

**DEFICITS OF GAIT INITIATION AND STEADY STATE GAIT
ARE EXACERBATED BY POSTURAL THREAT
IN PARKINSON'S DISEASE PATIENTS**

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Dedication

I dedicate this thesis to my family and my fiancé Audrey. All of you have taught me the value of perseverance, hard work and to believe in myself.

Abstract

The effects of postural threat on gait initiation and steady state gait among Parkinson's disease (PD) patients and age-matched adults were examined. Ten healthy adults (CTRL; mean age= 68.8 ± 8.4 , range 56-80 years) and ten PD patients (PD_{OFF} / ON ; mean age= 69.7 ± 10.3 , range 54-81 years) initiated gait and continued with steady state walking along a walkway of two different height conditions. PD patients were first tested in a non-medicated state followed by testing in a medicated state. The results showed that gait initiation and steady state gait deficits inherent to PD are exacerbated in a postural threatening environment. As well, medication efficacy for overcoming parkinsonian deficits may be context dependent. These findings confirm the dynamic nature of movement deficits characteristic of parkinsonian patients and provide empirical evidence for specific environments that can create movement difficulties for people with PD.

Acknowledgements

Well we finally did it. This thesis has been a project for the past two years and without the help, support, and encouragement from my family, friends, and co-workers this thesis would not have been possible. I would just like to thank and acknowledge the people who have helped make this thesis possible.

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General Introduction

1. Introduction

Postural control describes the process of maintaining the position of the body in space for the purpose of stability and orientation (Shumway-Cook & Woollacott, 2000). Normal aging is associated with difficulties in controlling posture (Horak, Diener, & Nashner, 1989), a problem manifest by compromised postural stability, gait initiation, and steady state gait among the elderly (Tinetti, Speechley, & Ginter, 1988; Brunt, Liu, Trimble, Bauer, & Short, 1999; Hass et al., 2004). Balance and locomotion become increasingly difficult for adults who have Parkinson's disease (PD). PD patients have a fall rate that is the highest among all neurological diseases, with patients experiencing twice the amount of falls that age-matched healthy adults encounter (Stolze et al., 2004). Possible reasons for this increased fall rate are the difficulties that PD patients experience in controlling momentum during gait initiation (Hass et al., 2004) and the subsequent deficiencies of slow shuffling and low ground clearance of the feet during steady state gait (Overstall, 2001).

A common observation among patients and therapists alike is that PD motor symptoms associated with control of locomotion can fluctuate across environmental contexts, with novel or challenging situations exacerbating disease symptoms (Morris, Iansek, Smithson, & Huxham, 2000). Specific examples that create difficult situations for PD patients include busy road crossings (Fahn, 1995), cluttered home environments (Morris et al., 2000; Rochester et al., 2004; Stolze et al., 2004), and narrow spaces (Giladi et al., 1992; Macht & Ellgring, 1999). However, despite these observations and patient reports, little empirical study has been conducted to document how a challenging environmental context can influence motor performance in PD patients. This thesis addresses a critical need to determine how challenging environments affect movement patterns among PD patients.

This chapter presents a literature review that serves to demonstrate the potential for a modulating effect for environmental context on motor control among patients with PD. This literature review has been categorized into four different sections. The *Parkinson's disease literature* section consists of work that underlines the fundamental principles of the hypothesized causes of PD, the influence of PD on motor control, as well as treatment methods for the care and management of this disease. The *gait initiation and steady state gait* section presents an overview of the biomechanical principles of gait initiation and steady state gait. The third section, *gait initiation and steady state gait in Parkinson's disease* reviews current research regarding how Parkinson's disease influences gait initiation and steady state gait. The final section, *environmental context*, explores the role that changes in environmental context, and more specifically postural threatening situations, can have on the regulation of locomotion.

2. Parkinson's Disease Literature

2.1 Epidemiology

PD is a neurodegenerative disease that is characterized by tremor (involuntary shaking), rigidity (stiffness surrounding the joint), bradykinesia (slowness of movement), gait disturbance, and postural instability. PD is the second most common neurodegenerative disease in today's population and one of the most common causes of disability among the elderly (Jankovic, 2002). This disorder affects about 1% of the population over the age of 60, and it has been stated that 1 person in 40 will develop parkinsonian symptoms over their lifetime (Jankovic, 2002). Advancing age is the most important risk factor for developing PD, with the peak onset at age 60 years. However, PD is not just a disease of middle or old age: 15% of PD patients are 50 years or less, and 10% are 40 years or less (Jankovic, 2002) .

PD is caused by the degeneration of dopaminergic neurons in the substantia nigra pars compacta (SNc). In addition, neuronal loss in the cerebral cortex, anterior thalamus, hypothalamus, amygdala and basal forebrain has shown to play a major role in developing Parkinson's disease symptoms (Bowers, Maguire-Zeiss, Harvery, & Federoff, 2001). However, almost 80 per cent of brain dopamine is found in the striatonigral complex comprising the putamen, caudate, and the SNc (Stewart, 2001) (Figure 1). The putamen and caudate receive the majority of dopamine from the dopaminergic neurons located in the SNc. Neuronal loss in the SNc is correlated with the extent of dopaminergic depletion in the putamen and caudate, with dopamine depletion more evident in the putamen (Stewart, 2001).

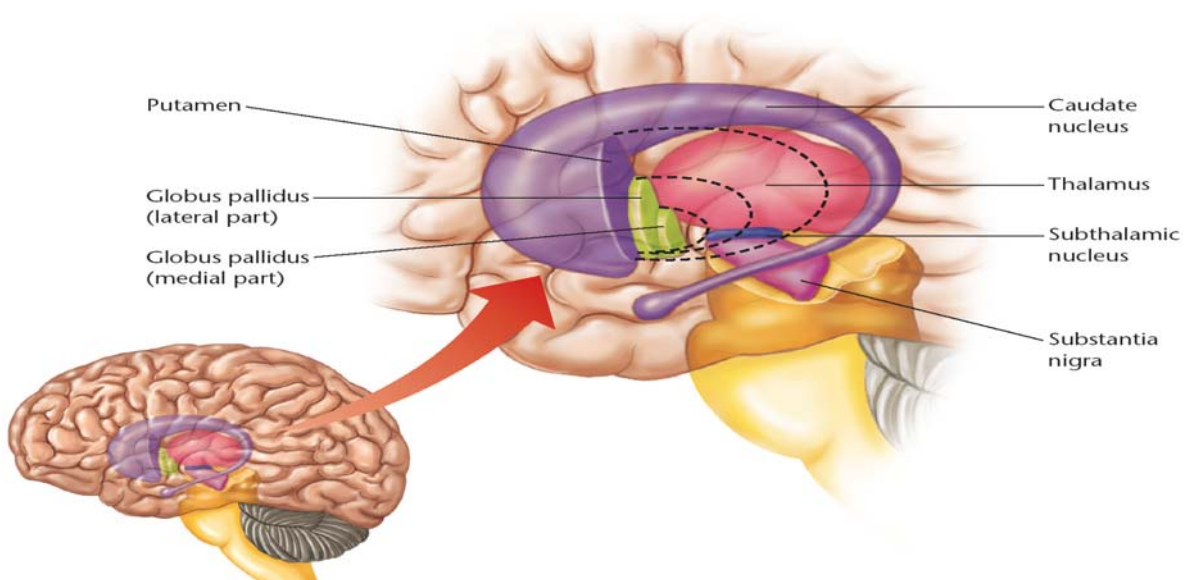


Figure 1. Diagram of the human brain, highlighted are the basal ganglia

Adapted from <http://cti.itc.virginia.edu>

PD exists as both a sporadic and familial disorder. The common pathway of both sporadic and familial PD is a loss of dopamine neurons. Importantly, it has been stated that early symptomatic PD can be produced when dopamine neurons reach a number that is below a

critical threshold (Duvoisin, 1992). Research shows that cell loss in excess of 50 percent of normal levels is required for clinical symptoms to develop (Stewart, 2001). Environmental factors such as pesticides, herbicides, industrial chemicals and genetic mutations have been identified as potential risk factors for PD. It is theorized that either alone or in combination, these triggers can play a role in developing PD symptoms (Olanow & Tatton, 1999). Bowers (1997) suggests a 'common pathway' model that involves the theory that multiple triggering mechanisms such as genetic, toxicant and environmental triggers plus genetic vulnerability, increases the risk of cell death. To date there has been no cure to either eradicate all symptoms for life or to replenish dopamine producing cells.

2.2. Anatomical Review

The degeneration of the dopaminergic nigrostriatal projections in the basal ganglia leads to disruption of the motor circuit. Both voluntary and involuntary movements are controlled by this circuit, which is comprised of several subcircuits which interact in a complex manner (Stewart, 2001) (Figure 2).

The function of the basal ganglia in controlling movement is governed by excitatory and inhibitory outputs. The ventrolateral thalamus (VL) has an excitatory output to the motor cortex and thus acts to facilitate movement. On the other hand, the globus pallidus interna (GPi) and the substantia nigra pars reticulata (SNr) have an inhibitory output to the VL and thus acts like a brake on movement. The GPi receives input from the putamen via two pathways: 1) the direct pathway and 2) the indirect pathway. The direct pathway runs from the putamen to GPi and its effects are inhibitory (ie. to release the brake on movement exerted by GPi). The indirect pathway runs from the putamen via globus pallidus externa (GPe) and subthalamic nucleus (STN). STN has an excitatory effect on GPi and the

resulting effect is to increase the braking on movement from GPi. Normal dopamine released from the SNc acts on both these pathways.

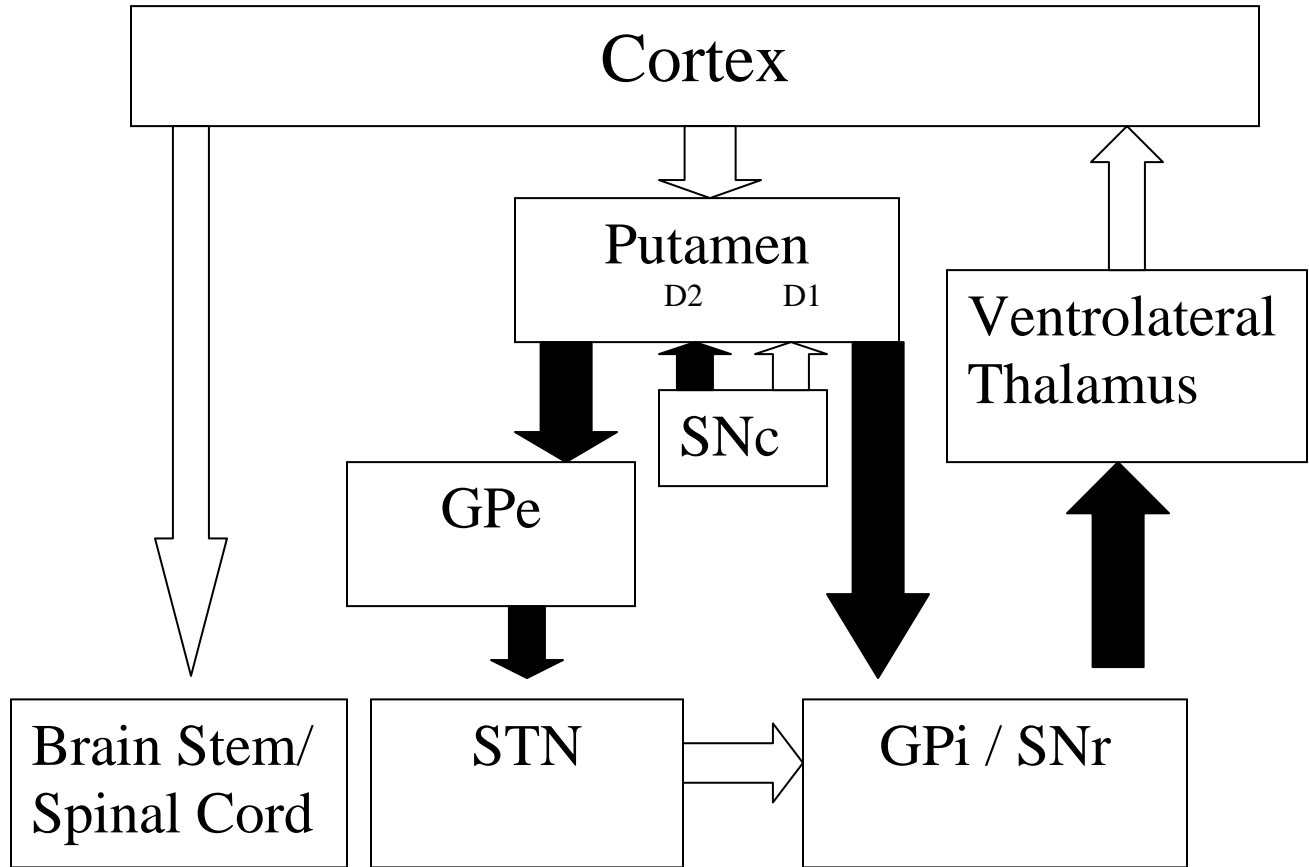


Figure 2. The basal ganglia. Open arrows represent excitation; solid arrows indicate inhibition.

Adapted from Stewart, 2001

The role of dopamine D1 receptors is to stimulate the direct pathway, this action results in a decrease of the braking effect on movement from GPi. By acting on dopamine D2 receptors, the indirect pathway is inhibited, decreasing the stimulus for GPi to exert a braking effect. Normal SNc function therefore results in a low braking effect from GPi to VL and thus allows VL to facilitate movement via its excitatory effects on the motor cortex (Stewart, 2001).

In PD, decreased dopamine release from SNc disrupts this complex mechanism. Understimulation of the direct pathway and underinhibition of the indirect pathway result in an increased inhibitory output or increased braking effect from the GPi. Thus, the excitatory effects of VL on the motor cortex are diminished and movement inhibited (Stewart, 2001). It has been stated that abnormal functioning of the direct and indirect pathways is the cause of dyskinesias and motor fluctuations within advanced cases of PD (Elble, 2002).

2.3 Basal Ganglia Function

The basal ganglia are involved in the maintenance of motor, cognitive, and patterned and sequential behavior such as locomotion (Hindle, 2001). One role of the basal ganglia is to maintain cortically preselected movement amplitude during repetitive movements (Morris, Ianssek, McGinley, Matyas, & Huxham, 2005). Although the basal ganglia do not directly scale movement size, these structures are responsible for matching performance outcomes with original motor plans (Ianssek, Bradshaw, Phillips, Morris, & Cunnington, 1995). In an example of stride length amplitude in gait, the motor cortical regions are responsible for selecting movement amplitude based on the desired outcome or goal of the task, for example stepping over an obstacle. The role of the basal ganglia is to provide the correct motor response and appropriately timed cues to enable the motor plan to run to completion and allow the patient to achieve a successful step over the obstacle. This is advantageous to locomotion because the cortex is 'freed up' to control other tasks that require attention (Bond & Morris, 2000). It is believed that the basal ganglia in the PD brain cannot match the preselected motor plan to the intended amplitude. Consequently, a mismatch between the pre-selected and actual amplitude of movement occurs. In the hypothesized situation presented, this would lead to a shorter step and possible obstacle contact (Morris et al., 2005).

2.4 Treatment

Pharmacological and medical treatments exist to combat the symptoms and movement difficulties of PD. Drug therapy remains the primary intervention to treat PD, with levodopa replacement being the most effective drug strategy to treat the symptoms of this disease. Levodopa medication is used by depleted dopaminergic neurons to increase synaptic dopamine concentrations (Playfer, 2001). In addition, levodopa replacement has been shown to be effective in improving locomotor deficits associated with PD (Burleigh-Jacobs, Horak, Nutt, & Obeso, 1997). The alleviation of bradykinesia and rigidity helps PD patients ambulate more effectively within activities of daily living. In the task of gait initiation levodopa medication has been shown to be effective in improving force production and increasing velocity of movement (Burleigh-Jacobs, Horak, Nutt, & Obeso, 1997), both factors that have been implicated to reduce the likelihood of sustaining a fall during gait initiation (Cummings & Nevitt, 1989). For steady state gait, levodopa medication has been shown to improve the range of motion achieved at the hip, knee, and ankle joints throughout the gait cycle (Shan, Lee, Chao, & Yeh, 2001). In addition, stride length, stride velocity, and foot ground clearance also increase when levodopa is used (Knutsson, 1972; Morris et al., 2005).

Summary

The symptoms of rigidity, tremor, bradykinesia, and postural instability can be very incapacitating for patients with PD. These symptoms are the result of a loss of dopamine producing neurons in the basal ganglia of the brain. The motor cortex relies on the basal ganglia to maintain preselected movements. However, in PD patients dopamine depleted basal ganglia create a mismatch between preselected and actual movement amplitudes; the result are substantial movement deficiencies. There are attempts to relieve some of the

symptoms of PD through drug therapy, however no cure has been found to eradicate all symptoms associated with this disease. Further understanding and continued research of the basal ganglia, medication effectiveness, and the impact of this disease on movement is needed to implement improved treatment techniques and effective therapeutic strategies.

3. Gait Initiation / Steady State Gait

Relevant Background: Biomechanics of gait initiation and steady state gait

3.1 Gait Initiation

The intricate relationship between center of pressure (COP) and center of mass (COM) is a fundamental concept that must be investigated prior to the discussion of gait initiation. COM is the weighted average of the COM of each body segment in 3D space. Balance is maintained when the vertical projection of the COM on the ground is kept within the support base of the body, which is defined by the boundaries of the feet. In contrast, COP is the location of the vertical reaction force that is projected onto the ground, and as such, represents a weighted average of all force acting on the ground. The position of the COP depends on the relative weight distribution between the feet (Winter, 1991).

The initiation of gait is a task that challenges balance because of the requirement to move from a relatively static position to periodically unstable gait. The gait initiation process requires the coordination of anticipatory postural adjustments to move the COM forward and over the stance leg (the second leg to leave the ground) (Figure 3). This shift in body mass is essential to achieving single-limb support during the first step.

Gait Initiation

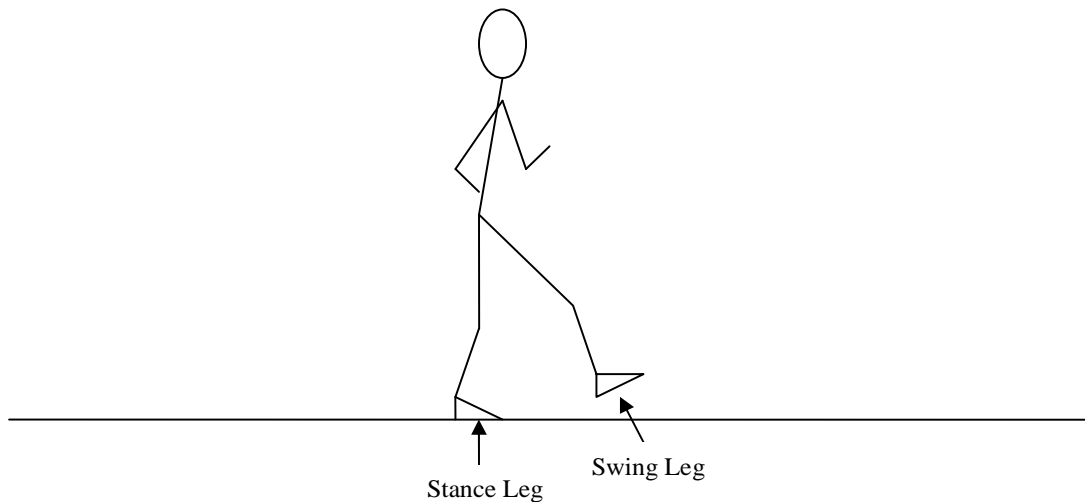


Figure 3. Gait initiation process, figure depicts single-limb support and corresponding swing leg and stance leg.

The postural adjustments involved in gait initiation produce both vertical and horizontal forces that move the COP from a location between the feet, to a position backwards and toward the swing leg (Figure 4). This process is referred to as the *initiation phase*, and is characterized by the COM moving forward and laterally over the stance leg (Burleigh-Jacobs et al., 1997). The COP then moves laterally towards the initial stance leg, and as a result the COM completes positioning over the initial stance leg. This phase is referred to as the *transfer phase*. It is midway through the transfer phase that the heel of the foot from the initial swing leg lifts off the ground. This is closely followed by the toe of the foot from the initial swing leg lifting off the ground and is achieved when the COP reaches the most lateral position under the stance leg (Dibble et al., 2004).

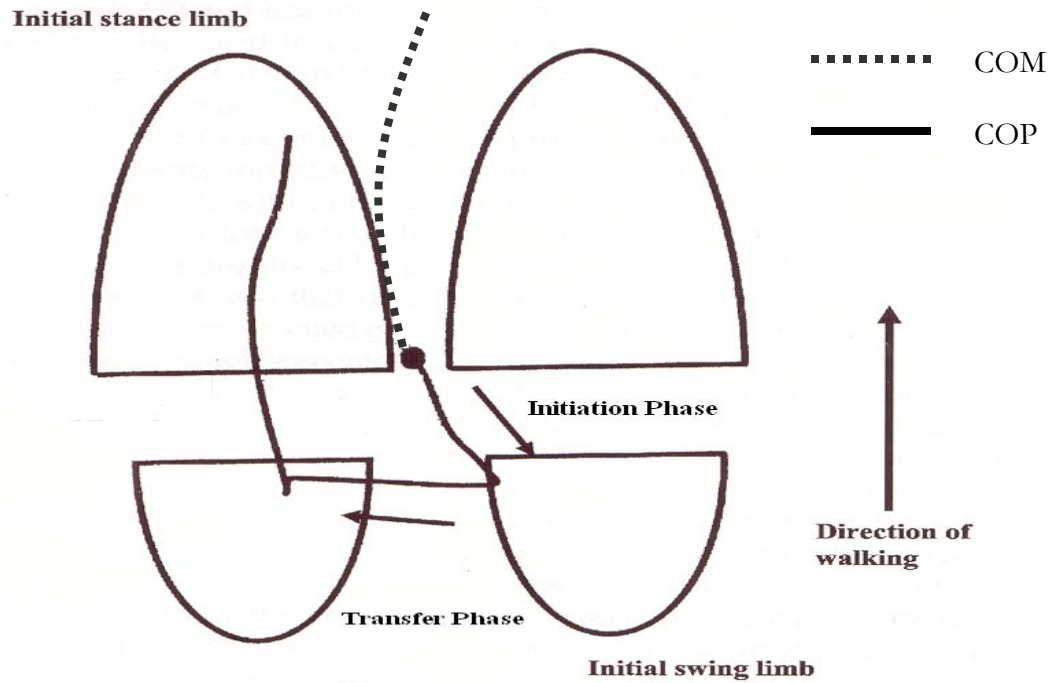


Figure 4. COP and COM movement pattern. The COP begins at a static position between the feet (dark circle). Initiation phase consists of the COP moving backwards and lateral towards the initial swing leg. COP then moves laterally toward the initial stance leg, referred to as the transfer phase. The COM moves forward and laterally toward the initial stance leg.

Adapted from Dibble et al., 2004

3.2 Steady State Gait

The human body is inherently unbalanced due to two-thirds of our body mass being located two-thirds of our body height above the ground. As a result, the central nervous system (CNS) is in a constant challenge to maintain our COM within our base of support (Winter, 1991). Gait is a challenging task because locomotion is dependent on the continued self-initiation of a fall, whereby the COM moves beyond the base of support. Bipedal gait involves alternating sequences of movement in which the body is supported first by one limb, which is contacting the ground, and then by the other limb. The period of support in which both feet are in contact with the ground is referred to as double-limb support (DLS) and the period in which only one foot is in contact with the ground is referred to as single-limb support (SLS) (Figure 5). These intervals are marked by two events: 1) heel contact: the time at which the heel contacts the ground and 2) toe off: when the opposite foot leaves the

ground. Gait cycles are defined relative to these events. For example, one complete gait cycle is typically from the right foot leaving the ground to when the right foot leaves the ground a second time, this process is defined as one stride (Enoka, 1994).

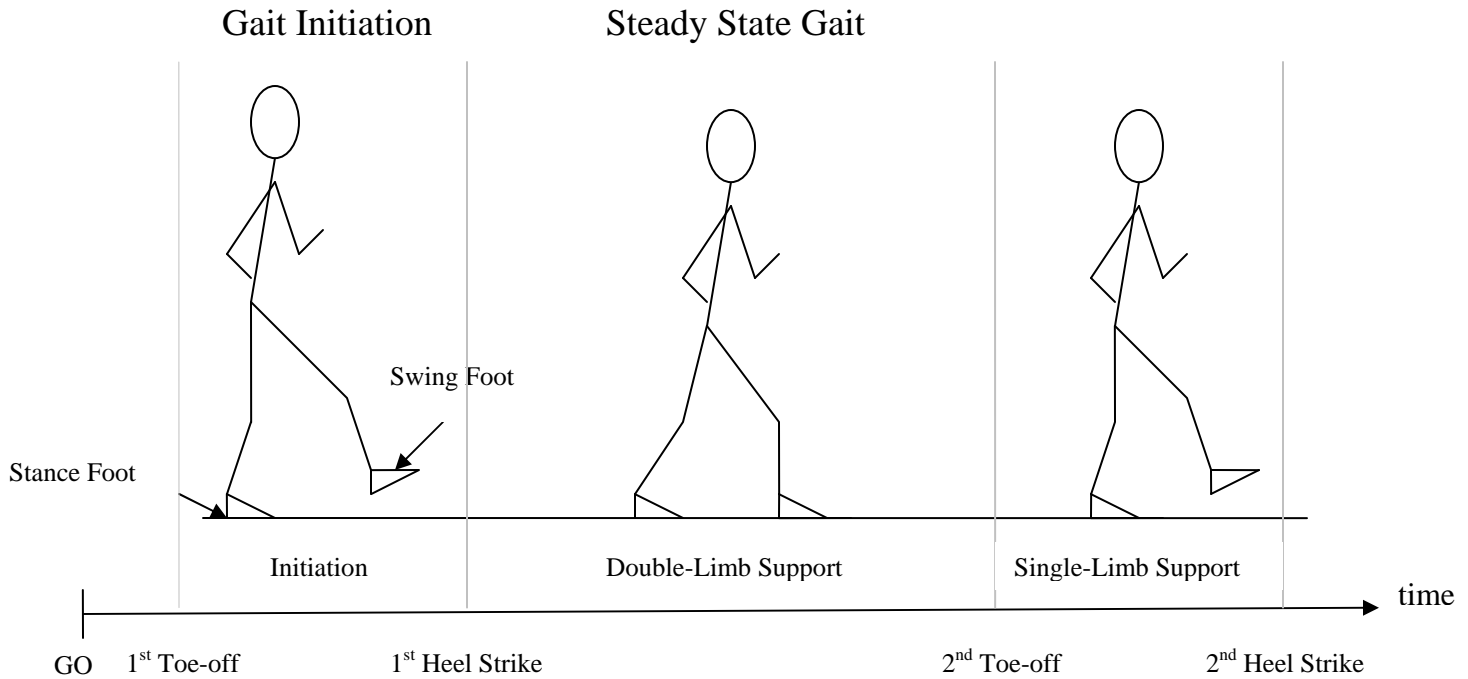


Figure 5. Illustration of human gait and the different support phases of the gait cycle.

Summary

Locomotion is produced by successful gait initiation and the continuation of steady state gait. Gait initiation is comprised of an intricate relationship between COP and COM dynamics. The goal of gait initiation is to produce a sufficient amount of force that will generate the momentum necessary to move the COP first towards the swing-leg and then towards the stance-leg. The result is a transfer of the location of the COM toward the stance-leg, thus enabling a step to be taken safely. Steady state gait is characterized by continuous gait cycles which consist of a SLS phase and a DLS phase. Together these two

movement processes provide adequate opportunity to study human movement and possible modifications or adaptations made by age, disease, or environment.

4.0 Gait Initiation and Steady State Gait in PD

4.1 Gait Initiation

For patients with Parkinson's disease, gait initiation disorders emerge concomitantly with problems associated with postural control (Vaugoyeau, Viallet, Mesure, & Massion, 2003). On physical examination, the gait initiation impairment can be aggravated to such an extent that the patient becomes "frozen to the spot" (Narabayashi, 1980) or "suddenly blocked" (Giladi et al., 1992). As Vaugoyeau et al. (2003) suggest, these freezing episodes indicate that the impairment of gait initiation could reach a stage beyond which step triggering would no longer be possible. This is significant because such a severe impairment could lead to an increase in fall rate. Many patients report falling when they freeze because their feet remain fixed on the ground while their upper body continues to move or turn (Overstall, 2001).

The parkinsonian posture and the subsequent symptoms of PD have a considerable effect on gait initiation. The parkinsonian posture is described as a 'stooped posture' with the neck and head inclined forward and the trunk flexed forward. As well, the dorsal spine shows kyphosis (Knutsson, 1972). Moreover, the arms are slightly abducted, the elbows are flexed and the hands are carried in front of the body with the fingers partially flexed. In addition, the hips and knees are flexed, and the angle of the ankle decreases as the disability increases, which causes PD subjects to stand more on their toes compared to adults of the same age without the disease (Knutsson, 1972) (Figure 6).



Figure 6. Illustration of the typical parkinsonian posture.

Adapted from www.va.gov

Previous research has shown that persons with PD exhibit increased movement time, decreased movement amplitude, and decreased velocity through all phases of gait initiation when compared to healthy older adults (Dibble et al., 2004). More specifically during the *initiation phase* (refer to figure 7) of gait initiation, persons with PD exhibit decreased posterior and lateral displacement of the COP compared to older adults without PD (Dibble et al., 2004). As well, Halliday et al. (1998) showed that during this phase, despite the decreased COP displacement PD patients took longer to initiate gait. Likewise during the *transfer phase* (refer to figure 7) PD patients have shown to not only take longer to complete this phase, but do so with a slower velocity. These results may suggest why PD patients also have a shorter step length when initiating gait (Halliday, Winter, Frank, Patla, & Prince, 1998).

Interestingly, the deficiencies that PD patients exhibit in gait initiation have been found to improve with the use of levodopa medication. In particular, Burleigh-Jacobs et al. (1997) showed that levodopa medication reduced movement duration, and increased force production and velocity. These improvements may explain why the COP and COM trajectories during gait initiation still remain similar to healthy older adults despite the

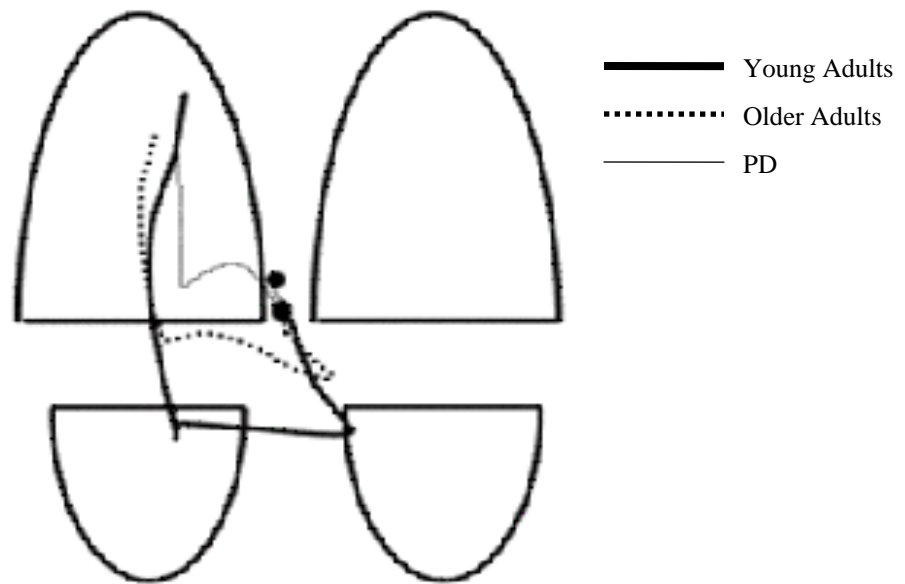


Figure 7. COP trace for gait initiation. Comparison between healthy older adults (broken line) and PD patients (thin line)

Adapted from Halliday et al., 1998

reported deficiencies in timing, velocity, and amplitude (Halliday et al., 1998).

4.2 Steady State Gait

Recent research has confirmed that PD patients experience a greater number of falls compared to healthy older adults and that the majority of these falls occur during locomotion (Ashburn, Stack, Pickering, & Ward, 2001; Bloem, Valkenburg, Slabbekoorn, & van Dijk, 2001). The explanation of high fall risk and incidence may lie within the parkinsonian posture (Schaafsma et al., 2003). PD gait is characterized by a stooped posture, reduced arm movements, reduced gait velocity, and reduced stride length (Schaafsma et al., 2003), which results in a slow shuffling pattern. This type of walking pattern is characterized by a reduction in knee flexion and heel elevation, as well as increased flexion of the trunk. In advanced stages of PD, gait becomes reduced to sliding of the feet and forward movement is accomplished through short quick steps. The influence of dysfunctional basal ganglia cannot be discounted as a primary cause of these deficits. It is proposed that the short steps PD patients take during gait is the result of a loss of automaticity in the ability to create smooth sequential movements, and that PD gait is comprised of separate small steps (Overstall, 2001).

Despite these deficits, levodopa medication has shown to be beneficial in reducing the difficulties that PD patients encounter during steady state gait. Levodopa therapy has been shown to increase stride length, stride velocity, steps per minute, as well as reducing the amount of time spent in double limb support (Blin, Ferrendez, Pailhous, & Serratrice, 1991; Morris et al., 2005). These results would suggest that dopamine may regulate the amplitude of the gait motor plan (Overstall, 2001).

Summary

The tasks of gait initiation and steady state gait are essential for activities of daily living. However for PD patients, these tasks can become very difficult and disabling. Research has shown that PD patients initiate gait with smaller amplitude, slower velocity, and longer duration compared to healthy older adults. For steady state gait, reduced stride length, slower stride velocity and walking speed, as well as an increase in DLS characterizes the deficiencies that PD patients exhibit. The proposed source of these deficits stems from dysfunctional basal ganglia, with both gait initiation and steady state gait parameters improving with levodopa medication.

5.0 Environmental Context

Movement is constantly being adapted or modified to suit the environment. For example, when walking on an icy surface our movement changes to adapt to the environment and the result is a more cautious and conservative movement pattern. The adaptability of the CNS to modulate movement in response to a challenging or changing environment is crucial to the success of goal-directed movement. Numerous studies have addressed the need for investigating the role of environmental context on locomotion; changes in surface, obstacle negotiation, and postural threatening situations have unequivocally demonstrated locomotion is modulated to meet the demands imposed by the

environment (McKenzie & Brown, 2004; Brown, Gage, Polych, Sleik, & Winder, 2002; Brown, McKenzie, & Doan, in press).

Anecdotal observations and patient reports indicate that PD patients have increased movement deficiencies in challenging environmental contexts (Morris et al., 2000). For example, busy road crossings (Fahn, 1995), cluttered home environments (Morris, 2000; Rochester et al., 2004; Stolze et al., 2004) and narrow spaces (Giladi et al., 1992; Macht & Ellgring, 1999), are a few of the challenging environments that affect movement for PD patients. Yet, beyond patient report and clinical observation, further research is vital to understanding how challenging environmental contexts influence movement among PD patients.

Objective of the Thesis

The purpose of this thesis was to explore how patients with PD modulate the initiation and control of gait in an environmental context that presents a threat to postural control. Moreover, this thesis also examined whether environmental context influences the efficacy of levodopa therapy for alleviating typical locomotor-dependent symptoms of Parkinson's disease.

In accordance with previous work from our laboratory the postural threat environment consisted of two testing conditions. 1) A floor condition (non-elevated, low postural threat), in which subjects initiated gait and continued with steady state gait while walking on the ground, and 2) an elevated condition (increased postural threat) in which all subjects initiated gait and continued with steady state gait while walking on the elevated surface.

It was hypothesized that Parkinson's disease patients in the postural threatening environment would show an increase in the already disabling motor deficits. In addition, it was hypothesized that the efficacy of parkinsonian medication may be compromised in the elevated testing condition. This hypothesis was based on patient reports and anecdotal evidence suggesting PD patients have difficulties with movement in challenging environments.

Deficits of Gait Initiation and Steady State Gait are Exacerbated by Postural Threat in Parkinson's Disease Patients

1. Introduction

Balance and locomotor deficits are among the hallmark symptoms of Parkinson's disease (PD) (Morris et al., 2000; Morris, 2000; Morris, Huxham, McGinley, Dodd, & Iansek, 2001; Nilsson, Tornqvist, & Rehncrona, 2005; Sohng, Moon, & Lee, 2004), and it is now recognized that these symptoms contribute to the high prevalence of falls in this population (Bloem et al., 2001; Gray & Hildebrand, 2000; Grimbergen, Munneke, & Bloem, 2004). It is this increased risk of falling (Wielinski, Erickson-Davis, Wichmann, Walde-Douglas, & Parashos, 2005), and the concomitant fear of falling (Adkin, Frank, & Jog, 2003), which develop with this disease that deprives patients of confidence and locomotor ability. This contributes to a loss of functional independence (Capecci et al., 2005), and a decrease in the subjective impression of physical and emotional functional quality of life (Chapuis, Ouchchane, Metz, Gerbaud, & Durif, 2005).

Currently, there is an extensive knowledge base confirming parkinsonian deficits in locomotor control during gait initiation (Crenna & Frigo, 1991; Gantchev, Viallet, Aurenty, & Massion, 1996; Halliday et al., 1998) and steady-state gait (Bowes et al., 1990; Morris et al., 2005; Schaafsma et al., 2003) compared to age-matched non-neurological participants. A key finding to emerge from these studies is that movement deficits are exacerbated in situational contexts that impose added motor or cognitive demands, such as walking while carrying a tray of glasses (Bond & Morris, 2000; Canning, 2004) or performing a cognitive task concurrent to gait initiation (Melzer, Benjuya, & Kaplanski, 2003) or gait (Rochester et al., 2004). Disease-related degeneration of dopamine-producing cells in the substantia nigra causing excessive inhibition of striatothalamic output and a lack of facilitation to the motor area of the cortex (Burch & Sheerin, 2005; Lefaucheur, 2005) provides foundation for

parkinsonian motor deficits in non-challenging contexts (Morris, 2000). The exacerbated deficit seen in situational contexts that impose added motor or cognitive demand is suggested to reflect a compromised ability to direct cognitive resources to movement execution, a strategy used by PD patients to overcome movement deficits (Morris, 2000). Yet, despite these findings, anecdotal evidence and clinical observations indicate that the motor symptoms associated with the movement disorder of PD also fluctuate across environmental contexts, with novel or challenging contexts exacerbating disease symptoms (Morris, 2000). For example, cluttered home environments (Morris, 2000; Rochester et al., 2004; Stolze et al., 2004), busy road crossings (Fahn, 1995), and narrow spaces (Giladi et al., 1992; Macht & Ellgring, 1999) are reported to make disease symptoms more troublesome for PD patients.

The environmental context in which a movement is performed plays a significant role in how the movement is expressed. Numerous examples of this phenomenon across a diverse range of movements are available in the literature, each providing justification for the adaptability of human movement. The existence of adaptability ensures task execution despite any imposed constraints. Extensive research on healthy older adults demonstrates how gait patterns are modulated to accommodate environmental constraints that increase the risk for falling and/or present the possibility for injurious consequences should a fall occur. Gait pattern adjustments according to the presence and characteristics of obstacle contingencies (Chen et al., 1996; Zettel, McIlroy, & Maki, 2002), or the conditions and challenge imposed by the walking surface (Brown, Gage et al., 2002; Marigold & Patla, 2002; Richardson, Thies, DeMott, & Ashton-Miller, 2004) substantiate this now well-documented finding. Yet, despite these observations, the effect of environmental context on motor symptoms of PD remains unexplored beyond clinical observation and patient report. Our

purpose in this study was to explore the effect of environmental context on locomotor control among patients with PD. We incorporated the elevated platform paradigm as a manipulation of environmental context. This paradigm presents a threat to postural control by a heightened potential for injurious consequences (Brown, Gage et al., 2002; Gage, Sleik, Polych, McKenzie, & Brown, 2003; McKenzie & Brown, 2004). Following clinical report of aggravated parkinsonian symptoms in challenging environmental contexts, we expected that locomotor deficits inherent to the processes of gait initiation (Halliday et al., 1998) and steady-state gait (Morris et al., 2005) among PD patients would be exacerbated in the threatening environmental context. We suggest this work addresses the documented need for research studies investigating how environmental context influences motor performance in people with PD (Morris, 2000).

2. Methods

2.1 Participants

Ten levodopa dependent (mean age= 69.7 ± 10.3 , range 54-81 years) PD patients and ten age-matched healthy control subjects (mean age= 68.8 ± 8.4 , range 56-80 years) participated in this study. All participants provided their informed consent prior to the beginning of testing. Clearance to conduct this study was provided by the Human Research Ethics committee of the University of Lethbridge. All control participants were free from any neurological disease or any other medical conditions that may affect gait function. PD subjects were recruited from local PD support groups and invited to participate if they were able to ambulate independently. Patients had mild to moderate severity PD according to the Hoehn and Yahr scale (Hoehn & Yahr, 1967). All subjects completed a questionnaire prior to testing to determine medical history, medication use, and fall history. Table 1 provides a summary of clinical characteristics of PD subjects as well as details relevant to falls history.

Table 1A: PD Subject Demographics

Subject	Age (years)	Gender	Years Diagnosed	Hoehn and Yahr (off/on)	UPDRS III (off / on)	Medication	Daily Dosage of L-Dopa	Number of Falls Last Year
1	81	M	7	2.0 / 2.0	33 / 16	Sinemet CR / Mirapex	160mg / 100mg	1
2	54	F	10	1 / .5	14 / 5	Sinemet CR / Permax	160mg / 1mg	0
3	54	F	22	2.5 / 1.5	43 / 21	Sinemet CR / Mirapex	50mg / 1mg	1
4	80	F	2	3 / 2.5	54 / 38	Sinemet CR / Amantadine	100mg / 100mg	1
5	75	M	2	1.5 / 1	17 / 6	Sinemet	100mg	1
6	63	F	1.5	3 / 1.5	58 / 22	Sinemet	200mg	3
7	65	F	11	2.5 / 1	34 / 21	Sinemet CR / Mirapex	50mg / 1mg	1
8	80	M	15	3 / 2.5	45 / 28	Sinemet	100mg	0
9	69	M	4	3.0 / 1.0	40 / 18	Sinemet	100mg	1
10	76	M	8	1.5 / 1	24 / 6	Sinemet/Sinemet CR	100mg / 160mg	0

Table 1B: CTRL Subject Demographics

Subject	Age (years)	Gender	Number of Falls Last Year
1	56	F	0
2	57	F	0
3	77	M	0
4	80	M	0
5	73	F	0
6	62	F	0
7	69	F	1
8	74	F	1
9	75	M	0
10	65	F	0

PD patients were tested in the non-medicated state (PD_{OFF} : following a minimum 12 hour withdrawal of anti-Parkinsonian medication), and post medication (PD_{ON} : minimum one hour post medication). All patient testing was conducted on the same day with “off” state testing occurring first for all patients. The motor subscale component of the UPDRS (Fahn and Elton, 1987) was used to assess disease severity in each subject for both the “off” and “on” medication states. PD subjects also self-reported on the quality of their medicated state to confirm a good “on”.

2.2 Manipulation of Environmental Context

Participants were asked to walk the length of a walkway, which was 4.70 m in length and 0.60 m wide, in two environmental context conditions. In one testing condition (floor) the walkway was outlined on the floor using black tape strips, in the other condition (elevated) the walkway was 0.60m above the ground (See Figure 8). The elevated walkway system was constructed of wood and was rigidly connected to maximize stability. Two force platforms (Bertec Corporation, Columbus OH) were placed side by side at the leading edge of the walkway in each testing condition. In the elevated condition the force platforms were placed on top of a hydraulic lift (Pentalift, Guelph Ontario) and were flush with the walkway. In the non-elevated testing condition a ramp (length 0.9 m, inclination angle of 5.5 degrees) was used to bridge the height differential between the force platforms (0.09 m) and the ground (0.0 m)(See Figure 8).

2.3 Instrumentation

Infrared-reflective markers were placed bilaterally at the head of the fifth metatarsal, lateral malleolus, heel, lateral epicondyle of the femur, iliac crest, lateral epicondyle of the humerus, acromion process, and single markers were placed on the sternal notch and forehead. Kinematic data were collected using a 6-camera infrared motion analysis data

collection system (Peak Performance Technologies and Peak Motus 2000 software, Englewood, Colo.) at a collection frequency of 120 Hz. Ground reaction force and moment of force data were collected from each force platform at a sampling frequency of 600 Hz and stored off-line for further analysis. Kinematic and force plate data were collected synchronously using the Peak Performance system. In addition, frontal and sagittal digital video was captured using tripod-mounted digital video cameras.

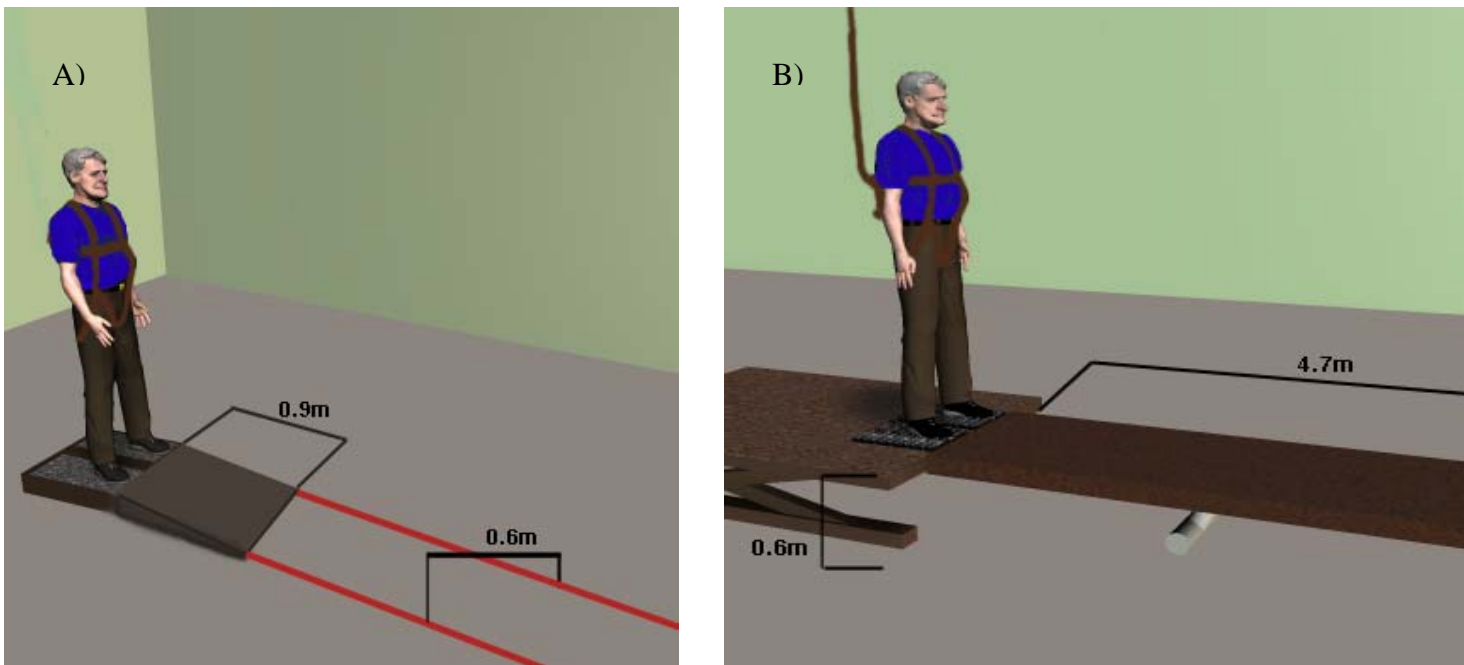


Figure 8. Two testing conditions. A) Floor condition and B) Elevated condition

2.4 Protocol

All subjects began each trial by standing with each foot on a separate force platform. Foot positions were marked prior to the first data collection to ensure consistency between trials. Participants were asked to walk at a comfortable speed across the entire length of the walkway. Subjects were instructed to initiate gait following the onset of an auditory cue and to walk the entire length of the walkway without stopping. There were no restrictions placed on the selection of the limb or speed used for gait initiation.

There were 18 test trials and one practice trial in each testing condition. Fifteen of the eighteen trials for each testing condition involved an obstacle avoidance task. These data were collected for future research and were not included in this thesis. The remaining three trials were void of any obstacle and provided the data for the results presented in this thesis. Trial order was fully randomized within each condition, and the order of test condition (floor/elevated) was counterbalanced between subjects. This method was used to prevent carry over between testing conditions. All participants wore a T-shirt, shorts, comfortable walking shoes, and a safety harness over their clothes while being tested. When walking on the elevated walkway the safety harness was attached to a coupling that moved along a steel track anchored to the ceiling above the walkway. All participants were guarded by a spotter who walked behind the subjects for each test trial.

2.5 Data processing

Custom written algorithms were used to process kinematic and analog data and to determine event occurrences (Matlab, The MathWorks, Natick MA USA). Raw marker data were filtered using a 4th order Butterworth low pass digital filter at a cut-off frequency of 10 Hz. Whole-body center of mass (COM) in the anterior-posterior dimension was calculated using a 7-segment model using the anthropometric values provided by Winter (1990). These segments included the foot, leg, and thigh bilaterally, and the trunk (including arms and head with the trunk segment). COM velocity was calculated using the finite differences method. Force platform data were filtered using a 4th order Butterworth low pass digital filter at a cut-off frequency of 10 Hz. Coordinates for the anterior-posterior (y) and medial-lateral (x) positions of the center of pressure (COP) from each force plate were calculated using the following equation:

$$COP_x = \frac{My}{F_z}$$

$$COP_y = \frac{Mx}{F_z} \quad \text{Where } M = \text{moment of force and } F = \text{force}$$

The net COP location between the two force platforms was then calculated using the algorithm provided by Winter et al.(1991):

$$COP_{NET} = COP_L \times \left(\frac{R_L}{R_L + R_R} \right) + COP_R \times \left(\frac{R_R}{R_R + R_L} \right)$$

Where COP_L and COP_R are the COP from under the left and right foot respectively; R_L and R_R are the ground reaction forces from the left and right foot respectively.

2.6 Measures of Interest

Gait Initiation

Previous studies of gait initiation have separated the COP trace into different phases based on specific events (Dibble et al., 2004; Hass et al., 2004; Martin, 2002). Accordingly, we identify three events that occur consecutively in time: COP_{ONSET} , $COP_{RELEASE}$, and COP_{UNLOAD} (Figure 9). COP_{ONSET} is described as the first detected COP movement after the audio signal. $COP_{RELEASE}$ is determined as the maximum lateral and posterior COP displacement towards the extremity taking the first step. COP_{UNLOAD} is defined as the point at which lateral deviation of COP crosses the midline of the two force platforms to terminate under the stance limb, prior to anterior displacement. This event was determined using a velocity algorithm. These events were then used to separate the gait initiation cycle into two phases: initiation (INIT) and transfer (TRANS). INIT consists of the period from the COP_{ONSET} to $COP_{RELEASE}$, and TRANS is defined as the period between $COP_{RELEASE}$ and COP_{UNLOAD} (Figure 9). Five dependent variables were established for each phase: 1) Event

Time, defined as the absolute duration of time between relevant events, 2) Resultant (RST) COP displacement, defined as the total displacement between relevant events independent of direction, 3) Medial-lateral (ML) COP displacement, defined as the range of COP displacement in the ML dimension between relevant events, 4) Anterior-posterior (AP) COP displacement, defined as the range of COP displacement in the AP dimension between relevant events, and 5) Peak COP velocity, defined as the maximum velocity reached within each phase.

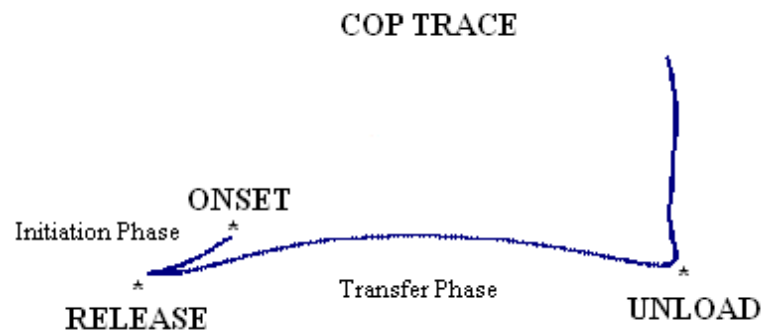


Figure 9. COP trace. Highlighted are three specific events: 1) Onset, 2) Release, 3) Unload. As well as two specific phases: 1) Initiation phase and 2) Transfer Phase. Dependent variables were measured using these events and phases.

Steady State Gait

Kinematic data were cropped into gait cycles using the event of right heel contact. For each trial we used the last gait cycle captured by the motion analysis system (minimum 4th gait cycle). Kinematic measures include: 1) Stride length, 2) Stride velocity, 3) COM velocity in the AP direction, and 4) Percentage of gait cycle duration spent in double limb support (%DLS), as per our previous work in this area (Brown et al., 2001).

2.7 Statistical Analysis

Subject anthropometric and demographic details were compared between groups using independent t-tests. The effect of postural threat on gait initiation and gait was assessed using separate ($PD_{OFF}/CTRL$, $PD_{ON}/CTRL$, PD_{ON}/PD_{OFF}) Group x Height

(elevated/non-elevated) Repeated Measures Multivariate Analyses of Variance (RM MANOVA) for each category of measures. Factors found to be significant in the multivariate analyses were followed up by univariate analyses: separate (PD_{OFF}/CTRL, PD_{ON}/CTRL, PD_{ON}/PD_{OFF}) Group x Height (elevated/non-elevated) Repeated Measures Analyses of Variance (RM ANOVA). Bonferroni adjusted pairwise comparisons were used as post-hoc analysis for significant univariate RM ANOVA results. Results were considered significant at the 0.05 level.

3. RESULTS

Results are presented independently for the tasks of gait initiation and steady state gait. A summary of statistical findings for gait initiation and gait are provided in Tables 2a and 2b respectively. Descriptive statistics detailing the effects of Group and Height for each task are provided in Tables 3a and 3b.

3.1 Subject Characteristics

There were no significant differences between groups in height or body weight (height: $t(18) = 0.15$, $p > .05$; body weight: $t(18) = 0.25$, $p > .05$). However, there was a trend that was nearing significance when comparing number of falls in the past year between groups ($t(18) = 2.26$, $p = .077$). Only two CTRL subjects reported falling in the past year, while six PD subjects also reported falling in the last year.

Table 2a: Summary of statistical findings for gait initiation.

INITIATION PHASE	PD _{OFF} vs. CTRL			PD _{ON} vs. CTRL			PD _{ON} vs. PD _{OFF}		
	Height	Group	Height	Height	Group	Height	Height	Group	Height
			x Group			x Group			x Group
MANOVA	*	*	*						*
Event Time	*	*	*						*
RST COP Displacement									
ML COP Displacement									
AP COP Displacement			*						*
Peak COP Velocity									

TRANSFER PHASE	PD _{OFF} vs. CTRL			PD _{ON} vs. CTRL			PD _{ON} vs. PD _{OFF}		
	Height	Group	Height	Height	Group	Height	Height	Group	Height
			x Group			x Group			x Group
MANOVA		*		*	***	*			*
Event Time	0.061	*		***	*	*			*
RST COP Displacement		*							
ML COP Displacement		*			0.082				
AP COP Displacement	*			0.082					
Peak COP Velocity		*		0.094		*			*

*

*p<.05; ***p<.001

Table 2b: Summary of statistical findings for steady state gait.

STEADY STATE GAIT	PD _{OFF} vs. CTRL			PD _{ON} vs. CTRL			PD _{ON} vs. PD _{OFF}		
	Height	Group	Height x Group	Height	Group	Height x Group	Height	Group	Height x Group
MANOVA	*	***	*	*	***	*	***	0.088	
Stride Length	*	***	0.074	*	***	*	*		
Stride Velocity	0.076	***		*	***	*	*		
AP COM Velocity	*	***	*	*	***	*	*		
%DLS	0.073	***	*		***		*		

*=p<.05; ***p<.001

Table 3a: Summary of descriptive statistics for gait initiation for each condition of postural threat.
Data are presented as mean \pm standard error for each test group.

INITIATION PHASE	FLOOR			ELEVATED		
	CTRL	PD _{ON}	PD _{OFF}	CTRL	PD _{ON}	PD _{OFF}
Event Time (s)	0.39 (0.08)	0.60 (0.06)	0.72 (0.13)	0.37 (0.08)	0.76 (0.13)	1.04 (0.09)
RST COP Displacement (m)	0.023 (0.03)	0.026 (0.006)	0.017 (0.01)	0.029 (0.03)	0.014 (0.006)	0.024 (0.01)
ML COP Displacement (m)	0.02 (0.01)	0.02 (0.01)	0.008 (0.01)	0.02 (0.01)	0.009 (0.01)	0.013 (0.01)
AP COP Displacement (m)	0.015 (0.01)	0.017 (0.01)	0.013 (0.01)	0.016 (0.01)	0.007 (0.002)	0.002 (0.003)
Peak COP Velocity (m/s)	0.23 (0.05)	0.24 (0.05)	0.10 (0.05)	0.17 (0.02)	0.12 (0.02)	0.11 (0.02)

TRANSFER PHASE	FLOOR			ELEVATED		
	CTRL	PD _{ON}	PD _{OFF}	CTRL	PD _{ON}	PD _{OFF}
Event Time (s)	0.24 (0.09)	0.48 (0.09)	0.53 (0.10)	0.29 (0.04)	0.67 (0.09)	0.67 (0.14)
RST COP Displacement (m)	0.05 (0.02)	0.04 (0.03)	0.03 (0.01)	0.05 (0.04)	0.03 (0.01)	0.03 (0.01)
ML COP Displacement (m)	0.04 (0.01)	0.026 (0.01)	0.025 (0.01)	0.05 (0.01)	0.027 (0.005)	0.024 (0.006)
AP COP Displacement (m)	0.026 (0.01)	0.006 (0.009)	0.004 (0.009)	0.003 (0.006)	0.005 (0.008)	0.007 (0.006)
Peak COP Velocity (m/s)	1.20 (0.23)	1.10 (0.25)	0.53 (0.08)	1.24 (0.16)	0.58 (0.06)	0.37 (0.07)

Table 3b: Summary of descriptive statistics for steady state gait for each condition of postural threat.
Data are presented as mean \pm standard error for each test group.

STEADY STATE GAIT	FLOOR			ELEVATED		
	CTRL	PD _{ON}	PD _{OFF}	CTRL	PD _{ON}	PD _{OFF}
Stride Length (m)	0.94 (0.05)	0.76 (0.04)	0.63 (0.04)	0.93 (0.05)	0.58 (0.04)	0.48 (0.03)
Stride Velocity (m/s)	0.92 (0.05)	0.71 (0.04)	0.51 (0.04)	0.89 (0.05)	0.45 (0.04)	0.35 (0.04)
AP COM Velocity (m/s)	1.02 (0.03)	0.84 (0.03)	0.69 (0.04)	0.98 (0.03)	0.59 (0.03)	0.45 (0.04)
%DLS	15.3 (2.4)	22.0 (2.3)	24.4 (2.1)	14.8 (2.4)	25.0 (2.2)	33.8 (2.1)

3.2. Gait Initiation

3.2.1 PD_{OFF} / CTRL

3.2.1.1 Initiation Phase (INIT). The MANOVA revealed significant main effects for Group ($F(1,18) = 7.03, p < .05, \lambda = .29$), and Height ($F(1,18) = 5.08, p < .05, \lambda = .36$), and a significant Group by Height interaction ($F(1,18) = 3.83, p < .05, \lambda = .42$). Follow-up univariate tests revealed that event time was the only measure to reach significance for the Group and Height main effects, while event time ($F(1,18) = 6.76, p < .05$) and AP COP displacement ($F(1,18) = 4.26, p = .05$) reached significance for the Group by Height interaction. PD_{OFF} took significantly longer than CTRL subjects to initiate gait ($F(1,18) = 5.16, p < .05$; CTRL=0.387s; PD_{OFF}= 0.882s), and event times for this phase were significantly longer in the elevated condition versus the floor condition ($F(1,18) = 29.84, p < .05$; Elevated=0.711s; Floor =0.557s). Follow-up comparisons showed that this effect of Height was driven by the PD_{OFF} group, who took significantly longer to initiate gait in the elevated versus the floor condition ($p = 0.026$), while CTRL subjects showed no difference for this measure between testing conditions (Figure 10a). Moreover, PD_{OFF} used significantly less AP COP displacement in the elevated testing condition for the INIT phase ($p = 0.036$), while CTRL subjects did not alter the range of AP displacement during this phase. For all subjects, the direction of displacement during INIT was posterior (Figure 10b).

3.2.1.2 Transfer Phase (TRANS). A main effect for Group ($F(1,18) = 19.81, p < .05, \lambda = .13$) emerged from the multivariate analysis, however, no significant results were revealed for Height or the Group by Height interaction. A follow-up univariate test showed that RST COP displacement ($F(1,18) = 5.14, p < .05$), ML COP displacement ($F(1,18) = 5.40, p < .05$), event time ($F(1,18) = 8.53, p < .05$), and peak COP velocity ($F(1,18) = 10.54, p < .05$) were significantly different between groups for this phase of gait initiation. In particular, PD_{OFF}

showed less resultant COP displacement ($p=.036$; CTRL=0.052m; PD_{OFF}= 0.033m) and less ML COP displacement than CTRL subjects ($p=.032$; CTRL=0.045m; PD_{OFF}=0.025m). Yet, despite this reduced range of displacement, PD_{OFF} took significantly longer to complete the TRANS phase than CTRL subjects ($p=.009$; CTRL=0.26s; PD_{OFF}=0.60s). Consequently, PD_{OFF} reached a significantly slower peak COP velocity than CTRL subjects during this phase ($p=.004$; CTRL=1.23m/s; PD_{OFF}= 0.45m/s).

3.2.2 PD_{ON} / CTRL

3.2.2.1 *Initiation Phase (INIT)*. No significant effects emerged for this phase of gait initiation.

3.2.2.2 *Transfer Phase (TRANS)*. Significant main effects for Group ($F(1,18) = 11.10$, $p<.05$, $\lambda=.20$) and Height ($F(1,18) = 3.94$, $p<.05$, $\lambda=.42$), and a significant Group by Height interaction ($F(1,18) = 4.13$, $p<.05$, $\lambda=.40$) were detected. Univariate follow-up testing showed that event time was the only measure to reach significance for the Group and Height main effects, while the Group by Height interaction was supported by the measures of event time ($F(1,18) = 6.38$, $p<.05$) and peak COP velocity ($F(1,18) = 4.26$, $p=.05$). PD_{ON} subjects took longer to complete the TRANS phase of gait initiation than CTRL subjects ($F(1,18) = 11.39$, $p<.05$; CTRL=0.26s; PD_{ON}=0.58s), and regardless of group, event times for the TRANS phase were significantly longer in the elevated condition versus the floor condition ($F(1,18) = 17.35$, $p<.05$; ELEVATED=0.48s; FLOOR=0.36s). This main effect for Height was driven by the performance of the PD_{ON} group, who took significantly longer to complete the TRANS phase in the elevated condition compared to the floor condition ($p=0.004$), while CTRL subjects showed no differences between the two testing conditions ($p>.05$; Figure 10c). Similarly, PD_{ON} subjects showed a significantly reduced peak COP velocity ($p=0.043$) in the elevated height condition, despite having velocity values that approximated CTRL values for the floor condition (Figure 10d).

3.2.3 PD_{ON} / PD_{OFF}

3.2.3.1 *Initiation Phase (INIT)*. A significant Height effect ($F(1,18) = 6.50, p < .05, \lambda = .30$) emerged from the multivariate analysis, however, no significant Group effect ($F(1,18) = 1.92, p > .05, \lambda = .59$) or Group by Height interaction were revealed ($F(1,18) = 2.27, p > .05, \lambda = .55$). The univariate test showed that the main effect for Height was supported by the measures of event time ($F(1,18) = 7.13, p < .05$) and AP COP displacement ($F(1,18) = 12.54, p < .05$). More specifically, both PD_{ON} and PD_{OFF} took less time to initiate gait in the floor condition ($PD_{ON} = 0.60s, PD_{OFF} = 0.71s$) than in the elevated condition ($PD_{ON} = 0.76s, PD_{OFF} = 1.04s$). In addition, both PD_{ON} and PD_{OFF} showed an increased amount of posterior displacement in the floor condition ($PD_{ON} = 0.017m, PD_{OFF} = 0.013m$) than in the elevated condition ($PD_{ON} = .007m, PD_{OFF} = .002m$).

3.2.3.2 *Transfer Phase (TRANS)*. A significant Height effect ($F(1,18) = 3.57, p < .05, \lambda = .44$) was detected from the multivariate analysis, however, no significant Group effect ($F(1,18) = 1.50, p > .05, \lambda = .65$) or Group by Height interaction was revealed ($F(1,18) = 1.67, p > .05, \lambda = .63$). The univariate test showed that the main effect for Height was supported by the measures of event time ($F(1,18) = 7.13, p < .05$) and peak COP velocity ($F(1,18) = 12.54, p < .05$). Both PD_{ON} and PD_{OFF} took less time to conduct the transfer phase in the floor condition ($PD_{ON} = 0.48s, PD_{OFF} = 0.53s$) than in the elevated condition ($PD_{ON} = 0.67s, PD_{OFF} = 0.67s$). In addition, both PD_{ON} and PD_{OFF} showed a decrease in COP velocity in the elevated condition ($PD_{ON} = 0.58m/s, PD_{OFF} = 0.37m/s$) than in the floor condition ($PD_{ON} = 1.10m/s, PD_{OFF} = 0.53m/s$).

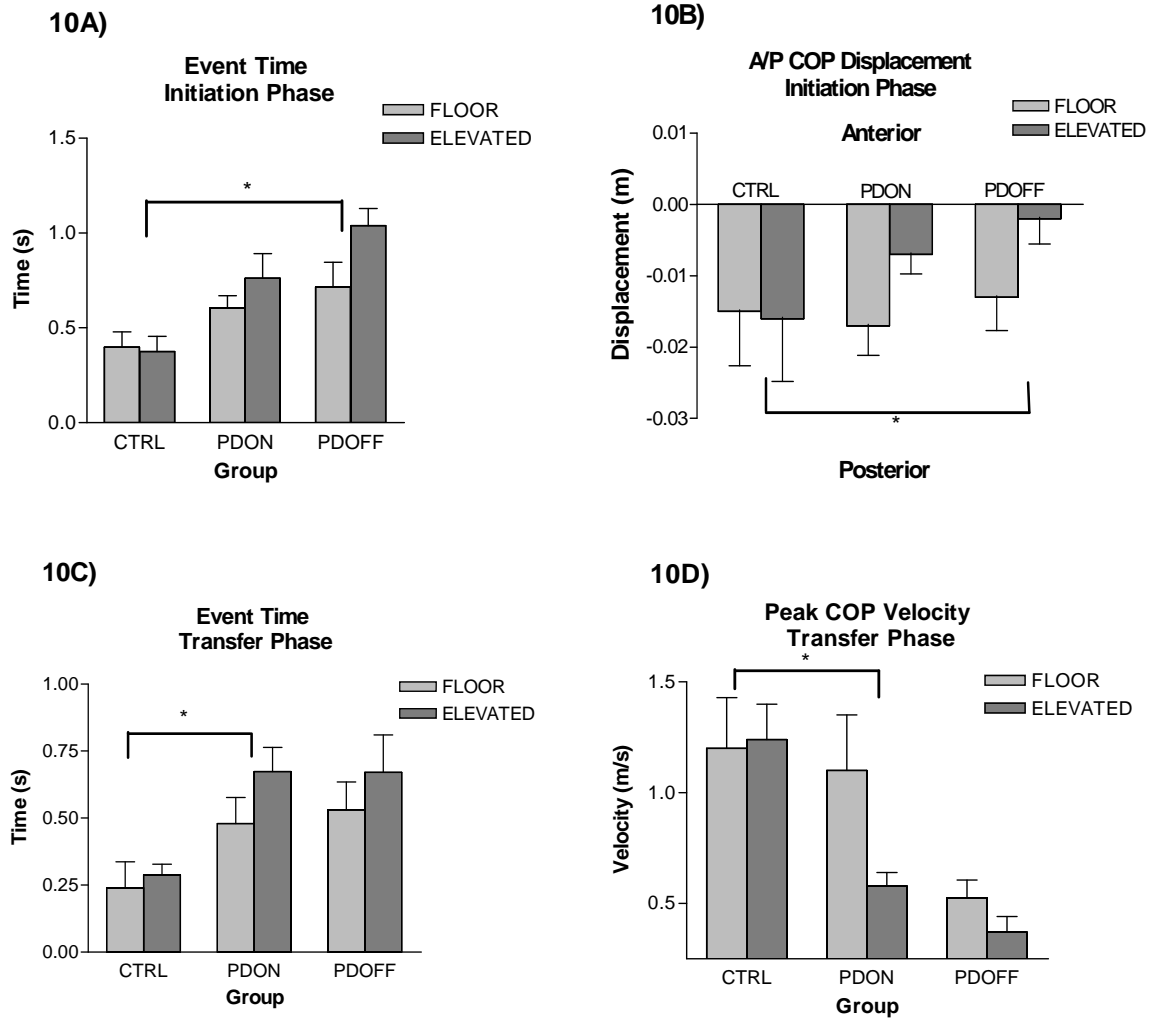


Figure 10. COP kinematics during gait initiation in floor and elevated (dark grey) testing conditions for control subjects (CTRL) and Parkinson’s disease patients on (PDON) and off (PDOFF) medication. Results illustrated represent measures that reached significance for a group by height interaction. Data provided represent mean \pm standard error values. A) Initiation phase: event time, B) Initiation phase: COP displacement (posterior), C) Transfer phase: event time, D) Transfer phase: peak COP velocity.

* $p \leq .05$

3.3. Steady State Gait

3.3.1 PD_{OFF} / CTRL. The multivariate analysis revealed main effects for Group ($F(1,18) = 20.30, p < .05, \lambda = .16$) and Height ($F(1,18) = 4.22, p < .05, \lambda = .47$), as well as a significant Group by Height interaction ($F(1,18) = 3.48, p < .05, \lambda = .52$). Follow-up comparison showed that PD_{OFF} exhibit a shorter stride length ($F(1,18) = 59.67, p < .05; CTRL = 0.94\text{m}; PD_{OFF} = 0.56\text{m}$) and reduced stride velocity ($F(1,18) = 52.15, p < .05; CTRL = 0.91\text{m/s}; PD_{OFF} = 0.43\text{m/s}$) compared to CTRL subjects. PD_{OFF} subjects also had a slower AP COM velocity ($F(1,18) = 80.76, p < .05; CTRL = 1.01\text{m/s}; PD_{OFF} = 0.58\text{m/s}$), and concurrently spent more time in double limb support (%DLS) ($F(1,18) = 36.314, p < .05; CTRL = 15.08\%; PD_{OFF} = 29.12\%$) than CTRL subjects. Interestingly, stride length ($F(1,18) = 4.31, p < .05; elevated = 0.71\text{m}; floor = 0.79\text{m}$) and AP COM velocity ($F(1,18) = 9.52, p < .05; elevated = 0.72\text{m/s}; floor = 0.86\text{m/s}$) were reduced in the elevated condition compared to the floor condition. Univariate follow-up tests revealed that these measures were supported by Group by Height interactions (AP COM velocity: ($F(1,18) = 4.90, p < .05$), %DLS: ($F(1,18) = 4.57, p < .05$)) (Figure 11a and 11b), and that significant Height effects for these measures emerged among the PD_{OFF} group only. Specifically, PD_{OFF} walked significantly slower in the elevated versus the floor condition ($p = 0.005$), while CTRL subjects did not alter walking velocity between testing conditions. Similarly, PD_{OFF} subjects spent a longer period of time in double limb support in the elevated condition compared to the floor condition ($p = 0.05$), while CTRL subjects showed no significant differences ($p > 0.05$).

3.3.2 PD_{ON} / CTRL. Main effects for Group ($F(1,18) = 8.10, p < .05, \lambda = .32$) and Height ($F(1,18) = 4.41, p < .05, \lambda = .46$), and a significant Group by Height interaction ($F(1,18) = 3.00, p = .05, \lambda = .56$) emerged from the MANOVA. PD_{ON} walked slower ($F(1,18) = 25.75, p < .05; CTRL = 1.01\text{m/s}; PD_{ON} = 0.72\text{m/s}$) and with a shortened stride length ($F(1,18) =$

27.03, $p < .05$; CTRL=0.94m; PD_{ON}=0.67m) than CTRL subjects. This resulted in a slower stride velocity ($F(1,18) = 20.36$, $p < .05$; CTRL=0.91m/s; PD_{ON}=0.59m/s) and a longer double limb support time (% DLS) ($F(1,18) = 16.23$, $p < .05$; CTRL=15.08; PD_{ON}=24.01) compared to CTRL subjects. In the elevated condition, participants walked slower ($F(1,18) = 9.75$, $p < .05$; elevated=0.79m/s ; floor=0.93m/s), with a shortened stride length ($F(1,18) = 5.08$, $p < .05$; elevated=0.76m; floor=0.86m), and slower stride velocity ($F(1,18) = 6.96$, $p < .05$; elevated=0.67m/s; floor=0.82m/s) compared to the floor testing condition. There were no changes in % DLS time between testing conditions. Nevertheless, the Group by Height interaction showed that the manipulation of environmental context affected gait among PD_{ON} subjects differently than CTRL subjects. Specific differences emerged in AP COM velocity ($F(1,18) = 5.25$, $p < .05$), stride length ($F(1,18) = 4.37$, $p = .05$), and stride velocity ($F(1,18) = 4.26$, $p = .05$) (Figure 11a, 11c, and 11d). More specifically, PD_{ON} showed significantly slower walking speed ($p = 0.006$), shorter stride length ($p = 0.006$), and slower stride velocity ($p = 0.002$) in the elevated condition versus the floor condition. CTRL subjects did not show any differences between testing conditions.

3.3.3 PD_{ON} / PD_{OFF}. A significant main effect for Height ($F(1,18) = 12.11$, $p < .05$, $\lambda = .24$) was revealed through the multivariate analysis. However, a Group by Height ($F(1,18) = .92$, $p > .05$, $\lambda = .80$) interaction failed to emerge even though a main effect for Group ($F(1,18) = 2.48$, $p = .08$, $\lambda = .60$) did approach significance. Stride length ($p = .000$), stride velocity ($p = .000$), AP COM velocity ($p = .000$), and %DLS ($p = .034$) were all found to be significantly different between height conditions.

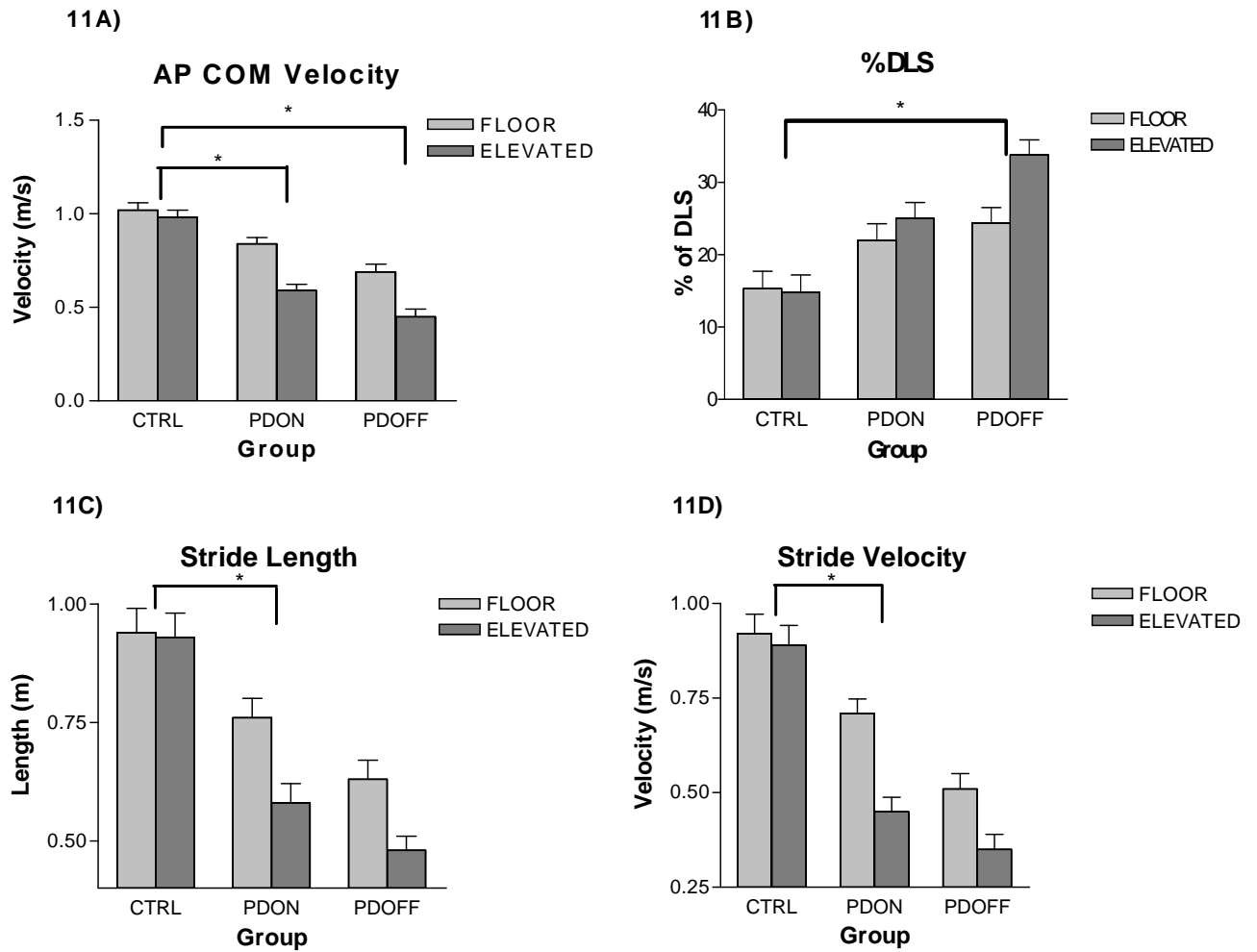


Figure 11. Steady-state gait kinematics in floor and elevated (dark grey) testing conditions for control subjects (CTRL) and Parkinson’s disease patients on (PDON) and off (PDOFF) medication. Results illustrated represent measures that reached significance for a group by height interaction. Data provided represent mean \pm standard error values. A) AP COM Velocity, B) %DLS, C) Stride Length, D) Stride Velocity.

* $p \leq .05$

4.0 Discussion

The purpose of this study was to determine how environmental context influences locomotor control among patients with PD. Healthy adult control participants and PD patients in both a non-medicated and medicated state were asked to initiate gait and continue with steady state gait in two environmental contexts that differed in the potential consequences of instability should a fall occur. Our results showed that in the absence of levodopa therapy, PD patients exhibited exacerbated deficits in gait initiation and steady state gait in the elevated compared to the floor condition. In addition, our findings demonstrated that medicated PD patients showed comparable results with CTRL subjects in the floor condition, however, in the elevated condition medicated PD patients showed deficits similar to their non-medicated state. These findings suggest that: 1) gait initiation and steady state gait deficits inherent to PD are aggravated in an environmental context that presents a threat to postural control and 2) medication efficacy for overcoming parkinsonian deficits may be context dependent. These findings confirm the dynamic nature of parkinsonian motor deficits (Morris, 2000) and provide empirical support for specific situations that can create movement deficits for PD patients.

Previous research has shown that parkinsonian deficits in gait initiation and steady state gait are characterized by a decreased velocity and a reduction in movement amplitude typical of bradykinesia (Crenna & Frigo, 1991; Halliday et al., 1998; Morris et al., 2005; Nallegowda et al., 2004; O'Sullivan, Said, Dillon, Hoffman, & Hughes, 1998). For gait initiation these effects emerge as decreased velocity during the INIT and TRANS phase. For steady state gait, a slower walking velocity, characterized by an increase in DLS time, decrease in stride length, and stride velocity exemplify the difficulties PD patients encounter when walking (Morris et al., 2005). Our findings substantiate this well documented

phenomenon by demonstrating that regardless of context PD_{OFF} show significant reductions in movement amplitude and velocity for gait initiation and steady state gait compared to CTRL subjects. Our findings also support a beneficial effect of parkinsonian medications for alleviating the deficits observed in gait initiation and steady state gait (Morris et al., 2005; Nallegowda et al., 2004; O'Sullivan et al., 1998), with PD_{ON} showing improvement beyond the non-medicated state. These changes however, emerged only in the non-threatening context.

A key finding from our study was that parkinsonian deficits typical of gait initiation and steady state gait were aggravated in the threatening context. This effect was revealed by temporal and spatial COP kinematics during gait initiation and gait cycle kinematics during steady state gait among non-medicated patients. Specifically, during the INIT phase of gait initiation PD_{OFF} required a longer duration of time, yet moved through a shorter range of displacement when comparing the elevated and floor conditions. Deficits in steady state gait were manifest among PD_{OFF} as a decreased walking speed with a greater proportion of the gait cycle spent in the DLS phase. Concurrently, there was also a trend for stride length to decrease in the threatening environmental context among PD_{OFF}. These findings confirm that parkinsonian bradykinesia is exacerbated by situational context.

The most compelling finding we present is that the PD response to levodopa therapy for alleviating motor deficits associated with gait initiation and steady state gait was context dependent. Specifically, improvements in timing and amplitude parameters of gait initiation and gait typically associated with levodopa medication (Burleigh-Jacobs et al., 1997; Morris et al., 2005) emerged only in the non-threatening context. In particular, event time and peak COP velocity within the TRANS phase of gait initiation, as well as gait velocity, stride length, and stride velocity for steady state gait showed significant improvements following

medication in the non-elevated condition, but there were no significant changes beyond non-medicated state in the elevated testing condition. This finding presents the possibility that the efficacy of medication therapy for overcoming movement deficits is compromised in a threatening environmental context. One implication of context-dependent drug efficacy is that PD patients when encountering a postural challenging situation may experience an increase in movement difficulty, despite the possibility of not experiencing any difficulties in a non-challenging situation. An alternate explanation to this proposition is that medication efficacy is not compromised in the elevated testing condition, and PD patients responded to the threatening context by adopting extremely conservative movement patterns. Although this may be the case, the effectiveness of these movement pattern alterations for reducing fall risk cannot be determined from the present study. However, we suggest that the similarity of these adaptations to parkinsonian bradykinesia and akinesia will limit the capacity for timely reactive movements such as would be necessary when required to preserve stability under time-restricted conditions, for example if an obstacle suddenly appeared underfoot (McKenzie & Brown, 2004). To this end we expect that the movement pattern alterations that emerged among PD patients in the elevated testing condition, which are not alleviated by levodopa, will not be beneficial to reducing fall risk. Our current work is exploring this possibility.

Contrary to parkinsonian patients, CTRL subjects did not alter movement patterns when the environmental context presented heightened consequences of instability. These findings contradicted previous work from our laboratory that demonstrated older adults do modify gait kinematics when postural threat is heightened. We suggest that the wider walkway used in this study was insufficient to impose the level of threat necessary to necessitate movement modifications among CTRL subjects.

4.1 Context dependent changes in PD gait initiation and gait: Potential underlying mechanisms

Morris et al (2000) argue that PD patients rely on conscious processes to regulate movements that, for the non-parkinsonian population, require little conscious input. One implication to arise from this theory is that motor performance may be compromised in situations that impose added cognitive demands. Indeed, carrying a tray of glasses while walking (Bond & Morris, 2000) or talking while walking are two situations that have been shown to change parkinsonian walking patterns (Bloem, Grimbergen, Cramer, & Valkenburg, 2000). In previous work from our laboratory (Brown, Gage et al., 2002) we demonstrated that walking in an environmental context that threatens postural control, such as the testing conditions imposed in this study, is more attentionally demanding than walking in a non-threatening context. One explanation for the added demand is that participants direct attention to the source of the threatening stimuli (Williams, Hadjistavropoulos, & Asmundson, 2004); a draw for attentional resources that is unnecessary if threat is absent. In the protocol of the study, this threat was presented by the environment in which the movement is being performed. Therefore, it remains possible that the changes in locomotor control that emerged among PD patients (on/off) in the threatening context reflect a compromised capacity to consciously regulate motor output in this testing condition. To this end, we suggest that the capacity to consciously regulate movement may be limited by the added 'draw' for attentional resources that is presented by the threatening environmental context.

Curiously, parkinsonian medication was less effective for overcoming movement deficits in the threatening environment than it was in the non-threatening environment. This finding may represent a detrimental effect of anxiety on medication efficacy. Recent research has shown that anxiety is significantly more prevalent in PD patients compared to age

matched adults without the disease (Walsh & Bennett, 2001). In addition, it has been noted that an increase in anxiety may be associated with decreased mobility in PD patients (Walsh & Bennett, 2001), suggesting that parkinsonian medication may not be as effective when anxiety levels are increased. Interestingly, abnormalities in the dopaminergic system have been thought to play a major role in the elevated levels of anxiety that PD patients experience. Both the ventral tegmental area (dopamine projection) and the locus ceruleus show substantial change in neurochemical activity in PD patients. Dopamine inhibits the firing rate of the locus ceruleus and the loss of dopaminergic inhibition that results from PD degeneration is proposed to cause the increase in both trait and state anxiety (Walsh & Bennett, 2001). The implications of this finding suggest that in the present study the exacerbated movement deficits may be the result of increased anxiety concomitant with insufficient dopaminergic inhibition. PD patients have decreased levels of endogenous dopamine and the use of synthetic dopamine replacement can restore dopaminergic functions. This is evident in the floor condition with medicated PD patients showing significant reductions of movement deficits compared to non-medicated patients. However, conventional dopamine dosages do not provide adequate inhibition to control anxiety responses in challenging environments and anxiety-evoked movement deficits result. The end result is that medicated PD patients perform similar to non-medicated patients in the high threat condition which may be increasingly dangerous if they are expecting to have full medication benefits. Regardless, these results show that the benefit of levodopa medication is compromised in a postural threatening environment.

5.0 Conclusion

Gait initiation and steady state gait are dynamic locomotor movements that require challenging control of COP and COM. These tasks become more difficult for PD patients, and as our results show become increasingly difficult in a postural threatening environmental context. Our findings indicate that PD patients have significant deficiencies in gait initiation and steady state gait compared to CTRL subjects and that these deficits are exacerbated by postural threat. PD patients in the absence of medication show a bradykinesia that is beyond typical parkinsonian slowness in the postural threatening environment. In addition, PD patients in their medicated state show that the effectiveness of their medication may be context dependent. These results have significant implication for PD patients especially under situations that require additional attention (ie. crossing a street, walking in a crowd) or environments that may create anxiety from a fear of falling (ie. slippery sidewalks, steep stairs).

General Discussion

This thesis compared how patients with PD and age matched older adults without PD alter the regulation of locomotion in an environmental context that presents a threat to postural control. In addition, this thesis examined the context dependent efficacy of parkinsonian medication for alleviating locomotor deficits. These questions were addressed for the tasks of gait initiation and steady state gait. The postural threat paradigm consisted of two different testing conditions, a low threat non-elevated (FLOOR) condition and a high threat elevated (ELEVATED) condition as per previous work from our laboratory. Both healthy older adults (CTRL) and PD patients initiated gait and continued walking along a walkway in these two conditions. PD patients were tested in a non-medicated and medicated state within the same day.

1. Effects of Postural Threat on Gait Initiation and Steady State Gait

Results from this thesis confirm and support the findings from previous studies regarding PD deficits for the tasks of gait initiation and steady state gait. Specifically, PD patients relative to CTRL subjects exhibited significant deficits when initiating gait and walking. Moreover, PD deficits were exacerbated in a non-medicated state. Previous studies have documented that non-medicated PD patients have reduced lateral and posterior COP displacement and slower velocity during gait initiation (Burleigh-Jacobs et al., 1997) and smaller stride length, increased DLS time, and slower walking velocity (Morris et al., 2005) during steady state gait compared to medicated PD patients. Our results substantiate these findings and provide additional evidence for context-dependent medication efficacy for PD patients in these types of movement tasks.

The unique finding presented in this thesis was that PD deficits are exacerbated in a postural threatening environment. More specifically, our results suggest that in a threatening

environmental context non-medicated PD patients show deficits that are beyond their typical levels of parkinsonian movement difficulty. In particular, when the environmental context presented a threat to postural control, PD_{OFF} patients showed an increase in timing, reduced magnitude of COP displacement, and slower COP velocity for both the INIT and TRANS phases of gait initiation. For steady state gait, PD_{OFF} movement was characterized by a reduced walking velocity, increased time in DLS, decreased stride length, and a reduced stride velocity.

The most compelling result to emerge from this thesis was that the effectiveness of parkinsonian medication for overcoming the movement difficulties associated with gait initiation and gait appears to be context dependent. Specifically, the effectiveness of PD medication for overcoming the deficits that emerged in the non-medicated state was limited to the non-threatening (floor) testing condition. This finding was demonstrated by an increase in event time, reduced COP displacement, and decreased velocity compared to the floor condition in both phases of gait initiation. For steady state gait, compromised medication efficacy was demonstrated by a slower walking velocity, increased time spent in DLS, reduced stride length, and a slower stride velocity of steady state gait. This finding provides a unique contribution to the literature, demonstrating a confirmed effect for environmental context on medication efficacy.

Unlike PD patients, our CTRL subjects did not show any variations to their movement patterns in the elevated testing condition. This is in contrast to previous research from our laboratory in which it was concluded that older adults exhibit modifications to gait kinematics in an environmental context of increased postural threat. (Brown, Gage et al., 2002; Gage et al., 2003; McKenzie & Brown, 2004). A wider walkway and possible disparity in subject demographics (ie. number of previous falls, fear of falling, physical activity levels)

between healthy older adult groups provide reasons for the differences between the current results and previous findings using this paradigm.

2. Potential Mechanisms: Implications of Results

The first proposed explanation for the observed movement deficits is based on the notion that PD patients are allocating more of their attention to the postural threatening environment. As such, PD patients are leaving less cognitive capacity available to concentrate on executing movement. This theory is based on the premise presented by Morris et al. (2004) where it is argued that PD patients rely more heavily on conscious attentional motor control processes compared to CTRL subjects in order to bypass defective basal ganglia. The simultaneous need to concentrate on environment and task is proposed to account for the difficulties that PD patients have in challenging environments (Rochester et al., 2004). Since the pharmacological schedule for drug therapy promotes constant medication dosing, PD patients rarely experience the full ‘OFF’ state tested in this study (Playfer, 2001). Consequently, these results lend themselves to the common reported effect of “wearing-off”, which happens when parkinsonian medication levels are not at peak dose and are at the end of a medication cycle (Jankovic, 2002). In this instance, it is important for PD patients to realize that when faced with a challenging situation they will be vulnerable to experiencing movement difficulties. Moreover, although PD medication can alleviate movement deficits, these benefits seem limited to non-challenging situations. The results presented in this thesis imply that in a non-challenging situation medication efficacy is beneficial to overcoming movement deficits. However, when faced with a situation that may impose a threat to postural control (ie. slippery sidewalks, steep stairs), the benefits of parkinsonian medication may be compromised. This finding carries the implication that

encountering a postural challenging situation may increase the risk for movement difficulties beyond the inherent risk associated with this disease.

The second explanation that cannot be overlooked is the notion that perhaps PD patients in the increased postural threat environment are adapting their movement to comply with a more conservative or safe behavior. Previous research in this area has confirmed that the gait pattern alterations adopted by non-neurological older adults in the threatening context serve well to reduce the risk of falling (Brown, Polych, & Doan, in press). Although this may be the case for the results presented in this thesis, it is hypothesized that a conservative movement strategy for PD patients may be detrimental. More specifically, if movement amplitude and velocity are substantially minimized, the necessary force production and displacement of COP and COM could lead to an inability to create successful and meaningful movements, with the most severe circumstance resulting in freezing of gait and the subsequent loss of balance.

A unique finding to emerge from this thesis is that medication efficacy is reduced in a postural threatening environment. This finding suggests that medication efficacy is context dependent. One possible explanation for the unresponsiveness of parkinsonian medication in the postural threatening environment may be the detrimental effect of anxiety on medication efficacy. It has been reported that 5% - 40% of the PD population experience some form of anxiety (Starkstein, Robinson, & Leiguardia, 1993). Interestingly, PD patients have shown to have a decrease in mobility when anxiety levels increase, leading to the notion that perhaps the reduction in mobility is associated with an attenuation in medication efficacy (Walsh & Bennett, 2001). The results presented in this thesis seem to support such a notion, as medicated PD patients showed an increase in movement deficits when the environmental context became more challenging. It is unknown if the PD patients in the

present study had an increase in anxiety levels in the elevated testing condition. However, previous studies from our laboratory that have utilized the same postural threat paradigm and have been able to show that anxiety levels increase in response to an increase in postural threat. Taken together these results suggest that medication efficacy may be compromised in the elevated threat condition because of an increase in anxiety.

3. Implications for Therapy

The findings presented in this thesis suggest an integral role for assisting in the development of therapeutic strategies for managing situations of daily living. Typical assessments of PD impairment, such as the single-task measures of gait, may offer little insight into actual difficulties patients could have in home environments, busy streets, and changes in walking surface (Rochester et al., 2004). However, based on the results presented in this thesis, it is possible that the degree of movement impairment can be better understood when the movement is required to meet context demands. Consequently, therapeutic interventions can be prescribed accordingly. Visual, auditory, and cutaneous cues are types of therapeutic interventions that have been shown to improve the spatial and temporal parameters of locomotion for PD patients. In non-challenging situations visual and auditory cues have been shown to improve the gait parameters of stride length and stride velocity (Darmon, Azulay, Pouget, & Blin, 1999), while cutaneous cues have been successful in improving the timing associated with gait initiation (Burleigh-Jacobs et al., 1997; Dibble et al., 2004). However, implications of this thesis suggest that therapists using sensory cues as a therapeutic intervention should consider the medication level of PD participants and the environmental context in which these cues are used. In situations where the environment requires a challenge in postural control or redirection of attention, the degree of movement difficulty may outweigh the benefits of such a strategy.

4. Future Research

The results presented in this thesis offer the foundation for further research in this field. Future research in the areas of obstacle negotiation, fear of falling, and dual-task paradigms that involve a postural threat environment could yield new knowledge regarding the movement capabilities of patients with PD. Obstacle negotiation research could offer unique insight into how PD patients both medicated and non-medicated respond to situations that challenge both their attention to a task and how successful they are at completing the task. The implications for such research would have significant real-world application. Research in this area could give greater insight into the role of extrinsic factors and the possibility for falls in the PD population. As well, future research is needed to explore how PD patients who are identified as having a fear of falling modulate their movement in a postural challenging context, and at the same time the benefits or detriments of using a more conservative approach to movement could be assessed. These results would be important to the further understanding of the psychological constraints of fear of falling on movement in challenging environments.

5. Limitations of Study

Some limitations of this thesis must be acknowledged. First, the PD patients included in this study were tested both in a non-medicated and medicated state. The UPDRS scale was used to ensure a difference between medication states, however subjects were only given one hour to be considered medicated. It is possible that PD patients did not reach peak dose in their medication cycle until later. Thus, the reported 'on' state of our subjects may not be a true measure of the full benefit of parkinsonian medication or indicative of capable movement behavior when medicated for a longer period of time.

The second limitation of this thesis is the inability to use collected galvanic skin conductance (GSC) data. GSC measures the perspiration of the skin, and more specifically perspiration of the fingers. GSC is a validated and reliable measure of anxiety (Ashcroft, 1991; Naveteur & Roy, 1990). GSC was collected for each subject and for all trials, however due to unforeseen problems with the hardware used to collect GSC, the corresponding data was unusable. This is unfortunate because it would have added to the findings of this study, as the observed results could have also been attributed to increased levels of anxiety in our PD patients in the elevated condition. Previous studies that have used this postural threat paradigm have collected GSC and results have shown that as the environmental context becomes more challenging, subjects become more anxious. In addition, previous work has shown that anxiety modifies gait parameters (Brown, Gage et al., 2002; Gage et al., 2003; McKenzie & Brown, 2004). However, in the present study it is uncertain if PD patients were more anxious than CTRL subjects or all subjects were equally as anxious. Future research is needed to substantiate this notion.

6. Conclusion

The purpose of this thesis was to investigate the effect of environmental context on locomotor control among patients with PD. The results presented in this thesis suggest that environmental context exacerbates the deficits associated with PD and that medication efficacy may be context dependent.

Results from this thesis support previous findings in the area of gait initiation and gait, but also provide experimental support for the effects of environmental context on movement patterns in PD patients. A compelling finding of this thesis is that PD movement deficits in the absence of levodopa therapy were exacerbated in the threatening environmental context. These findings confirm that parkinsonian bradykinesia is exacerbated

by situational context. Yet, the most compelling finding presented in this thesis is that medicated PD patients have a reduction in medication efficacy in an environmental context that presents instability. These results suggest that parkinsonian medication may be context dependent, and offer unique insight for the design and implementation of therapeutic strategies for the care and management of Parkinson's disease.

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Figure 6.
Illustration of
the typical
parkinsonian
posture.

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