IMPROVING WALKING IN INDIVIDUALS WITH PARKINSON'S DISEASE THROUGH WEARABLE TECHNOLOGY

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by
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ABSTRACT

Movement problems related to Parkinson's disease (PD) have been shown to have a profound effect on functional independence and reported quality of life. Within the constellation of movement signs of PD (tremor, muscle rigidity, bradykinesia/hypokinesia, and postural instability), impaired arm swing is often the earliest-recognized symptom. It is also a strong independent predictor of greater fall risk and morbidity/mortality risk. Early treatment for movement problems such as impaired arm swing is associated with the greatest improvement in these impairments. However, movement problems often coincide with impaired processing of sensory information, leaving many people with PD with inadequate awareness of their posture and limb position. Thus, PD-related gait deficits are difficult for people to correct by themselves.

External cueing techniques (such as visual cues in the environment or auditory cues for pacing and rhythm) have shown promise in improving parameters such as gait speed, step length, and freezing incidence for people with PD. To date, techniques such as these have not been applied to improving arm swing. Considering the prevalence of arm swing deficits and their strong association with global function, arm swing provides a compelling target for external cueing strategies that may help normalize movement patterns in individuals with PD. Therefore, the primary objective of this project was to determine how cues for increased arm swing may affect gait parameters within a single session of training, as well as after a longer training period with arm swing cues. This series of studies included work involving neurotypical young volunteers, multiple groups of individuals with Parkinson's disease, and neurotypical volunteers age-matched to the volunteers with Parkinson's disease. Arm swing cues for all studies were delivered using

a novel wireless wrist-worn device developed by our group (ArmSense, patented) to measure arm swing and deliver cues for larger, more mechanically normal movement. All studies involved an assessment of baseline walking parameters, training with individualized arm swing cues (or dose-matched walking without cues), and a post-training assessment. Gait parameters of interest included gait velocity, cadence, step length, lateral trunk sway, anterior-posterior trunk sway, interlimb coordination, and surface electromyography (sEMG) characteristics of muscle activation in the anterior deltoid, posterior deltoid, gluteus medius, gastrocnemius (medial head), and peroneus longus. In addition to gait parameters, one study (Chapter 5) involved a month-long training program and measured volunteers at the beginning and end on the Activities-specific Balance Confidence Scale (ABC), the Functional Gait Assessment (FGA), the Timed Up-and-Go (TUG), and the 39-item Parkinson's Disease Questionnaire (PDQ-39).

Chapter 2 provides results of single-session testing of ArmSense in young neurotypical adults. Ten volunteers participated in this study as a single group, wore an ArmSense device on each wrist, and walked at comfortable speed. Walking before ArmSense training was assessed both on a 20-foot walkway and on a self-paced treadmill. Subjects were then provided with individualized arm swing targets in the form of vibratory cues elicited when their anterior arm swing amplitude reached 120% of baseline amplitude. They completed a bout of treadmill walking with the cues in place, instructed only to swing each arm high enough on each step that they got the vibratory feedback. After treadmill training, subjects completed post-test over-ground and treadmill walking bouts with no cues.

As a group, subjects were able to respond to the arm swing cues and showed several changes to their gait pattern with arm swing feedback, including faster walking, increased step length and postural extension, and increased activity in the anterior deltoids and peroneus longii bilaterally. Velocity, step length, and arm swing amplitude remained significantly above baseline during the post-test conditions. Changes across multiple body segments are of note since the only instruction the subjects were given was to "try to swing your arm enough to feel the vibration on every swing." This study, though a preliminary proof-of-concept for the ArmSense device, demonstrates that multisegment changes in kinematics and muscle activation can be elicited in young neurotypical individuals solely through cues for a larger arm swing.

Chapter 3 provides results of single-session testing of ArmSense versus floor-based visual cues in a cohort of individuals with PD. Twelve individuals with PD participated as a single group, wore an ArmSense device on each wrist and walked under five conditions: baseline, visual cues, retention of visual cues (no cues), ArmSense cues, and retention of ArmSense cues (no cues). A balanced crossover design was used (half of the subjects received the visual cue and retention conditions before ArmSense, while half received the ArmSense cue and retention conditions first). All conditions involved walking trials of 10m over ground, with half the trials completed at a self-selected comfortable speed, and half completed at a self-selected fast speed. For the ArmSense cue condition, subjects received vibratory cues elicited when their anterior arm swing amplitude in each arm reached 120% of baseline amplitude (the same type of cue as the study in Chapter 2). Subjects rested for five minutes after each cue condition before beginning the corresponding retention condition.

At a comfortable pace, step length increased during both visual cueing and ArmSense cueing. However, we observed increased lateral trunk sway with visual cueing, possibly suggesting decreased gait stability. In contrast, no statistically significant changes in trunk sway were observed with ArmSense cues compared to baseline walking. At a fast pace, changes in gait parameters were less systematic. Interestingly, even though ArmSense cues only specified changes in arm swing amplitude, we observed changes in multiple other gait parameters, reflecting the active role arm swing plays in gait and suggesting a new therapeutic path to improve mobility in people with PD.

Chapter 4 provides results of single-session testing of ArmSense in three groups: people with PD who received ArmSense cues (PD-C), age-matched older adults who received ArmSense cues (CTL-C), and people with PD who wore ArmSense units but received no cues (PD-NC). Subjects with PD were randomized to the PD-C group or the PD-NC group. Eight subjects were included in each of the three groups. All groups performed 50 baseline walking trials on a 20-foot walkway in a motion capture environment. Cue groups then received individualized targets for increasing their arm swing, set to 110% of baseline amplitude for the more involved arm in the PD-C group or the non-dominant arm in the CTL-C group. All subjects then performed 15 minutes of walking in a quiet gym, during which the PD-C and CTL-C groups received cues and PD-NC group wore ArmSense but received no cues. All subjects then performed 25 over-ground uncued post-training walking trials.

Comparing uncued walking before and after arm swing training (or after dose-matched uncued walking), increases in step length, velocity, and arm swing amplitude were seen after training in the PD-C group, but not the PD-NC group or CTL-C groups.

Arm swing amplitude increased significantly in the more affected arm of subjects in the PD-C group, but not in the other two groups. Analysis of interlimb coordination indicated that while not all subjects had a discernible swing with each arm during each gait cycle, that a higher proportion of those in the PD-C group had a discernible arm swing after training than before (with no corresponding change in the PD-NC group), perhaps indicating a partial normalization of severely impaired arm swing. Finally, the PD-C group demonstrated significantly increased anterior deltoid activity after training, with no other widespread changes in muscle activity with training in the other groups. Though groups were small, this study design included two control/comparison groups (age-matched healthy older adults and a group of individuals with PD who walked without cues), potentially leading to more robust conclusions that arm swing cues may lead to improved gait parameters that cannot be fully explained by the effects of age or time spent walking.

Chapter 5 provides results of the final study in the series, a randomized controlled trial exploring the effects of a 30-day training program for larger arm swing on gait parameters, balance confidence, gait stability, and quality of life. This study included the same volunteers with PD who participated in the single-session study described in Chapter 4 (eight subjects in each group). Following the initial lab session described above, the PD-C and PD-NC groups were issued ArmSense units to wear while walking in their own community environment (walking 30 mins/day, 4-5 days/week, for 30 days). The PD-C group received vibratory cues for a larger arm swing during this walking training while the PD-NC wore the units but received no cues. Both groups then returned to the lab for a second walking session (taking place 24-48 hours after their last training

walk). At this second session, all subjects completed 50 trials of uncued over ground walking, as they had done at the first session. Additionally, both groups completed the ABC, TUG, FGA, and PDQ-39 at both sessions.

Comparing uncued walking in session 1 vs session 2, increases in step length, velocity, arm swing amplitude, and anterior deltoid activity were seen after training in the PD-C group, but not the PD-NC group. FGA and TUG showed a significant session 2 vs session 1 improvement in the PD-C group but not the PD-NC group. ABC, PDQ-39, and other measures did not show significant changes between sessions or between groups. Though groups were small, this randomized controlled trial demonstrated that after training with arm swing cues, individuals with PD may demonstrate improved gait parameters and functional gait stability even 1-2 days after the last training session.

The studies included in this dissertation systematically explored the effects of arm swing cues during gait in neurotypical young adults, in a single-group study with individuals with PD, in individuals with and without PD in a single session with a non-cued control group, and after a month of training with arm swing cues. Though questions remain about the optimal cue dosage and how to integrate this training into a larger physical activity program, this series of studies provides compelling initial evidence that arm swing cues via a portable wireless system may improve gait characteristics including step length velocity, arm swing amplitude, and functional gait stability.

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CHAPTER 1

INTRODUCTION AND REVIEW OF LITERATURE

Parkinson's Disease and Movement Impairments

Parkinson's disease (PD) is the second most common neurodegenerative condition in the U.S. (only Alzheimer's disease is more common). PD affects 1 million Americans and 7-10 million people worldwide (Parkinson's Disease Foundation Inc, 2016), and frequently leads to gait disturbance and falls (Crouse, Phillips, Jahanshani, & Moustafa, 2016; Nieuwboer et al., 2007; Wood, Bilclough, Bowron, & Walker, 2002). The primary pathology related to PD is a dopamine deficiency due to the death of dopaminergic neurons in the basal ganglia, especially in the substantia nigra (Jankovic, 2008).

While PD causes impairments in multiple body systems, some of the earliest and most functionally devastating effects are due to movement-related problems (Bovonsunthonchai, Vachalathiti, Pisarnpong, Khobhun, & Hiengkaew, 2014; Jankovic, 2008; Wood et al., 2002). The cardinal signs of PD are the movement problems of tremor, rigidity, bradykinesia/hypokinesia, and postural instability (Parkinson's Disease Foundation Inc, 2016). In walking, these signs lead to impairments such as small shuffling steps, slow velocity, stiff flexed posture, and reduced or asymmetrical arm swing (Lewek, Poole, Johnson, Halawa, & Huang, 2010; Wood et al., 2002; Wright, Gurfinkel, Nutt, Horak, & Cordo, 2007).

There are long-established associations between these movement problems and profound functional deficits, including increased fall risk, decreased independence, and

decreased reported quality of life (Crouse et al., 2016; Martin & Hurwitz, 1962; Peterson & Horak, 2016; Wood et al., 2002). Conversely, early treatment of movement problems in people with PD is associated with improvement in both pathology-related impairments such as hypokinesia and rigidity, and associated functional and societal participation problems (Morris, Martin, & Schenkman, 2010; Nieuwboer, De Weerdt, Dom, & Lesaffre, 1998; Peterson & Horak, 2016; Wood et al., 2002). Treatment of PD-related movement problems commonly involves a combination of several interventions: dopaminergic medications (such as dopamine replacement or agonists), deep brain electrical stimulation, assistive devices/technology, and/or physical rehabilitation.

The goal of dopaminergic medication is to preserve or supplement dopamine within the brain. In fact, decreased symptoms in response to increased dopamine is a common method of confirming a diagnosis of idiopathic PD (Parkinson's Disease Foundation Inc, 2016). These medications have been shown to be effective in reducing tremor, bradykinesia and rigidity, and are almost always a part of an individual's treatment program (Jankovic, 2008; Parkinson's Disease Foundation Inc, 2016). However, dopaminergic medications can have disruptive side effects such as unwanted voluntary movements (dyskinesia), and have not been shown to be effective in alleviating posture or gait related impairments (Curtze, Nutt, Carlson-Kuhta, Mancini, & Horak, 2015; Rocchi, Chiari, & Horak, 2002; Wright et al., 2010)

Deep brain electrical stimulation (DBS) is a more recent treatment technique in which a device that generates an electrical current is surgically implanted in the brain at a site that alleviates the symptoms(s) being treated. Such implanted devices, most often at the globus pallidus or subthalamic nucleus, have been shown to be effective in relieving

tremor, rigidity, and bradykinesia with fewer side effects than dopaminergic medications (Curtze et al., 2015; Fasano et al., 2011; Rocchi et al., 2002; St. George, Nutt, Burchiel, & Horak, 2010). However, there is conflicting information about whether DBS improves postural and gait impairments or may slightly worsen these impairments, especially in the short term (Fasano et al., 2011; Rocchi et al., 2002; St. George et al., 2010). With both medications and DBS, treatment may be complicated by side effects, treatment contraindications or precautions, and the additional risks involved in DBS implantation surgery.

By contrast, physical activity and movement-based rehabilitation do not involve the risks of surgery or side effects, and have been shown to be effective for short-term improvements in posture and gait (Farley & Koshland, 2005; Fox et al., 2012; McNeely et al., 2015; Mehrholz et al., 2010; Morris et al., 2010). Common interventions in skilled therapy or community exercise sessions include walking/general full-body exercise (Ebersbach et al., 2010; Farley & Koshland, 2005), Tai Chi (McNeely et al., 2015), tango dancing (McNeely et al., 2015), treadmill walking (Mehrholz et al., 2010), and tandem or spin-cycling (McGough et al., 2016; Ridgel, Abdar, Alberts, Discenzo, & Loparo, 2013; Wu, Hallett, & Chan, 2015). A popular recent physical activity intervention focusing on increasing the amplitude of movements is LSVT®BIG, in which certified therapists encourage maximal-amplitude movements in a range of functional positions to alleviate hypokinesia (Ebersbach et al., 2010; Farley & Koshland, 2005; Fox et al., 2012). Common denominators in all these physical activity regimens include high frequency, high intensity training in proper movement patterns to maximize carryover to post-

treatment activity. Training may involve multiple hours of exercise per day for three to five days per week, and frequent external coaching for desired movement parameters.

Parkinson's Disease and Sensory Processing Impairments

One of the likely reasons why such a high volume of training seems necessary for success in treating PD-related movement problems is that PD pathology involves an element of impaired sensory integration, especially proprioception (Almeida et al., 2005; Hwang, Agada, Grill, Kiemel, & Jeka, 2016; Jacobs & Horak, 2006; Ketzef et al., 2017; Konczak et al., 2009; Vaugoyeau, Hakam, & Azulay, 2011; Wright, Gurfinkel, King, & Horak, 2007). Impaired sensory integration may complicate physical activity intervention by affecting an individual's ability to accurately detect errors in their movements (Bertolini, Wicki, Baumann, Straumann, & Palla, 2015; Hwang et al., 2016; Konczak et al., 2009). It is not surprising, then, that if sensory information is not properly being interpreted, basal ganglia impairments related to starting, stopping, scaling, and pacing movements could be very difficult to correct (Jankovic, 2008; Ketzef et al., 2017; Wu et al., 2015). Compensatory techniques have traditionally involved focusing an individual's conscious attention on the motor task in order to recruit additional cognitive pathways in place of impaired basal ganglia pathways, but these attentional demands can become so great that tasks are exhausting and not conducive to normal function (Behrman, Teitelbaum, & Cauraugh, 1998; Nieuwhof et al., 2017).

With these considerations in mind, significant recent research has explored the concept of combining physical activity training with cues, "using external temporal or spatial stimuli to facilitate movement (gait) initiation and continuation" (Nieuwboer et

al., 2007). As augmented feedback from external sources, cues may help to bridge the gap of missing or poorly integrated sensory information (Rubinstein, Giladi, & Hausdorff, 2002), whether through visual cues, auditory cues, or tactile/vibratory information. Visual cues are commonly used to improve the spatial parameters of a task, such as using pieces of tape on the floor to encourage proper foot placement (Lim et al., 2010; Nieuwboer et al., 2007; Nieuwboer et al., 2009; van Wegen, Hirsch, Huiskamp, & Kwakkel, 2014). Auditory cues are commonly used to improve the temporal/rhythmic parameters of a task (Lim et al., 2010; Rubinstein et al., 2002). Tactile/vibratory information has been used mostly for temporal/rhythmic cues, but is the least studied cueing modality (El-Tamawy, Darwish, & Khallaf, 2012; Nieuwboer et al., 2007).

While modalities of external feedback combined with physical activity can lead to immediate short-term improvements, these changes must be trained with high-frequency high-intensity regimens for the changes to persist after the external feedback is withdrawn. Additionally, it is difficult for many types of cues to be transferred from the clinic environment to the community, perhaps due to the permanent nature of the cueing mechanisms themselves (such as pieces of tape on the floor), or the risk that the cues could interfere with necessary sensory information from the environment (such as using auditory cues from headphones while walking on a busy city street). At this time, there is no clear consensus in the literature as to the best method, modality, or site on the body to deliver optimum cues for improving gait.

Parkinson's Disease and Arm Swing Impairments

Arm swing represents a significant yet understudied motor symptom of PD during gait. Impaired arm swing is the most common motor symptom of PD (Lewek et al., 2010; Mirelman et al., 2016), sometimes even detected before clinical diagnosis (Mirelman et al., 2016), and is an independent predictor of increased fall risk (Crouse et al., 2016; Wood et al., 2002). However, arm swing has only recently been quantitatively described in the PD literature, and little attention has been paid to arm swing when walking in natural environments (Lewek et al., 2010; Roemmich et al., 2013; Roggendorf et al., 2012; Zampieri et al., 2010).

The Role of Arm Swing in Gait

In considering arm swing as a gait-related movement impairment to be treated in individuals with PD, it is also important to note that the relationship between arm and leg movements seen in healthy persons (Bruijn, Meijer, Beek, & van Dieën, 2010; Eke-Okoro, Gregoric, & Larsson, 1997; Massaad et al., 2014; Meyns, Bruijn, & Duysens, 2013; Sylos-Labini et al., 2014) persists to some extent even in people with PD, though the relative phase and coordination may be different in people with PD (Bondi, Zeilig, Bloch, Fasano, & Plotnik, 2017; Lewek et al., 2010; Plotnik, Giladi, & Hausdorff, 2007; Roemmich et al., 2013). While arm swing impairments may co-exist with other impairments such as increased trunk or limb rigidity or proprioceptive integration deficits (Jacobs & Horak, 2006; Wright, Gurfinkel, Nutt, et al., 2007), it is unclear from the literature whether impaired arm swing is a consequence of another PD symptom or the result of a combination of symptoms. To our knowledge, arm swing measurement has

never been combined with cueing for a specific movement target. However, arm swing could provide a promising application for external cues. Where arm swing abnormalities are detected early in the pathology of PD, these deficits may provide the earliest opportunity to apply cues for improving gait. Additionally, a cueing mechanism worn on the upper extremity could be easier to put on and remove and potentially more socially acceptable for the user than placement at other body sites. Finally, the higher incidence of peripheral sensory loss in the lower extremities versus the upper extremities (Jankovic, 2008; Morris et al., 2010) could make the upper extremity a preferable location for a cueing device.

In working towards a better understanding of arm swing impairment in people with PD, the research questions are compelling: Can impaired arm swing be treated? If so, using what type of cueing? And how might such cues affect the rest of the individual's gait pattern?

The ArmSense System for Arm Swing Cues

To explore these questions, we have developed a wrist-based wireless device (ArmSense), which measures arm swing during walking using accelerometers and gyroscopes and delivers a customized real-time cue to encourage a larger arm swing. The goal of this series of experiments is to demonstrate whether ArmSense cueing is a viable concept for changing arm swing, determine the immediate effects of arm swing cueing on spatiotemporal gait parameters and trunk posture, and explore the longer-term effects of ArmSense cue training on gait impairments, balance, and quality of life.

To best answer these questions with an efficient paradigm adaptable to clients at different mobility levels, we propose a theoretical framework of augmented feedback to guide the delivery of cueing, both in a supervised clinic/lab environment and in a person's home and community environment. A tracking and cueing device may make a significant difference in the lives of these patients, allowing them to receive helpful movement cues in their home and community when not receiving clinical treatments. However, most commercially-available technology for monitoring movement (such as fitness trackers or mobile apps) cannot deliver precise feedback that is tuned to aid mobility in real-time, limiting the usefulness of these devices to people with PD. Here, we propose to improve mobility using ArmSense.

The ArmSense device (Figure 1-1) consists of triaxial accelerometers and gyroscopes, a small vibrating motor, a microprocessor board, and components for transcribing/saving the data (either to an on-board SD card or transmitted through Bluetooth to a nearby desktop/laptop computer or smartphone). As measurements of angular acceleration and velocity are obtained by the triaxial sensors, they are combined with a fusion algorithm similar to that used by Madgwick (Madgwick, Harrison, & Vaidyanathan, 2011), in order to minimize measurement errors associated with underestimation in the accelerometer or drift in the gyroscope.

a) b)

Figure 1-1. ArmSense device prototypes in position on wrists. a) Version 1 (2015) b) Version 2 (2017).

ArmSense has the potential for increasing movement amplitude and coordination in walking, with widespread health, economic, and quality of life benefits for individuals with conditions impairing arm movement during walking, including those with PD. The primary objective of this project was to determine how cues for increased arm swing may affect gait parameters within a single session of training, and whether any observed benefits transfer to more permanent changes with repetitive use of such cueing after a longer training period. It is proposed that the following specific aims will be addressed in this dissertation:

Specific Aims

Specific Aim 1: To determine short-term improvements in gait with ArmSense cues in individuals with PD. To better understand how increased arm swing affects step length, gait speed, muscle activity and arm/leg coordination, we will examine single-session walking with and without a vibration cue to increase arm swing.

Hypothesis 1a. ArmSense cues will lead to increased step length.

Hypothesis 1b. ArmSense cues will lead to improved arm/leg coordination.

Hypothesis 1c. ArmSense cueing will lead to reduced variability of arm/leg relative phase.

Hypothesis 1d. ArmSense cueing will lead to more normalized muscle activity in arm and leg muscles as compared with people without PD.

Specific Aim 2: To determine if there are sustained improvements in gait and quality of life with ArmSense cues in individuals with PD. To apply the effects of ArmSense in a more relevant and impactful setting, people with PD will use ArmSense while walking at home for four weeks, with half of the subjects receiving tracking and arm swing vibration cueing while the other half receive tracking only. Pre- and post-tests will assess subjects' performance on gait parameters, quality of life and motor-related PD symptoms.

Hypothesis 2a. Arm swing amplitude during uncued walking will increase after intervention.

Hypothesis 2b. Step length and velocity during uncued walking will increase after intervention.

Hypothesis 2c. Arm/leg coordination during uncued walking will improve after intervention.

Hypothesis 2d. Assessment of balance confidence, balance in gait, and quality of life will improve after intervention.

Through these fundamentally related aims, we propose to use the ArmSense cueing device to facilitate gait improvements first in a laboratory environment, then in

home and community environments. We believe this technology, the first to our knowledge to encourage changes in arm swing through precise individualized cues, can improve mobility with every walk, even outside the therapy clinic.

CHAPTER 2

GAIT CHANGES WITH USE OF AN ARM SWING CUEING DEVICE IN NEUROTYPICAL YOUNG PEOPLE

Introduction

The role of arm swing in human gait has been the focus of considerable research for most of the last century, including how arm movements are generated during walking (through active muscle contractions, as a passive consequence of movements in other body segments, or as a context-dependent combination of the two mechanisms), and how reciprocal arm swinging movements are neurologically and biomechanically coupled with reciprocal leg stepping movements. Elftman (1939) was one of the first to study arm swing behavior and hypothesized about possible connections between arm swing and leg movements (Elftman, 1939). Researchers since then have demonstrated that larger arm swing is correlated with increased gait speed and step length (Bruijn et al., 2010; Meyns et al., 2013), indicating a mechanical coupling between the two movement patterns. In 2014, Sylos-Labini and colleagues showed that periodic arm movements in a "gait-like pattern" (Sylos-Labini et al., 2014) are associated with increased cyclical EMG activity in leg muscles even if the legs are unweighted and immobilized. Most recently, the same group showed temporal associations between the EMG burst associated with deltoid activity in arm swing and muscle activity associated with stepping in the legs (La Scaleia et al., 2014). Though this body of work serves to further characterize the connection between gait movement patterns in the arms and legs in neurotypical individuals, it is still

unknown whether an external cue specific to arm motion will also generate changes in muscle activation in other body segments.

The purpose of this study was to investigate possible gait changes associated with larger arm swing in young neurotypical individuals. ArmSense, a novel portable cueing device that delivers an individualized vibratory cue to encourage a larger arm swing, has recently been developed to study gait effects of cues for larger arm swing (Thompson, Agada, Wright, Reimann, & Jeka, 2017), but without any precise spatiotemporal, kinematic or muscle activation information. To further explore the effects of this device on gait in a laboratory environment, we used motion capture technology and surface electromyography (sEMG) to detect changes in both kinematic parameters and muscle activation patterns with the use of ArmSense to encourage a larger amplitude arm swing. Based on previous pilot work, we hypothesized that a sample of neurotypical young adults would demonstrate increased arm swing amplitude in response to the cues, as well as increased gait velocity, step length, and increased amplitude of muscle activation in the body segments that show increased movement amplitude. We hypothesized that the cues would have a minimal positive effect, and perhaps even a disruptive effect, on interlimb coordination, as young healthy individuals have been shown to walk with one arm and the opposite leg in-phase, and with the ipsilateral arm and leg antiphase (Perry, Burnfield, & Cabico, 2010; Plotnik et al., 2007).

Methods

Subjects

Ten neurotypical young adults were included in this study (3 females, 7 males, mean age 25.3±5.8, all right hand dominant). Volunteers were recruited through fliers located on the university campus where the laboratory is housed. All subjects were free from history of neurological injury or illness, orthopaedic surgeries that affected walking, and any other medical condition that could preclude safe and comfortable walking. The study was approved by the institutional review board (protocol #22499). Written consent was obtained from all subjects before participation.

Procedures

Subjects wore an ArmSense device on each dorsal wrist, as seen in Figure 1-1 (a) and described by Thompson et al. (2017). Each device consisted of a microprocessor, wireless communication hardware, vibration motor, and tri-axial accelerometers, gyroscopes and magnetometers (all components through SparkFun Electronics, Boulder, CO, USA). Sensor data were streamed in real-time from the microprocessor boards housed in each sensor to a desktop computer. The accelerometer and gyroscope data were fused together on the desktop in a custom-written LabVIEW program (National Instruments, Austin, TX, USA) to generate 4D quaternion angles, as in Madgwick et al (Madgwick et al., 2011). By fusing these sensor data, an estimate was generated of the rotation of the ArmSense device relative to vertical (person's arms placed at their sides perpendicular to the floor). Additionally, subjects wore 45 passive reflective markers attached to the skin according to Vicon's Plug-In Gait marker set with 6 additional markers placed on the anterior thighs, anterior tibias, and 5th metatarsal heads as seen in

Figure 2-1 (Reimann, Fettrow, Thompson, & Jeka, 2018). Finally, subjects wore eight wireless Trigno sEMG sensors (Delsys Inc., Natick, MA, USA), with placement on bilateral anterior deltoid, peroneus longus, gluteus medius, and medial gastrocnemius muscles as per SENIAM international guidelines ("Surface ElectroMyoGraphy for the Non-Invasive Assessment of Muscles," 2017).

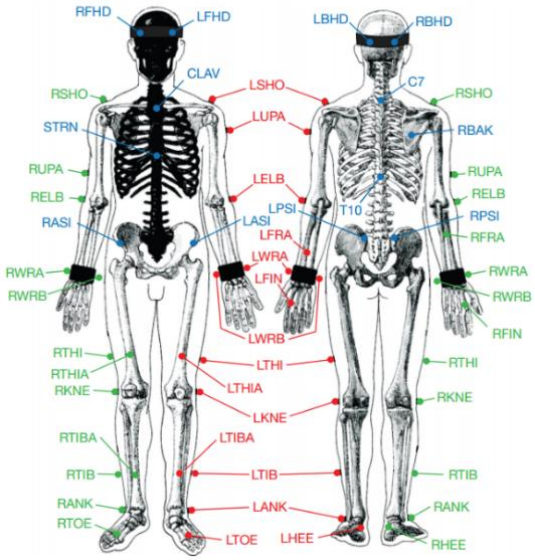

Figure 2-1. Marker placement for 45 passive markers (same placement used for treadmill and over ground collection environments.)

Subjects walked under five conditions in two motion capture environments, all at a self-selected comfortable walking speed. Over ground walking was captured at baseline-and post-training, with conditions named baselineOG and postOG, respectively. Over ground walking was performed on a 20-foot walkway with a safety harness for support (see Figure 2-2), with 20 trials of the length of the walkway conducted under each condition. Positions of the passive markers were recorded by 12 Qualisys Oqus cameras (Qualisys AB, Goteborg, Sweden) at 100 Hz.

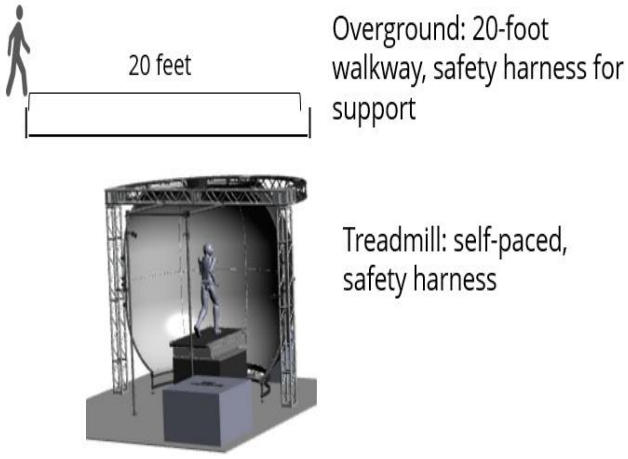

Figure 2-2. Data collection environments.

In addition to the two over ground conditions, three walking conditions were performed on a self-paced treadmill, consisting of a split-belt treadmill with belts tied and running at the same speed (Bertec Corporation, Columbus, Ohio, USA). Treadmill conditions were named baselineTM, feedback, and postTM. Treadmill belt speed was varied by a proportional-derivative controller custom-created in LabView (National Instruments, Inc., Austin, TX, USA), with the controller programmed to keep the position of the markers on the subject's posterior superior iliac spines in the anterior-posterior midline of the treadmill. When the subject walked faster and moved forward on the treadmill belts, the controller sped up the belts. When the subject walked more slowly and moved backward on the treadmill belts, the controller slowed down the belts accordingly. This protocol was used so that subjects would have no external velocity imposed on walking but were in control of their own speed throughout all conditions. To provide visual flow consistent with each participant's speed, a virtual environment was projected onto a hemispherical shell partially surrounding the treadmill (see Figure 2-2). The virtual environment was custom-programmed in Unity3d (Unity Technologies, San

Francisco, CA, USA), and consisted of a tiled floor with floating cubes distributed randomly on a sky background as discussed in (Reimann et al., 2018) and pictured in Figure 2-3. Perspective in the scene was linked to the two markers on subject's temples (front head markers in Figure 2-1), and speed of the visual flow varied according to the treadmill belt speed. Positions of the passive markers in the treadmill environment were recorded by nine Vicon cameras (Vicon Motion Systems, Oxford, UK) at 250 Hz.

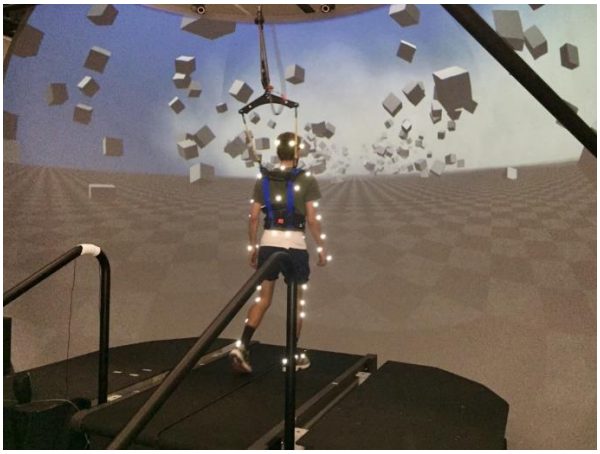

Figure 2-3. Self-paced treadmill and virtual walking environment.

Subjects walked five 2-minute trials in the baselineTM condition, ten 2-minute trials in the feedback condition, and (following a five-minute rest period) five 2-minute trials in the post-TM condition. Before any data collection on the self-paced treadmill, subjects walked on the treadmill for 15 minutes to acclimate themselves to the environment. The total order of conditions for all subjects was as follows: baselineOG, 15-minute treadmill acclimation period, baselineTM, feedback, five-minute rest period, postTM, postOG. The self-paced treadmill environment is pictured in the diagrams in Figures 2-2 and 2-3.

Following the two baseline conditions, the arm swing amplitude for each arm was determined, calculated as the median angular change from vertical during all trials of the baselineTM condition. The baselineTM condition was chosen since it offered a larger data set and pilot testing showed no significant difference in arm swing amplitude between baselineOG and baselineTM conditions. Target arm swing amplitude was set at 120% of median baseline swing amplitude for each arm, and vibratory cues were delivered during each anterior arm swing that the subject reached the target amplitude. During all trials in the feedback condition, subjects received vibratory feedback on each arm swing of sufficient amplitude, with occasional repetition of the verbal cue, "Try to swing your arm high enough to get the vibration on every step." Following the feedback trials, subjects rested in sitting for five minutes, then completed the postTM and postOG conditions.

Data Analysis

Arm swing was measured by the ArmSense devices to record baseline swing and ensure subjects were reaching target angle and triggering vibration during the feedback condition. Gait velocity was measured using the treadmill belt speed and the velocity per step as detected by movement of the heel markers. Step length was measured as the anterior-posterior distance between heel markers at each heel contact. Lateral and anterior-posterior trunk sway were measured as the angular change relative to vertical of the line connecting the marker on the C7 spinous process and the midpoint between the markers on the left and right posterior superior iliac spines. Interlimb coordination was measured by tracking the anterior-posterior local maxima of the heel markers and the midpoint of the two wrist markers on each side. The position of the markers was used to

calculate phase based on the formula presented by Plotnik (Plotnik et al., 2007), using the swing time of each arm and leg. Phase between the ipsilateral arm and leg should have a value of approximately 180 degrees, since the maximum anterior arm swing should occur at the halfway point between adjacent heel strikes of that leg. (Conversely, the phase between one arm and the contralateral leg should have a value of zero, since the maximum anterior arm swing should occur at the same time as heel strike of the contralateral leg.) Figure 2-4 further illustrates expected phase relationships between ipsilateral and contralateral limbs.

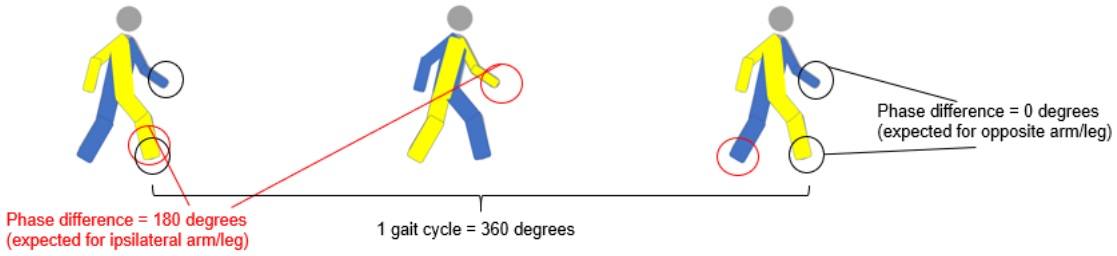

Figure 2-4. Typical expected phase relationships (180 degrees for arm versus ipsilateral leg, 0 or 360 degrees for arm versus contralateral leg).

Surface electromyography (sEMG) data were collected at 1100 Hz, rectified, and then low pass filtered at 10 Hz to create a linear envelope shape to allow for clear comparison of timing and amplitude patterns across conditions, similar to sEMG processing procedures previously used by this group (Logan et al., 2014). sEMG data are presented here with a unitless amplitude, normalized to the resting activity of each subject, to allow for comparison of mean gait cycle traces across conditions. Custom-written programs in MATLAB (Mathworks, Natick, MA, USA) were used in data analysis.

Separate repeated-measures ANOVA analyses were performed on each discrete gait parameter (velocity, step length, ipsilateral arm-leg phase), with each analysis comparing the five testing conditions. Continuous variables (arm swing amplitude, trunk extension, and muscle activity) were plotted as averages of all gait cycles in a given condition, with mean and 95% confidence interval traces, from which visual inspection was used to determine points of significant difference between conditions. Level of significance (alpha) was set a priori to 0.05. When significant main effects were noted in the ANOVA analysis, *post hoc* paired *t*-tests with Bonferroni corrections for multiple comparisons were used (since Kruskal-Wallis test showed normal distribution for velocity and step length). All calculations were performed in SPSS 23 (IBM, Armonk, NY, USA) and Microsoft Excel 2016 (Microsoft, Redmond, WA, USA). Results plots show combined results for all 10 subjects and are averaged across all gait cycles for each condition.

Results

ANOVA test for step length yielded main effect for condition (*F=8.912, sig=0.009)*. ANOVA test for velocity yielded main effect for condition (*F=4.142, sig=0.011).* Findings for these and other variables of interest are further described below. Figures below provide a summary of responses by variable across conditions, with significant differences indicated when they were found by *post hoc* testing relative to the baselineTM condition. No main effect of condition was found for phase difference.

Step Length

Figure 2-5 illustrates increases in step length relative to the baselineTM condition. Increased step length was first noted during the feedback condition ($p = 0.011$) and

remained significantly above baselineTM in both postTM (p = 0.009) and postOG (p = 0.012) conditions. There was no significant difference between the baselineTM and baselineOG step lengths.

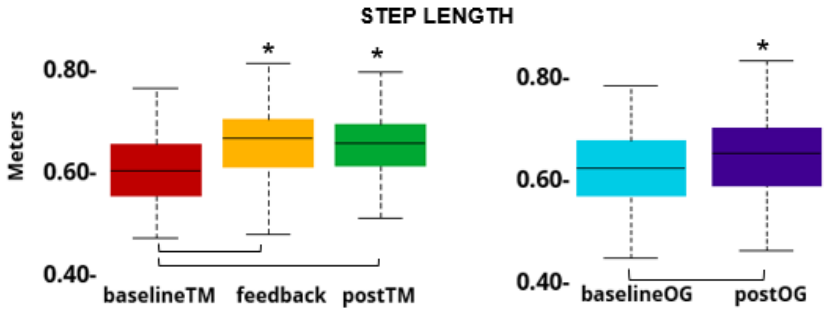

Figure 2-5. Step length by condition (TM = treadmill; OG = over ground). Asterisks indicate statistically significant difference between the condition indicated and baselineTM, with statistical significance defined with Bonferroni correction as $p \leq 0.0125$. (Please refer to text for exact p values.)

Velocity

Figure 2-6 illustrates increases in velocity relative to the baselineTM condition. Increased velocity was first noted during the feedback condition (p = 0.012) and remained elevated in the postTM condition (p = 0.011). There was a nonsignificant trend towards increased velocity in the postOG condition relative to the baselineTM and baselineOG conditions (p = 0.031).

Interlimb Coordination

Figure 2-7 shows phase difference across condition, with no main effect found for condition. There appears to be a slight deviation from anti-phase in the feedback condition, which subsided in the post-test conditions.

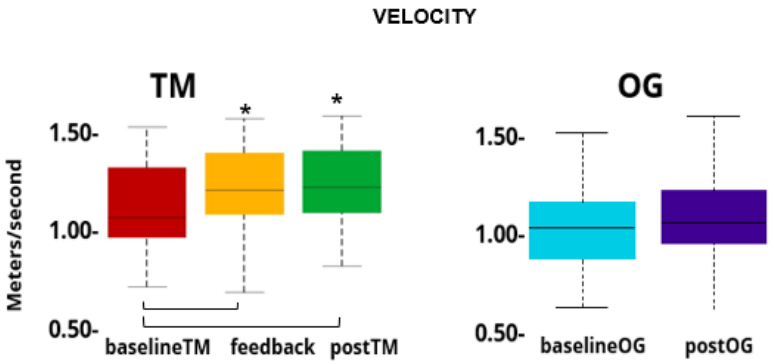

Figure 2-6. Velocity by condition (TM = treadmill; OG = over ground). Asterisks indicate statistically significant difference between the condition indicated and baselineTM, with statistical significance defined with Bonferroni correction as $p \leq 0.0125$. (Please refer to text for exact p values.)

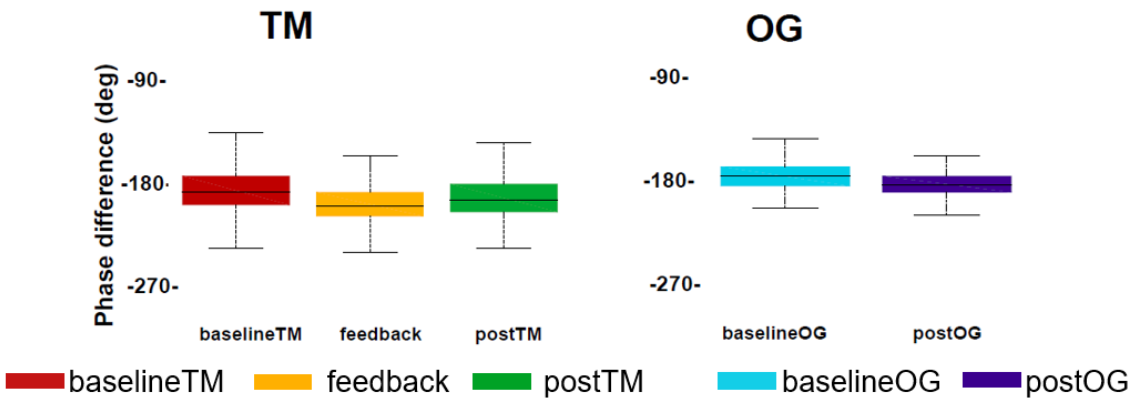

Figure 2-7. Ipsilateral arm-leg phase by condition (TM = treadmill; OG = over ground). 180 degree phase difference indicates the expected anti-phase relationship between the arm and leg on the same side. Asterisks indicate statistically significant difference between the condition indicated and baselineTM, with statistical significance defined with Bonferroni correction as $p \leq 0.0125$. (Please refer to text for exact p values.)

Anterior-Posterior Trunk Position

Figure 2-8 illustrates significantly increased trunk extension during the feedback condition versus baselineTM ($p < 0.01$), with subjects returning to their original posture after the washout period (no difference between baselineTM and postTM condition.)

Both baselineOG and postOG demonstrated slightly but not significantly increased trunk extension versus baselineTM (p = 0.089), and there was no difference between the over ground conditions.

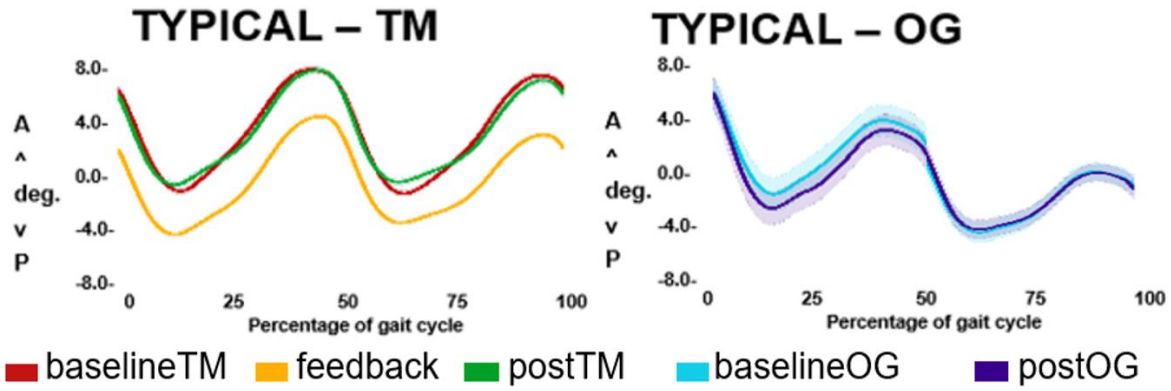

Figure 2-8. Anterior-posterior trunk sway by condition. "A" on the vertical axis indicates more anterior trunk lean (flexion), "P" indicates more posterior trunk lean (extension). Dark lines indicate mean trajectory for each condition; surrounding shading indicates 95% confidence interval. Statistically significant differences are indicated by traces without overlapping confidence intervals.

Arm Swing Amplitude

Figure 2-9 shows increased arm swing amplitude during the feedback condition versus baselineTM, which lessened somewhat in postTM but remained above baseline amplitude. Additionally, increased arm swing amplitude was seen in the postOG condition relative to the baselineOG condition.

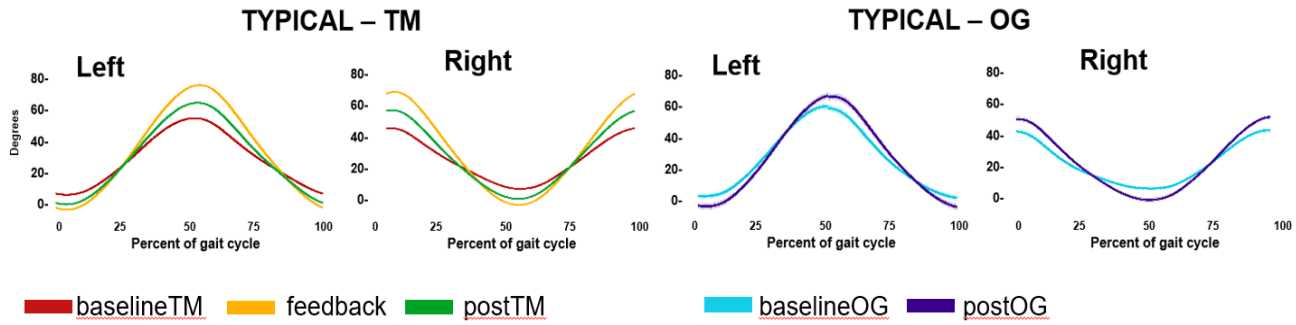

Figure 2-9. Arm swing amplitude by condition. Dark lines indicate mean trajectory for each condition; surrounding shading indicates 95% confidence interval. Statistically significant differences are indicated by traces without overlapping confidence intervals.

Muscle Activity

Figure 2-10 shows muscle activation in each anterior deltoid and peroneus longus muscle, where the right anterior deltoid activity was significantly increased in the feedback and postTM conditions versus baselineTM, and in the postOG versus baselineOG conditions. No consistent differences were seen in the left anterior deltoid. In the peroneus longus, activity was increased bilaterally in the feedback and postTM conditions during pushoff, relative to the baselineTM condition. This difference is smaller (not exceeding the shaded 95% confidence interval), but the trend is still present in the postOG condition relative to the baselineOG condition on the left side.

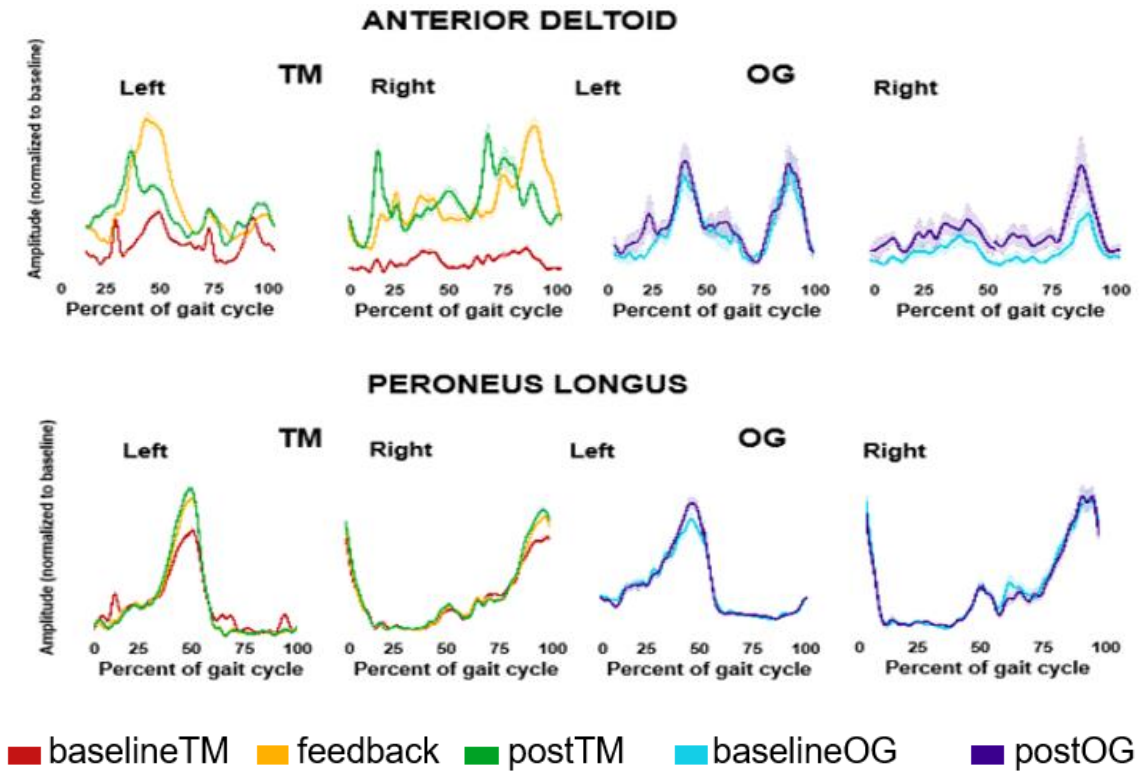

Figure 2-10. Muscle activity by condition for the anterior deltoid and peroneus longus. Dark lines indicate mean trajectory for each condition; surrounding shading indicates 95% confidence interval. Statistically significant differences are indicated by traces without overlapping confidence intervals.

Discussion

This work reports the single-session response of a cohort of ten young neurotypical adults who received cues to walk with a larger arm swing. Considering the pilot nature of the study and the small sample size, some design choices were made to ensure the results could be as widely generalizable as possible. First, a repeated-measures study design was chosen to allow each participant to act as their own control. Secondly, the study included both treadmill and over ground walking. The self-paced treadmill with proportional visual flow attempted to replicate an over ground environment as much as possible, while providing the long periods of uninterrupted stepping in a motion capture environment that could only occur on a treadmill. However, there are still conflicting opinions in the literature about how generalizable treadmill walking is to over ground walking (Mehrholz et al., 2010). Out of an abundance of caution in this regard, conditions of true over ground walking were included both before and after treadmill walking. Over the course of the conditions, subjects showed several changes to their gait pattern with arm swing feedback during treatment and post-test walking.

Feedback Condition

As expected, subjects were able to significantly increase their arm swing during feedback trials in response to the cues. Other changes seen during the feedback trials included increased speed, step length, postural extension, and activity in the peroneus longii and anterior deltoids (but not in the gluteus medius or medial gastrocnemius). Increased trunk extension in the presence of larger arm swing could reflect a difference in

muscle recruitment or trunk inertia as the arm motion changed. Indeed, recent work in runners has demonstrated a change in "back functional line" muscle activity (including the latissimus dorsi, gluteus maximus, and vastus lateralis) with changes in arm swing (Agresta, Ward, Wright, & Tucker, 2018). However, these findings have not yet been replicated in walking, and placement of the safety harness and limitations of the EMG collection system precluded the monitoring of these muscle groups in addition to those already being studied. Additionally, the fact that the trunk extension effects were limited to the feedback condition while other kinematic and muscle activity changes persisted into the post-test conditions (see below) indicates that the trunk extension may not be fully attributable to increased arm swing. Trunk extension changes may instead reflect changes in attention to task with arm swing cues or even biomechanical compensation to try to raise the arms higher in anterior swing.

Increased gait speed and step length on their own could reflect increased volitional effort in walking when arm swing was voluntarily increased or could simply reflect the biomechanical relationship in which a greater arm swing and rotational velocity in the trunk and pelvis could lead to increased step length. However, when the increased step length and velocity are considered along with the increased muscle activity in both upper and lower extremities, it seems more likely that these changes reflect an increased active effort to walking. Interestingly, the muscle activity differences with feedback were not symmetric, but were greater on the right deltoid and left peroneus longus. One possible explanation could be that all subjects were right-handed and may have thus shown a greater voluntary response in their right versus left arms. Additionally, since left leg motion is coordinated with the right arm during normal gait (Bondi et al.,

2017; Perry et al., 2010) and peroneus longus serves as a secondary propulsion muscle during straight-line walking, left leg propulsion might have increased with the greater change in right anterior deltoid activation. Finally, it is possible that as a group subjects may have had a larger baseline arm swing on the right, an asymmetry that could have been further increased with the 120% baseline amplitude target for each arm. Gait changes that occurred during the feedback condition, particularly those in the trunk and lower extremities, are notable since the only instruction the subjects were given was to "try to swing your arm enough to get the vibration on every step."

PostTM and PostOG Conditions

Arm swing amplitude, velocity, and step length were not as increased in the postTM condition as in the feedback condition but were still significantly different than baselineTM. Changes in the post-test conditions are especially interesting since arm swing cues and instructions were only given during the feedback condition, and there was a five-minute rest between the feedback condition and the start of the postTM condition. Less pronounced changes from baseline were noted in postOG than in postTM, though step length, arm swing amplitude, and anterior deltoid activity remained elevated in postOG. The blunted changes in postOG versus postTM may have been seen for several reasons. First, postOG walking always followed postTM walking, so it is possible that subject fatigue or simply the passage of time could have led to smaller effects in the postOG condition. Also, the motion capture environment for over ground walking was limited to 20 feet. Though no significant differences were found between baselineOG and baselineTM, it is possible that the shorter continuous walking periods in postOG may have limited the ability to detect more subtle differences from baseline.

There were several limitations to this study. The small sample size and repeated-measures design (with lack of a separate control group) were practical for an initial proof-of-concept investigation but could restrict generalizability of the results. Additionally, the inclusion of both treadmill and over ground conditions, while intended to ensure the results could be generalizable beyond treadmill walking, could have added to the fatigue of subjects and affected their walking in post-test conditions. Finally, the self-paced treadmill and virtual environment required a significant adaptation period to ensure that data collection would not capture a "learning effect" in which subjects' gait changed simply from getting used to the treadmill. While such an adaptation period is common in treadmill studies (Mazzà, Donati, McCamley, Picerno, & Cappozzo, 2012; Mehrholz et al., 2010), this added walking may have added to participant fatigue and could pose a more significant challenge were this protocol applied to populations with impaired walking endurance.

It should be noted that there were several variables monitored during the study that did not significantly differ across any of the study conditions: gluteus medius activity, medial gastrocnemius activity, lateral trunk sway, and interlimb coordination (change in phase difference between arm and leg). Of particular interest is the behavior of interlimb coordination in feedback and post-test conditions. While ipsilateral arm and leg remained close to the expected 180 degree anti-phase throughout all conditions, the largest change from anti-phase was seen during the feedback condition. This indicated that in these unimpaired subjects, cues for a larger arm swing may have actually disrupted their interlimb coordination. However, it should be noted that subjects were

only allowed ten minutes of walking with cues and may have required more time to further acclimate to walking with a larger arm swing.

Conclusion

Literature indicates that arm swing is intimately connected to spatiotemporal parameters of gait and activity in other segments, whether the movements are largely passive or active. Changes in arm swing frequency and amplitude have been seen with changes in speed and step length (Perry et al., 2010), but it is unknown whether a change in arm swing can precipitate a change in other gait parameters. Considering that many types of impaired gait (such as gait seen in those with stroke or Parkinson's disease) also involve impaired arm swing, an intervention using arm swing to target larger gait behavior could represent a new path in functional mobility rehabilitation. This study, though a preliminary proof-of-concept for the ArmSense device in a sample of young neurotypical individuals, demonstrates that multisegment changes in kinematics and muscle activation can be elicited solely through cues for a larger arm swing.

CHAPTER 3

SPATIOTEMPORAL GAIT CHANGES WITH USE OF AN ARM SWING CUEING DEVICE IN PEOPLE WITH PARKINSON'S DISEASE

This work has been published in *Gait and Posture* (Thompson, Agada, et al., 2017)**.** As per Elsevier publishing company, no permissions are necessary to use this work.

Introduction and Abstract

Abstract

Impaired arm swing is a common motor symptom of Parkinson's disease (PD), and correlates with other gait impairments and increased risk of falls. Studies suggest that arm swing is not merely a passive consequence of trunk rotation during walking, but an active component of gait. Thus, techniques to enhance arm swing may improve gait characteristics. There is currently no portable device to measure arm swing and deliver immediate cues for larger movement. Here we report pilot testing of such a device, ArmSense, using a crossover repeated-measures design. Twelve people with PD walked in a video-recorded gym space at self-selected comfortable and fast speeds. After baseline, cues were given by either visually using taped targets on the floor to increase step length or through vibrations at the wrist using ArmSense to increase arm swing amplitude. Uncued walking then followed, to assess retention. Subjects successfully reached cueing targets on >95% of steps. At a comfortable pace, step length increased during both visual cueing and ArmSense cueing. However, we observed increased medial-lateral trunk sway with visual cueing, possibly suggesting decreased gait stability. In contrast, no statistically significant changes in trunk sway were observed with ArmSense cues compared to baseline walking. At a fast pace, changes in gait parameters

were less systematic. Even though ArmSense cues only specified changes in arm swing amplitude, we observed changes in numerous gait parameters, reflecting the active role arm swing plays in gait and suggesting a new therapeutic path to improve mobility in people with PD.

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease in the US, affecting one million Americans and 7-10 million worldwide (Parkinson's Disease Foundation Inc, 2016). Its cardinal symptoms of tremor, rigidity, bradykinesia, and postural instability lead to progressive deficits, and in many cases to gait disturbance and falls (A Nieuwboer et al., 2007). Symptoms of PD during walking include small, shuffling steps that may become uncontrollably fast (festinating), slow velocity, stiff flexed posture, and reduced arm swing (Lewek et al., 2010; M. E. Morris, Huxham, McGinley, Dodd, & Iansek, 2001; Wood et al., 2002). These deficits are associated with reduced function (A Nieuwboer et al., 2007; Wood et al., 2002), lower reported quality of life (Wood et al., 2002), increased fall risk (Plotnik et al., 2007; Wood et al., 2002), and increased risk of morbidity and mortality (Wood et al., 2002). Impaired arm swing is the most common motor symptom of PD (A Nieuwboer et al., 1998). It is an early sign (sometimes even preceding clinical diagnosis) (Lewek et al., 2010), and is in itself a significant predictor of increased fall risk (Wood et al., 2002). However, arm swing has only recently been quantitatively described in PD, first by lab-based techniques (Lewek et al., 2010; Roemmich et al., 2013; Roggendorf et al., 2012), then also with portable instruments (Zampieri et al., 2010).

While multiple impairments contribute to gait problems in PD, recent work has uncovered deficits in proprioception and central processing of somatosensory information (Hwang et al., 2016; Jacobs & Horak, 2006; Konczak et al., 2009; Wright et al., 2010). Results of such studies indicate that individuals with PD may not accurately perceive and interpret information about where their limbs are in space. This impairment in self-monitoring makes it challenging for patients to carry over the effects of rehabilitation into their lives outside therapy. Movement impairments in PD have long been known to be amenable to external cues, whether visual, auditory, or haptic (Behrman et al., 1998; I Lim et al., 2005; Martin & Hurwitz, 1962; Rubinstein et al., 2002; Spaulding et al., 2013). Cues use "external temporal or spatial stimuli to facilitate movement … initiation and continuation" (A Nieuwboer et al., 2007). The positive effects of gait cues include increased walking speed and smoothness, increased step length, and improved postural extension (Behrman et al., 1998; I Lim et al., 2005; Martin & Hurwitz, 1962; Rubinstein et al., 2002; Spaulding et al., 2013). However, these improvements are notoriously short-lived, with movement often returning to pre-cueing patterns within minutes or even seconds of cue removal (El-Tamawy et al., 2012; I Lim et al., 2005; Spaulding et al., 2013). More recent evidence shows that carryover may be longer if cues are given during high-frequency, high-intensity training (Ebersbach et al., 2010; Farley & Koshland, 2005; van Wegen et al., 2014). There are, however, concerns that such training may not be appropriate for all people with PD, including those who are medically fragile or lack the social support to attend frequent appointments.

The approach we propose is to develop a wrist-based wireless device (ArmSense) that measures arm swing during gait and delivers a real-time cue to encourage a person

with PD to use larger arm swing while walking. In the study reported here, we analyzed whether such cueing also changes gait parameters in the trunk and legs.

The ArmSense device measures arm swing amplitude and delivers a vibratory cue when a designated angle has been reached relative to vertical, encouraging patients to achieve a target angle with their arm swing at each step. We measured the response of subjects with PD to arm swing cueing with ArmSense using a crossover repeated-measures design, and assessed its effects on step length, cadence, velocity and lateral trunk movement. These gait parameters have been identified as likely to change in PD (A Nieuwboer et al., 1998; Wood et al., 2002), and are associated with postural instability and increased fall risk (Adkin, Bloem, & Allum, 2005; Wood et al., 2002). Additionally, lateral trunk sway has been shown to be increased in individuals with elevated fall risk and individuals performing challenging gait tasks (Adkin et al., 2005; de Hoon et al., 2003), with and without PD.

To compare cueing with ArmSense to common physical therapy practice, we included a condition where visual cues on the floor encouraged increased step length (Martin & Hurwitz, 1962; Son & Kim, 2015; Spaulding et al., 2013). We hypothesized that subjects would be able to successfully respond to vibratory cues, and that increased arm swing amplitude would correlate with increased step length. After pilot tests, we further hypothesized that since the experiment would only include one session, any gait changes associated with cueing would dissipate within a brief washout period.

Methods

Subjects

Twelve individuals with PD were included in this study. Volunteers were recruited through community support groups and exercise groups, and from people who had participated in past studies within our department. All were classified at H&Y stage II (5 females/7males, mean age 63.5±9.5, mean disease duration 5.4 yrs±4.6 mean UPDRS Part III score 34.9±16.5). A diagnosis of idiopathic PD was made by each participant's neurologist prior to enrollment. All were responsive to dopaminergic or dopamine agonist medications, none demonstrated atypical Parkinson's syndromes, and none reported neurologic injury besides PD. All were tested in their "on" medication state (medication taken within one hour of the start of testing) to maximize the generalizability of the findings. All scored a minimum of 24/30 on the Mini-Mental State Exam and walked >15 meters without assistive devices or assistance from another person. Functional mobility was examined by a licensed physical therapist experienced with treating PD and certified in administering the UPDRS. The study was approved by the institutional review board (protocol #22499). Written consent was obtained from all subjects before participation.

Procedures

Subjects wore an ArmSense device on each dorsal wrist. The device consisted of a microprocessor, wireless communication hardware, vibration motor, and tri-axial accelerometers, gyroscopes and magnetometers (all components through SparkFun Electronics, Boulder, CO, USA). Sensor data were streamed to a laptop in real time to estimate the rotation of the ArmSense device relative to vertical (person's arms placed at

their sides perpendicular to the floor) (Madgwick et al., 2011). The accelerometer and gyroscope data were fused together in a custom-written LabVIEW program (National Instruments, Austin, TX, USA) to generate 4D quaternion angles, as in Madgwick et al (Madgwick et al., 2011). The quaternion angles were then converted into a (3-2-1) sequence of Euler angles without filtering (Madgwick et al., 2011). The yaw angle of the Euler angle representation was used as the relevant variable for arm swing in the sagittal plane. Additionally, subjects wore markers taped on the skin over their dorsal wrists, acromion processes, lateral malleoli, and medial malleoli for identification of body landmarks during video analysis. Subjects wore their own shoes with laces or hook-loop closures. Subjects walked 15m over ground in a quiet gymnasium while being videotaped in the sagittal (2 cameras) and frontal (1 camera) planes. The middle distance of 10m was used for analysis and the initial and terminal distances were discarded. Subjects were asked to refrain from pronating or supinating their arms to ensure that the yaw angle of the ArmSense devices consistently represented sagittal plane motion.

Subjects walked at two self-selected paces: comfortable and fast. Five trials at each pace were performed with no cueing (baseline). We used average arm swing (angular change from vertical) and step length at comfortable speed during baseline to calculate individualized movement amplitude targets depending on condition. In the visual cueing condition, targets for foot placement were taped on the floor at intervals of 120% of baseline step length. In the ArmSense cueing condition, vibratory cues for arm swing were delivered at 120% of baseline arm swing. Subjects performed ten trials in each cueing condition at each pace. Each cueing condition was followed by five minutes rest and a retention condition of uncued walking (Retention-V and Retention-A, five

trials at each pace), for a total of five cueing conditions and two paces. Fewer trials were obtained during baseline and retention conditions than cueing conditions to minimize fatigue. Within each testing block, the order of comfortable-pace trials and fast-pace trials was randomized. The order of cueing blocks (visual vs ArmSense) was randomized in a crossover design for each subject to reduce possible carryover effects. Response by cueing condition and pace was analyzed for each of the following parameters: lateral trunk sway, step length, cadence, and gait velocity.

Data Analysis

As discussed in the Introduction, the parameters chosen for analysis have been identified in the literature as being commonly affected in PD and associated with negative health outcomes such as fall risk, gait independence, and quality of life (Adkin et al., 2005; de Hoon et al., 2003; A Nieuwboer et al., 1998; Wood et al., 2002). Arm swing was measured by the ArmSense devices in order to record baseline swing and ensure subjects were reaching target angle and triggering vibration during ArmSense cueing trials. Gait velocity, cadence, step length, and lateral trunk sway were measured by video analysis in Dartfish 7.0 (Dartfish Corporation, Fribourg, Switzerland) and custom-written programs in MATLAB (Mathworks, Natick, MA, USA). Velocity was determined based on the amount of time between the pelvis crossing the start of the 10m course and the end of the course. Cadence was calculated by extrapolating number of steps and time taken over the 10m distance to one minute. Step length was determined using a meter stick placed alongside the walking course in the video for reference, and using that reference to calculate the sagittal-plane horizontal distance between the lateral malleolus of one lower extremity and the medial malleolus of the contralateral lower

extremity at each foot contact. Average step length for each trial was calculated and used for subsequent analysis. Lateral trunk sway was defined for each step as the difference between the maximal lateral excursion of the acromion marker at mid-stance of one step and the subsequent step with the contralateral foot. It is important to distinguish between lateral trunk sway and trunk rotation, which often decreases due to trunk rigidity in PD (Wright, Gurfinkel, Nutt, et al., 2007). Due to limitations of the cameras and environment, trunk rotation was not measured in this protocol.

Separate five-by-two two-way repeated-measures ANOVA analyses were performed on each gait parameter, with each analysis considering the five testing conditions and two paces. Bonferroni corrections for multiple comparison and *post hoc* paired t tests were used, when significant main effects were noted, to compare each testing and retention condition with baseline. All calculations were performed in SPSS 20 (IBM, Armonk, NY, USA) and Microsoft Excel 2013 (Microsoft, Redmond, WA, USA).

Results

Subjects met step length and arm swing targets on >95% of steps during cueing trials. ANOVA tests for step length (*F=8.585, sig=0.005)*, cadence (*F=12.740, sig=0.002),* and lateral trunk sway (*F=11.212, sig=0.004)* yielded significant main effects for condition, while no main effect was detected for gait velocity (*F=2.208, sig=0.158).* Figures 2-2 through 2-5 provide a summary of responses by gait parameter, pace, and condition, with significant differences indicated when they were found between cueing or retention conditions and baseline.

Step Length

Comfortable pace. Figure 3-1 illustrates increases in step length during visual cueing ($p<0.001$) and ArmSense cueing ($p=0.002$). In the retention conditions, increases in step length compared to baseline walking were observed only after ArmSense cueing ($p=0.002$).

Fast pace. Figure 3-1 shows that patients increased step length ($p=0.007$) in visual cueing relative to baseline walking, but no other conditions differed significantly from baseline.

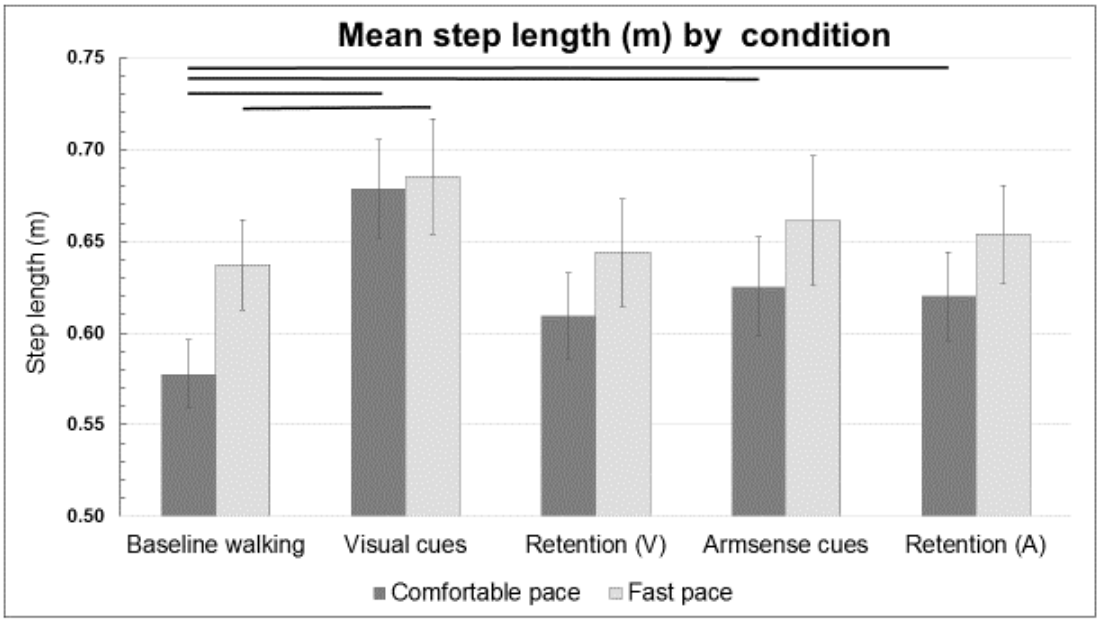

Figure 3-1. Summary of results for step length by pace and condition. Horizontal lines indicate statistically significant difference between the conditions indicated, with statistical significance defined with Bonferroni correction as $p\leq0.0125$. (Please refer to text for exact *p* values.)

Lateral Trunk Sway

Comfortable pace. Figure 3-2 shows that patients demonstrated an increase in lateral trunk sway ($p<0.001$) in visual cueing relative to baseline walking, but no other conditions differed significantly from baseline.

Fast pace. Figure 3-2 shows an increase in lateral trunk sway ($p<0.001$) in visual cueing relative to baseline walking, but no other conditions differed significantly from baseline.

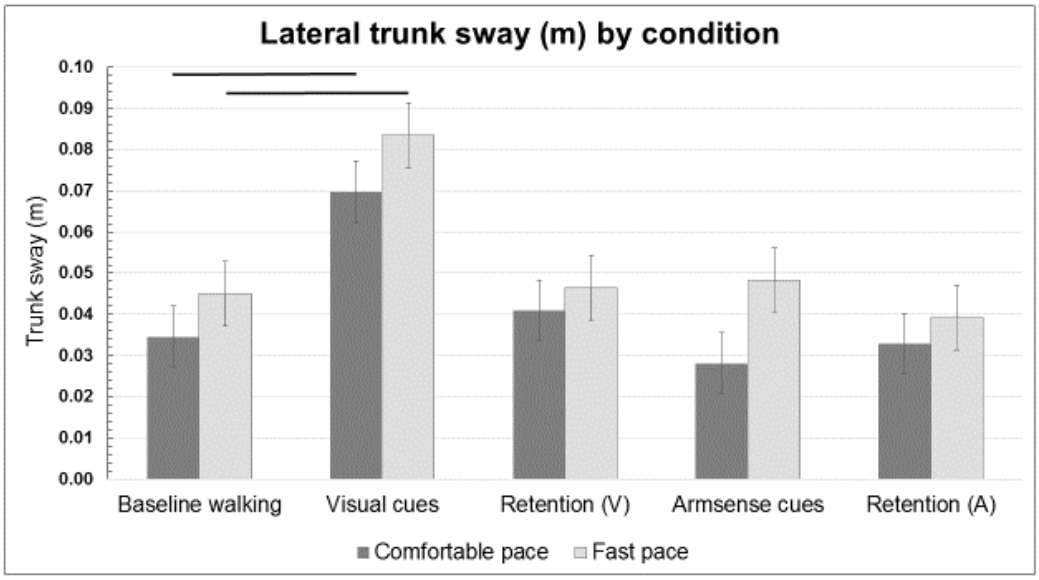

Figure 3-2. Summary of results for lateral trunk sway by pace and condition. Horizontal lines indicate statistically significant difference between the conditions indicated, with statistical significance defined with Bonferroni correction as $p\leq0.0125$. (Please refer to text for exact p values.)

Cadence

Comfortable pace. Figure 3-3 illustrates that cadence was lower during visual cueing ($p=0.004$) and ArmSense cueing ($p<0.01$). In the retention condition, cadence was lower only with ArmSense cueing ($p<0.001$) compared to baseline walking.

Fast pace. Figure 3-3 shows that cadence was lower during ArmSense cueing than baseline ($p<0.001$). Additionally, there was a trend noted towards lower cadence during visual cueing ($p=0.018$).

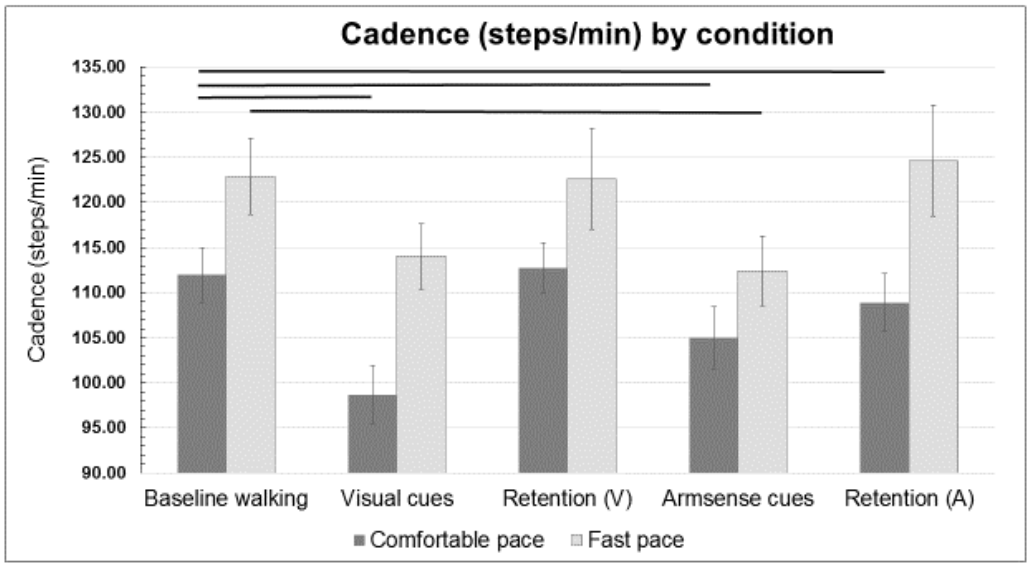

Figure 3-3. Summary of results for cadence by pace and condition. Horizontal lines indicate statistically significant difference between the conditions indicated, with statistical significance defined with Bonferroni correction as $p\leq0.0125$. (Please refer to text for exact *p* values.)

Velocity

Comfortable pace. As Figure 2-4 shows, there were no significant differences between conditions at comfortable pace ($p=0.658$).

Fast pace. There were no significant differences between conditions at self-selected fast pace ($p=0.725$).

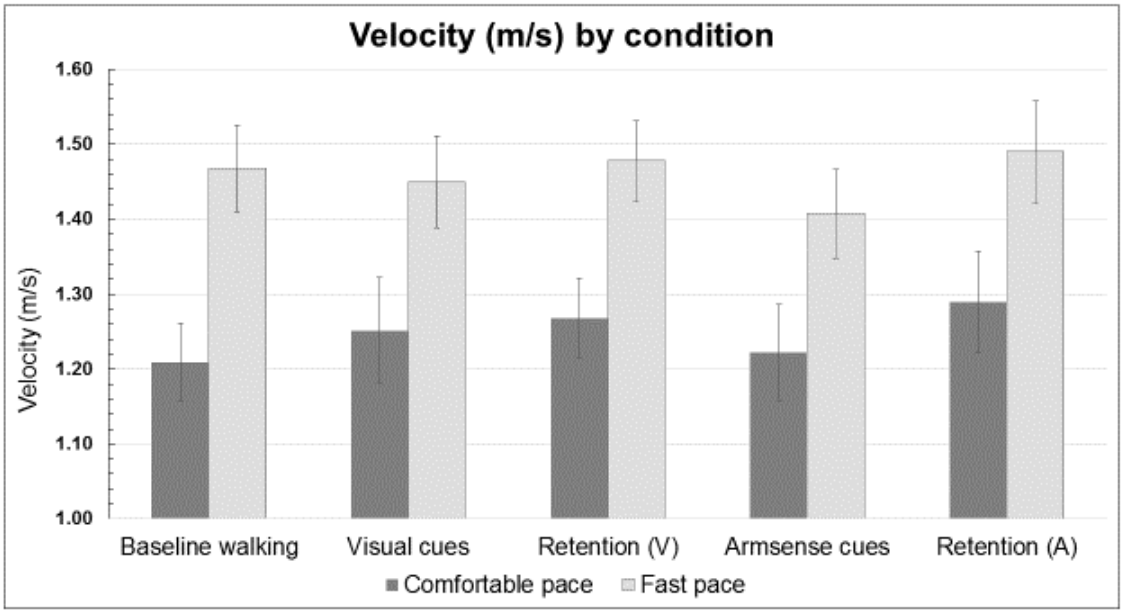

Figure 3-4. Summary of results for velocity by pace and condition. Horizontal lines indicate statistically significant differences between the conditions indicated, with statistical significance defined with Bonferroni correction as $p \leq 0.0125$. (Please refer to text for exact p values.) For gait velocity, no statistically significant differences were noted between cueing or retention conditions and baseline at either comfortable or fast pace.

Discussion

This study reports the first results of a device to monitor arm swing amplitude outside a laboratory and provide real-time feedback to encourage larger movement. Due to the heterogeneity of PD motor effects across patients, a repeated-measures design was used. The main findings indicate that subjects can respond to vibratory cues for larger movement even after only brief exposure (~15 minutes of cueing). Larger arm swing can lead to larger step length and lower cadence than during uncued walking. Finally, amplitude changes in the limbs with ArmSense cues can occur without significant increase in lateral trunk sway.

The decision to use vibratory cues to increase arm swing was made to maximize ease and user acceptance. Many cueing systems that encourage larger movements utilize visual cues (Spaulding et al., 2013), which are difficult to transfer from clinic to home (e.g., strips of tape on the floor). In other systems, the equipment may limit the ability to interact with the environment or call attention to impairments (e.g., augmented-reality goggles or devices that project a laser target on the floor). By contrast, auditory and vibratory cues are used to encourage changes in the pacing or rhythm of movement (A Nieuwboer et al., 2007), but have not been found to be as effective in changing amplitude of movement (El-Tamawy et al., 2012). Additionally, auditory cues often require headphones, which may limit the ability to freely interact with the environment. By using a vibratory cue as a target that is elicited when the movement is of sufficient amplitude, we hope to combine the best of all cueing modalities: a "low-profile" cue that does not limit interaction with the environment or call attention to a person's walking impairments, but may still effectively encourage larger movements.

In considering the results of cueing at two different speeds, it is notable that more between-condition differences were noted at comfortable pace than fast pace. This could be attributed to subjects needing to maintain larger and more frequent steps to sustain a higher velocity, which may have placed them closer to their biomechanical limits and left little room to change other parameters. Additionally, faster walking speed is correlated with increased step length and arm swing regardless of the task or context (Meyns et al., 2013). However, faster walking may even increase fall risk in those with gait deficits (Krasovsky, Lamontagne, Feldman, & Levin, 2014), and thus would not be an optimal

way to encourage larger movements. Therefore, we expect that the changes noted during comfortable-pace walking are more valid for community-dwelling people with PD.

Longer steps were noted in both visual and ArmSense cueing. While larger arm swing has been associated with longer steps both in healthy and PD populations (Meyns et al., 2013), this is the first work to our knowledge to assess the effects on step length from cueing for arm swing. Both visual and ArmSense cues specified a 20% increase in amplitude over baseline, but ArmSense cues did not result in a 20% increase in step length, perhaps because there is not a 1:1 relationship between arm swing and step length. This relationship should be investigated in future studies.

While we compared ArmSense to a common clinical method for increasing step length (targets on the floor) and observed longer steps under both conditions, there were kinematic differences in the subjects' responses to these different cues. Visual cues resulted in increased lateral trunk translation, while ArmSense did not. This might be because increased arm swing is associated with increased trunk rotation (Meyns et al., 2013), which may have changed the forces on the upper body and reduced lateral trunk sway. This difference in trunk sway is of note because lateral sway during gait may be less stable and require greater effort to control than anterior posterior sway (de Hoon et al., 2003), potentially placing a person with PD at greater fall risk. Additionally, though eye tracking was beyond the scope of our analysis, several subjects reported that the visual cues led them to spend more time looking at the floor, making them more anxious than when looking at their surroundings. While the precise reason for the trunk sway difference could be the focus of future work, these results indicate there may be multiple movement patterns used in PD to increase step length. From this work alone, however, it

appears that even a brief encounter with arm swing cueing leads to increased step length, with less detrimental side effects to lateral balance.

Because the period of cueing was brief and previous work (Farley & Koshland, 2005) indicates that substantial training is required to obtain carryover of effects after cue withdrawal, we hypothesized that the effects of visual or ArmSense cueing would not persist beyond a brief washout period. For visual cues, that hypothesis was supported – step length during the retention period decreased such that it was no longer significantly different from baseline uncued walking. However, during ArmSense retention trials, step length remained significantly greater than baseline.

There were several limitations in the design of this pilot study. Small sample size with heavy representation of H&Y stage 2 may restrict generalizability, especially considering the heterogeneity of gait and posture impairments in PD. Additionally, recruitment through support groups and exercise groups could have biased the sample towards those who were enthusiastic about both physical activity and research participation, which may have influenced their responses. Use of video analysis instead of motion capture technology limited precision of results, including inability to capture transverse-plane trunk motion, but allowed for the use of over-ground walking in a more natural environment, hopefully increasing the generalizability. Use of yaw rotation to quantify arm swing necessitated instruction to subjects to minimize pronation/supination, which may have changed their arm swing pattern. Finally, while the goal of this device is independent home use by patients (to regularly exercise or "tune up" their movement pattern, similar to using a treadmill for home fitness), results observed during these sessions (and reinforced by subjects' opinions) indicate that there is a need for training

with the devices first. One subject even reported, “it’s been so long since I moved my arms while walking, I think I forgot how.” Future studies would include several training sessions and a pilot of independent use during walking at home. Whether to reinforce gains made during physical therapy treatments or to maintain function when not receiving therapy, there continues to be a profound need for a portable device to monitor movement and deliver detailed online feedback that can be immediately integrated to improve movement patterns and maximize independent mobility for individuals with PD.

Conclusion

Visual cueing is often used to change gait parameters in PD. We found that vibration cues at the wrist might be even more effective at changing and retaining gait characteristics, despite the indirect nature of the vibration cue. During comfortable-pace walking, vibration cues not only reinforced increased arm swing, but led to changes in step length and cadence, while leaving trunk sway unchanged. Such findings support the integrated nature of arm swing during gait, suggesting an indirect path to improve mobility in people with PD with a device that is compatible with daily life activity.

CHAPTER 4

SINGLE-SESSION GAIT CHANGES WITH USE OF AN ARM SWING CUEING DEVICE IN INDIVIDUALS WITH AND WITHOUT PARKINSON'S DISEASE

Introduction

External cueing techniques have shown promise in improving parameters such as gait speed, step length, and freezing incidence for people with Parkinson's disease (PD) (Mariani, Jiménez, Vingerhoets, & Aminian, 2013; Nieuwboer et al., 2007; Spaulding et al., 2013). Most frequently, these cues take the form of visual or auditory environmental stimuli provided at a constant spatial or temporal interval, designed to help individuals regulate their movements to align with the cues and "normalize" the amplitude, pace, or frequency of the movement pattern. Common examples of these types of walking cues include guides on the floor such as tape ladders or projected laser grids, metronomes, or music. Recently, new work has focused on the use of somatosensory cues such as vibration either to signal the need to change a movement pattern (El-Tamawy et al., 2012; Harrington et al., 2016) or as extrinsic feedback to indicate a proper movement pattern has been executed (Thompson, Agada, et al., 2017). Vibratory cues possess potential advantages over other types of sensory cues. For example, vibratory cues may be used with low-profile devices that fit close to the user's skin, are not immediately obvious to those around the user and might not interfere with gathering information from the environment like head-mounted displays or headphones could.

To our knowledge, we are the only group that has explored the use of vibratory techniques to cue arm swing during gait (Thompson, Agada, et al., 2017; Thompson, Reimann, et al., 2017; Thompson et al., 2018). Considering the prevalence of arm swing deficits in people with PD and the strong association of arm swing with global function (Lewek et al., 2010; Roggendorf et al., 2012; Wood et al., 2002), arm swing provides a compelling target for external cueing strategies that may help normalize gait patterns in individuals with PD. Previous work provides evidence that both neurotypical young adults and individuals with PD can voluntarily adjust the amplitude of their arm swing, and that changing arm swing leads to subsequent changes in other gait parameters such as velocity, step length, interlimb coordination, trunk posture, and muscle activity (Thompson, Agada, et al., 2017; Thompson, Reimann, et al., 2017; Thompson et al., 2018). However, these previous studies have used single-group repeated-measure designs with neurotypical young adults and individuals with PD. While these designs can provide compelling results in proof-of-concept pilot studies, the absence of a control group leaves it unclear whether the results may have been confounded by the effects of age, fatigue, or passage of time within the treatment session. Therefore, the main objective of this study was to compare single-session response to ArmSense cues in three groups: people with PD who receive ArmSense cues, people without PD who receive ArmSense cues, and people with PD who receive dose-matched walking but no cues. Arm swing cues were delivered using a wireless wrist-worn device developed by our group (ArmSense, patented) to measure arm swing and deliver cues for larger, more mechanically normal movement. We propose to use an over ground walking environment equipped with motion capture technology and surface electromyography (sEMG). Based on previous

work, we hypothesize that in individuals with PD with cueing, step length will increase, the relative phase (interlimb coordination) of opposite arm-leg will be closer to that neurotypical young adults or age-comparable peers without PD, the variability of the relative phase across gait cycles will decrease, and that muscle activity will be closer to that of neurotypical young adults or age-comparable peers without PD.

Methods

Subjects

Three groups of subjects were included in this study, with eight subjects per group: people with PD who received cueing (PD-C), people without PD who received cueing (CTRL-C), and people with PD who did not receive cueing (PD-NC). Initially, volunteers with PD were recruited through community support groups and exercise groups, from fliers distributed in the community, and from people who had participated in past studies within the department. Fifteen were classified at H&Y stage II, one at H&Y stage I. Further information about demographics and group comparison can be found in Table 4-1. A diagnosis of idiopathic PD was made by each participant's neurologist prior to enrollment. All were responsive to dopaminergic/dopamine agonist medications, none demonstrated atypical Parkinson's syndromes, and none reported neurologic injury besides PD. All were tested in their "on" medication state (medication taken within 90 minutes of the start of testing) to maximize the generalizability of the findings to the larger population of individuals with PD. Upon admission to the study, subjects with PD were assigned by randomized pairs to the PD-C group or the PD-NC group by coin flip. (For example, if Subject 1 was admitted to the study and randomized

by coin flip to the PD-C group, then the next subject admitted, Subject 2, was assigned to the PD-NC group.)

Subjects without PD were recruited from the spouses, relatives, and acquaintances of the subjects with PD as well as from fliers distributed in the community, ensuring that the group without PD (CTL-C) was comparable in age to the two groups with PD (PD-C group = 61.8 ± 7.6 yrs; PD-NC group = 61.8 ± 4.9 yrs; CTL-C group = 61.9 ± 10.1 yrs).

Table 4-1

Demographics of participants by group

Demographic variable	PD-C	PD-NC	CTL-C
n	8	8	8
age (yrs)	61.8 ± 7.6	61.8 ± 4.9	61.9 ± 10.1
sex (M;F)	3;5	5;3	2;6
more affected side (PD-C, PD-NC) or non-dominant side (CTL-C) (L;R)	4;4	4;4	7;1
MMSE score	29.9 ± 0.4	29.6 ± 1.1	29.9 ± 0.4
time since PD diagnosis (yrs)	6.0 ± 4.3	4.6 ± 3.7	N/A
UPDRS III score	24.4 ± 7.8	24.8 ± 3.8	N/A

Table 4-1. Summary of demographics for subjects by group. All demographics indicated as mean ± standard deviation. No significant between-group differences were noted for age or MMSE. Additionally, PD-C and PD-NC groups did not differ in UPDRS module III score or more affected side. PD-C and PD-NC groups were different in time since PD diagnosis, and all three groups were different in sex distribution of subjects.

All subjects scored a minimum of 24/30 on the Mini-Mental State Exam and could walk without an assistive device or assistance of another person. Functional mobility was examined by a licensed physical therapist experienced with treating PD and certified in administering the United Parkinson's Disease Rating Scale (UPDRS). The

study was approved by the institutional review board (protocol #22499). Written consent was obtained from all subjects before participation.

Procedures

Subjects wore wear an ArmSense device on each dorsal wrist, as seen in Figure 1-1 (b), with a dedicated mobile phone worn at the waist (LG Electronics, Seoul, South Korea). The ArmSense system functions like an earlier version described previously (Thompson et al, 2017), but was updated for smaller size, increased durability, and ability to function without a laptop or desktop for data processing. ArmSense uses triaxial gyroscopes and accelerometers (Metawear RG board, Mbient Corporation, San Francisco, CA, USA) along with a vibrating motor, all of which are mounted in a plastic case inserted in a wristband. Sensor data are streamed via low-energy Bluetooth connection to a mobile phone, where a custom-written Android Studio application (Android corporation, www.developer.android.com) receives and logs the data. In the application, sensor data from the accelerometer and gyroscope are fused to estimate the rotation of the ArmSense device relative to vertical (person's arms placed at their sides perpendicular to the floor) as in (Madgwick et al., 2011). Additionally, subjects wore 45 passive reflective markers attached to the skin according to the Plug-In Gait marker set with 6 additional markers placed on the anterior thighs, anterior tibias, and 5th metatarsal heads as seen in Figure 2-1 (Reimann et al., 2018). Finally, subjects wore ten wireless Trigno sEMG sensors (Delsys Inc., Natick, MA, USA), with placement on bilateral anterior deltoid, posterior deltoid, peroneus longus, gluteus medius, and medial gastrocnemius muscles as per SENIAM international guidelines ("Surface ElectroMyoGraphy for the Non-Invasive Assessment of Muscles," 2017).

Subjects walked over ground on a 20-foot level walkway, wearing a safety harness to prevent falling. For all walking, marker motion was recorded by 12 Qualisys Oqus cameras (Qualisys AB, Goteborg, Sweden) at 100 Hz. In the pre-test condition, subjects walked 50 trials of the walkway at a self-selected comfortable speed. Following baseline walking for subjects in the PD-C and CTL-C, the arm swing amplitude for each arm was calculated as the median angular change from vertical during all pre-test trials. Target arm swing amplitude was set at 110% of the amplitude of the more involved arm (PD-C group) or the non-dominant arm (CTL-C group), and vibratory cues were delivered during each anterior arm swing on which the subject reached the target amplitude. After the target was calculated and set via the mobile phone app, feedback training trials took place in a large quiet gym with three five-minute trials of walking with feedback. Subjects were only instructed to "try to swing your arm enough so that you feel the vibration on every swing." Following feedback training, subjects returned to the motion capture environment and completed 25 post-test trials on the walkway. Subjects in the PD-NC group were also taken to the gym following pre-test walking and completed three five-minute walking trials wearing the ArmSense system but received no cues and were just instructed to walk comfortably.

Data Analysis

Arm swing was measured by the ArmSense devices to record baseline swing and ensure subjects were reaching target angle and triggering vibration during ArmSense cueing trials. All other gait parameters used only the 4^{th} and 5^{th} steps of each trial, to ensure that steady-state walking was captured without gait initiation, acceleration or deceleration. Gait velocity was measured using the displacement and velocity of the heel

markers. Step length was measured as the anterior-posterior distance between heel markers at each heel contact. Interlimb coordination was measured by tracking the anterior-posterior local maxima of the heel markers and the midpoint of the two wrist markers on each side. The position of the markers was used to calculate phase based on the formula presented by Plotnik (Plotnik et al., 2007), using the swing time of each arm and leg. Phase between the ipsilateral arm and leg should have a value of approximately 180 degrees, since the maximum anterior arm swing should occur at the halfway point between adjacent heel strikes of that leg. (Figure 2-4 further illustrates expected phase values.) Surface electromyography (sEMG) data were collected at 1100 Hz, rectified, and then low pass filtered at 10 Hz to create a linear envelope shape to allow for clear comparison of timing and amplitude patterns across conditions, similar to sEMG processing procedures previously used by this group (Logan et al., 2014). sEMG data are presented here in microvolts, normalized to the mean of all trials for the session. Data were visually inspected to identify differences related to onset and relative amplitude, as in (Logan et al., 2014). Custom-written programs in MATLAB (Mathworks, Natick, MA, USA) were used in data analysis.

Separate three-by-two (three groups, two time points) ANOVA analyses were performed on each gait parameter that was quantified discretely for each condition (velocity, step length, ipsilateral arm-leg phase), with each analysis comparing the five testing conditions. Continuous variables (arm swing amplitude, trunk extension, and muscle activity) were plotted as averages of all gait cycles in a given condition, with mean and 95% confidence interval traces, from which visual inspection was used to determine points of significant difference between conditions. Level of significance

(alpha) was set a priori to 0.05. When significant main effects were noted in the ANOVA analysis, Bonferroni corrections for multiple comparisons where needed and *post hoc* Wilcoxon signed ranks tests were used for step length and velocity (since Kruskal-Wallis test showed non-normal distribution for velocity and step length), and *post hoc* paired *t* tests for arm swing, which was determined to be normally distributed. All calculations were performed in SPSS 23 (IBM, Armonk, NY, USA), MATLAB 2017b, and Microsoft Excel 2016 (Microsoft, Redmond, WA, USA). Unless otherwise indicated, results plots show combined results for all 8 subjects per group and are averaged across all gait cycles for each condition.

Results

ANOVA test for step length yielded main effects for condition (pre or post-training) (*F=13.346, sig=0.004)* and condition * group (*F=7.418, sig=0.004)*. ANOVA test for velocity yielded main effects for condition (*F=2.347, sig=0.01)* and condition * group (*F=1.446, sig=0.001)*. Findings for these and other variables of interest are further described below. Figures below provide a summary of responses by variable across groups and conditions, with significant differences indicated when they were found between pre and post-training conditions. No differences across condition were found for lateral or anterior-posterior trunk sway.

Step Length

Figure 4-1 shows step length in the pre and post-training conditions. All three groups differed in step length at baseline, but only the PD-C group significantly increased their step length after training (p = 0.000).

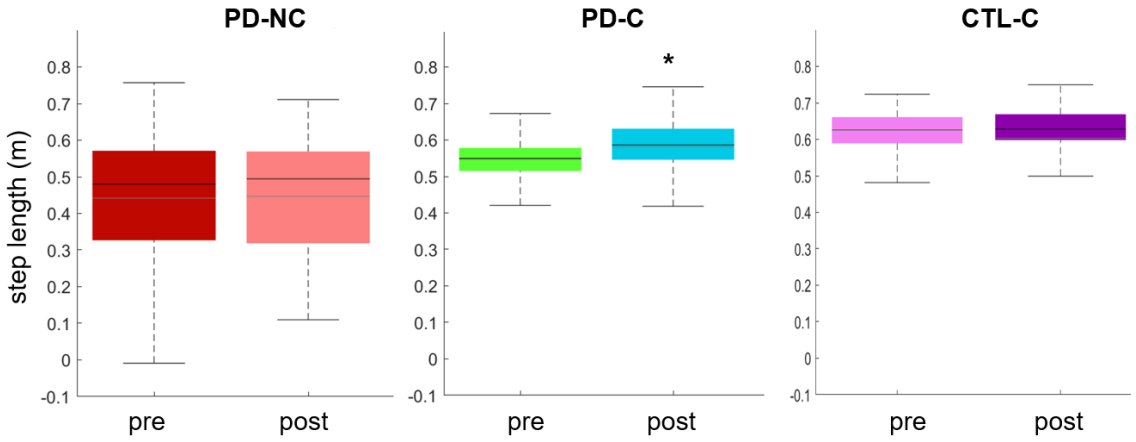

Figure 4-1. Step length by group and condition. Asterisks indicate statistically significant difference between the pre and post-training, with statistical significance defined with Bonferroni correction as $p \leq 0.0125$. (Please refer to text for exact p values.)

Velocity

Figure 4-2 shows velocity in the pre and post-training conditions. CTL-C differed from PD-NC and PD-C groups at baseline. Only the PD-C group significantly increased their step length after training ($p = 0.002$).

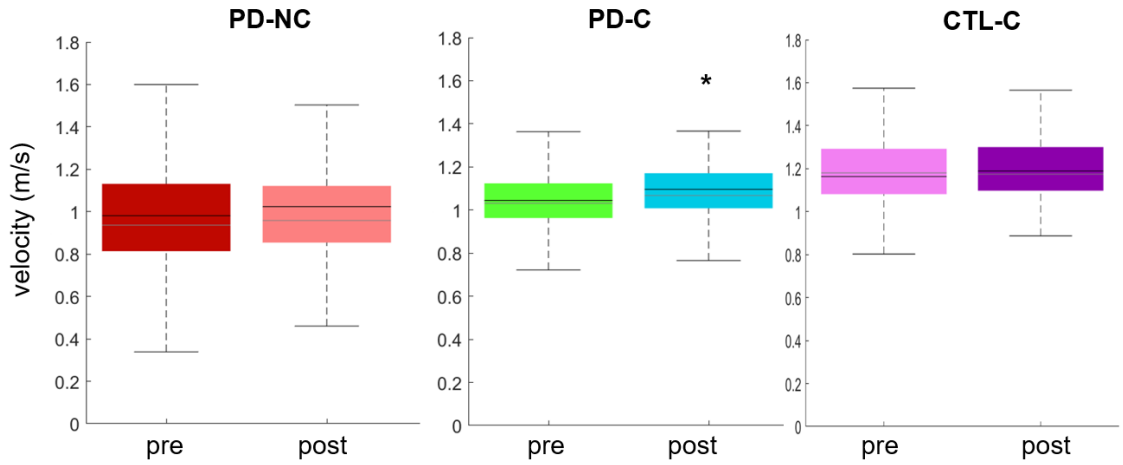

Figure 4-2. Asterisks indicate statistically significant difference between pre and post-training, with statistical significance defined with Bonferroni correction as $p \leq 0.0125$. (Please refer to text for exact p values.)

Arm swing amplitude

Figure 4-3 shows arm swing amplitude in the pre and post-training conditions by group, and by more affected vs less affected arm (or non-dominant vs dominant arm for the CTL-C group). Only the PD-C group's more affected arm demonstrated increased swing after training to an extent that exceeded the 95% confidence interval.

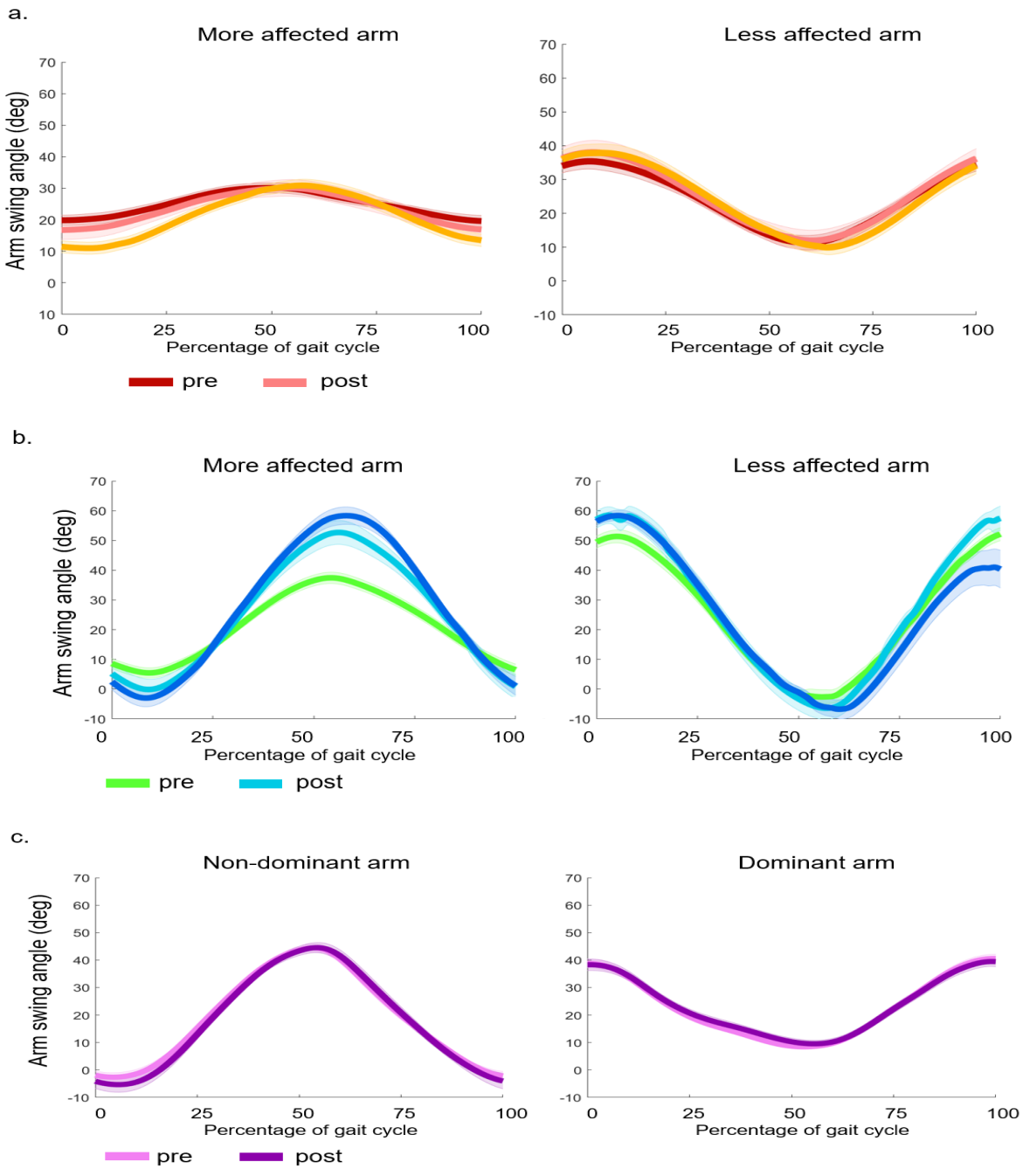

Figure 4-3. Arm swing amplitude, group, condition and arm, averaged across all gait cycles for each condition. Dark lines indicate mean trajectory for each condition; surrounding shading indicates 95% confidence interval. Statistically significant differences are indicated by traces without overlapping confidence intervals. Plots by group: a) PD-NC b) PD-C c) CTL-C. Note that the gold line for PD-NC and the dark blue line for PD-C indicate the results after 30-day training and are not discussed at this time. Please see Chapter 5 for a discussion of the results after 30-day training program.

Interlimb coordination

Unanticipated issues came to light in the analysis of interlimb coordination which, while impairing the ability to quantify interlimb phase as planned, could still shed significant light on the relationship between arm swing cues and interlimb coordination.

Ipsilateral arm-leg phase, as calculated in the Methods section above, required the detection one local maximum value of forward arm swing during each gait cycle (the period between adjacent heel strikes with the same foot). A value for phase could only be obtained for both conditions from one-third of the study subjects (1/8 in the PD-NC group, 2/8 in the PD-C group, and 4/8 in the CTL-C group). Phase data from one of the two conditions was available for the remainder of the subjects. Due to the missing data, the planned ANOVA and further analysis of variability by group and condition could not be performed. Please see Table 4-2 for full details about the availability of arm-leg phase information.

Table 4-2

Presence of detectable arm-leg phase by group and condition

Subjects	PD-NC		PD-C		CTL-C	
	pre	post	pre	post	pre	post
# of subjects with detectable arm-leg phase	5/8	4/8	4/8	6/8	7/8	5/8

Table 4-2. Subjects for whom a detectable arm-leg phase could be measured for all trials.

Muscle activity

In 9/10 monitored muscles, the CTL-C group (the healthy age-matched reference group) did not show significant differences between pre and post-training conditions (see Figure 4-4). The exception was the gastrocnemius muscle on the side of the dominant arm, which demonstrated decreased activation at push-off, which exceeded the 95% confidence interval after training. However, this change was not seen in either of the subject groups with PD. In the PD-NC group, there were no differences between conditions that exceeded the 95% confidence interval across any of the ten monitored muscles. In the PD-C group, there was a non-significant trend after training towards decreased activation of the gastrocnemius of the leg on the less affected side and significantly increased activation of the anterior deltoid on both sides.

Discussion

This study reports results of single-session testing of ArmSense in three groups: people with PD who received ArmSense cues (PD-C), age-matched older adults who received ArmSense cues (CTL-C), and people with PD who wore ArmSense units but received no cues (PD-NC). Previous work using the ArmSense system has involved single-group repeated measures designs; this study was the first to add control subjects. In fact, two control groups were added: a group of age-matched healthy older adults, and a group of subjects with PD who performed dose-matched uncued walking. These groups were added to explore the effects of ArmSense on persons with PD while minimizing the potential confounding effects of age, fatigue/passage of time, or effects that could have been seen purely due to walking.

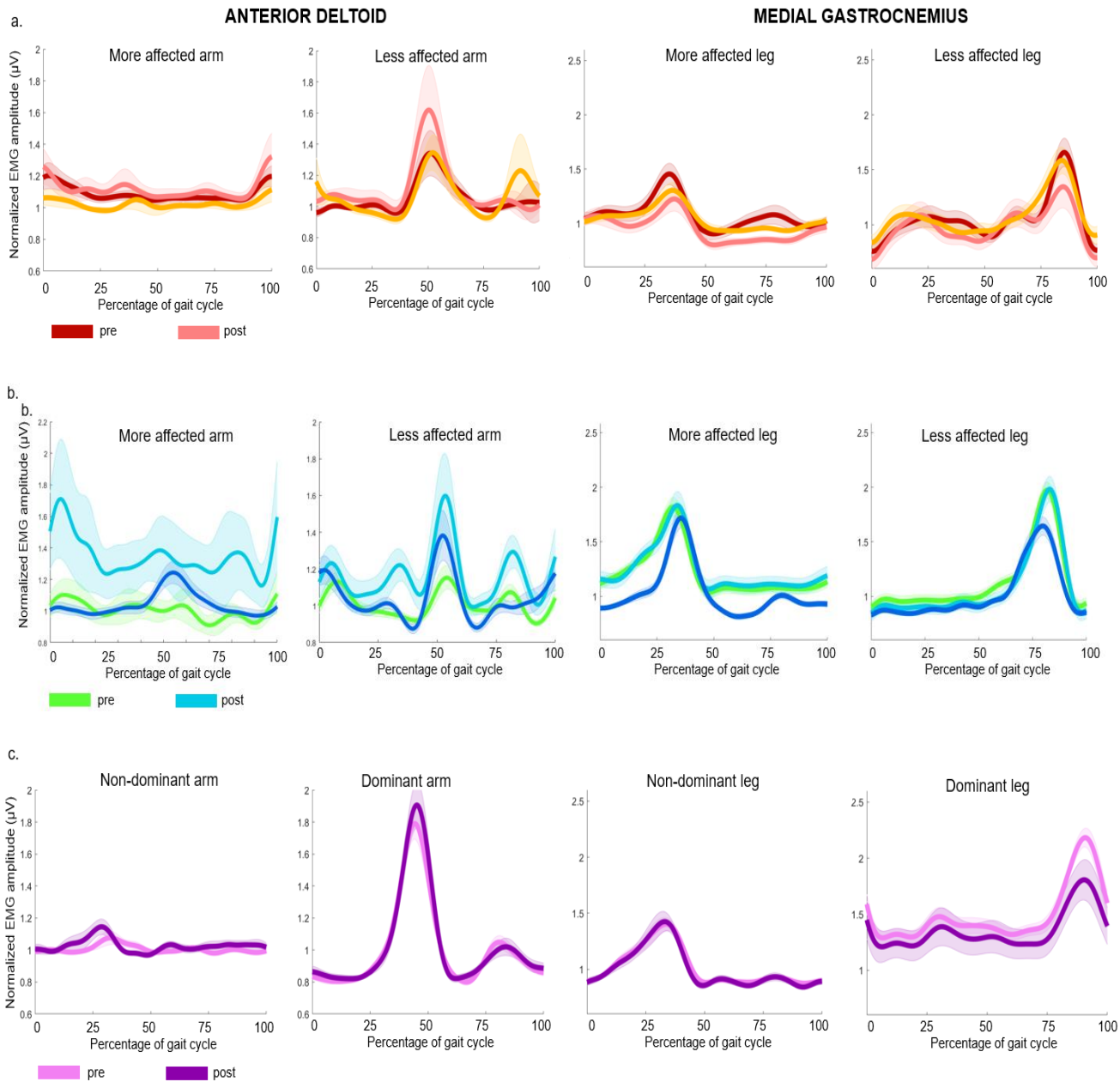

Figure 4-4. Muscle activity for the anterior deltoid and medial gastrocnemius, by group, condition, and leg, averaged across all gait cycles for each leg. Dark lines indicate mean trajectory for each condition; surrounding shading indicates 95% confidence interval. Statistically significant differences between conditions are indicated by traces without overlapping confidence intervals and are highlighted by asterisks. Plots by group: a) PD-NC b) PD-C c) CTL-C. Note that the gold line for PD-NC and the dark blue line for PD-C indicate the results after 30-day training and are not discussed at this time. Please see Chapter 5 for a discussion of the results after 30-day training program.

The present study also involved changes to the ArmSense cue calculation itself. Previous work used a target calculated as 120% of the baseline arm swing of each arm (Thompson, Agada, et al., 2017). This target demanded a sizable change in the swing of each arm but determining different targets for each arm also served to accentuate asymmetries that were present at baseline. Out of a desire to reinforce increased symmetry and make the task achievable for a wider range of individuals, the decision was made to change the target to 110% of the less involved arm. With this approach, both arms would be cued to increase their swing (with the largest increase being demanded of the more involved arm), but the cued amplitude was the same for each arm. While it is possible that this lower-amplitude cue may have led to less obvious gait effects, it is important to note that step length and velocity were still significantly increased in the PD-C group after training.

In addition to the changes in the cue amplitude, changes were made in the treatment environment and protocol. Previous work used either a 10-meter gym walking course or a self-paced treadmill for the majority of study walking. However, the gym did not allow for motion capture monitoring of kinematics, and the treadmill required a significant acclimation period of walking before data collection could even begin. Some pilot subjects expressed that the treadmill protocol felt very fatiguing. The investigators were concerned that excessive fatigue on the treadmill protocol could lead to diminished generalizability of results (since only the most fit and mobile individuals could participate). Additionally, it could be difficult to detect any effects of cueing if excessive fatigue changed an individual's gait pattern after training. Therefore, the decision was made to do all study walking in the over ground motion capture environment. While this

decision may have led to improved subject tolerance, it also decreased the number of consecutive steps that could be monitored on each trial and may have contributed to issues with detection of arm swing phase and analysis of interlimb coordination using the planned relative-phase method.

As expected based on previous work, subjects receiving cues (PD-C group) were able to significantly increase their arm swing following 15 minutes of training with the cues. This increase was greatest in the most affected arm, possibly due to the fact that the cue target was based on a small percentage increase in the less involved arm; therefore, a much greater proportional increase was expected in the more involved arm, which may have led to its greater demonstrated training effect.

Increased gait speed and step length were noted in the PD-C group as in previous single-group work. However, it is notable that these increases were not seen in either the healthy older adult group or the dose-matched walking group that did not receive cues. Had these gait parameter changes simply been due to a "warm-up effect" where rigidity and hypokinesia were alleviated by movement itself, one would have expected the dose-matched walking group to also exhibit post-training gain. However, no such result was seen. Based on our earlier work in younger subjects, it was surprising to see that the healthy older adult group did not show a carryover of increased arm swing after the cueing training. However, this lack of carryover in either arm swing or lower extremity gait parameters could have been due to the lower-amplitude cue target. Healthy older adults demonstrated greater (though not perfect) symmetry in their arm swing versus the subjects with PD. This finding is in line with research indicating that in healthy individuals, arm swing has a significant range of variability that is not considered to be

pathological (Goudriaan, Jonkers, van Dieen, & Bruijn, 2014; Meyns et al., 2013; Plate et al., 2015; Yoon et al., 2016). It is possible that the cue target used in this study did not represent a great enough change from baseline to be perceived as a new task element that required adaptation, and therefore did not generate gait changes retained after training in healthy older adults. As with previous work, lower extremity gait parameter changes that occurred after 15 minutes of training are notable since the only instructions the subjects were given were to "try to swing your arm enough to feel the vibration on every swing."

Analysis of interlimb coordination indicated that while not all subjects had a discernible swing with each arm during each gait cycle, that a higher proportion of those in the PD-C group had a discernible arm swing after training than before (with no corresponding change in the PD-NC group), perhaps indicating a partial normalization of severely impaired arm swing. When arm swing phase could be calculated, it did not demonstrate a significant change in variability before and after training but remained highly variable in both conditions. Perhaps this could be attributed to the fact that in order to standardize training, subjects only received instructions to enlarge their arm swing. To test this, further research could incorporate instructions for coordinating arm swing with leg movements while working on swing amplitude.

Finally, muscle activity results were in line with previous work, finding that the anterior deltoid activity was increased after training in the PD-C group. This result was not seen in the group with PD that received dose-matched walking or in the older adults receiving cueing. While this differs from earlier work on healthy younger subjects, it is likely due to the lower-amplitude cue used in this study.

There were several limitations to this study. A larger total number of subjects were used (24 total), but the three-group design meant there were only eight subjects in each group, so the sample size was still relatively small. Additionally, further research should explore more robust methods of analyzing interlimb coordination from a smaller number of strides in individuals with impaired arm swing. In considering subject attention/arousal during the task, we attempted to control for effects for attention and novelty by having all groups wear the same ArmSense system, the vibratory cues could have drawn more subject attention to their arms and changed motor behavior in a way not due to the amplitude of the cues themselves. Finally, as with any cues, attending to the vibration while walking likely introduced a dual task. While no subjects demonstrated a loss of balance during testing, it is unclear at this time whether there could be any possible detrimental effect on balance due to a dual task effect.

Conclusion

To our knowledge, this work is the first to support the use of arm swing cues to improve step length and gait velocity using a randomized controlled design. Though these are the results of just a single training session, findings provide stronger evidence that these gait benefits could be due to the cues themselves rather than the potential confounding effects of age or in-session walking.

CHAPTER 5

GAIT, BALANCE, AND QUALITY OF LIFE CHANGES IN PEOPLE WITH PARKINSON'S DISEASE FOLLOWING A 30-DAY TRAINING PROGRAM WITH AN ARM SWING CUEING DEVICE

Introduction

There is a growing body of evidence supporting the use of external cues to improve movement patterns in people with Parkinson's disease. Cues have been defined "using external temporal or spatial stimuli to facilitate movement (gait) initiation and continuation" (Nieuwboer et al., 2007). As augmented feedback from external sources, cues may be provided through visual, auditory, or somatosensory information (Harrington et al., 2016). In practice, cues can have an immediate and profound effect on movement patterns, but the effects quickly subside after the removal of the cue (Nieuwboer et al., 2009; Suteerawattananon, Morris, Etnyre, Jankovic, & Protas, 2004). Research indicates that one reason for the quick decay of cueing effects could be the sensory integration impairments that may increase difficulty with movement self-correction in the first place (Almeida et al., 2005; Hwang et al., 2016; Jacobs & Horak, 2006; Ketzef et al., 2017; Konczak et al., 2009; Rubinstein et al., 2002; Vaugoyeau et al., 2011; Wright, Gurfinkel, King, et al., 2007). These factors contribute to a situation in which individuals with PD experience an immediate benefit when using cues to guide movement, but find it very difficult to decrease the cues while retaining the improved movement pattern (Lehman, Toole, Lofald, & Hirsch, 2005; Rochester et al., 2010).

Recent work has also raised the possibility that the constant use of cueing may take a toll on performance in complex functional mobility due to the cognitive or attention load the cues add to task performance (Nieuwhof et al., 2017; Rochester et al., 2007; Wu et al., 2015). Taking into consideration the undeniable immediate benefits provided by external cues and the possible functional implications of using constant cues on a long-term basis, it is essential to gain a better understanding of how long the effects of cueing can be expected to last following training, and how much practice may be needed to attain any carryover effects. Additionally, while earlier research including the RESCUE trial studied both clinic-based and home-based cues and concluded that home-based cue training was underutilized (Jones et al., 2008; Lim et al., 2010; Nieuwboer et al., 2007), many cueing methods today are still predominantly clinic-based. Cue training that requires travel to attend a clinical session or the use of verbal or environmental cues that can only be provided in a clinical environment may require a frequency and intensity of clinical visits that may not be tolerable or logistically possible for some people with PD. Such individuals may benefit from a cueing-focused intervention that could be performed in and around their home, during mobility tasks the individuals are already performing.

Our group has recently explored the use of ArmSense, a patented portable cueing device designed to measure arm swing during gait and provide individualized vibratory feedback to indicate when a larger, more mechanically normal arm swing amplitude has been reached (Thompson, Agada, et al., 2017). Arm swing is an early predictor of profound functional changes, including increased fall risk, decreased independence, and decreased reported quality of life in people with PD (Crouse et al., 2016; Lewek et al.,

2010; Wood et al., 2002). Using this device, it has been demonstrated that in a single training session, individuals with PD can increase their arm swing to match the cues. While the cues delivered are limited to arm swing, single-session users also demonstrated changes in gait velocity, step length, and muscle activity in upper extremities and lower extremities (Thompson, Agada, et al., 2017; Thompson, Reimann, et al., 2017; Thompson et al., 2018). However, all previous research with ArmSense has been conducted in lab sessions. It is unknown whether a cueing intervention for arm swing that takes place solely in the patient's own immediate environment and in the context of functional mobility could demonstrate carryover after the cues have been removed. It is also unknown whether a physical activity program designed to increase arm swing amplitude during walking can also lead to positive changes in functional mobility and quality of life.

The purpose of this study was to explore the effects of a 30-day training program for larger arm swing on gait parameters, balance confidence, gait stability, and self-reported quality of life. Previous studies using the system have predominantly assessed kinematic and impairment-level variables such as gait velocity and step length. This study proposed to expand the variables being studied to show a larger picture of each individual's capacity, encompassing not just kinematics but also balance confidence, fall risk, and social participation. To work towards this goal, several clinical outcome measures were assessed before and after the training program: The Timed Up and Go (TUG), Activities-specific Balance Confidence Scale (ABC), Functional Gait Assessment (FGA), and the 39-item Parkinson's Disease Questionnaire (PDQ-39). The TUG instructs the subject to stand from a chair, walk three meters, turn, walk back to the chair and sit

down. Reported as the time it takes to negotiate this course, the TUG assesses speed of sit to stand, stand to sit, walking, and turning, and has been found to be reliable, valid, and predictive of fall risk in individuals with PD (Dal Bello-Haas, Klassen, Sheppard, & Metcalfe, 2011; Dibble & Lange, 2006). The ABC scale measures balance confidence by asking subjects to quantify how confident they feel that they can perform each of 16 specific tasks (such as getting out of a car or using an escalator) without feeling as though they will lose their balance. Reported as the percentage of balance confidence in each task (with 100% indicating total balance confidence), the ABC has also been found to be reliable and valid in individuals with PD and highly correlated to common clinical balance tests such as the TUG and FGA (Dal Bello-Haas et al., 2011; Lohnes & Earhart, 2010; Mak, Pang, & Mok, 2012). The FGA assesses balance and speed in a variety of gait-based tasks such as changing speed, head turning, and stair-climbing. With ten items evaluated on a zero to three ordinal scale (three indicating normal function), the FGA has been found to be reliable, valid, responsive, and with less of a ceiling effect than other common clinical gait tests (Dibble & Lange, 2006; Duncan et al., 2012; Petersen, Steffen, Paly, Dvorak, & Nelson, 2017). The PDQ-39 uses a self-reported ordinal scale to assess how frequently individuals with PD have experienced PD-related complications in the last month, such as carrying bags while shopping, feeling confined to the house, or feeling worried about other people's reactions to their symptoms. The questions are classified into eight domains: mobility, activities of daily living, emotional well-being, stigma, social support, cognition, communication, and bodily discomfort. Each domain is scored by the percentage of maximum points attained (higher scores represent greater perceived limitation and lower quality of life). As with the other tests discussed, the

PDQ-39 has been found to be reliable, valid, and responsive for use in individuals with PD (Dal Bello-Haas et al., 2011; Duncan & Earhart, 2011; Jenkinson, Peto, Fitzpatrick, Greenhall, & Hyman, 1995).

It was hypothesized that when assessed in uncued walking, individuals who received a month of ArmSense training would demonstrate larger arm swing amplitude, larger step length, higher velocity, and arm-leg relative phase closer to that of non-impaired age comparable peers. It was also hypothesized that these gains would be greater than those seen in a group of individuals with PD that receive dose-matched walking training but no ArmSense cues. Finally, it was hypothesized that those who received ArmSense cue training would demonstrate improved balance confidence, gait stability, and self-reported quality of life, and that these improvements would be greater than those seen in a group of individuals with PD that received dose-match walking training but no ArmSense cues.

Methods

Subjects

Two groups of subjects were included in this study, with eight subjects per group. These were the same subjects who participated in the single-session study reported in Chapter 4. As discussed in the previous chapter, the groups were people with PD who received cueing (PD-C) and people with PD who did not receive cueing (PD-NC). Volunteers with PD were recruited through community support groups and exercise groups, from fliers distributed in the community, and from people who had participated in past studies within the department. Fifteen were classified at H&Y stage II, one at

H&Y stage I. Further information about demographics and group comparison can be found in Table 5-1. A diagnosis of idiopathic PD was made by each participant's neurologist prior to enrollment. All were responsive to dopaminergic/dopamine agonist medications, none demonstrated atypical Parkinson's syndromes, and none reported neurologic injury besides PD. All were tested in their "on" medication state (medication taken within 90 minutes of the start of testing) to maximize the generalizability of the findings to the larger population of individuals with PD. Upon admission to the study, subjects with PD were assigned by randomized pairs to the PD-C group or the PD-NC group by coin flip. (For example, if Subject 1 was admitted to the study and randomized by coin flip to the PD-C group, then the next subject admitted, Subject 2, was assigned to the PD-NC group.)

Table 5-1

Demographics of participants by group

Demographic variable	PD-C	PD-NC
n	8	8
age (yrs)	61.8 ± 7.6	61.8 ± 4.9
sex (M;F)	3;5	5;3
more affected side (PD-C, PD-NC) (L;R)	4;4	4;4
MMSE score	29.9 ± 0.4	29.6 ± 1.1
time since PD diagnosis (yrs)	6.0 ± 4.3	4.6 ± 3.7
UPDRS III score	24.4 ± 7.8	24.8 ± 3.8

Table 5-1. Summary of demographics for participants by group. All demographics indicated as mean ± standard deviation. No significant between-group differences were noted for age, MMSE score, UPDRS module III score or more affected side. Groups were different in time since PD diagnosis and in sex distribution of participants.

All subjects scored a minimum of 24/30 on the Mini-Mental State Exam and could walk without an assistive device or assistance or another person. Functional mobility was examined by a licensed physical therapist experienced with treating PD and certified in administering the United Parkinson's Disease Rating Scale (UPDRS). The study was approved by the institutional review board (protocol #22499). Written consent was obtained from all subjects before participation.

Procedures

Subjects wore wear an ArmSense device on each dorsal wrist, as seen in Figure 1-1 (b), with a dedicated mobile worn on the waist (LG Electronics, Seoul, South Korea). The ArmSense system functions like an earlier version described previously (Thompson et al, 2017), but was updated for smaller size, increased durability, and ability to function without a laptop or desktop for data processing. ArmSense uses triaxial gyroscopes and accelerometers (Metawear RG board, Mbient Corporation, San Fransisco, CA, USA) along with a vibrating motor, all of which are mounted in a plastic case inserted in a wristband. Sensor data are streamed via low-energy Bluetooth connection to a mobile phone, where a custom-written Android Studio application (Android corporation, www.developer.android.com) receives and logs the data. In the application, sensor data from the accelerometer and gyroscope are fused to estimate the rotation of the ArmSense device relative to vertical (person's arms placed at their sides perpendicular to the floor) as in (Madgwick et al., 2011). Additionally, subjects wore 45 passive reflective markers attached to the skin according to the Plug-In Gait marker set with 6 additional markers placed on the anterior thighs, anterior tibias, and 5^{th} metatarsal heads as seen in Figure 2-1 (Reimann et al., 2018). Finally, subjects wore ten wireless Trigno sEMG sensors

(Delsys Inc., Natick, MA, USA), with placement on bilateral anterior deltoid, posterior deltoid, peroneus longus, gluteus medius, and medial gastrocnemius muscles as per SENIAM international guidelines ("Surface ElectroMyoGraphy for the Non-Invasive Assessment of Muscles," 2017).

Subjects walked over ground walk on a 20-foot level walkway, wearing a safety harness to prevent falling. For all walking, marker motion was recorded by 12 Qualisys Oqus cameras (Qualisys AB, Goteborg, Sweden) at 100 Hz. In the pre-test condition, subjects walked 50 trials of the walkway at a self-selected comfortable speed. Following baseline walking for subjects in the PD-C group, the arm swing amplitude for each arm was calculated as the median angular change from vertical during all pre-test trials. Target arm swing amplitude was set at 110% of the amplitude of the more involved arm (PD-C group), and vibratory cues were delivered during each anterior arm swing on which the subject reached the target amplitude. After the target was calculated and set via the mobile phone app, feedback training trials took place in a large quiet gym with three five-minute trials of walking with feedback. Subjects were only instructed to "try to swing your arm enough so that you feel the vibration on every swing." Following feedback training, subjects returned to the motion capture environment and completed 25 post-test trials on the walkway. Subjects in the PD-NC group were also taken to the gym following pre-test walking and completed three five-minute walking trials wearing the ArmSense system but received no cues and were instructed to walk comfortably.

Following the initial lab session described in Chapter 4, the PD-C and PD-NC groups completed the Activities-specific Balance Confidence Scale (ABC) to assess balance confidence, the Functional Gait Assessment (FGA) to assess gait stability, the

Timed Up and Go (TUG) to assess general walking and fall risk, and the 39-item Parkinson's Disease Questionnaire (PDQ-39) to assess self-reported PD-related quality of life. All subjects were issued ArmSense units to wear while walking in their own community environment (walking 30 mins/day, 4-5 days/week, for 30 days). The PD-C group received vibratory cues for a larger arm swing during this walking training (set at the same amplitude for each subject as they used during their initial lab session), while the PD-NC wore the units but received no cues. The cue application on the study mobile phone also recorded the arm swing amplitude data to a date and time-stamped text file, creating a digital "walking log" of the time spent walking and arm swing behavior. After the month of training, both groups then returned to the lab for a second walking session (taking place 24-48 hours after their last training walk). At this second session, all subjects completed 50 trials of uncued over ground walking, as they had done at the first session. Additionally, both groups completed the ABC, TUG, FGA, and PDQ-39 at their second session. All clinical tests were administered and scored by a licensed physical therapist with experience treating individuals with PD.

Data Analysis

Arm swing was measured by the ArmSense devices to record baseline swing and ensure subjects were reaching target angle and triggering vibration during ArmSense cueing trials. All other gait parameters used only the 4^{th} and 5^{th} steps of each trial, to ensure that steady-state walking was captured without gait initiation, acceleration or deceleration. Gait velocity was measured using the displacement and velocity of the heel markers. Step length was measured as the anterior-posterior distance between heel markers at each heel contact. Interlimb coordination was measured by tracking the

anterior-posterior local maxima of the heel markers and the midpoint of the two wrist markers on each side. The position of the markers was used to calculate phase based on the formula presented by Plotnik (Plotnik et al., 2007), using the swing time of each arm and leg. Phase between the ipsilateral arm and leg should have a value of approximately 180°, since the maximum anterior arm swing should occur at the halfway point between adjacent heel strikes of that leg. Surface electromyography (sEMG) data were collected at 1100 Hz, rectified, and then low pass filtered at 10 Hz to create a linear envelope shape to allow for clear comparison of timing and amplitude patterns across conditions, similar to sEMG processing procedures previously used by this group (Logan et al., 2014). sEMG data are presented here in microvolts, normalized to the mean of all trials for the session. All clinical outcome measures were scored according to the published instructions for the administration of each test. Custom-written programs in MATLAB (Mathworks, Natick, MA, USA) were used in data analysis.

For all variables, data were tested for normal distribution. Depending on the normality of the distribution the appropriate test was then used to detect statistically significant differences (unpaired *t* test or Mann Whitney U test for between-group comparisons, paired *t* test or Wilcoxon signed ranks test for within-group comparisons, with Bonferroni corrections for multiple comparisons). Continuous variables (arm swing amplitude, muscle activity) were plotted relative to time as averages of all gait cycles in a given condition, with mean and 95% confidence interval traces, from which visual inspection was used to determine points of significant difference between conditions. Level of significance (alpha) was set a priori to 0.05. All calculations were performed in SPSS 23 (IBM, Armonk, NY, USA), MATLAB 2017b, and Microsoft Excel 2016

(Microsoft, Redmond, WA, USA). All results plots show combined results for all 8 subjects per group and are averaged across all gait cycles for each condition.

Results

After the 30-day training program and 24-48 hours after the last cueing, significant increases in step length, velocity, and arm swing amplitude were observed in the PD-C group, but not the PD-NC group. Figures 5-2 through 5-4 below illustrate gait parameter results. Significantly increased muscle activity was noted in the bilateral anterior deltoids of the PD-C group after 30 days of training, but not the PD-NC group. In the lower extremities, decreased peak activation was noted in the gastrocnemius in the PD-C group after training, but plantar flexor activity was not consistently lower throughout the gait cycle. Please see Figure 5-5 for more detailed on these muscle activity results. Finally, results from the clinical outcome measures showed significant pre vs post-training differences in FGA and TUG score in the PD-C group, but not the PD-NC group. ABC and PDQ-39 scores did not show significant changes between or within groups. Please see Figure 5-6 below for detailed clinical outcome measure results.

Step Length

Figure 5-1 shows step length in uncued walking before and after the 30-day training. Data for the two groups were found not to have a normal distribution, therefore non parametric statistical testing was used. Mann-Whitney tests showed that the two groups differed in step length at baseline ($p = 0.000$). However, when looking at within-group differences over the course of training, Wilcoxon signed ranks tests revealed the

PD-C group significantly increased their step length after training (p = 0.000), while the PD-NC group did not (p = 0.122).

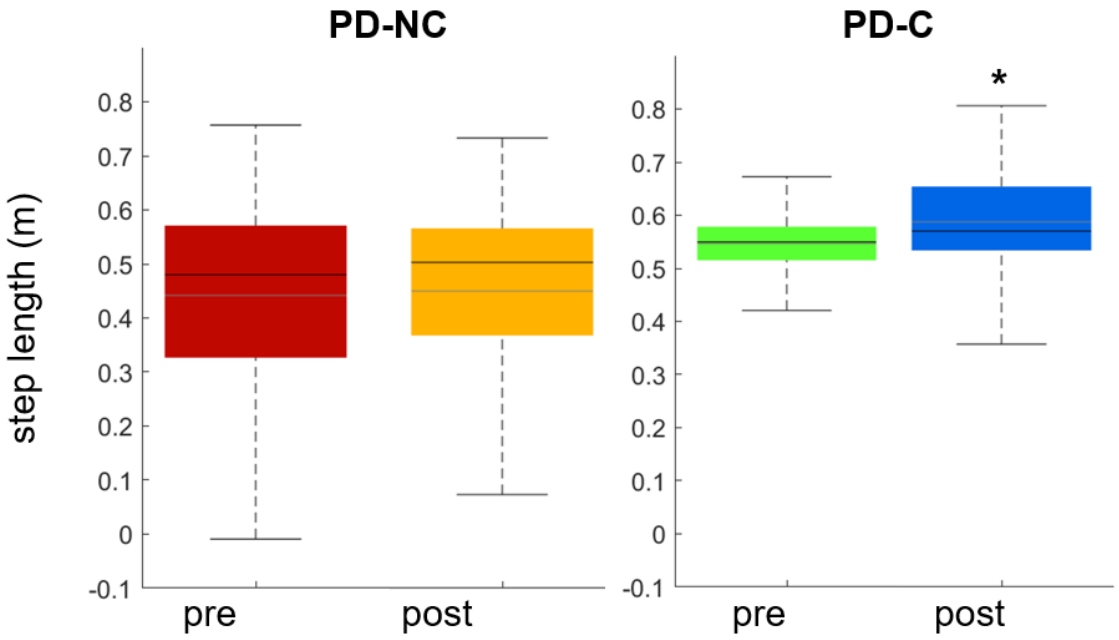

Figure 5-1. Step length by group and condition. Asterisks indicate statistically significant difference between the pre and post-training, with statistical significance defined with Bonferroni correction as $p \leq 0.0125$(Please refer to text for exact p values.)

Velocity

Figure 5-2 shows velocity in uncued walking before and after the 30-day training. Data for the two groups were found not to have a normal distribution, therefore non parametric statistical testing was used. As with step length, Mann-Whitney tests showed that the two groups' velocity differed at baseline (p = 0.027). However, when looking at within-group differences over the course of training, Wilcoxon signed ranks tests revealed the PD-C group significantly increased their step length after training (p = 0.000), while the PD-NC group did not (p = 0.261).

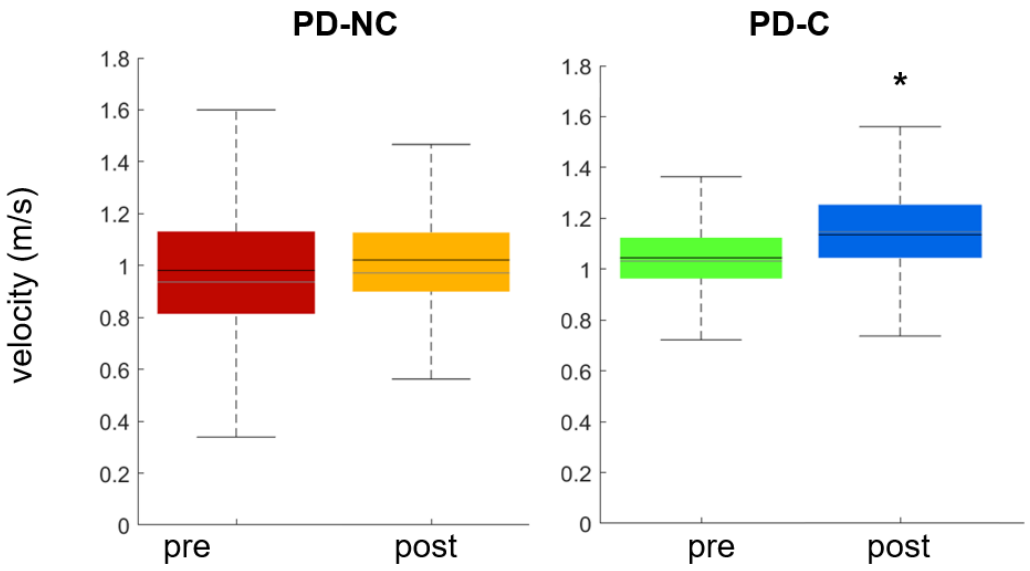

Figure 5-2. Velocity by group and condition. Asterisks indicate statistically significant difference between the pre and post-training,with statistical significance defined with Bonferroni correction as $p \leq 0.0125$. (Please refer to text for exact *p* values.)

Arm swing amplitude

Figure 5-3 shows arm swing in uncued walking before and after the 30-day training by group and by more affected vs less affected arm. For the PD-C group, both arms demonstrated significantly increased forward swing after training versus before, while no difference was seen in the PD-NC group.

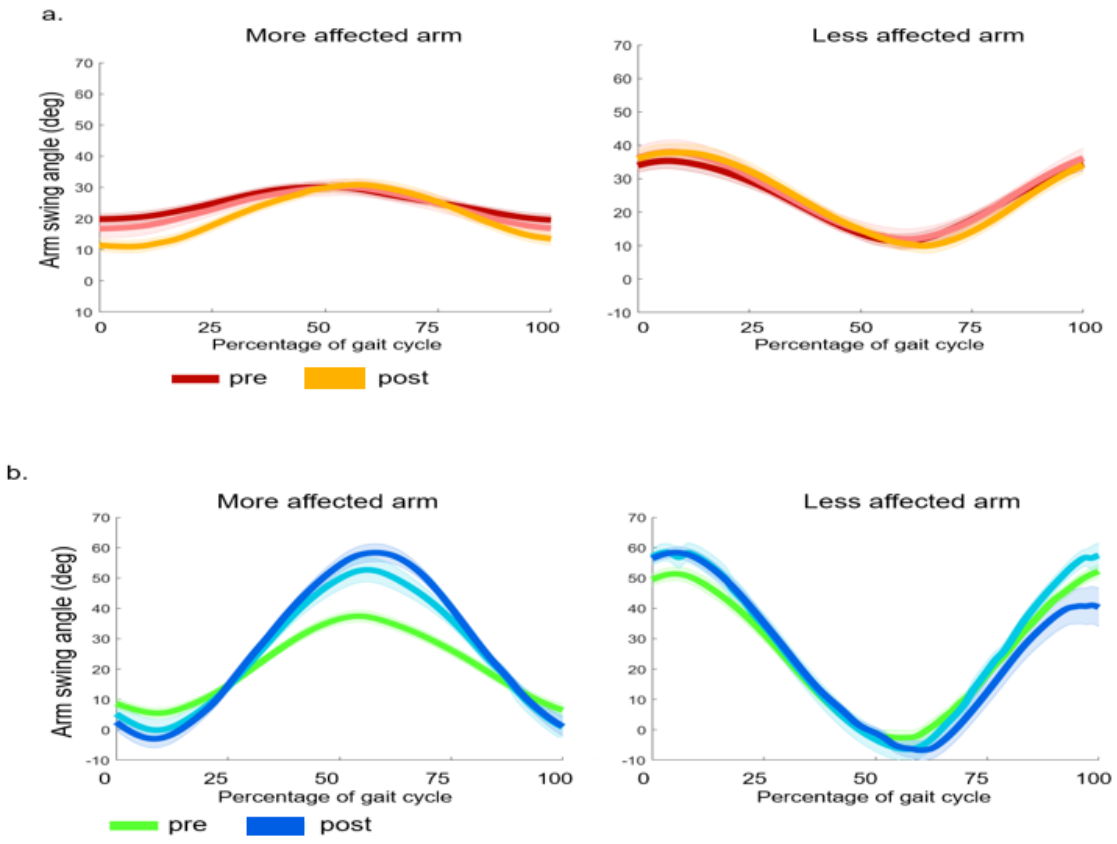

Figure 5-3. Arm swing amplitude, group, condition and arm, averaged across all gait cycles for before and after 30-day training. Dark lines indicate mean trajectory for each condition; surrounding shading indicates 95% confidence interval. Statistically significant differences are indicated by traces without overlapping confidence intervals. Plots by group: a) PD-NC b) PD-C. Note that the pink line for PD-NC and the light blue line for PD-C indicate the results after single-session training and were previously discussed in Chapter 4.

Interlimb coordination

Unanticipated issues came to light in the analysis of interlimb coordination which, while impairing the ability to quantify interlimb phase as planned, could still shed significant light on the relationship between arm swing cues and interlimb coordination.

Ipsilateral arm-leg phase, as calculated in the Methods section above, required the period between adjacent heel strikes with the same foot). A value for phase could only be obtained for both conditions from one-quarter of the study subjects (2/8 in the PD-NC

group, 2/8 in the PD-C group). Phase data from one of the two conditions was available for the remainder of the subjects. Due to the missing data, the planned ANOVA and further analysis of variability by group and condition could not be performed. Please see Table 5-2 for full details about the availability of phase data for one or both conditions.

Table 5-2

Presence of detectable arm-leg phase by group and condition

Subjects	PD-NC		PD-C	
	pre	post	pre	post
# of subjects with detectable arm-leg phase	6	4	4	6

Table 5-2. Subjects for whom a detectable arm-leg phase could be measured for all trials.

Muscle activity

In the PD-NC group, there were no differences between conditions that exceeded the 95% confidence interval across any of the ten monitored muscles. In the PD-C group, there was a non-significant trend after training towards decreased activation of the gastrocnemius of the leg on the less affected side and significantly increased activation of the anterior deltoid on both sides. (See Figure 5-4 for muscle activity results.)

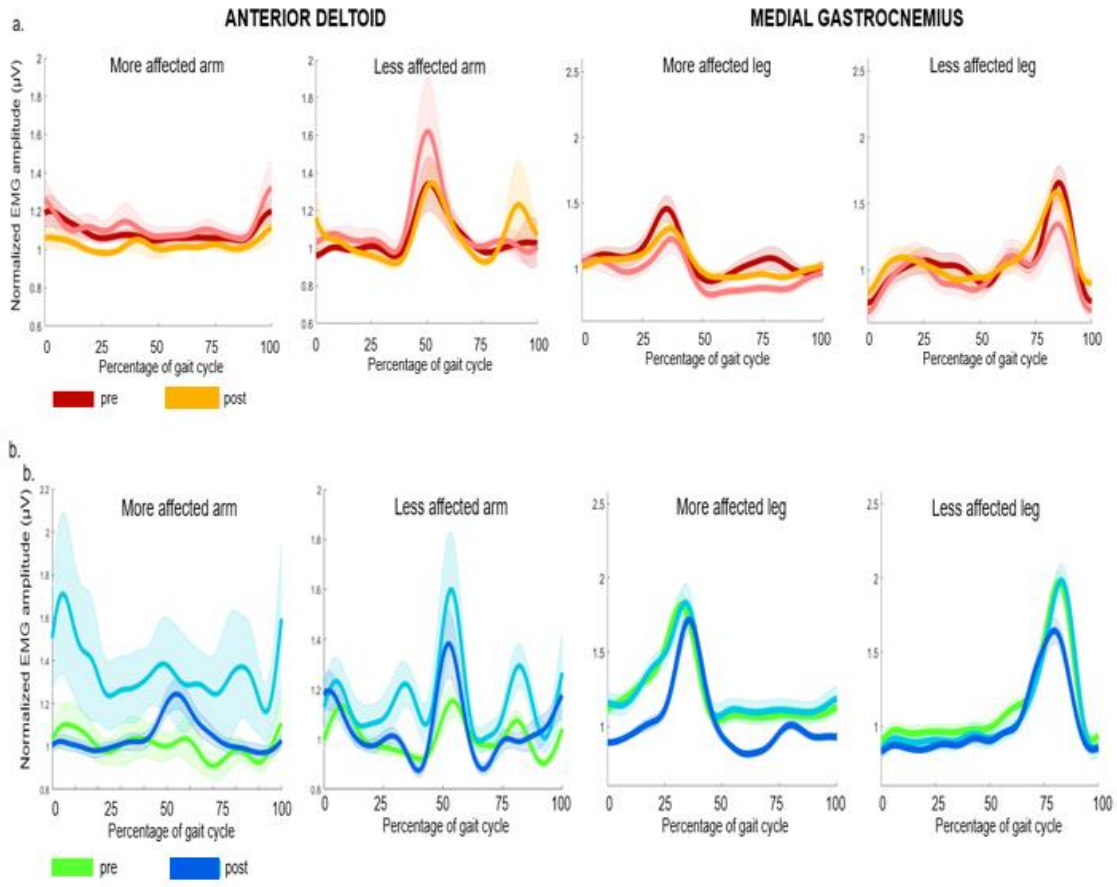

Figure 5-4. Muscle activity for the anterior deltoid and medial gastrocnemius by group, condition, and leg, averaged across all gait cycles for each leg. Dark lines indicate mean trajectory for each condition; surrounding shading indicates 95% confidence interval. Statistically significant differences between conditions are indicated by traces without overlapping confidence intervals and are highlighted by asterisks. Plots by group: a) PD-NC b) PD-C. Note that the pink line for PD-NC and the light blue line for PD-C indicate the results after single-session training and were previously discussed in Chapter 4.

Clinical Outcome Measures

The final set of results describes changes in outcome measures assessed both before and after the 30-day training, including for balance confidence (ABC, *higher score indicates better function*), functional balance during gait (FGA, *higher score indicates better function*), gait speed and fall risk (TUG, *lower time indicates better function*), and

self-reported PD-related quality of life (PDQ-39, *lower score indicates better function*). Separate paired *t*-tests compared the pre- and post-training scores for each group on each test. *The* FGA and TUG tests showed a significant improvement in the PD-C group after training ($p = 0.027$, $p = 0.048$ respectively) but not the PD-NC group ($p = 0.396$, $p = 0.267$ respectively). ABC and PDQ-39 scores did not show significant changes between or within groups. Figure 5-5 illustrates results of the clinical measures.

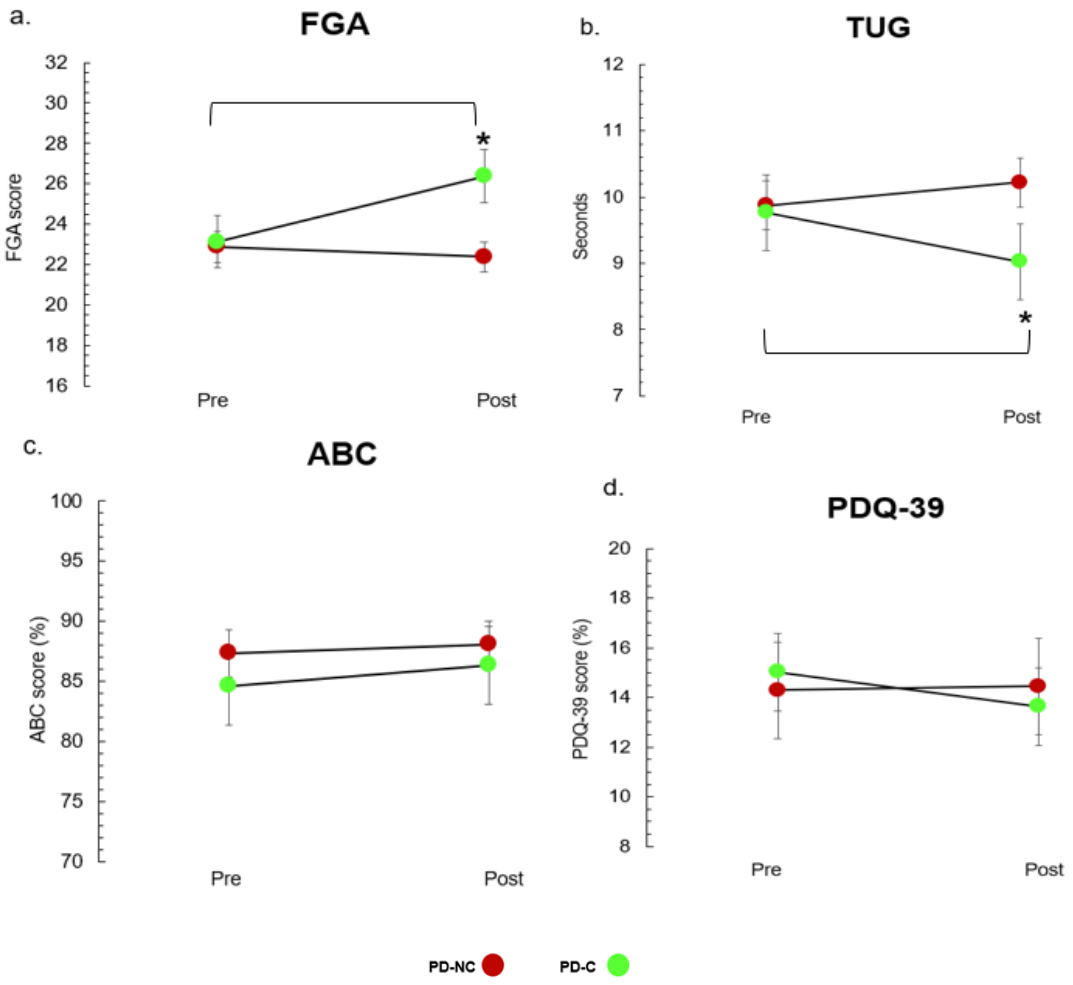

Figure 5-5. Clinical outcome measure changes by group and condition. Asterisks indicate statistically significant differences between the pre and post-training, with statistical significance defined at $p < 0.05$. Plots by test: a) FGA b) TUG c) ABC d) PDQ-39. (Please refer to text for exact *p* values.) Error bars indicate standard error above and below the mean.

Discussion

This study reports the results of a 30-day training program, which used external vibratory cues to encourage a larger arm swing during walking in individuals with PD. The effects of this intervention were examined relative to gait parameters, balance confidence, stability and balance during walking, and self-reported quality of life. As with the previous study described in Chapter 4, this current work incorporated a control group of individuals with PD who trained with equal dosage walking but did not receive cues. However, the current study represents an evolution from previous study designs, which may lead to increased robustness and validity of the conclusions. For example, to our knowledge this was the first study to explore potential training effects of vibratory arm swing cues for longer than one session, the first to conduct such training in the patient's own immediate environment (as opposed to a lab or clinic), and the first to employ clinically validated outcome measures as well as the previously-used gait parameter variables.

Walking dosage for both groups was 30 minutes per day, 4-5 days per week, for 30 days. Number of walks and time on each walk were logged on the ArmSense phone whenever the system was turned on, and subjects were also asked to keep a written diary of walking days and approximate times as a backup record. There was no difference between the two groups on number of walks and time spent on each walk, and each group was able to walk in accordance with the study dosage.

Several of the kinematic and gait parameter effects observed here mirrored those demonstrated in previous work, such as the cued group (PD-C) demonstrating increased step length, increased velocity, and increased arm swing amplitude after training, results

that were not demonstrated in the control group. Yet all previous work has explored these effects within one training session – post-training testing was carried out five to ten minutes after cue training. In this study, by contrast, post-training testing was carried out 24-48 hours after the last cue training, meaning that within-group and between-group differences indicate a longer retention of cue-related changes than had previously been shown. The retention of these gait changes for over a day after cueing demonstrates the exciting potential of this intervention and shows the need for future work to determine optimal frequency and intensity of training to maintain results over a manageable period of time. When considering kinematic variables, it is interesting to note that subjects' forward arm swing after 30 days was significantly increased in both arms, whereas after the single-session training discussed in Chapter 4 this variable only increased in the most affected arm. This difference in effect between one session and four weeks of training indicates that subjects might have changed their strategy to respond to cues as they trained independently. This raises the question of how the effects might change if arm swing cues were combined with some frequency of skilled physical therapy intervention over a sustained period of training. Finally, changes in velocity and step length should not be viewed in isolation, as it cannot be said that gait changes are necessarily "positive" changes (leading to improved balance or function, for instance). It could also be possible that changes could destabilize an individual's walking and lead to further impairment or imbalance. In light of this, we believe that further studies should continue to incorporate clinical assessment of balance and fall risk as well as gait parameters, to examine whether gait changes appear to lead to increased or decreased gait stability.

As with the single-session study reported in Chapter 4, the analysis of interlimb coordination using calculation of phase for arm swing vs heel strikes could not be completed in the method planned due to the fact that an arm swing was not detected during some trials for subjects. While this could have been due to their pre-existing arm swing impairment combined with a smaller number of strides per trial used to obtain gait parameter data, this finding is of interest as it indicates that quantification of interlimb coordination in this population may need to employ multiple and different methods instead of relying on one widely used method such as the phase calculation proposed and validated by Plotnik et al. (Plotnik et al., 2007).

Muscle activity results were in line with previous work, finding that the anterior deltoid activity was increased after training in the PD-C group. As with arm swing amplitude, this response seems to be even more pronounced after 30-day training than after a single session, a strong indicator that not only was the initial change retained, but that improvements and possible motor learning continued throughout the training month and was evident even 24-48 hours after the cues had been removed. As with the previous variables discussed, a post-training change was not evident in the dose-matched control group.

Finally, the present work provides interesting initial insights into how walking training with arm swing cues could impact other variables related to balance and self-reported confidence and quality of life. The clinical measures directly measuring gait performance (FGA and TUG) both demonstrated significant post-training improvements in the PD-C group that were not evident in the PD-NC group. It should be noted that the performance of both groups was generally very strong, possibly due to the possibility that

our sample of convenience from individuals active in community and exercise groups oversampled individuals who were more mobile and interested in physical activity. For this reason, our results did not indicate a significant group change related to their risk of falls, since both pre and post-training scores indicated high functional levels.

By contrast, the outcome measures related patient perception (ABC and PDQ-39) did not show significant improvement in either group after training. This implies that while subjects may have demonstrated aspects of "better" gait and balance performance after cueing training, they did not feel more confident in their balance or perceive a change in their quality of life. It could be argued that perception of mobility is only one of eight domains measured by the PDQ-39 (which also assesses such domains as social isolation, stigma, and bodily comfort) and thus improved perception of mobility might not be sufficient to shift the total score. However, even when the mobility-related questions were analyzed separately, there was still no change noted in either group after training. It could also be argued that the improvements associated with arm swing training are too task-specific to generalize to other functional tasks assessed by the ABC and PDQ-39. For example, the TUG and FGA contain such items as sit-to-stand, walking and turning, head movement while walking, walking backwards or with the eyes closed, and stair-climbing. While this battery of tasks tests a wide range of walking skills, the demonstrated improvement in these tasks might not generalize to ABC-related tasks such getting out of a car, picking an item off the floor, or standing on tiptoes to reach a high shelf. This is a possibility that merits further research, perhaps by adding clinical tests that assess a wider range of balance tasks than those directly related to walking. Adding a wider variety of functional tasks could help to determine whether the lack of change in

the ABC and PDQ-39 scores represents a lack of generalization of arm swing to other tasks, or that the benefits obtained weren't sufficient to change individuals' perceptions of how comfortable they were with functional mobility.

There were several limitations to this study. With only eight subjects per group, the sample size was relatively small, though pilot-based power analysis indicated that seven subjects per groups should be sufficient to detect differences at 80% power. Additionally, the recruitment and sampling method likely oversampled individuals who were very mobile and earlier in the PD pathology process, which may limit generalizability to people with PD who have more mobility impairments. This also likely meant that individuals in the sample had more functional (and closer to "normal") clinical test scores, so the scores changes noted may not reflect the same functional or safety implications as a score change could indicate in a more impaired individual. Additionally, a longer follow-up period than 24-48 hours could provide more information about the retention of different observed changes in gait and balance. Next, in considering subject attention/arousal during the task, we attempted to control for effects for attention and novelty by having all groups wear the same ArmSense system, the vibratory cues could have drawn more subject attention to their arms and changed motor behavior in a way not due to the amplitude of the cues themselves. Finally, as with any cues, attending to the vibration while walking likely introduced a dual task. While no subjects demonstrated a loss of balance during testing, it is unclear at this time whether there could be any possible detrimental effect on balance due to a dual task effect.

Conclusion

To our knowledge, this work is the first to use a home-based intervention paradigm to support the use of arm swing cues to improve step length, gait velocity, and functional balance using a randomized controlled design. This study also demonstrates that gait changes associated with a month of training may be retained for up to 24-48 hours after the last exposure to arm swing cues. These findings provide stronger evidence that changes in gait parameters following arm swing cues (but not dose-matched uncued walking) could have implications for improving functional balance in individuals with Parkinson's disease.

CHAPTER 6

DISCUSSION AND SUMMARY

Review of Specific Aims and Summary of Results

Parkinson's disease (PD) is the second most common neurodegenerative condition in the U.S., currently affecting 1 million Americans with a prevalence expected to double by 2040 (Kowal, Dall, Chakrabarti, Storm, & Jain, 2013; Parkinson's Disease Foundation Inc, 2016). PD results from a dopamine deficiency due to the death of dopaminergic neurons in the basal ganglia, especially in the substantia nigra (Jankovic, 2008) and frequently leads to gait disturbance and falls (Crouse et al., 2016; A Nieuwboer et al., 2007; Wood et al., 2002).

There are long-established associations between PD-related movement problems (such as tremor, rigidity, bradykinesia/hypokinesia, and postural instability) and profound functional deficits, including increased fall risk, decreased independence, and decreased reported quality of life (Crouse et al., 2016; Martin & Hurwitz, 1962; Peterson & Horak, 2016; Wood et al., 2002). When these movement problems are treated early, there can be significant gains at the impairment, activity, and social participation levels. However, many people with PD have impaired sensory integration (especially proprioception) and are unable to fully correct these deficits by themselves.

External cueing techniques (visual, auditory, or tactile/vibratory stimuli) have shown promise in improving parameters such as gait speed, step length, and freezing incidence for people with PD. To date, cueing techniques have not been applied to providing precise, individualized feedback for arm swing during walking. Considering

the prevalence of arm swing deficits and their strong association with global function in people with PD, arm swing provides a compelling target for external cueing strategies that may help normalize movement pattern in individuals with PD. Therefore, the primary objective of this project was to determine how cues for increased arm swing may affect gait parameters within a single session of training, as well as after a longer training period. This series of studies proposed to address the following specific aims:

Specific Aim 1: To determine short-term improvements in gait with ArmSense cues in individuals with PD. To better understand how increased arm swing affects step length, gait speed, muscle activity and arm/leg coordination, we will examine single-session walking with and without a vibration cue to increase arm swing.

Hypothesis 1a. ArmSense cues will lead to increased step length.

Hypothesis 1b. ArmSense cues will lead to improved arm/leg coordination.

Hypothesis 1c. ArmSense cueing will lead to reduced variability of arm/leg relative phase.

Hypothesis 1d. ArmSense cueing will lead to more normalized muscle activity in arm and leg muscles as compared with people without PD.

Specific Aim 2: To determine if there are sustained improvements in gait and quality of life with ArmSense cues in individuals with PD. To apply the effects of ArmSense in a more relevant and impactful setting, people with PD will use ArmSense while walking at home for four weeks, with half of the subjects receiving tracking and arm swing vibration cueing while the other half receive tracking only. Pre- and post-tests will assess subjects' performance on gait parameters, quality of life and motor-related PD symptoms.

Hypothesis 2a. Arm swing amplitude during uncued walking will increase after intervention.

Hypothesis 2b. Step length and velocity during uncued walking will increase after intervention.

Hypothesis 2c. Arm/leg coordination during uncued walking will improve after intervention.

Hypothesis 2d. Assessment of balance confidence, balance in gait, and quality of life will improve after intervention.

Summary of Results

This series of studies included work involving neurotypical young volunteers, multiple groups of individuals with Parkinson's disease, and neurotypical volunteers age-matched to the volunteers with Parkinson's disease. Arm swing cues for all studies were delivered using a novel wireless wrist-worn device developed by our group (ArmSense, patented) to measure arm swing and deliver cues for larger, more mechanically normal movement. All studies involved an assessment of baseline walking parameters, training with individualized arm swing cues (or dose-matched walking without cues), and a post-training assessment. Gait parameters of interest included gait velocity, cadence, step length, lateral trunk sway, anterior-posterior trunk sway, interlimb coordination, and surface electromyography (sEMG) characteristics of muscle activation in the anterior deltoid, posterior deltoid, gluteus medius, gastrocnemius (medial head), and peroneus longus. In addition to gait parameters, one study (Chapter 5) involved a month-long training program and measured volunteers at the beginning and end on the Activities-

Specific Balance Confidence Scale (ABC), the Functional Gait Assessment (FGA), the Timed Up-and-Go (TUG), and the 39-item Parkinson's Disease Questionnaire (PDQ-39).

Aim 1

Initial results in individuals with PD were obtained in a 12-subject repeated-measures study in which gait parameters were calculated by analyzing videotape of walking in a gym. Due to constraints of the data collection environment, muscle activity and interlimb coordination could not be described in this pilot study. Walking at a comfortable pace, step length increased during both visual cueing and ArmSense cueing, though velocity showed no significant difference. Increased lateral trunk sway was observed with visual cueing, possibly suggesting decreased gait stability. In contrast, no statistically significant changes in trunk sway were observed with ArmSense cues compared to baseline walking. At a fast pace, changes in gait parameters were less systematic. Even though ArmSense cues only specified changes in arm swing amplitude, we observed changes in multiple other gait parameters, reflecting the active role arm swing plays in gait and suggesting a new therapeutic path to improve mobility in people with PD.

The second study to address hypotheses in Aim 1 was a single-session testing of ArmSense in three groups (n=8 for each group): people with PD who received ArmSense cues, age-matched healthy older adults who received ArmSense cues, and people with PD who wore ArmSense units but received no cues. After baseline walking, then training with arm swing cues (or dose-matched uncued walking), subjects were re-assessed in uncued walking. Comparing uncued walking in before and after arm swing training (or dose-matched uncued walking), increases in step length and velocity were seen after

training in the PD-C group, but not the PD-NC group or CTL-C groups. Arm swing amplitude increased significantly in the more affected arm of subjects in the PD-C group, but not in the other two groups. Analysis of interlimb coordination indicated that while not all subjects had a discernible swing with each arm during each gait cycle, a higher proportion of those in the PD-C group had a discernible arm swing after training than before (with no corresponding change in the PD-NC group), perhaps indicating a partial normalization of severely impaired arm swing. The PD-C group demonstrated significantly increased anterior deltoid activity after training, with no other widespread changes in muscle activity with training in the other groups.

Though both studies had small numbers of subjects and encountered technical difficulties with quantification of interlimb coordination that did not present themselves during pilot work, Hypothesis 1a was supported and Hypothesis 1d partially supported (the noted increase in anterior deltoid activity in the PD-C group after training).

Aim 2

Aim 2 hypotheses addressed the possible effects of arm swing cue training on variables of gait, function, and quality of life. These hypotheses were addressed by the study described in Chapter 5. Comparing uncued walking in session 1 (the initial lab visit in Chapter 4) vs session 2 (subsequent lab visit after 30 days of walking training), significant increases in step length, velocity, and arm swing amplitude were seen after training in the PD-C group, but not the PD-NC group. Analysis of interlimb coordination indicated that while not all subjects had a discernible swing with each arm during each gait cycle, that a higher proportion of those in the PD-C group had a discernible arm swing after 30 days of training than before (with no corresponding change in the PD-NC

group). FGA and TUG showed a significant difference in the PD-C group but not the PD-NC group. ABC and PDQ-39 scores did not show significant changes between or within groups. Though interlimb coordination could not be analyzed as fully as planned, Aim 2 Hypotheses 2a, 2b, and 2d were supported by the results of this randomized controlled trial, demonstrating that after training with arm swing cues individuals with Parkinson's disease may demonstrate improved gait parameters and functional gait stability even 1-2 days after the last training session.

The studies included in this dissertation systematically explore the proof-of-concept for ArmSense in neurotypical young adults, in a single-group study with individuals with PD, and finally in a pair of controlled trials comparing the single-session responses of individuals with and without PD, and the training effects in two groups with PD. By exploring changes in gait and balance that occur following arm swing training, we hope to gain insights into possible benefits of an arm swing cueing device to improve functional mobility in individuals with PD.

Limitations

There are several limitations to this series of studies. First, our sample sizes were small, between eight and twelve subjects. While this is a common sample size range for this population and our pilot-based power analysis for the studies in Chapters 4 and 5 suggested that 80% power could be obtained with seven subjects per group (Faul, Erdfelder, Buchner, & Lang, 2009), it is possible that our groups were too small to adequately show all differences that were present.

Also, because the walking protocols required subjects to be able to walk without an assistive device or another person, we know that our sample could only include the most functional subset of individuals with PD. (This conclusion is supported by the fact that all 38 subjects with PD were in H&Y stages I-II, the earliest and most mobile stages of PD.) In addition to likely oversampling those in the early stages of PD, our recruitment through local community groups and previous research volunteers may have oversampled more mobile and motivated individuals, especially those who already wanted to engage in physical activity.

In addition to possible concerns about sampling technique, another possible source of excess variability could be that we did not standardize the training environment for the month-long intervention. Each individual walked in their own chosen environment, and subjects reported various walking locations including high school tracks, apartment building hallways, neighborhood or city streets, and beachside boardwalks. While this lack of standardization increased the environmental variability in the walking training, we feel the individualized environments were more representative of the community walking these individuals would likely engage in outside of a research study, and thus may have increased the generalizability of our findings as well as decreasing the logistical burden on our subjects.

Finally, we encountered greater variability and less improvement in interlimb coordination in individuals with PD than our pilot subjects led us to predict, including significant between-side differences in subject coordination with cues, even if clinical impairment measures were fairly symmetrical. Subsequent studies could consider adding

a training period or modifying the subject instructions to include a component to address interlimb coordination.

Future Research

This series of studies is the first to explore the effects of arm swing cues on gait, balance, and perceived quality of life in individuals with Parkinson's disease, using a patented portable, wireless system to deliver vibratory cues to encourage a larger arm swing. Results from these studies indicate that individuals with PD were able to successfully respond to the cues and increase their arm swing amplitude. Additionally, subjects receiving arm swing cues demonstrated increased gait speed and step length for several minutes after a single training session, and for up to one to two days after four weeks of training. Those receiving dose-matched walking without cues did not show these immediate or post-training changes in gait parameters. Finally, individuals with PD who trained with arm swing cues for one month demonstrated improved functional balance when tested one to two days after their last cueing training, including significantly improved TUG and FGA scores. None of these changes were seen in individuals receiving dose-matched walking without cues.

This initial set of studies measured subjects' responses to arm swing cues, but did not fully investigate possible mechanism behind changes in arm swing behavior. Future studies could explore these mechanisms by looking at possible associations between arm swing impairment and change in arm swing behavior and other PD-related symptoms, such as axial or limb rigidity, spatial inattention, or sensory integration impairment. Future studies could also include a standardized training regimen before independent

walking to provide instruction on integration of larger arm swing into a more globally functional gait pattern (including interlimb coordination). While we believed the use of self-selected training environments improved subject compliance and study validity, future work could also consider standardizing the environment for independent walking training, such as having all walking sessions occur at the same gym.

Other studies could also streamline the testing and training protocols to determine optimal training frequency and intensity. Such work could also enable less mobile or fit individuals to participate in ArmSense training and increase the generalizability of the findings.

Finally, we would enjoy the opportunity to explore new directions suggested by our research volunteers, including placing ArmSense sensors on the ankles as well as the wrists to cue heel strike and coordination, and even to tune the algorithm for use during jogging. By continuing to explore changes in gait and balance that occur following arm swing training, we hope to gain greater insights into benefits of an arm swing cueing device to improve functional mobility in individuals with PD.

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APPENDIX A

IRB-APPROVED INFORMED CONSENT (PROJECT #22499)

Title of research study	**Feedback Device to Increase Arm Swing During Walking**
Investigator and department	*The principal investigator for this project is Dr. W. Geoffrey Wright, PhD, Associate Professor of the Physical Therapy and Bioengineering Departments at Temple University.*
Why you are being invited to take part in a research study	*We are inviting you to participate in this research project because you are a person with Parkinson's disease (PD), or a person without PD who is interested in contributing to research about PD.*
Participant Rights **Who can I talk to?**	*If you have questions, concerns, or complaints, or think the research has hurt you, contact the research team at* W. Geoffrey Wright, PhD (Principal Investigator) Department of Physical Therapy Department of Bioengineering Temple University, Philadelphia, PA, 19140 215-707-9519 wrightw@temple.edu Elizabeth Thompson, DPT, NCS (Graduate Student Investigator) Department of Physical Therapy Department of Kinesiology Temple University, Philadelphia, PA 19122 215-204-0448 eliz.thompson@temple.edu Peter Agada (Laboratory Technician and Investigator) Department of Kinesiology Temple University, Philadelphia, PA 19122 215-204-0448 tuf30575@temple.edu Lei Ma, MS (Graduate Student Investigator) Department of Physical Therapy Temple University, Philadelphia, PA 19140 215-204-0448 leima1@temple.edu John J. Jeka, PhD (Co-Investigator)

	Department of Kinesiology and Applied Physiology University of Delaware, Newark, DE, 19716 Hendrik Reimann, PhD (Post-Doctoral Investigator) Department of Kinesiology and Applied Physiology University of Delaware, Newark, DE, 19716 Tyler Fettrow (Graduate Student Investigator) Department of Kinesiology and Applied Physiology University of Delaware, Newark, DE, 19716 *This research has been reviewed and approved by an Institutional Review Board. You may talk to them at (215) 707-3390 or e-mail them at: irb@temple.edu for any of the following:* • *Your questions, concerns, or complaints are not being answered by the research team* • *You cannot reach the research team* • *You want to talk to someone besides the research team* • *You have questions about your rights as a research subject* • *You want to get information or provide input about this research* *You are also encouraged to ask the research team any questions you may have, including before, during, or following the time that this consent form is discussed with you.*
Why are we doing this research?	*People who have Parkinson's disease (PD) may have trouble walking and moving their limbs. Giving them reminders about the right way to move can help, but it is very difficult to get those reminders when there is no doctor or physical therapist around. This research study is being conducted to understand more about how people with PD interpret sensory information when they are walking, and why they sometimes need reminders during walking. This research study is also being conducted to test a wireless, portable device that will detect a person's arm swing while walking and give reminders (through a vibration or "buzzing") of how to move the right way.* *We are including both people with PD and people without PD in our study. This way, we can compare any differences in responses to learn more about how PD affects walking and movement.*
How long will the research last?	*For the first part of the study, you will participate in 2 sessions that will last about 2 hours each.* *For the second part of the study, you will be asked to participate in 7 evaluation/training sessions with study staff, lasting 60 minutes per session. Six of the sessions will be conducted over a period of 2 weeks. You will then be asked to use the study devices when you walk for exercise at home, 30 minutes per day, 5 days per week for 6 weeks. After the period of home exercise, you will return for the final evaluation session with study staff.*

How many people will be studied?	*We expect about 180 people will be in this research study.*
What should I know about this research?	- *Someone will explain this research to you.* - *Whether or not you take part is up to you.* - *You can choose not to take part.* - *You can agree to take part and later change your mind.* - *Your decision will not be held against you.* - *You can ask all the questions you want before you decide.* - *If you agree to participate, you may change your mind at any time without penalty or loss of benefits to which you are otherwise entitled.*
What happens if I say yes, I want to be in this research?	*Evaluation and training sessions for the experiment will be performed at the Virtual Environment and Postural Orientation (VEPO) lab at Temple University. In some cases, walking trials with the cueing device may be help at Willingboro library, Willingboro, NJ, for people unable to travel to Philadelphia. You should plan to wear shorts, t-shirt or sleeveless shirt, and comfortable walking shoes. If you agree to participate, you will participate in 2 testing sessions for the first part of the experiment, with each session lasting 2 hours. For the second part of the experiment, you will participate in up to 7 evaluation/training sessions (lasting 1 hour each) and a 6-week home walking program. The 6-week home walking program will involve walking for 30 minutes per day (with rest as needed) for 5 days a week.* *All participants will be asked to complete the Mini-Mental Status Exam, a 30-question questionnaire designed to detect cognitive problems, to ensure you will be able to follow the study directions.* *You will be assessed by a rehabilitation professional experienced with treating persons with PD. This professional will give you tests to examine how well you are moving. If you have PD, you will be given the Hoehn and Yahr scale, the Timed up and Go (TUG) test, the miniBESTest, the Activities-specific Balance Confidence Scale (ABC), the Functional Gait Assessment (FGA), the Parkinson's Disease Questionnaire – 39 item (PDQ-39), and a part of the Unified Parkinson's Disease Rating Scale (UPDRS). If you do not have PD, you will just be asked to complete the TUG test, ABC, FGA, and miniBESTest. All participants will also be given a test to assess the sensation in your arms and legs using cotton swabs or thin bristles.* *We will videotape all of your walking.* *You will have adhesive markers attached to your skin with tape, to allow us to better see your movements on the videotape. You will also have adhesive sensors attached to your skin with tape to measure the activity in your muscles. For some trials, you will have electrodes attached to your skin on the back of your neck, which will deliver a small current while you are walking that may give a tingling sensation.* *You will be asked to walk short periods of time on a treadmill, wearing a harness for safety.* *You will be asked to walk certain distances (up to 2 minutes) on indoor and outdoor surfaces like tile, pavement, hardwood, or a treadmill. You may be asked to walk on an unobstructed path or on a path with one 7-inch tall obstacle which*

	will be visible to you. We will attach a small device to each arm (about the size of a wristwatch) by a fabric strap like a wristband, a small pouch or belt around your waist, and may ask you to wear another wristwatch-like device on your legs. The devices and videos will help us measure the length of your steps and your arm swing as you walk. Some of the devices will also have small vibrators inside them to give you cues for how to move as you walk. You will be asked to walk with the cues and without the cues. You may be asked to walk short distances repeatedly during the testing session. You will be given as much rest as you need in between walks. For the home walking program, you will be loaned a pair of sensors to wear on your wrists, and a device to gather and store the data, as well as to track your walking through a password-protected program. ***Sessions will be recorded using a video recorder to learn more about your walking. We may be interested in using these recordings to teach students or present the research to others, but this is optional; your selection of "yes" here indicates your permission for us to use the videos in education or presentations..*** ***Yes___ No___*** ***I agree that my session(s) may be used to present the research to others.*** *If you are a person with PD, you will be asked to participate while ON your anti-parkinsonian medication.*
Is there any way this research could be bad for me?	*No identifiable psychological, social, or legal risks exist for participating in this study.* *There may be some potential physical risks, including loss of balance and possible fatigue in feet, legs and back, and a potential risk of falling and injury. The measures in place to minimize this risk include having a member of study staff walking next to you during all the walking tests, and using a gait belt around your waist that the spotter can hold onto if you become unsteady. Whenever a study staff member is not walking with you, you will have a harness for safety and to prevent falling. There is also a potential risk of skin irritation at the site where the study device is attached by its band, or where the markers or electrodes attach to your skin. To minimize this risk, your skin will be examined before and after applying the device.* *There may be some potential privacy risk in this study. We take all possible steps to minimize the risk of disclosing your identity or information. Please see the section below, "What happens to the information collected for this research?" for more information about this.*
Will being in this research help me in any way?	*You are not expected to receive any direct medical benefits from your participation in this study. However, your participation may help researchers understand how cues can change a person's movement patterns. We hope that, in the future, other people might benefit from this study through more effective techniques to help them improve movement. If you complete each session, you will be paid $40 for each study session.*

What happens to the information collected for this research?	*To the extent allowed by law, we limit the viewing of your personal information to people who have to review it. We cannot promise complete secrecy. The IRB, Temple University, Temple University Health System, Inc. and its affiliates, and other representatives of these organizations may inspect and copy your information. If you are a person with PD, you will also need to sign a separate "Authorization to use and disclose your protected health information" to be a part of this research. If you are a person with PD, we will ask you for information regarding your PD diagnosis and current medications you are taking. This information will be kept in a secure location, such as a locked office and encrypted, password protected electronic data storage. We may publish the results of this research. However, we will keep your name and other identifying information confidential.* *Any potential loss of confidentiality will be minimized by storing data in a secure location such as: locked office and encrypted, password protected electronic data storage. All subjects are identified using an alpha-numeric (letters and numbers) identification system (such as "Subject1.") Videotaped testing sessions will be used for educational purposes and seminar presentations of the study findings and will be destroyed after 5 years. All data will be destroyed in 10 years. If we write a report or article about this research project, your identity will be protected to the maximum extent possible. Your information may be shared with representatives of Temple University or governmental authorities if you or someone else is in danger or if we are required to do so by law.*
Is there anything else I should know about this research study?	*Dr. Jeka has equity interests with Bertec, Inc., the company that holds joint ownership of the Armsense device. Further, Armsense, the device used in this study and developed by the principal investigator, has a US patent pending. This interest is considered a financial conflict of interest. If you would like more information, please use the contact information given in the Participant Rights section of this form.*
Statement of Consent	*Your signature indicates that you are at least 18 years of age; you have read this consent form or have had it read to you; your questions have been answered to your satisfaction and you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.* *If you agree to participate, please sign your name below.*
Signature and Date	**NAME OF SUBJECT[Please Print]**
	SIGNATURE OF SUBJECT
	DATE
	NAME OF RESEARCH STAFF Conducting Informed Consent
	SIGNATURE OF RESEARCH STAFF
	DATE

APPENDIX B

IRB-APPROVED RECRUITMENT FLIER (PROJECT #22499)

Do you have Parkinson's disease (PD)? Or do you have a friend or loved one with PD?

Researchers at Temple University are looking for volunteers for a study on walking in people with PD

- Who can participate?
  - Must have a diagnosis of Parkinson's disease
  - Must be able to walk for at least two minutes without an assistive device or anyone helping you
  - Must be able to follow multi-step directions and walk under different conditions
  - Cannot have an implanted deep brain stimulator (DBS) or pacemaker

- What does the study involve?
  - Walking in our lab on Temple's campus (1800 North Broad Street, Philadelphia)
  - Taking a cognitive test and quick examination of your PD symptoms
  - Walking over ground and on a treadmill
  - Walking in the community near your home
  - Using different sensors and cues while you walk

- If interested, please reach out to us!
  - Call our lab at 215-204-0448
  - Email us at TempleArmsense@gmail.com