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Effects of Cueing on Sit to Stand Transfers in Parkinson Disease

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The Effects of Cueing on Sit to Stand Transfers in Parkinson Disease

by

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We hereby certify that this dissertation, submitted by Rebecca A. Martin, conforms to acceptable standards and is fully adequate in scope and quality to fulfill the dissertation requirements for the degree of Doctor of Philosophy in Physical Therapy.

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Abstract

The Effects of Cueing on Sit to Stand Transfers in Parkinson Disease

Problem Statement: Individuals with Parkinson Disease (PD) often experience difficulty transferring from sit to stand (STS). Current evidence suggests cues which promote an external attentional focus improve gait and transfers for individuals with PD. However, this research utilizes cues which are difficult to replicate in clinical or natural environments making the findings difficult to generalize or implement. **Purpose:** The primary purpose of this study is to determine the effect of 3 different explicit cues on STS for individuals with PD. Additionally we sought to determine if, in this population, a relationship exists between latency of movement initiation and postural sway in early standing, changes in joint angle between conditions and postural sway in early standing, and cue provided during the transfer and postural sway in early standing. **Procedures/Methodology:** Thirteen individuals in both the experimental and control groups participated in this cross-over design study. Both groups completed trials of self-initiated uncued STS transfers. Those in the experimental group also completed trials of STS transfers in 3 conditions: with an external attentional focus of reaching to targets, with an external attentional focus of concurrent modeling, and with an explicit cue for an internal attentional focus. Data was collected by trained testers and utilized valid and reliable body worn inertial measurement unit sensors. ANOVAs were used to compare performance between conditions and to the performance of the healthy control group. Bonferroni corrections were completed to reduce the likelihood of accepting a false positive. **Results:** Both cues that elicit an external attentional focus improved motor control during the sit to stand transfer. However, only modeling was able to improve both motor control and postural control. Cueing that promoted an internal attentional focus resulted in decreased motor control and postural control. Additionally, a moderate positive

correlation was found between standing taller than typical and postural sway. **Clinical Implications:** Our results provide evidence for clinicians to better tailor treatment methodologies to the needs of individuals with PD. Optimal cueing can be utilized as compensations that reduce caregiver burden and increase independence of individuals with PD.

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Table of Contents

List of Tables

List of Figures

CHAPTER 1: INTRODUCTION

This dissertation study provides a fuller understanding of the effects of external cueing on sit to stand (STS) transfers for individuals with Parkinson Disease (PD). The introduction chapter presents the problem statement with relevant background information and justification for relevance of topic selection. Chapter 2 provides a thorough literature review of applicable theories and current evidence. Chapter 3 provides a detailed outline of methodology. Chapters 4, 5, and 6 include 3 fully completed manuscripts prepared for journal submission, which provide results of this dissertation study within clinical context.

1.1 Introduction to the Chapter

This chapter presents an overview of this dissertation study beginning with the problem statement and justification for selection and completion of this project. The research objectives and questions are identified, hypotheses proposed, and practical applications of the findings discussed. Finally, key terms, abbreviations, and operational definitions used throughout this dissertation study are defined.

1.2 Problem Statement

Individuals with PD often struggle with transferring from STS, due to multiple factors such as bradykinesia, rigidity,[1] and a lack of automaticity.[2] Current evidence suggests that cueing to promote an external attentional focus may improve gait and transfers for individuals with PD.[3-8] However, current cue research related to transfers within PD[8,9] utilize cues that are difficult to replicate in either the clinic or the patient's natural environment making the findings difficult to generalize or implement. Past studies have used audiovisual cues such as a small

yellow box on a computer screen that represents the patient's center of mass[9] or an 8 cm x 8 cm light on a wall at 1.5m distance at eye height.[8] During continuous tasks, like gait, individuals with PD have the ability to adapt their movements to the external cues provided over time. However, it remains unclear if the findings related to gait can be extrapolated to discrete tasks like STS. With discrete tasks, the individuals may not have the benefit of improving their performance over time to the external cues.

1.3 Relevance and Significance

According to a 2010 epidemiology study, an average of 1.6% of Medicare beneficiaries have PD.[10] However, in hundreds of counties in the United States, prevalence of PD reaches more than 13% of Medicare beneficiaries.[10] In 2013, it was estimated that the healthcare cost for individuals with PD in the United States was $14.4 billion, approximately $8.1 billion greater than their healthy counterparts.[11] This number is projected to increase at a high rate consistent with our country's aging population.[11]

Kowal, et al. compiled data from multiple national databases to allow for a comparison of the healthcare needs for individuals with PD to a similar population without PD.[11] It was estimated that, in 2010, there were approximately 630,000 people living with a diagnosis of PD in the United States. A sample of 630,000 Americans without PD were used to create a comparison that would allow for a fuller understanding of the impact of PD. Kowal, et al.'s results indicate that the population with PD is expected to require an additional 801,000 days of inpatient hospital care, 1.26 million physician visits, 31,000 emergency room visits, and 26,000 days of hospice care. [11]Additionally, it would be expected that an additional 96,000 individuals

in the PD group would require 24 hour nursing home care beyond the 8,000 expected in the without PD population.[11]

Studies have indicated that greater amounts of time spent in sedentary tasks by older adults, regardless of time spent in active tasks, was highly correlated with those individuals requiring additional assistance for completion of activities of daily living.[12] Individuals with PD experience bradykinesia and rigidity[1] that can make moving more difficult and burdensome. Accordingly, it has been found that even in mild to moderate stages of PD, individuals spent 75% of waking hours in sedentary activities.[13] Lack of automaticity has been suggested to be the cause of the bradykinesia experienced by those with PD,[2] which may lead to an increase in sedentary lifestyles. As a result, provision of external cueing has been theorized to improve motor capabilities of those with PD.

Health care professionals, family members, and caregivers of individuals with PD could benefit from the identification and translation of knowledge related to easily implemented strategies to improve the STS transfer of individuals with PD, such as external cues. Decreasing the burden on caregivers through the use of easily applied compensatory mechanisms to improve mobility could greatly reduce the number of individuals with PD living in nursing homes. In addition, increasing the independence of individuals with PD during STS transfers may reduce the risk of caregiver and patient injury.

The impact of many different types of cueing on gait for individuals with PD has been well studied.[4-7,14-17] Several of these studies reported on the result of auditory rhythmic cues on gait.[4-7,15,17,18] Rubinstein et al, reported on the results of verbal instruction prior to gait that had either an internal or external attentional focus. Others reported on the impact of visual cueing on gait through the use of tape or cardboard lines on the floor or a rhythmic flashing light.[7,15-17,19,20]

However, less evidence is available regarding non-gait related continuous tasks, such as writing and visual tracking. Currently, no systematic reviews or meta-analyses have been identified that focus on the impact of non-gait related external cueing within the PD field. The few studies available focus on continuous upper extremity tasks,[21] the effect of auditory cues and visual cues on sequencing for individuals with PD,[18] or the effect of visual and auditory cues on writing.[22,23] In addition, none of these studies specifically looked at the effect of cues that increase the internal attentional focus of the participants.

Likewise, limited evidence is available regarding the effect of cueing on discreet tasks, which have a definitive start and end. Because individuals with PD often lack automaticity and display motor patterns typical to those learning a new task even when completing familiar tasks,[2] the ability to integrate and adapt to external cues during continuous tasks may be easier than discrete tasks for individuals with PD. As a result, it may not be appropriate to generalize the results of studies which have evaluated the efficacy of cueing during continuous tasks to the significantly less studied discrete tasks. The proposed study would help physical therapists to better understand the most effective type of cueing to use during STS.

1.4 Research Questions

Research Question 1:

Which type of cue, external attentional focus of reaching to targets, external attentional focus of concurrent modeling, or an explicit cue for an internal attentional focus, will result in the most normalized STS transfer for individuals with PD?

Research Question 2: Is there a relationship between the latency of movement initiation and postural sway noted in the first 30 seconds of stand?

Research Question 3: Is there a relationship between hip joint angle changes from the uncued condition to the cued conditions and postural sway noted in the first 30 seconds of stand?

Research Question 4: Is there a difference in postural control during the first 30 seconds of standing based on the type of cues?

1.5 Research Objectives

Research Objective 1:

The primary purpose of this dissertation study was to determine the effect of 3 types of explicit cues on the task of STS for individuals with PD, external attentional focus of reaching to targets, external attentional focus of concurrent modeling, and an explicit cue for an internal attentional focus.

Research Objective 2: To determine if a relationship exists between the latency of movement initiation and postural sway noted in the first 30 seconds of stand following a STS in individuals with PD.

Research Objective 3: To determine if a relationship exists between hip joint angle changes from the uncued condition to the cued conditions and postural sway noted in the first 30 seconds of stand following a STS in individuals with PD.

Research Objective 4: To determine if there is a difference in postural control during the first 30 seconds of standing based on the type of cues presented during a STS transfer for individuals with PD.

1.6 Hypotheses

Null Hypothesis 1:

H_0: There will be no significant difference in STS metrics between types of cue provided.

Alternative Hypothesis 1:

It was hypothesized that an external attentional focus, provided either through reaching to targets or concurrent modeling, would be more successful than explicit cueing for an internal attentional focus in improving the mechanics and functionality of the STS transfer in individuals with mild to moderate PD. Mechanics will be considered "improved" if they change to be more consistent with the data collected from the healthy control group. Change scores of the following metrics were used to determine which type of cueing, if any, provides the greatest improvement in STS transfers for this sample: latency of movement initiation, duration of STS, losses of control of center of mass within the base of support, sway area, coronal sway, sagittal sway, sway jerk, sway velocity, change in hip angle as compared to the uncued condition, and change in overall height as compared to the uncued condition, and number of attempts. The findings of this dissertation study may also help to determine if there are greater benefits of externally focused cueing provided through modeling or reaching for targets for those with PD.

Null Hypothesis 2:

H_0: There is no relationship between the latency of movement initiation of the sit to stand motion and postural sway noted in the first 30 seconds of stand for individuals with PD.

Alternative Hypothesis 2:

A greater latency of movement initiation of the sit to stand motion will be related to increased postural sway during the first 30 seconds of stand for individuals with PD.

Null Hypothesis 3:

H_0: There is no relationship between hip joint angle changes from the uncued condition to the cued conditions and postural sway noted in the first 30 seconds of stand for individuals with PD.

Alternative Hypothesis 3:

Greater joint angle changes at the hip during a cued condition as compared to the uncued condition measurements will result in an increased postural sway noted in the first 30 seconds of stand for individuals with PD.

Null Hypothesis 4:

H_0: There is no significant difference in the effect of type of cues provided on postural control during the first 30 seconds of standing for individuals with PD.

Alternative Hypothesis 4:

The visual cue of modeling will result in improved postural control during the first 30 seconds of standing for individuals with PD.

1.7 Summary

The results of this dissertation study help clinicians to better tailor treatment methodologies to the needs of individuals with PD to maximize patient outcomes. It is important to maximize the effectiveness of cues utilized during therapy to optimize movements completed during every repetition of practice. This need is accentuated by the decreased rate of motor learning and increased need for repetitions of appropriate motor patterns experienced by individuals with PD.[24] Repetitions of poor movement patterns, which may result from inappropriate external cues, may impair motor learning and impede functional gains.

Beyond this, cues are a common compensatory mechanism that therapists and caregivers use to improve real time patient mobility. Understanding the best cue to give an individual may reduce the amount of physical assistance that is needed and reduce risk of injury to caregivers. Identification of optimal cueing may also help to design protocols used within long term care facilities. With an increased need for repetitions to achieve motor learning,[24] individuals with PD who have multiple caregivers may benefit from a more standardized approach to cueing for STS transfers.

Identifying treatment or compensation strategies that may improve an individual with PD's ability to complete a STS transfer could lead to a decrease in sedentary time. The idea that difficulty rising from a chair could lead to an individual choosing to sit longer has strong face validity, but there are no known correlation studies at this time. Improving one's ability to stand up increases independence. In turn, this could lead to a decrease in caregiver burden and an improved overall health condition for the individual with PD.

1.8 Definitions of Important Terms and Abbreviations

- BOS- base of support
- COM- center of mass
- External attentional focus – focus during a movement that draws a person's attention to the environment around them or to the effect they will have on the environment[25]
- External cue – an augmented cue that is not part of the task itself[26]
- Internal attentional focus – focus during a movement that directly draws attention to the person's own body during movement[25]
- LOB- loss of balance
- PD - idiopathic Parkinson disease
- PwP- People with Parkinson disease
- STS - sit to stand

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction to the Chapter

This purpose of this chapter is to present the reader with a concise but comprehensive review of current available literature as it relates to this dissertation study. First, an overview of current understanding of the neuropathology of PD will be covered with specific discussions of the role of genetics, alpha-synuclein, and the basal ganglia. A thorough discussion of commonalities and variations in clinical presentation if PD will follow. Next, motor learning in healthy adults will be compared to motor learning in individuals with PD. This chapter will end with a comprehensive review of the current evidence regarding sensory cueing as it relates specifically to individuals with PD.

2.2 Neuropathology of Parkinson Disease

PD is a neurodegenerative disorder that is characterized by a complex and variable clinical presentation of motor and non-motor symptoms, including cognitive[27] and motor learning changes.[24] While many recent advancements have shed light on the role that both genetics and environment play in the disease course of PD, the complete neuropathology of PD is not fully understood. Several disorders present with a clinical presentation similar to idiopathic PD, including multiple systems atrophy, progressive supranuclear palsy, corticobasilar degeneration, chronic traumatic encephalopathy, vascular parkinsonism, and drug-induced parkinsonism. For the purposes of this paper, the term PD will exclusively refer to idiopathic PD and not to any of the other disorders that can result in parkinsonian symptoms. Idiopathic PD is defined as “the selective degeneration of pigmented, dopaminergic neurons of the substantia

nigra pars compacta and other brainstem nuclei, with the presence of alpha-synuclein positive staining cytoplasmic inclusions (known as Lewy bodies) in the surviving neurons."[28]

2.2.1 Genetics and Parkinson Disease

Evidence strongly supports that genetics play an important role in PD[29,30] with some journal articles on this topic dating back to the early 1900s.[30,31] While 5-10% of individuals with PD develop the disease as a direct result of a genetic mutation, both common and rare genetic mutations have been found to place an individual at an increased risk of developing PD after certain environmental interactions.[32] The Movement Disorder Society maintains an up to date "genetic mutation database" that compiles current evidence regarding a growing list of genetic mutations that have been linked to PD. Currently, evidence regarding 1651 different mutations has been complied within the database.[33]

Many studies of environmental factors suggest a correlation between exposure to certain factors and an increased incidence of PD.[34-37] In 2015, Chin-Chan, et al. provided an in-depth overview of known correlations between exposure to environmental risk factors and incidence of PD.[35] Chin-Chan, et al. found positive correlations between incidence of PD and lifetime exposure to lead,[35] which has been found to suppress dopamine secretion into the synaptic cleft and reduce sensitivity of post-synaptic cleft receptors for dopamine,[38] a variety of pesticides, single large dose exposure to some solvents, and long term small dose exposure to other solvents.[35]

While it is clear that both genetics and the environment can play a causative role in PD, it is theorized that in most instances PD occurs secondary to a complex interaction of these 2 factors.[32,39] A common phrase used to describe this phenomenon, "genetics loads the gun and the environment pulls the trigger," can be traced back to a blog by Soania Mathur.[40] This analogy

provides a quick and patient friendly image of how genetics and the environment can interact to cause the degenerative process in PD.

2.2.2 Alpha-synuclein and Parkinson Disease

Alpha-synuclein proteins are produced in high levels in the healthy adult brain. They are found primarily in the areas surrounding the synaptic vesicles, within erythrocytes, and within platelets.[41] While the exact role of this protein within the body is not fully understood, most evidence supports that its function is to control the release of neurotransmitters.[42,43]

However, alpha-synuclein is now understood to play an important part in the disease process of PD.[43] Abnormal deposits of alpha-synuclein proteins have been found to occur early in the disease process for PD.[41] It is still unclear if the abnormal clumping of this protein is causative of PD or if it may develop as a result of another pathological process that occurs early in PD.[41]

2.2.3 Staging the Progression of Parkinson Disease Based on Pathology

Utilizing autopsy evidence regarding the presence of alpha-synuclein in individuals who passed away at varying stages of PD, Braak, et al. identified a 6 stage progression of alpha-synuclein in PD[44] that has been well accepted by researchers following its initial introduction in 2004. While Braak, et al. clearly outline within their article a comprehensive list of changes they noted throughout the central nervous system, this overview will focus on the most pertinent brain areas to understanding the clinical presentation of PD. During the stages presented by Braak, et al., there is a steady progression of abnormally clumped alpha-synuclein that forms in a distal to caudal distribution beginning in the brain stem. Braak, et al. suggested that the disease process in PD initiates during stage 1 at both the dorsal motor nucleus of the vagal nerve and the olfactory

bulb.[44] Stage 2 is characterized by increased damage to the dorsal motor nucleus and beginning damage in the medulla oblongata and pontine tegmentum.[44] It is in stage 3 that the disease process moves into the basal ganglia, but, at this point, the basal ganglia remain functional. Stage 4 is characterized by worsening of the disease process within the basal ganglia resulting in the emergence of clinically apparent PD.[44] Additionally, in stage 4 the disease process reaches the cortex, though the cognitive effects are not likely readily apparent at this phase.[44] In stages 5 and 6, the alpha-synuclein clumps have aggregated so heavily within the substantia nigra that this portion of the brain no longer has its characteristic dark coloring for which it was named. This coincides with significant worsening of motor symptoms.[44] Additionally, in these final stages, the alpha-synuclein plaques spread progressively throughout the motor cortex resulting in a steady decline in cognitive function.[44] A 2017 publication by Braak, et al., resulted in the author's affirmation that, in light of his more recent research, the framework presented above from their original publication still holds merit, though he points out that there may be additional sites of initiation for PD outside of the central nervous system.[45]

However, it is important to note that the accuracy of Braak, et al.'s staging has been questioned.[46] Burke, et al. point out that more recent case studies of "incidental Lewy body disease" may actually be pre-clinical PD due to the reduced number of dopamine producing cells within the substantia nigra of these subjects.[46] In autopsies, the individuals in these case studies did not develop alpha-synuclein clumping in the typical pattern described by Braak, et al.[47] Burke, et al. suggest that the diagnosis of dementia with Lewy Bodies should be considered to have the same neuropathological process as PD and continued on to state that the early presence of alpha-synuclein proteins in the cortical regions for individuals with dementia with Lewy bodies provides evidence that the Braak Stages are not an appropriate descriptor for progressive

development of PD.[46] Despite the flaws that Burke, et al. identify in the theoretical framework of Braak staging in relation to PD, the correlations between symptom onset and natural history of the disease have resulted in a general acceptance of Braak staging by research and clinical experts.[48] According to the Web of Science research database, the original Braak Stages article has 1,170 citations, which speaks to the importance of this staging scale within PD research.[48] In alignment with much research related to PD, this dissertation study utilizes the Braak stages to create a common language for further discussion of the disease.

2.2.4 Basal Ganglia Degeneration in Parkinson Disease

The onset of motor symptoms that comprise the cardinal symptoms of PD, tremor, rigidity, bradykinesia, and postural instability correlates with the degeneration of the basal ganglia and increased presence of abnormal clumping of alpha-synuclein proteins in and around the basal ganglia.[44] These are the hallmark clinical features associated with Braak Stage 3.[44] In a healthy individual, the basal ganglia assist with shifting between central sets, preparing for movements, and execution of action.[49] During the progression of PD, there is a selective and progressive loss of dopaminergic cells within the substantia nigra, part of the basal ganglia.[50] Dopamine is involved in multiple pathways within the brain that coordinate movement and lack of appropriate levels of dopamine is associated with tremor, rigidity, akinesia, and postural instability,[51] as well as difficulty with shifting between central sets, preparing for movements, and execution of actions.[49]

With many of the motor symptoms of PD being traced back to depletion of dopamine,[51] most medications to treat the primary symptoms of PD are designed to increase dopamine concentrations within the synaptic cleft.[52] Most symptoms of PD can be reduced with regular use of dopamine replacement therapy.[53] Two of the medications used by most individuals with PD in

the United States, carbidopa and levodopa, which act together to replace dopamine, result in a large fluctuation in the motor abilities throughout the day. These fluctuations, which occur due to a very short half-life of approximately 1.5 hours[54] of the carbidopa levodopa combination, results in what is known as the "on-off phenomenon." Without carbidopa, which helps the levodopa to cross the blood brain barrier, the half-life is decreased to only 50 minutes.[55] Patients are considered "on" when their medication dose is working most effectively and "off" when they are at the point of least effectiveness of the levodopa medication.[55] Carbidopa levodopa begins to release into the blood stream 30 minutes after the dose.[55] Peterson, et al. found greater improvements in movement related interventions during the "on" versus "off" stage of levodopa medications.[56] As a result, testing protocols must be carefully and optimally designed in order to capture all of an individual's motor capabilities while they are in the desired relationship to their therapeutic window. This means that researchers must work around the medication schedule of the individuals, as well as complete all of their motor testing within a 90-minute window in order to have a decreased likelihood that wearing off of medications is affecting the subject's motor function.

2.3 Clinical Presentation of Parkinson Disease

James Parkinson provided the initial written description of the clinical manifestation of PD in "An essay on the shaking palsy," which was published in 1817. [57] His essay begins with a basic definition of "shaking palsy," now known as PD: "involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend forward, and to pass from a walking to a running pace: the senses and intellects being uninjured."[58] While application of current research and known neuropathology allows for a

deeper understanding of the progression of the clinical presentation of PD over time, much of the observations made by James Parkinson are still widely accepted. The key difference in today's understanding of PD is that the "weakness" that was originally identified[58] is now better identified as bradykinesia or akinesia.

2.3.1 The Epidemiology of Parkinson Disease

A 2014 meta-analysis and systematic review of the prevalence of PD provides much insight on the epidemiology of PD.[59] The onset of the cardinal signs of PD rarely occurs prior to the fifth decade of life. However, there is a sharp increase in the prevalence of the disease with each decade of life.[59] The authors found no significant difference in prevalence between males and females. Certain lifestyle choices have been associated with an increased or decreased risk of developing PD. Likely due to the neuroprotective qualities of nicotine and caffeine, those who have a history of smoking or drinking coffee, respectively, have a decreased risk of developing PD.[60]

2.3.2 The Progression of the Clinical Presentation of Parkinson Disease

In the early Braak Stages, the non-motor symptoms of PD have not yet become apparent.[44] However, correlating with the progressive abnormal clumping of alpha-synuclein, other less obvious symptoms of PD are typically present. Leentjens, et al. found a statistically significant higher incidence of depression in patients in the pre-clinical stages of PD than in a "matched control population."[61] Excessive daytime drowsiness[62] and rapid eye movement (REM) cycle disorders[63] Haehner, et al. found that idiopathic anosmia, while not always present as a precursor to the onset of motor symptoms in PD and not always indicative of later development of PD, is significantly more likely to occur in individuals who will develop PD than

the general population.[64] Loss of sense of smell, which involves the olfactory bulb, and impaired sleep functions, which are controlled within the brain stem, are consistent with the early Braak stages that are characterized by alpha-synuclein protein clumping in these regions.[44] While some more recent research suggests that it may be possible to diagnose *some* cases of PD prior to the disease becoming clinically apparent,[65] PD is considered a diagnosis of exclusion, meaning that the presence of the cardinal signs without other known cause would indicate likely PD.[1]

While there are many different clinical presentations to Parkinson Disease, it is primarily characterized by the four cardinal signs, tremor, rigidity, bradykinesia, and postural instability.[50] These symptoms emerge during Braak stages 3 and 4,[44] when approximately 60% of the dopaminergic cells have died.[66] Most commonly, tremor within PD occurs at rest and is characterized by a "pill rolling" motion within the hands.[1] Similarly, rigidity within PD has a typical clinical presentation known as "cogwheel" rigidity which is hallmarked by a repetitive catch and release sensation when the patient is moved passively through the range of motion.[1] Additional motor signs include freezing or "motor blocks," hypomimia, dysphagia, dysarthria, decreased amplitude of arm swing during gait, festination of gait, difficulty with STS, difficulty with bed mobility, micrographia, difficulty with ADLs, glabellar reflex, blepharospasm, dystonia, striatal deformity, scoliosis, and camptocormia.[1] In addition to motor signs, individuals with Parkinson Disease also have a variety of non-motor signs and symptoms that emerge during Braak stages 3 and 4, including fatigue and orthostatic hypotension.[1,45] In addition, the depression, anxiety, apathy, sleep disorders, and anosmia may develop or worsen as the disease progresses.[1]

Due to the progressive nature of PD, both in the depletion of dopaminergic cells and the accumulation of abnormal alpha-synuclein clumping, the advanced stages of PD are hallmarked

by worsening of the motor and non-motor symptoms discussed above and the addition of cognitive decline.[1,45]

2.3.4 Measuring Progression of Parkinson Disease Based On Clinical Presentation

As Burke, et al. pointed out, staging Parkinson Disease based on the presence or absence of alpha-synuclein protein can be problematic, as the clinical presentation may not always correlate with this quantifier of disease progression.[46] Additionally, there is currently no way to test for the presence of alpha-synuclein clumping prior to autopsy. The Unified Parkinson's Disease Rating Scale was developed by Fahn and Elton[67] and later adopted and modified by the Movement Disorder Society (MDS-UPDRS).[68] Rather than staging the disease by neuropathological changes, this scale stages PD based on the clinical signs and symptoms of the disease.[68] The MDS-UPDRS is composed of questions and motor testing that evaluate the effect of PD and dopamine replacement medications on individuals with the disease, including items related to sleep, depression, anxiety, apathy, cognitive impairment, hallucinations, pain, bowel and bladder, fatigue, orthostatic hypotension, oral motor changes, activities of daily living, bed mobility, transfers, tremor, postural stability, gait, freezing, medications, rigidity, coordination, dysdiadochokinesia, motor fluctuations, dyskinesia, and dystonia.[68] Most of the 50 items on the test are scored on a 5 point Likert scale ranging from normal to severe, with the higher numbers indicating a more severe presentation of the signs or symptoms.[68]

2.4 Abnormalities of Motor Control in Parkinson Disease

Motor control has been operationally defined as "the ability to regulate or direct the mechanisms essential to movement."[26] Specific to PD, the aforementioned symptoms of PD that

demonstrate deficits in motor control include: tremor, bradykinesia, rigidity, postural instability, and difficulty switching between central sets. The study of motor control helps us to gain a fuller understanding of how movement occurs within healthy adults. Over the past several decades there have been many different theories of motor control presented. This chapter provides a brief overview of key historical theories, as well as more recent and applicable motor control theories as they apply to the task of STS.

2.4.1 Reflex Theory

Sherrington introduced his reflex based theory of motor control in 1925,[69] which suggests that all movement occurs in response to external stimuli. He suggested that even complex movements could be explained as a series of reflexes in succession.[69] However, this type of "bottom up" theory fails to explain voluntary movements that occur in the absence of external stimuli. One example of this could be a STS transfer that begins without an external stimulus. Despite proven instances of movement in the absence of external stimuli,[70] application of Sherrington's reflex theory helps to further understand the role of external stimuli and cues on overall movement.

2.4.2 Hierarchical Theories

Conversely, hierarchical theories of motor control suggest that cognition is divided into hierarchical levels that control all levels below them.[71] According to this theory, all movement occurs after input from the higher centers of the brain. As previously discussed, evidence supports that movement can occur in the absence of external stimulus. However, studies have shown that reflexive movements can occur in the absence of cortical input.[70] Perhaps most famous instance of this would be the decerebrate cat who is able to not only walk on the

treadmill without any cortical input, but able to respond to changes in treadmill speed with the correct cadence and resemblance of appropriate gait patterns.[72]

2.4.3 Information Processing Theory

In another approach to motor control theories, Mazzoni, et al.[27] adapted the three levels of information processing first described by David Marr[73] and applied them to the motor control difficulties experienced by those with PD. David Marr's description of information processing in 3 levels: computation, algorithmic, and implementation/hardware.[27,73] The computation level describes the output and the reason for the movement to occur. The algorithmic level describes how the motor outputs are achieved. The implementation level describes the anatomy of what actually performs the motor output.

Applying this concept to the difficulties often experienced by individuals with PD during the STS transfer provides a fuller understanding of how PD effects the motor control process during this task. Most easily understood are the deficits seen at the implementation, or hardware, level. According to Mazzoni, et al.'s theory, the implementation level would best be described through a thorough discussion of the reduction in the neurotransmitter dopamine and how this results in an increase in the output activity of the basal ganglia, which in turn will reduce activity within the motor cortex for the planned movement.[27] Additionally, others might add that the presence of abnormally clumping alpha-synuclein would also be appropriate to describe the implementation level of this motor theory.[41] Both descriptions of the implementation level provided explain how a defect at the implementation or "hardware" level impairs the ability of an individual with PD to rise from a surface. At the algorithm level, which discusses how motor outputs are achieved at a processes level, Mazzoni, et al. describe the individual with PD as having difficulty due to over activity of the basal ganglia resulting in under-excitement of the

associated motor cortex areas.[27] While there is some discussion of neuroanatomy at this level, the focus here is faulty connections between larger systems within the brain. At the level of computation, the focus is on the motor outputs and why the action occurs. This is the level at which this dissertation hopes to impact the STS transfer. For individuals with PD, bradykinesia, rigidity, and postural instability may result in a slow STS transfer with delayed onset and lack full extension phase, in addition to other deficits as detailed previously in this dissertation. This description focuses on the motor output created as a result of changes in motor control. For many individuals with PD the "why" or reason to complete the transfer, which is part of the consideration of the computation phase, has not changed. They would like to stand up, they attempt to stand up, but they are unsuccessful due to factors falling within the implementation and algorithm levels of motor control. However, as will be discussed later in this chapter, the possibility of changing the "why" for the initiation of a STS transfer from an internally driven stimulus to an external cue may allow for a bypass of some of the structures that have created difficulties within the implementation and algorithm levels.

2.4.4 Systems Theory

Many theories of motor control exist that are based on some combination of the reflex theory and hierarchical theories. However, perhaps the most commonly known within the field of physical therapy is the Shumway-Cook and Woollacott theory of motor control.[26] Referring to their theory as a "systems theory," Shumway-Cook and Woollacott theorize that all movement occurs through an interaction of the individual, the task, and the environment.[26] They continue on to break down the factors that may interact within the individual (cognition, perception, and action), the task (mobility requirements, postural control requirements, and upper extremity manipulation requirements), and the environment (regulatory and non-regulatory factors).[26]

Identifying all of these factors as important to motor control provides the researcher or clinician with multiple areas to consider when looking to promote change in the quality of movement.

Utilizing a Systems Theory approach can provide additional insight to the STS transfer. Within the individual, the most likely deficit for an individual with PD would be depletion of the dopaminergic cells with the basal ganglia. When PD has reached the Braak staging that coincides with difficulty in the STS transfer, the basal ganglia are no longer functioning optimally.[1] The basal ganglia would be considered to fall within the motor/action factor within the individual, according to the Shumway-Cook and Woollacott Systems Theory of Motor Control.[26] However, within the same subcategory, motor/action, there are many additional neuroanatomical structures and pathways that may allow for movement. For instance, many studies support positive effects from adding a regulatory cue within the environment for individuals with PD with the theory that this stimulates alternate pathways within the brain resulting in a bypass of the basal ganglia.[74] While sensation typically remains intact for individuals with PD, perceptual deficits in the form of decline of cognition and self-awareness progressive and appear in the later Braak stages of the disease.[1,75] This would be an additional example of deficits found within the individual, according to the Systems Theory, that is likely to impair the STS transfer.

The two remaining factors within movement, according to the Systems Theory, are the task and the environment. There are many sub-factors within the task and the environment that can be modified to improve the STS for individuals with PD. For instance, the seat height can be raised, dual tasks can be removed, support surfaces can be made more steady or firm, distractions can be minimized, and footwear with optimal traction can be utilized. However, the optimal outcome of therapy is to improve the transfer of the individual in their natural environment while making the least intrusive compensations. The above-named examples of factors within the

environment and task that can be modified may not be possible. However, there are some external cueing options, that would be easy to add to the environment, that may result in the aforementio ned alternate pathways and allow for an improved STS transfer.

2.5 Abnormalities in Motor Learning in Parkinson Disease

The manner in which new mechanisms are learned or current mechanisms are refined resulting in relatively permanent change is known as motor learning.[76] Like motor control, there are many known variances between motor learning processes employed by healthy individuals and those employed by individuals with PD.[24] An understanding of these differences allows for improved methodology of the proposed study.

Due to the progressive ineffectiveness of the basal ganglia in individuals with PD, there are some important differences in the manner in which motor learning occurs. Individuals with PD learn more slowly than healthy controls.[77-79] Since sleep plays an important role in skill acquisition, it is theorized that the sleep changes in PD may account for some of the difficulties in motor learning.[80] A meta-analysis suggests that implicit learning is negatively affected in PD.[81] However, many have demonstrated improved motor learning through repetitions of tasks during the presence of external cues. [3,5-8,14-23,82-86] Individuals with PD often demonstrate a greater reliance of task specific practice in order to learn a new task. Onla-or and Winstein found that, while individuals with PD learned easier tasks at an equal rate to a healthy control group regardless of setting, individuals with PD were less likely to achieve the ability to complete a more difficult motor task in a new context or environment.[87] With this in mind, it may be necessary for individuals with PD to take advantage of compensatory strategies when then are not in their optimal environments. Lastly, when awareness of learning is present or there is a

high level of cognitive demand, learning is impaired for individuals with PD.[80] In the earlier stages of PD, this means that individuals will have a more difficult time learning new tasks. However, in later stages of the disease, it also means that individuals with PD may not be able to interpret and react to longer or more complex cueing.

In other instances, motor learning principles that are applicable to healthy adults may also be applicable to individuals with PD. Wulf, et al. found that, like healthy adults, individuals with PD have improved postural stability when asked to maintain an external attentional focus, rather than an internal attentional focus.[88] While previous studies suggested a significantly decreased ability to learn through the use of random practice, Sidaway, et al. utilized a more clinically relevant task and found that individuals with PD improved more when utilizing a random practice schedule.[89] This is similar to healthy adults.[89] Observation of actions and motor imagery has been shown to improve motor learning for both healthy adults and individuals with PD, theoretically this occurs secondary to activation of similar brain structures.[90]

2.6 The Use of Sensory Cueing in Parkinson Disease

2.6.1 Cueing Pathways

Cunnington, et al. utilized fMRI to examine the areas of the brain with the greatest hemodynamic impact in response to both internally initiated movements and external cue initiated movements.[74] While both initiating factors resulted in an increase of blood flow to the primary motor area, the supplementary motor area, the superior parietal lobule, the insula cortex, and the cingulate cortex, the basal ganglia only demonstrated significant activation during those movements that were internally initiated.[74] The lack of involvement of the basal ganglia during externally cued movements provides a theory for why sensory cueing has been found to be an

effective way to improve motor outputs for individuals with PD. Morris hypothesized that external cueing is effective either because the external cue utilize the premotor cortex rather than the basal ganglia or because external cues utilize the dorsolateral prefrontal cortex as a means to bypass the basal ganglia.[91]

2.6.2 Concurrent Rhythmic Auditory Cueing During Gait and Parkinson Disease

Several studies have found an immediate improvement in the performance of gait with the presence of an external cue. A 2005 systematic review of cueing during gait reported a finding of "strong evidence" in support of utilizing rhythmic auditory cueing during gait to improve gait speed, stride length, and cadence for individuals with PD.[5] A 2014 systematic review including different studies due to more rigorous inclusion criteria and a greater body of research at the time of the study suggests that rhythmic auditory cueing can improve gait speed and cadence only, but does not improve step or stride length.[92] Additional important studies on this topic have been completed that were not part of either systematic review. Hove, et al. examined the differences in fractal scaling of gait, or the relationship in characteristics of strides over time, for individuals with PD from healthy controls during both uncued gait and gait with metronomes.[4] They found that when individuals with PD are asked to ambulate while listening to a metronome with the ability to adapt to minor changes in cadence, the individuals' gait patterns became more like those of the healthy control group.[4] The RESCUE trial[6] suggests that, for individuals with PD, regular in home training with a rhythmic auditory cue while ambulating for a 3 week period resulted in immediate increases in gait speed, increases in step length, decreases in cadence, and decreases in episodes of freezing indicating a more normalized gait pattern for this population. The therapists prescribing metronome frequency utilized a specific protocol to select optimal cue frequency. It must be noted that for this study, participants were also provided

with specific suggestions and methods to reduce freezing during the training period, which also may have contributed to the positive outcomes of the study.[6] Suteerawattananon, et al. found that auditory cueing in the form of a metronome that was set at a frequency that was 25% faster than their calculated maximum gait speed significantly increased gait speed for individuals with PD.[15] Rochester, et al. found that rhythmic auditory cueing consistent with the subject's preferred cadence elicited immediate improvements in gait speed and step length for individuals with PD and that gait values during dual tasking moved significantly toward measurements collected during single gait tasks in the same individual.[17] Niewboer, et al. looked at the effect of an auditory beep with a frequency set at the subjects' comfortable gait speed based on the 10 Meter Walk Test. They found a significant improvement in the speed of a complex dual task gait test.[19]

2.6.3 Visual Cueing During Gait in Parkinson Disease

Many researchers have reported an immediate impacted on the performance of gait in response to visual cues. Others reported on the impact of visual cueing on gait through the use of tape or cardboard lines on the floor or a rhythmic flashing light.[7,15-17,19,20] A 2005 systematic review found insufficient evidence to support the use of visual cueing during gait.[5] A 2014 systematic review found significant improvements cadence, gait speed, and step length.[92] Others reported on the impact of visual cueing on gait through the use of tape or cardboard lines on the floor or a rhythmic flashing light.[7,15-17,19,20] Suteerawattananon, et al. found that placing brightly colored lines perpendicular to the walkway at equal intervals based on a calculation of 40% of the subject's height resulted in a significantly improved step length for individuals with PD.[15] Rochester, et al. utilized a flashing light that was present on a pair of glasses worn by the subject to provide a visual cue during dual task gait and found that gait speeds and step length moved significantly toward measurements collected during single task gait in the same individual.[17]

Nieuwboer, et al.[19] looked at the effect of a light emitting device worn on a pair of glasses with a frequency set at the subjects' comfortable gait speed based on the 10 Meter Walk Test. They found no significant improvement in the speed of a complex dual task gait test.[6,19]

2.6.4 Somatosensory Cueing During Gait in Parkinson Disease

A 2005 systematic review identified only 1 study on this topic that met inclusion and exclusion criteria for the study. Due to the low quality of the study the authors of the systematic review report that, at that time, there was insufficient evidence to support the use of somatosensory cueing during gait.[5] Nieuwboer, et al.[19] looked at the effect of a pulsed vibration emitted from a wrist worn device with a frequency set at the subjects' comfortable gait speed based on the 10 Meter Walk Test. They found a significant improvement in the speed of a complex dual task gait test.[19]

2.6.5 Auditory Cueing in Parkinson Disease

Lehman, et al. utilized a pre-gait and during gait recurring cue to "take long steps" for daily training session occurring over 10 days. This use of external attentional focus during gait via verbal instruction resulted in improved gait speed, step length, and cadence as compared to the control group.[93] Pre-gait cueing was identified as an important factor during a 2002 systematic review. Rubinstein, et al. found that different pre-gait verbal instructions resulted in dramatically different gait outcomes. Cues to increase gait speed were effective in doing so, but also resulted in unwanted decreased step length and cadence changes.[7] This suggests careful consideration of the verbal cues provided. Verbal cues to increase step length or arm swing resulted in improved gait mechanics.[7]

2.6.6 Effects of Cueing on Non-Gait Continuous Tasks in Parkinson Disease

Research regarding cueing for non-gait related continuous tasks for individuals with PD is less readily available. In 2002, a study by Almeida et al, looking at the coordination of continuous upper extremity tasks, foundnac that external pacing cues did not improve the motor function of individuals with PD.[21] In 1995, Kritikos et al found that externally focused auditory cues were more effective than visual cues to complete proper sequencing for individuals with PD.[18] In 1997, Oliveria et al, found that both visual and auditory cues did improve the size of written letters immediately and with prolonged writing.[22] In 2016, Nackaerts et al completed a study that suggested visual cueing may actually impair handwriting for individuals with PD.[23] None of these studies specifically looked at the effect of cues that increase the internal attentional focus of the participants.

2.6.7 Effects of Cueing on Discrete Tasks in Parkinson Disease

Similarly, there is very limited information regarding the effect of cueing on discrete tasks that have a definitive start and end. All of the aforementioned studies looked at tasks that have an indistinct beginning and end. Because individuals with PD often lack automaticity, they typically display difficulty with beginning and ending tasks.[2] Therefore, once initiated, continuous tasks may be less difficult for individuals with PD. As a result, it may not be appropriate to generalize the results of studies looking at cueing during continuous tasks to the unstudied discrete tasks.

Few studies have actually looked at the effect of cueing on discrete tasks. Reaching for a target was improved when individuals reaching for a rolling ball initiated by the tester rather than a self-initiated reach to a stationary ball.[94] Mak, et al. found that a single auditory initiation cue could improve force production and reach duration in a pen retrieval task for individuals with PD.[95]

2.6.8 Effects of Cueing on Sit to Stand in Parkinson Disease

Only 1 study is known to have specifically looked at the effect of audiovisual cues on STS transfers for individuals with PD.[8] Mak and Hui-Chan compared the movements of individuals with PD to those of matched healthy controls during self-initiated and cue initiated STS transfers.[8] Self-initiated movements were guided by asking the patient to stand when they are ready with no further cues provided. The cue initiated movement was a paired initiation cue of both a verbal command to "get ready, stand up" and a visual cue of a 8cm x 8cm light appearing on a wall 1.5m away at a height equal to their standing eye level.[8] No additional cues were provided during the actual STS.

Mak and Hui Chan completed a later study looking at the effects of combined "audio-visual cued task-specific training" during STS transfers for people with PD. During this experiment individuals in the experimental group completed repetitions of STS transfers in 20 minute intervals, 3 times a week for a total of 4 weeks using the Equitest-Balance Master system by Neurocom.[83] The cues provided during this study were controlled by the computer system and included a visual cue of 2 boxes stacked vertical that included one colored box to indicate if the patient should be standing or sitting and a stickman representation of the subject that moved in real time with the patient to indicate if the pressure distribution was consistent with sitting or standing.[83] These cues would result in an initiation cue for each phase of the transfer. The researchers found that combined audiovisual training resulted in immediate reduced duration of the STS transfer and improved hip flexion torque with improvements still noted at the 2 week follow up.[83]

2.7 The Sit to Stand Transfer in Relation to Parkinson Disease

Several different groups have proposed strategies to breakdown the STS transfer to allow for clearer language to describe when deficits are occurring. Kotake, et al. suggest a 6 stage breakdown that allows for a clear understanding of what is happening at the hip, the knee, and the ankle in the sagittal plane during the STS process: (1) sitting in chair, (2) flexion of hip commences and buttocks clear surface, (3) maximum flexion of hip joint, (4) maximum dorsiflexion of ankle joint, (5) full standing, and (6) stabilization in standing.[96] While others have simplified the STS transfer into 2 phases, pre-extension and extension,[97] the additional phases suggested by Kotake, et al. allow for consideration of a period of time when the hip and knee joint are not working in a either a synchronized flexion or extension synergy which occurs in stage 4.[96]

However, the task analysis model presented by Hedman, et al.[98] provides a fuller examination of the STS transfer. Hedman suggests a 6 stage analysis process that includes initial conditions, preparation, initiation, execution, termination, and outcome.[98] Kotake, et al.'s suggested stages of the STS transfer nests under the "execution" phase of the task analysis presented by Hedman, et al. Hedman, et al. provided key qualifiers to look at within each phase of the task analysis, Table 2.1.

Table 2.1 Hedman, et al. Phases of Task Analysis[98]

PHASE OF TASK ANALYSIS	QUALIFIERS
INITIAL CONDITIONS	Posture, environmental context, ability to interact with environment
PREPARATION	Stimulus identification, response selection, response programming
INITIATION	Timing, direction, smoothness

EXECUTION	Amplitude, direction, speed, smoothness
TERMINATION	Timing, stability, smoothness
OUTCOME	Was the task successful?

The motor complications experienced by individuals with PD negatively impact many aspects of the STS transfer. Individuals with PD typically require additional time to complete a STS transfer[99,100] and demonstrate an increased latency of movement that may occur secondary to deficits in motor planning. [101,102] However, studies indicate that, with instruction to do so, individuals with PD are able to increase the velocity of their STS.[103] In a study of individuals in the early clinical stages of PD, Inkster and Eng found an exaggeration in hip flexion strategy and forward translation in center of mass during Kotake's stage 2 of the STS transfer.[104] Bishop, et al. found a correlation between difficulty recruiting the tibialis anterior during the early execution phases and overall difficulties with STS transfers in individuals with PD.[105] The STS transfer is problematic for individuals with PD at different phases and stages for different reasons, Table 2.2.

Table 2.2 Difficulties in Sit to Stand for Individuals with PD by Phase and Stage

Task Analysis Stage[98]	Adaptations Noted in the Literature or Probable Difficulties for Individuals with PD
Initial Conditions	- Kyphotic posture[1] - Rigidity[1] - Environmental conditions, such as seat height
Preparation	- When the basal ganglia are affected, there is difficulty switching between central sets resulting in hypothesized decrease in anticipatory control[49] - In the advanced stages of PD, cognitive changes may result in difficulty understanding the task.[1,44]
Initiation	- Akinesia, which presents during the middle stages of PD often results in a delay of movement initiation.[44] - Difficulty with shifting between central sets results[49]

Execution	Sit to Stand Stage[96]	Indicator	Adaptations Noted or Possible Difficulties for Individuals with PD
	1	Seated in Chair	- Kyphotic posture[1]
	2	Flexion of torso commences Buttocks leave chair surface	- Impaired ability to switch between central sets may make initiation of this stage difficult[49]
	3	Hip joint achieves maximum flexion	- Impaired ability to switch between central sets may make cessation of this stage difficult[49] - Increased hip flexion may result to improve postural stability[106] - Decreased hip flexion may result secondary to lack of self-awareness[75] or fear of falling
	4	Ankle joint achieves maximum dorsiflexion	- Impaired ability to switch between central sets may make initiation of this stage difficult[49] - Difficulty recruiting tibialis anterior[105]
	5	Standing	- Impaired ability to switch between central sets may make initiation of this stage difficult[49]
	6	Stabilize in standing position	- Orthostatic hypotension[1] - Impaired ability to switch between central sets may make cessation of standing difficult[49]
Termination			- Likely to undershoot due to a lack of awareness of body position[75] - Likely to undershoot due to kyphotic posture[1]
Outcome			- Lack of adequate forward translation may result in an ineffective transfer of center of mass into the standing base of support

*While some impairments or characteristics noted may be present in any stage, this table provides the phase or stage where it is most likely to affect the transfer.

2.8 Summary

Previous research has demonstrated that cueing can improve movement patterns in individuals with PD in certain situations.[3,5,6,8,15-23,82,85,86,92] However, literature is limited for discrete tasks and, specifically, in relation to STS transfers. While Mak and Hui-Chan were able to show that cue-initiated STS resulted in decreased duration of the STS transfer and increased hip torque[8,83] as compared to their matched healthy controls, there are several factors that warrant additional research on this topic. The cues provided during the Mak and Hui Chan's studies are not easily reproducible in the clinical or natural environments. Additionally, much

research supports that cues can improve movement for individuals with PD, however, the benefits of different cues can be context specific.[89] There is no known research at this time that looks to identify the best type of cue to provide during the STS transfer. This dissertation study helps to better understand the most appropriate type of cueing to use during the STS transfer. Additionally, it may provide greater insight for the best type of cue to provide during interventions or as compensations to improve performance on other discrete tasks and to begin research to determine if the results of previous studies that have suggested the benefit of external cues on continuous tasks can be generalized to discrete tasks.

CHAPTER 3: METHODOLOGY

3.1 Introduction to the Chapter

This chapter is a thorough presentation of the methodology of this dissertation project. Descriptions for participant recruitment and selection, data collection, and data analysis are provided. Relevant supporting evidence are provided to justify the methods used.

3.2 Research Methods

The primary purpose of this study is to determine the effect of 3 types of explicit cues on the task of STS for individuals with PD, external attentional focus of reaching to targets, external attentional focus of concurrent modeling, and an explicit cue for an internal attentional focus. As shown in the literature review, there is ample research to support that external cues have the potential to improve the motor output for individuals with PD. However, it is currently unclear what type of cue is best during STS transfers. With the only studies on cueing during STS transfers utilizing cues that are impractical to use in everyday life or within most clinics,[8,83] the specific cues selected for this proposed study were selected because of ease of implementation by both therapists and caregivers in any setting. Both reaching to targets and concurrent modeling utilize a primarily external attentional focus, which current research supports improves motor learning and motor control in both healthy individuals and individuals with PD.[88] Reaching to targets may utilize the same principles as tape line targets during gait, which has been shown to improve step length and gait speed for individuals with PD.[16] For the purpose of this dissertation study, the tester drew attention to the targets at the time that the subject was to reach for the targets taking advantage of the effect of the moving target effect described by Masjsak, et al.[94] The final cue, which promotes an internal attentional focus, was selected not for its likelihood of producing the best motor outcome, but because it is a commonly utilized

strategy both in the clinic and by caregivers. It is important to further investigate if this strategy is helpful, neutral, or unhelpful in improving the STS for individuals with PD.

A cross-over design that exposes each study participant to each type of cue was utilized as it was the best type of study to investigate the research objectives. Due to the great variations in clinical presentation of individuals with PD,[1] utilizing different patients for each group would require an extremely large sample size. Utilizing the same group of subjects for each condition reduced the likelihood of impact by covariates.[107]

To investigate the primary purpose of the proposed study, the main design of the study will have 1 factor (cue provided) and 10 dependent variables that look at kinematics, bradykinesia, and postural stability, Table 3.1. In addition, this design can be utilized to investigate research question 4, which looks at the effect of type of cue on the first 30 seconds of stand. For research question 2, which asks if a relationship exists between latency of movement initiation and postural sway noted in the first 30 seconds of stand for individuals with PD, and research question 3, which asks if a relationship exists between hip joint angle changes from the uncued condition to the cued condition and postural sway in the first 30 seconds for individuals with PD, a separate correlation estimation will be completed.

Table 3.1 Factors of Main Design

Factor 1- Cue Provided	Dependent Variables
Uncued sit to stand	Change in hip angle compared to the uncued condition
External attentional focus of reaching to targets	Change in total height compared to the uncued condition
External attentional focus of concurrent modeling	Number of attempts
Explicit cue for internal attentional focus	Latency of movement
	Duration of the transfer
	Sway area
	Coronal sway

	Sagittal sway
	Sway jerk
	Losses of control of center of mass within the base of support

red=kinematic measurements; yellow = measures of bradykinesia; blue=postural sway measurements

3.2.1 Participants

Two groups of participants were recruited for this study, a PD group and an age matched healthy control group, with a minimum of 13 participants in each group. Sample size estimation was completed utilizing a 0.05 level of significance, a power of 0.8, and an effect size of 0.85.[108,109] The level of significance and power was selected based on norms within the research field. The effect size was calculated from data presented in a similar study[3] which identified the effects of different types of external cues on gait. The researchers for the aforementioned study looked at the effect of cueing individuals to ambulate while deliberately swinging their arms, counting out loud, taking large steps, or walking quickly. For each condition, the researchers measured the effect of the cue provided on right step length, left step length, velocity, shoulder excursion, elbow excursion, and cadence. The researchers did not indicate which of the variables the primary outcome measure for their study, therefore the effect sizes were calculated from the variables most similar to the present study and a range was identified. Those variables that were considered most similar to the present study include the effect of cueing for large steps or to walk fast on right step length, left step length, or gait velocity and the effect of cueing for deliberate arm swing on shoulder or elbow excursion. These were selected because of the use of an external attentional focus of the cue for improved movement on a related body part. The table below shows the calculated effect sizes based on the AI-Therapy Statistics® online calculator. (Table 3.2) Calculations of the effect sizes resulted in a range of 0.85-2.5. To decrease risk of not

having enough power in the present study, the lower end of the range was utilized in the sample size calculation for this study.

Table 3.2 Effect Size Calculations[3]

Cue	Measurement	Effect Size Calculated
Walk fast	Right step length	0.85*
	Left step length	0.85
	Gait velocity	2.17
Take large steps	Right step length	1.85
	Left step length	1.52
	Gait velocity	1.69
Swing arms	Shoulder excursion	1.37
	Elbow excursion	2.5**

Key: *lowest effect size found, ** highest effect size found

The estimated sample size is consistent with similar studies completed recently with 15 subjects with PD and 15 healthy controls should provide adequate power for the proposed study.[8,16,23,94] A 2005 systematic review of effects of cueing during gait in individuals with PD included 24 studies, 14 of which had experimental groups with 15 or less subjects.[5] These studies included sample sizes as low as 6, 7, 8, 8, 10, 10, 11, and 12.[5] An additional 5 studies had 16 subjects in the experimental groups and the remaining 6 studies from 21-68 subjects.[5] The study identified that is most similar in methodology and purpose to the proposed study utilized 15 subjects in the experimental group and 15 subjects in the healthy control group[8] and was published in 2004 in *Movement Disorders.*

3.2.1.1 Inclusion Criteria

Participants were required to meet specific inclusion criteria, Table 3.3. Participants in the PD group were diagnosed by a neurologist with idiopathic PD and were on stable dosages of anti-Parkinson's medication, when applicable. All participants were able to follow directions and properly respond to the cues provided. All participants reported during the screening interview that they had at least occasional difficulty rising from a standard height chair, but are able to do so independently a majority of the time. All participants were able to stand from a chair independently without the use of their arms at least 1 of every 4 attempts during uncued testing. As individuals with PD often have difficulty with initiation of movement due to bradykinesia[1] and difficulties changing between central sets,[49] it was anticipated that it would take multiple attempts to stand for some participants. If every attempt was considered an independent STS this would likely skew the data, however, this was controlled for within this study by the assessor documenting the number of attempts to stand prior to the patient giving up or successfully standing. Additionally, all participants achieved the minimum score of 22 points on the Montreal Cognitive Assessment (MoCA). One subject was excluded from the study for not attaining the minimum cut-off score. This cut-off was selected based on research validating the MoCA for use in determining the ability of individuals with PD to provide informed consent for research.[110]

3.2.1.2 Exclusion Criteria

Participants were required to meet specific exclusion criteria, Table 3.3. Candidates for this dissertation study were be excluded if they have a history of brain surgery for treatment of PD or are currently participating in a medication study, both of which could introduce an unnecessary covariate into the study. Other than idiopathic PD, all participants were required to be free of neurological, musculoskeletal, or other health conditions or cognitive impairments that

could impact the results of this dissertation study. Additionally, individuals with a body mass index greater than 35 were excluded from this study in order to reduce the likelihood of the presence of a covariate related to anthropomorphic outliers, since 85.7% of the United States population have a body mass index of less than 35.[111] The World Health Organization recommends utilizing body mass index norms for the country of interest rather than height or weight norms.[112]

Table 3.3 Inclusion and Exclusion Criteria

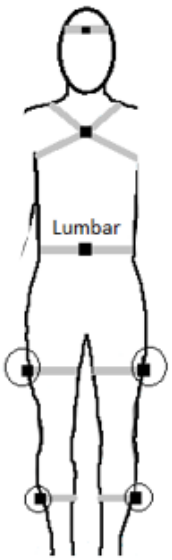
Inclusion Criteria	Exclusion Criteria
Diagnosed by a neurologist with idiopathic PD (PD group only)	Brain surgery for the treatment of PD
Stable on medications	Currently participating in a medication study
Able to follow directions	Body mass index greater than 35
Able to stand from a chair independently without the use of their arms at least 1 of every 4 attempts during uncued testing	Other than idiopathic PD, all participants will be required to be free of neurological, musculoskeletal, or other health conditions that impair the ability of the subject to complete a sit to stand.
Report at least occasional difficulty rising from a standard chair.	
Between the ages of 45 and 90	
Minimum Montreal Cognitive Assessment score of 22[110]	

3.2.2 Reliability of Tests and Measures

Kinematic and postural sway metrics were collected using APDM Mobility Lab's Opal Sensors and the Moveo Explorer Data Collection Program.[113] Mobility Lab's Opal Sensors are valid, reliable, and responsive to change in both individuals with PD and healthy adults.[114-116] The Opal Sensors weigh less than 25 grams, have dimensions of approximately 44x40x14 mm, and attach with lightweight straps. They utilize accelerometers, gyroscopes, and magnetometers in all 3 axes to gather data that is sent wirelessly to a computer in real time. Seven opal sensors were utilized,1 on each leg, 1 on each thigh, 1 attached to the lumbar spine, 1 attached to the

sternum, and 1 attached to the forehead, Figure 3.1.[117] Body worn sensors were not applied to the upper extremities for the purpose of this experiment. This sensor placement allowed for collection of the following kinematic metrics: neck flexion-extension; trunk flexion-extension; hip flexion-extension; knee flexion-extension; ankle dorsiflexion-plantarflexion.[113] Regarding the STS process, this sensor placement captured the following metrics: latency of initiation of movement, duration of the STS transfer. In addition, this sensor placement will allow for the following postural control data to be collected: coronal, sagittal, and transverse plane range of motion.[118]

Figure 3.1 Body Worn Inertial Measurement Unit Placement[118]



The MDS-UPDRS[119] was collected to grade the staging of PD for the experimental group. The MDS-UPDRS is valid, reliable, and responsive to change.[68,120] All testing was completed by a Movement Disorder Society trained rater. Scores on the MDS-UPDRS range from 0-199, with higher scores indicating a greater impact of PD symptoms.

The Parkinson's Disease Questionnaire-39 (PDQ-39) was utilized to measure the impact of PD on the participants' health related quality of life. The PDQ-39 is a self-report questionnaire that measures participation, is valid, reliable, and sensitive to change.[121-123] Scores on the PDQ-39 are calculated as a percentage and range from 0-100, with higher scores indicating a greater impact of symptoms.

As a measure of demographics, the 10 Meter Walk Test (10MWT) was completed by all participants. The 10MWT, a commonly utilized measure to determine gait speed (GS), is reliable and sensitive to change in those with PD.[124] A slower GS is indicative of a greater difficulties with ambulation. A 10-meter straight walkway was utilized in a hallway with solid colored flooring with tape lines marked on the wall near the floor at 0, 2, 8 and 10 meters. Tape will not be placed on the floor as it may provide an external cue that would provide altered results. Participants began at the first tape line and were instructed to "walk at a comfortable pace until I say stop," which occurred at the last tape line. The average of 3 trials was used as the 10MWT score.[125]

The MoCA was completed by all participants to determine their ability to provide informed consent and has been validated for this purpose. The MoCA is a 16-item test that measures visuo-spatial and executive functioning, memory, language, abstraction, and orientation. Karlawish, et al., validated the MoCA for use in determining the ability of an individual with PD to provide informed consent within research studies and recommended a cut off score of 22 or higher.[110]

3.2.2 Procedures

3.2.2.1 *Recruitment*

Subjects were recruited through a sample of convenience from local support groups, local health care providers, and already established pools of research subjects. Subjects were initially screened for appropriateness for inclusion in this study via telephone conversation following a group specific protocol (Appendices 1 and 2). Telephone screening included an overview of the study, including possible risks and benefits, time commitments, and location of the data collection, questions to ensure inclusion and exclusion criteria are met, and scheduling of sessions as appropriate. All candidates signed an informed consent form at the data collection site prior to data collection.

3.2.2.2 *Setting*

Data collection occurred within a university setting or at a community exercise facility in a quiet area with minimal distractions. All locations will be standardized for regulatory environmental factors.

3.2.2.3 *Training of Testers*

The MDS-UPDRS was completed by a Movement Disorder Society trained tester. Testers who collected the remaining demographic information of age, height, weight, years with symptoms, years since the diagnosis, gender, GS, and PDQ-39 score completed a standardized training to ensure consistency of all data collection. Data collection for both the uncued and cued STS transfers was completed by a tester who is trained in the use of the body worn sensors and patient cueing.

3.2.2.4 *IRB Approval and Informed Consent*

Institutional Review Board approval was attained for the proposed research project from Nova Southeastern University and Clarkson University and informed consent attained from each

participant prior to data collection. Site permission was gained from Rock Steady Boxing Syracuse.

3.2.2.5 *Data Collection*

For all participants, data collection occurred on a single date. Subjects were scheduled to begin testing 30 minutes after taking their regularly scheduled carbidopa-levodopa. This timeframe was selected as Hauser, et al found that "on" phase typically initiated around 45 minutes following immediate release or extended release levodopa was ingested.[126] No motor related testing took place until 1 hour following the medications being ingested. The 1-hour timeframe was selected to ensure that the "on" phase had been reached and motor measurements were taken during their period of optimal movement. Upon arrival, participants were educated about the purpose of the study, the process of the study, and their ability to opt out of continuing at any time. Each participant signed an informed consent form and underwent the MoCA to determine that they are able to provide informed consent. Then, the tester confirmed the last time they took their dopamine replacement medications and their next scheduled dose. Non-motor portions of the MDS-UPDRS, the PDQ-39, confirmation of date of birth, height, weight, confirmation of years with symptoms, and confirmation of years since diagnosis were completed between peak "off" and peak "on" time as time permits or following the completion of all time sensitive data collection. Sixty minutes following the patient taking their regularly scheduled PD medications, measurements that are time sensitive for the "on" phase were collected. These included uncued and experimental STS transfer kinematics, immediate standing "on" postural sway, the 10MWT, and "on" motor portions of the MDS-UPDRS, Appendix 3. A standard, backless, armless tub bench was used for all testing. Seat height for this study was standardized with knees in approximately 100 degrees of flexion in order to better understand the kinematics

of the movement beginning from a standardized joint position. Knee angle was confirmed in sitting through the use of a goniometer. Lowering the seat beyond 100 degrees of knee flexion alters the STS transfer significantly requiring greater hip angular velocity.[127] However, having the seat height lower than 90 degrees is more reflective of the situations during which individuals may need more assistance to perform a STS transfer in their daily lives. Additionally, all transfers began from a position with feet shoulder width apart and feet positioned 10 cm posterior to placement when the tibia is in vertical alignment, which are consistent with typical initial conditions of successful STS transfers.[128]

Prior studies have shown impaired motor learning in individuals with PD,[24] making it possible to increase the repetitions with a low risk of the effect of learning on STS transfers within a single session. Protocols for consistency were created, Appendix 4.

To ensure that uncued transfers were self-initiated, participants were given a prompt to complete a brief verbal recall activity then stand up after they are done. The prior study on the effects of audiovisual cueing during the STS transfer for people with PD reported a self-initiated uncued transfer. However, the authors report asking the patients to stand when they were ready.[8] It is possible that subjects utilized this prompt as an external cue to initiate standing. Completion of a cognitive task prior to standing reduced the likelihood of this occurring in the proposed study. Rest breaks between all transfers were provided and required to be at least 1 minute in duration, but longer as requested by the test subject, to reduce the effects of fatigue. The protocol to collect the STS data under the 3 conditions was randomized for each participant to decrease the learning effect. However, the protocol for each condition remained standardized, Appendix 4.

During the condition of external attentional focus of reaching to targets, the task was separated into 2 subcomponents of the transfer that was completed in a specific order to be

consistent with the suggested "cognitive movement strategies" suggest by Keus, et al.[129] For this condition, the tester was positioned to the more affected side of the patient in order to prevent falls. During the condition of external attentional focus of concurrent modeling, the tester was positioned directly opposite of the patient at a distance of 2.5 times the subject's arm length in order to prevent the tester and patient from touching during the transfer. If the tester and subject touch hands, the trial was stopped and the distance increased to 3 times the subject's arm length with the change documented on the data collection sheet. The tester was in an excellent position to guard the patient in this condition to prevent falls. During the condition of explicit cue for an internal attentional focus, the area in front of the patient was cleared from all potential "targets" that may increase the likelihood for an external attentional focus. To prevent falls, a tester was positioned to the more affected side of the subject. The tester was properly trained in guarding techniques for each condition.

For individuals in the healthy control group, all data collection occurred on the same day, Appendix 5. Uncued testing of STS will occur in the same manner as described for the PD groups in Appendix 4. However, data from the remaining 3 conditions was not collected since the research questions of this dissertation study focused on the effect of various types of cueing as measured by assimilation of dependent variables toward those of the healthy control group.

3.3 Data Analysis

Demographics were calculated and included age, gender, years with diagnosis, years with symptoms, health related quality of life as reported on the PDQ-39, disease severity as indicated by the MDS-UPDRS, and gait speed, as applicable. Mean and standard deviations were provided for interval and ratio level data.[107] For nominal and ordinal level data, medians and mode were presented.[107]

All dependent variable data was first analyzed to determine whether parametric assumptions were met. Only the kinematic data of change in hip angle compared to the uncued condition and change in height compared to the uncued condition were found to have a normal distribution. Selection of statistical analyses was based on the ability of the data to meet the assumptions for the test, the research questions, and the data available.

Data analysis for research questions 1 and 4 were completed as part of the first manuscript and details can be found in Chapter 4. Data analysis for question 3 was completed as part of the second manuscript and details can be found in Chapter 5. Data analysis for question 2 "is there a relationship between the latency of movement initiation and postural sway noted in the first 30 seconds of stand?" resulted in the acceptance of the null hypothesis and will be discussed here. Assessment of distribution of data determined that the sway data was not normally distributed. A Spearman Rank Order correlation was used to identify if a relationship between sway and latency was present. No relationship was identified.

3.4 Presentation of Results

Three manuscripts have been prepared for submission based on this dissertation study. The first "Modeling improves postural control following sit to stand in Parkinson disease" can be found in Chapter 4. The second "Impact of cues on motor control in sit to stand transfers for individuals with Parkinson disease" can be found in Chapter 5. The third "Standing taller than typical effects postural control in Parkinson disease" can be found in Chapter 6.

CHAPTER 4: First Manuscript: *Modeling improves postural control following sit to stand in Parkinson disease*

4.1 Contribution of Authors

CHAPTER FOUR

MODELING IMPROVES POSTURAL CONTROL FOLLOWING SIT TO STAND IN PARKINSON DISEASE

Contribution of Authors and Co-Authors

Author: Dr. Rebecca A Martin
Contributions:
Research project: Conceived, organized, and executed.
Statistical analysis: Designed and executed the statistical analysis.
Manuscript preparation: Wrote the first draft of the manuscript. Integrated feedback to complete the final draft of the manuscript.

Co-Author: Dr. Jennifer Canbek
Contributions to the research project:
Research project: Helped conceive the study design. Review and critique.
Data Analysis: Review and critique.
Manuscript preparation: Review and critique.

Co-Author: Dr. George Fulk
Contributions to the research project:
Research project: Helped conceive the study design. Review and critique.
Data Analysis: Review and critique.
Manuscript preparation: Review and critique.

Co-Author: Dr. Lee Dibble
Contributions to the research project:
Research project: Helped conceive the study design. Review and critique.
Data Analysis: Review and critique.
Manuscript preparation: Review and critique.

Co-Author: Dr. Ali Boolani
Contributions to the research project:
Data Analysis: Review and critique.

4.2 Manuscript Information Page

Rebecca Martin, George Fulk, Lee Dibble, Ali Boolani, Jennifer Canbek

Movement Disorders

Status of the Manuscript:

_x___ Prepared for submission to a peer-reviewed journal

_____ Officially submitted to a peer-review journal

_____ Accepted by a peer-reviewed journal

_____ Published by a peer-reviewed journal

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4.3 Manuscript in Journal Form

ABSTRACT

Background: Explicit cues are commonly used to overcome the effects of motor symptoms associated with Parkinson disease (PD). While much is known about the effects of explicit cues on gait for people with PD, little is known about the impact of explicit cues on postural sway during discrete tasks like sit to stand (STS) transfers. **Objective:** To identify if three different types of explicit cues provided during STS transfers of people with PD will result in postural sway during immediate standing that was more similar to healthy controls. **Methods:** This crossover study had 13 subjects in both the PD and healthy control groups. All subjects completed three trials of uncued STS transfers. The PD group additionally completed three trials of STS transfers in three conditions: external attentional focus of reaching to targets, external attentional focus of concurrent modeling, and explicit cue for an internal attentional focus. Body worn sensors collected sway data. Sway characteristics between the healthy control and PD groups was compared with Mann Whitney U tests. Friedman's Tests were used to compare sway characteristics between conditions. **Results:** Modeling was the only cue that resulted in decreased sway. The reaching to target and internal attentional focus cues had no impact on sway. However, incidences of the center of mass moving outside of the base of support were present for both reaching to targets and cues for an internal attentional focus. **Conclusions:** Modeling as a cue during STS for people with PD may safely reduce sway more than other commonly used cues.

Introduction

Postural instability is one of the cardinal signs of Parkinson disease (PD).[50] Long before people with Parkinson disease (PwP) develop a positive Pull test, they exhibit increased postural sway during static standing in both the sagittal and coronal planes as compared to healthy age matched peers.[130] Changes in postural sway have been linked to fall risk within this population.[130] Additionally, when verbal-cognitive dual tasking is introduced, individuals with PD experience significantly more sway.[130] Because of the progressive neurodegeneration seen with PD,[44] postural instability increases over time and impairs the ability of PwP to complete motor tasks like ambulation and transfers.

In addition to increases in postural sway, individuals with PD experience akinesia, bradykinesia, tremor, rigidity, and lack of automaticity. Explicit cues are one common intervention used to overcome the effects of many of these motor symptoms, though their effects on postural sway during discrete tasks are unclear. Functional magnetic resonance imaging has shown that explicit cues utilize neural circuits which bypass the basal ganglia.[74] Studies indicate that explicit cueing during gait can result in increased gait speed,[5,92] increased step length,[5,17] and decreased episodes of freezing during gait.[6] Five studies looked at the impact of continuous or discrete tasks in sitting, but did not provide any insight into the impact of cues on postural sway.

Multiple studies have examined the impact of providing explicit cues during the task of sit to stand (STS) transfers on the motor control of PwP.[8,83] One study reported that visual and auditory cues may result in decreased duration of the transfer, improved peak horizontal and vertical velocities, and improved joint torque time to peak.[8] Another study reported that explicit cues provided during the STS which had an external attentional focus reduced the duration of the

transfer and number of attempts to attain standing, but cues for an internal attentional focus resulted in a longer duration and latency period for the STS transfer (See Chapter 5). A third study reported a shorter duration of transfer and improved hip flexion torque after four weeks of training with explicit cues.[83] Each of these studies provide support for the use of explicit cues to improve motor control of PwP during the transfer. However, it is also important to understand the impact of these cues on postural control in immediate standing balance.

To the best of the authors' knowledge, no studies have examined the effect of cues provided during the STS transfer on postural control during immediate standing in PwP. Identifying the potential positive or negative impact of commonly applied cues on postural control will allow clinicians to make informed decisions regarding selection of cues and intervention designs. The purpose of this study was to identify whether three different types of explicit cues provided during STS transfers of people with PD led to postural control during immediate standing that was more similar to healthy controls. It was hypothesized that explicit cues which elicited an external attentional focus, modeling or reaching to targets, would result in improved postural control, while the cue that elicited an internal attentional focus would result in reduced postural control.

METHODS

Study Sample

A PD group and a healthy control (HC) group, each with 13 subjects, were recruited from exercise and support groups throughout central and northern New York. Inclusion criteria were: stable on medications for the past two months, able to follow directions, able to rise from a chair without assistance or use of their arms at least one of every four attempts during uncued testing,

be between the ages of 45 and 90, and score a minimum of 22 on the Montreal Cognitive Assessment (MoCA).[110] In addition, those in the PD group were required to have a diagnosis of idiopathic PD by a neurologist. Potential subjects were excluded from the study if they had brain surgery for the treatment of PD, were participating in a medication study, had a body mass index greater than 35 as this could significantly alter the mechanics of a STS transfer,[111,112] or had any other health conditions that would impair their ability to complete a STS transfer. Institutional Review Board approval was attained from Clarkson University and Nova Southeastern University. All subjects signed an informed consent form prior to participation in the study.

Study Design

A cross-over design was used in which all subjects in the experimental group completed each condition of the STS transfer. The HC group completed only the uncued STS condition to allow for comparison of postural sway for the individuals with PD across conditions against neurologically healthy controls.

Demographic Measures

To determine the profile of the sample additional data was collected. Age, gender, height, weight, and gait speed were collected from all subjects. Gait speed via the 10MWT has been found to be valid and reliable within healthy adults and adults with PD.[124] Additionally, those in the PD group completed the Parkinson Disease Questionnaire 39[121,122] and were tested by a trained rater on the Movement Disorder Society's Unified Parkinson's Disease Rating Scale.[68,121] These tests and measures have been found to be valid and reliable in adults with PD to assess the impact of PD on quality of life and disease severity.

Equipment and Dependent Variables

Sway data was collected during all STS trials utilizing an inertial measurement unit sensor (Opal Sensors and Moveo Explorer Data Collection Program, APDM Wearable Technologies, Portland, Oregon) placed on the lumbar spine. This sensor utilized gyroscopes, magnetometers, and accelerometers to collect sway data during the first 30 seconds of standing following a STS transfer. These sensors have been found to be valid and reliable in both healthy adults[131] and individuals with PD.[114,115] The unit communicated with a nearby computer to collect data in real time. Sway data collected included sway area, amount of sway in the sagittal plane, amount of sway in the coronal plane, sway jerk, and sway velocity. Sway area was defined as the 95% of the total area in which the individual sways and combines movement in both the sagittal and coronal planes.[118] Sway in the sagittal and coronal planes was defined as the total degrees of sway experienced in the related plane.[118] Sway jerk was a derivative of acceleration and provides information regarding the smoothness of movements.[131] Sway velocity was the average speed of sway movements[118]. Additionally, any incidences of the center of mass (COM) moving outside of the base of support (BOS), as demonstrated by the subject stepping or requiring assistance to prevent a fall, were operationally defined as a loss of balance (LOB) and the number was recorded.

Experimental Protocol

All data was collected in a private location in a university setting or a similar room in a community exercise facility during a single session. In order to ensure that all data for those in the PD group was collected during the same phase of medication, all motor data was collected in a 60-minute window that began exactly 60 minutes following the consumption of their regularly

scheduled dopamine replacement therapy.[55] This timing would result in data collection during peak "on" time.[132]

Both the HC and PD groups completed three trials of uncued STS trials. All STS trials began from a standardized position. Subjects were seated on a tub bench with the seat height adjusted such that their knees were in 100 degrees of flexion when their tibia were vertical. Then, the subjects' feet were placed shoulder width apart and moved posteriorly 10 cm to place the subjects' feet in the position most optimal for completing the STS transfer. Subjects were provided with a verbal prompt requesting that they respond in a single sentence and then stand immediately. The subjects were required to provide a verbal response prior to standing so that they could not use a cue from the tester to initiate their sit to stand motion. Sway data was collected during the first 30 seconds of standing using the inertial measurement unit sensor. In addition, subjects were monitored for incidences of COM moving outside the BOS that resulted in a step or required physical assistance to recover.

Those in the PD group additionally completed three STS trials in each of three conditions. The nine experimental trials were completed in a random order (Randomizer.org, Social Psychology Network, Middletown, Connecticut). Prior to each trial, the tester read a condition specific set of directions that asked the subject to focus on the current set of directions. Condition 1 (Modeling for External Attentional Focus): Each subject began in the standardized position with a second tub bench placed opposite the subject at a distance from the subject's toes equal to two and a half times the length of the subject's arm. The tester provided a verbal prompt of "when I stand up, stand with me" then the tester stood up. Condition 2 (Reaching to Targets for External Attentional Focus): Each subject began in the standardized position with a second tub bench placed opposite the subject at a distance from the subject's toes equal to the length of the

subject's arm. The tester provided the prompt to "reach to my hand" as the tester placed the dorsum of their hand on the front of the opposing chair. When the subject contacted the tester's hand, the test immediately cued the subject to "stand to the ceiling." Condition 3 (Cued for Internal Attentional Focus): Each subject began in the standardized position. All objects were removed from in front of the subject. The tester provided the cue to "bend forward at your hips and stand until your back is straight."

Data Analysis

Data were analyzed using *SPSS Version 26.0*. Demographics were calculated for both the PD and HC groups. Each dependent variable was assessed for normality utilizing the Shapiro-Wilk Test. Results were assessed for skewness and kurtosis. Sway data was graphed and reviewed looking for indications of learning or fatigue, such as trend lines suggesting improvement or decline throughout the course of trials. No trends were identified.

Comparison of Postural Sway Between the PD and HC Groups

Sway metrics observed during the uncued condition were compared between the PD and HC groups using Mann Whitney U tests with a significance level of $p < 0.013(0.5/4)$. For those sway metrics with significant differences found between the PD and HC groups during the uncued conditions, separate Mann Whitney U tests were completed between the uncued condition of the HC group and each experimental condition of the PD group. This was completed to identify if any experimental condition resulted in postural sway characteristics that were not significantly different than the HC group.

Comparison of Postural Sway Across Conditions for the PD Group

Separate Friedman's tests were utilized to compare postural sway area, sagittal plane sway, coronal plane sway, sway jerk and sway velocity of the PD group across all conditions of the STS transfers (uncued, modeling, reaching, and internal focus). Because we performed five separate Friedman tests (one for each measure of postural control) Bonferroni correction factors were applied, resulting in a $p<0.01$ (0.05/5) for statistical difference. If a significant difference was identified in the Friedman's test a post-hoc Mann Whitney U test was performed to identify between which cueing conditions the difference was. Because there were six potential comparisons a Bonferroni correction factor was applied resulting in $p<0.008$ (0.5/6). A McNemar Test (Bonferroni corrected $p < 0.008$, 0.05/6) was utilized to compare the occurrences of COM moving outside of the BOS across conditions.

RESULTS

Subjects in the PD group included eight males and five females with a mean age of 68.46(+/-9.11) years and gait speed of 0.87(+/-0.21) m/s. Subjects in the HC group included seven males and six females with a mean age of 67.31(+/-10.41) and gait speed of 1.23(+/-0.12) m/s. One candidate for the PD group was excluded from the study for not meeting the minimum criteria during cognitive testing. Additional demographic information can be found within Table 1.

[Insert Table 1 around here]

Comparison of Postural Sway Between the PD and HC Groups

There was a statistically significant difference ($p< 0.013$) between the PD and HC groups during the uncued condition with those in the PD group demonstrating increased sway area (PD= 5.192 degrees^2, HC= 0.767 degrees^2) and sway jerk (PD=5.03 m/s^3, HC= 0.644 m/s^3). No significant difference was noted between the PD and HC groups during the uncued condition for coronal

sway, sagittal sway, or sway velocities. When sway area was compared between the uncued condition of the HC group and the experimental conditions of the PD group, the significant difference remained across all conditions. However, when sway jerk was compared between the uncued condition of the HC group and the experimental conditions of the PD group, the significant difference was no longer present in the modeling condition (PD= 2.361 m/s^3, HC= 0.644 m/s^3). See Table 2. Additionally, no LOB occurred for either group in the uncued condition.

[Insert Table 2 around here]

Comparison of Postural Sway Across Conditions for the PD Group

There was a statistically significant difference between conditions ($p < 0.01$) for the PD group in coronal sway. Post-hoc testing identified that the modeling cue resulted in significantly less coronal sway than the uncued, reaching to target, or internal attentional focus conditions (uncued= 0.272 degrees, reach to targets= 0.265 degrees, modeling= 0.197 degrees, internal attentional focus= 0.288 degrees). See Table 3. Additionally, LOB occurred during both the reaching to target and internal attentional focus conditions. Two LOB incidents occurred during the reaching to target condition, one which was self-corrected with a step and one which required tester assistance to recover. One LOB incident occurred during the internal attentional focus condition and the subject required tester assistance to recover. A McNemar Test found no statistical significance ($p < 0.008$) regarding incidences of LOB between conditions for the PD group. See Table 4.

[Insert Table 3 around here]

[Insert Table 4 around here]

DISCUSSION

This study examined the effects of three different types of cueing on postural sway immediately following a STS transfer for PwP who experience occasional difficulty completing a STS from a standard height chair. When not cued, individuals with PD were found to have significantly greater sway areas and sway jerk in immediate standing than their healthy counterparts. A verbal cue paired with a modeling cue resulted in decreased postural sway during the first 30 seconds of standing without LOB. Neither a verbal cue paired with reaching to targets or a verbal cue for internal attentional focus decreased postural sway during the first 30 seconds of standing. However, both cues introduced LOB incidents that were not present during the uncued condition for either the HC or PD groups. Our study provides insight on the clinical application of cues utilizing modeling, target, and internal attentional cues during STS transfers and the impact of these cues on postural stability.

Modeling

An explicit verbal cue paired with modeling of the STS transfer was the only cue that resulted in improved balance during early standing for the PD group. This suggests that, especially for individuals with clinically important postural instability, modeling may be a safe way to cue individuals while completing standing tasks. Prior research suggested that increases in sway jerk may be the best sway characteristic to identify untreated PD.[131] In our study, modeling was able to reduce the level of sway jerk to not significantly different from the HC group.

In this study, modeling was completed in “mirror image” positioning with the tester directly across from the subject. However, this may not be possible in all environments. Consideration of

the theoretical basis for why modeling was effective suggests that replicating the paired verbal command and modeling from beside the patient, or even utilizing a squatting position without a seat, should provide similar results. Modeling with a paired verbal command provides an explicit cue, which functional magnetic resonance imaging[74] has shown utilizes neural pathways that are not reliant on the basal ganglia. Additionally, electromyography (EMG) studies have shown that, even in the absence of movement, similar activation occurs in the motor cortex when observation of familiar movements occurs.[133] This activation is known as the mirror neuron system and explains how humans can predict what happens next during a familiar sequence of events.[133] Research indicates that action observation, like watching a sit to stand transfer, could activate the mirror neuron system and prime the motor cortex for improved movements.[134]

Incidents of Loss of Balance

While no statistically significant changes in sway area, coronal sway, sagittal sway, sway jerk, or sway velocity were found when subjects completed the reaching to target or internal attentional focus conditions, incidences of LOB were present in both of these conditions. A McNemar Test indicated that the incidences of COM moving outside the BOS were not statistically significant. However, a Delphi study reported that a 25% decrease in falls should be considered a significant improvement following interventions for PwP.[135] While the authors of this study did not provide an operational definition for "fall," it is likely the losses of balance which required tester assistance to recover would have fit within their operational definition. It is less likely that the self-initiated step would fit into this definition. If we considered the sample as a whole, the percentage of LOB incidents by condition would still be under this criterion. However, with all three LOB incidents occurring with different subjects, it is important to note that based on the suggested MCID, two to three different subjects may have experienced clinically important

increases LOB incidents with the addition of an explicit cue. Two out of 13 subjects may have experienced a clinically meaningful increased in LOB incidents within the reaching to target cue. One out of the 13 subjects likely experienced a clinically meaningful increased in LOB incidents within the reaching to target cue.

Selection and Placement of Targets

Our findings of introduction of LOB incidents suggest that targets should be carefully selected to reduce risk of falls. During the reaching to target condition, individuals were cued to reach to the tester's hand, which occurred at the end of the pre-extension phase, then to "stand to the ceiling" to complete the extension phase. All subjects were able to reach the tester's hand without signs of imbalance. However, the two LOB incidents that occurred during the reaching to target condition occurred at the end of the extension phase, which could indicate that the ceiling was not an appropriate target.

Prior research has reported improved motor control during discrete tasks completed by PwP with the introduction of targets, but did not add to our understanding of the impact of utilizing targets on postural sway and balance since studied reaching tasks were completed in sitting.[94,95] To the best of these authors' knowledge, this is the first study to report on the impact of reaching to targets on postural sway. Based on prior research[15,62,94] and the additional findings within the current study, targets are likely an effective strategy to improve motor control for individuals with PD, but clinicians should strive to place targets in attainable locations that result in optimal movement. In the case of the STS transfer, it may have been better to have the tester place a hand at shoulder height for the subject to stand to. In the clinic, if a therapist is seeking to improve

upper extremity swing during a pre-gait stepping activity, it may be better to place a target at the maximally attainable distance than to encourage the patient to "reach toward that wall."

Cueing for an Internal Attentional Focus

Despite frequent use in clinical and home settings of the cue used in this study for an internal attentional focus, or similar phrases, this study adds to the limited body of evidence that questions the clinical utility of such cues for this population (See Chapter 5). No benefits were seen regarding improvements in postural sway, but rather one LOB incident was introduced with the addition of this cue. In combination with other reports that cues which elicit an internal attentional focus during STS transfers reduce the speed of the transfer, cueing for an internal attentional focus during STS transfers are not recommended at this time (See Chapter 5).

Limitations and Future Research

The sample size of this study, while adequate to find significance, is still relatively small and represents a limited range of disease severity. At this time, it is unclear if these findings would apply to individuals with more severe cognitive or motor impairments due to PD. Many different cues are provided in the clinic, however, in this study we only looked at 3 cues. Therefore, there may be other cues that are more effective at improving the postural stability of PwP in early standing that were not examined here. Lastly, this study looked at the effects of a one-time cue rather. Further research should examine the effects of practice on skill acquisition and retention of cued STS transfers.

CLINICAL IMPLICATIONS

Modeling while providing a succinct verbal cue may improve postural control while completing discrete standing tasks providing caregivers and clinicians with a useful cue that can be provided in most settings. With an understanding of the theoretical basis of modeling, caregivers and clinicians should complete modeling cues from any location that allows for PwP to clearly see what is being modeled and maximizes safety for both individuals.

Table 1. Subject Demographics

Characteristic	Healthy Control (n=13)	Subjects with PD (n=13)	95% CI
Gender (male/female)	7/6	8/5	
Age in years Mean(SD)	67.31 (10.41)	68.46 (9.11)	-9.07, 6.77
Height in cm Mean(SD)	165.72 (10.49)	172.00 (8.72)	-14.09, 1.52
Weight in kg Mean(SD)	82.36 (14.41)	84.73 (12.54)	-13.69, 8.95
10MWT (m/s) Mean(SD)	1.23 (0.12)	0.87(0.21)	-3.09, -1.03
Years with symptoms Mean(SD)		10.38 (9.18)	
Years with diagnosis Mean(SD)		5.38 (3.3)	
MDS-UPDRS – total score Median(range) Possible range: 0-199		70 (48-112)	
PDQ-39 - median(range) Possible range: 0-100		34 (4-74)	

10MWT= 10 Meter Walk Test; MDS-UPDRS= Movement Disorder Society's Unified Parkinson Disease Rating Scale; PDQ-39= Parkinson's Disease Questionnaire 39

Table 2. Comparing Sway Characteristics Across Parkinson Disease Conditions to the Healthy Control Uncued Condition

Postural Sway Characteristic	Healthy Control Mean (SD)	Parkinson Disease Mean (SD)			
	Uncued	Uncued	Reach to Targets	Modeling	Internal Focus
Sway Area (degrees^2)	0.767 (0.303)	5.192(7.074)*	4.824(7.100)*	3.147(3.893)*	4.316(4.798)*
Coronal Sway (degrees)	0.158(0.103)	0.272(0.177)	0.265(0.200)	0.197(0.141)	0.288(0.218)
Sagittal Sway (degrees)	0.445(0.248)	0.816(0.724)	0.702(0.425)	0.542(0.340)	0.601(0.396)
Sway Jerk (m/s^3)	0.644(0.417)	5.030(7.28)*	2.564(2.69)*	2.361(3.061)	2.320(2.501)*
Sway Velocity (m/s)	0.149(.153)	0.215(.178)	0.204(0.181)	0.157(0.141)	0.207(0.143)

*Sway characteristic of the PD group is significantly different than the HC group after the Bonferroni correction ($p<0.013$)

Table 3. Sway Characteristics Compared Across Conditions in Parkinson Disease Group

Sway Characteristic	Condition Mean (SD)			
	Uncued	Reach to Targets	Modeling	Internal Attentional Focus
Sway Area (degrees^2)	5.192(7.074)	4.824(7.100)	3.147(3.893)	4.316(4.798)
Coronal Sway* (degrees)	0.272(0.177) †	0.265(0.200) †	0.197(0.141) †	0.288(0.218)
Sagittal Sway (degrees)	0.816(0.724)	0.702(0.425)	0.542(0.340)	0.601(0.396)
Sway Jerk (m/s^3)	5.030(7.28)	2.564(2.69)	2.361(3.061)	2.320(2.501)
Sway Velocity (m/s)	0.215(.178)	0.204(0.181)	0.157(0.141)	0.207(0.143)

*Statistical significance was found for this postural sway characteristic through Friedman's test after Bonferroni correction ($p<0.01$)

† Statistical significance was found with post-hoc Mann Whitney U after the Bonferroni correction ($p<0.008$). Modeling resulted in significantly less coronal plane sway than the uncued or reaching to target conditions.

Table 4. Incidences of Loss of Balance*

Incidences of the COM moving outside the BOS	Uncued	Reaching to Target	Modeling	Internal Attentional Focus
Step	-	1	-	-
Assistance	-	1	-	1

COM= center of mass, BOS= base of support; No statistical significance was found after Bonferroni correction ($p < 0.008$) * Loss of balance operationally defined as the COM moving outside the BOS.

4.4 Instructions to Authors

Instructions to Authors from *Movement Disorders*

Excerpt from "Author Guidelines" for *Movement Disorders:*

> **Documentation of Author Roles**
> At the end of the manuscript, all authors must be listed, along with their specific roles in the project and manuscript preparation. These should include but not be restricted to: 1. Research project: A. Conception, B. Organization, C. Execution; 2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique; 3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique;

Excerpt from "Author Guidelines" for *Movement Disorders:*

> • **Research Articles:** Full-length articles should present new clinical or scientific data in a field related to movement disorders. The format should include: Structured Abstract: (Background, Objectives, Methods, Results, Conclusions) Up to 250 words with no abbreviations. Text: Up to 3700 words excluding of abstract, legends and references. Minimal abbreviations. Tables and/or figures: Up to 5. Legends: Should be concise and describe results without repeating data in text.

Excerpt from "Author Guidelines" for *Movement Disorders:*

> The text of the manuscript should be in the following sequence:
>
> **(2) Abstract**
>
> Structured Abstract: We require that authors submit structured abstracts. The page following the title page of Full-Length Articles should include an abstract of up to 250 words. The abstract should be structured. The page following the title page of a Brief Report should include a structured abstract of up to 150 words. Reviews should include an unstructured abstract. Viewpoints do not need any abstract.
>
> **(3) Introduction**
>
> Give a brief description of the background and relevance of the scientific contribution.
>
> **(4) Methods**
>
> Describe the methodology of the study. For experimental investigation of human or animal subjects, please state in this section that an appropriate institutional review board approved the project. For those investigators who do not have formal ethics review committees, the principles outlined in the "Declaration of Helsinki" should be followed. For investigations in human subjects, state in this section the manner in which informed consent was obtained from the subjects. A letter of consent must accompany

all photographs, patient descriptions, and pedigrees in which a possibility of identification exists. The authors are responsible for ensuring anonymity.

(5) Results

No specific regulations.

(6) Discussion

No specific regulations.

(7) Acknowledgment

No specific regulations. These may be published on line at the discretion of the editor.

(8) Authors' Roles

List all authors along with their specific roles in the project and preparation of the manuscript.

These may include but are not restricted to:

1) Research project: A. Conception, B. Organization, C. Execution;

2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique;

3) Manuscript: A. Writing of the first draft, B. Review and Critique.

Excerpt from “Author Guidelines” for *Movement Disorders:*

(13) Tables

Tables should be typed neatly, each on a separate page, with a title above and any notes below. Explain all abbreviations. Do not repeat the same information in tables and figures that is present in text. Tables and figures should be uploaded as individual files and not part of the manuscript text. (You do not need to mail hard copies of your manuscript).

***Tables and Figure Legends**

Double-space legends of fewer than 40 words for tables and figures.

CHAPTER 5: Second Manuscript: *Impact of cues on motor control in sit to stand transfers for individuals with Parkinson disease*

5.1 Contribution of Authors and Co-Authors

CHAPTER FIVE

IMPACT OF CUES ON MOTOR CONTROL IN SIT TO STAND TRANSFERS FOR INDIVIDUALS WITH PARKINSON DISEASE

Contribution of Authors and Co-Authors

Author: Dr. Rebecca A Martin
Contributions:
Research project: Conceived, organized, and executed.
Statistical analysis: Designed and executed the statistical analysis.
Manuscript preparation: Wrote the first draft of the manuscript. Integrated feedback to complete the final draft of the manuscript.

Co-Author: Dr. Jennifer Canbek
Contributions to the research project:
Research project: Helped conceive the study design. Review and critique.
Data Analysis: Review and critique.
Manuscript preparation: Review and critique.

Co-Author: Dr. George Fulk
Contributions to the research project:
Research project: Helped conceive the study design. Review and critique.
Data Analysis: Review and critique.
Manuscript preparation: Review and critique.

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Research project: Helped conceive the study design. Review and critique.
Data Analysis: Review and critique.
Manuscript preparation: Review and critique.

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Contributions to the research project:
Data Analysis: Review and critique.

5.2 Manuscript Information Page

Rebecca Martin, George Fulk, Lee Dibble, Ali Boolani, Jennifer Canbek

Journal of Neurologic Physical Therapy

Status of the Manuscript:

_x___ Prepared for submission to a peer-reviewed journal

_____ Officially submitted to a peer-review journal

_____ Accepted by a peer-reviewed journal

_____ Published by a peer-reviewed journal

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5.3 Manuscript in Journal Format

Abstract

Background and Purpose: Individuals with Parkinson disease (PD) often experience difficulty transferring from sit to stand (STS). Current evidence suggests cues which promote an external attentional focus improve gait and transfers for individuals with PD. However, current research utilizes cues which are difficult to replicate in clinical and home environments making the findings difficult to generalize or implement. The purpose of this study is to identify if three different types of explicit cues provided during STS transfers of people with PD will result in motor control characteristics that are more consistent with healthy controls. **Methods:** Twenty-six participants completed trials of self-initiated uncued STS transfers. Those in the experimental group also completed trials of STS transfers in 3 conditions: an external attentional focus of reaching to targets, an external attentional focus of concurrent modeling, and an explicit cue for an internal attentional focus. Data was collected by trained testers using valid and reliable body worn inertial measurement units. Unpaired t-tests compared movement characteristics between the healthy control and experimental groups. Repeated-measures ANOVAs were used to compare movement characteristics between conditions, with paired t-tests used for post-hoc analysis. **Results:** Modeling shortened the duration of the transfer. Reaching to targets likely resulted in a clinically meaningful decrease in attempts to attain stand. Cueing for an internal attentional focus resulted in increased latency and duration of the STS. **Discussion and Conclusions:** Cues for an external attentional focus were most effective at reducing the impact of motor impairments on STS for individuals with PD.

INTRODUCTION

As Parkinson disease (PD) progresses, individuals develop motor signs and symptoms that significantly impair movement. For example, bradykinesia increases time required to complete activities [1] while hypokinesia causes a decrease in the amplitude of movement.[136] Akinesia can make beginning motor tasks problematic.[137] Lack of automaticity may cause people with PD (PwP) to utilize motor control patterns similar to those just learning the motor task. Kyphotic posture can alter mechanics and impair function.[1] These and other impairments contribute to progressive functional decline throughout the course of the disease.[44]

In particular, PwP often struggle with STS transfers and experience increased latency of movement,[137] task duration,[1] and number of attempts to complete STS transfers and may need assistance. Even in mild to moderate stages of PD, many individuals spend up to 75% of their waking hours in sedentary activities.[13] Evidence suggests that when controlling for active task participation, a high association exists between time spent performing sedentary tasks and need for assistance to complete activities of daily living.[12] As PD progresses, caregiver burnout increases concurrently with an increased need for caregiver assistance,[138] which may include transfer assistance. One way to reduce caregiver burnout is to identify ways for PwP to improve their motor capabilities and complete STS transfers with less assistance.

Explicit cuing is theorized to compensate for akinesia, bradykinesia, and lack of automaticity and found to improve motor capabilities for PwP in certain contexts, such as during gait[5,92] and reaching tasks.[94,95] Functional magnetic resonance imaging suggests that explicit cues which draw an external attentional focus bypass faulty basal ganglia circuits found in PwP.[74] During gait, several studies report improved gait mechanics including improvements in speed,[5,92]

increased step length,[5,92] and reduced freezing with the provision of auditory rhythmic cues.[6] Common cueing methods used to improve gait speed and increase step length include brightly colored tape[15]on the floor, and lights shown on a pair of glasses.[17,19] Verbal cues to "take long steps" improved gait speed but produced varied effects on step length, and cadence.[93] The varied impact of different verbal cues suggests the importance of carefully selecting verbal cues for this population.

While research supports providing cues during gait, it is unclear whether these findings are generalizable beyond gait due to less evidence and conflicting results regarding non-gait related continuous tasks and discrete tasks. Improved speed and accuracy of button pushing were found with externally focused auditory cues as compared to visual cues provided during upper extremity sequencing tasks.[18] One study identified improved letter size from visual or auditory cues during writing.[22] Another suggests visual cueing impairs handwriting for PwP.[23] Two studies reported explicit cueing increased force production and speed during reaching.[94,95]

Specific to the discrete task of STS transfers, limited evidence is available regarding optimal cueing for patients with PD. A verbal cue to "get ready, stand up" paired with a visual cue of an 8x8cm light appearing at eye level resulted in increased horizontal and vertical speeds with a decreased duration of transfer.[8] A training program of biofeedback and cues to sit or stand based on highlighted boxes on a monitor reduced STS transfers duration and improved hip flexion torque.[83] While providing some support for the use of external cues for transfers, the strategies utilized within these studies are not transferable to home or most clinical settings. Additionally, these studies did not compare the use of cues that result in an internal versus external attentional focus.

While auditory, visual, verbal, and tactile cueing have been successful in gait and upper extremity tasks, based on current evidence, it is unclear if the external cueing during continuous tasks can be applied to the discrete task of a STS transfer for PwP. Therefore, the purpose of this study is to identify if three different types of explicit cues provided during STS transfers of people with PD will result in motor control characteristics that are more consistent with healthy controls: external attentional focus of concurrent modeling; external attentional focus of reaching to targets; and an explicit cue for an internal attentional focus. It was hypothesized that PwP would respond better to cues that create an external attentional focus, rather than the cue for an internal attentional focus.

METHODS

Study design

This is a cross-over design study with all participants in the PD group participating in an uncued condition and 3 experimental STS conditions. A healthy control (HC) group participated in the uncued condition to allow for comparison of motor control for the PwP across conditions against typical.

Study Sample: Twenty-six participants, 13 with PD and 13 healthy controls (HC), were recruited for this study from PD support groups and exercise classes throughout New York. Inclusion criteria included being between the ages of 45 and 90, being able to follow directions, being stable on medications for the past two months, report occasional difficulty rising from a standard chair but have the ability to stand independently without the use of their arms at least one of every four attempts during uncued testing, and score a minimum of 22 on the Montreal Cognitive Assessment (MoCA).[110] In addition, those in the PD group were required to have been

diagnosed with idiopathic PD by a neurologist. Candidates were excluded from the study if they had a history of brain surgery for the treatment of PD, were currently participating in a medication study, had a body mass index of greater than 35,[111,112] or had a comorbid neurological, musculoskeletal, or other health condition that impaired their ability to complete a STS transfer. All participants signed an informed consent prior to data collection and this study was approved by the Institutional Review Boards of Clarkson University and Nova Southeastern University.

Participants in both groups completed all data collection during a single session in a private location within either a university setting or a similar room located within a community exercise facility. All participants completed the MoCA[110] and the 10 Meter Walk Test[124] to determine gait speed, both of which are valid and reliable within healthy adults and PwP. In addition, those in the PD group completed the Parkinson Disease Questionnaire 39 (PDQ-39)[121] and all sections of the Movement Disorder Society's Unified Parkinson's Disease Rating Scale (MDS-UPDRS).[68] These measures are reliable and valid measures of impact of PD on health-related quality of life and disease severity, respectively. The MDS-UPDRS was administered by a rater trained in the proper administration and rating of this measure.

To reduce the impact of phase of medications on results of this study, all motor testing for PwP were completed between 60 and 120 minutes after taking the dopamine replacement therapies during the on phase of the medications.[55]

Instrumentation and Dependent Variables

Inertial measurement unit sensors (Opal Sensors and Moveo Explorer Data Collection Program, APDM Wearable Technologies, Portland, Oregon) were used to collect latency, duration of the

transfer, and joint angle changes during each trial. The sensors utilize accelerometers, gyroscopes, and magnetometers to infer joint kinematics and communicate with a nearby computer in real time. These sensors have been found to be valid, reliable, and sensitive to change in both healthy adults[116] and PwP.[114,115] Latency was measured as the time from the completion of the prompt until the moment of meaningful movement initiation. Duration was measured as the time from movement initiation until movement termination in standing. Joint angle changes were measured by subtracting the joint angles measured by the sensors in the pre-trial cued erect posture from the post-trial standing posture. Joint angle changes were measured at the hip in isolation as well as a combination of knee, hip, trunk, and cervical spine through seven sensors that were worn by each participant, one on each lateral leg, one on each lateral thigh, one attached to the lumbar spine, one attached to the sternum, and one attached to the forehead. Number of attempts was recorded as the number of times that the participant initiated or re-initiated movement to complete the STS transfer and was recorded by the tester.

STS Data Collection

All participants completed three trials of uncued STS transfers. For each trial, sensors were calibrated in cued erect quiet standing (tactile cueing to sternum and lumbar spine with verbal cue to stand tall). Following calibration participants sat on a height adjustable tub bench that allowed for the participant's knee to be in 100 degrees of flexion while sitting with the tibia in vertical. This is the lowest seat height prior to a significant change in STS mechanics.[127] The participant's feet were moved posteriorly 10 centimeters and placed at shoulder width apart, the foot positioning most consistent with successful STS transfers.[128] The participant was then provided with a prompt requiring them to provide a one sentence response then immediately

stand up. This prompt removed the possibility of the tester providing an initiating cue for the transfer.

Following uncued STS data collection, individuals in the PD group also completed three trials in each of the three experimental conditions: external attentional focus of modeling cue, external attentional focus of reaching to target cue, and internal attentional focus cue. The order in which the experimental trials were completed was randomized for each participant using an online randomizer (Randomizer.org, Social Psychology Network, Middletown, Connecticut). All trials in the experimental conditions began in the same standardized position described above. Prior to each trial, participants were reminded to focus on the current cue and not to try to utilize the strategy they felt was most effective. Then they were provided with a brief description of the current trail. For the modeling cue, a secondary tub bench was placed at a distance equal to 2.5 times the length of the participant's arm in front of their toe when the foot was in the standardized STS positioning. The tester sat on the opposing tub bench and provided the verbal cue "when I stand up, stand with me." For the reaching to target cue, a secondary tub bench was placed at a distance equal to the length of the participant's arm in front of their toe when the foot was in the standardized STS positioning. The tester placed the back of their hand on the front edge of the opposing tub bench and provided a verbal cue to "reach to my hand." Immediately upon contact of the participant's hand with the tester's hand the tester provided a verbal cue to "stand to the ceiling." For the internal attentional focus cue, all objects were removed from in front of the participant. The tester provided the verbal cue to "bend forward at your hips, then stand until your back is straight."

Data Analysis

Data were analyzed using *SPSS Version 26.0*. Gender, age, height, weight, and gait speed were calculated for both groups. In addition, years with symptoms, years with diagnosis, total scores for the MDS-UPDRS, and the PDQ-39 were calculated for the PD group. All dependent variables were graphed and reviewed for the presence of trend lines that may indicate fatigue or learning. No trend lines were identified.

Comparison of Motor Control Between the HC and PD Groups

Motor control characteristics during the uncued condition were compared between the HC and PD groups using paired t-tests or their non-parametric alternative with a significance of $p < 0.013(0.5/4)$. When a significant difference was identified between the characteristics in the uncued conditions, additional t-tests were completed between the uncued condition of the HC group and the experimental conditions of the PD group. This was completed to determine if any of the experimental conditions resulted in the elimination of the significant difference found between uncued conditions for that characteristic.

Comparison of Motor Control Between Conditions of the PD Group

Separate repeated measures ANOVAs for parametric data or their non-parametric alternative were utilized to identify overall between task condition differences in each motor control characteristic. Because five separate ANOVAs were performed (one for each dependent variable) the Bonferroni correction factor resulted in a $p<0.01$ (0.05/5) for statistical difference. When significance was found through the ANOVA, post-hoc paired t-tests or their non-parametric alternative were performed to identify which conditions were statistically different.

Because six combinations of conditions were possible, the Bonferroni correction factor was set at $p<0.008$ (0.5/6).

RESULTS

The PD group consisted of eight males and five females (mean age=68.46+/-9.11 years, gait speed=0.87+/-0.21 m/s). The HC group consisted of seven males and six females (mean age=67.31+/-10.41, gait speed=1.23+/-0.12 m/s). Participant characteristics are presented in Table 1. One candidate was excluded from the PD group secondary to not attaining the minimum score on the MoCA. Twelve of the 13 participants in the PD group were taking dopamine replacement therapies. No incidences of the center of mass (COM) moving outside of the base of support (BOS) occurred during the uncued condition for either group. However, 2 incidences of the COM moving outside of the BOS occurred during the reaching to target condition and 1 incidence of the COM moving outside of the BOS occurred during the internal attentional focus condition. These trials were included in the data analysis. No other adverse events occurred.

---Insert Table 1 around here---

Comparison of Motor Control Between the HC and PD Groups

We found a statistically significant difference ($p<0.013$) between the HC and PD groups with the PD group demonstrating a longer duration of the transfer (PD= 3.80sec, HC=1.8sec), longer latency (PD=3.22sec, HC=0.58sec), significantly different combined joint angle changes (PD=2.10 degrees, HC=2.18 degrees), and significantly different hip angle changes (PD=2.51degrees, HC=0.83 degrees) between the PD and HC groups. No significant difference in number of attempts was found between groups. When latency, change in combined joint angles, and change in hip angle were compared between the experimental conditions of the PD

group and the uncued condition of the HC group, the significant differences remained. However, when duration was compared between the experimental conditions of the PD group and the uncued condition of the HC control group, it was found that the significant difference was no longer present during the modeling condition (Modeling=2.85sec, HC1.8sec). See Table 2.

--- Insert Table 2 around here ---

Comparison of Motor Control Across Conditions for PD

We found a statistically significant difference ($p \leq 0.01$) between conditions of the PD group for duration of the transfer and latency. Internal attentional focus condition resulted in a significantly longer duration (5.60sec) than the uncued (3.80sec), reaching to targets (3.12sec), or modeling (2.85sec) conditions. Modeling (2.85sec) resulted in a significantly shorter duration than uncued (3.80sec) condition. The reaching to targets (1.34sec) and modeling (1.93sec) conditions both resulted in significantly shorter latency periods as compared to the internal attentional focus condition (5.40sec). No statistically significant different was found between conditions for change in combined joint angles or change in hip angle. See Table 3.

--- Insert Table 3 around here ---

DISCUSSION

We investigated the effects of three different types of explicit cueing on STS transfers in PwP on motor control, modeling, reaching to targets, and an explicit cue for an internal attentional focus. Modeling resulted in a statistically significant reduction in bradykinesia, while reaching to targets may have resulted in a clinically important reduction in hypokinesia during the pre-extension phase of the STS transfer. A degradation in motor control was noted in response to an

explicit cue for an internal attentional focus. The results of this study suggest that there are important considerations for each type of cue, modeling, provision of targets, and cueing for an internal attentional focus.

Modeling

The modeling condition resulted in reduced bradykinesia of the STS transfer as compared to the uncued and internal attentional focus conditions for the PD group, indicating that it may be an appropriate strategy to improve movement speed. Additionally, the modeling condition was the only condition during which the PD group did not require significantly more time than the HC group to complete the transfer. Modeling reduced the duration of the transfer by nearly 25% from 3.8 seconds to 2.8 seconds, bringing the duration closer to those in the HC group who had a duration of 1.8 seconds. One potential mechanism that has been proposed to explain the effect of modeling is the activation of mirror neurons.[133] This could mean that the tester modeling the STS just prior to the individual with PD completing it may have resulted in a motor priming effect[134] which increased the automaticity of the movement. No incidences of the COM moving outside of the BOS occurred with this cue, suggesting that it may be appropriate for implementation by caregivers and clinicians who are not able to provide substantial physical assistance. To the best of the authors' knowledge, this is the first study to look at the impact of modeling in isolation on motor control in PD. However, our findings are consistent with prior research that suggest improvements in motor control for PwP when cues elicit an external attentional focus.[6,15,17]

Reaching to Targets

Concise verbal cues combined with appropriate targets may be the most efficient cue for individuals who experience akinesia. While reaching to targets did not result in a statistically

significant reduction in attempts to stand, it is likely that a clinically important reduction is present. The HC group never required more than one attempt to stand. However, additional attempts were needed in all conditions for the PD group (uncued=1.31, reaching to targets=1.07, modeling=1.28, and internal attentional focus=1.47). If the typical person stands up 46+/-17 times in a day,[139] that could mean that the provision of targets during transfers may reduce attempts by up to 15 per day. Because prior research has shown that failed attempts at motor tasks leads to a decreased attempts to complete the task,[140] it is important to reduce the number of failed attempts experienced during STS transfers.

The STS transfer has 2 main components of the execution phase, the pre-extension and extension phases. A failed attempt to complete a STS may result from inadequate forward weight transfer during the pre-extension phase due to hypokinesia. Providing a target in front of an individual with PD at a distance equal to their arm's length in front of their foot provides an external cue for how far forward they need to translate their weight to be within their new BOS and complete a successful transfer. This is consistent with prior research that found improvements in amplitude of movements with the introduction of targets.[15,17,22] Because 2 incidences of the COM moving outside of the BOS occurred during the reaching to target condition, clinicians and caregivers who cannot provide adequate physical assistance to recover from a loss of balance should consider the use of modeling over this cue.

Internal Attentional Focus

The explicit cue for an internal attentional focus did not provide compensations for any motor signs or result in improved motor control during the STS transfer for PwP. In fact, the cue to "bend forward at your hips, then stand until your back is straight" resulted in a significantly

longer transfer than all other conditions, including the uncued condition. This indicates that this type of cue may worsen the effects of bradykinesia. Additionally, the internal attentional focus cue resulted in a significantly longer latency period than the other two experimental conditions and was the only condition with a latency period that was significantly longer than the HC group indicating that it may also worsen the impact of akinesia. This cue was included within this study because it is similar to commonly provided cues within clinical and home settings. While it was not expected that this cue would improve motor control during STS transfers for PwP, it was important to include in order to better understand the impact of commonly utilized clinical cues. With a worsening of bradykinesia and akinesia and the introduction of an incidence of the COM moving outside of the BOS, the evidence would suggest that cues which elicit an internal attentional focus are not optimal for PwP.

Limitations and Directions for Future Research

Only three commonly used types of cues were studied in this project. Other cues that could be easily implemented in all settings may be effective and should be studied in the future. The sample size is relatively small and included a limited range of disease severity making it unclear if the results of this study would apply to those individuals with more severe impairments due to PD. Additionally, the results of this study provided information about the effect of a single cue during one training session. For this reason, these results should not be generalized to which type of cue may be retained and continue to be effective after a period of no practice. Future research should examine the skill acquisition and retention of such training programs.

CONCLUSIONS

The results of this study support that cues which provide an external attentional focus may result in important improvements in motor control during STS for PwP. This finding is consistent with cue and reaching studies related to gait and PD[5,6,92,94] and provides further evidence of the utility of cues during a functionally relevant discrete task. The cues provided within this study which elicit an external attentional focus, reaching to targets and modeling, both improved motor control, but only modeling significantly reduced the duration of the transfer.

Table 1. Participant Demographics

Characteristic	**Healthy Control (n=13)**	**Participants with PD (n=13)**	**95% CI**
Gender (male/female)	7/6	8/5	
Age (years)	67.31 (10.41)	68.46 (9.11)	-9.07, 6.77
Height (centimeters)	165.72 (10.49)	172.00 (8.72)	-14.09, 1.52
Weight (kilograms)	82.36 (14.41)	84.73 (12.54)	-13.69, 8.95
10MWT (meters/second)	1.23 (0.12)	0.87(0.21)	-3.09, -1.03
Years with Diagnosis		5.38 (3.3)	
Years with Symptoms		10.38 (9.18)	
PDQ-39 - median(range) Possible range: 0-100		34 (4-74)	
MDS-UPDRS –total score Median(range) Possible range: 0-199		70 (48-112)	

CI= Confidence Interval, PDQ-39= Parkinson's Disease Questionnaire 39, MDS-UPDRS= Movement Disorder Society's Unified Parkinson's Disease Rating Scale

Table 2. Movement Characteristics Compared to the Healthy Control Group

Motor Control Characteristic	Healthy Control Mean(SD)	Parkinson Disease Mean(SD)			
	Uncued	Uncued	Reach to Targets	Modeling	Internal Focus
Attempts to attain standing	1(0)	1.31(0.54)	1.07(0.16)	1.28(0.51)	1.47(0.76)*
Duration in seconds	1.80(0.65)	3.8(1.67)*	3.12(1.34)*	2.85(1.45)	5.6(3.36)*
Latency in seconds	0.58 (0.14)	3.22(3.73)*	1.34(0.80)*	1.93(1.68)*	5.4(6.30)*
Change in Combined Joint Angle (degrees) (lower # is taller)	2.18(4.05)	2.10(5.60)*	-1.22(7.50)*	8.21(11.36)*	-2.19(15.31)*
Change in Hip Angle (degrees) (lower # is taller)	0.83(1.4)	2.51(3.37)*	-0.43(4.27)*	4.85(5.27)*	1.79(3.65)*

*Motor control characteristic of the PD group is significantly different than the HC group after the Bonferroni correction ($p<0.013$)

Table 3. Comparison of Movement Characteristics Across Conditions in Parkinson Disease Group

Motor Control Characteristic	Condition Mean (SD)			
	Uncued	Reach to Targets	Modeling	Internal Focus
Attempts to attain standing	1.31(0.54)	1.07(0.16)	1.28(0.51)	1.47(0.76)
Duration in seconds*	3.8(1.67)†	3.12(1.34)†	2.85(1.45)†	5.6(3.36)†
Latency in seconds*	3.22(3.73)	1.34(0.80)†	1.93(1.68)†	5.4(6.30)†
Change in Combined Joint Angle (degrees) (lower # is taller)	2.10(5.60)	-1.22(7.50)	8.21(11.36)	-2.19(15.31)
Change in Hip Angle (degrees) (lower # is taller)	2.51(3.37)	-0.43(4.27)	4.85(5.27)	1.79(3.65)

*Statistical significance was found for this postural sway characteristic through Friedman's test after Bonferroni correction ($p<0.01$)

† Statistical significance was found with post-hoc Mann Whitney U after the Bonferroni correction ($p<0.008$); Internal attentional focus had a significantly longer duration than the uncued, reaching to targets, or modeling conditions. Modeling had a significantly shorter duration than baseline. The reaching to targets and modeling conditions both had significantly shorter latency periods as compared to the internal attentional focus condition.

5.4 Instructions to Authors

Excerpt from "Instructions for Authors" for *Journal of Neurologic Physical Therapy:*

> **Manuscript Preparation**
> All manuscripts should be prepared in Microsoft Office Word, manuscripts should be double-spaced using 1-inch margins and at least 12-point font. All text pages created using Word (including Tables and References) should be contained in a single document.

Excerpt from "Instructions for Authors" for *Journal of Neurologic Physical Therapy:*

The first submission of a manuscript may not exceed 3500 words of text (not including the Abstract, Figure Legends, and References). Unless otherwise stated (see Manuscript Categories), materials should be prepared in the following order.

Abstract. An abstract not exceeding 250 words should be included at the beginning of the MS Word document. This Abstract should be the same as the Abstract that is entered into Editorial Manager during submission. For Systematic Reviews and Research Articles, abstract content should be organized according to the following headings: Background and Purpose, Methods, Results, Discussion and Conclusions.

Excerpt from "Instructions for Authors" for *Journal of Neurologic Physical Therapy:*

Text. For Systematic Reviews and Research articles, the text is divided into sections including: Introduction, Methods, Results, Discussion, and Conclusions.

Excerpt from "Instructions for Authors" for *Journal of Neurologic Physical Therapy:*

Text must be free of ageist and sexist terminology. The nomenclature of disorders should be referred to without the possessive form (ie use Parkinson disease rather then Parkinson's disease). Manuscripts must be prepared using *person-first* language. Language such as "*persons with stroke*" is preferable to "patients with stroke" as the former recognizes that the individual is a partner in the health care process. If the individuals who are being referred to have consented to participate in a study, then the term "participants" is appropriate.

Excerpt from "Instructions for Authors" for *Journal of Neurologic Physical Therapy:*

As noted in the general instructions, comparative studies should report between-groups differences in the form of mean between-group differences or odds ratios with 95% confidence intervals, or other description of effect size.

Tables. Each table should be single-spaced and placed on a separate page at the end of the manuscript text document. Each table should have a brief title and should be numbered consecutively in the order of their citation in the text. Any references cited within a table must be numbered in sequence with the preceding text relative to the location at which the table is to be inserted. Authors must indicate in in the text file the approximate location where tables are to be inserted (eg, "---insert Table 1 about here---")

CHAPTER 6: Third Manuscript: *Standing taller than typical effects postural control in Parkinson disease*

6.1 Contribution of Authors

CHAPTER SIX

STANDING TALLER THAN TYPICAL EFFECTS POSTURAL CONTROL IN PARKINSON DISEASE

Contribution of Authors and Co-Authors

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Contributions:
Research project: Conceived, organized, and executed.
Statistical analysis: Designed and executed the statistical analysis.
Manuscript preparation: Wrote the first draft of the manuscript. Integrated feedback to complete the final draft of the manuscript.

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Contributions to the research project: Helped conceive the study design. Review and critique.
Contributions to the data analysis: Review and critique.
Contributions to the manuscript preparation: Review and critique.

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Contributions to the data analysis: Review and critique.
Contributions to the manuscript preparation: Review and critique.

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Contributions to the data analysis: Review and critique.
Contributions to the manuscript preparation: Review and critique.

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Contributions to the data analysis: Review and critique.

6.2 Manuscript Information Page

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Neurorehabilitation and Neural Repair

Status of the Manuscript:

_x___ Prepared for submission to a peer-reviewed journal

_____ Officially submitted to a peer-review journal

_____ Accepted by a peer-reviewed journal

_____ Published by a peer-reviewed journal

Published by Lippincott Williams & Wilkins

6.3 Manuscript in Journal Format

Abstract

Objective: Falling is a common problem for individuals with Parkinson disease (PD). Studies show that sit to stand transfers challenge postural stability within this population. Explicit visual and verbal cues can impact motor outputs for individuals with PD. The purpose of this study was to determine if a relationship exists between standing taller than typical as a result of an external cue and postural stability immediately following sit to stand transfers for individuals with PD. *Methods:* Thirteen subjects completed nine sit to stand trials across three different experimental conditions. A Spearman-rank test was used to analyze data for a relationship between standing taller than typical and postural sway. *Results:* A moderate positive correlation between standing taller than typical and postural sway, indicating a decrease in postural stability. *Conclusions:* External cues that result in the most erect posture following a sit to stand transfer may also decrease postural stability for individuals with PD.

Keywords

Parkinson disease, posture, balance, cues, fall

Introduction

A 2013 systematic review supports that somewhere between 35 and 95% of individuals with Parkinson disease (PD) fall each year.[141] Of those who have fallen in the past year, 70% are likely to experience recurrent falls.[141] Falls resulted in a decreased quality of life for individuals with PD across all domains of the Parkinson's Disease Questionnaire-39 (PDQ-39), but most significantly for the domains of activities of daily living and mobility.[142] Additionally, falls are an important predictor of self-reported caregiver burden in those caring for individuals with

PD.[143] In a 2017 United States study of 16,368 patients with PD who fell within the past year, an average cost per fall of $1,471, with a range of $715-2,553 (95% CI) was reported.[144] With an average of 1.6% of Medicare beneficiaries having a diagnosis of PD,[10] reducing fall risk in this population could create significant cost savings, improvements in quality of life, and decreased caregiver burden.

Transfers have been identified as a key cause of falls for individuals with PD, with up to 21% of falls being linked to transfers.[145] Difficulty during transfers may occur for a number of reasons for this population, including difficulty with switching between central sets,[49] lack of self-awareness of body positioning,[75] poor muscle recruitment patterns,[99,105] lack of automaticity,[2] and kyphotic posture.[1] While not considered one of the four cardinal signs of PD, which are tremor, rigidity, bradykinesia, and postural instability,[1] kyphotic posture is a common sign of PD that becomes increasingly problematic as the disease progresses.[146] Kyphotic posture may be problematic for both the initiation of the sit to stand (STS) transfer, as it may make forward translation of the center of mass (COM) more difficult, and the termination of the STS transfer, as it may reduce the overall amplitude of the transfer resulting in an early termination. Kyphotic posture has been linked to an increase in falls[147] in some research, but other researchers have suggested that kyphotic posturing may be a compensation for poor balance that reduces fall risk.[148]

Current research indicates that external cues, such as visual cues[7,15-17,19] or auditory cues,[4-6,15,17,19] can improve gait mechanics for individuals with PD when appropriately applied. Successful visual cues include tape lines on the floor[15] a flashing light presented on the lens of glasses worn by the subject,[17] or light flashing to a rhythm on the lens of glasses worn by the subject.[6,19] Verbal cues to take longer steps or increase arm swing have shown improvements in gait[7,93]

while verbal cues to increase gait speed reduced step length and had undesirable effects on cadence.[7]

Because the forward stooped posture commonly seen in individuals with PD is atypical as compared to the healthy population, healthcare professionals and caregivers may provide similar cues that result in a more erect posture in an attempt to normalize the appearance or function of these individuals. Currently, it is unclear what effect cues to stand taller than typical may have on standing postural sway for this population. Therefore, the purpose of this study was to determine if a relationship exists between joint angle changes from uncued to the cued conditions and postural sway noted in the first 30 seconds of stand following a STS transfer in individuals with PD. It was hypothesized that cues which resulted in a taller than typical standing posture following the sit to stand transfer would decrease postural stability.

Methods

Subjects

Prior to recruitment, this study was jointly approved by the Institutional Review Boards (IRB) of both Nova Southeastern University and Clarkson University and was completed in accordance with the ethical principles outlined in the Declaration of Helsinki. Informed consent was attained from all subjects prior to data collection. A sample size estimation was completed utilizing a 0.05 level of significance, a power of 0.8, and an effect size of 0.85. The level of significance and power was selected based on norms within the research field. The effect size was calculated from data presented in a similar study which identified the effects of different types of external cues on gait.[3]

Subjects were recruited from support groups and exercise classes in upstate New York. Subjects met the following inclusion criteria: diagnosed by a neurologist with idiopathic PD, on stable dosages of any dopamine replacement therapies, attain a minimum score of 22 points on the Montreal Cognitive Assessment,[110] report during the screening interview that they "have at least occasional difficulty rising from a standard height chair but are able to do so independently a majority of the time," and stand from a chair independently without the use of their arms at least one of every four attempts during uncued testing. Candidates were excluded from the study if they had a history of brain surgery for the treatment of PD, were currently participating in a medication study, had a body mass index greater than 35,[111,112] or had a comorbid neurological, musculoskeletal, or other health related condition that impaired the ability of the subject to complete a sit to stand transfer.

Study Design

A secondary analysis was completed of data collected during an investigation into optimal cueing during sit to stand transfers for individuals with PD. The original study was a cross-over design that asked all subjects to complete a total of 24 sit to stand transfers divided evenly across four conditions, which included an uncued condition and in response to three types of explicit cues on the task of STS for individuals with PD, external attentional focus of reaching to targets, external attentional focus of concurrent modeling, and an explicit cue for an internal attentional focus. After 6 uncued trials, the remaining 18 trials were randomized (Randomizer.org, Social Psychology Network, Middletown, Connecticut). Both kinematic and sway data was collected together during the first three trials of each condition. The uncued condition was utilized to determine "typical" for the subject. Therefore, nine experimental trials were completed by each subject for a total of 117 trials across subjects.

Data collection

Kinematic and postural sway metrics were collected using inertial measurement units (IMUs) (Opal Sensors and Moveo Explorer Data Collection Program, APDM Wearable Technologies, Portland, Oregon). [113] The IMUs are valid, reliable, and responsive to change in individuals with PD.[114-116] The IMUs utilize accelerometers, gyroscopes, and magnetometers in all three axes to gather data that is sent wirelessly to a computer in real time. Seven IMUs were utilized, one on each lateral leg, one on each lateral thigh, one over the lumbar spine, one over the sternum, and one on the forehead.[117] This IMU placement allowed for collection of bilateral knee, bilateral hip, lumbar spine, and cervical spine flexion-extension joint angle changes. Kinematics were derived from joint angle changes. Postural sway data in immediate standing, including average sway area, coronal sway range, sagittal sway range, sway jerk, and sway velocity, was collected through the IMU placed over the lumbar spine.[113,118] Sway data collected included 95% sway area, sway in the sagittal and coronal planes, sway jerk, and sway velocity. Sway area was defined as the 95% of the total area through which the IMU traveled in both the sagittal and coronal planes.[118] Sway in the sagittal and coronal planes was measured as the total degrees of sway in the related plane.[118] Sway jerk provides information regarding the smoothness of movements and was a derivative of acceleration.[131] Sway velocity was defined as the average speed of all sway movements[118].

Data was collected during a single session. To ensure that all subjects were tested in the same phase of medication, all applicable subjects were scheduled to begin testing 30 minutes after taking their regularly scheduled carbidopa-levodopa during the peak on phase of dopamine replacement therapies.[55] Following attainment of informed consent, non-motor testing was initiated and carried out until one hour after the subject ingested their dopamine replacement

therapy medications, at which time motor testing was completed. No motor testing exceeded a one-hour time frame. Any remaining non-motor testing was completed following the motor testing. Non-motor testing included the Montreal Cognitive Assessment, non-motor portions of the Movement Disorder Society's Unified Parkinson's Disease Rating Scale,[68] the Parkinson Disease Questionnaire-39,[121] height, weight, and confirmation of date of birth, years with symptoms, and years since diagnosis. Motor testing included uncued and experimental sit to stand transfer kinematics, immediate standing postural sway, the 10MWT, and motor portions of Movement Disorder Society's Unified Parkinson's Disease Rating Scale.

Data collection for the sit to stand transfers was standardized. A single, armless tub bench was used for all testing. Seat height for this study was standardized with knees in 100 degrees of flexion when both tibia were positioned vertically, the lowest seat height prior to a significant change in transfer mechanics.[127] All transfers began with feet positioned shoulder width apart and 10 cm posterior to the foot placement with tibia in vertical alignment.[128] Recalibration of sensors took place in standing prior to each sit to stand transfer with the tester providing tactile cueing at the lumbar spine and sternum while saying "stand tall" to cue subjects into their fully erect posture. Sensors collected data from the time of calibration through stand to sit, a wash out period, STS, and the first 30 seconds of standing.

Data Analysis

To better understand the impact of standing taller than typical, the trial with the greatest increase in normalized combined joint angle was identified for each study subject. Normalized combined joint angles of the knees, hips, back, and neck as compared to the subject's uncued average was calculated for each trial utilizing the following formulas:

Formula 1. Trial combined joint angle change

$$combined\ joint\ angle\ in\ standing\ post\ trial$$
$$-\ combined\ joint\ angle\ in\ standing\ pretrial$$
$$= trial\ combined\ joint\ angle\ change$$

Formula 2. Normalized combine joint angle change

$$\frac{(trial\ combined\ joint\ angle\ change - uncued\ average\ combined\ joint\ angle\ change)}{uncued\ average\ combine\ joint\ angle\ change}$$
$$= normalized\ combined\ joint\ angle\ change$$

Sway data from the same trial for each patient was analyzed to determine if a correlation was present. Sway data analyzed within the study included sway in the sagittal plane, sway in the coronal plane, sway area, sway jerk, and sway velocity. Normalized sway data was calculated utilizing the following formula:

Formula 3. Change in sway metric

$$\frac{trial\ sway\ metric\ - baseline\ average\ sway\ metric}{baseline\ average\ sway\ metric} = change\ in\ sway\ metric$$

Sway data was converted to an ordinal scale with each trial being ranked as a separate level to allow for the inclusion of loss of control of the COM within the base of support (BOS) ranked as the greatest amount of sway. With the ordinal level data, Spearman rank-order correlations were used to identify relationships between the degree of normalized combined joint angle increase as compared to uncued and the change in normalized sway characteristics. The a priori sample size calculation needed to identify a statistically significant different, with 80% power and an alpha level of 0.05, was 13 subjects.

Results

Thirteen subjects [age in years= 68.46(9.11); eight male/ five female; disease severity as measured by the Movement Disorder Society's Unified Parkinson's Disease Rating Scale= 70/199(48-112)] participated in this study. Complete sample demographics are reported in Table 1.

[Insert Table 1 around here]

Each subject within this study had at least one trial that resulted in more erect than typical standing posture. A moderate level positive correlation was identified between normalized combined joint angle change and normalized change in coronal plane sway, sagittal plane sway, and sway velocity with $p<.05$ when the subject was standing more erect than typical, indicating increased sway in a more erect posture. See Table 2.

[Insert Table 2 around here]

Discussion

According to our findings, individuals with PD who stand with a more erect posture than typical may experience a decrease in standing postural control. We found a moderate, positive relationship between a more erect posture at the culmination of the STS transfer and postural sway in early standing. This provides further evidence to support the theory that kyphotic posturing may be a compensation to reduce the risk of falls for this population.[148] While explicit cues are commonly utilized to improve motor performance for individuals with PD, our findings suggest that visual and verbal cues which create the most erect posture for an individual may also

result in the greatest increase in postural sway in both the coronal and sagittal planes within this population.

Our findings are consistent with multiple studies which have indicated that kyphotic posturing may be a mechanism by which individuals can compensate for impaired postural stability.[148,149] Some research supports that is it important to differentiate types of balance challenges when looking at the effects of a stooped posture.[149] One study found that a stooped posture may compensate for impaired postural stability during rotational balance challenges, such as STS transfers,[149] while noting that a stooped posture decreased postural stability in response to transverse plane shifts of the base of support.[149] Another study compared reactive responses of healthy adults (22-33 years of age) during erect posturing to simulated kyphotic posturing with the subjects placed in 30 degrees of forward lean that resulted in hip and knee flexion.[148] This study found that voluntarily adopting a kyphotic posture resulted in a significant decrease in the latency of reactive responses, greatest in the backward direction.[148] With posterior losses of balance being problematic for individuals with PD, an increase in time to recover a posterior loss of balance could be important.

The results of this study suggest that patients should be supervised during task specific practice that results in more erect than typical standing postures. Early during a rehabilitation episode of care, clinicians may not want to recommend a more erect than typical standing posture for individuals with PD. While many rehabilitation experts choose to teach caregivers to correct or patients to self-correct into a more erect standing posture, this may decrease the standing balance of individuals with PD until the patient has had time to practice within the more erect range. Additionally, research indicates that individuals with PD have a more difficult time transferring motor learning into new contexts.[24] As a result, it may be important to practice taller than typical

standing in a variety of contexts prior to encouraging patients to adopt taller than typical posturing during higher risk activities, such as when dual tasking. More erect posturing should not be completely avoided as physical therapy interventions designed to improve erect standing posture have been found to be correlated with improved scores on common balance assessments.[150]

The positive correlation noted within our study between postural sway and increased height as compared to typical may be partially explained by the lack of self-awareness that many individuals with PD experience.[75] Individuals with PD may not realize when they are reacting to a cue that they are moving more than typical and as a result they may not be aware that their COM is moving to or beyond their posterior limit of stability until it results in a stepping reaction, a significant sway response, or a fall. Practice of relevant tasks may improve their self-awareness. In addition to practicing tasks in a more erect posture, practice of finding limits of stability[151] and taking compensatory steps[152] appropriately have been shown to result in improved postural control for individuals with PD.

Even though sit to stand transfers should result in relatively little movement within the coronal plane, significant increases of coronal plane movement was identified during initial standing when the subjects attained the most erect posturing. This indicates that the increased sway is not simply a result of overshooting and corrective movements, but rather a multidirectional decrease in stability. It is unclear if a final target to aim for would impact the coronal sway in early standing.

Limitations

This study has a relatively small sample size that represents a limited spectrum of disease severity making the results of this study not generalizable to all individuals with PD. Force plate data would have added to the understanding of impact of cues on postural sway, specifically gaining a fuller understanding of the path of the center of mass within the base of support.

Future Research

The findings of this study indicate that individuals with PD may be less stable when they are cued to stand more erect than typical following at STS transfer. What cannot be known from this study is whether individuals with PD are able to attain postural stability within a more erect standing posture following the STS transfer in response to practice. Additionally, further research to determine optimal cueing for the STS transfers in PD should include an external cue that works to terminate the STS at an optimal time, such as a verbal cue or a target for the shoulder to touch.

Conclusions

Based on our findings, it is recommended that clinicians complete task specific practice in erect postures under supervision prior to making recommendations for erect posturing with a task in the home and community environments. Additionally, this study supports the recommendation for skilled rehabilitation experts to oversee postural retraining programs.

Table 1. Subject Demographics

Characteristic	Subjects (n=13)
Age (years) **Mean (standard deviation)**	68.46 (9.11)
Sex (male/female)	8/5
Height (cm) **Mean (standard deviation)**	172.00 (8.72)
Weight (kg) **Mean (standard deviation)**	84.73 (12.54)
10MWT (meter/second) **Mean (standard deviation)**	6.92 (1.73)
Years with Diagnosis **Mean (standard deviation)**	5.38 (3.3)
Years with Symptoms **Mean (standard deviation)**	10.38 (9.18)
PDQ-39 **Mean (range)** **possible range: 0-100**	34 (4-74)
MDS-UPDRS **Mean (range)** **possible range: 0-199**	70 (48-112)

10MWT= 10 Meter Walk Test; PDQ-39= Parkinson's Disease Questionnaire 39; MDS-UPDRS= Movement Disorder Society's Unified Parkinson's Disease Rating Scale

Table 2. Correlation Between Change in Height and Postural Sway

Trials	**Postural Sway Characteristic**	**Sig (p<.05)**	**R (Spearman Rank Order Correlation)**	**95% Confidence Interval**
Trials with greatest increase in height	Sway area (degrees^2)	0.059		-46.082, 20.097
	Coronal sway (degrees)	0.008*	.654	-46.068, 20.124
	Sagittal sway (degrees)	0.025*	.555	-46.085, 20.096
	Sway Jerk (m/s^3)	0.162		-46.076, 20.118
	Sway Velocity (m/s)	0.029*	.538	-46.092, 20.067

* indicates statistical significance ($p<0.05$)

6.4 Instruction to Authors

Excerpt from “Instructions to Authors” for *Neurorehabilitation and Neural Repair:*

> Three typewritten copies of each manuscript must be submitted, in English, double-spaced throughout with a 2.5 cm (1 inch) left margin.

Excerpt from “Instructions to Authors” for *Neurorehabilitation and Neural Repair:*

> Full length original research articles should have an Abstract, Introduction, Methods, Results, and Discussion.

Excerpt from “Instructions to Authors” for *Neurorehabilitation and Neural Repair:*

> Abstract: Abstracts may contain up to 200 words. For original research articles and brief communications the abstract should be structured with the following subheadings: Objective, Methods, Results, Conclusions. Up to six key words or terms should be included for use by referencing sources.

Excerpt from “Instructions to Authors” for *Neurorehabilitation and Neural Repair:*

> Tables and Illustrations: All tables should have a title and should be typed double-spaced, including all headings, each on a separate page. All abbreviations should be defined.

Excerpt from “Instructions to Authors” for *Neurorehabilitation and Neural Repair:*

> DETAILS OF STYLE General: An important goal of Neurorehabilitation and Neural Repair is to foster communication between the basic and clinical research communities whose work is relevant to recovery from neural injury. Therefore, basic science articles should include sufficient explanatory information in the Introduction and elsewhere to permit reading by clinician readers, and vice versa. All abbreviations and jargon terms should be defined and kept to a minimum. The rationale and significance of the reported research should be explained in terms of its relevance to recovery of neurological function. At the end of Discussion, a subheading Implications may be added. Slightly greater latitude to speculate on clinical implications of basic research findings will be permitted here. Clinical researchers may use this subheading to suggest what basic science advances would be needed in order to move the clinical research to the next level.

Chapter 7: Discussion

7.1 Summary of the Findings

This dissertation study examined the effects of three different types of explicit cues on motor control during and postural control immediately following a STS transfer for individuals with PD. The results of this study can be applied to individuals with PD who experience occasional difficulty completing a STS transfer from a standard height chair. Additionally, this dissertation study sought to determine the effects of standing taller than typical on postural control for individuals with PD.

Significant findings were identified when examining the impact of explicit cues on postural sway immediately following STS transfers for individuals with PD. When not cued, individuals with PD were found to have significantly greater sway areas and sway jerk in immediate standing than their healthy counterparts. A verbal cue paired with a modeling cue resulted in decreased postural sway during the first 30 seconds of standing without LOB. Neither a verbal cue paired with reaching to targets or a verbal cue for an internal attentional focus decreased postural sway during the first 30 seconds of standing. However, both cues introduced LOB incidents that were not present during the uncued condition for either the HC or PD groups.

Significant findings were identified when examining the effects of explicit cues on motor control during STS transfer for individuals with PD. Modeling resulted in a statistically significant reduction in bradykinesia, while reaching to targets may have resulted in a clinically important reduction in hypokinesia during the pre-extension phase of the STS transfer. A degradation in motor control was noted in response to an explicit cue for an internal attentional focus.

According to the findings of this dissertation study, individuals with PD who stand with a more erect posture than typical may experience a decrease in standing postural control. A moderate, positive relationship between a more erect posture at the culmination of the STS transfer and postural sway in early standing was identified. While explicit cues are commonly utilized to improve motor performance for individuals with PD, our findings suggest that visual and verbal cues which create the most erect posture for an individual may also result in the greatest increase in postural sway in both the coronal and sagittal planes within this population.

7.2 Integration of the Findings with Previous Literature

7.2.1 Modeling

The results of this dissertation study demonstrated that an explicit verbal cue paired with modeling during the STS of an individual with PD may reduce bradykinesia and improve postural control during early standing balance. To the best of the primary investigator's knowledge, this is the first study to look at the impact of an isolated modeling cue on motor control in PD. However, modeling creates an external attentional focus, which has been well studied and found to be effective in improving motor control in this population,[6,15,17] consistent with the findings of this dissertation study. Modeling with a paired verbal command provides an explicit cue, which functional magnetic resonance imaging[74] has shown utilizes neural pathways that are not reliant on the areas of the brain most affected by PD. The results of this dissertation study were consistent with prior research indicating that the use of explicit cueing that creates an external attentional focus may improve the motor control of individuals with PD.[6,15,17] One potential mechanism that has been proposed to explain the effect of modeling is the activation of mirror neurons.[133] When the tester modeled the STS motions just prior to the individual with PD

completing them, it may have resulted in a motor priming effect[134] increasing the automaticity of the movement. Regarding postural control, prior research reported a direct link between increases in sway jerk and PD.[131] In this dissertation study, modeling was able to reduce the level of sway jerk to not significantly different from the HC group. To the best of the primary investigator's knowledge, this study is the first to look at the impact of modeling on postural sway in standing.

7.2.2 Reaching to Targets

To the best of the primary investigator's knowledge, this dissertation study is the first to report on the effect of reaching to targets on postural control during discrete tasks. However, the findings of this dissertation study are consistent with prior research[94,95] regarding a positive impact of use of targets on motor control for individuals with PD. Some studies have reported improvements in amplitude of movements with the introduction of targets.[15,17,22] However, this dissertation study found no change in the amplitude of movement, as indicated by inferred joint angle changes. This may be because prior studies noting increases in amplitude of movement looked at the continuous tasks of gait[15,17] or handwriting[22] and participants may have been able to improve their movement patterns over time in response to the cues. This dissertation study found a 25% reduction in the amount of time to complete the STS transfer. This decreased duration is consistent with prior studies indicating an increased gait speed[5,17] and decreased reach duration.[95]

7.2.3 Internal Attentional Focus

While there is a strong body of evidence to suggest the use of cues eliciting an external attentional focus, to the best of the primary investigator's knowledge, this is the first study to

compare the effects of cues eliciting an external versus internal attentional focus on individuals with PD. In some gait studies, individuals were cued to increase their arm swing[7] and improved gait speed and arm movements were noted. While some might consider this an internal attentional focus, when an individual is told to increase their arm swing they are likely focusing on their improving the final reach of their hand rather than their shoulder movements. Therefore, it would not be appropriate to consider this a cue eliciting an internal attentional focus.

7.2.4 Effects of Standing Taller than Typical

According to our findings, individuals with PD who stand with a more erect posture than typical may experience a decrease in standing postural control. Our findings are consistent with multiple studies which have indicated that kyphotic posturing may be a mechanism by which individuals can compensate for impaired postural stability.[148,149] Some research supports that is it important to differentiate types of balance challenges when looking at the effects of a stooped posture.[149] One study found that a stooped posture may compensate for impaired postural stability during rotational balance challenges, such as STS transfers,[149] while noting that a stooped posture decreased postural stability in response to transverse plane shifts of the base of support.[149] Another study compared reactive responses of healthy adults (22-33 years of age) during erect posturing to simulated kyphotic posturing with the subjects placed in 30 degrees of forward lean that resulted in hip and knee flexion.[148] This study found that voluntarily adopting a kyphotic posture resulted in a significant decrease in the latency of reactive responses, greatest in the backward direction.[148]

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a cue that they are moving more than typical and as a result they may not be aware that their COM is moving to or beyond their posterior limit of stability until it results in a stepping reaction, a significant sway response, or a fall.

7.3 Implications of the Findings

7.3.1 Implications for Physical Therapy Clinical Practice

Use of Modeling Cues

The modeling condition resulted in reduced bradykinesia during the STS transfer and improved postural control immediately following the STS transfer as compared to the uncued and internal attentional focus conditions for the PD group, indicating that it may be an appropriate strategy to improve movement speed during this task. While recommended in some commonly utilized exercise programs, to the best of the primary investigator's knowledge, this is the first study to examine the impact of modeling on motor control or postural sway during discrete tasks

Additionally, the modeling condition was the only condition during which the PD group did not require significantly more time than the HC group to complete the transfer. Modeling reduced the duration of the transfer by nearly 25% from 3.8 seconds to 2.8 seconds, bringing the duration closer to those in the HC group who had a duration of 1.8 seconds. No incidences of the COM moving outside of the BOS occurred with this cue, suggesting that it may be appropriate for implementation by caregivers and clinicians who are not able to provide substantial physical assistance.

Use of Targets as Cues

Based on prior research[15,62,94] and the additional findings within the current study, targets are likely an effective strategy to improve motor control for individuals with PD, but clinicians should strive to place targets in attainable locations that result in optimal movement. In the case of the STS transfer, it may have been better to have the tester place a hand at shoulder height and prompt the subject to stand until they reach the hand. In the clinic, if a therapist is seeking to improve upper extremity swing during a pre-gait stepping activity, it may be more appropriate to place a target at the maximally attainable distance than to encourage the patient to "reach toward that wall."

While reaching to targets did not result in a statistically significant reduction in attempts to stand, it is likely that a clinically important reduction is present. The HC group never required more than one attempt to stand. However, additional attempts were needed in all conditions for the PD group (uncued=1.31, reaching to targets=1.07, modeling=1.28, and internal attentional focus=1.47). If the typical person stands up 46+/-17 times in a day,[139] that could mean that the provision of targets during transfers may reduce attempts by up to 15 per day. Because prior research has shown that failed attempts at motor tasks leads to a decreased attempts to complete the task,[140] it is important to reduce the number of failed attempts experienced during STS transfers.

Use of Cues that Elicit an Internal Attentional Focus

The explicit cue for an internal attentional focus did not provide compensations for any motor signs or result in improved motor control during the STS transfer for individuals with PD. In fact, the cue to "bend forward at your hips, then stand until your back is straight" resulted in a significantly longer transfer than all other conditions, including the uncued condition. This

indicates that this type of cue may worsen the effects of bradykinesia. Additionally, the internal attentional focus cue resulted in a significantly longer latency period than the other two experimental conditions and was the only condition with a latency period that was significantly longer than the HC group indicating that it may also worsen the impact of akinesia. This cue was included within this dissertation study because it is similar to commonly provided cues within clinical and home settings. While it was not expected that this cue would improve motor control during STS transfers for Individuals with PD, it was important to include in order to better understand the impact of commonly utilized clinical cues. With a worsening of bradykinesia and akinesia and the introduction of a LOB incident the evidence would suggest that cues which elicit an internal attentional focus are not optimal for individuals with PD.

Use of Cues that Lead to Taller than Typical Standing

The results of this dissertation study suggest that patients should be supervised during task specific practice that results in more erect than typical standing postures. Many rehabilitation experts choose to teach caregivers to correct or patients to self-correct into a more upright standing posture. This may decrease the standing balance of individuals with PD until the patient has had time to practice within the range. It may not be appropriate for clinicians to recommend a more erect standing posture early during a rehabilitation episode of care. Additionally, research indicates that individuals with PD have a more difficult time transferring motor learning into new contexts.[24] As a result, it may be important to practice taller than typical standing in a variety of contexts prior to encouraging patients to adopt taller than typical posturing during higher risk activities, such as when dual tasking. However, more erect posturing should not be completely avoided as physical therapy interventions designed to improve erect standing posture have been found to be correlated with improved scores on common balance assessments.[150] Practice of

relevant tasks may improve their self-awareness. In addition to practicing tasks in a more erect posture, practice of finding limits of stability[151] and taking compensatory steps[152] appropriately have been shown to result in improved postural control for individuals with PD.

Even though sit to stand transfers should result in relatively little movement within the coronal plane, significant increases of coronal plane movement were identified during initial standing when the subjects attained the most erect posturing. This indicates that the increased sway is not simply a result of overshooting and corrective movements, but rather a multidirectional decrease in stability. It is unclear if a final target to aim for would impact the coronal sway in early standing.

7.3.2 Implications for Clinical Practice of Other Healthcare Providers

The findings of this dissertation study are not uniquely applicable to physical therapists and physical therapist assistants. Many healthcare professionals provide cues aimed to improve the ability of individuals with PD to attain standing. Primary care providers, certified nursing assistants, respiratory therapists, occupational therapists, optometrists, and many more providers may cue a patient who is demonstrating increased latency or amplitude during a STS transfer. In these instances, health care providers should utilize modeling when able to improve the motor control and postural control of the individuals with PD. Reaching to targets is an acceptable cue when the provider is not able to model, but is able to provide the patient with physical assistance to recover a from a LOB if needed. Use of cues that elicit an internal attentional focus should be avoided.

7.3.3 Implications for Individuals with Parkinson Disease and Their Caregivers

Decreasing the burden on caregivers through the use of easily applied compensatory mechanisms to improve mobility could greatly reduce the number of individuals with PD living in nursing homes. Additionally, it is known that even in mild to moderate stages of PD, individuals spent 75% of waking hours in sedentary activities.[13] Improving the ability of individuals with PD and their caregivers to attain standing may reduce the time spent in sedentary activities. This, in turn, may affect their overall cardiovascular health. In addition, increasing the independence of individuals with PD during STS transfers may reduce the risk of caregiver and patient injury. Modeling and the provision of targets are easy to provide compensatory strategies that could reduce the level of physical assistance required. Additionally, if caregivers are currently providing a cue that elicits an internal attentional focus, the change to model or use of targets could result in greater improvements. Any increase in independence for the patient or decrease in burden to the patient may result in clinically meaningful improvements in quality of life.

7.4 Limitations and Recommendations

Several limitations of this dissertation study are acknowledged. First, only three commonly used types of cues were studied in this project. These cues were selected because, based on available knowledge, they were believed by the researchers to either be the most effective cues possible in a wide variety of settings or because they are commonly utilized in the clinic and home setting. Other cues that could be easily implemented in all settings may also be effective and should be studied in the future. Additionally, other commonly used cues may not be effective and should be studied to determine their clinical utility. Specifically, it is recommended that future studies

utilize fully attainable targets to determine if the target of "stand to the ceiling" resulted in the backward LOB because it was unattainable. A cue to "stand to my hand" with a hand placed at the participant's self-selected shoulder height may improve postural sway.

The sample of this study decreases the generalizability of the findings. While adequate to find significance within this study, the sample size is relatively small. Additionally, the sample included a limited range of disease severity, making it unclear if the results of this study would apply to those individuals with more severe impairments due to PD. Lastly, because of the short half-life cycle of dopamine replacement therapies, sit to stand data collection needed to be completed within a standardized time frame with respect to medications. All data was collected during the peak "on" phase of medications. Therefore, it is unclear if the findings can be generalized to how individuals with PD would perform during the "off" phase of medications. Repeating this study with a larger and more diverse sample during both their "on" and "off" medication phases would make the results more generalizable and robust.

Many researchers attempt to utilize more testers and locations to increase the generalizability of the findings. Because of the small sample size, it was important to minimize testers to reduce the impact of the tester as a covariate. To reduce the impact of minimal testers, cues utilized in this study were designed to be easy to administer in a consistent manner by caregivers and clinicians. However, further research to ascertain if caregivers and clinicians can replicate these findings are warranted.

Importantly, the results of this dissertation study provide information about the effect of a single cue during one training session. For this reason, these results should not be generalized to which type of cue may be retained and continue to be effective after a period of no practice. It is

possible that the best one-time cue is different from the best type of cue to utilize consistently for individuals with PD. Future research should examine the skill acquisition and retention of such training programs.

The findings of this study indicate that individuals with PD may be less stable when they are cued to stand more erect than typical following at STS transfer. What cannot be known from this study is whether individuals with PD are able to attain postural stability within a more erect standing posture following the STS transfer in response to practice. Future research should examine the skill acquisition and retention of training programs to improve postural control following STS transfers in this population.

7.5 Chapter Summary

This dissertation study has several important findings. Based on the data, modeling may be an effective cue to reduce bradykinesia and improve standing balance during discrete tasks for individuals with PD. The findings of this dissertation study are consistent with prior research indicating that use of cues that elicit an external attentional focus may reduce bradykinesia. However, this dissertation study adds to the literature that reaching to targets may reduce postural control during discrete tasks for this population. Additionally, the data collected in this dissertation study support theories presented in other research which suggested that individuals with PD may stoop to prevent a posterior LOB. In this dissertation study, findings demonstrated a positive relationship between standing taller than typical and increase postural sway.

Based on these findings, several clinical recommendations can be made. It is recommended that physical therapists utilize modeling cues to reduce bradykinesia and improve postural control during practice of new tasks with a patient. While targets can improve motor control, it is

recommended that targets are carefully selected to optimize movement without causing an unwanted LOB. Use of cueing that elicits an internal attentional focus should be avoided with this patient population. Lastly, the decision of when and if posture should be corrected through cueing for patients with PD should be based on their ability to maintain their COM within their BOS safely within their new, more erect posture.

Appendices

Appendix 1: Phone Screening Checklist for PD Group

Phone Screening Checklist- Parkinson Disease Group	
Read opening script	
Have you been diagnosed with Parkinson Disease by a neurologist?	
Have you ever been told that you have a "different kind" of Parkinson's, such as: multiple systems atrophy, Parkinson's caused by a stroke or brain attack, or progressive supranuclear palsy?	
Are you able to stand up from a chair on your own with or without the use of your arms?	
Are you able to walk 30 feet with or without an assistive device such as a cane or walker?	
Are you currently taking any medications for PD? If so, what are you taking? Have you recently changed medications or are you working with your physician to find the appropriate dose of medications?	
Do you have any other medical diagnoses that limit your ability to stand up from a chair?	
Have you undergone any kind of surgery as a method for treating your Parkinson Disease?	
What is your date of birth?	
If appropriate, provide date for scheduled baseline testing	

Appendix 2: Phone Screening Checklist for the Healthy Control Group

Phone Screening Checklist- Healthy Control Group	
Read opening script	
Are you able to stand up from a chair on your own with or without the use of your arms?	
Are you able to walk 30 feet with or without an assistive device such as a cane or walker?	
Do you have any other medical diagnoses that limit your ability to stand up from a chair?	
What is your date of birth?	
If appropriate, provide date for scheduled baseline testing	

Appendix 3: Testing Protocol for Parkinson Disease Group

Testing Protocol- Parkinson Disease Group	
Time sensitive data collection indicated in green boxes and should begin at: *(After item 7, the placement of time sensitive data can occur at any point within the protocol.)*	
1. Explanation and signing of informed consent	
2. MoCA	Score:
3. Confirmation of D.O.B.	
4. Placement of sensors (APDM) on head, anterior chest, lumbar spine, bilateral lateral thighs, bilateral anterior legs, and bilateral dorsum of feet	
5. Type of PD medication regularly taken	
6. Time of last dose	Indicate time here: Items sensitive to time should begin 1 hour after the last dose of PD medications.
7. Time for next dose	Indicate time here: Items sensitive to time should begin 1 hour after the last dose of PD medications.
8. Height	
9. Weight	
10. Uncued Sit to Stand Testing Protocol (Table 3.4)	# of attempts
11. Comfortable gait speed measured through the 10MWT	
12. Motor portion of the MDS-UPDRS	
13. Randomized collection of STS data under 3 conditions (see standardized protocol, Table 3.4)	
14. Years with symptoms	
15. Years since diagnosis	
16. Non-motor portions of the MDS-UPDRS	

17. PDQ-39	

Appendix 4: Sit to Stand Data Collection Protocols

Sit to Stand Data Collection Protocols		
Pre-testing measurements		
Ensure the seat height is properly adjusted to allow for 100 degrees of knee flexion while tibia are positioned vertically in sitting.		
Then position the feet shoulder width apart and 10 cm posterior to the most anterior aspect of the knee. Place a tape marking on the floor to allow for easy return to starting position.		
In upright sitting, ask the patient to raise one arm to shoulder height. Measure from the anterior axilla to the tip of extended fingers.	*Record "arm length" here:*	
Pre-testing Subject Instructions		
Say to subject, "I will be providing you with a variety of different directions. I would like you to focus on *only* the directions for your current task and not try to combine directions or improve your movements by thinking about the strategy that you feel works best. Remember, please focus on the directions given to you for *that* task. You will be asked to stand up several times. Each time it is important that you remain standing for a period of time to allow the computer to record your data. I will let you know when you may return to sitting. Can you please tell me the 2 important things that I just told you?" Repeat directions until the subject is able to state that they should focus on the current set of instructions and remain standing until told otherwise.		
Uncued Sit to Stand Testing Protocol		# of attempts
Have the patient sit on pre-height adjusted tub chair and position their feet.		

Ask the subject to “say a few sentences about their favorite meal, then immediately stand up. Maintain quiet standing for 1 minute until I tell you may return to sitting.”		
1 minute rest break – discuss their favorite meal during break time		
Reposition feet		
Ask the subject to “say a few sentences about their favorite place, then immediately stand up. Maintain quiet standing for 1 minute until I tell you may return to sitting.”		
1 minute rest break- discuss their favorite place during break time		
Reposition feet		
Ask the subject to “say a few sentences about their favorite teacher, then immediately stand up. Maintain quiet standing for 1 minute until I tell you may return to sitting.”		
1 minute rest break- discuss their favorite teacher during break time		
Reaching to Target Sit to Stand Testing Protocol		
Have the patient sit on height-adjusted tub chair		
Reposition feet		
Adjust a second tub chair to the patient’s knee height and place it one arm length from the subject’s toes while the ankle is ankle is dorsiflexed to 15 degrees.		
Say to the subject, “Reach to my hand.”		
Place back of hand on nearer edge of second tub chair so that palm is facing the test subject.		
Then when they touch the tester’s hand, “stand to the ceiling.”		
Concurrent Modeling Sit to Stand Testing Protocol		
Have the subject sit on height-adjusted tub chair		
Reposition feet		
Place a second tub chair opposite the patient at a 2.5 arms’ length from subject’s front chair legs		
Say to the subject, “When I stand up, I would like you to stand up with me.”		

Model an exaggerated forward reach and stand to full erect posture.		
Internal Attentional Focus Sit to Stand Testing Protocol		
Have the subject sit on height-adjusted tub chair		
Reposition feet		
Remove all targets from in front of the subject		
Say to the subject, “Please bend at your hips and knees, then stand until you feel your back is straight.”		

Appendix 5: Testing Protocol for Healthy Control Group

Testing Protocol- Healthy Control Group		
Explanation and signing of informed consent		
Placement of sensors (APDM)		
Adjustment of tub bench to allow for 90 degrees of knee flexion in sitting with tibia vertical	Indicate height here:	
Uncued STS		
Comfortable gait speed measured through the 10 Meter Walk Test		
Height		
Weight		
Confirmation of D.O.B.		
Randomized collection of STS data under 3 conditions (see standardized protocol, Table 3.6)		
Uncued Sit to Stand Testing Protocol		# of attempts
Have the patient sit on pre-height adjusted tub chair and position their feet.		
Ask the subject to "say a few sentences about their favorite meal, then immediately stand up. Maintain quiet standing for 1 minute until I tell you may return to sitting."		
1 minute rest break – discuss their favorite meal during break time		
Reposition feet		
Ask the subject to "say a few sentences about their favorite place, then immediately stand up. Maintain quiet standing for 1 minute until I tell you may return to sitting."		
1 minute rest break- discuss their favorite place during break time		
Reposition feet		
Ask the subject to "say a few sentences about their favorite teacher, then immediately stand up. Maintain quiet standing for 1 minute until I tell you may return to sitting."		

1-minute rest break- discuss their favorite teacher during break time		

References

1. Jankovic J. Parkinson's disease: clinical features and diagnosis. *Journal of Neurology, Neurosurgery & Psychiatry.* 2008;79(4):368-376.
2. Wu T, Hallett M, Chan P. Motor automaticity in Parkinson's disease. *Neurobiology of disease.* 2015;82:226-234.
3. Behrman AL, Teitelbaum P, Cauraugh JH. Verbal instructional sets to normalise the temporal and spatial gait variables in Parkinson's disease. *Journal of Neurology, Neurosurgery & Psychiatry.* 1998;65(4):580-582.
4. Hove MJ, Suzuki K, Uchitomi H, Orimo S, Miyake Y. Interactive rhythmic auditory stimulation reinstates natural 1/f timing in gait of Parkinson's patients. *PloS one.* 2012;7(3):e32600.
5. Lim I, van Wegen E, de Goede C, et al. Effects of external rhythmical cueing on gait in patients with Parkinson's disease: a systematic review. *Clinical rehabilitation.* 2005;19(7):695-713.
6. Nieuwboer A, Kwakkel G, Rochester L, et al. Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. *Journal of Neurology, Neurosurgery & Psychiatry.* 2007;78(2):134-140.
7. Rubinstein TC, Giladi N, Hausdorff JM. The power of cueing to circumvent dopamine deficits: a review of physical therapy treatment of gait disturbances in Parkinson's disease. *Movement Disorders.* 2002;17(6):1148-1160.
8. Mak MK, Hui-Chan CW. Audiovisual cues can enhance sit-to-stand in patients with Parkinson's disease. *Movement disorders.* 2004;19(9):1012-1019.
9. Bhatt T, Yang F, Mak MK, Hui-Chan CW, Pai Y-C. Effect of externally cued training on dynamic stability control during the sit-to-stand task in people with Parkinson disease. *Physical therapy.* 2013;93(4):492-503.
10. Wright Willis A, Evanoff BA, Lian M, Criswell SR, Racette BA. Geographic and ethnic variation in Parkinson disease: a population-based study of US Medicare beneficiaries. *Neuroepidemiology.* 2010;34(3):143-151.
11. Kowal SL, Dall TM, Chakrabarti R, Storm MV, Jain A. The current and projected economic burden of Parkinson's disease in the United States. *Movement Disorders.* 2013;28(3):311-318.
12. Dunlop DD, Song J, Arntson EK, et al. Sedentary time in US older adults associated with disability in activities of daily living independent of physical activity. *Journal of Physical Activity and Health.* 2015;12(1):93-101.
13. Wallén MB, Franzén E, Nero H, Hagströmer M. Levels and patterns of physical activity and sedentary behavior in elderly people with mild to moderate Parkinson disease. *Physical therapy.* 2015;95(8):1135.
14. Rochester L, Nieuwboer A, Baker K, et al. The attentional cost of external rhythmical cues and their impact on gait in Parkinson's disease: effect of cue modality and task complexity. *Journal of neural transmission.* 2007;114(10):1243.
15. Suteerawattananon M, Morris G, Etnyre B, Jankovic J, Protas E. Effects of visual and auditory cues on gait in individuals with Parkinson's disease. *Journal of the neurological sciences.* 2004;219(1):63-69.
16. Azulay J-P, Mesure S, Blin O. Influence of visual cues on gait in Parkinson's disease: contribution to attention or sensory dependence? *Journal of the neurological sciences.* 2006;248(1):192-195.
17. Rochester L, Hetherington V, Jones D, et al. The effect of external rhythmic cues (auditory and visual) on walking during a functional task in homes of people with Parkinson's disease. *Archives of physical medicine and rehabilitation.* 2005;86(5):999-1006.

18. Kritikos A, Leahy C, Bradshaw JL, Iansek R, Phillips JG, Bradshaw JA. Contingent and non-contingent auditory cueing in Parkinson's disease. *Neuropsychologia.* 1995;33(10):1193-1203.
19. Nieuwboer A, Baker K, Willems A-M, et al. The short-term effects of different cueing modalities on turn speed in people with Parkinson's disease. *Neurorehabilitation and neural repair.* 2009.
20. Lim I, van Wegen E, Jones D, et al. Does cueing training improve physical activity in patients with Parkinson's disease? *Neurorehabilitation and Neural Repair.* 2010;24(5):469-477.
21. Almeida QJ, Wishart LR, Lee TD. Bimanual coordination deficits with Parkinson's disease: the influence of movement speed and external cueing. *Movement Disorders.* 2002;17(1):30-37.
22. Oliveira RM, Gurd JM, Nixon P, Marshall JC, Passingham RE. Micrographia in Parkinson's disease: the effect of providing external cues. *Journal of Neurology, Neurosurgery & Psychiatry.* 1997;63(4):429-433.
23. Nackaerts E, Nieuwboer A, Broeder S, et al. Opposite effects of visual cueing during writing-like movements of different amplitudes in Parkinson's disease. *Neurorehabilitation and neural repair.* 2016;30(5):431-439.
24. Nieuwboer A, Rochester L, Müncks L, Swinnen SP. Motor learning in Parkinson's disease: limitations and potential for rehabilitation. *Parkinsonism & related disorders.* 2009;15:S53-S58.
25. Wulf G, Höß M, Prinz W. Instructions for motor learning: Differential effects of internal versus external focus of attention. *Journal of motor behavior.* 1998;30(2):169-179.
26. Shumway-Cook A, Woollacott MH. *Motor control: translating research into clinical practice.* 5th ed: Lippincott Williams & Wilkins; 2017.
27. Mazzoni P, Shabbott B, Cortés JC. Motor control abnormalities in Parkinson's disease. *Cold Spring Harbor perspectives in medicine.* 2012;2(6):a009282.
28. Foltynie T, Brayne C, Barker RA. The heterogeneity of idiopathic Parkinson's disease. *Journal of neurology.* 2002;249(2):138-145.
29. Lazzarini A, Myers R, Zimmerman T, et al. A clinical genetic study of Parkinson's disease Evidence for dominant transmission. *Neurology.* 1994;44(3 Part 1):499-499.
30. Allan W. Inheritance of the shaking palsy. *Archives of Internal Medicine.* 1937;60(3):424-436.
31. Bell J, Clark AJ. A pedigree of paralysis agitans. *Annals of Human Genetics.* 1926;1(4):455-464.
32. Lill CM. Genetics of Parkinson's disease. *Molecular and cellular probes.* 2016;30(6):386-396.
33. Lill CM MA, Hartmann C, Lohmann K, Marras C, Lang AE, Klein C, Bertram L. Launching the movement disorders society genetic mutation database (MDSGene). 2016;31(5):607-609.
34. Petrovitch H, Ross GW, Abbott RD, et al. Plantation work and risk of Parkinson disease in a population-based longitudinal study. *Archives of neurology.* 2002;59(11):1787-1792.
35. Chin-Chan M, Navarro-Yepes J, Quintanilla-Vega B. Environmental pollutants as risk factors for neurodegenerative disorders: Alzheimer and Parkinson diseases. *Frontiers in cellular neuroscience.* 2015;9:124.
36. Priyadarshi A, Khuder SA, Schaub EA, Shrivastava S. A meta-analysis of Parkinson's disease and exposure to pesticides. In:2000.
37. Brown TP, Rumsby PC, Capleton AC, Rushton L, Levy LS. Pesticides and Parkinson's disease—is there a link? *Environmental health perspectives.* 2006;114(2):156.
38. Kala SV, Jadhav AL. Low level lead exposure decreases in vivo release of dopamine in the rat nucleus accumbens: a microdialysis study. *Journal of neurochemistry.* 1995;65(4):1631-1635.
39. Polito L, Greco A, Seripa D. Genetic profile, environmental exposure, and their interaction in parkinson's disease. *Parkinson's disease.* 2016;2016.
40. Mathur S. With Diseases, Genetics Loads the Gun and Environment Pulls the Trigger. In. *HuffPost.* Vol 2018. United States2013.
41. Stefanis L. α-Synuclein in Parkinson's disease. *Cold Spring Harbor perspectives in medicine.* 2012;2(2):a009399.

42. Lansbury PT, Lashuel HA. A century-old debate on protein aggregation and neurodegeneration enters the clinic. *Nature.* 2006;443(7113):774.
43. Bendor JT, Logan TP, Edwards RH. The function of α-synuclein. *Neuron.* 2013;79(6):1044-1066.
44. Braak H, Ghebremedhin E, Rüb U, Bratzke H, Del Tredici K. Stages in the development of Parkinson's disease-related pathology. *Cell and tissue research.* 2004;318(1):121-134.
45. Braak H, Del Tredici K. Neuropathological staging of brain pathology in sporadic Parkinson's disease: separating the wheat from the chaff. *Journal of Parkinson's disease.* 2017;7(s1):S71-S85.
46. Burke RE, Dauer WT, Vonsattel JPG. A critical evaluation of the Braak staging scheme for Parkinson's disease. *Annals of neurology.* 2008;64(5):485-491.
47. Fearnley JM, Lees AJ. Ageing and Parkinson's disease: substantia nigra regional selectivity. *Brain.* 1991;114(5):2283-2301.
48. Citation Report for "Stages in the development of Parkinson's disease-related pathology" by Braak, et al. . Clarivate Analytics. Accessed June 3, 2018.
49. Monchi O, Petrides M, Strafella AP, Worsley KJ, Doyon J. Functional role of the basal ganglia in the planning and execution of actions. *Annals of neurology.* 2006;59(2):257-264.
50. Dickson DW. Neuropathology of Parkinson disease. *Parkinsonism & related disorders.* 2018;46:S30-S33.
51. Lotharius J, Brundin P. Pathogenesis of Parkinson's disease: dopamine, vesicles and α-synuclein. *Nature Reviews Neuroscience.* 2002;3(12):932.
52. . Parkinson's Disease Therapy Algorithm. 2017.
53. Fahn S. Parkinson disease, the effect of levodopa, and the ELLDOPA trial. *Archives of neurology.* 1999;56(5):529-535.
54. Drugs.com. Carbidopa and Levadopa: Professional. https://www.drugs.com/pro/carbidopa-and-levodopa.html. Published 2017. Accessed April 10, 2017.
55. Sinemet®(Carbidopa-Levodopa) [press release]. FDA.
56. Peterson DS, Horak FB. The effect of levodopa on improvements in protective stepping in people with Parkinson's disease. *Neurorehabilitation and neural repair.* 2016;30(10):931-940.
57. James P. An essay on the shaking palsy. *The Journal of Nervous and Mental Disease.* 1924;60(4):441.
58. Parkinson J. An essay on the shaking palsy. *The Journal of neuropsychiatry and clinical neurosciences.* 2002;14(2):223-236.
59. Pringsheim T, Jette N, Frolkis A, Steeves TD. The prevalence of Parkinson's disease: A systematic review and meta-analysis. *Movement disorders.* 2014;29(13):1583-1590.
60. Hernán MA, Takkouche B, Caamaño-Isorna F, Gestal-Otero JJ. A meta-analysis of coffee drinking, cigarette smoking, and the risk of Parkinson's disease. *Annals of neurology.* 2002;52(3):276-284.
61. Leentjens AF, Van den Akker M, Metsemakers JF, Lousberg R, Verhey FR. Higher incidence of depression preceding the onset of Parkinson's disease: a register study. *Movement Disorders.* 2003;18(4):414-418.
62. Abbott R, Ross G, White L, et al. Excessive daytime sleepiness and subsequent development of Parkinson disease. *Neurology.* 2005;65(9):1442-1446.
63. Postuma RB, Lang AE, Massicotte-Marquez J, Montplaisir J. Potential early markers of Parkinson disease in idiopathic REM sleep behavior disorder. *Neurology.* 2006;66(6):845-851.
64. Haehner A, Hummel T, Hummel C, Sommer U, Junghanns S, Reichmann H. Olfactory loss may be a first sign of idiopathic Parkinson's disease. *Movement disorders.* 2007;22(6):839-842.
65. Nalls MA, McLean CY, Rick J, et al. Diagnosis of Parkinson's disease on the basis of clinical and genetic classification: a population-based modelling study. *The Lancet Neurology.* 2015;14(10):1002-1009.

66. Dauer W, Przedborski S. Parkinson's disease: mechanisms and models. *Neuron.* 2003;39(6):889-909.
67. Fahn SElton R. Unified Parkinson's Disease Rating Scale. Fahn SMarsden MCCalne DBGoldstein M Recent developments in Parkinson's disease. In: NJ: Macmillan Healthcare Information; 1987.
68. Goetz CG, Tilley BC, Shaftman SR, et al. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. *Movement disorders.* 2008;23(15):2129-2170.
69. Sherrington CS. Remarks on some aspects of reflex inhibition. *Proc R Soc Lond B.* 1925;97(686):519-545.
70. Taub E, Berman A. Movement and learning in the absence of sensory feedback. *The neuropsychology of spatially oriented behavior.* 1968:173-192.
71. Foerster O. The motor cortex in man in the light of Hughlings Jackson's doctrines. *Brain.* 1936;59(2):135-159.
72. Whelan PJ. Control of locomotion in the decerebrate cat. *Progress in neurobiology.* 1996;49(5):481-515.
73. Marr D. Early processing of visual information. *Phil Trans R Soc Lond B.* 1976;275(942):483-519.
74. Cunnington R, Windischberger C, Deecke L, Moser E. The preparation and execution of self-initiated and externally-triggered movement: a study of event-related fMRI. *Neuroimage.* 2002;15(2):373-385.
75. Maier F, Prigatano GP, Kalbe E, et al. Impaired self-awareness of motor deficits in Parkinson's disease: Association with motor asymmetry and motor phenotypes. *Movement Disorders.* 2012;27(11):1443-1446.
76. Schmidt RA, Lee TD. *Motor control and learning: A behavioral emphasis.* Human Kinetics; 1999.
77. Ghilardi M-F, Eidelberg D, Silvestri G, Ghez C. The differential effect of PD and normal aging on early explicit sequence learning. *Neurology.* 2003;60(8):1313-1319.
78. Smiley-Oyen AL, Lowry KA, Emerson QR. Learning and retention of movement sequences in Parkinson's disease. *Movement disorders.* 2006;21(8):1078-1087.
79. Michel J, Benninger D, Dietz V, van Hedel HJ. Obstacle stepping in patients with Parkinson's disease. *Journal of neurology.* 2009;256(3):457-463.
80. Marinelli L, Quartarone A, Hallett M, Frazzitta G, Ghilardi MF. The many facets of motor learning and their relevance for Parkinson's disease. *Clinical Neurophysiology.* 2017;128(7):1127-1141.
81. Siegert RJ, Taylor KD, Weatherall M, Abernethy DA. Is implicit sequence learning impaired in Parkinson's disease? A meta-analysis. *Neuropsychology.* 2006;20(4):490.
82. Benoit C-E, Dalla Bella S, Farrugia N, Obrig H, Mainka S, Kotz SA. Musically cued gait-training improves both perceptual and motor timing in Parkinson's disease. *Frontiers in human neuroscience.* 2014;8:494.
83. Mak MK, Hui-Chan CW. Cued task-specific training is better than exercise in improving sit-to-stand in patients with Parkinson's disease: A randomized controlled trial. *Movement Disorders.* 2008;23(4):501-509.
84. Spildooren J, Vercruysse S, Meyns P, et al. Turning and unilateral cueing in Parkinson's disease patients with and without freezing of gait. *Neuroscience.* 2012;207:298-306.
85. Stolwyk RJ, Triggs TJ, Charlton JL, Iansek R, Bradshaw JL. Impact of internal versus external cueing on driving performance in people with Parkinson's disease. *Movement Disorders.* 2005;20(7):846-857.
86. Willems AM, Nieuwboer A, Chavret F, et al. Turning in Parkinson's disease patients and controls: the effect of auditory cues. *Movement disorders.* 2007;22(13):1871-1878.

87. Onla-or S, Winstein CJ. Determining the optimal challenge point for motor skill learning in adults with moderately severe Parkinson's disease. *Neurorehabilitation and neural repair.* 2008;22(4):385-395.
88. Wulf G, Landers M, Lewthwaite R, Toöllner T. External focus instructions reduce postural instability in individuals with Parkinson disease. *Physical therapy.* 2016;89(2):162-168.
89. Sidaway B, Ala B, Baughman K, et al. Contextual interference can facilitate motor learning in older adults and in individuals with Parkinson's Disease. *Journal of motor behavior.* 2016;48(6):509-518.
90. Abbruzzese G, Avanzino L, Marchese R, Pelosin E. Action observation and motor imagery: innovative cognitive tools in the rehabilitation of Parkinson's disease. *Parkinson's Disease.* 2015;2015.
91. Morris ME. Movement disorders in people with Parkinson disease: a model for physical therapy. *Physical therapy.* 2000;80(6):578-597.
92. Rocha PA, Porfírio GM, Ferraz HB, Trevisani VF. Effects of external cues on gait parameters of Parkinson's disease patients: a systematic review. *Clinical neurology and neurosurgery.* 2014;124:127-134.
93. Lehman DA, Toole T, Lofald D, Hirsch MA. Training with verbal instructional cues results in near-term improvement of gait in people with Parkinson disease. *Journal of Neurologic Physical Therapy.* 2005;29(1):2-8.
94. Majsak MJ, Kaminski T, Gentile AM, Flanagan JR. The reaching movements of patients with Parkinson's disease under self-determined maximal speed and visually cued conditions. *Brain: a journal of neurology.* 1998;121(4):755-766.
95. Ma H-I, Trombly CA, Tickle-Degnen L, Wagenaar RC. Effect of one single auditory cue on movement kinematics in patients with Parkinson's disease. *American journal of physical medicine & rehabilitation.* 2004;83(7):530-536.
96. Kotake T, Dohi N, Kajiwara T, Sumi N, Koyama Y, Miura T. An analysis of sit-to-stand movements. *Archives of physical medicine and rehabilitation.* 1993;74(10):1095-1099.
97. Shepherd RB, Gentile A. Sit-to-stand: functional relationship between upper body and lower limb segments. *Human movement science.* 1994;13(6):817-840.
98. Hedman LD, Rogers MW, Hanke TA. Neurologic professional education: linking the foundation science of motor control with physical therapy interventions for movement dysfunction. *Journal of Neurologic Physical Therapy.* 1996;20(1):9-13.
99. Mak MK, Hui-Chan CW. Switching of movement direction is central to parkinsonian bradykinesia in sit-to-stand. *Movement Disorders.* 2002;17(6):1188-1195.
100. Mak MK, Levin O, Mizrahi J, Hui-Chan CW. Joint torques during sit-to-stand in healthy subjects and people with Parkinson's disease. *Clinical Biomechanics.* 2003;18(3):197-206.
101. Rogers MW, Chan CW. Motor planning is impaired in Parkinson's disease. *Brain research.* 1988;438(1-2):271-276.
102. Chan CW. Could Parkinsonian akinesia be attributable to a disturbance in the motor preparatory process? *Brain research.* 1986;386(1-2):183-196.
103. Mak MK, Hui-Chan CW. The speed of sit-to-stand can be modulated in Parkinson's disease. *Clinical neurophysiology.* 2005;116(4):780-789.
104. Inkster LM, Eng JJ. Postural control during a sit-to-stand task in individuals with mild Parkinson's disease. *Experimental brain research.* 2004;154(1):33-38.
105. Bishop M, Brunt D, Pathare N, Ko M, Marjama-Lyons J. Changes in distal muscle timing may contribute to slowness during sit to stand in Parkinsons disease. *Clinical biomechanics.* 2005;20(1):112-117.

106. Schultz AB, Alexander NB, Ashton-Miller JA. Biomechanical analyses of rising from a chair. *Journal of biomechanics.* 1992;25(12):1383-1391.
107. Portney LG, Watkins MP. Foundations of clinical research: applications to practice. 2009.
108. Ltd. AC. Sample Size Calculator. https://www.ai-therapy.com/psychology-statistics/sample-size-calculator. Published 2019. Accessed May 11, 2019.
109. Zint M. Power Analysis, Statistical Significance, & Effect Size. My Environmental Education Evalutation Resoursce Assistant. http://meera.snre.umich.edu/power-analysis-statistical-significance-effect-size. Accessed May 11, 2019.
110. Karlawish J, Cary M, Moelter ST, et al. Cognitive impairment and PD patients' capacity to consent to research. *Neurology.* 2013;81(9):801-807.
111. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999-2008. *Jama.* 2010;303(3):235-241.
112. de Onis M, Habicht J-P. Anthropometric reference data for international use: recommendations from a World Health Organization Expert Committee. *The American journal of clinical nutrition.* 1996;64(4):650-658.
113. APDM I. Full-body Kinematics Analysis. 2017.
114. Hulbert S, Ashburn A, Robert L, Verheyden G. A narrative review of turning deficits in people with Parkinson's disease. *Disability and rehabilitation.* 2015;37(15):1382-1389.
115. Zampieri C, Salarian A, Carlson-Kuhta P, Aminian K, Nutt JG, Horak FB. The instrumented timed up and go test: potential outcome measure for disease modifying therapies in Parkinson's disease. *Journal of Neurology, Neurosurgery & Psychiatry.* 2010;81(2):171-176.
116. Mancini M, King L, Salarian A, Holmstrom L, McNames J, Horak FB. Mobility lab to assess balance and gait with synchronized body-worn sensors. *Journal of bioengineering & biomedical science.* 2011:007.
117. APDM I. Research-Grade Wearable Sensors. 2017.
118. APDM I. Comprehensive Gait and Balance Analysis. https://www.apdm.com/mobility/. Published 2017. Accessed2018.
119. Goetz CG, Fahn S, Martinez-Martin P, et al. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Process, format, and clinimetric testing plan. *Movement Disorders.* 2007;22(1):41-47.
120. Goetz C, Poewe W, Dubois B, Schrag A, Stern M, Lang A. The MDS-UPDRS: how to apply the new UPDRS in practice and research settings. *The Movement Disorder Society.* 2006.
121. Siderowf A, McDermott M, Kieburtz K, Blindauer K, Plumb S, Shoulson I. Test–retest reliability of the unified Parkinson's disease rating scale in patients with early Parkinson's disease: results from a multicenter clinical trial. *Movement disorders.* 2002;17(4):758-763.
122. Martínez-Martín P, Payo BF. Quality of life in Parkinson's disease: validation study of the PDQ-39 Spanish version. *Journal of Neurology.* 1998;245(1):S34-S38.
123. Peto V, Jenkinson C, Fitzpatrick R. Determining minimally important differences for the PDQ-39 Parkinson's disease questionnaire. *Age and Ageing.* 2001;30(4):299-302.
124. Sofuwa O, Nieuwboer A, Desloovere K, Willems AM, Chavret F, Jonkers I. Quantitative gait analysis in Parkinson's disease: comparison with a healthy control group. *Arch Phys Med Rehabil.* 2005;86.
125. Palmer E, Matlick D, Council RO. 10-Meter Walk Test. 2015.
126. Hauser RA, Ellenbogen A, Khanna S, Gupta S, Modi NB. Onset and duration of effect of extended-release carbidopa-levodopa in advanced Parkinson's disease. *Neuropsychiatric disease and treatment.* 2018;14:839.
127. Janssen WG, Bussmann HB, Stam HJ. Determinants of the sit-to-stand movement: a review. *Physical therapy.* 2002;82(9):866-879.

128. Kawagoe S, Tajima N, Chosa E. Biomechanical analysis of effects of foot placement with varying chair height on the motion of standing up. *Journal of Orthopaedic Science.* 2000;5(2):124-133.
129. Keus SH, Bloem BR, Hendriks EJ, Bredero-Cohen AB, Munneke M, Group PRD. Evidence-based analysis of physical therapy in Parkinson's disease with recommendations for practice and research. *Movement disorders.* 2007;22(4):451-460.
130. Błaszczyk JW, Orawiec R. Assessment of postural control in patients with Parkinson's disease: sway ratio analysis. *Human movement science.* 2011;30(2):396-404.
131. Mancini M, Carlson-Kuhta P, Zampieri C, Nutt JG, Chiari L, Horak FB. Postural sway as a marker of progression in Parkinson's disease: a pilot longitudinal study. *Gait & posture.* 2012;36(3):471-476.
132. *Whitepaper.* Mobility Lab by APDM;2015.
133. Rizzolatti G, Craighero L. The mirror-neuron system. *Annu Rev Neurosci.* 2004;27:169-192.
134. Stoykov ME, Madhavan S. Motor priming in neurorehabilitation. *Journal of neurologic physical therapy: JNPT.* 2015;39(1):33.
135. Henderson EJ, Morgan GS, Amin J, Gaunt DM, Ben-Shlomo Y. The minimum clinically important difference (MCID) for a falls intervention in Parkinson's: A delphi study. *Parkinsonism & related disorders.* 2019;61:106-110.
136. Van Hilten J, Van Eerd A, Wagemans E, Middelkoop H, Roos R. Bradykinesia and hypokinesia in Parkinson's disease: what's in a name? *Journal of neural transmission.* 1998;105(2-3):229-237.
137. Hallett M. Clinical neurophysiology of akinesia. *Revue neurologique.* 1990;146(10):585.
138. Abendroth M, Lutz BJ, Young ME. Family caregivers' decision process to institutionalize persons with Parkinson's disease: A grounded theory study. *International journal of nursing studies.* 2012;49(4):445-454.
139. Bohannon RW. Daily sit-to-stands performed by adults: a systematic review. *Journal of physical therapy science.* 2015;27(3):939-942.
140. Uswatte G, Taub E. Implications of the learned nonuse formulation for measuring rehabilitation outcomes: Lessons from constraint-induced movement therapy. *Rehabilitation psychology.* 2005;50(1):34.
141. Allen NE, Schwarzel AK, Canning CG. Recurrent falls in Parkinson's disease: a systematic review. *Parkinson's disease.* 2013;2013.
142. Michalowska M, FIszer U, Krygowska-Wajs A, Owczarek K. FALLS IN PARKINSON'S DISEASE CAUSES AND IMPACT ON PATIENTS'QUALITY OF LIFE. *Functional neurology.* 2005;20(4):163-168.
143. Schrag A, Hovris A, Morley D, Quinn N, Jahanshahi M. Caregiver-burden in Parkinson's disease is closely associated with psychiatric symptoms, falls, and disability. *Parkinsonism & related disorders.* 2006;12(1):35-41.
144. François C, Biaggioni I, Shibao C, et al. Fall-related healthcare use and costs in neurogenic orthostatic hypotension with Parkinson's disease. *Journal of medical economics.* 2017;20(5):525-532.
145. Ashburn A, Stack E, Ballinger C, Fazakarley L, Fitton C. The circumstances of falls among people with Parkinson's disease and the use of Falls Diaries to facilitate reporting. *Disability and rehabilitation.* 2008;30(16):1205-1212.
146. Brakedal B, Tysnes O-B, Skeie GO, Larsen JP, Müller B. The factor structure of the UPDRS motor scores changes during early Parkinson's disease. *Parkinsonism & related disorders.* 2014;20(6):617-621.
147. McDaniels-Davidson C, Davis A, Wing D, et al. Kyphosis and incident falls among community-dwelling older adults. *Osteoporosis international.* 2018;29(1):163-169.
148. Choi CJ, Lim HW, Park MK, Cho JG, Im GJ, Chae SW. Does the kyphotic change decrease the risk of fall? *Clinical and experimental otorhinolaryngology.* 2011;4(3):118.

149. Bloem BR, Beckley DJ, van Dijk JG. Are automatic postural responses in patients with Parkinson's disease abnormal due to their stooped posture? *Experimental brain research.* 1999;124(4):481-488.
150. Capecci M, Serpicelli C, Fiorentini L, et al. Postural rehabilitation and Kinesio taping for axial postural disorders in Parkinson's disease. *Archives of physical medicine and rehabilitation.* 2014;95(6):1067-1075.
151. Jessop RT, Horowicz C, Dibble LE. Motor learning and Parkinson disease: refinement of movement velocity and endpoint excursion in a limits of stability balance task. *Neurorehabilitation and Neural Repair.* 2006;20(4):459-467.
152. Jöbges M, Heuschkel G, Pretzel C, Illhardt C, Renner C, Hummelsheim H. Repetitive training of compensatory steps: a therapeutic approach for postural instability in Parkinson's disease. *Journal of Neurology, Neurosurgery & Psychiatry.* 2004;75(12):1682-1687.