Fluoroscopic unit a 63-kV, 1.2-m-A output with a full field of view mode. The field of view included the lips and teeth,

anteriorly, nasal spine superiorly, cervical spine superiorly, and upper esophageal sphincter inferiorly.

Participants completed 10, 5 mL trials of thin liquid (Liquid E-Z Paque Barium Sulfate Suspension; 60% w/v, 41% w/w; from E-Z-EM) by cup. During the swallow examinations all participants self-fed in order to closely replicate "natural" feeding conditions. The investigator gave the cup to the participants and prompted him or her to “place the liquid in your mouth and swallow when ready.”

Expiratory Muscle Strength Training Protocol

For both the active and sham treatment group, the EMST device was weekly set to 75% of the participant's average maximum expiratory pressure (MEP) (see procedures below). A clinician, blinded to treatment randomization, visited participants weekly for 4 weeks to adjust the EMST device settings based on the MEP performance score. The sham device was physically no different than the EMST device but was non-functioning, as it did not produce a pressure threshold load during use.

During the weekly visit by the clinician, participants were reminded how to properly use their device to ensure independent daily treatment trials. Participants were trained to wear nose clips, take a deep breath, hold their cheeks lightly (to reduce labial leakage), and “blow as hard as they could into the device” and identify that air was flowing freely through the device (once they reached threshold pressure). Each participant trained at home (independent of the clinician) completing five sets of five repetitions five days out of the week [123-125, 131]. Compliance with the training was tracked daily using a form provided by the clinician, which was checked weekly.

Maximum Expiratory Pressure

Using a standardized protocol at each time point for assessment, participants stood and occluded the nose with the nose clips. Maximum expiratory pressure measurements were taken using a pressure manometer (FLUKE 713-30G) coupled to a mouthpiece via 50 cm, and 2 mm inner diameter tubing, with an air-leak created by a 14-gauge needle. Participants were instructed to place the device with the mouthpiece between the lips and behind the teeth, to inhale as deeply as possible (i.e. to a lung volume approximating total lung capacity) and to blow into the manometer tube quickly and forcefully. Three values within 5% of each other were required to achieve an average for the participants' individualized MEP score. This score set the EMST device for the subsequent training as indicated above.

Physiologic Measures

Respiratory-swallow events were interpreted from the respiratory signals collected by the Kay Elemetrics Signal Lab that were identified as surrounding the swallow event. The polarity of the respiratory signal determined airflow. A positive polarity signal represented expiratory events and a negative polarity signal represented inspiratory events. The respiratory-swallow events were documented as respiratory events that occurred before and after swallow apnea. Swallow apnea duration (SAD) was represented by a plateau of the air flow signal along the x-axis and the duration was measured from the digital display of the respiratory signal in milliseconds (ms).

Functional Measures of Swallow

The penetration-aspiration (P-A) scale score [138, 139] was used to quantify the presence of penetration and aspiration during the swallowing of the 3 oz sequential bolus. The P-A scale is a validated scale using ordinal measures, where 1 indicates the safest swallow and 8 indicates the least safe swallow, or silent aspiration. The scale measures whether or not material entered the airway and if it entered the airway, whether the residue remained or was expelled.

Statistical Analysis

Descriptive statistics describe the frequency of each possible respiratory event before and after swallow apnea. Pearson r correlations were conducted across the data set, before training to assess relationships between respiratory events before and after swallow apnea and SAD. Data was first analyzed without averaging across events (all 10 swallow trials were analyzed individually) and then averaged across trials. Pearson r correlations were conducted with collapsed data to determine relationships between respiratory events pre and post-swallow, SAD and P-A score. A t-test with aggregates was used to compare measures among swallow safety (P-A score ≤ 2 ; P-A score ≥ 3). A series of repeated measures ANOVA was conducted after training (EMST or Sham) to determine time effect on the dependent variables. A post hoc analysis using ANOVA repeated measures was conducted to investigate groups separated by P-A score (non-P-A 1-2, P-A 3-8). Individuals with P-A scores of 3 or greater have increased swallow severity and may be at increased risk if swallows are followed by inspiration.

Demographics

Refer to Table 2-1 and 2-2 for participant demographics.

Table 2-2. Demographics: Experimental group

Participant	Age	Sex	H & Y
1	50	M	2
2	71	M	2
3	74	M	2
4	57	M	2
5	64	M	2
6	64	M	2
7	65	M	2.5
8	63	M	2.5
9	74	F	2.5
10	64	M	2.5
11	68	M	3
12	72	M	3
13	74	M	3
14	70	M	3
15	77	M	3
16	73	M	3
17	56	F	3
18	60	M	3
19	81	F	3
20	78	F	4
M	67.75		N/A
SD	8.097		N/A

Age, sex, and Hoehn & Yahr (H & Y) severity

Table 2-3. Demographics: Sham group

Participant	Age	Sex	H & Y
1	66	M	2
2	64	M	2
3	60	M	2.5
4	70	M	2.5
5	68	F	2.5
6	81	M	2.5
7	77	M	2.5
8	42	F	2.5
9	64	M	2.5
10	78	M	3
11	64	F	3
12	71	M	3
13	82	M	3
14	45	M	3
15	67	M	3
16	68	F	3
17	70	F	3
18	77	F	4
19	76	M	4
M	67.895		N/A
SD	10.619		N/A

Age, sex, and Hoehn & Yahr (H & Y) severity

CHAPTER 3 RESULTS

Total Number of Swallows Analyzed Pre-training Collapsed across Group

A total of 339 swallows of a possible 390 swallows (10 trials by 39 participants) was collected before implementing expiratory muscle strength or sham training. Fifty one of the possible 390 swallows were not analyzed for various reasons. Of those 51, 10 were not analyzed due to image file corruption, 35 could not be analyzed because the respiratory signal was absent or not of great enough amplitude to identify respiratory events, and 6 swallows were not included because there was presence of piece meal swallows that resulted in a bolus size less than 5 mL.

Total Number of Swallow Events Analyzed Pre-training Collapsed across Group

A possible total of 780 swallow events (39 participants swallows by 10 trials by 2 respiratory events) should have existed. However, a total of 670/780 swallow events were only analyzed. The reason 110 swallow events could not be analyzed was because a portion of the signal did not have significant signal gain or there was image file corruption. Collapsed data combining experimental and sham group participant swallows showed that expiration preceded the swallow event 70.1% of the time and inspiration preceded the swallow event 29.9% of the time. Expiration followed the swallow event 86.4% of the time and inspiration followed the swallow event 13.6% of the time. See Table 3-3 for frequencies of respiratory events associated with swallow pre-training collapsed across groups.

Total Number of Swallows Analyzed Post-training Collapsed across Group

A total of 328 swallows from 33 participants were collected (10 trials by 32 participants and 8 trials by 1 participant) after implementing expiratory muscle strength (EMST) or sham training. Six participants by 10 trials were lost in the data set because the files were corrupt or missing. Additionally, one participant did not tolerate the 5 mL thin barium and completed 8

swallows instead of 10 trials. Fifty two of a possible 328 swallows were not analyzed due minimal or absent respiratory signals secondary to mouth breathing or image file corruption.

Total Number of Swallow Events Analyzed Pre-training Collapsed across Group

A possible total of 656 swallow events (32 participants by 10 trials by 2 respiratory events and 1 participant by 8 trials by 2 respiratory events) should have existed. However, a total of 569/656 swallow events were only analyzed. The reason 87 swallow events could not be analyzed was because a portion of the signal did not have significant signal gain or there was image file corruption. Collapsed data across the experimental and sham groups showed that expiration occurred 70.1% before the swallow and inspiration occurred 29.9% before the swallow. Expiration occurred 91.0% after the swallow and inspiration occurred 9.0% after the swallow. See Table 3-4 for frequencies of respiratory events associated with swallow post-training.

Total Number of Swallow Events Analyzed Post-training Collapsed across Group

A possible total of 656 swallow events (32 participants by 10 trials by 2 respiratory events and 1 participant by 8 trials by 2 respiratory events) should have existed. However, a total of 565/656 swallow events were only analyzed. The reason 91 swallow events could not be analyzed was because a portion of the signal did not have significant signal gain or there was image file corruption. Collapsed data across the experimental and sham groups showed that expiration occurred 76.5% before the swallow and inspiration occurred 23.5% before the swallow. Expiration occurred 94.8% after the swallow and inspiration occurred 5.2% after the swallow. See Table 3-4 for frequencies of respiratory events associated with swallow post-training.

Pre-training Analysis of Swallow Events Produced by Experimental Group

Accounting for the missing swallow files as indicated above, there were 316/360 swallow events analyzed for the experimental group pre-training. Descriptive statistics showed expiration preceded 68.4% of swallows and followed 92.5% of the swallows. Inspiration preceded 31.6% of swallows and followed 7.5% of swallows (Table 3-5) Mean SAD was 1.173 seconds pre-training for the experimental group (Table 3-6).

Pre-training Analysis of Swallows Event Produced by Sham Group

Accounting for the missing swallow files as indicated above there were 253/300 swallow events analyzed in the sham group pre-training. Descriptive statistics showed expiration preceded 72.2% of the swallows and followed 88.9% of the swallows. Inspiration preceded 27.8% of swallows and followed 11.1% of swallows (Table 3-5). Mean SAD was 0.766 seconds pre-training for the sham group (Table 3-6).

Post-training Analysis of Swallow Events Produced by Experimental Group

Accounting for the missing swallow files as indicated above there were 293/360 swallow events analyzed in the experimental group post-training. Descriptive statistics showed expiration preceded 72.9% of the swallows and followed 96.6% of the swallows post-EMST training. Inspiration preceded 27.1% of swallows and followed 3.4% of swallows (Table 3-5). Mean SAD was 1.573 seconds post-training for the experimental group (Table 3-6).

Post-training Analysis of Swallow Events Produced by Sham Group

Accounting for the missing swallow files as indicated above there were 272/300 swallow events analyzed in the sham group post-training. Descriptive statistics showed expiration preceded 80.5% of the swallows and followed 92.8% of the swallows. Inspiration preceded 19.5% of the swallows and followed 7.2% of the swallows (Table 3-5). Mean SAD was 0.814 seconds post-training for the sham group (Table 3-6).

Correlation Analysis

Pre-training respiratory events and SAD were averaged across trials and groups. Pearson r statistics revealed significant positive correlation before training between SAD and respiratory event pre-swallow ($r = 0.357$, $p = 0.000$), while there was a significant negative correlation before training between SAD and respiratory event post-swallow ($r = -0.162$, $p = 0.005$) (Table 3-7).

After running the initial correlation analysis, P-A score and respiratory events were averaged across trials and collapsed across groups. A correlation existed between P-A score and post-swallow respiratory event ($r = 0.590$, $p = 0.000$) (Table 3-8).

Post-training respiratory events and SAD data were collapsed across groups. Pearson r statistics revealed a significant positive correlation between SAD and respiratory event pre-swallow ($r = 0.497$, $p = 0.000$). Additionally, there was a significant positive correlation between post-training respiratory event pre-swallow and pre-training respiratory event pre-swallow ($r = 0.476$, $p = 0.000$) as well as post-training post-swallow respiratory event and pre-training post-swallow respiratory event ($r = 0.341$, $p = 0.000$) (Table 3-9).

To further examine the factors that may have contributed to the relationship between P-A score and respiratory events, participants were divided into groups by P-A score (Group 1, $P-A \leq 2$; Group 2, $P-A \geq 3$). A t-test for equality of means, with equal variances assumed, was then conducted and a significant difference was found for post-swallow respiratory event ($t = -2.253$, $df = 36$, $p = 0.03$) with Group 2, having higher P-A scores, and more inspiratory events post-swallow (Table 3-10 and Figure 3-2).

Analysis of Training Effects: EMST and Sham

A repeated measures ANOVA revealed a significant difference ($F(4,167) = 2.587$, $p = 0.039$) between the experimental and the sham groups as a function of training. There were no

significant differences within groups (Table 3-11). For further illustration of P-A score as a function of training refer to Figure 3-1.

Post hoc testing, using pairwise comparisons to assess differences between group, showed only a significant difference in SAD between the experimental and sham groups ($p = 0.002$) with the experimental group producing a longer SAD mean by 0.272 seconds compared to the sham group (Table 3-12). Figure 3-2 displays the mean SAD for experimental and sham groups across time.

Post hoc analysis was conducted for both experimental and sham groups using paired sample t-tests. There was no significant difference within the experimental group (Table 3-13) or sham group (Table 3-14) before and after training for pre-post-swallow respiratory events or SAD.

A post hoc repeated measures ANOVA also showed a significant interaction ($F = 9.912$, $df = 1$, $p = 0.002$) occurred across time, group, and swallow safety ($P-A \text{ score} \leq 2$; $P-A \geq 3$) with SAD (Table 3-15 and Figure 3-3).

Table 3-3. Collapsed data across the experimental and sham group for swallow events pre-training, n= 39.

Pre-Training (All)	Expiration	Inspiration
Pre-Swallow Respiratory Event	70.1 % (232/331)	29.9 % (99/331)
Post-Swallow Respiratory Event	86.4 % (293/339)	13.6 % (46/339)

Table 3-4. Collapsed data across the experimental and sham group for swallow events pre and post-training, n= 33.

Respiratory Event	Pre-Training (All)		Post-Training (All)	
	Pre-Swallow	Post-Swallow	Pre-Swallow	Post-Swallow
Expiration	70.1% (197/281)	91.0% (262/288)	76.5 % (212/277)	94.8 % (273/288)
Inspiration	29.9% (83/281)	9.0% (26/288)	23.5 % (65/277)	5.2 % (15/288)

Table 3-5. Respiratory events associated with swallow for the experimental and sham groups

Group	Pre-training			Post-training		
	Respiratory Event	Expiration	Inspiration	Respiratory Event	Expiration	Inspiration
Experimental N = 18	Pre-Swallow	68.4% (106/155)	31.6% (48/155)	Pre-Swallow	72.9% (105/144)	27.1% (39/144)
	Post-Swallow	92.5% (149/161)	7.5% (12/161)	Post-Swallow	96.6% (144/149)	3.4% (5/149)
Sham N = 15	Pre-Swallow	72.2% (91/126)	27.8% (35/126)	Pre-Swallow	80.5% (107/133)	19.5% (26/133)
	Post-Swallow	88.9% (113/127)	11.1% (14/127)	Post-Swallow	92.8% (129/139)	7.2% (10/139)

Table 3-6. Mean swallow apnea duration for experimental and sham groups pre-post-training

Group	Swallow Apnea Duration	
	Pre-training	Post-training
Experimental	1.173 seconds	1.573 seconds
Sham	0.766 seconds	0.814 seconds

Table 3-7. Pearson r correlations for experimental and sham groups collapsed pre-training

Measures		SAD	Respiration Pre-swallow	Respiration Post-swallow
SAD	Pearson Correlation	1	0.357**	-0.162**
	Significance (2-tailed)		0.000	0.005
	N	333	290	298
Pre-swallow Respiratory Event	Pearson Correlation	0.357**	1	-0.051
	Significance (2-tailed)	0.000		0.356
	N	290	331	330
Post-swallow Respiratory Event	Pearson Correlation	-0.162**	-0.051	1
	Significance (2-tailed)	0.005	.356	
	N	298	330	339

Table 3-8. Pearson r correlations for mean swallow apnea duration and penetration-aspiration score of experimental and sham groups collapsed pre-training

		Respiration Pre-swallow (mean)	Respiration Post-swallow (mean)
SAD (mean)	Pearson Correlation	.550**	-.322
	Significance (2-tailed)	.001	.059
	N	35	35
P-A score	Pearson Correlation	-.232	.590**
	Significance (2-tailed)	.160	.000
	N	38	38

Table 3-9. Pearson r correlation of respiratory measures for experimental and sham groups collapsed post-training

			Post-training	
			Pre-swallow Respiratory Event	Post-swallow Respiratory Event
Post-training	Pre-swallow Respiratory Event	Pearson Correlation Sig. (2-tailed) N	1 277	-0.020 0.746 277
	Post-swallow Respiratory Event	Pearson Correlation Sig. (2-tailed) N	-0.020 0.746 277	1 288
	SAD	Pearson Correlation Sig. (2-tailed) N	0.497** 0.000 222	-.040 0.543 231
Pre-training	Pre-swallow Respiratory Event	Pearson Correlation Sig. (2-tailed) N	0.476** 0.000 239	-.138* 0.030 248
	Post-swallow Respiratory Event	Pearson Correlation Sig. (2-tailed) N	-0.042 0.510 243	0.341** 0.000 252

Table 3-10. Results of the pairwise comparisons (t-tests) using aggregates for equality of means for the non-penetrator-aspirators versus penetrators-aspirators pre-training.

		t	df	Sig. (2-tailed)	Non-P-A Mean	P-A Mean	Mean difference	Standard Error
Pre-swallow Respiratory Event	Equal variances assumed	0.579	36	0.566	1.3420	1.2750	0.0669	0.1156
Post-swallow Respiratory Event	Equal variances assumed	-2.253	36	0.030	1.0629	1.2306	-0.1677	0.0744
SAD	Equal variances assumed	1.963	33	0.058	1.4553	1.7565	0.3991	0.2033

Table 3-11. Repeated measures ANOVA for analysis of experimental and sham group differences

Effect		F	df	p
Between Subjects	Group	2.587	(4.00,167.000)	0.039
Within Subjects	Time	0.816	(4.00, 167.000)	0.516
	Time x Group	1.405	(4.00, 167.000)	0.234

Table 3-12. Pairwise comparisons (t-tests) of means for experimental and sham groups

Measure	Group	Group	Mean Difference (Exp – Sham)	Std. Error	Sig.
Pre-swallow Respiratory Event	Exp	Sham	0.43	0.057	0.457
Post-swallow Respiratory Event	Exp	Sham	-0.058	0.035	0.098
SAD	Exp	Sham	0.272	0.088	0.002

Table 3-13. Paired sample t- test for the experimental group pre-post-training

Pre-Post-training	t	df	p
Pre-swallow Respiratory Event	0.852	127	0.396
Post-swallow Respiratory Event	0.576	134	0.566
SAD	-0.906	128	0.367

Table 3-14. Paired sample t-test for the sham group pre-post-training

Pre-Post-Training	t	df	p
Pre-swallow Respiratory Event	1.521	110	0.131
Post-swallow Respiratory Event	1.215	116	0.277
SAD	-1.673	115	0.097

Table 3-15. Repeated measures ANOVA for analysis of penetration-aspiration score as a function of experimental and sham groups and swallow safety severity.

Source	Measure Pre-Post-training	df	F	p
Time x Group 2 (Pen-Asp)	Pre-swallow Respiratory Event	1	1.195	0.276
	Post-swallow Respiratory Event	1	0.167	0.683
	SAD	1	0.252	0.616
Time x Group1 x Group 2	Pre-swallow Respiratory Event	1	0.488	0.486
	Post-swallow Respiratory Event	1	0.713	0.400
	SAD	1	9.912	0.002**

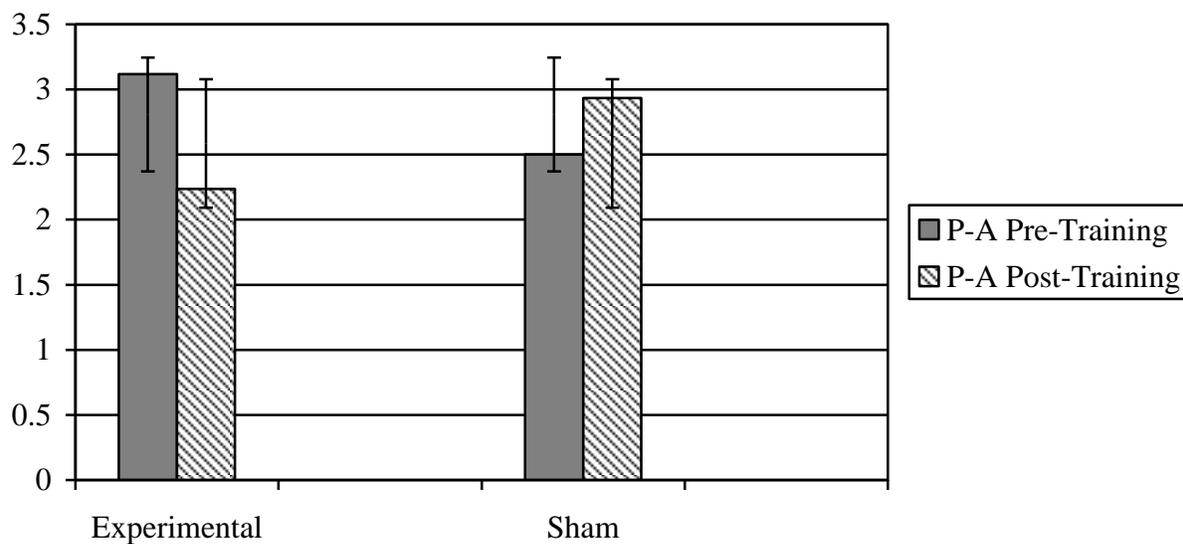


Figure 3-1. Mean P-A scores with standard deviations of experimental and sham groups before and after training. There were no significant differences.

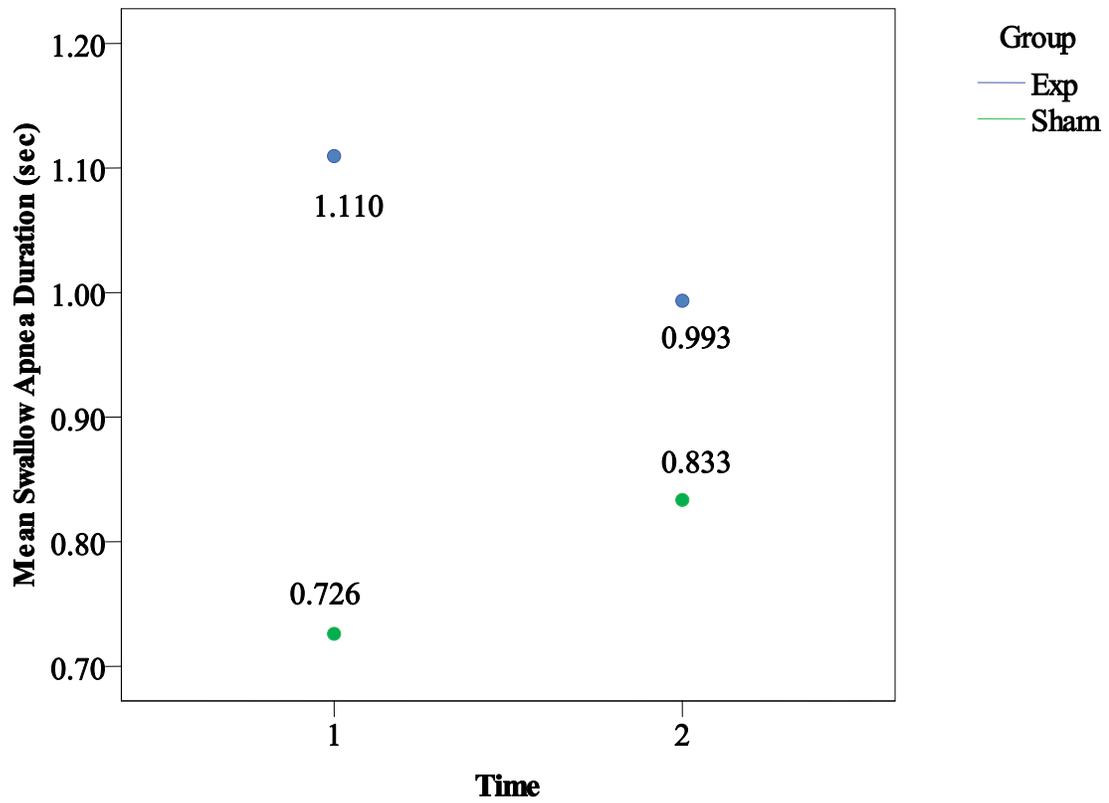


Figure 3-2. Comparison of mean swallow apnea duration, pre and post-training. Significant difference ($p=0.002$) between groups at time 1, where time 1 is before training and time 2 is after training. There were no significant differences within groups by time.

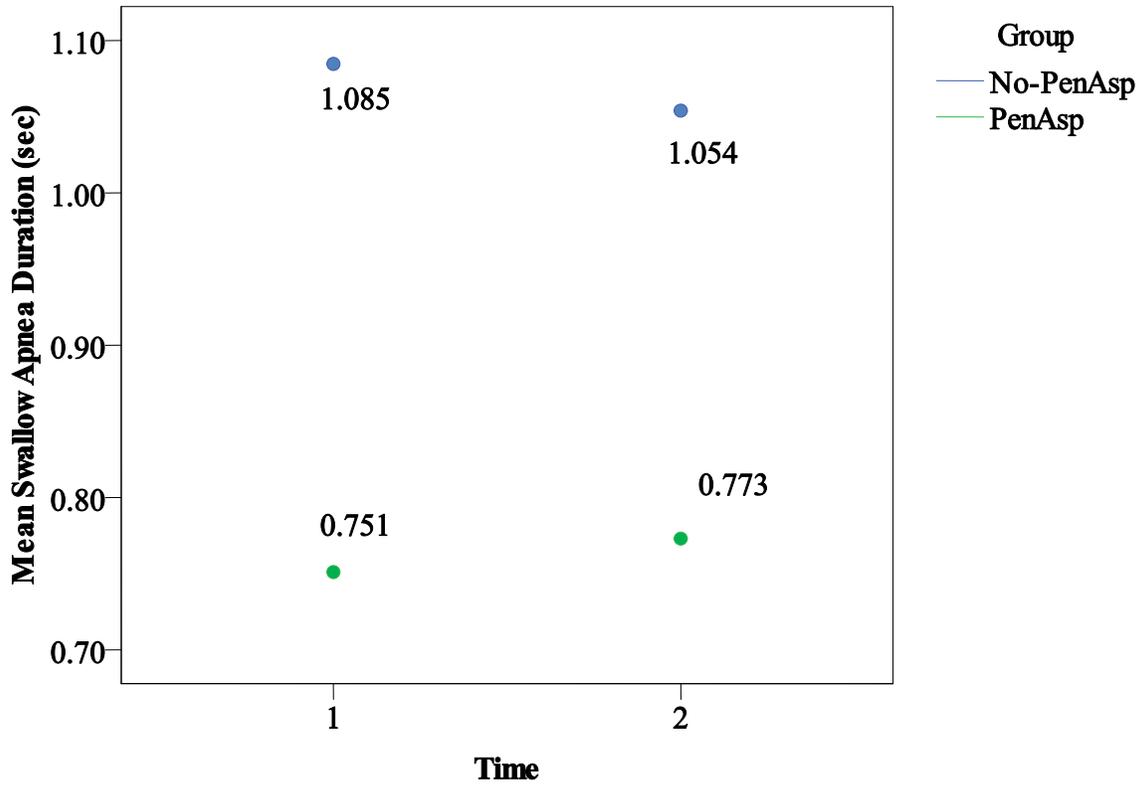


Figure 3-3. Comparison of mean SAD by swallow safety across time. For the No-PenAsp group, individuals received a P-A score of 1 or 2. For the PenAsp group, individuals received a P-A score from 3-8. Time 1 is before training and Time 2 is after training. A significant difference was found between groups.

CHAPTER 4 DISCUSSION

Findings of this study demonstrated that expiration is the predominant respiratory event occurring both before and after swallow apnea for individuals with Parkinson's disease (PD) during swallows of 5 mL thin boluses. Additionally, this study identified significant positive relationships that exist among respiratory events, swallow apnea duration (SAD) and penetration-aspiration (P-A) score. Pre-swallow inspiratory events were positively related to longer durations of swallow apnea. Post-swallow inspiratory events were positively related to shorter SADs. Post-swallow inspiratory events were positively related to higher P-A scores. To further investigate the relationship of swallow safety to SAD, individuals were divided into two groups by P-A score. Individuals with P-A scores of 1-2 were designated as non-penetrator-aspirators and those with P-A scores of 3-8 were designated as penetrator-aspirators. Those individuals who penetrated or aspirated demonstrated significantly shorter SADs compared to the non-penetrator aspirator group. Finally, there was a significant difference between the experimental and sham groups before expiratory muscle strength training (EMST) intervention, in which participants in the sham group demonstrated shorter mean SAD by 0.272 seconds. However, there were no significant differences within participants for the experimental or sham groups as a function of EMST, thus EMST did not alter the respiratory events before or after a swallow.

As seen in Table 3-3, the initial analysis of swallows of the 39 individuals with PD before EMST or sham intervention revealed that 70.1% (232/331) of swallows were preceded by expiration and 86.4% (293/339) of swallows were followed by expiration. Of the 33 individuals whose swallows were analyzed before and after training, 70.1% (197/281) of swallows were preceded by expiration and 91.0% (262/288) of swallows were followed by expiration (Table 3-

4). It was hypothesized that in general individuals with PD would show an increased percentage of swallows followed by inspiration. Although there was not a healthy control group included in the present study, individuals in the current study generated about 6-7% less swallows followed by expiration compared to a similar study conducted by Martin-Harris et al. [82], which described the respiratory-swallow events associated with a 5 mL thin bolus in 76 healthy adults using videofluoroscopy and a nasal cannula. In the study conducted by Martin-Harris et al. [82], it was determined that approximately 76-79% of swallows began in expiration and 93% end in expiration when averaged across two trials [82]. Additional studies using non-invasive methods to assess breathing and swallowing coordination in healthy adults have generated similar results. Hirst et al. [83] reported 91% of swallows of 5 mL water boluses produced by 29 older healthy adults were followed by expiration. Klahn and Perlman [84] examined the swallows of 5 mL water boluses produced by 12 young healthy adults (18-25 years) and reported 100% of swallows were followed by expiration.

Previous investigations of breathing and swallowing coordination in individuals with PD which included healthy controls for comparison, found significant differences in respiratory events surrounding a swallow [37, 38]. Pinnington et al. [37], used the Exeter Dysphagia Assessment Technique (EDAT) to analyze respiratory events surrounding the swallow of a 5 mL thin bolus in 12 individuals with PD and 14 elderly controls and found that those with PD followed 80% of swallows with an expiratory event and that healthy adults followed 99% of swallows with expiration. Important to note is that Pinnington et al. [37] gave participants either 5 mL of water or orange squash; however, the analysis did not indicate if swallow events were differentiated between boluses, nor did the study indicate the distribution of bolus presentation to participants. It was assumed that the swallows for the different bolus types were collapsed for

analysis. The two bolus types differed by taste and texture, both of which have the potential to impact the oral and pharyngeal phases of swallow. Gross et al. [38] presented both pudding and cookie boluses to 25 persons with PD and 25 healthy controls. In the pudding condition, persons with PD followed 74.5% of swallows with expiration and the healthy adults followed 92.7% of swallows with an expiratory event. When presented with the cookie bolus, persons with PD followed 75.3% of swallows with expiration. In comparison, the healthy adults followed 90.7% of swallows with expiration [38]. Caution should be used when comparing results of these studies to the present study because the different bolus types used could potentially impact the swallow and respiratory events. Results of the previously conducted studies [37, 38] indicate that individuals with PD have a significantly higher percentage of inspiratory events following a swallow, compared to healthy adults. A closer look at the percentages of post-swallow events reveals the majority of swallow are followed by expiration. It is possible that the conditions in which the participants with PD were tested were not representative of real-life eating situations where they may be more susceptible to inspire after swallowing. During daily eating tasks, where larger boluses or multiple sips of liquid may be consumed at one time, persons with PD may show more difficulty in coordinating respiration with swallowing. In healthy controls, respiratory events have been shown to be altered when boluses are consumed that are 50 mL or larger [83, 86, 89]. Preiksaitis and Mills [86] reported boluses of 200 mL resulted in a greater number of swallows followed by inspiration. Dozier et al. [89] investigated respiratory-swallow coordination with a 50 mL bolus in healthy adults. The investigators found that individuals required an average of 4.35 swallows to ingest this bolus size and that individuals maintained apnea for more than one swallowing event. The investigators used the term ingestion cycle to describe the occurrence of multiple swallows within a single apneic period [89]. The initial

swallow of the 50 mL bolus showed 44% were followed by an expiratory event. After the first ingestion cycle, 93% of swallows were followed by an expiratory event. It would seem that individuals with PD might be at greater risk for aspiration during sequential swallow tasks, with the chances of inspiration being greatest after the first swallow based on these above mentioned studies. Sequential swallows are more representative of swallowing behaviors in everyday life and should be further investigated in persons with PD. No studies to date have investigated respiratory events associated with sequential swallows in individuals with PD.

The present investigation also sought to determine the relationship between respiratory events, swallow apnea duration and P-A scale scores. Swallows initiated during inspiratory events were positively related to longer SADs. Possibly individuals who inspired before the swallow have a disordered oral phase with decreased bolus control [30-32, 36], resulting in longer SAD although this was not the case in the study by Gross et al. [38]. In fact, Gross et al. [38] reported that healthy adults produced significantly longer SADs with cookie and pudding boluses when swallows were initiated in inspiration; however, they did not observe this same pattern in the participants with PD. The type of bolus may account for the different findings between the Gross et al. [38] study and the present study which tested a 5 mL thin liquid. In general, longer oral transit times have been associated with thicker consistencies in both healthy individuals [146] and in persons with PD [36]. Less well documented is the study of apnea duration. The distinctions between the Gross et al. [38] study and the current study for the measure of apnea duration may simply be due to the distinct bolus types used and have little to do with the influence of PD on SAD. In order to determine the influence of PD on SAD compared to bolus type another investigation of bolus type would have to be designed so that group difference could be elucidated. In conjunction with this analysis, it would be interesting to

look at oral transit times across bolus consistencies as they related to pre-swallow respiratory events and SAD. This further analysis would contribute to the suggestion that there is a relationship between oral transit time, SADs, and inspiratory events before the swallow. Since our study focused on just a small, thin bolus type and the Gross et al. [38] study focused on thicker consistencies, it is too premature to conclude that PD alone is contributing to longer SADs.

Post-swallow inspiratory events were positively related to shorter SADs as well as higher P-A scores. This finding supported the hypothesis of the second aim. Shorter SAD followed by inspiration indicates a possible relationship between respiratory events and swallow severity in individuals with PD. Poor bolus containment, premature spillage of liquid into the valleculae and pyriform sinuses and delayed swallow reflex [29, 30, 32, 35] have been reported in individuals with PD. In combination with these factors, individuals who demonstrated penetration or aspiration (P-A score 3-8) were also more likely to have shorter SADs. Morton, Minford, Ellis, and Pinnington [147] studied the relationship of pharyngeal dwell time and aspiration in 32 individuals with dysphagia of varied origins. The investigators reported that among those who aspirated, a greater percentage of the pharyngeal dwell time occurred in inspiration. Inspiratory events coupled with the presence of residue in the pharynx leaves the airway more susceptible to aspiration events. Shortened SAD may be related to the delay in triggering the swallowing reflex. Individuals with greater impairment in swallow functioning which results in shorted SAD may also experience poor integration of the swallow and respiratory signals, in which case inspiration events are more likely to occur.

Based on the evidence from Potulska et al. [29], Nagaya et al.[32], Ali et al. [30], and Robbins et al. [35], further analysis of the swallows generated by the participants in the present

study is warranted. In order to confirm the relationship between post-swallow inspiration and swallow severity, oral and pharyngeal phases of swallow should be investigated more thoroughly, including objective temporal measures, hyoid displacement, and qualitative observations or oral bolus manipulations. It may be that swallow severity is also related to higher P-A scores. Individuals with P-A scores of 3 to 8 are considered to have decreased swallow safety. The finding that inspiratory events post-swallow was positively related to higher P-A scores confirms the suggestions of others who have stated that post-swallow inspiration is associated with decreased swallow safety [76, 81-89, 148].

The final aim of the present study was to determine if the predominant respiratory events associated with the 5 mL thin bolus would alter after 4 weeks of EMST. Findings indicated that there were no significant differences in respiratory events surrounding the swallow for both the experimental or sham groups pre to post-training. There was a trend toward an increase in expiratory events for both groups both preceding and following the swallow. The hypothesis was that the amount of swallows followed by inspiration would decrease after 4 weeks of EMST training. When the groups were separated pre-training, individuals in the experimental group inspired before 31.6% of swallows and inspired after 7.5% of swallows. Following EMST training for the experimental group, inspiratory events before swallow decreased to 27.1%, a difference of 4.5%. Inspiratory events post-swallow decreased to 3.4%, a difference of 4.1%. Participants in the sham group, pre-training, inspired 27.8% before the swallow and inspired 11.1% after the swallow. Interestingly, after sham training, inspiratory events before swallow decreased 19.5% a difference of 8.3%. Following the swallow, inspiratory events decreased by 3.9% to 7.2%.

Swallow apnea duration was also compared pre to post-training. The average SADs for individuals with PD enrolled in this study at the pre-training time point was 1.173 seconds (sec) for the experimental group and 0.766 sec for the sham group, and at post-training was 1.573 sec for the experimental group and 0.814 sec for the sham (Table 3-6). The average SADs between groups prior to intervention were significantly different, but following the intervention arm were not significantly different between groups. This change between groups pre to post, was mainly due to an increase in SADs for the experimental group; although this did not reach significance. Additionally, it was found that longer SADs were positively correlated with lower P-A scores. These results, in light of past findings describing improved swallow safety following EMST intervention [149-153], may provide further insight into the underlying mechanisms of changes to swallow outcomes. It is possible that in addition to improved hyoid displacements [150], changes in respiratory-swallow relationships and possibly swallow coordination are contributing to improvements in swallow safety secondary to intervention with EMST. These hypotheses require further study.

Expiratory muscle strength training has been used as an intervention protocol for a variety of patient groups with positive results in EMST's ability to increase maximum expiratory pressure (MEP) following 4 to 5 weeks of training [67, 116, 125, 129, 131, 135, 136]. There is evidence that EMST alters the force activation of the submental muscles in healthy adults during training [130, 140]. Recently, persons with PD demonstrated improved voluntary cough production and decreases in P-A scores after 4 weeks of EMST, specifically in individuals who exhibited penetration or aspiration [69]. Changes in MEP, cough and swallow safety, secondary to intervention with EMST, may be a result of improvements in the central nervous system's ability to respond to varying physiological demands. Neural adaptations occur relatively quickly

during training with increased motor unit recruitment and muscle coordination [121, 142, 154], due in part to decreased neural inhibitory reflexes [155]. Evidence that cortical changes might result from strength training is based on reports that strength gains occur before peripheral changes occur such as muscle hypertrophy [156-159] and that a loss of strength occurs even before peripheral atrophy during detraining [160, 161] or disuse [162]. Additional support for neural adaptations preceding strength gains comes from studies demonstrating cross-training effects in which unilateral limb strength training produces increased strength in the contralateral limb [121, 154, 163, 164]. Recently, experimental evidence comes from Chhabra [165], who used transcranial magnetic stimulation, to test whether strength training of abdominal muscles might influence central nervous system drive. Specifically, she reported decreases in active motor thresholds in the lateral oblique abdominal muscles of healthy adults following 4 weeks of training with EMST. Chhabra [165] suggested this change in active motor thresholds indicate an increase in cortical excitability of excitatory interneurons and corticospinal neurons associated with EMST.

In part, Chhabra's [165] findings supported the hypothesis that EMST might alter swallow coordination. However, the findings of the current study indicate that respiratory-swallow integration appears to be relatively hard-wired and difficult to modulate with strength training. This may be due to the complex interaction of central pattern generators and the cerebral cortex [77, 166-168] on respiratory-swallow patterns. Possibly, skill specific training is more appropriate for rehabilitation of dysfunctional respiratory-swallowing coordination, rather than strength training. Several studies using rat animal models have compared strength training to motor skill training in forelimb muscles [169-174]. Investigations of strength training and its impact on the motor cortex suggest that it does not cause central nervous change such as

synaptogenesis. Rather, cortical changes observed after strength training are due to angiogenesis, or growth of new blood vessels [169, 171]. Furthermore, comparisons have been made to differentiate strength training and skill training changes in motor map representation [169, 171, 174]. Remple et al.[174] investigated strength versus skill training in reaching movements of rats. Both the skill and strength training groups demonstrated increases in wrist and digit motor map representations, however, the group that also performed the strength training movement did not show additional increases in shoulder and elbow representation. Although these studies are limited to limb motor representation, of the effects of strength and skill training may translate to respiration and swallowing. Perhaps the lack of change in swallow pattern secondary to EMST intervention in this study was due to the fact that the task itself is nonspecific to swallowing. The emphasis is placed on strength rather than skill.

In cases where swallow dis-coordination exists, rehabilitation utilizing swallow-specific tasks may be more appropriate, yet one must still realize the importance of proper muscle force generation. A combined modality approach utilizing strength training (like EMST) and swallow-specific tasks may maximize treatment benefits secondary to increased central drive and peripheral adaptations leading to physiologically based improvements in swallow safety.

Limitations

The current study did not include a healthy age-matched control group. Inclusion of such a group would allow further discussion of the effects of neurodegeneration on respiratory-swallow events. The effects of this confounding factor were mitigated, in part, by comparing this study's results to those in Martin-Harris et al. [82] which employed similar methodology and investigated respiratory events surrounding the swallow of a 5 mL thin bolus in healthy adults. Additionally, where as respiratory-swallow patterns and swallow apnea measures were made from the multiple 5 mL thin bolus presentations, P-A scores were determined from a 3 oz

sequential thin liquid trial. This allowed for the identification of participants who were at risk for penetration-aspiration, but restricted the direct comparison of swallow pattern and swallow safety. This study utilized nasal cannula signals as the single source of acquiring respiratory data. The validity of these measures would be enhanced by supplementing with respiratory plethymography. Finally, individuals who participated in the present research study did not present with abnormal respiratory events before or after the swallow. It is likely that this significantly impacted EMST intervention effects due to a ceiling effect. Intervention cannot change that which is not disordered. Future studies investigating affects of EMST on respiratory-swallow coordination should select individuals who have abnormal swallow-respiratory events. By including a cohort of individuals who produce abnormal respiratory events before treatment, the influence of a ceiling effect may be eliminated and statements regarding EMST's influence on respiratory events associated with swallowing can be made.

Conclusion

This study contributes to the growing literature of respiratory-swallow coordination in impaired populations, specifically PD. This is the first study, to our knowledge, investigating the respiratory events associated with swallowing using videofluoroscopy and the P-A scale. It is also the first study to investigate the affects of rehabilitation on respiratory-swallow coordination in those with PD. In individuals with mild to moderate PD severity (H&Y II-IV), expiration is the predominant event, occurring after approximately 70% of swallows. Comparisons of respiratory-swallow events in the present study to reports of respiratory-swallow events of healthy adults indicate that individuals with PD follow a greater percentage of swallows with an inspiratory event. In consideration of post-swallow inspiration and swallow safety, individuals with P-A scores 3-8 show a greater predominance of inspiratory events occurring after a swallow. Additionally, those with decreased swallow safety also show shorter SADs. The

occurrence of inspiratory events after a swallow as well as shorter SADs may serve as important indicators during clinical swallow assessments in patients at risk for penetration or aspiration. Complete patient care not only requires the identification and origin of impairment, but also appropriate treatment. Strength training using the EMST paradigm improves measures of swallow safety (defined by decreases in P-A scores) as well as cough. Expiratory muscle strength training intervention in the present study did not show an effect on respiratory-swallow coordination. In consideration of swallowing rehabilitation in individuals with PD and other progressive diseases, EMST has been shown to reduce penetration-aspiration. EMST should not be discounted as an intervention tool for respiratory-swallow dis-coordination and further investigation is warranted for individuals with increased disease severity and in populations who demonstrate greater abnormality of respiratory events.

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BIOGRAPHICAL SKETCH

Irene graduated from the University of Florida with a Bachelor of Arts degree in communication sciences and disorders in 2007. She graduated cum Laude. She completed a Master of Arts degree in speech pathology from the University of Florida in May 2009. Irene works as a speech-language pathologist in an adult outpatient setting, with an emphasis on dysphagia. In the future, she also plans to return to school to pursue a doctoral degree in speech-language pathology.

THE EFFECTS OF EMST ON RESPIRATORY EVENTS DURING SWALLOW IN PARKINSON'S DISEASE

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The ability to swallow and protect the airway is impaired in individuals with Parkinson's disease (PD) and contributes to an increased risk of developing aspiration pneumonia. The present study sought to describe the respiratory events associated with a liquid swallow, to elucidate contributing factors associated with abnormal respiratory events, and to determine if intervention would change the events for increased swallow safety. It was found that the majority of swallows were followed by expiration, which is the same as healthy adults, suggesting that individuals with PD may not demonstrate impairment in breathing - swallowing coordination. However, it was determined that individuals who did breathe in after the swallow were more likely to have liquid enter the airway. Expiratory muscle strength training, an intervention technique which has shown improvements in swallow safety in persons with PD, was also completed. The present study did not show changes in respiratory events, but this is likely because the participants were normal before training.