ATTENTIONAL RESOURCE ALLOCATION AND SWALLOW FUNCTION IN PARKINSON'S DISEASE

By

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A DISSERTATION PRESENTED TO THE GRADUATE SCHOOL
OF THE UNIVERSITY OF FLORIDA IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA

2009

To all those who have journeyed with me on the road to graduation:
your faithfulness and love have not gone unnoticed. This document is dedicated to each of you.

ACKNOWLEDGMENTS

"It takes a village" seems to fall short as I write these acknowledgments. I have been immensely blessed throughout my educational trajectory with amazing people who have been placed in my path; people who have changed my professional and personal life in ways which I cannot begin to express in these few words. To God I am thankful for the grace given each of those special people and given me during this journey. I must thank my parents who always advised that I should stay in school until I ran out of degrees and who provided me with all the love, guidance, and care that I would need to achieve that end. To my brother, who is my greatest pride, I give many thanks for standing close during every peak and valley, especially in the last sprint towards this degree. The roller coaster would never have been bearable or as enjoyable without him. Many thanks to Lali and Heather, for listening ears, giving hearts, and for being pillars during this process; I am eternally grateful to both of them. I must also thank Bethany, Leidi, Vivi and the rest of the "corillo" through whom I have learned many invaluable life lessons; especially the true definition of "work hard, play hard." For every moment of escape and for your selflessness I am so thankful. You are much more than friends, you are family.

Many thanks go out to the small army of graduate students: Lauren, Sarah, April, Katie, and Stacie, who made data acquisition possible, a joy, and seamless for the participants. I am also thankful to my labmates, the exceptional women of the laryngeal function lab (past and present), who poured so many resources into making my completion of this document possible, their friendship and support have been invaluable through the years. Much appreciation to my dissertation comrade and partner in crime, Christina del Toro, who is the best classmate, roommate, and friend any nerd could ask for.

My heartfelt thanks go to my dissertation committee, the members of which have seen me grow from an eager undergraduate, to an excited Masters student with many questions, to a doctoral candidate and student. The educational journey would never have been as fruitful as it was without their diehard support and guidance. To Christine Sapienza I give many thanks. She always saw potential in me and provided me with all the resources I would need to have a well-rounded educational experience: she has been much more than a "scientific" mentor, she has been a friend. I look forward to many more years of collaboration and friendship. To Jay Rosenbek, I am appreciative for all the lessons learned as a student and office mate, through him I have been taught the delicate balance of mixing science and heart into every research and clinical experience. In Lori Altmann I found a mentor who helped me learn the language "lingo" and whose statistical expertise and empathetic, caring spirit were essential to my formation as a researcher. Since I stepped foot on Movement Disorders soil Michael Okun was available to assist in every research endeavor. His willingness to offer expertise and resources was essential to the successful completion of this project.

Very special thanks also go to the participants and families who were enrolled in this study. It was their willingness and openness to research which made this project possible and a joy to complete.

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LIST OF ABBREVIATIONS

PD	Parkinson's disease
CPG	Central pattern generator
EEG	Electroencephalogram
SMA	Supplemental motor area
fMRI	Functional magnetic resonance imaging
DSG	Dorsal swallow group
VSG	Ventral swallow group
NTS	Nucleus tractus solitarius
NA	Nucleus ambiguous
UES	Upper esophageal sphincter
L-Dopa	Levodopa
VFES	Videofluoroscopic evaluation of swallowing
EMST	Expiratory muscle strength training
PA score	Penetration-aspiration score
VAMC	Veterans Administration Medical Center
UPDRS	Unified Parkinson's Disease Rating Scale
H&Y score	Hoehn & Yahr score
DBS	Deep brain stimulation
MDC	Movement Disorders Centers
UK	United Kingdom
BRRC	Brain Rehabilitation Research Center
UF	University of Florida
DRS	Dementia Rating Scale

SPSS	Statistical Package for the Social Sciences
Dx	Diagnosis
OOT	Onset oral transit
BHR	Bolus head passed ramus of the mandible
BTR	Bolus tail passed ramus of the mandible
BV	Bolus at vallecula
AEE	Arytenoids elevate
AEC	Arytenoid cartilage contacts epiglottis
OTT	Oral Transit Time
PTT	Pharyngeal Transit Time
TSD	Total Swallow Duration
DSF	Digit span forward
DSB	Digit span backward
DO	Digit Ordering

Abstract of Dissertation Presented to the Graduate School
of the University of Florida in Partial Fulfillment of the
Requirements for the Degree of Doctor of Philosophy

ATTENTIONAL RESOURCE ALLOCATION AND SWALLOW FUNCTION IN PARKINSON'S DISEASE

By

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December 2009

Chair: Christine M. Sapienza
Major: Communication Sciences and Disorders

The goal of this study was to test whether swallow safety could be disrupted by increasing cognitive demands during the motor task of swallowing. To achieve this end, twenty participants with Parkinson's disease (PD) and dysphagia were tested completing a dual task experimental paradigm under videofluoroscopy. Results revealed that there were differential effects to swallow safety based on baseline scores on measures of cognitive flexibility and attention. Participants who were mildly impaired in cognitive flexibility and attention demonstrated cognitive-motor interference with worsening of both swallow and cognitive performance. Participants who were most impaired in the domains of cognitive flexibility and attention actually had improvements in swallow safety in the dual task condition. Additionally, decreased swallow timing durations were found overall when comparing single and dual task conditions, but no significant changes were found in measures of airway coordination. The results of this study support the hypothesis that fronto-limbic top-down drive can influence the swallow plan resulting in changes to swallow performance (in this case, swallow safety). Future studies should focus on further specifying the cognitive mechanisms influencing the

swallow plan and focus on use of cognitive targets for the treatment of swallow dysfunction.

CHAPTER 1
INTRODUCTION AND REVIEW OF LITERATURE

Dysphagia, or disordered swallowing, can lead to significant deterioration of health and quality of life. Of particular concern is the associated risk of aspiration or ingestion of foreign particles into the airway, a potential cause of aspiration pneumonia resulting in high morbidity and mortality (Langmore, Skarupski, Park, & Fries, 2002; Langmore, et al., 1998). Studies suggest that 40% of adults aged 60 years and older have dysphagia (Doggett, Turkelson, & Coates, 2002; Feinberg, Knebl, Tully, & Segall, 1990). Additionally, pneumonia is the 5th leading cause of death in persons 65 years or older and the 3rd leading cause of death in persons 85 years and older (LaCroix, Lipson, Miles, & White, 1989). In fact, aspiration pneumonia is often the leading cause of death in persons with neurodegenerative diseases, including Parkinson's disease (PD; Fernandez & Lapane, 2002; Gorell, Peterson, Rybicki, & Johnson, 2004; Hoehn, 1967; Shill & Stacy, 1998; Singer, 1992). By the year 2010 an estimated 18 million adults will require care for dysphagia-related impairment (Feinberg, et al., 1990; Robbins, et al., 2008). Despite the staggering statistics, there is an incomplete understanding of the mechanisms underlying swallow function and dysfunction, its assessment, and management. A more comprehensive understanding of these mechanisms should result in improved assessment and management techniques for dysphagia.

Swallow Function

Physiology of Healthy Swallow

Swallowing is a complex process during which the bolus, a cohesive mass of food/liquid, is successfully transported from the oral cavity to the esophagus and into the stomach. Traditionally the process of swallowing has been considered to be comprised of three main phases: 1) the oral phase, 2) pharyngeal phase, and 3) esophageal phase. The oral phase can be parsed into the oral-preparatory and oral transit phases (Perlman, Booth, Grayhack, 1994). In the oral-preparatory phase, food is brought to the mouth and manipulated in the oral cavity preparing the bolus for swallowing (Kahrilas & Logemann, 1993). The oral transit phase follows with transport of the bolus to the oropharynx (Blitzer, 1990; Dodds, Stewart, & Logemann, 1990). More specifically, the tongue tip elevates or dips, the soft palate raises, and the posterior tongue depresses (Dodds, et al., 1990; Shaker, Cook, Dodds, & Hogan, 1988). Classically, these swallow phase have been considered to be under voluntary control (e.g., Leopold & Kagel, 1983). The pharyngeal phase involves various laryngeal airway protective mechanisms including adduction of the true and false vocal folds and inversion of the epiglottis, ultimately resulting in transport of the bolus from the oropharynx, passed a closed laryngeal vestibule, and through the upper esophageal sphincter (Logemann, 1983; Perlman & Christensen, 1997). During the esophageal phase peristalsis transports the bolus through the esophagus and into the stomach (Logemann, 1983). The latter two stages are classically considered to be under involuntary control, but there is a literature to suggest that voluntary mechanisms can influence these phases (Leopold & Kagel, 1997a; Leopold & Kagel, 1983; Logemann, 1983; McGuire & Rothenberg, 1986; Pimental & Kingsbury, 1989), at least in part.

Neural Substrates of Swallow

From initiation to completion, swallowing is a patterned sensorimotor process controlled by both automatic and volitional control systems within a complex neural network (Hamdy, et al., 1996; Hamdy, et al., 1999; Hamdy, Xue, Valdez, & Diamant, 2001; Martin, Goodyear, Gati, & Menon, 2001; Martin & Sessle, 1993; Mosier, et al., 1999; Zald & Pardo, 1999). Literature suggests the involvement of the cortex, subcortical structures, brainstem, and cerebellum in the production of a healthy, safe swallow. Studies have reported activation of neural structures including the cingulate cortex, insula, inferior frontal gyrus, supplementary motor area, sensorimotor cortex, supplementary sensory area, premotor cortex, antereolateral and posterior parietal cortex, basal ganglia, thalamus, and cerebellum (Hamdy, et al., 1996; Hamdy, et al., 1999; Hamdy, et al., 2001; Martin, et al., 2001; Martin, Murray, Kemppainen, Masuda, & Sessle, 1997; Martin & Sessle, 1993; Mosier, et al., 1999; Zald & Pardo, 1999) as well as indirect pathways between cortical motor planning regions and lower motor neurons (Huckabee, Deecke, Cannito, Gould, & Mayr, 2003). These data have been accepted in part, but not without controversy as some of the activation identified in these studies may be representative of innervations of the tongue and face which are not necessarily specific to swallowing (Martin, et al., 2001).

Cortical areas (e.g. inferior frontal gyrus, supplementary motor area, sensorimotor cortex, supplementary sensory area, premotor cortex, antereolateral and posterior parietal cortex) involved in swallowing have been implicated in sensorimotor integration, motor planning, and execution of the swallow. The function of subcortical structures for swallowing is less clear, but these are considered essential for refining the swallow pattern. The thalamus, for instance, is bilaterally activated during swallowing (Malandraki, Sutton, Perlman, Karampinos, & Conway, 2009) and it is considered that this activation is suggestive of sensory and motor input processing through thalamic connections with cortical and striatal structures resulting in transfer of this information to higher cortical structures (Mosier, et al., 1999; Simonyan, Saad, Loucks, Poletto, &

Ludlow, 2007). Pharyngeal stage components of swallowing, specifically laryngeal closure, result in yet higher activation of subcortical areas (i.e. posterior insula). Albeit limited evidence, Malandraki and colleagues (2009) suggest that more automatic components of swallowing rely more heavily on subcortical networks. Additionally, the insular cortex, also highly activated during swallowing, has been considered essential to sensory-motor integration between primary cortical and subcortical sites (Augustine, 1996; Mosier, et al., 1999). Mosier and colleagues (1999) also described the importance of the insular cortex to regulation of kinematic movement and temporal sequencing of events during swallowing.

Studies describing the neural substrates of swallowing have not parsed out the effects of motor planning/programming from motor execution; this may be due in part to the complex interaction of these processes and their interaction with the central pattern generator (CPG; which will be further described below). Huckabee and colleagues (2003) investigated cortical activation during swallow planning versus swallow execution using electroencephalography (EEG) in 20 healthy older adults through identification of a premotor potential. EEG activity was found in the supplementary motor cortex with a rapid declination before the initiation of movement, suggesting the role of the supplemental motor area (SMA) during swallow planning. Malandraki and colleagues (2009) addressed swallow planning vs. execution in an experimental design using functional magnetic resonance imaging (fMRI) during swallowing and throat clearing tasks. Their results supported those of previous studies finding activation of pericentral and perisylvian areas, the cingulate gyrus, the insula, the thalamus, premotor and prefrontal regions, parieto-occipital areas, and the cerebellum during swallow (Hamdy et al., 1999; Hartnick, et al., 2001; Kern et al., 2001a,b; Martin et al., 2001, 2004, 2007; Mosier & Bereznaya, 2001; Mosier et al., 1999; Suzuki et al., 2003; Toogood et al., 2005; Zald & Pardo, 1999). There were no statistical differences in activation during the planning (throat clearing, tongue tapping) and the execution of the swallow. Further support for the presence of a “swallow plan” is the occurrence of swallow specific apraxia most commonly occurring in persons with stroke (Daniels, 2000; Robbins & Levin, 1988; Robbins, Levine, Maser, Rosenbek, & Kempster, 1993).

Unique from other motor acts, swallowing can occur independent of cortical control. Decerebrate animals are able to sustain functional swallowing patterns (Janczewski & Karczewski, 1990; Mitchell & Berger, 1975; Zheng, Barillot, & Bianchi, 1991). This is attributed to the presence of a CPG for swallowing located in the brainstem (Yajima & Larson, 1993). CPGs are groups of neurons which can fire in a rhythmic and patterned manner independent of sensory or central input. The swallow CPG is hypothesized to be made up of two distinct groups of neurons, the dorsal swallow group (DSG) in the rostrocaudal nucleus tractus solitarius (NTS) and the ventral swallow group (VSG) in the nucleus ambiguous (NA; Broussard & Altschuler, 2000a, 2000b; Zheng, et al., 1991). It appears that the DSG are a group of premotor neurons which send information to the VSG which then transmit information to selected cranial and spinal motor nuclei resulting in the execution of the swallow (Wheeler & Sapienza, 2005). Further description of the CPG is to follow. The swallowing and respiratory CPGs are in close proximity within the brainstem, likely improving efficiency and coordination of swallow and respiration.

Respiratory-Swallow Relationships

Sharing upper airway anatomic and neuro-anatomic space, respiratory and swallow functions are intricately linked. Both respiratory and swallow function are susceptible to modification based on changes to oropharyngeal and laryngeal structures. To date, the majority of the literature assessing respiratory-swallow relationships has focused on respiratory pattern during swallow; most often assessed through the use of nasal cannulas during videofluoroscopic evaluation. These studies suggest that although the swallow can be triggered during the inspiratory or expiratory phases of respiration, the vast majority of people expire prior to swallowing and end the swallow with expiration (Feroah, et al., 2002; Klahn & Perlman, 1999; Martin-Harris, et al., 2005; Martin-Harris, Brodsky, Price, Michel, & Walters, 2003; Martin, Logemann, Shaker, & Dodds, 1994; Perlman, He, Barkmeier, & Van Leer, 2005).

There is also mounting evidence that sensory information from the upper airways influences lung volume and subglottal pressure during swallowing. Wheeler and colleagues (Wheeler Hegland, Huber, Pitts, & Sapienza, 2009) found that lung volume at swallow onset ranges from 50 – 55% vital capacity in healthy young adults, and remains unchanged during effortful swallow (Wheeler, 2007). Lung volume initiation is higher for thin boluses than thick boluses. Additionally, swallow safety improves with increased subglottal pressure during swallow (Gross, Steinhauer, Zajac, & Weissler, 2006). The effects of perturbations to these factors are not well understood as of yet.

Sensation and Swallowing

An exquisitely coordinated process, swallowing is an integrated sensory-motor experience, and therefore is highly modifiable based on sensory input. Sensory receptors responsible for identifying changes in taste, smell, visual appearance, and temperature, in addition to mechanoreceptors which identify changes in the respiratory and deglutitive systems, among others, are likely responsible for modifying the motor act of swallowing (Ding, Logemann, Larson, & Rademaker, 2003; Gross, Atwood, Grayhack, & Shaiman, 2003; Gross, et al., 2006; Hiss, Strauss, Treole, Stuart, & Boutilier, 2004; Logemann, et al., 1995; Mistry, Rothwell, Thompson, & Hamdy, 2006; Sciortino, Liss, Case, Gerritsen, & Katz, 2003). There is evidence, that increasing bolus volume, viscosity, and changing taste will result in physiological changes of the swallowing act (Chee, Arshad, Singh, Mistry, & Hamdy, 2005; Dantas & Dodds, 1990; Ertekin, et al., 1997; Kuhlemeier, Palmer, & Rosenberg, 2001; Leow, Huckabee, Sharma, & Tooley, 2007; Raut, McKee, & Johnston, 2001; Shaker, et al., 1993; Smith, Logemann, Burghardt, Zecker, & Rademaker, 2006; Troche, Sapienza, & Rosenbek, 2008; Wheeler Hegland, et al., 2009). Additionally, changes in lung volume and respiratory pattern also result in functional changes to swallow (Gross, Atwood, et al., 2003; Gross, et al., 2008; Gross, Atwood, Ross, Olszewski, & Eichhorn, 2009; Gross, Mahlmann, & Grayhack, 2003; Gross, et al., 2006; Wheeler Hegland, et al., 2009; Wheeler, 2007). While the data suggest that the swallow motor plan/program is highly plastic and modifiable based on sensory information; significant empirical study is needed. This is of particular importance as changes in bolus consistency and stimulation of oral structures are often utilized in clinical practice for improvement of swallow function (Bulow, Olsson, Ekberg, 2003; Dantas & Dodds, 1990; Kendall, Leonard, McKenzie, 2001; Kuhlemeier, Palmer, Rosenberg, 2001; Power, Fraser, et al., 2006; Troche, Sapienza, & Rosenbek, 2008).

Cognition and Swallowing

The influence of cognitive systems on motor functioning has recently garnered significant research interest (e.g., Bensoussan, et al., 2007; Plummer-D'Amato, et al., 2008; Singhal, Culham, Chinellato, & Goodale, 2007; Yogev-Seligmann, Hausdorff, & Giladi, 2008). There is some literature, mainly deductive in nature, describing the effects of cognitive changes on swallow function, with an emphasis on the influence of cognition on the oral-preparatory phase of swallowing. These changes include, but are not limited to, the development of hyperphagia and feeding aversion secondary to impulsiveness, altered attention, disinhibition, and poor judgment (Leopold & Kagel, 1997a; Leopold & Kagel, 1983; Logemann, 1983; McGuire & Rothenberg, 1986; Pimental & Kingsbury, 1989). Very little controlled investigation exists into the effects of cognitive processes on the pharyngeal phase of swallow, and only one study has empirically tested the effects of varying cognitive load on any phase of swallow.

There is one study which experimentally explored the involvement of attentional processes on oral-pharyngeal swallowing and reaction times utilizing a dual task paradigm. There was no inclusion of videofluoroscopy or other more direct swallow visualization measures. The results of this study (Brodsky, 2006), a dissertation which is not yet published, demonstrated differential changes in swallow function during single and dual task conditions. Baseline durational measures of oral-preparatory and oropharyngeal phases of swallow were completed (single task condition). Following this, a dual task condition was completed during which participants listened for a target non-word presented aurally while swallowing 5 ml of water from a cup. These aural stimuli were presented during the oral-preparatory and oropharyngeal phases of swallow. Durational measures of oral-preparatory and oropharyngeal phases and reaction times revealed that the oral-preparatory phase was more highly influenced by changes in attention than was the oral-pharyngeal phase of swallow, but both the oral-preparatory and oropharyngeal phases of swallowing increased in duration during the dual task condition. The paradigm used in this study had durational measures of oral-preparatory and oropharyngeal phases of swallow and reaction time as its primary outcomes. Additionally, no measures of swallow safety were completed. Despite this, the results suggest that although the pharyngeal phase of swallow has long been considered reflexive it can be influenced by other mechanisms, including cognition, as evidenced by increased latency in reaction times during the pharyngeal phase and differential effects on durational measures.

Other evidence supporting the involvement of cognitive systems during swallow include the activation of fronto-cortical structures during swallowing (Earles, Vardaxis, & Koceja, 2001; Martin, et al., 1999) and the presence of dysphagia in persons with cognitive disorders, independent of neuromuscular deficit (Langmore, Olney, Lomen-Hoerth, & Miller, 2007). Nonetheless, direct empirical study testing the influence of cognitive factors on the pharyngeal phase of swallow specifically has not been completed to date.

A more complete understanding of the mechanisms underlying a healthy vs. dysfunctional swallow along with the development and testing of evidence/physiologically-based treatment paradigms for dysphagia is hindered by the absence of a model/framework of swallow function. Currently there is no framework of sensorimotor swallow control which accounts for both motor and nonmotor aspects of swallowing; more specifically, cognitive functioning, motor planning/programming, motor execution, and sensory feedback. The following section will elaborate on the development of a proposed framework for studying swallow function.

A Proposed Theoretical Framework of Sensorimotor Swallow Control

The proposed framework presented here (Figure 1-1) is based on the literature related to healthy swallow physiology and that from participants with dysphagia. The motor control literature with specific attention to motor speech and Van der Merwe's model of speech production was also utilized to shape the proposed framework (Van der Merwe, 1997). Such a model has utility for the description of healthy swallow processes. A sound theoretical framework is also necessary for the characterization and appropriate management of pathological swallow sensorimotor control; issues which will be expounded upon later in this chapter. The following section will provide information regarding: 1) the function of each of the specified domains comprising the framework; 2) the literature to support the presence of these domains; and 3) the neural areas which likely contribute to the function completed by each domain. It is important to note that the proposed framework is theoretical and hypothetical and as such, there are many unanswered questions whose solutions will provide further support for the proposed domains and insight related to the factors influencing the domains.

This theoretical framework of swallow function includes four main domains: 1) cognitive-affective; 2) swallow plan; 3) swallow execution; and 4) CPG. The influence of feedback throughout the swallow system is also specified. Each of the domains will be explained in further detail below. Arrows indicate the possibility of top down and bottom up processing. This framework allows for the production of swallow independent of cortical control: *CPG* to *Execution* and swallowing influenced by cortical control which would involve *Cognitive-Affective Input*, *Motor Planning*, and *Execution*, the latter of which are also influenced by the presence of the CPG.

Cognitive-Affective Input

Literature suggests that “limbic drives” are essential to the development and implementation of motor goals; processes which likely take place in the higher association cortex (Brooks, 1986). The fronto-limbic systems which are essential to various cognitive processes may gain access to the motor systems via the nucleus accumbens (Mogenson, Jones, & Yim, 1980). In an alert and awake person, cognitive-affective input (including motivation, awareness, etc) will influence the drive for swallowing. There is evidence of dementia inducing dysphagia (Langmore, et al., 2007) and clinically it seems that mood, arousal, memory, attention and other cognitive-affective factors often influence swallow performance. Additionally, persons with swallow dysfunction may develop marked fear or anxiety of swallowing resulting in changes to swallow function (i.e. posturing of swallow structures, aversion; adverse reactions to eating or to specific foods).

Cognitive-Affective input for swallowing can be susceptible to change via feedback in various ways: varying taste, smell, and visual appeal, for instance, may trigger an association which may result in an adverse limbic response to swallowing. Although there is no direct evidence testing the effects of cognition or affect on the safe execution of a swallow, patients will often report worsening swallow function with increased distraction, implicating cognitive-affective systems in the production of a safe swallow.

The influence of cognitive processes on motor performance has garnered increased research support in recent years; particularly in the area of gait and balance (e.g., Bensoussan, et al., 2007; Plummer-D'Amato, et al., 2008; Singhal, Culham, Chinellato, & Goodale, 2007; Yogev-Seligmann, Hausdorff, & Giladi, 2008). Since there has been no empirical testing of the effects of cognitive-affective system changes on swallow function, the gait and balance literature can be used to inform the framework of swallow functioning, especially given the involvement of a CPG for gait. The effects of cognitive processes on gait function have been studied, in large part, through the use of dual task paradigms. In these paradigms, a person performs two tasks simultaneously. The performance in the dual task condition is then compared to the performance in the single task condition. Cognitive motor interference refers to the phenomenon in which simultaneous performance of a cognitive task and a motor task interferes with the performance of one or more tasks. This interference is presumed to occur because of competing demands for attentional resources. The dual task paradigm is a well-respected paradigm for assessing shared attentional resources among two cognitive tasks or cognitive and motor tasks (e.g., Bensoussan, et al., 2007; Kemper, McDowd, Pohl, Herman, & Jackson, 2006; Melzer, Benjuya, & Kaplanski, 2001; Plummer-D'Amato, et al., 2008; Riby, Perfect, & Stollery, 2004; Singhal, Culham, Chinellato, & Goodale, 2007; Yogev-Seligmann, Hausdorff, & Giladi, 2008).

The concept of attention has been modified significantly over the years. It is now considered essential for the distribution/allocation of resources to given cognitive and motor tasks. At times termed “cognitive effort”, “resources”, or “capacity” it is influenced by internal and external stimuli, resulting in bottom-up and top-down modulation of function. There are still various theories as to what “attention” really is, how much “attention” exists, and how the “resources” are allocated (McNeil, Odell, & Tseng, 1990). There is relative agreement, though, that cognitive-motor interference, a phenomenon often observed during dual task paradigms, can be explained utilizing capacity-sharing models of attention allocation where two functions are competing for similar resources; therefore, when these functions are completed at the same time, there are decrements in one or both of the functions. Kahneman (1973, p. 8) expands on this idea; describing two assumptions: 1) "there is general limit on capacity to perform mental work" and 2) "this limited capacity can be allocated with considerable freedom among concurrent activities." This has implications for swallow given that it is a life sustaining function and thus should result in prioritization within allocated resources.

McNeil and colleagues (1990) identify several other factors associated with attention from which theories regarding allocation of resources for swallowing can be extrapolated:

- Attentional allocation is influenced by arousal. If a person is not sufficiently aroused, the ability to allocate attention to a given task and/or the amount of attentional resources available is reduced. This phenomenon might explain the increased incidence of dysphagia related to dementia (Langmore, et al., 2007) or the increased incidence of aspiration pneumonia in nursing home residents (Langmore, et al., 2002; Langmore, et al., 1998).

- Attention is organized in a dynamic manner. Attention can therefore be shared across cognitive and potentially motor domains, and this might result in unequally distributed attentional resources across domains.

- The attentional system has the capacity to evaluate task demands, therefore, allocating the appropriate amount of resources to a task. This might result in tasks which are cognitively underdriven, not because of reduced amounts of cognitive effort or attention but secondary to deficient analysis of task demands. This may be of particular concern in persons with sensory-motor involvement. Additionally, this might result in variability of performance secondary to varying feedback influencing decisions relative to task demands.

- The more complex and less automatic a task, the more cognitive effort is required. Swallowing is a complex task, but relatively automatic in nature. It is possible that in pathological cases, there is a decrement in the automaticity of the task resulting in the need for additional attentional resources for successful completion of the task.

Swallow Plan

Common understanding in the area of motor control describes several hierarchical levels of organization, including planning, programming, and execution for successful motor control (e.g., Gracco & Abbs, 1987; Schmidt, 1975, Van der Merwe, 1997). In the speech motor control literature, it has been suggested that a *clinical* distinction cannot be made between motor planning and programming (Van der Merwe, 1997). In the swallowing literature, little to no distinction has been made between motor execution and the “swallow plan” therefore, this model, for now, will join planning and programming into one domain termed “swallow plan.” The term “swallow plan” has been used very limitedly in the swallow literature (Huckabee et al., 2003; Malandraki et al., 2009). Therefore, the “swallow plan” will involve both the motor plan and motor program. Evidence for the presence of this domain include EEG and fMRI studies (Huckabee, et al., 2003; Malandraki, et al., 2009), the occurrence of swallow apraxia (Daniels, 2000; Robbins & Levin, 1988; Robbins, et al., 1993), and the extensive motor control literature (e.g., Gracco & Abbs, 1987; Schmidt, 1975). This domain is essential to understanding the coordinated and modifiable nature of swallowing function secondary to feedback. Changes in the motor plan/program which are sent to the motor units are highly dependent upon sensory information from the bolus (e.g. changes in bolus size, viscosity, consistency) or internal changes in the respiratory or deglutative systems, for instance. This swallowing plan is then executed.

Swallow Execution

In the execution phase of swallowing, the swallow plan is transformed into automatic reflexive motor movements (Brooks, 1986). There is evidence from the motor control literature that despite the relatively reflexive nature of this domain there may be influence of feedback on the execution of a motor plan/program (Crutcher & Alexander, 1990; Eccles, 1977). This may occur with unexpected (especially transient) changes in peripheral muscle strength or range of motion or perhaps secondary to afferent information being relayed from mechanoreceptors within the swallow mechanism.

Central Pattern Generator (CPG)

The CPG, defined as, “premotor neurons or interneurons which can initiate or organize the swallowing motor sequence” (Ertekin & Aydogdu, 2003, pg. 2233) has mainly been studied in non-human mammals. These neurons are located in the NTS and the reticular formations surrounding the NTS (dorsal swallowing group – DSG) and the nucleus ambiguous (ventral swallowing group - VSG) (Jean, 1984, 2001; Kessler and Jean 1985; Broussard & Altschuler, 2000b). The involvement of the CPG on execution and motor planning is not completely clear, although it has been suggested that the DSG may be more closely linked to motor planning and the VSG to execution driving motorneuron pools of cranial nerves V, VII, IX, X, and XII (Ertekin & Aydogdu, 2003; Holstege, Kuypers, & Dekker, 1977; Jean et al., 1983; Jean, 2001; Wheeler & Sapienza, 2005). The extent of its involvement on motor planning/programming and execution during “automatic” swallowing (i.e. sleep) versus swallowing in an awake, aware state is unclear and an empirical question.

The neural correlates of the various domains of swallow function as per the proposed framework are identified in Figure 1-2. These are based on the motor control literature and areas activated during fMRI and EEG studies of swallowing.

Feedback

Unarguable is the role of feedback via various sensory systems for proper motor control of swallowing. Feedback can influence cognitive-affective input, motor planning/programming, and execution as described above and each of the domains can subsequently provide information which will alter future swallowing performance (Ding, et al., 2003; Gross, Atwood, et al., 2003; Gross, et al., 2006; Hiss, et al., 2004; Logemann, et al., 1995; Mistry, et al., 2006; Sciortino, et al., 2003).

Examples of feedback mechanisms via baroreceptors, chemoreceptors, hydroreceptors, mechanoreceptors (and muscle spindles), nociceptors, proprioceptors, thermoreceptors, etc. are listed below:

- Bolus Taste
- Bolus Smell
- Visual appearance of bolus
- Bolus size
- Bolus consistency
- Bolus temperature
- Auditory cue from a clinician or caretaker
- Kinesthetic information from oral structures
- Kinesthetic information from the hands as food is manipulated, cut, etc.
- Receptors within the gastrointestinal tracts detecting hunger
- Mechanoreceptors in the airways

Swallow Framework in a Pathological Model

The proposed framework of swallow function has implications for the understanding of dysphagia. The proposed framework can be utilized to define loci of dysfunction secondary to pathology. This leads to specific research questions used to examine factors which can influence swallow function in a given population. Following, the proposed model will be considered in light of pathology, in this case, PD. PD was selected as it is the population of interest in the current study. PD results in changes to both motor and non-motor functions. The susceptibility to cognitive and swallow dysfunction in PD, specifically, is of particular importance for this study. Further description of motor and non-motor symptoms secondary to PD is to follow.

Parkinson's Disease (General)

PD has long been considered an illness caused by dopamine depletion in the substantia nigra that affected only motor function, but the current conceptualization of PD acknowledges that it affects distributed neuroanatomical regions, disrupting multiple motor and non-motor systems (Braak, Ghebremedhin, Rub, Bratzke, & Del Tredici, 2004). The cardinal symptoms include bradykinesia, rigidity, resting tremor, and postural instability. In addition to basal ganglia specific changes, it is now considered that the PD process begins in the dorsal motor nucleus of the vagal nerve and, from there, proceeds upward until it arrives at the cerebral cortex (Braak et al., 2004). This conceptualization of PD progression has particular implications for swallowing, given the particular involvement of brainstem structures. Braak and colleagues (Braak, et al., 2004) delineate six stages in the progression of PD; in the first of which the dorsal motor nucleus of the vagal nerve in the brain stem is always involved. Involvement of the substantia nigra follows the pathology of the medulla. It isn't until stages 3 and 4 of the disease that the clinical presentation of PD may begin. In stage 3, there is an upward moving process of the disease into the forebrain and development of pathological changes to the striatal loop centers. The 4th stage, results in bilateral impairment with dysfunction in memory and cognition. It is in stages 5 and 6 that the substantia nigra appears "unmistakably pale". Braak's model has not been accepted without controversy, but provides support for the understanding of pathology secondary to PD which is not solely dependent on basal ganglia mediated functions (i.e. swallow, speech, cognition, autonomic systems, etc).

Parkinson’s Disease and Dysphagia

James Parkinson (1817) in his first published description of the PD, *An Essay on the Shaking Palsy,* identified swallow disturbance. He reported prepharyngeal abnormalities of ingestion, including difficulty initiating the swallow, maintaining self-feeding, impaired oral containment of both saliva and food, and labored lingual movements. His observations have proven quite accurate (Ardran & Kemp, 1967; Blonsky, Logemann, Boshes, & Fisher, 1975; Bosma, 1957; Logemann, 1983).

The incidence of dysphagia in persons with PD has been reported to be anywhere between 18.5% to 100% of the patients studied (Bassotti, et al., 1998; Coates & Bakheit, 1997; Hunter, Crameri, Austin, Woodward, & Hughes, 1997; Logemann, Blonsky, & Boshes, 1975) with silent aspiration in at least a third of patients (Mari, et al., 1997) many of which are asymptomatic (Bushmann, Dobmeyer, Leeker, & Perlmutter, 1989). Additionally, there is six times greater risk of death secondary to pneumonia in PD (Morgante, et al., 2000), with aspiration pneumonia being the leading cause of death (Fernandez & Lapane, 2002; Gorell, et al., 2004; Hoehn, 1967; Shill & Stacy, 1998; Singer, 1992). This is thought to be a consequence of a combination of chronic immobilization and swallow impairment (Fall, Saleh, Fredrickson, Olsson, & Granerus, 2003).

Widespread impairment in PD results in swallow deficits of every stage of swallow. Dysfunction is commonly seen in oral manipulation of the bolus including lingual pumping, labial bolus leakage, lingual tremor, slowed or limited mandibular function, piecemeal deglutition, pre-swallow spill, delayed swallow triggering, and post swallow residue (Ali, et al., 1996; Blonsky, et al., 1975; Born, Harned, Rikkers, Pfeiffer, & Quigley, 1996; Coates & Bakheit, 1997; Ertekin, et al., 2002; Leopold & Kagel, 1996, 1997b, 1997c; Nagaya, Kachi, Yamada, & Igata, 1998; Stroudley & Walsh, 1991). Changes to the pharyngeal phase of swallow include slow pharyngeal transit, abnormal/delayed contraction of the pharyngeal wall, coating of the pharyngeal walls with bolus material, deficient epiglottic positioning, decreased epiglottic range of motion, stasis in the vallecula and pyriform sinuses, slow laryngeal elevation and excursion, penetration, aspiration, and upper esophageal sphincter (UES) discoordination (Ali, et al., 1996; Blonsky, et al., 1975; Born, et al., 1996; Bushmann, et al., 1989; Coates & Bakheit, 1997; Eadie & Tyrer, 1965; Ertekin, et al., 2002; Leopold & Kagel, 1996, 1997b, 1997c; Nagaya, et al., 1998; Stroudley & Walsh, 1991). Other associated impairments include vocal fold bowing, drooling and difficulty swallowing saliva in up to 78% of persons with PD, and deficits in swallow-respiratory relationships as evidenced by more swallowing during inhalation and swallowing at low tidal volume (Gross, et al., 2008; Lim, Leow, Huckabee, Frampton, & Anderson, 2008; Pinnington, Muhiddin, Ellis, & Playford, 2000).

The etiology of swallow dysfunction in persons with PD has not been well defined. Changes have been attributed to the cardinal symptoms of PD with decline in motoric abilities due to rigidity, hypokinesia, and tremor; processes controlled by dopaminergic pathways (Lieberman, et al., 1980). Rigidity and bradykinesia have been implicated specifically as responsible for difficulty chewing and drooling. Eadier & Tyrer (1965) and Ertekin et al. (2002) hypothesized that the hypokinetic, reduced rate of spontaneous swallowing movements, and the “slowness of segmented but coordinated sequential movements” (pg 948), may be the most significant cause of swallow dysfunction in PD. Lastly, swallow dysfunction in PD has also been attributed to involvement of the dorsal motor nucleus of the vagus nerve and of “Lewy bodies in the myenteric plexus of the esophagus” (Edwards, Quigley, & Pfeiffer, 1992, pg. 730).

Severity and degree of motor involvement in PD do not necessarily correlate with severity of swallow dysfunction (Ali, et al., 1996). Similarly, clinical staging does not predict swallow difficulty (Bushmann, et al., 1989). In fact, Ali et al. (1996) found no relation between limb tremor and lingual tremor and no relation between muscular rigidity and dysmotility of the pharyngeal wall. Additionally, Levodopa (L-Dopa), the gold standard for the treatment of PD related symptoms, has not been found to be efficacious for the treatment of dysphagia in PD (Born, et al., 1996; Hunter, et al., 1997; Leopold & Kagel, 1997c); nor does L-Dopa improve/influence respiratory-swallow relationships (Lim, et al., 2008).

Parkinson’s Disease and Cognition

Concurrent cognitive and motoric dysfunction is inevitable in PD. Cognitive deficits in PD have long been identified in the literature. Subtle cognitive impairments exist in most of the population (Brown & Marsden, 1984) and changes which are often unidentifiable clinically but can be evidenced with comprehensive neuropsychological testing (Muslimovic, Post, Speelman, & Schmand, 2005). Dementia has deleterious effects on quality of life, prognosis, and increases risk for placement in a nursing home (which also happens to be a risk factor for development of aspiration pneumonia) (Aarsland, Zaccai, & Brayne, 2005; Langmore, et al., 2002; Nussbaum, Treves, Inzelberg, Rabey, & Korczyn, 1998). A recent study in a large cohort of newly diagnosed persons with PD revealed cognitive dysfunction in 24% of patients. Deficits in the domains of memory, attention, and executive function constituted the core dysfunction (Muslimovic, et al., 2005). Other studies have identified a yet higher prevalence of cognitive dysfunction in persons with PD (Williams-Gray, Foltynie, Brayne, Robbins, & Barker, 2007). More specifically, cognitive deficits have been reported in the areas of language, memory, visuospatial function, and concept formation and behavioral regulation, with executive functioning being the first affected and visuospatial dysfunction most frequently reported (for a review see Owen, 2004)

Deficits in the domain of memory include deficits in episodic memory, paired associate learning, auditory verbal learning, and visual reproduction of geometric designs (Beatty, Staton, Weir, Monson, & Whitaker, 1989; Bowen, Burns, Brady, & Yahr, 1976; Huber, Shuttleworth, & Paulson, 1986; Huber, Shuttleworth, Paulson, Bellchambers, & Clapp, 1986; Massman, Delis, Butters, Levin, & Salmon, 1990). Impaired verbal and nonverbal short and long term recall have also been observed with preserved long term recognition. At the level of executive function, anticipation, planning, initiation, and monitoring of goal-directed behaviors are negatively affected. Additionally, there is evidence supporting decrements in attentional processes (Litvan, Mohr, Williams, Gomez, & Chase, 1991; Taylor, et al., 2008).

The pathophysiology of dementia in PD is not completely defined but has been thought to involve limbic and neocortical Lewy body deposition, neurofibrillary tangles, senile plaques, and dysfunction of non-dopaminergic neurotransmitter systems, most specifically the cholinergic system (review Williams-Gray et al., 2007). Additionally, later onset disease has been found to predict cognitive dysfunction (Muslimovic, et al., 2005).

In the section below PD is presented as a pathological model in light of the proposed framework (Figure 1-3).

Cognitive-Affective Input

Persons with PD have been found to have deficits in multiple cognitive and affective domains as described in the literature (Aarsland, et al., 2003; Altgassen, Phillips, Kopp, & Kliegel, 2007; Bayles, et al., 1996; Beatty, et al., 1989; Berg, Bjornram, Hartelius, Laakso, & Johnels, 2003; Braak, Rub, Jansen Steur, Del Tredici, & de Vos, 2005; Brown, MacCarthy, Gotham, Der, & Marsden, 1988; Brown & Marsden, 1990; Elwan, et al., 1996; Lees & Smith, 1983; Levin, Llabre, & Weiner, 1989; Levin, Tomer, & Rey, 1992; McDonald, Richard, & DeLong, 2003; Menza, Forman, Goldstein, & Golbe, 1990; Mortimer, Pirozzolo, Hansch, & Webster, 1982; Muslimovic, et al., 2005; Okun & Watts, 2002; Owen, 2004; Pirozzolo, Hansch, Mortimer, Webster, & Kuskowski, 1982; Richard, 2007; A. E. Taylor & Saint-Cyr, 1995; Veazey, Aki, Cook, Lai, & Kunik, 2005). These changes may influence the *amount* and *allocation* of attentional resources or cognitive effort for swallow performance in persons with PD. The following theories will be specific to attentional resource allocation for swallowing in PD given the use of a dual task paradigm as was utilized in the current study.

- A reduction in the total amount of resources may result in less resources allocated overall and therefore less available resources for swallowing.
- Reductions in level of arousal might result in an inability to properly allocate resources to swallowing at any given time.
- Deficient sensory processing may provide inaccurate information regarding swallowing task demands at any given time, resulting in an improper allocation of resources to swallowing.
- Reductions in attentional resources and executive function deficits may result in improper prioritization of resources for swallowing.
- It may also be the case that for persons with motor disturbance a given motor task may require more attentional resources or cognitive effort resulting in insufficient resources for swallowing. In this case, the deficit may not be caused by reduced attentional resources, but by increased task demands secondary to motor deficits.

It is likely that persons with cognitive and motor dysfunction will be especially vulnerable to dual task effects on swallow function. This discussion will focus on the influence of attentional mechanisms on swallow function given the aims of the proposed study, but dysfunction in other cognitive domains and affective changes (i.e., apathy, depression, anxiety, etc) will inevitably interact to influence swallow performance as well. Although this has only been studied once in the area of swallow function (Brodsky, 2006), these assumptions are also supported by the gait and balance literature which has found decrements in speed and accuracy of gait function with concurrent cognitive and motor tasks (Bensoussan, et al., 2007; Plummer-D'Amato, et al., 2008; Singhal, Culham, Chinellato, & Goodale, 2007; Yogev-Seligmann, Hausdorff, & Giladi, 2008); with results being exaggerated in populations with known cognitive-motor deficits, such as PD (Rochester, et al., 2004; Yogev-Seligmann, et al., 2008). These changes have been attributed to: 1) exceeding the limited attentional resource capacity, 2) less automaticity compared with normal controls, and 3) deficits in central executive function.

Swallow Plan

The basal ganglia are an important structure for the development of the motor plan/program; therefore, dysfunction of the basal ganglia may inherently result in changes to motor plans/programs. In addition, sensory disturbance associated with basal ganglia impairment may also further influence motor plans/programs. Swallow planning/programming can be altered due to several changes which occur secondary to PD:

- Inappropriate feedback or deficient sensory information results in the selection of an inappropriate motor plan/program within a given context.
- Distorted or inappropriate knowledge of results or performance over time reinforces an inappropriate or deficient motor plan/program.

- Difficulty integrating sensory information results in an inability to modify the motor plan/program online.

Swallow Execution

Although weakness of peripheral structures is not always implicated in the early stages of motor dysfunction secondary to PD, there is evidence suggesting that muscle strength weakness is common (Falvo, Schilling, & Earhart, 2008; Koller & Kase, 1986). There is evidence, for instance, of vocal fold bowing in PD which may be secondary to reduced drive to the thyrovocalis muscle over time (Blumin, Pcolinsky, & Atkins, 2004). Similarly, maximum range of motion of oropharyngeal and laryngeal structures may also decrease over time (Nagaya, Kachi, Yamada, & Igata, 1998). Therefore, execution level deficits secondary to weakness and reduced range of motion may occur. The CPG will not be discussed specifically, but evidence from Braak et al, 1994 would suggest that the nucleus ambiguous and nucleus tractus solitarius are not implicated in the brainstem lesions identified in the progression of PD; these may exist but have not yet been identified.

Feedback

Feedback is without a doubt impaired in PD; deficits may be present at the level of the receptors or in the integration of sensory information in the basal ganglia. The impact of sensory disturbance on swallow function in PD is not completely understood. Evidence suggesting a high prevalence of silent aspiration provides additional support for influence of sensory dysfunction on swallow impairment (Mari, et al., 1997). Other identified changes in PD which might influence the feedback loop necessary for safe swallowing include changes in taste, ability to self feed, and changes in smell, among others (Simuni & Sethi, 2008). Additionally, there is evidence that external cuing improves dual task cost in persons with PD suggesting that feedback, in this case, can improve function (Baker, Rochester, & Nieuwboer, 2008).

Swallow Framework: Influences on Evaluation and Management of Dysphagia

Evaluation of Swallowing Disorders

Proper evaluation of swallow impairment is necessary for refined identification of dysfunction and selection of salient therapeutic targets. The videofluoroscopic evaluation of swallowing (VFES) is considered by many to be the gold standard for assessment of swallowing function. This is especially the case in neurodegenerative disease which often involves dysfunction of all the phases of swallow and is also associated with sensory impairment. VFES allows for the visualization of the swallow mechanism before, during, and after the swallow. VFES is completed in a radiographic suite. VFES only provides a snapshot of swallowing function as repeated ingestion of barium and radiation exposure for patients limits the acquisition of longer more elaborate samples of swallow function. Careful attention should be directed towards the development of clinical assessment protocols which evaluate all domains of swallow function. Assessment protocols should be guided by detailed medical history and patient report, and during instrumental assessment (be it with VFES or swallow endoscopy), the swallowing mechanism should be taxed and challenged in order to properly identify loci of dysfunction.

Figure 1-4 provides examples of possible questions which should be answered utilizing current assessment methods in order to address changes at the various levels of swallow function and enhance assessment improving the comprehensiveness of evaluative techniques. Methods for assessment of the proposed domains of swallow are delineated below.

Cognitive-Affective Input

- Administer cognitive screening or obtain information regarding cognitive function from the medical record/history;
- Have patient complete dual cognitive and motor (swallow) task and assess changes in *cognitive* performance in single vs. dual task conditions;
- Have patient complete dual cognitive and motor (swallow) task and assess changes in *swallow* performance in single vs. dual task conditions;
- Assess whether an external cue to prioritize swallow improves swallow function

Swallow Planning

- Assess variability of performance over several trials
- Assess coordination of structures

Swallow Execution

- Test the strength of the muscles of swallowing in a task other than swallowing
- Test the strength of the muscles of swallow during swallowing
- Test the range of motion of swallow structures in tasks other than swallowing
- Test the movement of swallow structures during swallowing

Feedback

- Assess patients awareness of the bolus in the oral and pharyngeal cavities
- Note patient awareness of penetration/aspiration
- Note patients ability to self-feed (or lack thereof)
- Ask or assess patient awareness of changes in smell or taste

Treatment of Swallowing Disorders

Most techniques for clinical management of dysphagia lack empirical evidence for their use. There have been only two randomized clinical trials specific to dysphagia management; one of a compensatory technique (Robbins, et al., 2008) and the second a recent study exploring the utility of expiratory muscle strength training (EMST), a restorative technique, for the management of dysphagia in PD (Troche, Wheeler-Hegland, Musson, Rosenbek, Okun, & Sapienza, 2008). As evidence has mounted regarding peripheral and central plasticity, rehabilitative and restorative techniques have received more research and clinical attention (Ludlow, et al., 2008). These techniques often target improved strength and/or coordination, but an incomplete understanding of the factors and domains influencing dysphagia limit the specificity of training to identified loci of dysfunction.

Dysfunction of varying domains of the proposed theoretical framework will require adaptation of selected therapeutic techniques. More specific treatment targets should allow for greater exploitation of plasticity resulting in robust change/improvement to swallow function. In cases of persons with cognitive-motor impairment, for example, training to dual task, training to prioritize the more important task, or training to attend to swallowing when swallowing, may be most appropriate. Training to improve cognition overall, may also improve swallow performance in these cases. Dysfunction in swallow planning, for instance, may require treatments which are very task-specific in conjunction with enhanced and specific knowledge of performance and results in order to strengthen appropriate motor plans/programs. Repetition in varying contexts specific to those encountered in everyday feeding conditions may also be necessary. Dysfunction in execution may rely more heavily on the principle of overload; therefore resulting in improved strength and range of motion of the swallow mechanism thus improving swallow function (Figure 1-5).

Specific Aims and Hypotheses

The repercussions of dysphagia in populations with cognitive-motor involvement, particularly PD, are often deadly secondary to the development of aspiration pneumonia. Currently, there is an incomplete understanding of the factors which contribute to a safe and timely swallow. No studies have tested the effects of increased cognitive load on swallow safety and physiology under direct visualization with videofluoroscopy. The mechanisms controlling swallow safety have long been considered to be mainly reflexive in nature mediated by processes of the swallow CPG in the brainstem (e.g., Ertekin & Aydogdu, 2003; Holstege, Kuypers, & Dekker, 1977; Jean et al., 1983; Jean, 2001; Wheeler & Sapienza, 2005). The expectation that swallowing function might be influenced by cognitive changes is not unfounded as other processes like gait, also mediated via a CPG, have demonstrated dual cognitive-motor task effects (e.g., Bensoussan, et al., 2007; Plummer-D'Amato, et al., 2008; Singhal, Culham, Chinellato, & Goodale, 2007; Yogev-Seligmann, Hausdorff, & Giladi, 2008). A more comprehensive understanding of the mechanisms influencing and modulating swallow function is important for the development of appropriate interventions for the remediation of swallow impairments. Therefore, the primary goal of this study was to assess the influence of attentional resource allocation on swallow performance in PD by testing the effects of completing a cognitive task while swallowing on swallow safety.

Specific Aim 1

To test the hypothesis that performing concurrent cognitive (digit span forward) and swallow tasks would result in decrements of swallow safety (as measured by penetration-aspiration score, PA score) (Rosenbek, Robbins, Roecker, Coyle, & Wood, 1996) secondary to increased attentional demands via dual task paradigm. It was predicted that persons with PD and dysphagia would have significantly higher PA scores in the dual task versus single task conditions.

Specific Aim 2

To test the hypothesis that performing concurrent cognitive (digit span forward) and swallow tasks would result in disruptions of swallow timing and swallow coordination (a proxy of the swallow plan/program). It was predicted that persons with

PD and dysphagia would demonstrate significantly shorter oral transit times, pharyngeal transit times, and total swallow duration and would also have less swallow coordination in the dual task versus single task conditions.

Exploratory Aim

To test the hypothesis that performing a more complex concurrent cognitive task (digit span backward) would result in greater disruptions to swallow safety, as measured by PA score, when performing a less complex cognitive task or no concurrent cognitive task. It was predicted that PA scores would be significantly higher for the dual task with digits span backward than the single task and dual task – digits forward conditions.

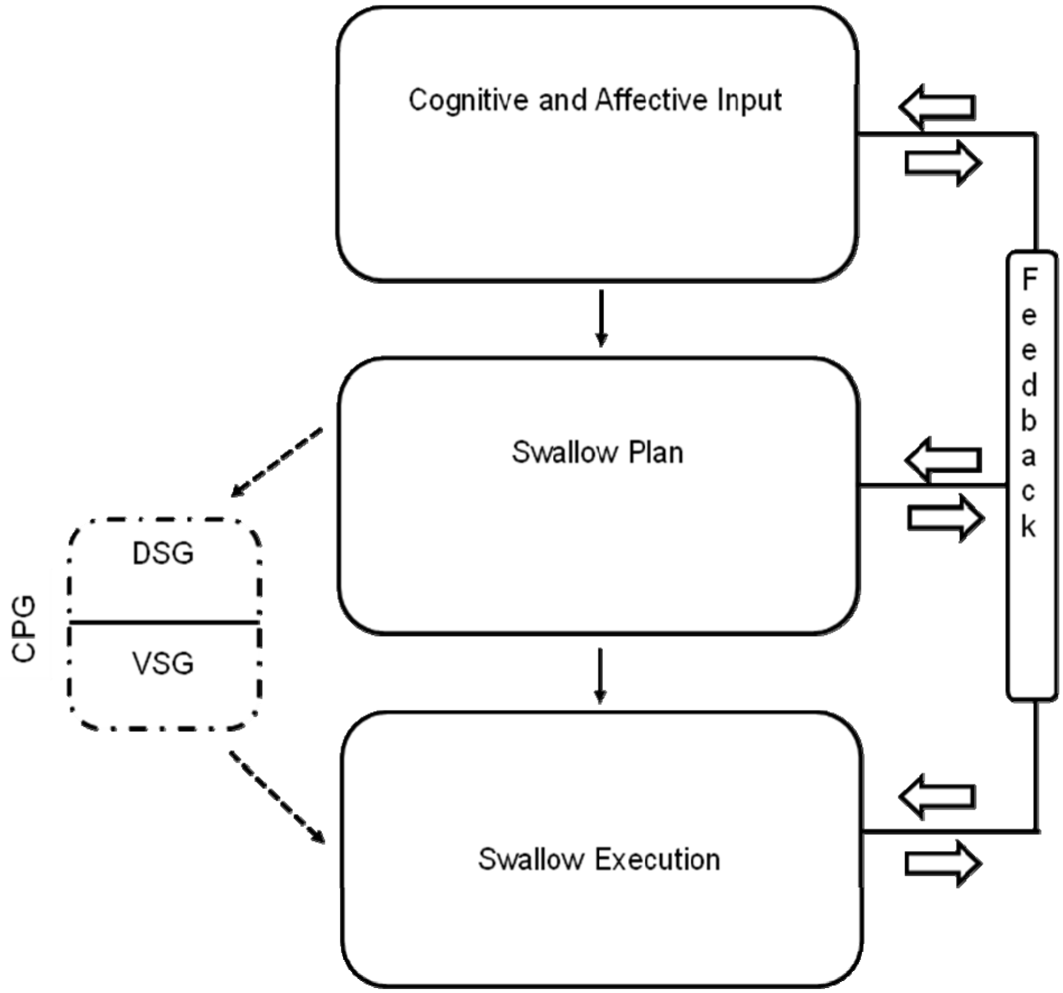

Figure 1-1. Proposed theoretical framework of sensorimotor swallow control whereby the CPG represents the patterned brainstem control of swallow and the domains of 1) cognitive-affective input, 2) swallow plan, 3) swallow execution, and 4) feedback are proposed to understand the mechanisms modulating swallow function.

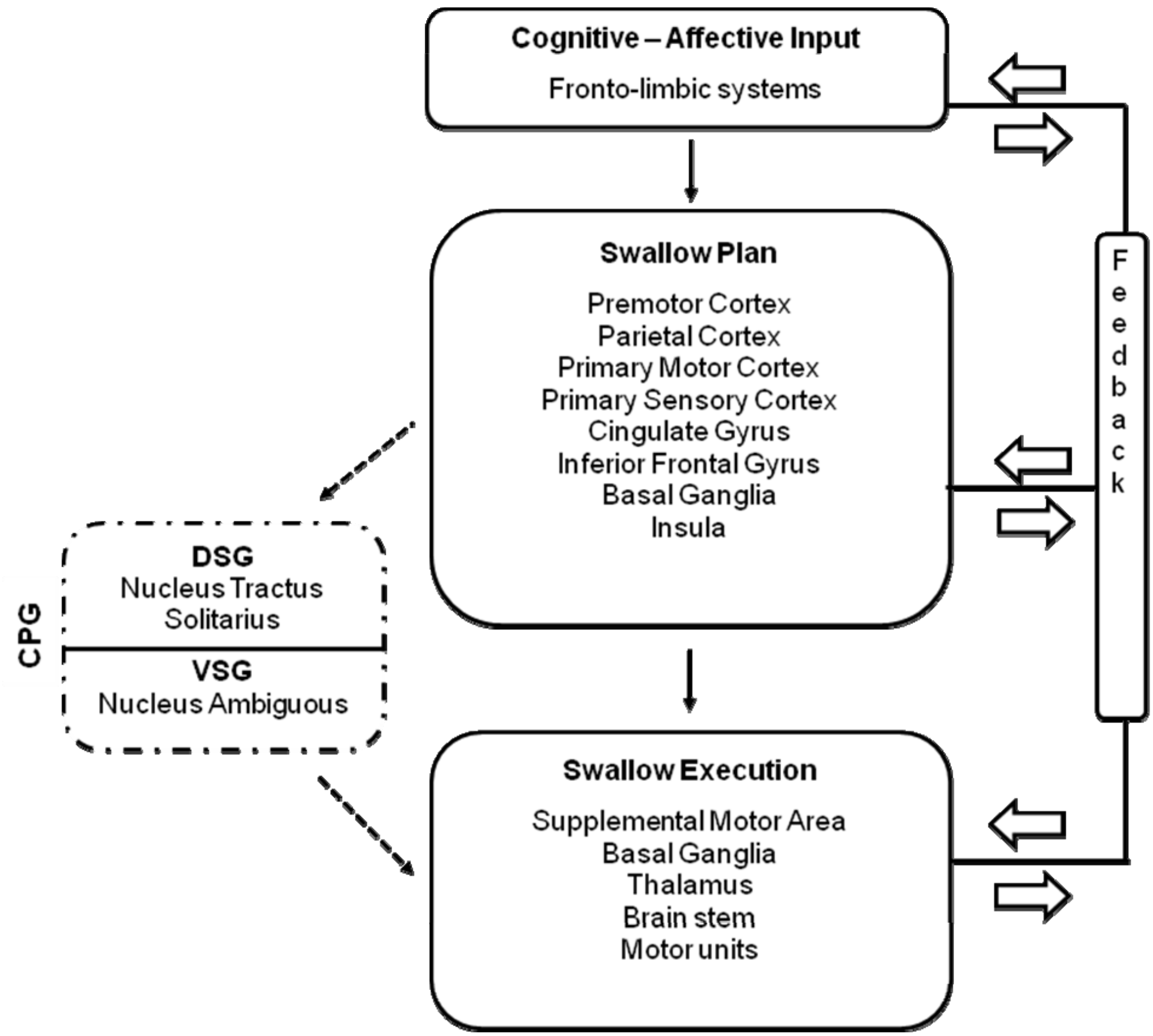

Figure 1-2. Neural correlates of the proposed framework of sensorimotor swallow control.

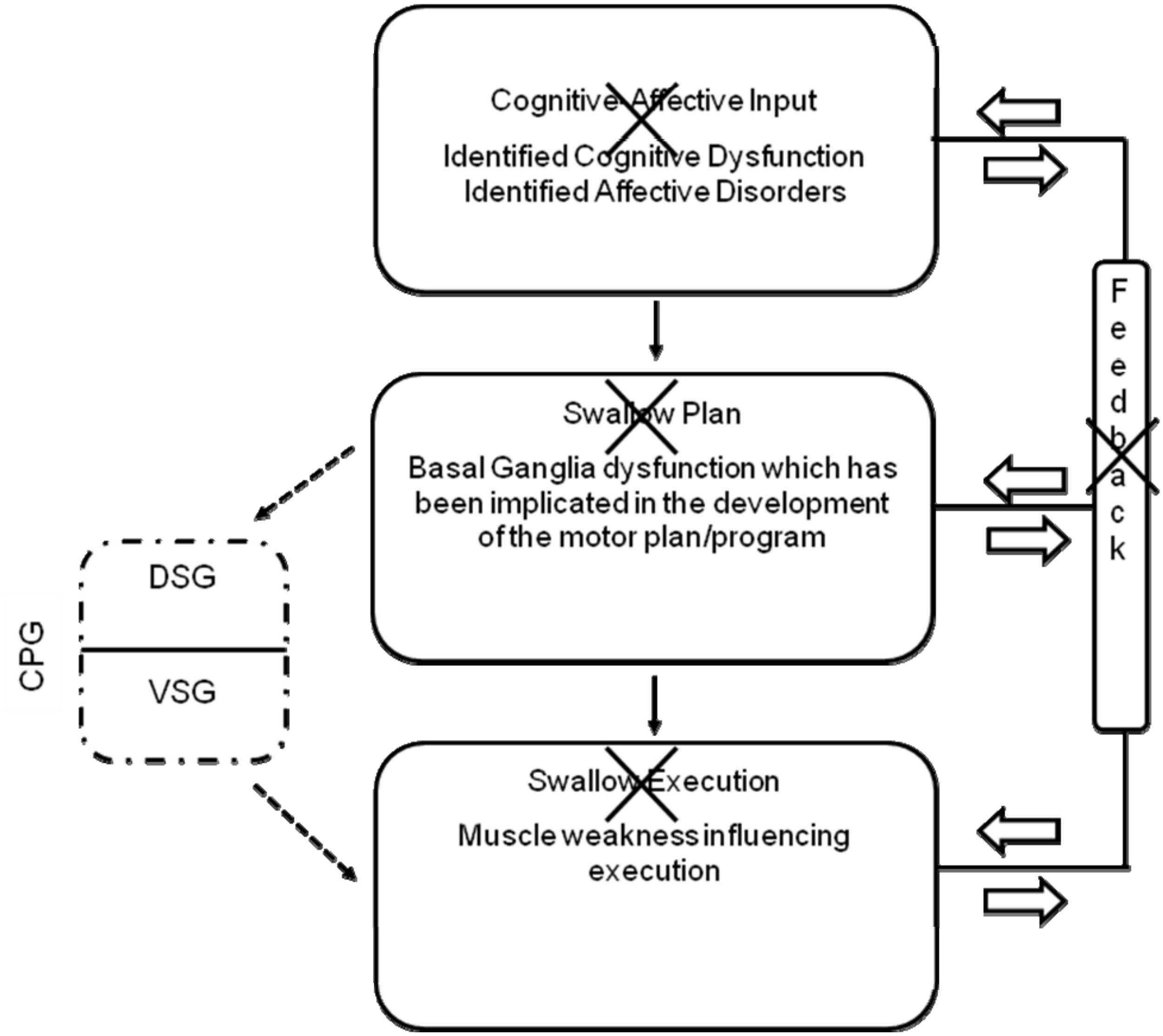

Figure 1-3. A proposed framework of sensorimotor swallow control: a PD pathological model. It is proposed that PD results in changes of all the domains of the proposed framework.

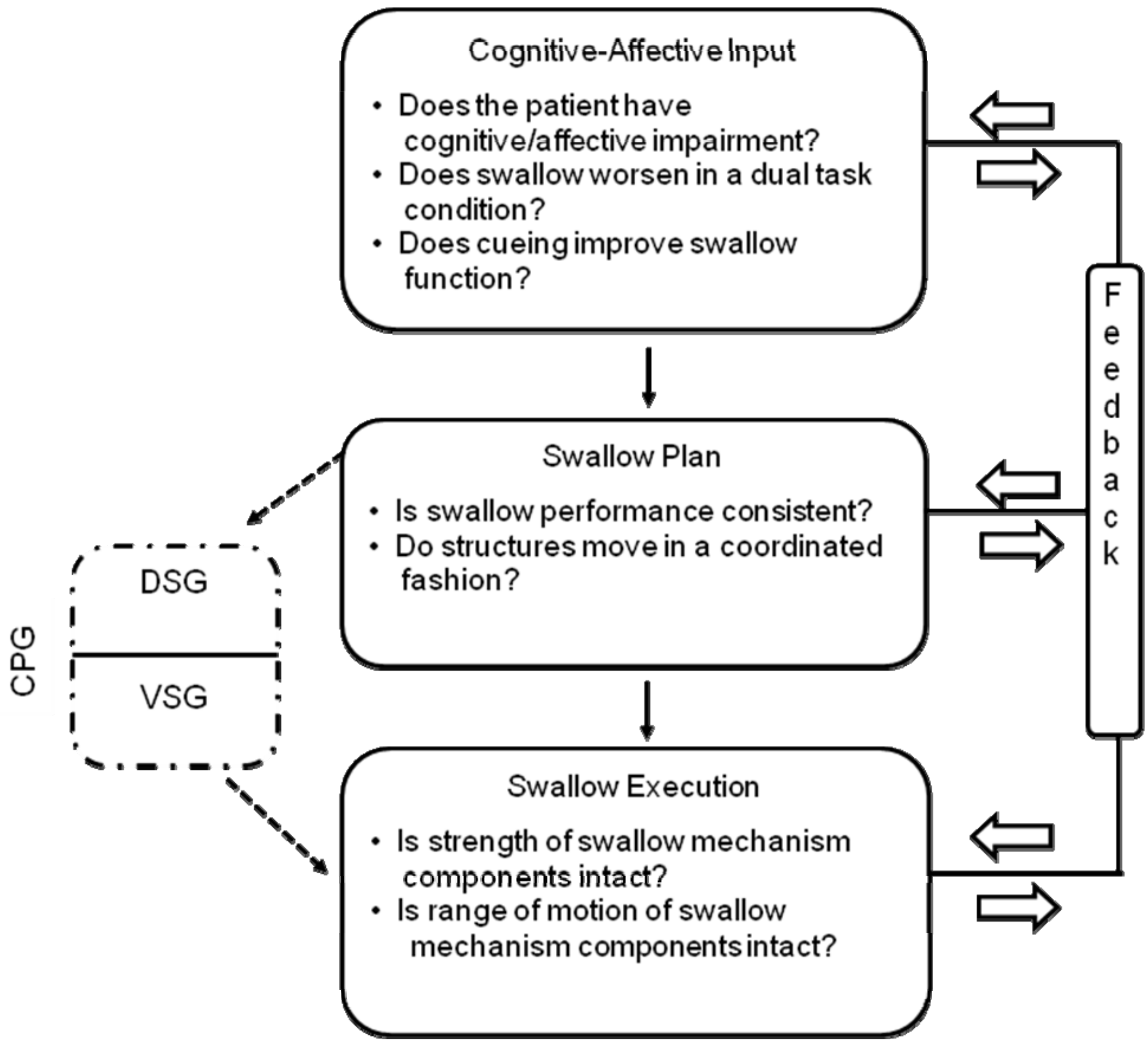

Figure 1-4. A proposed framework of sensorimotor swallow control: Evaluation of Dysphagia.

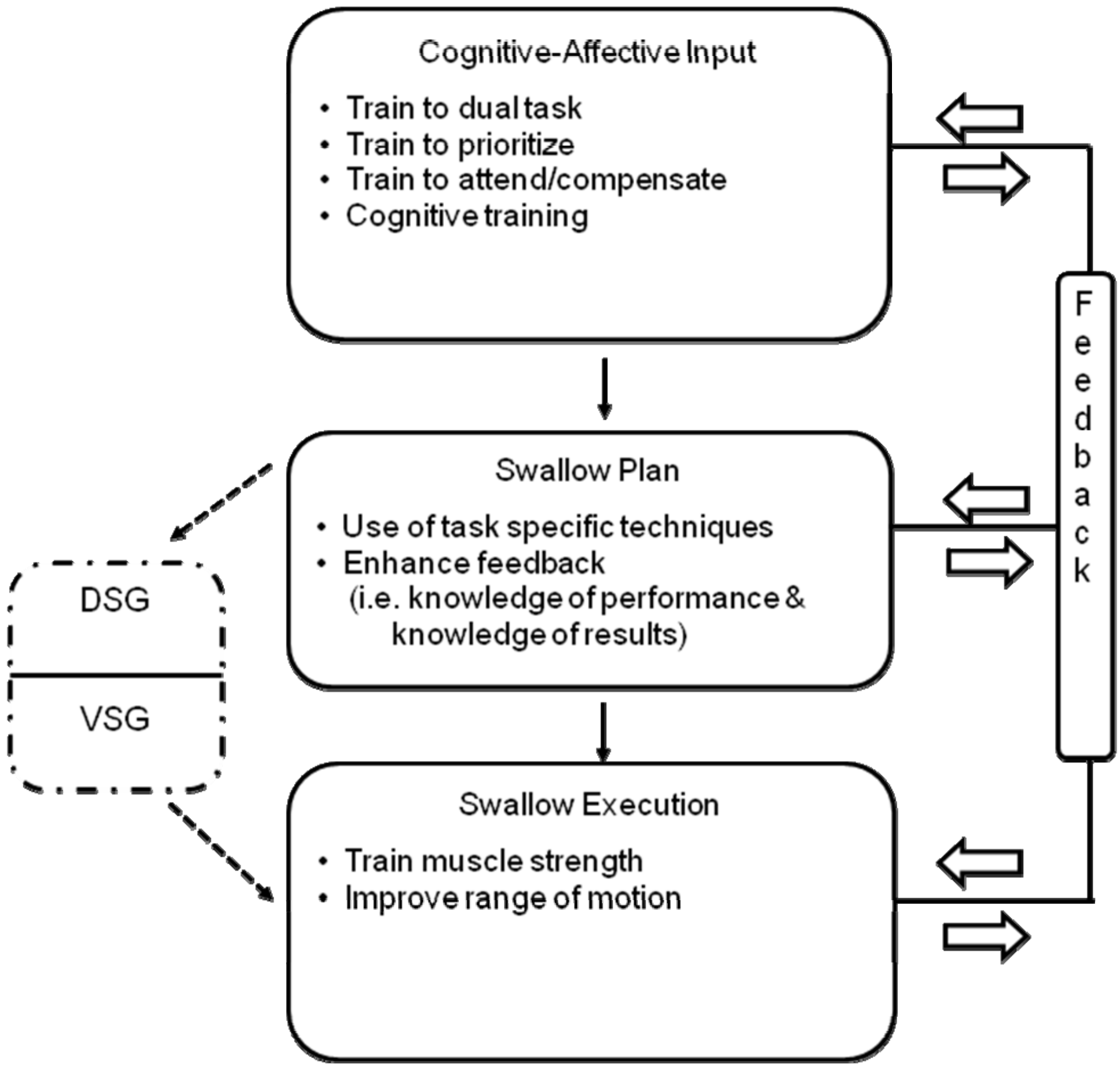

Figure 1-5. A proposed framework of sensorimotor swallow control: Treatment of Dysphagia.

CHAPTER 2
METHODS

Participants

Twenty participants with idiopathic PD were recruited and participated in this study. There were 4 females (ages 72 to 77, mean=75) and 16 males (ages 65 to 80, mean=70.5). Persons with PD were recruited from the University of Florida (UF) and Malcom Randall Veterans Administration Medical Center Movement Disorder Centers. All participants had complaints of dysphagia with evidence of penetration of thin liquid barium on videofluoroscopic evaluation of swallowing (VFES) as assessed by a licensed and certified speech-language pathologist. Demographic information, including age, Unified Parkinson's Disease Rating Scale (UPDRS), Hoehn &Yahr (H&Y) score, years since diagnosis, and education, is presented in Table 2-1.

Inclusion/Exclusion Criteria

Criteria for inclusion in the study included:

- Diagnosis of Idiopathic Parkinson's Disease (either tremor-predominant or rigid-predominant) by a certified movement disorders neurologist
- Hoehn & Yahr (1967) stage II-III
- Stabilized on one or more anti-PD meds
- Adult between the ages of 60 and 85 years
- Non-demented as measured by the Dementia Rating Scale-II (DRS-II; Jurica, Leitten, & Mattis, 2001)
- Willing and capable of providing informed consent
- Normal hearing thresholds for the participant's age or appropriately aided

Criteria for exclusion from the study included:

- History of Deep Brain Stimulation (DBS), pallidotomy, or thalamotomy
- History of any other neurological disorder

- History of developmental speech or language disorder
- History of any other motor speech or language disorder
- Diagnosis of Alzheimer's disease or semantic dementia
- History of severe depression, anxiety, or apathy
- History of attention deficit disorder

Diagnosis and Clinical Assessment of PD

Fellowship trained Movement Disorders Neurologists from the UF and Malcom Randall VAMC Movement Disorders Centers (MDC) diagnosed PD using the United Kingdom (UK) brain bank criteria (Hughes, et al., 1992).

Research Design

Overview

The following protocol was developed and implemented in order to test the hypothesis that attentional resource allocation plays an important role in a safe, timely, and coordinated swallow in PD. To achieve this end, a group of participants with PD and known dysphagia were enrolled. All participants underwent two different phases of study. Phase one included complete baseline testing of cognitive functioning and training on the experimental paradigm and phase two included the dual task experimental paradigm completed in the radiologic suite under videofluoroscopy. Both phases were completed on the same day. Participants with PD were tested within the window of optimized medication function (i.e. one hour after taking anti-PD medications).

Phase 1: Cognitive Testing Procedures

The first half of the experimental visit included assessment of study eligibility and neuropsychological status and took place in the Oral Motor Performance Lab at the Malcom Randall VAMC, Brain Rehabilitation Research Center (BRRC), Gainesville, FL. Prior to completion of any tests, the participant signed the informed consent form for project IRB# 518-2008 which was approved by University of Florida (UF) and Malcom Randall VAMC Institutional/Scientific Review boards and accompanying radiation safety committees. The participants' medical histories were obtained through chart review and query of the UF Movement Disorders Database, which maintains complete data on all neuropsychological function, UPDRS scores, Hoehn & Yahr scores, Mini Mental Status Examination, and scores related to depression, anxiety, and apathy (e.g., Beck Depression Index and Marin Apathy Index).

Given the novelty of the research questions, a comprehensive neuropsychological screening was necessary in order to identify any possible covariates contributing to the obtained results. The neuropsychological testing included: 1) DRS-II (Jurica, Leitten, & Mattis, 2001); 2) digit span forward/backward (Wechsler, 1987); 3) digit ordering (Hoppe, Muller, Werheid, Thone, & von Cramon, 2000); 4) Trails A & B (Spreen & Strauss, 1998); and 5) Stroop color XXXs and color words.

The DRS-II is a valid mental screening test of cognitive functioning in patients with PD (Brown, et al., 1999) and was used to assess eligibility for study inclusion. Administration of the DRS-II results in a global measure of dementia. Subtests, which were designed to mirror bedside examinations of cognitive functioning, test attention, initiation and perseveration, construction, conceptualization, and verbal and nonverbal short term memory. Digit span, performance of alternating movements, design copying, description of similarities, sentence recall and design recognition are among the tasks included in the DRS (Jurica, Leitten, & Mattis, 2001). The *Wechsler Memory Scale*—Revised (Wechsler, 1987) was used to assess working memory. The subtests administered were digit span forward, digit span backward, and digit ordering. For all three, stimuli gradually increased in length and digits were read at a rate of one per second. For digit span forward and backward participants were instructed to listen to the string of digits and then repeat the numbers either forward or backward depending on the task. There were two sets of stimuli for each corresponding length/amount of numbers. The test was stopped once the participant failed both sets of a given length. For digit ordering, participants were presented with a string of numbers which they were then to place in ascending order. There were four sets of stimuli at each selected length.

Cognitive flexibility and attention was assessed using the Trails A & B tests and the Stroop color XXXs and color words tests. For the Trails A, participants were presented with a sheet containing numbers one through 25. They were then instructed to draw lines from number to number in ascending order. For Trails B, participants were to alternate numbers and letters in ascending order. For both Trails tests, total time to complete the test was determined. Lastly, the Stroop test, also a measure of attention and cognitive flexibility, consisted of a sheet of paper containing five rows of ten items each. For the Stroop color XXXs the participants read the color names (i.e. blue, green, red) of the XXXs which were printed in colored ink. Participants were then administered the Stroop color words, in this case, participants were presented with five rows of ten color words each. The color words were printed in a color other than the one printed. Participants were asked to disregard the color word, and instead say the color of the ink the word was printed in. For both parts, participants were given 45 seconds to list as many of the colors correctly as possible. The investigator and/or trained graduate research assistants administered all tests to the participants. This phase of the experimental protocol lasted approximately 45 minutes per participant.

Training on experimental procedures

Prior to the experimental videofluoroscopic evaluation of swallowing, participants were trained on the experimental task. Participants were then given small cups (identical to the ones used in the experimental design) filled with water (instead of barium) to swallow. They were instructed to keep their heads as still as possible, tiling the cup more than their heads when swallowing. They were also instructed to hold the cup, listen for the numbers, swallow, and then repeat the numbers as requested following the swallow in the dual task condition. They practiced taking single and dual task swallows. They were trained to 90% success prior to enrollment in the experimental paradigm described below.

Phase 2 : Experimental Procedures

Videofluoroscopic procedures

The experimental dual task procedures took place in the department of radiology at the Malcom Randall VAMC, Gainesville, Fl. using videofluoroscopy. Participants were seated upright and images of barium swallows were recorded in the lateral view. A properly collimated Phillips Radiographic/ Fluoroscopic unit that provides a 63-kV, 1.2-m-A type output for full field of view mode was utilized. Fluoroscopic images were recorded to a Kay Elemetrics Swallowing Signals Lab (Kay Elemetrics, Lincoln Park, NJ) using a digital scan converter and electronically recorded at 30 frames per second.

It was requested of the resident radiologist that the field of view include, at the very least, the lips and teeth anteriorly, nasal spine superiorly, cervical spine posteriorly, and upper esophageal sphincter inferiorly, allowing for a complete visualization of the oral and pharyngeal structures involved in swallow. Specifically, the structures needing to be visualized for measurement included the tongue, ramus of the mandible, hyoid bone, and upper esophageal sphincter. Figure 2-1 provides a still picture as visualized on the Kay Elemetrics Digital Swallow Station program.

Cognitive task

The cognitive task used in the experimental paradigm was a modified digit span. Digits forward using six digits and digits backward with five digits were both completed in the dual task condition. The participants were instructed to listen to the aurally presented span of digits and then provide the digits back in a forward or backward order, depending on the trial. Accuracy of responses was assessed by determining number of correctly recalled digits over total number of digits which should have been recalled. Previous studies (Troche, Altmann, Hudson, et al., 2008; Troche, Altmann, Rosenbek, & Sapienza, 2008) revealed that participants began to demonstrate greatest breakdown in digit span forward following presentation of five digits. Therefore, six digits were chosen in order to challenge participants, while still allowing sufficient success to determine dual task effects. Responses were transcribed online and accuracy was assessed following the experimental paradigm. Online information regarding accuracy of responses was not provided to the participants.

Motor task

The motor task for the dual task paradigm was the swallowing of 10 cc’s of thin barium contrast by small cup (Liquid E-Z Paque Barium Sulfate Suspension; 60% w/v, 41% w/w; from E-Z-EM). The cup for self-feeding was selected in order to approximate everyday feeding conditions despite the fact that the swallow study was taking place in a synthetic environment; the radiological suite. In the single swallow task participants were instructed to “empty the barium into [your] mouth and swallow when [you’re] ready.” Participants were instructed to keep their heads as still as possible during all swallows in order to reduce any movement artifact.

Dual task

The experimental paradigm consisted of single (cognitive and swallow) and dual task (cognitive plus swallow) conditions. Participants at times completed the cognitive task independent of the swallow task (single task cognitive condition) or the swallow task independent of the cognitive task (single task swallow condition). Under dual task conditions, the participants were given the cup of barium to hold and instructed, “I will now read you [six or five] numbers, please give me the numbers [forward or backward] after you swallow.” The numbers were then read aloud by the examiner, at a rate of approximately one per second. Single task and dual task conditions were randomized. Each single task (digits forward and swallow) was completed five times, the dual task (digits forward while swallowing) was completed five times, and the dual task (digits backward while swallowing) was completed three times. The number of total possible swallows was limited so as not to create over exposure to radiation and excessive ingestion of barium for participants. Table 2-2 presents the stimuli used for each participant. The same stimuli were used for all participants, but recall that the trials were randomized.

Data Analysis and Outcome Measures

All swallow measurements were completed by an examiner trained in the analysis of modified barium swallow studies and blinded to participant identity and condition. Swallow-related measures were completed on swallow studies which were recorded to the Kay Elemetrics Swallow station. Analysis was completed frame by frame to ensure accuracy and reliability of measurement.

Primary Outcome : Swallow Safety

Swallow safety in the single versus dual task conditions, was quantified using the PA scale (Table 2-3; Rosenbek et al., 1996). Each swallow was measured individually and assigned a PA score. The P-A Scale is a validated, ordinal scale used to measure whether or not material entered the airway and if it did, whether the residue remained or was expelled.

Physiological Measures of Swallow Timing and Coordination

The Kay Elemetrics Swallow station software allows for the electronic tagging of videofluoroscopic swallow studies upon frame-by-frame playback. This in turn allows for the tagging of specific swallow events with extraction of time-specific information. The following swallow event tags were placed in order to assess swallow timing and airway coordination changes in response to dual task conditions. The following tags were made by the principal investigator who was blinded to participant identity and experimental dual/single task condition (Table 2-4).

Measures of Swallow Timing

Measures of swallow timing included oral transit time, pharyngeal transit time, and total swallow duration (e.g., Ali, Laundl, Wallace, deCarle, & Cook, 1996; Cook, et al., 1989; Kendall, 2002; Kendall, Leonard, & McKenzie, 2003; Kendall, McKenzie, Leonard, Goncalves, & Walker, 2000; Power, et al., 2009; Troche, Sapienza, & Rosenbek, 2008). These measures were determined from the swallow event tags described above. Oral transit time was defined as the duration of time it took a participant to clear the bolus from the oral cavity. Initiation of oral transit time was defined as the point when the tongue tip was raised and the bolus began posterior movement in the oral cavity with the end of oral transit time being defined by the point when the bolus tail passed the level of the ramus of the mandible. Pharyngeal transit time was defined as the time it took the bolus to clear the pharyngeal cavity. Onset of pharyngeal transit was defined as the point when the bolus head passed the level of the ramus of the mandible and offset when the bolus tail passed through the UES. Total swallow duration was defined as the amount of time it took the bolus to move through the oral cavity and clear the pharyngeal cavity. Onset of total swallow duration was defined as the point when the tongue tip was raised and the bolus began posterior movement in the oral cavity and the offset when the bolus tail cleared the UES. Calculation of swallow timing measures from swallow event tags is described in Table 2-5.

Measures of Airway Coordination

Airway coordination (Table 2-6) was assessed using a measurement scheme defined by Kendall & Leonard (2001). Measurements were based on swallow event tags listed above in Table 2-4. The four selected airway coordination measures allowed for, in theory, the description of: 1) onset of aryepiglottic fold elevation relative to the initiation of the pharyngeal swallow, 2) the time required for aryepiglottic folds to elevate in order to achieve glottic closure, 3) aryepiglottic fold elevation relative to location of the bolus in the pharynx, and 4) aryepiglottic fold closure relative to location of the bolus in the pharynx.

Dual Task Response

Comparisons between single and dual task performance within cognitive and swallow measures was completed by participant in order to assess whether participants were “responders” to the dual task condition. Difference scores (single task performance minus dual task performance) were calculated for each trial completed by each participant. These scores were then averaged by participant within condition. To assess cognitive response to dual task conditions, percent correct for digits forward in the dual task was subtracted from percent correct for digits forward in the single task. To assess swallow (motor) response to dual task conditions, PA score in the dual task condition was subtracted from PA score in the single task condition. A score of zero placed participants in the *no change group* for both swallow and cognitive performance. Participants who *worsened* in cognitive task performance in the dual vs. single task condition were identified as those with positive difference scores. Those with negative difference scores were identified as participants who had improved in cognitive performance in the dual vs. single task condition. Participants who *worsened* in swallow safety in the dual vs. single task condition were identified as those with negative difference scores. Those with positive difference scores were identified as participants who had improved in swallow safety in the dual vs. single task condition. Based on these difference scores participants were divided into groups based on dual task response for both cognitive and swallow tasks (i.e. no response, worsening in dual task, improvement in dual task condition).

Reliability

Inter and Intra-rater reliability for the primary outcome measure, PA score, was completed on 25% of the obtained swallow data. The primary rater was the principal investigator and the intra rater reliability was completed by a trained graduate speech-language pathology student.

Statistical Analyses

Reliability

Statistical analysis of the data was completed using the Statistical Package for the Social Sciences (SPSS) software version 17.0. Both inter and intra-rater reliability was completed on 25% of the sample for the primary outcome measure and were assessed statistically using intraclass correlational analyses providing a Cronbach's alpha. Given the ordinal nature of the primary outcome of PA score, a Wilcoxon signed rank test for two related samples was utilized to test differences in the single vs. dual task conditions. Baseline cognitive scores were then separated by dual task swallow response group (i.e. no change, worsened, improved) in order to identify any differences in baseline cognitive functioning which may have influenced dual task response. Analysis of cognitive measures by dual task response group was completed using nonparametric Kruskal Wallis testing. Paired samples t-tests were utilized to test any difference in the single and dual tasks for transit time measures and measures of airway coordination. Lastly, for the exploratory aim, non-parametric Friedman test for related samples was completed comparing PA scores in the single, dual-forward, and dual-backward conditions. Statistical significance was set at $p \leq .05$.

Table 2-1. Demographic information, including sex, age, UPDRS, Hoehn & Yahr (H & Y) score, years since diagnosis (PD Dx), and education for each participant. Compiled from medical record review and responses from participant inquiry.

Participant Code	Sex	Age	UPDRS	H & Y	PD Diagnosis	Education
1	M	66	32	2	1998	14
2	M	74	23	2	2003	20
3	M	65	58	3	2000	20
4	M	80	37	3	2000	20
5	M	65	22	2	2005	20
6	M	66	43	2	1999	20
7	F	76	33	2	2001	12
8	F	77	29	2	2005	12
9	M	60	27	2.5	2001	16
10	M	80	44	2	2004	16
11	M	71	25	2	2008	11
12	F	75	24	2	2005	16
13	M	74	25	2	2008	20
14	M	75	48	3	1999	20
15	M	70	28	2	2004	16
16	M	73	33	3	1998	20
17	M	67	24	2	2007	20
18	F	72	35	3	1998	16
19	M	75	29	2	2001	16
20	M	67	42	2.5	1999	12

Table 2-2. List of stimuli used for each participant during the experimental dual task paradigm completed under videofluoroscopy during phase II of the study.

Task Condition	Stimuli
Cognitive (single)	7 - 9 - 6 - 3 - 5 - 8
Cognitive (single)	2 - 5 - 6 - 1 - 8 - 3
Cognitive (single)	3 - 2 - 8 - 5 - 9 - 6
Cognitive (single)	5 - 8 - 9 - 2 - 4 - 3
Cognitive (single)	3 - 7 - 2 - 4 - 1 - 5
Swallow (single)	n/a
Swallow (single)	n/a
Swallow (single)	n/a
Swallow (single)	n/a
Swallow (single)	n/a
Dual task (forward)	4 - 5 - 9 - 7 - 3 - 6
Dual task (forward)	9 - 1 - 5 - 2 - 7 - 3
Dual task (forward)	3 - 8 - 2 - 6 - 9 - 1
Dual task (forward)	8 - 7 - 3 - 2 - 6 - 4
Dual task (forward)	2 - 4 - 1 - 7 - 5 - 8
Dual task (backward)	2 - 7 - 5 - 4 - 6
Dual task (backward)	5 - 7 - 1 - 3 - 4
Dual task (backward)	8 - 5 - 3 - 4 - 1

Table 2-3. Penetration-Aspiration Scale (Rosenbek, et al., 1996) used as the primary outcome measure.

1	Contrast does not enter the airway
2	Contrast enters the airway, remains above the vocal folds
3	Contrast remains above the vocal folds with visible residue
4	Contrast contacts vocal folds, no residue
5	Contrast contacts vocal folds, visible residue
6	Contrast passes glottis, no sub-glottic residue
7	Contrast passes glottis, visible sub-glottic residue despite patient response
8	Contrast passes glottis, visible sub-glottic residue, absent of patient response

Table 2-4. Measurement tags of physiological swallow function completed by the principal investigator who was blinded to participant identity and experimental dual/single task condition. Measures of swallow timing and airway coordination were derived from these tags.

Tag	Description
OOT	Onset of posterior movement by the bolus in the oral cavity. Point at which the tongue tip was raised and the bolus began posterior movement towards the posterior aspect of the oral cavity.
BHR	Point at which the leading edge of the bolus passed the level of the ramus of the mandible.
BTR	Point at which the tail of the bolus passed the level of the ramus of the mandible
BV	Point at which the bolus arrived at the level of the vallecula. If the bolus did not appear to arrive in the vallecula BV was identified as the point when the bolus passed the level of the base of the vallecula.
UES	Point at which the tail of the bolus passed through the UES.
AEE	Point when the most superior part of the arytenoids began to elevate.
AEC	Point when the Arytenoid cartilage made contact with the inverting epiglottis.

Table 2-5. Description of calculations used to derive swallow timing measures from swallow event tags described in Table 2-4.

Timing Measures	Calculation
Oral Transit Time	BTR – OOT
Pharyngeal Transit Time	UES – BHR
Total Swallow Duration	UES – OOT

Table 2-6. Description of calculations used to derive airway coordination measures. Both calculations and definitions of measures are delineated.

AEE – BHR	Onset of aryepiglottic fold elevation relative to start of swallow
AEC – AEE	Time required for aryepiglottic fold elevation to achieve supraglottic closure
BV-AEE	Aryepiglottic fold elevation relative to location of the bolus in the pharynx
AEC-BV	Aryepiglottic fold closure relative to location of the bolus in the pharynx

Figure 2-1. Still radiographic image representing one frame of swallow sequence (lateral view) as visualized on the Kay Elemetrics Digital Swallow Station program.

CHAPTER 3
RESULTS

Reliability

Intraclass correlation analyses revealed that interrater reliability was excellent with a Cronbach's alpha of .968, $p<.001$. Intrarater reliability was also found to be excellent with a Cronbach's alpha of .966, $p<.001$.

Baseline Cognitive Measures

Table 3-1 contains raw scores, means and standard deviations for baseline cognitive measures (i.e. DRS, Stroop 1 & 2, DSF, DSB, Digit ordering, Trails A & B). Participant 20 was excluded from further analysis given that his DRS score was in the demented range (DRS = 116). Participants 1-19 all performed within the non-demented range (DRS ≥ 130) and all further results excluded participant 20 from analysis.

Primary Outcome: Penetration-Aspiration Score

Comparison of Single versus Dual Task

Table 3-2 shows average PA scores for each participant, group means and standard deviations. Wilcoxon signed rank test revealed that PA scores were not significantly different in the single versus dual task conditions ($Z=-1.259$, $p= -.208$)

Dual Task Response

Fourteen of 20 participants worsened in their cognitive performance (percent correct on digits forward) in the dual task condition, 3 of 20 had no change in percent correct in the two conditions, and 3 of 20 had an improvement in percent correct on digits forward in the single vs. dual task conditions.

8 of 20 participants worsened in swallow safety in the dual vs. single task conditions, 5 of 20 participants demonstrated no change in swallow safety in the two conditions, and 7 of 20 participants demonstrated an improvement in swallow safety in the dual task condition. Table 3-3 presents difference scores and corresponding groups (for groups: 1=no change, 2=worsened, 3=improved).

Baseline Cognitive Function by Dual Task Response

Table 3-4 displays means and standard deviations of all baseline cognitive measures by dual task swallow response group. Non-parametric Kruskal Wallis testing revealed significant differences among dual task response groups for several cognitive measures (Table 3-4). The measures which demonstrated significant differences or trends towards significant differences were those which measured cognitive flexibility and attention (i.e. Trails and Stroop). Significant differences were found for Stroop color XXXs (Chi-square=9.430, *p=.009)* and Trails A (Chi-square=12.20, *p=.002*). In both cases, least impaired scores were found for the group which demonstrated no change in the dual vs. single task conditions and most impaired scores were found for the group which improved in swallow safety in the dual vs. single task conditions. Trends towards significance were found for Stroop color words (Chi-square=9.430, *p=.088*) and Trails B (Chi-square=4.852, *p=.088*). Again, in this case, least impaired scores were found for the group which demonstrated no change in the dual vs. single task conditions and most impaired scores were found for the group which improved in swallow safety in the dual vs. single task conditions.

Secondary Outcome

Swallow Timing

Table 3-5 presents means, standard deviations, and *p*-values. Paired samples t-tests assessing change in swallow timing secondary to task condition revealed a significant shortening of OTT (t=2.524, df=17, p=.022), PTT (t=2.141, df=17, p=.047), and TSD (t=2.731, df=17, p=.014) in the dual task condition.

Airway Coordination

Means, standard deviations, and *p*-values can be found in Table 3-6. Paired-samples t-tests completed to assess changes in airway coordination secondary to task condition demonstrated no significant differences in the single vs. dual task conditions. There was a trend towards change in airway coordination (aryepiglottic fold closure relative to location of the bolus in the pharynx) (t=1.807, df=17, p=.088).

Exploratory Aim

A non-parametric Friedman Test for related samples revealed no significant difference in PA score in the single, dual – forward, and dual –backward conditions between groups (Chi-square=.241, p=.886). Given no significant difference in PA, timing and airway coordination measures were not tested.

Table 3-1. Raw scores, means, and *standard deviations* for baseline cognitive measures (i.e. Dementia Rating Scale, Stroop XXXs & color words, digit span forward (DSF), digit span backward (DSB), digit ordering (DO), Trails A & B)

Participant	DRS	Stroop XXXs	Stroop Color Words	DSF	DSB	DO	Trails A	Trails B
1	143	83	47	7	7	19	91	140
2	139	76	56	12	14	20	64	90
3	140	66	32	8	4	13	75	239
4	135	55	29	9	7	14	188	192
5	142	47	32	10	6	14	108	148
6	137	57	34	9	7	14	145	227
7	142	30	22	7	6	12	197	219
8	139	46	16	7	6	11	188	485
9	139	58	51	7	4	3	125	148
10	142	19	27	8	7	17	120	260
11	139	64	28	7	5	14	82	197
12	137	80	36	10	3	13	147	176
13	130	64	33	7	6	13	152	309
14	141	43	26	6	4	14	164	284
15	140	73	32	5	6	12	214	687
16	137	46	31	8	8	12	222	413
17	141	77	32	3	4	11	94	122
18	142	69	39	6	7	16	109	204
19	131	83	22	6	4	9	101	364
20	116	27	13	6	2	3	344	629
Means	137.60	58.15	31.90	7.40	5.85	12.70	146.50	276.65
StDevs	*6.18*	*18.93*	*10.60*	*1.98*	*2.50*	*4.23*	*66.35*	*163.87*

Table 3-2. Average PA scores for each participant, along with group means and *standard deviations.*

Participant	PA Mean Single	PA Mean Dual	PA *SD* Single	PA *SD* Dual
1	1.00	1.00	*0*	*0*
2	1.00	1.00	*0*	*0*
3	5.00	5.60	*0*	*1.34*
4	2.80	1.00	*1.48*	*0*
5	2.80	4.80	*1.48*	*0.45*
6	2.25	2.80	*1.89*	*2.05*
7	1.20	1.00	*0.45*	*0*
8	4.00	3.80	*0*	*0.45*
9	1.20	2.20	*0.45*	*1.64*
10	2.20	2.60	*1.79*	*2.19*
11	1.40	1.40	*0.89*	*0.89*
12	1.00	1.25	*0*	*0.50*
13	1.20	1.00	*0.45*	*0*
14	2.20	2.00	*1.30*	*1.22*
15	2.00	2.40	*0.71*	*0.55*
16	3.40	2.80	*1.52*	*1.30*
17	1.00	1.00	*0*	*0*
18	3.00	4.20	*1.22*	*1.79*
19	1.00	1.00	*0*	*0*

Table 3-3. Differences scores (single minus dual task) and corresponding groups by participant for cognitive and swallow tasks. For response code, 1=no change, 2=worsened, 3=improved

Participant	Cog Dual Task	Cognitive Response Code	Swallow Dual Task	Swallow Response Code
1	0.00	1	0.00	1
2	0.00	1	0.00	1
3	0.03	2	-0.60	2
4	0.00	1	1.80	3
5	0.10	2	-2.00	2
6	0.23	2	-0.55	2
7	0.23	2	0.20	3
8	0.23	2	0.20	3
9	-0.03	3	-1.00	2
10	0.10	2	-0.40	2
11	-0.13	3	0.00	1
12	0.01	2	-0.25	2
13	0.13	2	0.20	3
14	0.03	2	0.20	3
15	0.01	2	-0.40	2
16	0.10	2	0.65	3
17	0.03	2	0.00	1
18	-0.03	3	-1.20	2
19	0.10	2	0.00	1
20	0.13	2	0.30	3

Table 3-4. Means, *standard deviations,* significance based on Kruskal Wallis non-parametric statistical analyses of scores on baseline cognitive scores by dual task response groups.

Dual Task Motor Response	Cog Perf	UPDRS	DRS	Stroop 1	Stroop 2	DSF	DSB	DO	Trails A	Trails B
No change	0.00	26.60	138.60	76.60	37.00	7.00	6.80	14.60	86.40	182.60
	0.09	*3.78*	*4.56*	*7.77*	*14.07*	*3.24*	*4.21*	*4.83*	*14.26*	*108.60*
Worsened	0.05	35.13	139.88	58.63	35.38	7.88	5.50	12.75	130.38	261.13
	0.09	*12.40*	*2.11*	*19.03*	*7.21*	*1.81*	*1.60*	*4.27*	*40.79*	*176.93*
Improved	0.12	34.40	137.33	47.33	26.17	7.33	6.17	12.67	185.17	317.00
	0.10	*8.82*	*4.412*	*11.48*	*6.31*	*1.03*	*1.33*	*1.21*	*24.74*	*112.98*
Chi-square	3.907	2.711	1.345	9.430	4.865	1.052	.429	.748	12.20	4.852
Asymp. Sig	*.142*	*.258*	*.510*	*.009*	*.088*	*.591*	*.807*	*.688*	*.002*	*.088*

Table 3-5. Means, *standard deviations*, and *p*-values for swallow timing measures by condition.

	Single Task	Dual Task	*p-values*
Oral Transit Time	0.4982	0.449	*.022*
	0.1610	*0.1337*	
Pharyngeal Transit Time	0.8443	0.7771	*.047*
	0.1944	*0.1550*	
Total Swallow Duration	1.0213	0.9381	*.014*
	0.2125	*0.1997*	

Table 3-6. Means, *standard deviations*, and *p*-values for airway coordination measures by condition.

Airway Coordination Measures	Single Task	Dual Task	*p*-values
AEE – BHR	0.8419	0.8091	*.261*
	0.2194	*0.1768*	
AEC – AEE	0.6700	0.6428	*.186*
	0.1497	*0.1374*	
BV-AEE	0.9749	1.0058	*.293*
	0.2162	*0.1976*	
AEC-BV	0.7939	0.7370	*.088*
	0.2255	*0.1940*	

CHAPTER 4
DISCUSSION

The current study was designed to test the hypothesis that changes to oropharyngeal swallowing occur with increasing cognitive demand in persons with PD. Despite the fact that the mechanisms controlling swallow safety have long been considered to be mainly under involuntary control, the expectation that swallowing function might be influenced by changes in cognitive drives is not unfounded. Gait, for example, also mediated via a CPG, has demonstrated dual cognitive-motor task effects (Bensoussan, et al., 2007; Plummer-D'Amato, et al., 2008; Singhal, Culham, Chinellato, & Goodale, 2007; Yogev-Seligmann, Hausdorff, & Giladi, 2008), which are exaggerated in populations with cognitive-motor dysfunction (Rochester, et al., 2004; Yogev-Seligmann, et al., 2008). With the progression of PD, cognitive and swallow dysfunction worsen, with death usually occurring secondary to dysphagia related changes (i.e. aspiration pneumonia) (Fernandez & Lapane, 2002; Gorell, Peterson, Rybicki, & Johnson, 2004; Hoehn, 1967; Mari, et al., 1997; Shill & Stacy, 1998; Singer, 1992). Therefore, the current project was timely in that the findings provide insight for improvements in evaluation and management of dysphagia in persons with PD.

The design of the current study is novel as it is the first study to use a dual task paradigm to test swallow function under videofluoroscopy in those with PD. The study involved 20 persons with PD whose baseline cognitive function was tested extensively prior to completing a digit span task while swallowing. The following discussion highlights the results of the study in light of their clinical and research implications, particularly addressing their influence on the proposed theoretical framework for sensorimotor oropharyngeal swallowing which was presented in Chapter one.

Dual Task Effects on Swallow Safety

The primary aim of this study was to test the hypothesis that swallow safety would worsen, as measured by PA score, when persons with PD completed a concurrent motor (swallowing) and cognitive (digit span forward) task as compared to swallowing without the cognitive task. The results of this study did not demonstrate a significant worsening of swallow safety when comparing the two task conditions. In fact, seven participants were found to improve in swallow safety when in the dual task condition. This is compared to eight participants who worsened under the dual task condition and five which demonstrated no change in the dual task vs. single task conditions. Further, post-hoc statistical analyses were completed in order to determine whether baseline cognitive functioning influenced dual task response/effect.

Once baseline cognitive scores were separated by group (i.e. no change, worsened, improved) differential effects of cognition on dual task swallow response were revealed. On average, participants with no change in swallow performance in the dual vs. single task conditions (i.e. non-responders), also had no change in cognitive performance between the two conditions. Basically, these participants were non-responders to the cognitive and motor aspects of the dual task paradigm. It can be hypothesized that in order for cognitive input to result in decrements of the swallow plan, there must be a given degree of swallow and cognitive impairment, making both more susceptible to change. It is possible that the swallow plan does not become disrupted by cognitive input until a certain threshold of motor and/or cognitive impairment is reached. This apparently was not achieved with the simple digit span forward task in the five participants who were non-responders.

Significant differences in baseline cognitive functioning were found among the three dual task swallow response groups on two measures of cognition. The Stroop color XXXs and Trails A tests showed significant differences between groups (as a function of dual task response). Additionally, trends towards significance were found for the Stroop Color words and Trails B. In all four cases, non-responders were least impaired, followed by those who worsened in the dual task, and with those who improved in the dual task performing the worst on these measures. These cognitive tests are considered to test cognitive flexibility and attention, specifically (Spreen and Strauss, 1998). This result provides insight into the domains of cognition which when dysfunctional, may cause most significant change to swallow performance. For Stroop color XXXs, persons who worsened in the dual task condition demonstrated a 23.5 percentage reduction in Stroop and those who improved in the dual task condition a 38.2 percentage worsening as compared to the non responders. For Trails A, persons who worsened in the dual task condition demonstrated a 50.9 percentage reduction in Stroop and those who improved a 114.3 percentage worsening as compared to the non responders.

Our prediction of higher PA scores (less safe swallow) in the dual task condition was supported in the subgroup of the tested sample who demonstrated mild impairment in cognitive flexibility and attention. These findings are consistent with the gait and balance dual task literature, where persons with PD have been found to have breakdowns in postural stability and gait in the dual task versus single task conditions (Rochester, et al., 2004; Yogev-Seligmann, et al., 2008). This subgroup of participants demonstrated cognitive-motor interference, supporting the theory that the modified digit span task and the swallowing task shared attentional resources; therefore, resulting in a breakdown in both swallowing safety and digit span performance in the dual task condition.

It was unexpected that a group would actually benefit from the dual task conditions and it was even more surprising that the group with the most impaired scores on cognitive testing showed this benefit. It is possible that for those with the most impaired cognitive flexibility and attention the dual task condition served as a treatment for improved swallowing. The simple fact that the participant knew they would be completing a more difficult task may have increased arousal during the dual task, thus increasing available attentional resources for the swallow and cognitive tasks. This is compatible with the McNeil et al., (1990) description of attention. As described in Chapter 1, the amount of available attentional resources is highly dependent upon the level of arousal. Increased arousal results in increased amount of attentional resources.

Similarly, the dual task condition may have resulted in increased arousal thus leading to improved allocation of attentional resources. Or, perhaps prioritization of the swallowing task was improved in the dual task condition as compared to the single task condition. Prioritization of a task is considered important for resource allocation. A task which is more highly prioritized is likely to receive more resources quicker, than a less prioritized task. Prioritization, along with amount of resources available for allocation, fluctuate with arousal level. In the case of this study, both the cognitive task and the swallow task were competing for resources. Swallow, being a biological function necessary for survival, should be prioritized. It is possible that bringing greater attention to the task resulted in just that, prioritization of swallow.

Regardless, the fact that a change in swallow safety was observed in a cohort of persons with dysphagia as a function of completing a concurrent motor (swallowing) and cognitive task supports the hypothesis that varying cognitive load results in changes to swallow safety. This has significant research and clinical implications given that the pharyngeal phase of swallowing has long been thought to be controlled completely or at least in large part by involuntary processes with little susceptibility to change from top-down mechanisms. Further description of these mechanisms will be described below when implications for the framework of sensorimotor oropharyngeal swallow are addressed.

Dual Task Effects of Swallow Timing and Airway Coordination

In order to better understand any physiological adjustments which might have occurred with the dual task condition, measures of swallow timing and airway coordination were completed. It was hypothesized that timing measures would shorten in the dual task condition and airway coordination measures would reveal diminished swallow coordination in the dual task condition. Oral transit time, pharyngeal transit time, and swallow duration were all significantly shortened in the dual vs. single task conditions. Historically, shorter transit times have been associated with improved swallow function but more recently this theory has been refuted. Many researchers have revised this idea and instead consider that faster swallowing is not necessarily more functional or safe (Kendall, 2002; Kendall & Leonard, 2001). Rather it may be that there is a minimum time requirement for coordination of airway protection and bolus propulsion/flow through the oropharynx and laryngopharynx. It is very possible that shorter transit times particularly in a neuropathological condition (model) may be indicative of reduced coordination of oropharyngeal swallowing. Unfortunately, the literature on swallow transit times is not complete enough to allow for the comparison of transit times obtained in this study to expected values in healthy elderly and/or persons with PD for a 10 cc bolus of thin liquid barium.

Oral transit times shortened from .498 to .449 seconds in the dual task condition, a reduction of ten percent from the single task condition. Total swallow duration shortened from 1.0213 to 0.9381 seconds in the dual task condition, an 8% reduction from the single task condition. Lastly, pharyngeal transit time shortened from .844 to .777 seconds in the dual task condition, an 8 % reduction from the single to dual tasks. Current literature suggests that the oral phase of swallow is completely under voluntary control and should therefore be more highly influenced by intrinsic and extrinsic factors, like cognitive load, affect, and motor disruption (e.g., Leopold & Kagel, 1983). Therefore the fact that oral transit time was most susceptible to change in the dual task condition is not unfounded. Brodsky (2006) tested the effects of a dual task on durational measures of swallow and reaction times during a go- no go task with swallowing. During the dual task participants listened for a target non-word while swallowing 5 cc of water from a cup. Videofluoroscopy was not completed but reaction times as well as durational measures were completed. Brodsky found that duration of oral preparatory transit was much more susceptible to change than was duration of oropharyngeal transit.

Interestingly, Brodsky (2006) found that transit times significantly increased in duration. The current study found that there was a significant decrease in transit times. in the current study. These differences may be explained by different methodologies. Both the cognitive and motor tasks were quite different between studies. In the Brodsky

(2006) study participants were swallowing a smaller bolus (5 cc) but were also required to react motorically (by switch) to the target stimuli. Additionally, the cognitive task required attentional resources to be prioritized to the cognitive task as stimuli were being presented aurally during the act of swallowing. In the current study, the bolus size was larger but no motoric response was required in response to the cognitive task. Additionally, the cognitive task allowed for prioritization of either the cognitive or motor task during swallow, as digits were presented before swallow and response following swallow. Direct visualization of swallow in the current study should have also allowed for more exact assessment of duration of swallow phases. Despite the methodological differences, the fact that pharyngeal transit time, in both Brodsky (2006) and the current study, were significantly influenced by task condition, although less so than oral transit time, is further support for the hypothesis that mechanisms of swallow, which have been historically perceived to be reflexive in nature, are influenced by cognitive factors and are much more modifiable and adaptable to change than historically thought. It is likely that these factors disturb the development of the proper swallow plan, particularly in a neuropathological model.

The pharyngeal mechanisms of swallow were further described through the measures of airway/swallow coordination. The selected measures have been described by Kendall and Leonard (2001) but have not received extensive study by other researchers. Of the measures described by Kendall and Leonard (2001) we selected the measures which provided specific information pertaining to airway coordination. These measures included: 1) onset of aryepiglottic fold elevation, 2) time required for glottal closure, 3) aryepiglottic fold closure relative to bolus position in the pharynx, and 4) onset of aryepiglottic fold elevation relative to bolus arrival in the vallecula. Of those, only one measure demonstrated a trend towards significant change in the dual task as compared to the single task: the onset of aryepiglottic fold elevation relative to bolus arrival in the vallecula. The fact that no significant change was demonstrated in any of the airway coordination measures, may be their lack of sensitivity or specificity to detect these subtle changes change rather than a lack of change in airway/swallow coordination in the dual vs. single task conditions. The same may be true of PA score. Further discussion of these measurement issues follows.

Implications for the Proposed Framework Of Sensorimotor Oropharyngeal Swallowing

The results of this study support the importance of including a domain specific to cognition in the framework of sensorimotor oropharyngeal swallowing. In the case of this study, completing a digits forward task while swallowing resulted in changes to swallow transit times with differential effects on swallow safety as a function of baseline cognitive functioning. It can be suggested that in an awake and alert human, the function of the CPG is not enough to overcome the descending drive from fronto-limbic systems which can influence/shape/disrupt the swallow plan and subsequently disturb swallow performance. The improvement in swallow safety observed in those with most impaired cognitive functioning provides insight for swallow therapy. It can be hypothesized that increasing descending cognitive drive in persons with baseline reductions/impairments in arousal, amount of attentional resource, or attentional resource allocation can result in normalization of swallow function. Further study should test what person-specific or task-specific factors cause some to improve in function in the dual task and others to worsen.

Although the current study provides support for the hypothesis that attentional resources are important for a safe, timely swallow, less is clear as to the mechanism of action. The most likely explanation would be that dysfunctional attentional processes result in a “deficient” swallow plan. Some theories include:

- Reduced attentional resources result in faulty prioritization and therefore faulty allocation of resources to swallowing during swallowing.
- Reduced attentional resources results in an under driven motor system which results in global changes to motor functioning, including swallowing.
- Reduced attentional resources impair feedback loops which result in the inappropriate selection of a swallow plan within a given context.
- Reduced attentional resources impair the swallow mechanisms ability to modify the swallow plan online.
- Increased motoric task demands for swallowing may result in an insufficiency of attentional resources for safe swallowing.

Therefore, in summary, when asleep the pathway for swallow function is CPG to swallow execution (possibly through swallow planning) directly. When awake the cognitive/affective system increases its influence on the swallow plan, with the CPG still essential for swallow execution and function. Figure 4-1 depicts the results of this study in relation to the proposed framework.

Implications for Evaluation and Treatment of Dysphagia

Despite the fact that the repercussions of dysphagia (i.e. aspiration pneumonia, malnutrition, and dehydration) are life threatening and often the leading cause of death in populations with neurodegenerative disease, there are few treatments for dysphagia which have been identified and studied appropriately. There are currently no effectiveness studies for any dysphagia rehabilitation paradigm and the only efficacy studies have been for diet modification techniques (Robbins et al., 2008) and most recently, expiratory muscle strength training (e.g., Troche et al., 2008). Additionally, even less is known about the long term outcomes associated with dysphagia treatment. In fact, most studies testing outcomes of dysphagia rehabilitation involve very small sample sizes and effect sizes. It may be that dysphagia rehabilitation is hindered not only by a lack of understanding of the factors influencing dysphagia, but also by restricted evaluation methods which do not properly locate the loci of dysfunction.

Moreover, the act of swallowing does not occur in isolation. Swallowing usually surrounds a social event often taking place in the context of multiple cognitive and motor distractions and requirements. At home, eating is rarely a silent, solitary experience. Instead, families gather, discuss their day and share stories, sometimes while the television is on in the background and the dog is barking. At a restaurant, yet more affective, cognitive, and motor load is added as background noise, social pressures, and distractions are enhanced. Additionally, the sole act of eating is cognitively loaded. One must decide on bolus sizes, order of bolus presentation, and then complete the motor task of bringing the food to the mouth successfully.

Current evaluation methods for dysphagia do not consider the cognitive and affective complexity surrounding eating and thus swallowing. Instead patients are in an isolated, usually quiet, environment when evaluated. During the time of evaluation patients are usually completely focused/concentrated on swallowing; the task at hand. Patients are then presented with a controlled set of boluses, the type and size of which are usually selected by the clinician. The evaluation loses ecological validity as it no longer represents the reality of the swallowing/eating experience. This study highlights the need for cognitive taxing during swallow evaluation in order to elucidate changes which may be occurring during a real meal. It is only through more complete and specific evaluation of swallowing that we can identify true loci of dysfunction influencing everyday swallow changes.

The results of this study also provide preliminary evidence for the utility of dual tasks or tasks of varying cognitive load as treatment for dysphagia. In the case of this cohort of participants with PD, a substantial group of participants demonstrated improvement in swallow function in the dual task. Further research must identify the bounds of how much cognitive load is enough and when it is too much. These are empirical questions which must be answered in order to identify what cognitive tasks are most effective in increasing arousal and improving the amount of available attentional resources for swallowing. Further study is also needed in order to identify whether swallow or cognitive therapy, particularly in more impaired populations, results in improvement to swallow function, particularly in swallowing situations which are more highly loaded cognitively.

Additionally, it is possible that pharmacological management may also be of benefit in these situations. A survey-based pilot study of 8 persons with PD revealed that persons with lower levels of arousal were more likely to have dysphagia, a finding which supports the results of this study (Sengupta et al., 2007). In these cases, it has been suggested that pharmacological agents targeting increased arousal, may improve swallowing function. This requires significant study in order to identify whether pharmacological agents can improve arousal for swallowing and identify which pharmacological agent is most appropriate.

Strengths and Limitations

While still exploratory the current study's implementation and design were quite novel. Each participant underwent the same number of swallows, as participants were not cued to swallow more than normal in order to reduce differential effects of fatigue from participant to participant. Additionally, single/dual task conditions were randomized. Although the same stimuli were used for all participants, the order in which the stimuli were presented changed in order to, again, control for possible swallow fatigue, a phenomenon which may not be uncommon in persons with known dysphagia. All participants underwent extensive baseline cognitive testing allowing for the identification of cognitive factors which should receive further testing; factors which may very well contribute to increased susceptibility to worsening of swallow function. Additionally, disease severity was controlled in this group of persons with PD and testing was completed when participants were optimized ON their medications. This is especially essential in this population where heterogeneity of presentation is not uncommon. Although participants had swallow dysfunction it was mild to moderate in severity, in order to minimize floor and ceiling effects and the need to bail out prior to completion of the protocol. Ensuring that participants were non-demented further homogenized our experimental sample. Lastly, all measures were made by raters who were blinded to participant and swallow condition.

This study was not without limitation. The small sample size of 20 persons with PD, may have limited the degree to which subtle changes could be assessed statistically secondary to reduced power. This is particularly influential given that the outcome measures selected may not have been sensitive enough to detect the level and intricacy of change associated with pharyngeal coordination. The PA scale is a valid, and clinically relevant tool for assessing swallow safety. Evaluating presence/absence of penetration/aspiration is essential for determining an appropriate management plan in dysphagia. This being said, further development of measurement tools/schemes to completely, accurately, and precisely describe the physiology of swallow are needed. Current measures are quite gross in their assessment of swallow physiology. Although measures of timing and airway coordination are important to swallow physiology, it is the interplay between swallow phase durations, coordination of swallow structures, timing of key swallow events, location of bolus material, and respiratory-swallow relationships together which truly provide insight into physiology. The development of new measures and improvement of current measures of swallow physiology are necessary for the proper identification of change in swallow physiology secondary to perturbation and treatment.

More bolus types/sizes should be tested in future experimental designs. The bolus type/size selected was 10 cc of thin liquid barium. This is a relatively small bolus size compared to the bolus sizes present in everyday eating conditions, but is one often utilized in the swallow literature. The smaller bolus size allowed for the relative control of bolus residue in these participants with known oropharyngeal dysphagia. Too much residue could have obscured measurement, making it more difficult to reliably assess safety and coordination of swallow. It was also thought that the selected bolus size would diminish the possibility of a floor effect by restricting the incidence of aspiration during the swallow exams and control the ceiling effect, by allowing for enough swallow deterioration. An empirical question to be assessed in the future is whether varying bolus size from swallow to swallow creates changes in swallow safety given the need to rapidly change the swallow plan.

Another limitation of the study is that each participant's cognitive system was likely taxed to a different degree with the digit span forward task. For instance, a person whose baseline function only allowed for the recalling of 6 digits forward was taxed maximally by our experimental task, but a person who could recall 11 digits maximally on baseline cognitive functioning was taxed less so in the digits forward design. It is also possible that the selected cognitive task (i.e. modified digit span) was not difficult enough to truly tax the attentional system. This concern is mitigated by the results showing cognitive-motor interference in a subgroup of the tested sample. Despite this we believe that the current design was most appropriate for this *first* study using a dual task paradigm for swallowing under videofluoroscopy. Future studies should test differential effects on swallow function when varying the degree to which an individual's cognitive system is taxed during the dual task paradigm (i.e. basing the cognitive task within the dual task paradigm on baseline cognitive functioning). The exploratory aim of this study was to test whether there would be differential effects on swallow safety if a more cognitively taxing task was utilized in the dual task condition. In the case of this study, digits backward vs. digits forward did not result in differential effects on swallow safety.

Future Research

This study serves as impetus for further research testing the non-motor contributions to dysphagia. What may seem clinically intuitive to some requires substantial examination to answer the questions surrounding this topic and subsequently enhance the care of persons with dysphagia. The following topics and questions require study:

- Can the results of this study be replicated in a larger sample size?
- Do the phenomena elucidated in this study also exist in healthy older and younger adults? Or are they specific to populations with some sort of pathology? Or do they only occur in populations with concomitant cognitive and swallow disturbance?
- How impaired does baseline cognitive functioning have to be to result in decrements of swallow safety when in the dual task?
- What is the dual task cost for swallow safety when the cognitive task is made more difficult?
- Can a simple distraction task lead to reductions in swallow safety?
- Is there truly a population in which dual tasking can function as a treatment for dysphagia?
- Can cognitive treatment (specifically treatment for attention and cognitive flexibility) improve swallowing indirectly?
- Can pharmacological agents be used for the improvement of arousal and subsequently, the reduction in incidence of swallow dysfunction in persons with PD?
- Can combined modality treatments (i.e. cognitive rehabilitation + swallow exercises or swallow exercises + pharmacological management) result in more maintainable and generalizable outcomes for swallow?
- How can dysphagia evaluation methods be improved in a way which more appropriately mirrors the realities of everyday meals?

Summary

The goal of this study was to test whether swallow safety could be disrupted by increasing cognitive demands during the motor task of swallowing. To achieve this end, 20 participants with PD and dysphagia were tested completing a dual task experimental paradigm under videofluoroscopy. Results revealed that there were differential effects to swallow safety based on baseline scores of cognitive flexibility and attention.

Participants who were mildly impaired in cognitive flexibility and attention demonstrated cognitive-motor interference with worsening of both swallow and cognitive performance. Participants who were most impaired in the domains of cognitive flexibility and attention actually had improvements in swallow safety in the dual task condition. Additionally, shorter transit times were found overall when comparing single and dual task conditions, but no significant changes were found to measures of airway coordination. The results from this study support the hypothesis that fronto-limbic top-down drive can influence the swallow plan resulting in subsequent change to swallow performance.

A. Single Task Swallow Performance

B. Dual Task Swallow Performance in those with most impaired cognitive functioning

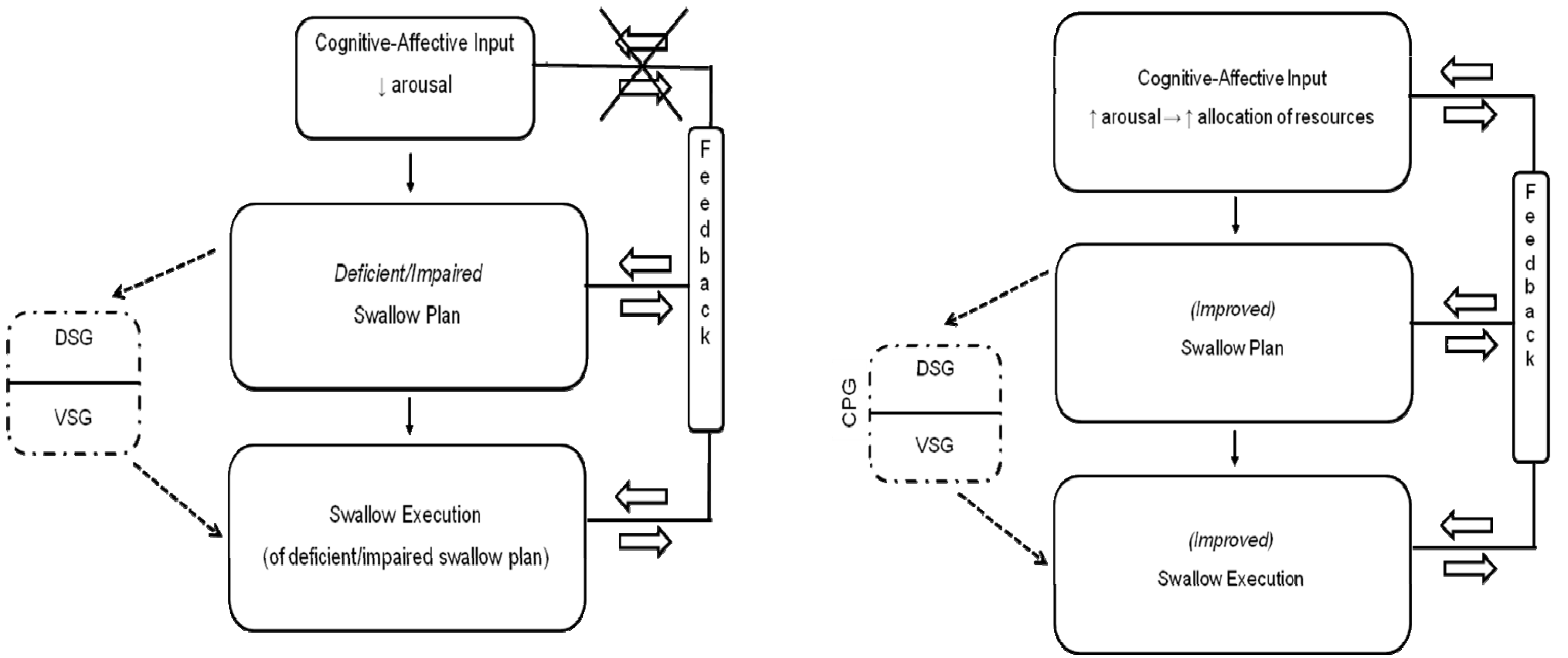

Figure 4-1. The results of the current study overlaid on the proposed model of sensorimotor oropharyngeal dysphagia

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BIOGRAPHICAL SKETCH

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