Real-Time Feedback Training to Improve Gait and Posture in Parkinson's Disease

by

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ABSTRACT

Progressive gait disorder in Parkinson's disease (PD) is usually exhibited as reduced step/stride length and gait speed. People with PD also exhibit stooped posture, which can contribute to reduced step length and arm swing. Since gait and posture deficits in people with PD do not respond well to pharmaceutical and surgical treatments, novel rehabilitative therapies to alleviate these impairments are necessary. Many studies have confirmed that people with PD can improve their walking patterns when external cues are presented. Only a few studies have provided explicit real-time feedback on performance, but they did not report how well people with PD can follow the cues on a step-by-step basis. In a single-session study using a novel-treadmill based paradigm, our group had previously demonstrated that people with PD could follow step-length and back angle feedback and improve their gait and posture during treadmill walking. This study investigated whether a long-term (6-week, 3 sessions/week) real-time feedback training (RTFT) program can improve overground gait, upright posture, balance, and quality of life. Three subjects (mean age 70 ± 2 years) with mild to moderate PD (Hoehn and Yahr stage III or below) were enrolled and participated in the program. The RTFT sessions involved walking on a treadmill while following visual feedback of step length and posture (one at any given time) displayed on a monitor placed in front of the subject at eye-level. The target step length was set between 110-120% of the step length obtained during a baseline non-feedback walking trial and the target back angle was set at the maximum upright posture exhibited during a quiet standing task. Two subjects were found to significantly improve their posture and overground walking at post-training and these changes were retained six weeks after RTFT (follow-up) and the third subject improved his upright posture and gait rhythmicity. Furthermore, the magnitude of the improvements observed in these subjects was greater than the improvements observed in reports on other neuromotor interventions. These results provide preliminary evidence that real-time feedback training can be used as an effective rehabilitative strategy to improve gait and upright posture in people with PD.

To my parents, Latha and Baskaran

To my sister & family, Krutheeka, Jayendiran and Adhvaith

To my support system, friends and mentors

This work is dedicated to you!

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CHAPTER 1

INTRODUCTION

SIGNIFICANCE

Parkinson's disease is the most common movement disorder besides essential tremor and is the second most common neurodegenerative disease after Alzheimer's disease (Tanner & Aston, 2000). Approximately 1-2% of the population aged over 65 years suffers from PD (Alves, Forsaa, Pedersen, Dreetz Gjerstad, & Larsen, 2008); this prevalence increases to 3 – 5% in people 85 years and older (Fahn, 2003). The degradation of dopamine-producing cells in the substantia nigra of the basal ganglia was found to be the primary cause of this disease. No cure being available, some researchers and clinicians focus on alleviating the dysfunctions caused by PD.

Four prominent features of PD are tremor, rigidity, bradykinesia, and gait and postural instability (Meg E Morris, Iansek, Matyas, & Summers, 1996). In addition, flexed posture and freezing (motor blocks) have been included among the classic features of parkinsonism (Jankovic, 2008). Gait impairments in PD may be classified into two types: continuous, which includes impairments such as reduction of stride length and gait speed, increased double support time, and left-right asymmetry); and episodic, which includes impairments such as festination and freezing (Frazzitta, Pezzoli, Bertotti, & Maestri, 2013). In addition to these features that are clinically observable, PD is also characterized by increased stride-to-stride variability, which manifests as increased coefficient of variation (COV) in some gait indices and contributes to gait instability in persons with PD (Hollman, Kovash, Kubik, & Linbo, 2007). Furthermore, stooped posture exhibited by people with PD, which appears as rounding of the shoulders and flexion of the hips and knees (Benatru, Vaugoyeau, & Azulay, 2008), also contributes to reduced step length and arm swing. Asymmetry in parkinsonian gait has gained significance recently as an indicator for potential freezing of gait (FOG) which can lead to falls (Ricciardi et al., 2012). Plotnik et al. (2005) hypothesized that asymmetrical and uncoordinated activation of legs during walking are characteristics of PD+FOG patients and asymmetric gait can lead to FOG (Plotnik, Giladi, Balash, Peretz, & Hausdorff, 2005). Gait and posture deficiencies in PD are disabling and can increase age-related risk of falling and affect quality of life for persons with PD; postural instability, rigidity, and bradykinesia being the strongest clinical predictors of falls (Rogers, 1996).

Symptoms of PD have been mainly treated with dopaminergic medication such as levodopa. Medication is generally successful in managing classical symptoms of PD, helping preserve mobility for some years but still is only partially effective (Rogers, 1996). McNeely et al. assessed 24 PD patients (in medication ON and OFF conditions) and 20 healthy control subjects while they performed several walking and balance tests. While medication ON condition helps to maintain walking in persons with PD by improving velocity and stride length significantly when compared to medication OFF condition, both parameters were lower than those of healthy controls. The effects of medication on postural instability and balance are unclear, as some impairments were retained and observed regardless of medication status (McNeely, Duncan, & Earhart, 2012). Also, it has been found that most patients treated with levodopa experience medication-induced motor fluctuations, dyskinesias or other complications after approximately 5 years of treatment (Jankovic, 2005). Over time, people with PD experience fluctuating phases characterized by an on/off reemergence of Parkinson's symptoms between medication doses as medication becomes less effective. Physical therapy (PT) can provide a beneficial supplement to standard medication (Gage & Storey, 2004), though it is not known if it directly addresses the underlying pathology of PD (Rubinstein, Giladi, & Hausdorff, 2002). These issues have led researchers to explore additional rehabilitation techniques to supplement traditional pharmacological treatments to address the symptoms of PD and improve quality of life.

Physical therapy may serve as an adjunct to pharmacological and neurosurgical treatments as these are able to reduce but not eliminate the deficits of PD (Kwakkel, de Goede, & van Wegen, 2007). In a review of physical therapy interventions for PD, Tomlinson et al. identified several studies that implemented motor activities to focus on improving various gait and balance issues in PD, which included: physiotherapy, aerobic training, group box training, Lee Silverman Voice Treatment (LSVT) BIG training, treadmill walking, tango, tai chi, body weight supported treadmill training etc. (Tomlinson et al., 2014). Novel approaches such as partial body weight-supported treadmill training, polestriding (Krishnamurthi et al., 2017) and structured treadmill training were also used as a rehabilitation intervention and were found to be superior to usual PT approaches for increasing gait velocity (Moroz et al., 2009). Recently, many studies conducted physical therapy sessions that included external sensory cues which were provided to persons with PD while they carried out gait and balance activities. The incorporation of external cues is found to be beneficial since PD involves a generalized dysfunction of sensorimotor integration and proprioception which is a result of impaired basal ganglia functions that relate to processing and integrating sensory input to organize and guide movement and posture (Schneider, Diamond & Markham, 1987).

EXTERNAL SENSORY CUES

External sensory cues can be defined as sensory facilitators that use spatial or temporal information to initiate and carry out functional activities in individuals with motor dysfunction (Rubinstein et al., 2002). The use of auditory, visual and/or tactile cues that provide spatial or temporal information on walking for persons with PD have been the subject of many investigations been investigated by many over the years.

The most widely used auditory cue is a metronome at the desired step frequency. Additionally, researchers have used externally-voiced words, musical beat, ‘cluck’ and ‘ding’ sounds (Cassimatis, Liu, Fahey, & Bissett, 2016). Rhythmic auditory stimulation (RAS) using the above-mentioned cues have produced promising results during and immediately after cued training sessions. Single session studies have reported that patients were able to match their cadence to a beat that was set at 10% faster than their baseline values, significantly improving their velocity, cadence and stride length (Cunnington, Iansek, Bradshaw & Phillips, 1995). There is no clear explanation for how RAS helps to improve gait, but it is suggested that perhaps it provides an external rhythm that can compensate for the defective internal rhythm of the basal ganglia (McIntosh, Brown, Rice, & Thaut, 1997).

Tactile cues in the form of vibrations have recently been studied, more investigations will be required to determine their efficacy with respect to correction and regulation of walking in PD. Nieuwboer et al. (2007) used a wrist worn vibratory device as one of the three cued interventions (visual, auditory or somatosensory cues) in an effort to assess improvements in step length and walking speed of PD subjects in the home environment. Although this study reported small but significant effects of cues on performance, it did not provide evidence regarding which cue contributed to these improvements. In a single-session study, step synchronized vibration stimulation was applied to the plantar region of 8 PD subjects and 8 healthy subjects' feet via insoles and the effect was studied with and without the stimulus (Link, Novak, & Novak, 2017). This study provided evidence of improvements in walking speed, step duration, step length, cadence, and reduction of variability in gait requiring investigation of its long-term effects in a larger cohort and development of better devices.

Visual cues have been mainly used as a technique to regulate stride length. Floor markers were reported to be effective in improving gait of PD patients as early as 1967 (M E Morris, Iansek, Matyas, & Summers, 1994). Other forms of visual cues include virtual reality glasses, optical stimulating glasses, white stripes, white tape and subject mounted light device and light flashes (Spaulding et al., 2013). Notably, there are specific configurations in which these cues are found to work, for example, transverse lines on the floor spaced by appropriate distance on the floor achieve good results whereas zigzag or parallel lines do not (Rubinstein et al., 2002). Visual cues help to fill in for the motor set deficiency by providing visual data on appropriate stride length (Meg E. Morris & Iansek, 1996). These cues generate an optical flow that may activate a cerebellar visual-motor pathway (Azulay et al., 1999). Many single session studies have reported improvements in stride length and velocity when floor markers were presented to PD patients. In comparison to RAS, visual cues work better in improving stride length (Suteerawattananon, Morris, Etnyre, Jankovic, & Protas, 2004).

Visual cueing in conjunction with a physical therapy technique such as treadmill training has been implemented by a very few research groups. Treadmill training (TT) with and without body-weight supported treadmill training (BWSTT) have been shown to be effective in improving gait in PD (Frenkel-Toledo et al., 2005; Herman, Giladi, Gruendlinger, & Hausdorff, 2007; Pohl, Rockstroh, Rückriem, Mrass, & Mehrholz, 2003). It is hypothesized that walking on a moving walkway (i.e., a treadmill) inherently provides external cueing that in turn generates repetitive sensory input to the central nervous system (Mathiowetz & Haugen, 1994). Recently, two studies

(Frazzitta, Maestri, Uccellini, Bertotti, & Abelli, 2009; Schlick et al., 2015) have explored the use of visual cueing in the form of step/stride length cues to study the improvements in the same. In a forty-subject study, conducted by Frazzitta et al. (2009), visual and auditory cued performance with and without treadmill walking was compared. A group of 20 participated in a cueing protocol that included visual cues in the form of a target displayed on a monitor which the subject had to reach while taking an appropriate stride (alternating right and left feet were displayed on the screen) and an auditory cue in the form of musical beats that were synchronized with the visual cues. The other 20 subjects participated in a rehabilitation protocol that included overground walking with cues (not on the treadmill) and visual cues in the form of transverse tapes placed on the floor. Results indicate the cued treadmill training group had better improvements in gait indices than the other. In a pilot study, Schlick et al. (2015) recruited 23 subjects and assigned them to two groups: one group was provided with visual cues while walking on the treadmill and the other performed only treadmill walking. Visual cues were presented in the form of foot projections on the treadmill belt while the subjects walked over it in 12 training sessions over the course of five weeks. Comparisons were made between the two groups receiving cued TT with another receiving only TT. Findings indicated that patients with higher freezing scores (FOG-Questionnaire) had greater benefit (increase in stride length) from cued TT than those with lower scores. In a follow-up assessment, 2 months after the dynamic cued TT period, it was reported that although there was a decrease in gait indices such as stride length, cadence and gait speed in the cued TT group, the decrease was less than that of the TT group and these indices remained above baseline performance.

In most studies that investigated the impact of cues on gait patterns, step/stride length was improved by visual cues. However, these cues were usually provided as transverse lines on the floor which is not suitable for outside the laboratory environments (for long continuous walking encountered during daily activities). Almost all studies involving visual cues (except Frazzitta, Maestri, Uccellini, Bertotti, & Abelli, 2009; Ginis et al., 2016; Schlick et al., 2015) did not provide feedback to participants about their performance on a step-by step basis. Other studies on a variety of tasks have demonstrated that immediate feedback can enable individuals to modulate their effort to achieve established goals (Alice Nieuwboer, Rochester, Muncks, & Swinnen, 2009). Moreover, there are some other important limitations with some of the studies. In the study reported by Frazzita et al. (2009), it is difficult to ascertain which type of cue (visual or auditory) contributed improvements in gait performance. In addition, only gait indices such as speed and stride cycle were evaluated. The study by Schick et al. (2015) enables us to identify visual cues as a contributor to enhanced performance, but the technique of projecting foot prints on the treadmill requires the subjects to look down walking, which is different from normal walking, and may worsen the stooped posture already experienced by many people with PD.

A recent study developed a wearable smartphone-based application (CuPID system) to provide real-time feedback on gait performance to PD patients in the home environment (Ginis et al., 2016). In this feasibility study, forty participants were recruited and allocated to two groups: the intervention group, who used the CuPID system, and the control group, who were advised by a researcher about gait and freezing. In the CuPID group, inertial measurement units were worn on the feet and the mobile phone application provided audio feedback in real-time via earphones about performances on four different gait parameters: stride length, cadence, symmetry and gait speed. Significant improvements in gait speed and balance tests were observed. Although this system was found to be feasible and well accepted by participants, providing feedback about stride length may not be easy to follow on a step-by-step basis. Also, since feedback on different gait parameters was provided at different time points, it is difficult to ascertain which gait parameter (stride length, cadence, symmetry or gait speed) led to improvement in performance.

In a feasibility study to overcome the above-mentioned drawbacks, Jellish et al. implemented a treadmill-based real-time feedback (RTF) protocol in which explicit visual cues on step length and back angle were provided to subjects (Jellish et al., 2015). This single-session study demonstrated that subjects with PD could successfully utilize the visual cues to improve their step length and upright posture. The improvements in step length and upright posture were sustained even during the non-feedback trials that immediately followed the feedback trials. However, the effects of regular use of RTF on these outcomes are not clear, thus warranting an investigation to determine if the effects of RTF are retained and/or cumulative across days.

Importantly, it is also unknown whether long-term RTF can lead to translation of benefits to overground walking.

Given the need for investigating long-term benefits of RTF for gait and posture rehabilitation in PD, this intervention study investigated the long-term effects of a six-week RTF training (RTFT) program in subjects with PD on gait during overgound walking. We tested the following hypotheses:

(i) RTFT will improve gait in people with PD: The overground gait parameters collected at pre-RTFT will be compared to post-RTFT. Any increases in stride length and gait speed and/or decreases in stride length/step time variability will indicate improvement in overground gait due to RTFT.

(ii) RTFT will improve upright posture in people with PD: The back angle measured during treadmill gait at pre-RTFT will be compared to post-RTFT. An increase in back angle at post-RTFT will indicate an improvement in upright posture

(iii) These gait and posture improvements will be sustained at six weeks after completion of the RTFT intervention (follow-up). Improvements in the above-mentioned gait and upright variables at follow-up-RTFT when compared pre-RTFT will indicate that the effect of RTFT on walking and posture is preserved six weeks after the training is completed.

CHAPTER 2

MATERIALS AND METHODS

SUBJECTS

Four subjects with PD (Hoehn and Yahr stage 3 or below; Goetz et al., 2004) were recruited to participate in the study (Table 2.1). Of them, three subjects (mean age 70 ± 2 years) completed the study and were included in the analysis; one subject had difficulty walking on the treadmill during the first (pre-RTFT) evaluation session and hence did not continue. This study was approved by the Institutional Review Board of Arizona State University and all subjects provided their written informed consent and permission for photography and videography (see Appendix A for IRB approval form).

Table 2.1

Participant information

Subjects	Sex	Age	H&Y Score	# years since diagnosis
S01	F	68	2	4
S02	M	72	3	6
S03	M	70	2	8

Inclusion criteria for the study were: diagnosis of idiopathic PD according to UK brain bank criteria (Hughes, Daniel, Kilford, & Lees, 1992), age between 50-80 years, UPDRS walking and freezing score ≥ 1 during 'medication-on' state, stable dosing of PD medication for 4 weeks prior to the study, ability and willingness to perform the 6-week intervention and evaluation sessions including ability to walk overground (50 meters continuously) and over the treadmill (for 5 minutes continuously) while wearing lightweight sensors. The experimental sessions were conducted approximately one hour after regular dose of PD medication to ensure participation during the "medication-on" state, during which the medication effectively controls PD and to avoid motor fluctuation resulting from end of dose deterioration.

Subjects were excluded if they: exhibited dementia according to DSM-IV criteria; regularly used assistive gait device such as walker or cane, had prominent dyskinesia (> 50% of day or UPDRS dyskinesia score > 1); had on/off motor fluctuations (> 25% throughout day) , prone to frequent falling (UPDRS fall score > 1); experienced freezing leading to falls; had

UPDRS postural stability > 2 in medication on state or other balance impairment which in the opinion of the movement specialist (Dr. Mahant or Dr. Ospina) would affect subjects' safety or compliance with the study protocols; had a recent history of unstable heart or lung disease, evidence of pregnancy, or major neurological disease except PD (e.g., stroke), or metabolic (e.g., diabetes) problems; had postural hypotension, cardiovascular disorders, musculoskeletal disorders, or vestibular dysfunction limiting locomotion or balance; had currently or recently participated in any other study involving exercise to improve gait or posture; or had been prescribed to take anti-parkinsonian medication for every 4 hours or less to avoid confounding factors of medication dosage due to necessity to take medication during data collection sessions.

Subjects who lacked approval from their cardiologist or primary care physician to participate in the study, failed to provide consent to this study, had a history of non-compliance with medical or research procedures, had cardiac pacemaker or any implanted stimulatory device, had an untreated chemical addiction or abuse, or uncontrolled psychiatric illness were excluded from this study as well.

STUDY PROTOCOL

Each subject participated in a pre-RTFT evaluation session, 6-week RTFT intervention (three 45-minute sessions per week), post-RTFT evaluation session (at 7th week of the study) and follow-up-RTFT (13th week of the study) requiring 21 visits to the Center for Adaptive Neural Systems, Arizona State University. The post-RTFT and follow-up-RTFT evaluations enabled investigation of the immediate and long-term effects of RTFT intervention, respectively. This study protocol is depicted in Figure 2.1 along with the tasks performed during each evaluation and training session.

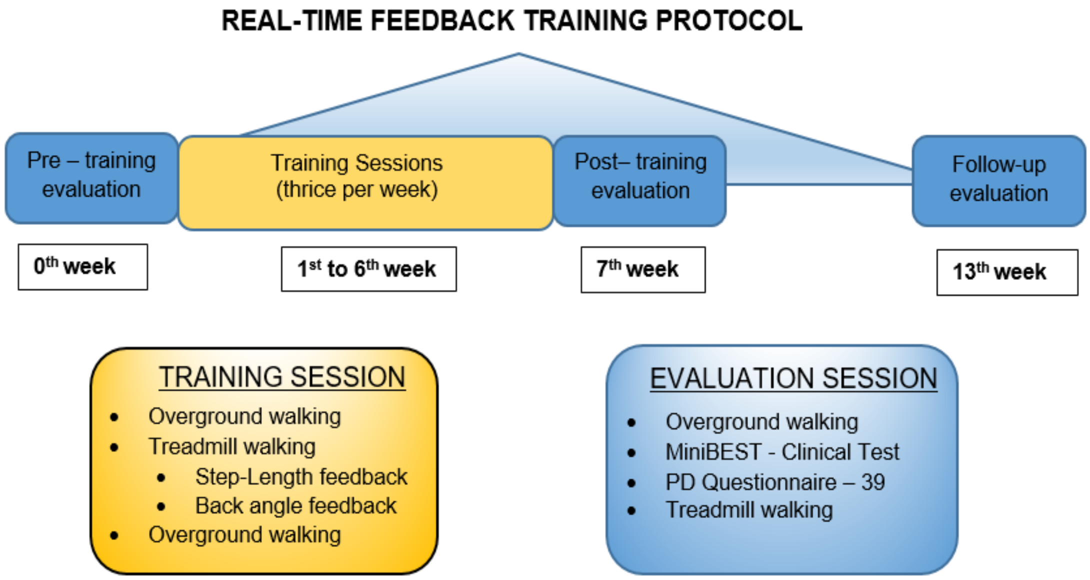


Figure 2.1. Experimental timeline and protocol

Training sessions were carried out during subjects' "medication-on" condition. Table 2.2 gives an overview of the experimental tasks performed during each training session. During each session, subjects walked overground for about 120 meters before and after the set of treadmill trials. These overground trials helped to investigate the effects RTF provided during earlier days and the immediate effects of RTF.

Table 2.2.

Experimental tasks performed during RTFT sessions

Task		# of trials /description	Task descriptor
Overground walking		1/ 120-meter walking	Pre-RTF walking
Treadmill walking	Back angle feedback	3/ 5 minutes each	ON- 0^{th}-2^{nd} minute
			OFF- 2^{nd}-3^{rd} minute
			ON- 3^{rd}-4^{th} minute
			OFF- 4^{th}-5^{th} minute
	Step length feedback	3/ 5 minutes each	ON- 0^{th}-2^{nd} minute
			OFF- 2^{nd}-3^{rd} minute
			ON- 3^{rd}-4^{th} minute
			OFF- 4^{th}-5^{th} minute
Overground walking		1/ 120-meter walking	Post-RTF walking

Each treadmill trial with feedback involved real-time feedback (RTF) of step length or back angle; only one type of feedback was provided at a given time to avoid dual tasking. Before the feedback trials, the subject selected a comfortable speed by walking on the treadmill for a few minutes; this comfortable speed was then used to carry out all the subsequent treadmill training tasks. Each RTFT session comprised of participation in a total of six 5-minute treadmill walking trials: three 5-minute step length feedback trials and three 5-minute upright feedback trials. The sequence of type of feedback administration was alternated for each day of participation in order to determine if changes in gait parameters during overground walking depended upon the type of feedback training received just before the post-RTF overground walking session. During each of the 5-minute feedback trials, the following sequence of feedback conditions were administered to avoid developing dependence on the feedback for modulating their performance: 0 to 2nd minute – feedback provided; 2nd to 3rd minute – no feedback; 3rd to 4th minute – feedback provided; 4th to 5th minute – no feedback. The time periods without feedback were intended to encourage the subjects to internally conceptualize the effort needed to walk with targeted step length and uprightness. Parameters such as step length, step time and upright posture were calculated during all these trials. Sufficient rest periods were provided between each of these trials as required.

Evaluation sessions were conducted during the "medication-on" condition. Table 2.2 gives an overview of the experimental tasks performed during each evaluation session. For all walking/balance tasks, Mobility Lab^{TM} (APDM, USA) sensors were worn. During the treadmill walking sessions, reflective markers were worn in addition to the wearable sensors. This setup will be explained in the upcoming sections.

Table 2.3

Experimental tasks performed during evaluation sessions

Task	# of trials/time	Task descriptor
Overground walking	1	120-meter walking
Mini-BEST	N/A	Figure 2.2
PD-Questionnaire 39	N/A	N/A
Treadmill walking	2/10 minutes or 4/5 minutes	No feedback; walking in self-selected speed

Each evaluation session started with an overground walking trial of about 120 meters. The subjects wore the APDM sensors and were asked to walk at their self-selected comfortable speed during this trial. From this task, parameters such as gait speed, stride length, step time, double support duration, gait asymmetry, and head accelerations were obtained. This was followed by tests for balance using the Mini-Balance Evaluation Systems Test (Mini-BESTest; Franchignoni, Horak, Godi, Nardone, & Giordano, 2010), which involved performing the activities shown in Figure 2.2

Mini-BESTest tasks

- sit to stand,
- rise to toes,
- stand on one leg,
- compensatory stepping correction in forward, backward, and lateral directions,
- standing eyes open on a firm surface,
- stance eyes closed on a foam surface,
- standing inclined eyes closed,
- change in gait speed,
- walk with horizontal head turns,
- walk with pivot turns,
- step over obstacles, and
- timed up & go with and without dual task (counting)

Figure 2.2 List of tasks in the Mini-BESTest

Adequate rest periods were provided between the tasks. After these tests, the subjects were asked to complete the Parkinson's Disease Questionnaire-39 (PDQ-39), which provides a validated measure of quality of life (Peto, Jenkinson, & Fitzpatrick, 1998). The 39 questions have 8 discrete scales: mobility, activities of daily living, emotional well being, stigma, social support, cognitive impairment, communication and bodily discomfort. The subjects were asked to consider how oftern in the last month they experienced certain events (e.g. difficulty in walking half a mile). According to the frequency of each event, they were asked to select one of 5 options, never/occasionally/sometimes/often/always or cannot do at all. The overall scores can be interpretted as 0 = no problem at all and 100 = maximum level of difficulty.

The subjects were then asked to walk on a treadmill for two 10-minute trials at their self-selected speed without any feedback. Shorter trials were used for subjects who were not comfortable in completing the 10-minute trials. From this task, parameters such as step length, step time and back angle were obtained.

EXPERIMENTAL SETUP

To obtain various indices such as stride length/time, gait speed, cadence, head accelerations, double support duration, elevation at mid-swing and variability and asymmetry measures, during both overground and treadmill walking, the subjects wore seven Mobility Lab^{TM} wearable sensors (APDM, USA) at different anatomical locations, on the left and right feet, left and right wrists, chest, hip and head as shown in Figure 2.3a. Each sensor has a set of accelerometers, a magnetometer and a gyroscope.

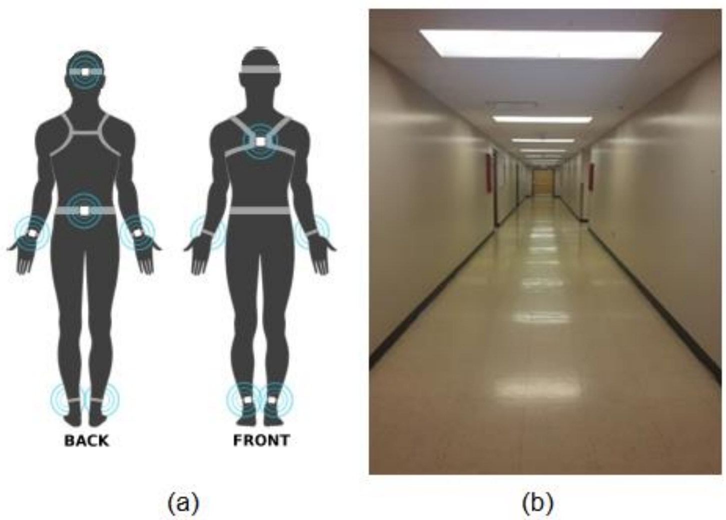


Figure 2.3 Anatomical locations at which the movement sensors are worn during overground and treadmill walking (a); Hallway used to perform overground walking tasks (b)

The 120-meter overground walking trials were performed in the hallway (38m x 2m x 3.3m) shown in Figure 2.3b, subjects made three 180 degree turns at every 30 meters. Treadmill training sessions were carried out with a set-up for motion capture and visual feedback. The main components of this setup were: 8 Optitrack cameras (Naturalpoint, USA) to quantify movement by tracking reflective markers placed on the subject, a motorized treadmill, computer software and system for data collection, and a monitor to present visual feedback.

The treadmill used in this study (TMX59, Trackmaster Treadmills, USA) allowed for adjustment of belt speed and inclination; in this study, the inclination was always set at zero. The stop tether was worn by the subject so that the treadmill belt would automatically stop in the case of a fall or loss of balance. In addition, subjects also wore a gait belt at all times to facilitate support by the experimenter in the event of any loss of balance. A monitor (22” x14”) was placed in front of the treadmill, at about 3 feet from the subject’s head and at eye-level, to provide visual feedback of step length and back angle. Eight Optitrack FLEX 3 V100 cameras were placed in a configuration around the treadmill that facilitated unobstructed viewing of reflective markers placed on the subject. Each camera operated at a frame rate of 100 frames per second with a latency of 10 ms. Tracking Tools™ (Naturalpoint, USA) software on a PC communicated with the cameras to acquire three-dimensional position of each of the markers. Custom-designed software used marker location data to calculate step length and back angle as well as other variables, display the selected variable on the monitor in real-time, and store the acquired and calculated variables.

(a) (b)

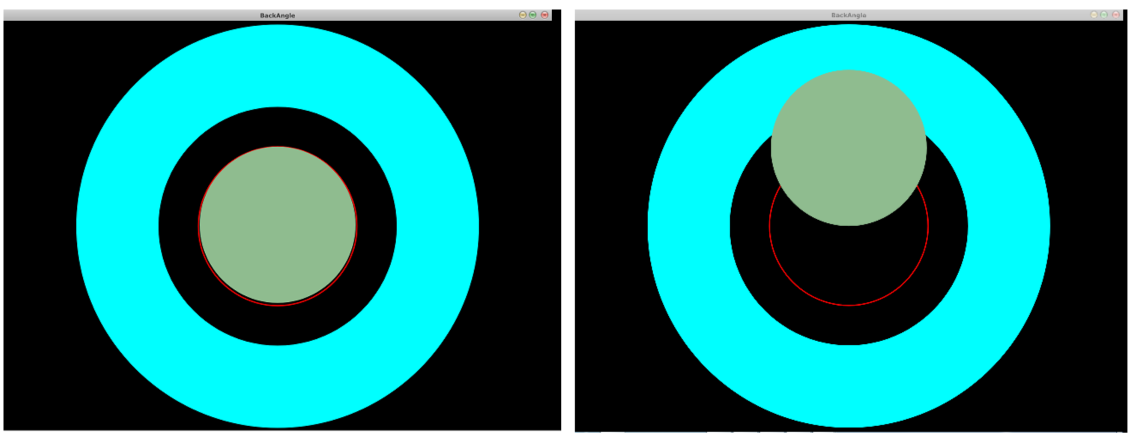
Figure 2.4. Ankle braces, modified gait belt and GoPro™ harness with the marker triads (a) *S*ubject wearing the markers and wearable sensors while on the treadmill and the monitor in front of the treadmill that displays real-time feedback (b).

Reflective markers were placed in triads at the specified anatomical locations. Each triad had a unique triangular configuration to allow the software to distinguish between the triads and track their centroids. Triads were placed on the on the upper back (center point between the shoulder blades), the lower back (center point at back of hips), and the lateral aspect of each ankle. A modified GoPro™ camera harness was utilized to attach the triad on the upper back while the waist triad connected to a gait belt. The ankle triads were affixed to straps worn over the subject's socks. Figure 2.4a shows the apparatus with the reflective markers and Figure 2.4b shows a subject wearing the sensors, the monitor that displays feedback, and the treadmill.

VISUAL FEEDBACK DESCRIPTION

Visual feedback of step length or upright posture was presented to the subjects; only one type of feedback was provided at any given time. Within each trial, the feedback display was switched on or off for the feedback-on and feedback-off conditions, respectively.

Back angle was calculated using the centroid positions of the triads on the upper back and the waist. Back angle was defined as the angle made by the line joining the two centroids with respect to the horizontal. Therefore 90 degrees corresponds to upright posture. The value for maximum uprightness of each subject was measured initially by asking the subject to stand as upright as possible before starting the back-angle feedback trial.



(a) (b)

Figure 2.5. Posture cursor (green circle) within the red target circle, indicating upright posture (a); the posture cursor relative (upwards) to the target circle, indicating subject leaned forward (b)

During presentation of feedback, the instantaneous uprightness of the subject was indicated on-screen by a filled green circle (posture cursor), with maximum uprightness represented on the display when the posture cursor overlapped completely with the red circular boundary (standing target) (Figure 2.5a). If the subject leaned forward, or stooped, the posture cursor moved up on the screen relative to the upright location; conversely, if the subject leaned backward, the posture cursor moved down on screen relative to the upright location (Figure 2.5b).

During walking, slight sagittal plane bending resulted in periodic variations in back angle. To account for these periodic movements, the target zone was increased and subjects were instructed to walk so that the posture cursor was kept within the inner boundary of the cyan circular region (walking target zone); the inner and outer radius of the walking target zone was set at 5º and 15º, respectively.

Step length was measured during the experimental session for both left and right feet separately (Figure 2.6). The instantaneous left and right step length was measured as the distance between heel strike and toe lift of the corresponding foot. Toe lift, and heel strike positions were determined by tracking the position of each ankle triad and determining minimum and maximum values along the anterior-posterior direction; step length for a given step was calculated as the difference between a sequential minimum and maximum value for each ankle triad.

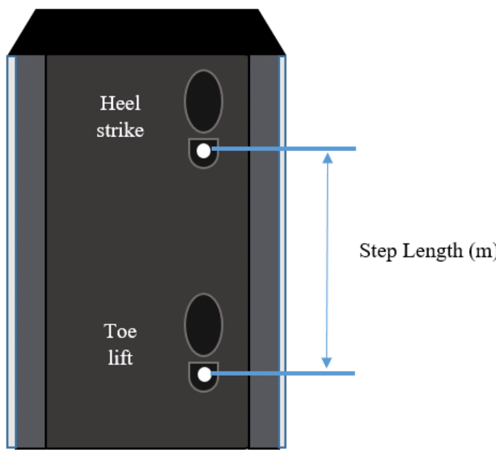


Figure 2.6. Top view of the treadmill surface with foot locations indicated for toe lift and heel strike. Left and right step lengths were measured as the distance between toe lift and heel strike of the respective foot.

During presentation of real-time feedback of step length, the instantaneous left and right step length was indicated on the monitor by black left and right foot icons on a white background (Figure 2.7a). Target step length was calculated by increasing the average step length (whichever side had a smaller value) obtained from a non-feedback treadmill walking trial. The percentage increase was set at a value in the range of 10 -20% and was gradually increased based on the subject's ability to reach the target zone. Blue target lines were displayed on-screen to indicate the desired upper and lower target bounds for step length calculated as 5% of the target step length. If a subject's left or right step length was larger or smaller than the target range (area between the two horizontal lines), the display of the corresponding foot icon relative to the target range indicated the amount of deviation as shown in Figure 2.7b. The step length feedback window could be adjusted to display any portion of the step length range between zero and one meter, thereby zooming in on a desired target range. During feedback off condition the display of footsteps and posture cursor & boundaries were removed.

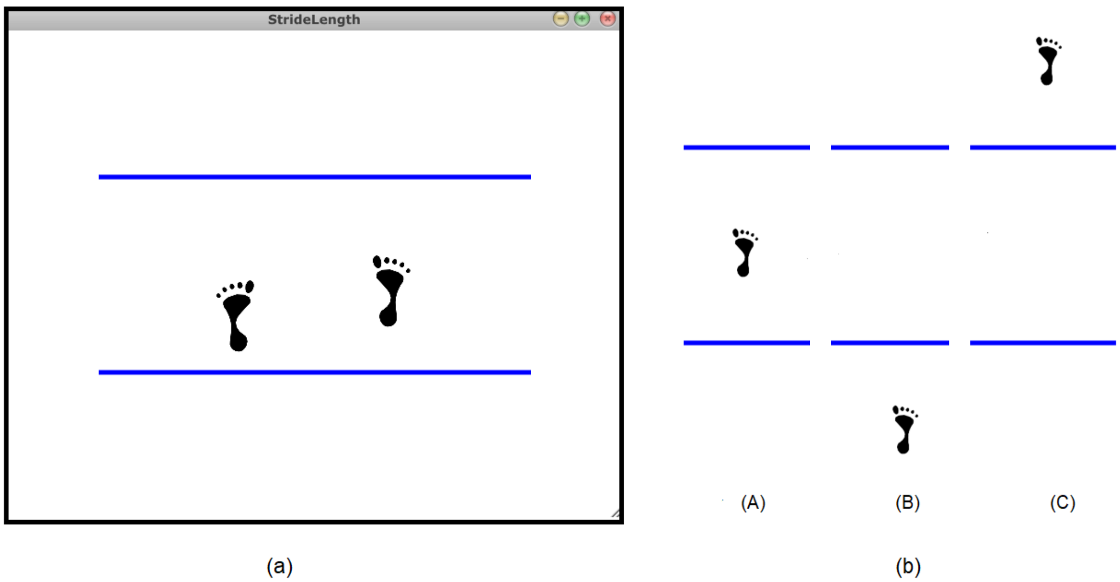


Figure 2.7. (a) Left and right step length was displayed on screen as left and right black footprints. Blue lines indicated the target range. (b) If the step length (right foot presented here) is within the target range, the footprint would fall between the blue lines (A); if the step length was larger or smaller than the target range, the footprint would fall below the bottom line (B) or above the top line (C)

STATISTICAL ANALYSIS:

Given that this is a pilot study with a very small sample size, the data from each subject was investigated separately using single-subject analysis. To compare the step-by-step gait indices obtained during each evaluation session and across training sessions, a one-way analysis of variance (ANOVA) test was used. A p-value < 0.05 was considered to be statistically significant. A Tukey post-hoc test was used to identify significant differences in each pairwise comparison. All analyses were run using SPSS 24 (IBM Corp., USA).

RESULTS

GAIT PARAMETERS DURING OVERGROUND WALKING

The changes across evaluation sessions in the mean and SD of stride length, step time, cadence, gait speed, and double support for each of the three subjects from the left and right sides were investigated (Figures 3.1 and 3.2).

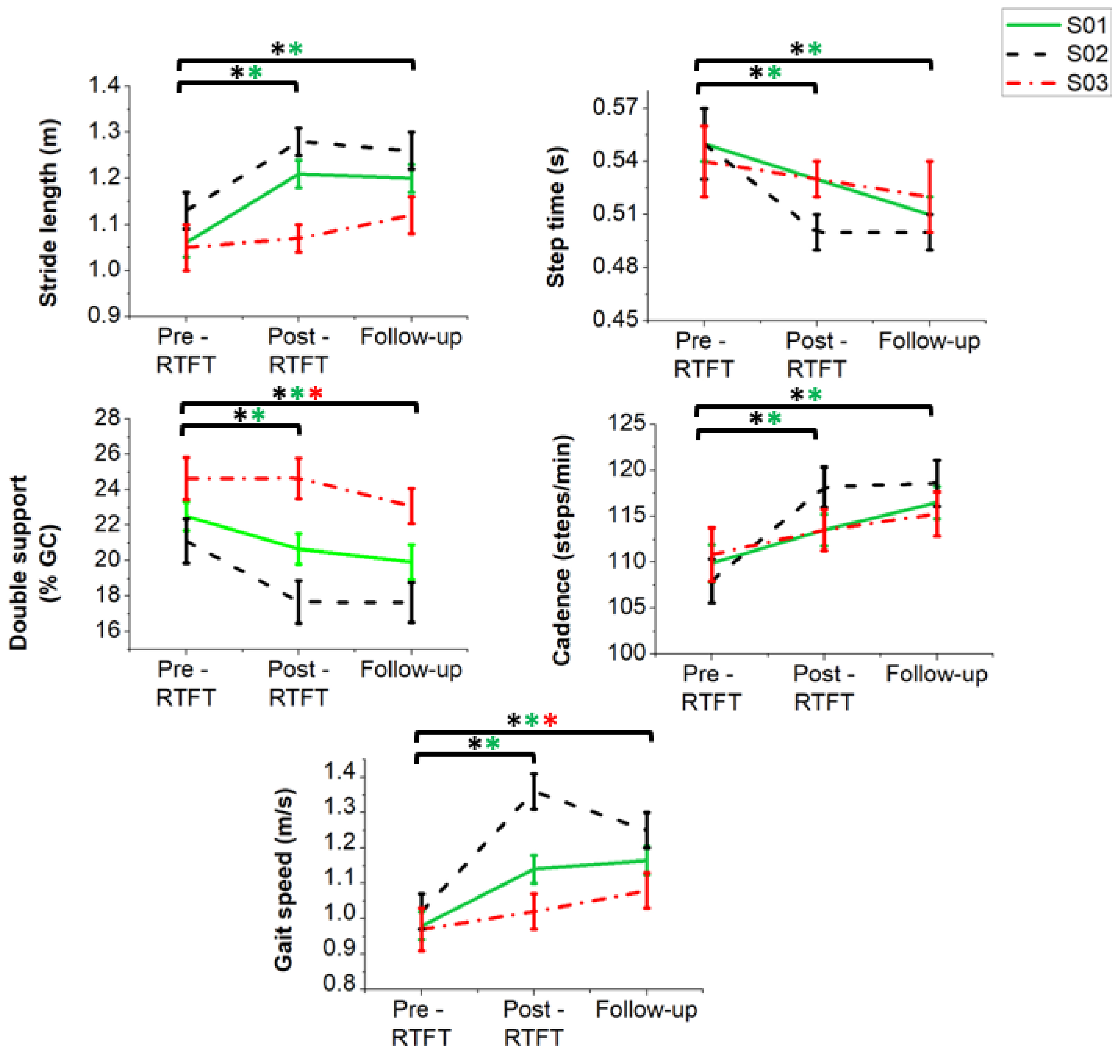


Figure 3.1 Mean and SD values of left side gait indices obtained at pre-RTFT, post-RTFT and Follow-up evaluation sessions

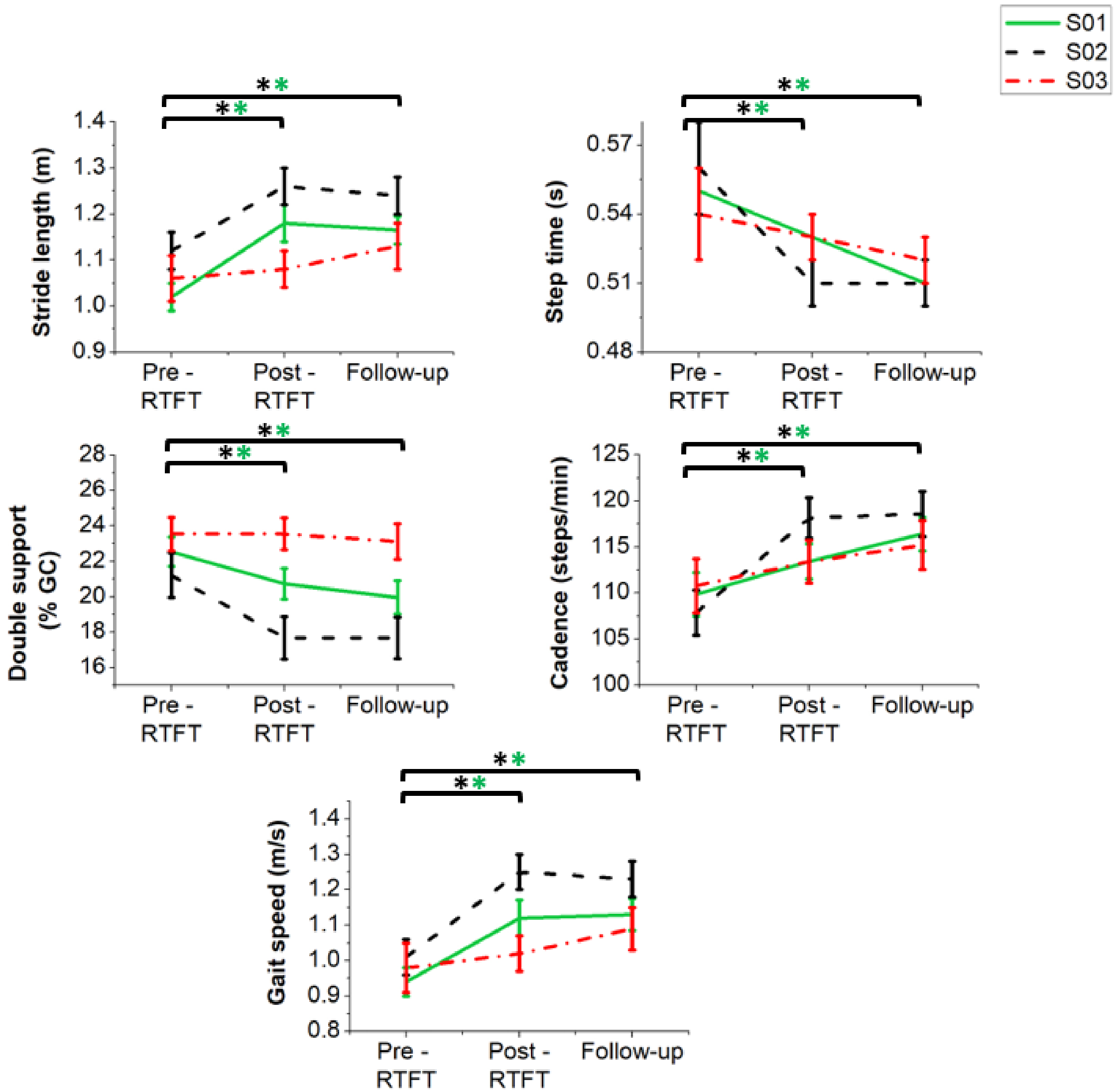


Figure 3.2 Mean and SD values of right side gait indices obtained at pre-RTFT, post-RTFT and follow-up evaluation sessions

A one-way ANOVA test comparing the step-by-step gait indices (n~80) obtained at each of the evaluation sessions showed that there were significant differences ($p<0.05$) between pre-RTFT and post-RTFT, and pre-RTFT and follow-up comparisons for subjects S01 and S02. A post-hoc Tukey's test, showed that they significantly improved ($p<0.05$) their stide length, gaid speed, cadence, double support, and step time at post-RTFT and follow-up when compared to pre-RTFT. In these subjects, stride length, gait speed, and cadece increased while step time and double support duration decreased. Although subject S03 did not show a significant improvement in overall overground walking, variability in stride length, in terms of coefficient of variation(COV), decreased for all three subjects at post and at follow-up when compared to pre-RTFT (Figure 3.3).

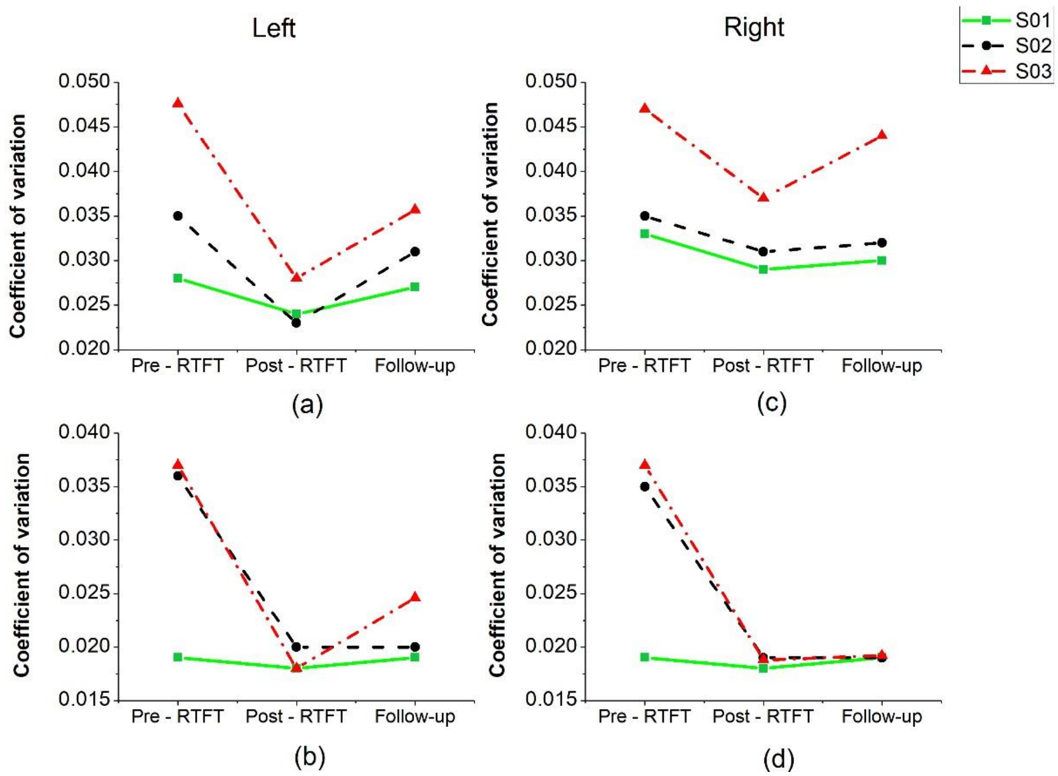


Figure 3.3 COV values of stride length (a and c) and step time (b and d) obtained at pre-RTFT, post-RTFT and follow-up evaluation sessions

Elevation at mid-swing parameter increased at post-RTFT and follow-up when compared to pre-RTFT in subjects S01 and S02 (Table 3.1). Only subject S01 showed a decrease in lateral step variability at post-RTFT and follow-up when compared to pre-RTFT.

Table 3.1

Additional outcome measures from overground walking

Parameter	Subject	Side	Pre-RTFT	Post-RTFT	Follow-up
Elevation at mid-swing (cm)	S01	Left	1.28 (0.27)	1.43 (0.28)	1.34 (0.31)
		Right	0.75 (0.31)	1.3 (0.28)	1.06 (0.34)
Mean (SD)	S02	Left	0.99 (0.34)	1.47 (0.53)	1.43 (0.39)
		Right	1.17 (0.42)	1.49 (0.47)	1.38 (0.4)
	S03	Left	1.77 (0.4)	1.3 (0.34)	1.53 (0.3)
		Right	2.25 (0.38)	1.29 (0.37)	1.63 (0.39)
Lateral step variability (cm)	S01	Left	3.86	2.99	3.68
		Right	3.97	3.21	3.23
Mean	S02	Left	2.36	2.49	2.2
		Right	2.25	2.7	2.23
	S03	Left	2.51	2.63	3.34
		Right	3.34	2.36	3.04

UPRIGHTNESS DURING TREADMILL WALKING

All the subjects improved the uprightness of their posture due to RTFT training. Back angle was higher at post-RTFT and follow-up when compared to pre-RTFT as seen from the mean and SD values obtained during treadmill walking sessions (Figure 3.4)

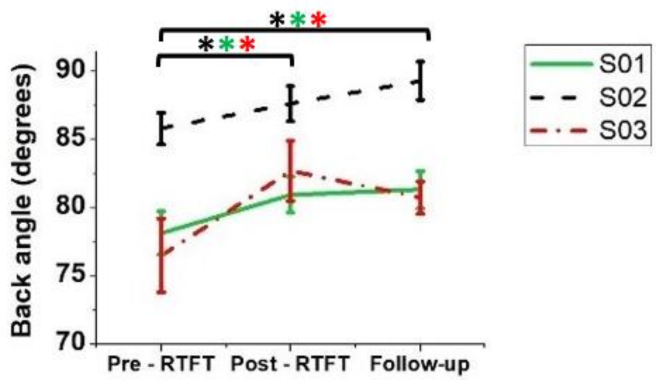


Figure 3.4. Mean and SD values of back angle obtained from treadmill walking during pre-RTFT, post-RTFT and follow-up evaluation sessions

BALANCE TEST AND PDQ – 39

Task performances and responses from the Mini-BESTest and PDQ-39 were evaluated and total scores were calculated (Table 3.2). Although no large differences were observed when comparing the overall scores across different evaluation sessions, the performance in individual tests in the Mini-BEST indicated an improvement in scores for subject S01 in the standing on one leg task from 0 (severe) at pre-RTFT to 1 (moderate) at post-RTFT and follow-up sessions, and from from 1 (moderate) at pre-RTFT to 2 (normal) at the follow-up session for subject S02. Subject S03 showed improvement in the rise to toes task 1 (moderate) at post-RTFT and follow up, when compared to pre-RTFT 0 (severe). For PDQ-39, the individual section scoring for mobility of S01 decreased from 10 at pre-RTFT to 5 at post-RTFT and to 0 at follow-up, and for stigma decreased from 18.75 at pre-RTFT to 12.5 at post-RTFT and follow-up. Subject S02's response scores of mobility in PDQ-39 decreased from pre-RTFT (10), when compared to post-RTFT (7.5). As for subject S03, along with overall score decrease at post- and follow-up, the individual section scores for mobility decreased from 25 at pre-RTFT to 10 at post-RTFT and 7.5 at follow up.

Table 3.2

Overall scores of the Mini-BESTest and the PDQ-39

Subjects	Pre-RTFT evaluation	Post-RTFT evaluation	Follow-up evaluation
	Mini-BESTest (/28)		
S01	23	22	25
S02	26	26	25
S03	23	24	24
	PD Questionnaire-39 (/100)		
S01	10.9	12.82	12.17
S02	17.94	21.79	16.66
S03	12.8	9.6	6.4

GAIT PARAMETERS DURING TREADMILLTRAINING SESSIONS

During the presentation of each type of feedback, subjects improved their walking and posture (Appendix B). The step length values obtained during baseline trial (treadmill walking with no feedback at the beginning of each session before they participated in the feedback trials), were compared with the step length values obtained during both feedback on and off conditions for a given session. For subjects S01 and S02, there was an increase in step length from the baseline values on almost all days. During walking trials, although subjects did not reach the maximum uprightness value that they obtained from a quiet standing task of each day, the back angle values obtained during the feedback sessions improved from the baseline value obtained during pre-RTFT.

Also, RTFT did not show any observable changes in step length asymmetry (Table 3.3). Subjects S01 and S02 had comparatively poor performance on the right side (-ve asymmetry) and S03 on the left side (+ve asymmetry), also confirmed by the information they provided about this during the consent process.

Table 3.3

Step length asymmetry indices of treadmill walking from evaluation sessions*

Subjects	Pre-RTFT evaluation	Post-RTFT evaluation	Follow-up evaluation
S01	-0.002	-0.031	-0.0317
S02	-0.012	-0.025	-0.016
S03	0.007	0.002	0.018

**Asymmetry* = 2 * $\frac{(Right\ step\ length - Left\ step\ length)}{(Right\ steplength + Left\ step\ length)}$

CHAPTER 4

DISCUSSION

External sensory cueing strategies have been found to be beneficial in improving gait deficiencies in PD (Cassimatis, Liu, Fahey, & Bissett, 2016; Lim et al., 2005; Rochester et al., 2005). More recently, a few groups have combined visual cues and treadmill training as a rehabilitation tool that provided better improvements than when either of these strategies was used in isolation (Frazzitta, Maestri, Uccellini, Bertotti, & Abelli, 2009; Schlick et al., 2015). Home-based monitoring and feedback systems are being developed as technologies that can enable real-time movement assessment and performance modulation (Ginis et al., 2016; A Nieuwboer et al., 2007). However, to the best of our knowledge, provision of explicit step-by-step visual feedback of step length and especially of posture as long-term training, and their effects on overground walking have not yet been investigated.

A real-time feedback system was developed and demonstrated to improve step length and upright posture in a single-session study in people with PD (Jellish et al., 2015). This system was updated and utilized for long-term training in this study. The following three hypotheses were investigated: (i) RTFT will improve gait in PD (ii) RTFT will improve posture in PD and (iii) These gait and posture improvements will be sustained at six weeks after completion of the RTFT intervention (follow-up). These hypotheses were addressed by using a 6-week intervention in a pilot study with 3 individuals mild-to-moderate PD by documenting outcome measures at pre-RTFT (0^{th} week), post-RTFT (7^{th} week) and follow-up (13^{th} week).

The results of this study suggest that real-time feedback can be used as a strategy to help persons with PD improve their gait and posture. Two subjects walked with increased stride length, cadence, and gait speed during overground walking at post-RTFT compared to pre-RTFT and these improvements were retained at follow-up. Although one subject did not exhibit significant improvements in those gait measures, variability in stride length and step time was reduced after RTFT, which indicates improvements in gait rhythmicity. Results also indicate that all three subjects improved posture, as shown by an increase in back angle at post-RTFT and follow-up compared to pre-RTFT. Thus, the first and the third hypotheses were supported by significant improvements in overground walking of subjects S01 and S03, and the second hypothesis was supported significant improvements in uprightness of all three subjects.

Sensory deficits in people with PD may limit their awareness of impairments to their walking pattern, such as reduced step length and stooped posture. Focusing attention on the task at hand has been shown to have beneficial effects on performance in persons with PD (Lohnes & Earhart, 2011). Feedback of their step length and posture in real-time facilitate awareness and attention to their movements and provide performance targets that can be used to modulate movements on a step-by-basis. Although there is a possibility that the subject's performance would revert to the baseline performance of a given session, the improvements in step length and back angle observed during the feedback-on condition were sustained during feedback-off trials that immediately followed. This may be due to the practice of increased attention to the task at hand and acute automatization of the performance due to RTFT.

This study utilized a small number of subjects in a pilot study. The hypotheses were tested for each subject using a single-subject design, but could not be tested across the set of subjects with such a small sample. To gain further insight into the potential importance of utilizing real-time feedback in the treadmill training paradigm, the magnitude of the changes observed in this study were compared to those from studies that used treadmill training without feedback.

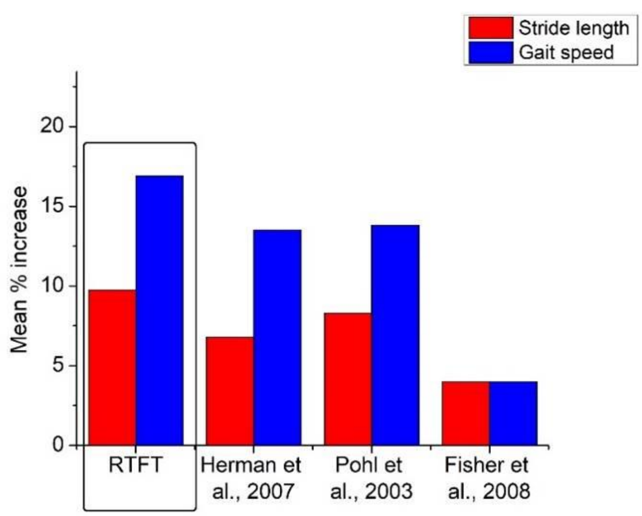


Figure 4.1 Mean percentage increase from pre-intervention to post-intervention in stride length and gait speed in RTFT and in other reports in the literature.

Improvements in stride length and gait speed observed in people with PD due to treadmill training without any real-time feedback reported in the earlier studies (Fisher et al., 2008; Herman, Giladi, Gruendlinger, & Hausdorff, 2007; Pohl, Rockstroh, Rückriem, Mrass, & Mehrholz, 2003) were compared to the results observed in this study. The mean percentage increase, in the pre- vs post- outcomes of stride length and gait speed from the treatment groups of these studies where compared to results from RTFT. This comparison indicates that RTFT produced better improvements in these gait indices than the other interventions (Figure 4.1). Also, only one study (Herman et al., 2007) performed a follow-up to assess retention of any benefits. A comparison of the pre- vs follow-up comparison of that study with our study indicates that after 6 weeks, the benefits were retained to a greater extent in RTFT (Figure 4.2). Although results from our study involved only 3 subjects, it included the subject who did not show significant improvements in overground gait, yet, RTFT performed better than treadmill training alone as an intervention. Results from the control groups of these studies were not presented due to lack of consistency, since only two studies had a control group where one had healthy individuals as controls.

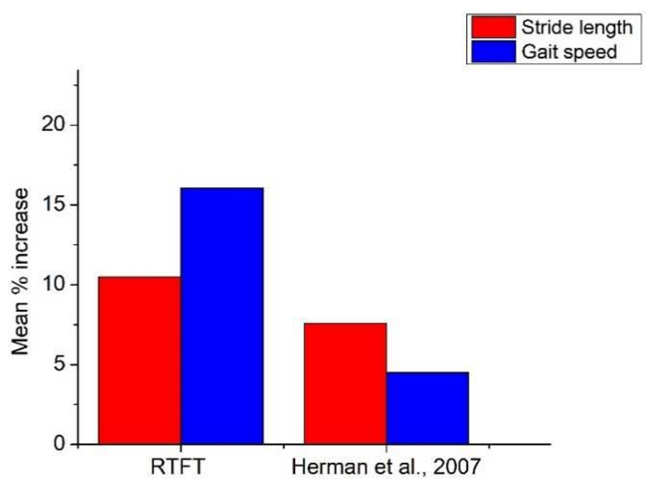


Figure 4.2 Mean percentage increase from pre-intervention to follow-up in stride length and gait speed in RTFT and one report from the literature.

In the future, a randomized control trial with a larger cohort has to be designed to isolate the effects of RTFT on gait and posture, where the control group will receive only treadmill training and no RTF. Additionally, a setup to measure upright posture, i.e. back angle, during overground walking could be implemented. Furthermore, an investigation of the possible mechanisms underlying the observed improvements, such as increased leg strength and improvements in proprioception, should be performed.

This long-term intervention has shown that two of three people with PD demonstrated significant improvements in their overground walking pattern and upright posture. Further investigation will be required to determine if this strategy can be generally beneficial to persons with PD. If a more comprehensive study demonstrates statistical and clinical significance, this system may serve as a precursor to a home-based feedback system to improve mobility and posture in the PD population.

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Tomlinson, C. L., Herd, C. P., Clarke, C. E., Meek, C., Patel, S., Stowe, R., Deane, K. H. O., Shah, L., Sackley, C. M., Wheatley, K., Ives, N. (2014) Physiotherapy for Parkinson's disease: a comparison of techniques. Cochrane Database of Systematic Reviews, Issue 6. Art. No.: CD002815. https://doi.org/10.1002/14651858.CD002815.pub2.

APPENDIX A

IRB APPROVAL

APPROVAL: EXPEDITED REVIEW

Narayanan Krishnamurthi
CONHI - Research Faculty and Staff
602/496-0912
Narayanan.Krishnamurthi@asu.edu

Dear Narayanan Krishnamurthi:

On 10/5/2016 the ASU IRB reviewed the following protocol:

Type of Review:	Initial Study
Title:	Real-Time Feedback Training to Improve Gait and Posture in People with Parkinson's Disease
Investigator:	Narayanan Krishnamurthi
IRB ID:	STUDY00004999
Category of review:	(4) Noninvasive procedures, (7)(a) Behavioral research
Funding:	Name: CONHI - Dean's Office
Grant Title:	
Grant ID:	
Documents Reviewed:	• RTFT - Evaluation session - walking part - 09-16-16.pdf, Category: Measures (Survey questions/Interview questions /interview guides/focus group questions); • RTFT - Letter of approval from PCP - 09-16-16.pdf, Category: Other (to reflect anything not captured above); • IRB application, Category: IRB Protocol; • Recruitment material - Flyer, Category: Recruitment Materials; • CITI training for Claire Honeycutt, Category: Other (to reflect anything not captured above); • RTFT - Evaluation session - balance part - MiniBEST data collection.pdf, Category: Measures (Survey questions/Interview questions /interview guides/focus group questions); • Responses to Pre-Review, Category: Other (to

	reflect anything not captured above); • RTFT - Training session data collection - 09-16-16.pdf, Category: Measures (Survey questions/Interview questions /interview guides/focus group questions); • RTFT - Statement of Eligibility - 09-16-16.pdf, Category: Screening forms; • RTFT- Patient Demographics and disease history-09-16-16.pdf, Category: Measures (Survey questions/Interview questions /interview guides/focus group questions); • Informed Consent, Category: Consent Form;

The IRB approved the protocol from 10/5/2016 to 10/4/2017 inclusive. Three weeks before 10/4/2017 you are to submit a completed Continuing Review application and required attachments to request continuing approval or closure.

If continuing review approval is not granted before the expiration date of 10/4/2017 approval of this protocol expires on that date. When consent is appropriate, you must use final, watermarked versions available under the "Documents" tab in ERA-IRB.

In conducting this protocol you are required to follow the requirements listed in the INVESTIGATOR MANUAL (HRP-103).

Sincerely,

IRB Administrator

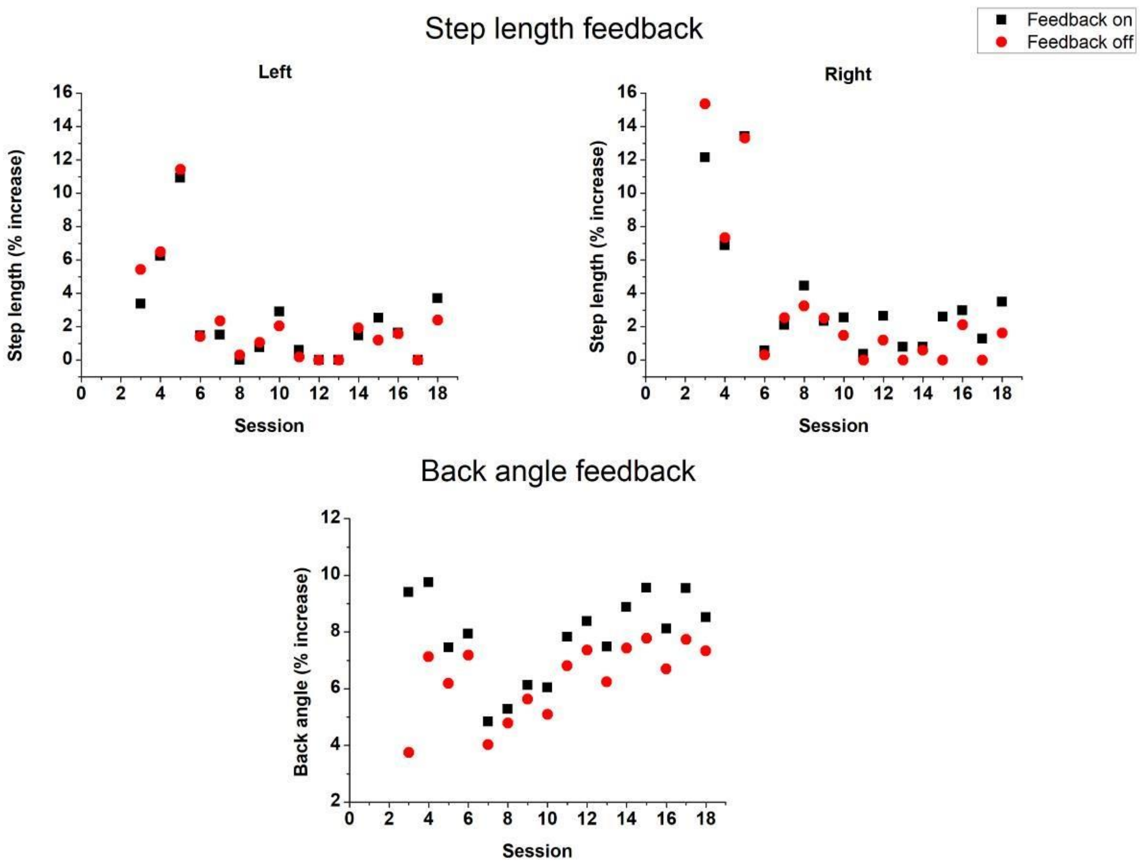
APPENDIX B

GAIT PARAMETERS FROM TREADMILL TRAINING SESSIONS

SUBJECT S01

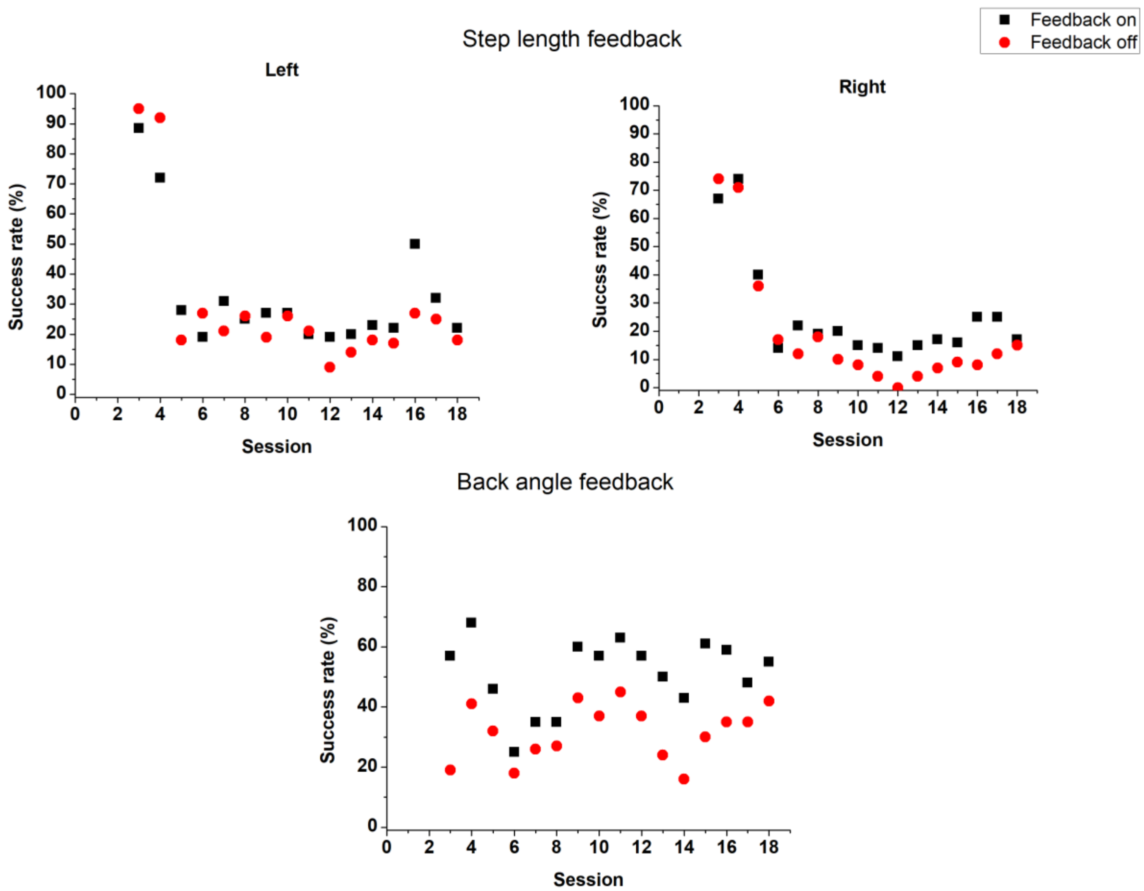
1. PERCENTAGE INCREASE IN STEP LENGTH AND BACK ANGLE

Percentage increase in step length represents changes from the baseline step length values obtained before each RTF session, and for back angle represents changes from the back angle value obtained at pre-RTFT.



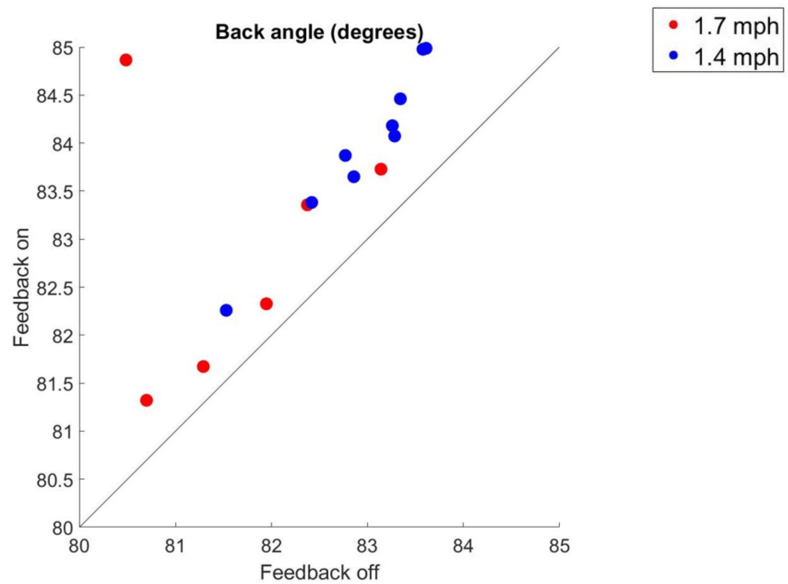
2. SUCCESS RATE DURING STEP LENGTH AND BACK ANGLE FEEDBACK

Results below present the performance during each session in terms of succss rate. For the step length feedback task, success rate was calculated as the percetage of the total number of steps that were within the target zone. For the back angle feedback task, success rate was calculated as the percentage of time the subject was within ±5% of the maximum uprightness.



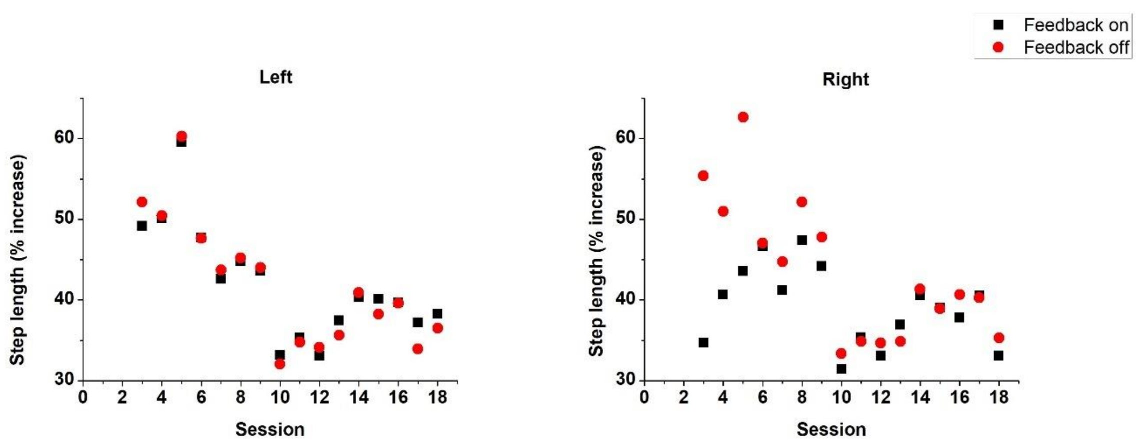
3. BACK ANGLE FEEDBACK

i. Back angle (degrees): Feedback-on vs Feedback-off condition

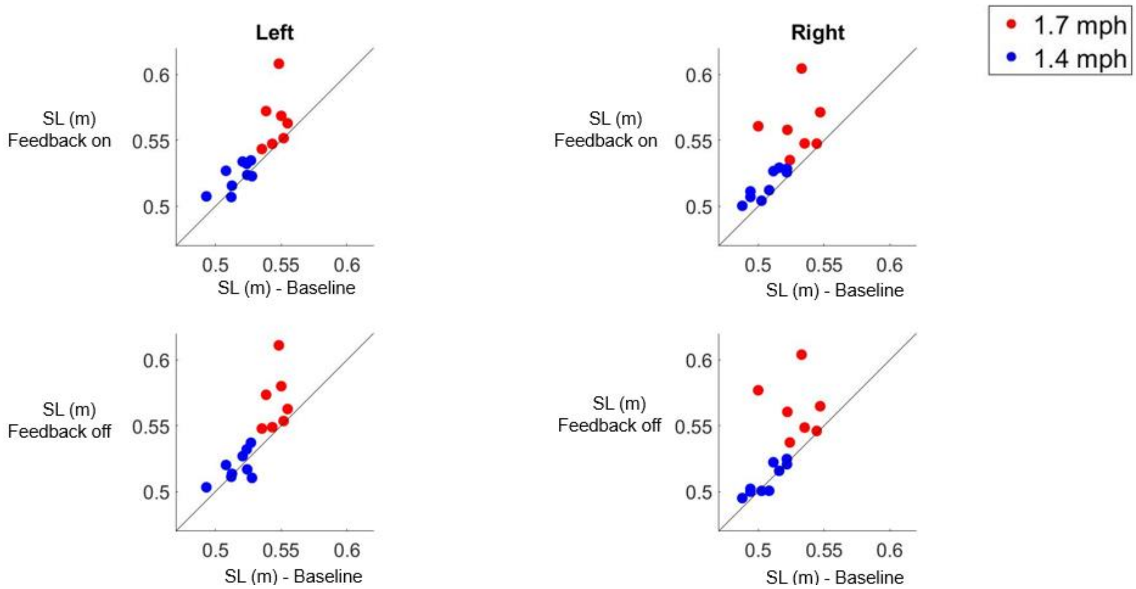


4. STEP LENGTH FEEDBACK OUTCOMES

i. Percentage increase from step length at pre-RTFT



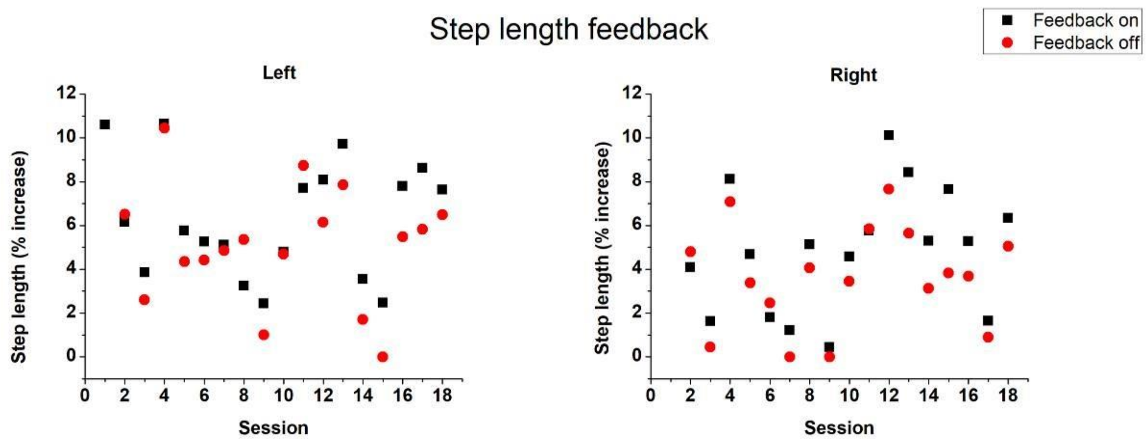
ii. Step length (m): Session baseline vs Feedback-on/off conditions

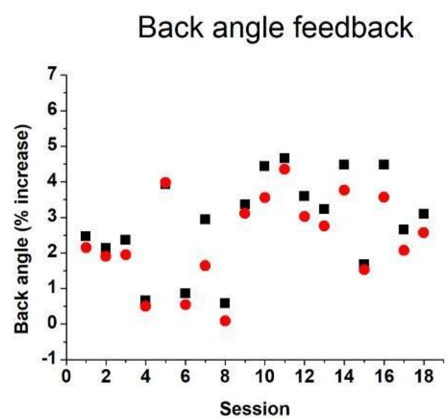


SUBJECT S02

1. PERCENTAGE INCREASE IN STEP LENGTH AND BACK ANGLE

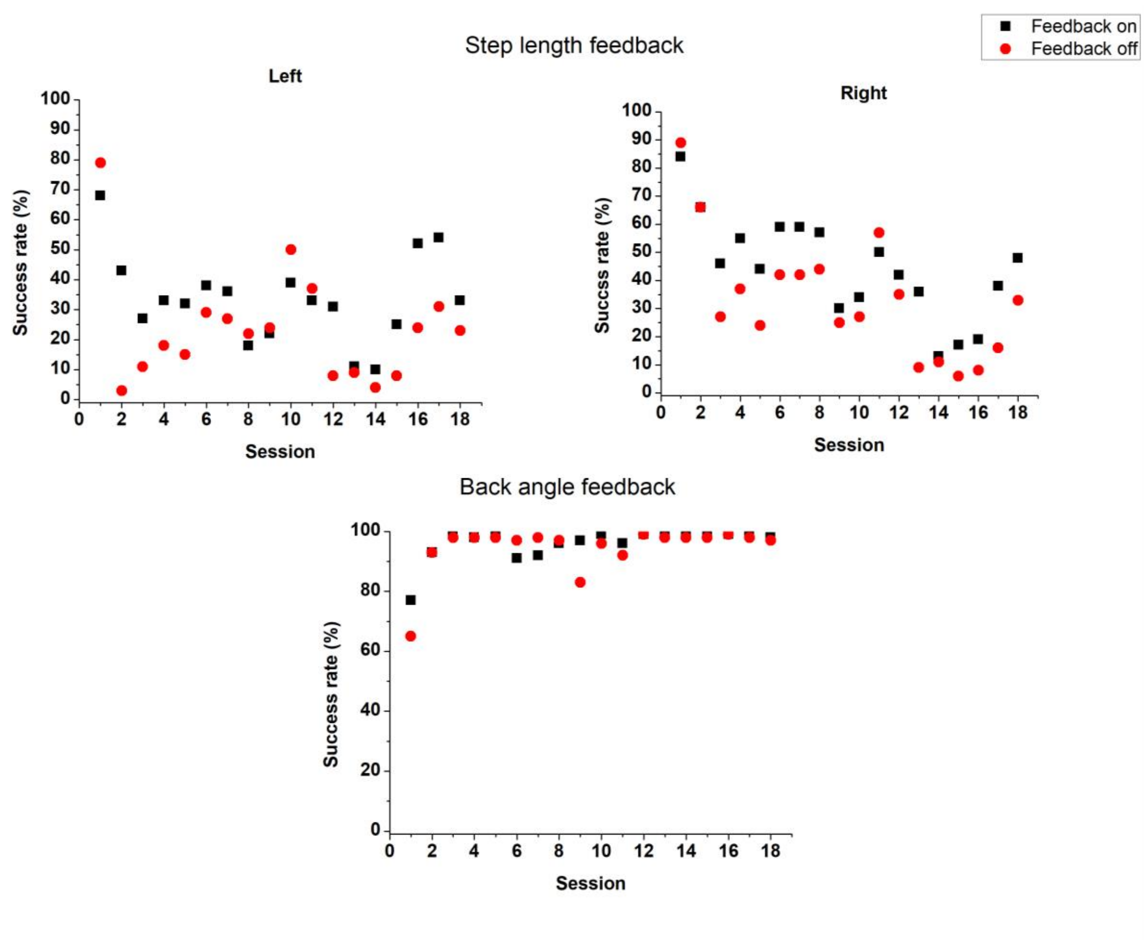
Percentage increase in step length represents changes from the baseline step length values obtained before each RTF session , and for back angle represents changes from the back angle value obtained at pre-RTFT.





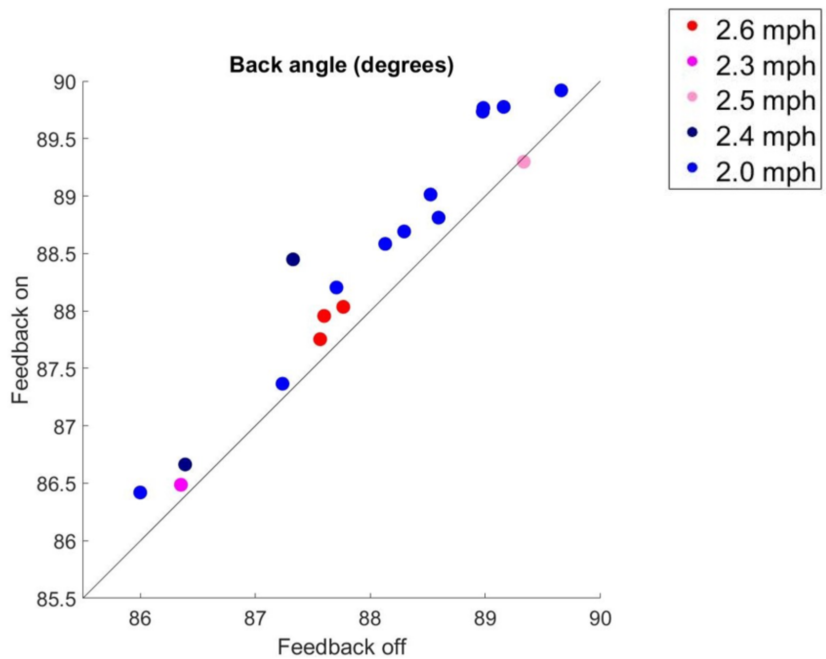
2. SUCCESS RATE DURING STEP LENGTH AND BACK ANGLE FEEDBACK

Results below present the performance during each session in terms of succss rate. For the step length feedback task, success rate was calculated as the percetage of the total number of steps that were within the target zone. For the back angle feedback task, success rate was calculated as the percentage of time the subject was within ±5% of the maximum uprightness.



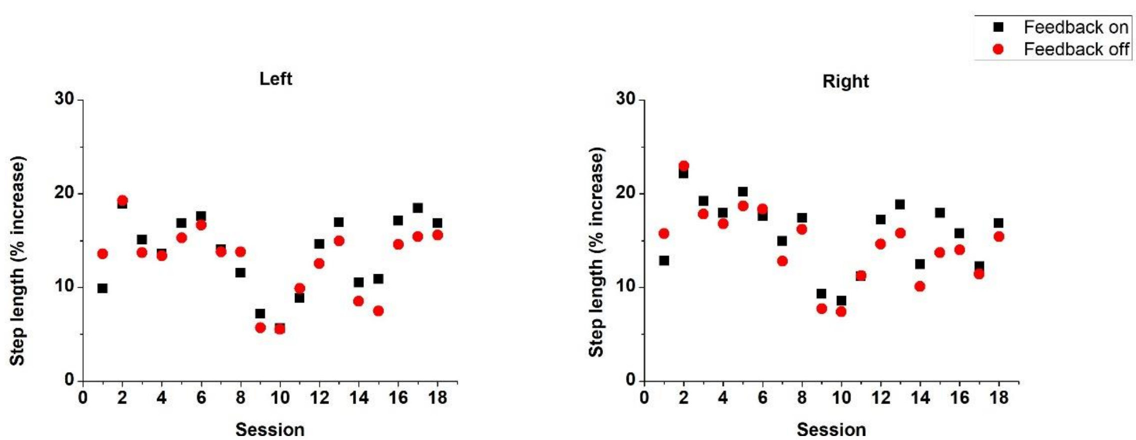
3. BACK ANGLE FEEDBACK

i. Back angle (degrees): Feedback-on vs Feedback-off condition

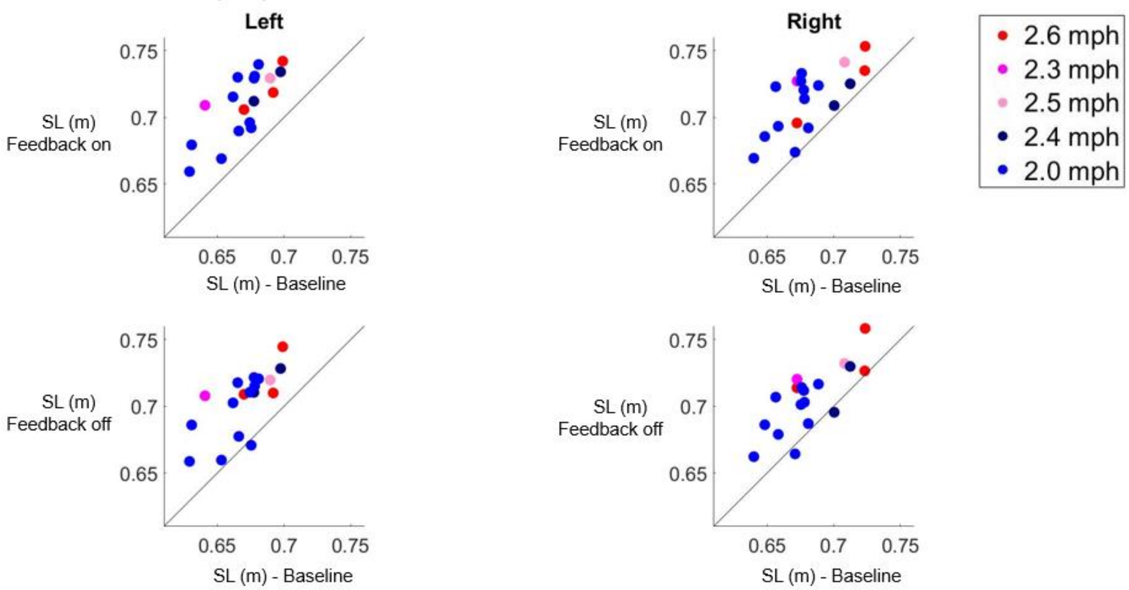


4. STEP LENGTH FEEDBACK

i. Percentage increase from step length at pre-RTFT



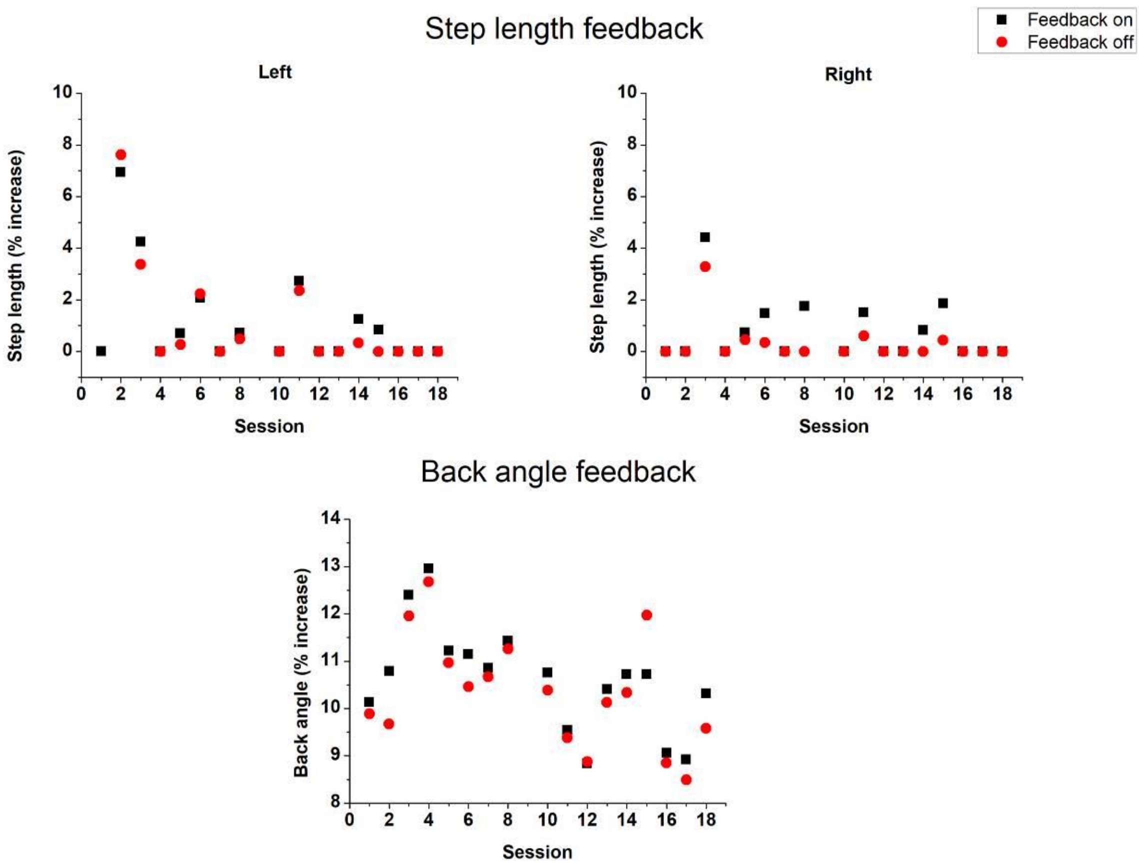
ii. Step length (m): Session baseline vs Feedback-on/off conditions



SUBJECT S03

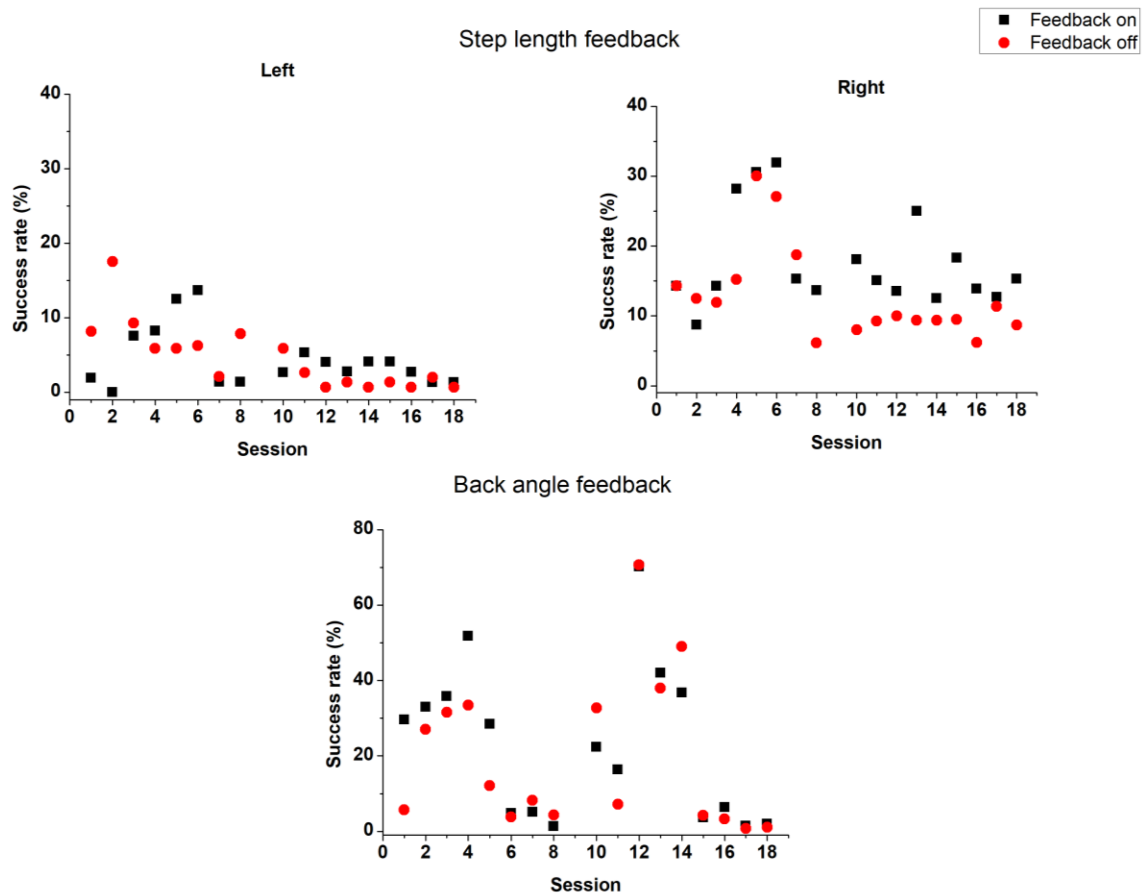
1. PERCENTAGE INCREASE IN STEP LENGTH AND BACK ANGLE

Percentage increase in step length represents changes from the baseline step length values obtained before each RTF session , and for back angle represents changes from the back angle value obtained at pre-RTFT.



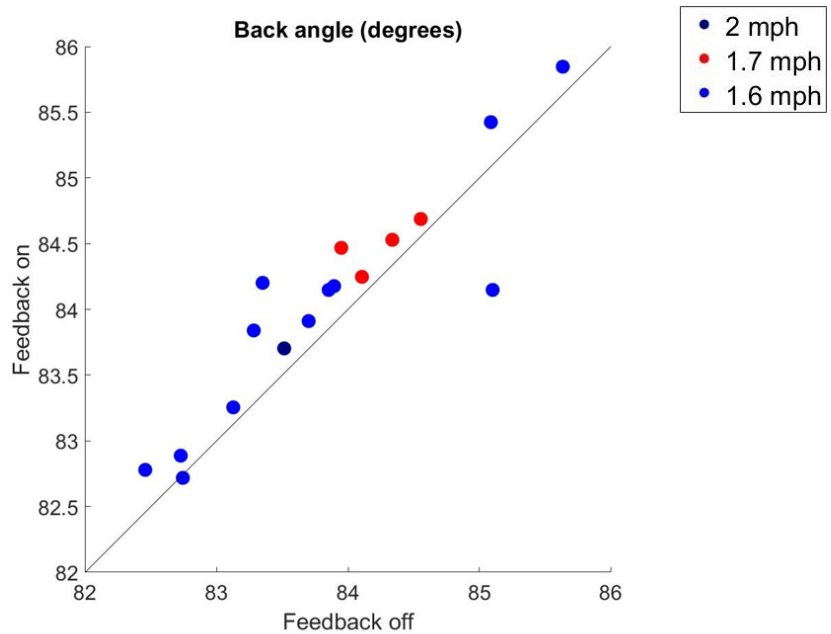
2. SUCCESS RATE DURING STEP LENGTH AND BACK ANGLE FEEDBACK

Results below present the performance during each session in terms of succss rate. For the step length feedback task, success rate was calculated as the percetage of the total number of steps that were within the target zone. For the back angle feedback task, success rate was calculated as the percentage of time the subject was within ±5% of the maximum uprightness.



3. BACK ANGLE FEEDBACK

i. Back angle (degrees): Feedback-on vs Feedback-off condition



4. STEP LENGTH FEEDBACK

i. Percentage increase from step length at pre-RTFT

No increase from pre-RTFT step length

ii. Step length (m): Session baseline vs Feedback-on/off conditions