THE CONTROL OF COMPENSATORY STEPPING RESPONSES TO UNPREDICTABLE PERTURBATIONS IN PERSONS WITH PARKINSON’S DISEASE

by

Natalie Kelly Damiano

A thesis submitted in conformity with the requirements for the Degree of Master of Science
Graduate Department of Rehabilitation Science
University of Toronto

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Master of Science, 2001

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Abstract

Parkinson’s disease (PD) patients demonstrate impairments in the control of voluntary stepping. It is unclear if they have similar difficulty controlling compensatory stepping used to recover postural stability. Compensatory stepping, evoked by backward platform perturbations, and forward-oriented voluntary stepping were recorded from four PD patients and four age-matched controls. Patients executed slower (289 ms at foot off, p=0.004), but stable, voluntary steps as compared to age-matched controls. In contrast, they demonstrated a significant amount of additional instability when executing compensatory reactions (multiple stepping 91.7% PD, 16.7% control). This occurred in spite of the fact the timing of the reactions was similar between the two groups (controls 467ms PD 464ms, p=0.9). Patients did, however, take shorter steps during compensatory stepping (step length: control 30cm, PD 21cm, p=0.04). Overall the results, which were not influenced by PD medication, highlight the specific control problem of hypometria (shorter steps) as opposed to delays in response initiation PD patients face when executing compensatory stepping responses. These results suggest that Parkinson’s disease impairs pathways that are crucial structures involved in the processing and execution of compensatory stepping responses to unpredictable and novel perturbations similar to those encountered in everyday life.
Acknowledgements

First and foremost, to my advisor, Dr. Bill McIlroy, for your enthusiasm and commitment to this project. Your ability to assist me in integrating the neurophysiology of postural control with a clinical population, as well as facilitating my ongoing learning and acquisition of the skills of scientific inquiry is truly appreciated. This degree has been a challenging but rewarding experience and I look forward to the challenges that lie ahead.

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<th>Description</th>
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<tbody>
<tr>
<td>5MT</td>
<td>Fifth metatarsal head</td>
</tr>
<tr>
<td>AP</td>
<td>Anterior-posterior</td>
</tr>
<tr>
<td>APA</td>
<td>Anticipatory postural adjustment</td>
</tr>
<tr>
<td>B</td>
<td>Hold handlebar</td>
</tr>
<tr>
<td>BG</td>
<td>Basal ganglia</td>
</tr>
<tr>
<td>BOS</td>
<td>Base of support</td>
</tr>
<tr>
<td>C7</td>
<td>7th cervical spinous process</td>
</tr>
<tr>
<td>CIS</td>
<td>Change in support</td>
</tr>
<tr>
<td>Cm</td>
<td>Centimetres</td>
</tr>
<tr>
<td>CNS</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>Co</td>
<td>Constrained trial</td>
</tr>
<tr>
<td>COM</td>
<td>Centre of mass</td>
</tr>
<tr>
<td>COMPT</td>
<td>Percentage of relative AP COM at FC/stepap</td>
</tr>
<tr>
<td>COP</td>
<td>Centre of foot pressure</td>
</tr>
<tr>
<td>Ctrl</td>
<td>Control subject</td>
</tr>
<tr>
<td>D</td>
<td>Distraction task</td>
</tr>
<tr>
<td>DBS</td>
<td>Deep brain stimulation</td>
</tr>
<tr>
<td>EC</td>
<td>Eyes closed</td>
</tr>
<tr>
<td>EMG</td>
<td>Electromyography</td>
</tr>
<tr>
<td>EO</td>
<td>Eyes open</td>
</tr>
<tr>
<td>FC</td>
<td>Foot contact</td>
</tr>
<tr>
<td>FO</td>
<td>Foot off</td>
</tr>
<tr>
<td>FS</td>
<td>Fixed support</td>
</tr>
<tr>
<td>GM</td>
<td>Gastrocnemius</td>
</tr>
<tr>
<td>GPI</td>
<td>Globus pallidus internus</td>
</tr>
<tr>
<td>Grtr Troch</td>
<td>Greater trochanter of femur</td>
</tr>
<tr>
<td>Hz</td>
<td>Hertz</td>
</tr>
<tr>
<td>IEMG</td>
<td>Integrated electromyography</td>
</tr>
<tr>
<td>LCD</td>
<td>Liquid crystal display</td>
</tr>
<tr>
<td>Li</td>
<td>Light cued trial</td>
</tr>
<tr>
<td>Lg</td>
<td>Large</td>
</tr>
<tr>
<td>LM</td>
<td>Lateral malleolus of fibula</td>
</tr>
<tr>
<td>m</td>
<td>Metres</td>
</tr>
<tr>
<td>Me</td>
<td>Medium</td>
</tr>
<tr>
<td>ML</td>
<td>Mediolateral</td>
</tr>
<tr>
<td>MPTP</td>
<td>1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine</td>
</tr>
<tr>
<td>ms</td>
<td>Milliseconds</td>
</tr>
<tr>
<td>N</td>
<td>Newton</td>
</tr>
<tr>
<td>OA</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>OFF</td>
<td>Off PD medication for twelve hours</td>
</tr>
<tr>
<td>ON</td>
<td>On PD medication-taken most recent dose</td>
</tr>
<tr>
<td>PD</td>
<td>Parkinson's disease</td>
</tr>
<tr>
<td>PEAK</td>
<td>Peak APA prior to foot off</td>
</tr>
<tr>
<td>Sm</td>
<td>Small</td>
</tr>
<tr>
<td>Stepap</td>
<td>Step length in AP direction</td>
</tr>
<tr>
<td>STN</td>
<td>Subthalamic nucleus</td>
</tr>
<tr>
<td>SWCHSC</td>
<td>Sunnybrook and Women's College Health Sciences Centre</td>
</tr>
<tr>
<td>T10</td>
<td>10th thoracic spinous process</td>
</tr>
<tr>
<td>TA</td>
<td>Tibialis anterior</td>
</tr>
<tr>
<td>Un</td>
<td>Unconstrained trial</td>
</tr>
<tr>
<td>UPDRS</td>
<td>Unified Parkinson's Disease Rating Scale</td>
</tr>
<tr>
<td>Yrs</td>
<td>Years</td>
</tr>
</tbody>
</table>
Glossary of Terms:

Anticipatory Postural Adjustment (APA):

Adjustment of COM prior to a volitional activity (arm raising, stepping or during gait) that is thought to decrease the effects of the impending perturbation to stability. APAs are examples of predictive balance control and are therefore most common when characteristics of upcoming perturbations are known.

Change in Support Strategy:

One of two main types of reactive balance strategies in which the base of support changes in order to recover stability after a perturbation. Commonly, compensatory stepping or grasping reactions are considered to be change in support strategies. Reactive balance strategies are utilized to recover stability after a person becomes unstable; they are therefore thought to be crucial to the maintenance of stability during the unpredictable activities of daily living.

Constrained Task Condition:

Task condition presented to subjects in which subjects were asked to step as quickly as possible to recover stability as soon as they felt the platform move. In this condition, subjects were given target step distances and were able to practice stepping prior to onset of the set of trials.
Fixed Support Strategy:

Reactive balance strategy in which the centre of mass moves within a fixed base of support in order to recover stability. Also called automatic postural reactions or ankle and hip strategies in the lower extremity.

Hoehn and Yahr Scale:

Clinical scale used to stage Parkinson’s disease progression. This scale was first described by Hoehn and Yahr (1967). The scale was modified by Fahn and colleagues (1987) and can be found on page 5 of this thesis. First clinical impression of balance impairment is noted at stage 2.5 on the scale.

Light Cued Task Condition:

Task condition presented to subjects in which subjects were asked to step as quickly as possible in response to a light cue presented at eye level on a LCD panel. Subjects were given target step distances and were able to practice stepping prior to onset of the set of trials. Demonstration of the light cue was also provided prior to onset.

Unconstrained Task Condition:

Task condition presented to subjects in which the platform moved forward or backward, at two magnitudes. Direction, magnitude and precise timing of onset of perturbation were randomized and unpredictable. Subjects were asked to do whatever came naturally so as to recover their balance and were not given any other instruction. As with all other trials, subjects
held a handlebar comfortably behind their back during these trials in order to minimize upper extremity motion. Unconstrained trials were always presented first.

**Unified Parkinson's Disease Rating Scale:**

A clinical rating scale commonly used in assessing PD patients. The scale is comprised of a series of questions, with scores of 0-4 including subjective assessment of symptoms (mentation, behaviour, mood, activities of daily living), as well as clinical assessment based on observation of specific tasks (motor examination). Higher scores on the scale indicate worsening of disease symptoms; a maximum score of 147 is possible. There is only one question on the scale that is specific to the assessment of postural stability, although a summation of four questions related to posture, rising from a chair, gait and postural stability make up a subscore of the UPDRS related to posture and gait.
Chapter 1.0 Introduction

Postural instability is a clinical hallmark of Parkinson’s disease (PD), particularly in the advancing stages of the disease process (Hoehn and Yahr, 1967; Bonnet et al., 1987; Klawans and Topel, 1974). This instability can lead to significant morbidity secondary to falls and associated injuries. Such functional impairments often result in further limiting the mobility and independence of community dwelling people with PD. Although many studies have investigated the changes seen in various postural control mechanisms in this population, our understanding of these changes and their role in the impairment of postural stability remains quite limited. Evidence suggests that the impairments of postural stability in the PD population affect, or are affected by, changes in predictive and reactive control of balance. Increased understanding of the control of postural stability in the PD population may help to improve strategies to minimize falls in addition to providing insight into the role the basal ganglia (BG) plays in the control of stability.

Lesions of the basal ganglia, occurring with Parkinson’s disease (PD), can lead to impairments in postural stability as reflected by changes in equilibrium reactions or feet in place strategies in this population (Beckley et al., 1993; Beckley et al., 1991; Bloem, 1992; Bloem et al., 1995; Chong et al., 2000; Chong et al., 1999b; Horak and Frank, 1993; Horak et al., 1992). As well, there is some evidence to suggest that the basal ganglia is involved in controlling anticipatory postural strategies (Lee et al., 1995; Rogers, 1989; Rogers, 1996; Rogers et al., 1987). There is also clear evidence that individuals with PD have difficulty controlling voluntary stepping movements (Burleigh-Jacobs et al., 1997; Halliday et al., 1998). In contrast, few studies have been completed investigating the role of compensatory stepping in maintaining upright stability in this population. In recent years, compensatory stepping has been shown to be
a key balance strategy to preserve upright stability (Maki and McIlroy, 1997). Recent studies have revealed important differences in this strategy between young and older subjects (Maki and McIlroy, 1996b: McIlroy and Maki, 1996), including increased incidence of multiple stepping in the healthy older adult. Given the apparent impairments in predictive and feet-in-place reactive balance control in the PD population, the successful execution of a compensatory step in response to perturbation is likely crucial in the maintenance of stability.

It is unclear, however, if there is a relationship between the control of compensatory stepping reactions and PD patients' difficulty in initiating voluntary stepping. The inability to scale "feet in place" reactions and failure to control the anticipatory phase of voluntary movements seen in the PD population are likely to have associated influences on the control of compensatory stepping. Compensatory stepping relies on scaling of response characteristics associated with the imposed instability and is often associated with predictive anticipatory adjustments prior to stepping (McIlroy and Maki, 1995). Limitations in scaling and control of these anticipatory adjustments at small magnitude perturbations are likely to be factors that will contribute to inappropriate compensatory stepping reactions. Consequently, the objective of this thesis is to determine if the ability to control compensatory stepping is compromised patients with Parkinson's disease.
Chapter 2.0 Review of the Literature

2.1 Overview of Parkinson's Disease

Parkinson's disease is a neurodegenerative disorder affecting over one million people in North America. PD is more prevalent in the older adult; it is thought that by the year 2040, neurodegenerative diseases (PD, motor neuron disease and dementia) will surpass cancer as the second most common cause of death in the elderly (Lilenfeld and Perl, 1993). James Parkinson first described the disease in 1817 in his "Essay on the Shaking Palsy" as a "paralysis agitans" in which there was a tremor at rest, lessened with movement, a propensity to flex at the trunk and tendency to pass from walking to running (Parkinson, 1817). In 1861, Charcot first included postural instability as a primary symptom of PD. He described this instability as the "patient loses the faculty of preserving equilibrium while walking" (Charcot and Vulpian, 1861 as cited in Tyler, 1992). The cause of PD remains unknown, although the underlying pathophysiology is well understood.

The gold standard for the differential diagnosis of idiopathic PD (from other Parkinsonian-like movement disorders) remains the neuropathological examination, in part secondary to the difficulty of measuring the striatal dopamine loss in vivo (Lang and Lozano, 1998a). Parkinson's disease is, however, diagnosed clinically, on the basis of a collection of four major symptoms: tremor, rigidity, bradykinesia and postural instability (Charcot and Vulpian, 1861 as cited in Tyler, 1992; Hoehn and Yahr, 1967; Lang and Lozano, 1998a; Knutsson, 1972; Martin, 1967; Muller et al., 1997; Nutt et al., 1993). The tremor is primarily a resting tremor, of 4-7 Hz, although tremor with increased effort is also seen. Tremor is often first noted in one upper extremity clinically and described as a "pill rolling tremor": EMG recordings in PD patients will demonstrate the tremor throughout muscles of upper and lower extremities.
Rigidity in PD patients is often of a “cogwheel” quality with some periodic “give” to the increased tone. Rigidity is worsened with voluntary movement in other body segments, as well as increased effort and arousal/anxiety. Patients with PD also demonstrate slow and small voluntary movement termed bradykinesia. Bradykinesia is seen in small movements of the hands as well as in the characteristic slow and festinating gait pattern of these patients. Particularly noticeable during gait, but also seen in other transitional movements, the bradykinesia in PD patients can worsen to the point of periods of freezing or akinesia as the disease progresses or when response to dopamine wears off. Akinesia, or complete arrest of movement, has been described in the literature as either a progression of the bradykinetic symptoms or as a separate entity, described as an increased onset latency prior to initiation of movement (Evarts et al., 1981). It is unclear, however, if PD patients truly have increased onset latencies to movement as a predominant symptom: Evarts and colleagues (1981) found significant variability between subjects and within the same subject over time in the occurrence of delayed initiation of movement. As well, many studies describing this apparent impairment use initial kinematic commencement of movement (of upper or lower extremity) to mark onset, as opposed to EMG or biomechanical onset as is commonly described in postural control literature. Regardless of this dispute, it is clear that PD patients have slowed execution of volitional movement, as well as periods of freezing. Posture instability and gait problems are so characteristic of PD that they are used as criteria for diagnosing the disease and assessing its severity and progression, with such tools as the Hoehn and Yahr scale and the Unified Parkinson’s Disease Rating Scale (UPDRS) (Hoehn and Yahr, 1967: Fahn et al., 1987: Martinez-Martínez et al., 1994; van Hilten et al., 1994). As noted in the Hoehn and Yahr scale, postural
instability becomes more prevalent in the middle to later stages of the disease process (see Table 1).

**Table 1: Modified Hoehn and Yahr Scale (adapted from Fahn, et al, 1987)**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Symptoms</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>No signs of disease</td>
</tr>
<tr>
<td>1</td>
<td>Unilateral disease</td>
</tr>
<tr>
<td>1.5</td>
<td>Unilateral plus axial involvement</td>
</tr>
<tr>
<td>2</td>
<td>Bilateral disease, without impairment of balance</td>
</tr>
<tr>
<td>2.5</td>
<td>Mild bilateral disease, with recovery on pull test *considered to be first stage with onset of postural instability</td>
</tr>
<tr>
<td>3</td>
<td>Mild to moderate bilateral disease: some postural instability physically independent</td>
</tr>
<tr>
<td>4</td>
<td>Severe disability; still able to walk or stand unassisted</td>
</tr>
<tr>
<td>5</td>
<td>Wheelchair bound or bedridden unless aided</td>
</tr>
</tbody>
</table>

### 2.2 Pathophysiology of Parkinson’s Disease

The current understanding of the pathophysiology of PD is based on neuropathological exam and more recently, the MPTP induced PD model in primates as well as pharmacological and surgical interventions in the treatment of the disease (Lang and Lozano, 1998a; Mink, 1998). Pathologically, Parkinson’s disease is characterized by the progressive death of numerous populations of neurons in the brain (Lang and Lozano, 1998a), including the dopaminergic neurons of the pars compacta of the substantia nigra. At the onset of clinical symptoms, loss of the dopaminergic cells in this area is estimated at 60-70%. Neuronal cell death is also seen in some aminergic brainstem nuclei, the cholinergic nucleus basalis of Meynert, hypothalamic neurons and small cortical neurons, particularly in the cingulate gyrus and entorhinal cortex. The
result of this cell loss is relatively specific to PD and results in a regional loss of striatal dopamine.

DeLong proposed a basal ganglia model that is currently used to describe the pathophysiology of PD (DeLong, 1990). It is also the basis for our understanding of the medical and surgical treatment of the disease. In both PD patients and the MPTP model, increased firing rates of the globus pallidus internus (GPI) and subthalamic nucleus (STN) neurons have been demonstrated (Bergman et al., 1990; Filion and Tremblay, 1991; Guridi et al., 1996; Hutchison et al., 1998; Hutchison et al., 1994). In accordance with the basal ganglia model, it is thought that these increased firing rates are a result of the degeneration of the nigrostriatal projections. Treatment with levodopa (dopamine precursor) relieves the hypokinetic symptoms of the disease (DeLong, 2000; Lang and Lozano, 1998a). Treatment with dopamine agonists has also been associated with decreasing the neuronal firing rates of the GPI and also relieves clinical symptoms (Hutchison et al., 1997). Lesions in either GPI and STN, as well as deep brain stimulation (DBS) in these areas, also decrease the firing rates of the neurons in these nuclei (Bergman et al., 1990; Lozano et al., 1995), and improves the hypokinetic symptoms of the disease (Baron et al., 2000; Masterman et al., 1998; Melnick et al., 1999; Skalabrin et al., 1998). This model of increased firing rates in the GPI and STN, coupled with the evidence that medical and surgical interventions decrease this firing and also improve clinical symptoms, particularly of hypokinetic nature has led to notion that the hypokinetic symptoms (bradykinesia, rigidity) are a result of the altered firing rates. It remains unclear if the postural instability seen in PD is also a direct result of the pathophysiology or a consequence of the hypokinetic primary motor symptoms. One recent study (Gross et al., 1999) has provided some indication that DBS in either GPI or STN improved features of volitional stepping as well as reactive balance strategies.
but these findings did not determine whether the postural dyscontrol seen in PD is a direct result of the increased firing rates or is secondary to another primary symptom.

Clinically, administration of levodopa is considered to be the most effective treatment of the motor symptoms of PD (Cotzias et al., 1967; Lang and Lozano, 1998a). However, it appears to lose its effectiveness after 5-7 years and is also associated with involuntary motor complications with long-term use. As well, many studies have found that levodopa does not improve the postural instability effectively in the PD population (Beckley et al., 1993; Bloem et al., 1996; Burleigh-Jacobs et al., 1997; Horak et al., 1996). Further details of these limitations can be found in section 2.4 of this thesis.

Stereotaxic DBS surgery for the relief of the hypokinetic symptoms of PD (bradykinesia, rigidity and postural instability) has recently been commenced and is now beginning to be considered as a standard treatment in some countries, although it remains experimental in North America (Hallett et al., 2000). From early studies, it appears that stimulation of the STN or GPi does have a preferential effect on the hypokinetic symptoms when compared to levodopa (Gross et al., 1999). As well, it appears to control hypokinetic symptoms during "off" periods associated with long-term levodopa use (Burchiel et al., 1999; Pinter et al., 1999; Volkmann et al., 1998). To date, these studies have measured hypokinetic symptoms mainly through clinical scores such as the UPDRS. One recent study (Siegel and Metman, 2000) has found that bilateral pallidotomy (lesions of the GPi) increased stride length and therefore gait speed in PD patients. This is the first study to quantify the changes in the gait pattern of PD patients after surgery. Increased insight into the pathophysiology of PD through the advent of new pharmacological and surgical interventions has begun to provide further information as to the CNS centres involved in the control of posture and balance in the PD population. Further research, quantifying changes in
postural control and gait will assist in determining the effectiveness of these treatments and the loci involved in the control of posture and gait.

2.3 Overview of Postural Control

In order to maintain upright stability, we must maintain our centre of mass (COM) over our base of support (BOS) in the face of destabilization caused by the effects of gravity as well as internal and external perturbations during interaction with the environment. In order to regulate the relationship between the COM and the BOS, the CNS uses a combination of both reactive and predictive balance control strategies (Frank and Earl, 1990). Predictive control features strategies executed prior to an anticipated perturbation in order to minimize the degree of instability (Cordo and Nashner, 1982; Belen'kai et al., 1967; Marsden et al., 1981). Such strategies are important during the execution of volitional movement or well-anticipated perturbations. Reactive strategies are fundamental in recovery of balance in the event of unpredictable perturbations such as slips or trips, or errors in volitional movement, and thus are likely critical strategies in falls prevention (Maki and McIlroy, 1996b).

2.3.1 Reactive Control Strategies

Reactive balance strategies are typically evoked and studied through the use of experimentally induced perturbations such as floor translations or tilts. Different types of reactions often arise as a result of different perturbation characteristics or environmental/instructional constraints placed upon the subjects. However, there are generally viewed to be two main categories of reactive balance strategies: fixed support and change in support strategies (Maki and McIlroy, 1997). Although these two categories have been identified and most often described separately in the literature, it is important to note that fixed
support and change in support strategies are not independent of one another, but rather are importantly related. Specifically, FS strategies are typically the initial responses to perturbations and are followed by CIS strategies if perturbation magnitudes are large enough. Fixed support (FS) strategies are strategies in which the base of support does not change, such as feet in place reactions (often termed automatic postural reactions). In contrast, change in support (CIS) strategies, such as compensatory grasping or stepping reactions, are distinguished by a change in base of support (through foot movement or grasping a handhold) in order to re-establish stability (see Figure 1).

FS strategies are motor strategies that display typical muscle synergy patterns of response (Nashner, 1977). Nashner and Horak and colleagues have characterized these responses as ankle or hip strategies based on initial muscular activation (Nashner, 1977),(Horak and Nashner, 1986). Ankle strategies are typically seen in response to small or slow anteroposterior translational perturbations; whereas hip strategies occur primarily in conditions where the anteroposterior stability is unstable (e.g. on a beam). These synergies appear, therefore, to be flexibly tuned to the specific biomechanical conditions (Horak and Nashner, 1986).

Anteroposterior oriented responses from lower limbs are characterized by muscle synergies most often activated distally to proximally (Nashner, 1976: Nashner, 1977). It is important to note that there are often important differences in the pattern of muscle activity and execution of the response evoked by AP or ML perturbations (Carpenter et al., 1999). However, the majority of studies conducted to date have emphasized responses to AP perturbations. In addition, the primary characteristics of FS reactions (onset latency, scaling) appear generalizable across responses evoked from different muscle groups (from perturbations of different directions).
"Fixed-support" (FS) strategies

"Change-in-support" (CS) strategies

Figure 1: Schematic description of anteroposteriorly oriented FS vs. CIS strategies. In FS strategies, the base of support does not change and stability is achieved by movement of the COM over a fixed BOS. In CIS strategies the BOS is changed to re-establish stability, in this case by stepping. Adapted from Maki and McIlroy, 1997.
Since the present study focuses on AP oriented stepping responses, the primary focus of the following review is on responses evoked by AP perturbations.

FS strategies are typically the earliest responses to surface translations, with latencies of approximately 100 ms (Nashner, 1977). The timing of the FS response is distinctive from that of the stretch reflex (40-50 ms) and voluntary reaction time (180-250 ms) (Kandel et al., 2000, p.662; Nashner and Cordo, 1981). When multiple reactive strategies are utilized in response to a perturbation during stationary stance (i.e. FS and CIS strategies), FS strategies from the lower limb typically begin first, with onset of CIS stepping strategies occurring 150-250 ms after platform perturbation (McIlroy and Maki, 1995). It was once thought that the CIS were responses of last resort initiated only when stability could not be maintained by a FS strategies (Nashner, 1989; Shumway-Cook and Horak, 1989 as cited in Horak et al., 1989b; Shumway-Cook and Woollacott, 1995). These authors have proposed that stepping strategies do not occur until the COM is outside of the fixed BOS (Nashner, 1989). More recently, however, it has been demonstrated that the initiation of compensatory stepping occurs too early to simply be a reaction of last resort (Maki et al., 1993). In fact, when the step is initiated the COM is well within the BOS stability limits. As well, McIlroy and Maki (1993b) have shown that when handrails are within reach, subjects demonstrate very early muscle activity in the arm muscles associated with upper limb CIS strategies, with latencies similar to those of FS strategies (average 88ms), in response to platform perturbations. Moreover, interaction between the FS strategy and pre-planned stepping occurs, modulating and attenuating the outcome of the FS strategy when subjects step in response to the perturbation cue (McIlroy and Maki, 1993a), (Burleigh et al., 1994).
Although FS strategies are the earliest response seen after support surface translation or rotation, the ability to execute a rapid CIS response (compensatory step or grasp) when perturbed is crucial to the maintenance of upright stance, particularly during the unpredictable activities of daily living. When the COM is perturbed significantly, executing an effective and efficient CIS strategy is the only means by which a person can maintain stability. Also important is that such CIS reactions become increasingly crucial when capturing stability when the BOS is changing as part of the ongoing movement such as during gait. If a person is unable to execute a fast and effective CIS (step or grasp/reach), they will likely fall. In fact, falls captured on videotape reveal compensatory stepping (primarily backward or lateral) in 35% to 45% of falls or near falls, and arm responses in 65% to 75% (Connell, 1995; Hollliday et al., 1990, as cited in (Maki and McIlroy, 1996b). As well, CIS strategies have been shown to be very common reactions when balance is perturbed unexpectedly in the experimental setting, even when perturbations are small and control could be regained without moving the arms or legs (McIlroy and Maki, 1993c). It is apparent that CIS strategies are key strategies in the maintenance of postural stability and are often strategies of choice even when they may be unnecessary.

2.3.1.1 CNS Control of Reactive Balance Strategies

Despite significant research in the area, how the CNS controls reactive balance strategies remains somewhat unclear. Review of the adaptation of the different responses in certain conditions as well as of the interaction and modulation of the different strategies may provide some insight into this CNS control. As well, a limited number of animal lesion studies have been completed, providing clues as to levels of control.

FS strategies are scaled in size in response to different velocities and displacement amplitudes of perturbation, especially if these variations in the stimulus are predictable (Diener
et al., 1988). As well, with practice, EMG activity of the lower limb muscles decreases, as does the force used to produce the reaction (ankle torque); however, body sway during the FS strategy as well as the latency of the reaction increases (Horak et al., 1989a). Nashner, Horak and colleagues have demonstrated that the CNS is able to adjust FS strategies to changes in sensorimotor and postural set. If the parameters of a perturbation (i.e. sensorimotor set) change after a number of perturbations, from platform translation to platform rotation, the response on the very first rotation is significantly different from that seen in the translations (Chong et al., 1999a). The CNS also appears to be able to take the initial position or posture into consideration when responding to perturbations (postural set). If the body is supported with a railing, the FS strategy evoked will be in the upper extremity and not lower extremity (Nashner, 1982). Similar findings hold true in experiments where postural set was altered from unsupported stand, to supported stand and free sitting (legs dangling) (Horak et al., 1992).

FS strategies can also be modified or suppressed by a person’s intent to move, particularly if that person is able to predict the characteristics of the upcoming perturbation during the movement (Burleigh et al., 1994; McIlroy and Maki, 1993a). If subjects are asked to step as soon as they feel the platform move, they will suppress their FS strategy to about 20% of normal. The inhibition is largest when the velocity of the perturbation is predictable (blocked trials). These characteristics demonstrate the adaptability in the CNS control of the FS strategy, indicating that reactive balance control strategies are not the product of hard-wired circuits.

Animal lesion studies also lend some insight into the CNS control of reactive balance strategies and provide some knowledge as to circuits that may be involved in the control of balance. McPherson and colleagues have shown that chronic spinalized cats are unable to maintain independent, unsupported stance for more than a few seconds and are unable to respond
appropriately to perturbations to their stance (Fung and Macpherson, 1999) (Macpherson et al., 1997). While some elements of postural orientation do appear to be organized at this spinal level, maintenance of postural equilibrium and reactive control require input from centres higher than the lumbosacral cord in the cat. It is important to note that studies to date in this field have centred on postural control in the quadruped animal. Comparative studies have not been completed in humans or primates and important differences may exist in the control of posture in the quadruped animal compared to the biped.

2.3.2 Predictive Control Strategies

As mentioned previously, predictive control of postural stability is important during volitional movement, including rapid arm movements, reaching and stepping or gait initiation, as reviewed by Massion (1994). It is thought that anticipatory postural adjustments (APAs) minimize instability that may arise due to the performance of the upcoming focal task. During upper extremity activities such as rapid arm raising during stance, EMG activity in the posterior muscles of the lower extremity increases prior to the movement in order to stabilize the COM prior to the upcoming anterior disturbance (Belen'kai et al., 1967; Bouisset and Zattara, 1981).

During volitional stepping, single leg lift or gait initiation, an APA is commonly observed (Brunt et al., 1991; Brunt et al., 1999). Typically, this APA consists of an initial displacement of the centre of foot pressure (COP) laterally towards the swing limb side and in the posterior direction, in order to propel the centre of mass (COM) toward the stance limb and forward for forward oriented stepping or gait (Brunt et al., 1991). This pattern of activity is stereotypical to the onset of walking in both young and older healthy adults (Elble et al., 1994;
Halliday et al., 1998) and the amplitude of the APA appears to be scaled to gait velocity (Halliday et al., 1998). During single leg flexion (leg lifts), the timing and gain properties of the APA are scaled as a function of the intended movement speed (Rogers, 1992). When the lower limb flexion is evoked by a noxious stimulus under the standing limb (spinal withdrawal reflex), the APA remains intact, even though it slows the time to foot off of that limb considerably (McIlroy et al., 1999a). It appears that, during gait initiation or voluntary, forwarded oriented stepping, APAs are typical, pre-programmed responses that can be scaled or tuned to the biomechanical properties of the focal movement. They also appear to be essential phenomena to the onset of forward oriented movement that generate the propulsive forces necessary to generate gait speed (Breniere et al., 1987) and are therefore inherent in the generation of volitional stepping.

2.3.2.1 Control of Compensatory Stepping Strategies vs. Volitional Stepping

Recent studies suggest that the control of compensatory stepping responses may be different than that of volitional stepping. The speed of the stepping response, when evoked by a platform perturbation, is significantly faster than when cued by a light or sound signal or a somatosensory cue. Also, the anticipatory postural adjustment (APA) usually seen prior to onset of volitional stepping is scaled down when steps are evoked by platform translation (McIlroy and Maki, 1993b; McIlroy and Maki, 1999). In fact, in response to a novel platform perturbation, the characteristic APA is often absent. As with the FS reactions, understanding of how the CNS controls compensatory stepping responses is not clear. It may be that the sequencing of muscle activation may be controlled by the same central pattern generators thought to be involved in locomotion, whereas initiation and scaling of the stepping responses may be controlled by the transcortical and subcortical pathways thought to be involved in the control of fixed support
strategies (Maki and McIlroy, 1997). The relationship between these two possible control mechanisms is of particular interest in the PD population, as control of volitional movement, especially gait initiation, is significantly compromised. Early studies of postural control/functional mobility in PD patients after stereotaxic DBS surgery or pallidotomy suggest that some of the pathways affected by PD may have some responsibility in reactive balance control. Thus, further study of the compensatory stepping response in this population may provide insight into the CNS pathways involved in the control of balance and posture.

2.3.3 Changes in Compensatory Stepping in the Older Adult

As mentioned previously PD is a disease that affects primarily older adults. In the present study, the PD patients were aged 62 to 71 years and therefore it is important to briefly review any changes seen in healthy older adults in their compensatory stepping behaviour. Although studies of the healthy elderly population did not reveal any significant differences in the timing of the compensatory stepping response, this group was more likely to take multiple steps in response to platform perturbation (McIlroy and Maki, 1996). It is suggested that multiple backward steps in response to a forward translation of the platform may be seen as a conservative strategy; during forward oriented stepping responses, however, over 30% of later steps in older adults were directed so as to recover lateral stability. This lateral stepping response may reflect an impaired ability to control the lateral displacement of the COM and may even distinguish fallers from non-fallers (Maki et al., 1994). Previous studies have suggested that increased lateral spontaneous sway amplitude was the best predictor for risk of future falling in the healthy elderly population (Maki et al., 1994). Measurement of control of lateral stability during stepping responses may also be useful in the PD population. In the present study,
incidence of multiple stepping and spatial coordinates of the multiple steps will also be examined as a measure of postural instability in the PD population.

2.4 Postural Control Strategies in the PD Patient

As noted previously, reactive balance control in the PD population is impaired. Numerous studies have demonstrated significant changes in the temporal and spatial characteristics of FS strategies, as well as the modifiability or scaling of such responses in this population in response to surface translation and rotation. In terms of temporal and spatial characteristics of FS strategies, Beckley and colleagues (Beckley et al., 1993), using platform tilts, found PD patients demonstrated long latency responses of normal latency in the tibialis anterior muscle group, in response to sudden toe up rotations. These responses were found to be smaller in amplitude than those of the control group (Bloem et al., 1996). Patients more severely affected by PD (stage IV, Hoehn and Yahr) also demonstrated increased amplitudes in their medium latency EMG responses of the posterior muscle group and a reversed (proximal to distal) activation sequence of the long latency responses that were correlated to disease severity (Beckley et al., 1993). In response to toes-up platform tilts, medium latency responses of the posterior muscle group are actually destabilizing as the body’s COM falls backward in response to such a platform tilt. Long latency responses of the anterior muscles re-stabilize the COM. Therefore, in the PD patients, all of these changes in response characteristics increase the instability of the subjects. When on PD medication, patients’ medium latency responses decreased in amplitude but remained larger than the control group; whereas long latency amplitudes were not different than those of the controls. Horak et al., (1992) found that when FS responses were evoked with backward support surface translations, PD subjects exhibited FS responses of normal latency but with an increase in antagonist muscle activity. As well they
generated decreased ankle torques during these responses and the initial velocity of their COM falling in response to the perturbation was slower than age-matched controls (Horak et al., 1996). Decreased initial velocity of the COM was thought to be secondary to increased baseline muscle tone and cocontraction (Horak, et al., 1996). Use of levodopa decreased the antagonist muscle activation in two of the eight PD patients (Horak et al., 1992). Levodopa administration further reduced the initial ankle torques in PD patients but did increase the initial velocity of COM displacement most likely by decreasing high baseline muscle tone seen in the PD patients (Horak et al., 1996).

PD patients have also been found to have difficulty modifying their responses to changes in perturbation parameters as well as to changes in postural set. Beckley and colleagues found that patients with PD (ON medication) failed to scale the size of their long latency response to changing magnitudes (displacement of rotation) of stimulus, even when this stimulus was predictable (Beckley et al., 1993). Horak and colleagues (1996) found that PD patients were able to scale their FS responses to changes in velocity of the platform translation, but not changes in displacement, even if the displacement was predictable. The difficulty seen in scaling to changing displacement was more pronounced at larger displacements. As well, when exposed to a changing postural set (unsupported stance, stance on a narrow beam, or legs dangling seated position), subjects with PD did not modify the EMG response of their lower limbs to the differing support conditions (Horak et al., 1992). Levodopa administration did not affect PD patients' ability to scale responses to changes in velocity; and their ability to scale to large amplitude displacements actually worsened when on medication (Horak et al., 1996).

Predictive control of balance is also affected in the PD population. Studies have shown impairments in the organization and temporospatial characteristics of anticipatory postural
adjustments prior to voluntary upper or lower limb movements. Rogers and colleagues (1989) found that in response to rapid arm raising, people with PD executed APAs less frequently and when they occurred they were of shorter duration. As well, the APAs included multiple EMG bursts extending into the agonist muscle activity, compared to age matched controls (Rogers, 1989). Latash and colleagues (1995) found that PD patients executed APAs similar to controls prior to making self-initiated fast upper extremity movements, but that there was an increase in the variability of the patterns of response, sometimes with clear EMG bursts in only one or two of the lower extremity muscles. In contrast, when APAs were elicited prior to a predictable load drop or catch, PD patients failed to produce an APA at all whereas control subjects demonstrated smaller but reproducible APAs (Latash et al., 1995). In another study, subjects were asked to quickly lift one leg laterally while maintaining stability in single leg stance. Subjects severely affected by PD (Hoehn and Yahr IV) demonstrated a marked reduction in the amplitude of the excursion of centre of pressure over the swing leg during the anticipatory postural adjustment necessary for the leg lift (Lee et al., 1995). They also found that the interval between initial force changes and onset of leg elevation was prolonged (i.e. an increased time to foot off). Subjects with mild-moderate PD (Hoehn and Yahr I-II) demonstrated either a normal or an increased amplitude in their APA but often had difficulty remaining in the lateral leg raise position. These findings suggest that the PD patients were unstable during single support stance; it is possible that the APA executed may not provide the stability necessary to maintain single support stance. Halliday and colleagues found that the APA of the PD patients prior to onset of walking was smaller in amplitude in both the lateral and posterior direction of the COP displacement (Halliday et al., 1998). This difference, however, was not significant if APA amplitude was normalized to gait speed. The PD patients tested were chosen secondary to
displaying significant akinesia (Hoehn and Yahr 2.5-3.0) and were significantly slower than the young or older healthy adults in terms of gait speed. PD patients were off medication but only for one medication period and therefore time off varied considerably (4-41 hours).

In contrast to FS reactions and voluntary stepping there has been little study of compensatory stepping in the PD population. Some recent studies have explored stepping that is cued, not evoked, by surface translations. Burleigh-Jacobs and colleagues found that PD subjects demonstrated self-initiated, self-generated steps characterized by decreased force production, as measured by slowed execution of the APA prior to the step and of the step itself (Burleigh-Jacobs et al., 1997). The APAs were also characterized by smaller peak COP changes prior to step onset. If, however, PD patients were cued to step by a small backward platform translation, they were able to decrease the duration of the APA, but could not decrease the overall time to foot off (unloading time). PD medication increased movement velocity, decreasing time to peak APA and to foot off in the self-generated, cutaneously cued steps, but did not affect the timing of the steps cued by the platform perturbations. It would appear that perturbation cues can be utilized by PD patients to decrease the duration of their stepping responses. Whether findings are similar when PD patients make compensatory stepping reactions in the face of novel perturbations remains unknown.

In summary, PD patients have been shown to be at an increased risk of instability secondary to FS strategies characterized by smaller ankle torques, posturally destabilizing amplitude changes, increased co-contraction of lower extremity muscles and reversed lower extremity muscle sequencing. As well, PD patients have demonstrated impairments in the scaling of such reactions to changes in perturbation magnitude, particularly if the changes are in displacement. In contrast, there is no evidence to date that PD patients are slower to initiate
balance reactions. Furthermore, the above studies demonstrate that PD patients have difficulty executing APAs prior to leg lifts and gait initiation. These APAs were sometimes absent, were of smaller amplitude and shorter duration and with increased co-contraction. Initial studies of perturbation cued stepping provide some indication that the speed of the APA can be improved with the cueing. In contrast to its effect on voluntary movement, medication has not been found to be effective in correcting the impairments found in the FS strategies or perturbation cued stepping.

2.5 Summary and Study Objectives

PD patients appear to have pronounced impairments in the maintenance of postural stability, in both predictive control and reactive FS strategies. If PD patients are unable to adequately prepare for upcoming instability or maintain stability through FS strategies, the importance of the CIS strategy will be even greater in this population. However, it has been documented that PD patients have difficulty executing self-generated as well as cued steps. Undoubtedly, if CIS strategies are mediated by similar mechanisms as either FS strategies or execution of volitional focal movement, then difficulty in executing CIS strategies will significantly contribute to the postural instability of PD patients. On the basis of these findings, the objectives of this study are:

- To determine the differences between PD patients and control subjects with respect to their postural stability and the spatial and temporal characteristics of their compensatory and volitional stepping, and

- To provide preliminary information as to the influence of PD medication in altering the control of compensatory stepping.
Ability to recover postural stability during compensatory stepping reactions will be measured by incidence of multiple stepping in response to the perturbations. It has been suggested that increased incidence of multiple stepping during forward oriented stepping responses is a useful indicator of postural instability, particularly when later steps are directed so as to recover lateral stability in response to AP oriented perturbations (McIlroy and Maki, 1996). Static and dynamic stability margins have also been suggested as measures of postural instability (Maki and McIlroy, 1999; Pai et al., 2000). In the present study, a complimentary measure of relative position of AP COM at foot contact as a factor of the new base of support was used to estimate static stability margins during stepping responses.

2.6 Hypotheses

When PD patients are OFF medication.

1. They will demonstrate increased postural instability, as measured by increased incidence of multiple stepping and increased COM excursion relative to their new base of support compared to age-matched controls.

2. The timing of their compensatory stepping responses (time to peak APA, time to FO, time to FC, but not latency to onset) will be slower than those of the age-matched controls.

3. PD patients will be unable to modify the temporal and spatial characteristics of their compensatory stepping responses to changes in perturbation magnitude.

Furthermore, on the basis of previous studies demonstrating little effect of medication on improving postural control in the PD population, this study will test the following secondary hypotheses:
4. The use of PD medications (levodopa/carbidopa) will not influence postural stability in the PD population, as evidenced by similar rates of multiple stepping compared with patients off medication.

5. The temporal and spatial characteristics of the volitional and compensatory stepping responses will not be affected by PD medications.
3.1 Subjects

3.1.1 Parkinson’s Disease Patients

Four subjects with a confirmed diagnosis, by a neurologist specializing in Movement Disorders, of idiopathic Parkinson’s disease were recruited for the study. Interested participants were screened with a telephone questionnaire to include subjects who were community dwelling, independently ambulatory (one subject used a cane outside the home), aged sixty to seventy-five, and classified as a Hoehn and Yahr 2.5-3.0 (Hoehn and Yahr, 1967; Fahn et al., 1987). Subjects were excluded from the study if they had a history of falls secondary to dizziness or vertigo, evidence of any other neurological or lower limb musculoskeletal impairment or were unable to effectively communicate verbally (secondary to experimental set-up). See Table 2 for complete inclusion and exclusion criteria.

Table 2: PD Patient Inclusion and Exclusion Criteria

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<thead>
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<th>Inclusion Criteria</th>
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<tr>
<td>Community Dwelling</td>
<td>History of Falls due to dizziness or fainting</td>
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<tr>
<td>Ambulatory</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Confirmed Diagnosis of PD (by Movement Disorders Neurologist)</td>
<td>Musculoskeletal Impairment of Lower Limb (arthroplasty, significant OA, recent fracture, amputation)</td>
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<tr>
<td>Aged 60-75</td>
<td>Other neurological disorders</td>
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<tr>
<td>Able to stand 1 minute unassisted</td>
<td>Diagnosed vestibular disorders</td>
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<tr>
<td>Able to walk 10 m unassisted (cane included)</td>
<td>Uncorrected visual impairments</td>
</tr>
<tr>
<td>Cognitively able to consent and participate in study</td>
<td>Recurrent episodes of dizziness</td>
</tr>
<tr>
<td>Hoehn and Yahr 2.5-3.0</td>
<td>Unable to effectively verbally communicate</td>
</tr>
<tr>
<td></td>
<td>Cardiovascular or other medical conditions that interfere significantly with daily activities</td>
</tr>
<tr>
<td></td>
<td>Medications that affect level of arousal</td>
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<tr>
<td></td>
<td>Medications taken for PD noted (see protocol)</td>
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</table>
Once screened, subjects were booked for a one day visit to the Centre for Studies in Aging at Sunnybrook and Women's College Health Sciences Centre, where all testing took place. PD subjects were all male and had an average age of 65.8 years. Table 3 details the clinical and demographic overview of each subject. Subjects were provided with full details of the experiment, including a demonstration of the platform, prior to signing informed consent as stipulated by the Research Ethics Board of Sunnybrook and Women's College Health Sciences Centre (SWCHSC) (See Appendix A).

3.1.2 Control Subjects

Age and sex-matched control subject raw data were retrieved from a previous study conducted at the Centre for Studies in Aging. The results were processed and analysed in the same manner as the PD subject data and used for comparison with the PD group. Control subjects completed a larger series of trials (please see Appendix B3 for details). Important to note from the control subject protocol is that the unconstrained task conditions remained the first perturbation series. Control subjects responded to unconstrained perturbations in 4 directions and there was one additional set of waveforms. As well, light cued stepping trials were split into two subsets with constrained trials placed in between and there was only one perturbation size (large) during constrained stepping trials in the control subjects. For comparison purposes, only responses to identical perturbation characteristics as the PD protocol were analysed in the control data.
Table 3: Demographic/Clinical Summary of Subjects:

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<th>PD Patients (n=4)</th>
<th>Controls (n=4)</th>
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</thead>
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<tr>
<td></td>
<td>Requip (mg)</td>
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</tr>
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3.2 Experimental Measures and Instrumentation

Perturbations were applied using the unique moving platform system, described in Figure 3, developed at the Centre for Studies in Aging, SWCHSC. Ground reaction forces were measured using three forceplates (one Kistler model 9281, 60 x 40 cm; two AMTI model OR6-5, 51-46 cm), embedded in the floor. During perturbation trials, the data were sampled at 200 Hz and during static sway trials the data were sampled at 50 Hz. Ground reaction force data were used to determine position of and displacement of centre of pressure, time of foot off and foot contact, onset of reaction, timing and magnitude of any anticipatory postural adjustments. Centre of mass displacement was calculated by double integrating shear forces. This technique has been confirmed to be a valid and reliable measure of COM displacement over the brief time periods used in this study (Eng and Winter, 1993: Maki and McIlroy, 1999).

Kinematics were recorded using four high-resolution video cameras shuttered at 1/500 sec. For the kinematic analysis, reflective markers were placed over T10 and S2 spinous...
processes, the sternal notch, xiphoid process, forehead, chin, bilateral temporomandibular joints, radial stylus processes, lateral epicondyles of the humerus, first and fifth metatarsal heads, lateral malleoli, posterior heels, lateral femoral condyles, and greater trochanters of the femur. Video tape recordings were later digitized and reconstructed into three-dimensional coordinates using a video-based motion analysis system (Peak Performance Technologies).

3.3 Platform Perturbations

For all portions of the experiment described, subjects stood on a custom designed moving platform, designed and built at the Centre for Studies in Aging (see Figure 2). The platform was a large, 2 m by 2 m, elevated floor with walls on three sides. There were handrails on all three walls and an overhead track with a safety harness attachment for safety precautions. The floor was marked into one inch squares and foot position markers were taped in place. Platform perturbations were computer controlled 600 ms waveforms with a 300 ms acceleration period followed by a deceleration of 300 ms. Perturbation magnitude details can be found in Table 4. Platform motion was triggered using a manual trigger by the experimenter.
Figure 2: Image of platform setup with subject in place. Forceplates are embedded in floor surface. Handrails are visible for support and front video cameras and light can be seen. Ample room for unconstricted movement in response to platform perturbation is noted.
Table 4: Perturbation Characteristics

<table>
<thead>
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3.4 Experimental Protocol

Each subject was tested in a one-day session at the Centre for Studies in Aging, SWCHSC. The experimental protocol consists of a series of short sets of trials, featuring different task conditions (See Appendix B). Subjects were provided with designated rest periods between sets of trials and were able to stop and rest at any time during testing. During all platform trials, subjects wore the safety harness and one experimenter was standing nearby to provide assistance if necessary.

In order to standardize effect of medication and the ON and OFF states, PD patients participating in the study arrived for the study OFF all PD medication for twelve hours (missing their morning doses), completed the entire sequence of tests described below, and then took their PD medications. A twelve-hour OFF period has been used in previous studies of effects of PD medication on postural control (Bloem et al., 1996; Burleigh-Jacobs et al., 1997; Horak et al., 1997; and 1998).
1996). As well, twelve hours OFF levodopa sufficiently exceeds the half-life of levodopa/carbidopa (2.25 hours) (Cedarbaum, 1990). After an average of forty-five minutes post-administration of PD medications, subjects were considered to be in the ON state. They walked around briefly, were scored on the Unified Parkinson’s Disease Rating Scale (UPDRS) and then repeated the entire sequence of tests (excluding initial baseline tests). All subjects were able to complete the entire experiment, although the protocol for the first subject had minor differences compared to the rest (see Appendix B); primarily he did not complete light cued trials.

3.4.1 Baseline Tests

Prior to commencing with the tests on the moving platform, PD subjects completed a pre-test questionnaire regarding their relative symptoms. Anthropometric measures, including height, weight, preferred base of support position and standardized base of support position were taken. To measure BOS dimensions, subjects stood on paper in their preferred stance and BOS outlines were taken, as well as malleoli height and position. For baseline measures and during all experimental trials, subjects were instructed to stand in standardized foot position markings (width between two heel centres = 11% of height, 14 degrees of external rotation between the medial borders of the two feet). Standardized foot placements were utilized based on average preferred stance positions in 262 healthy adults ranging in age from 19-97 years (McIlroy and Maki, 1997). Results from this study (McIlroy and Maki, 1997) demonstrated a wide range in preferred stance width and angle. Previous studies (Day et al., 1993; Kirby et al., 1987) have found that stance width may influence balance responses and thus standardization of stance width within an experimental paradigm is important to reduce these potential effects. BOS dimensions were also recorded in the standardized foot position used for all trials. As well,
subjects held a curved handlebar behind their backs (arms resting comfortably at sides) during all testing. The handlebar was used to minimize upper extremity responses during the compensatory balance reactions, as the purpose of this study was to examine lower extremity compensatory stepping responses. In order to standardize body position between dynamic and static tests, the handlebar was used throughout all testing.

The first set of trials consisted of two static standing trials, one with eyes open and one with eyes closed. Subjects were instructed to stand as still as possible, with feet in the standardized foot position, looking at a marker placed at eye level on the wall straight ahead as a focal point for eyes open conditions. The trial lasted 77 secs and was then repeated with eyes closed, and a blindfold in place.

3.4.2 Perturbation Induced Stepping Trials

For the rest of the trials, subjects started each trial in the standardized foot position with one foot on each of the anterior two forceplates. In the first series of trials, described as the unconstrained trials, subjects were instructed that after being told that the trial would begin, the platform would move suddenly and then stop in either the forward or backward direction, as detailed above. During all moving or stepping trials, subjects were never cued as to the direction or size of the next platform translation, nor the precise start time, so as to maximize unpredictability. During the unconstrained trials, subjects were presented with perturbations of two magnitudes and two directions (see Table 4). In order to maximize natural behaviour, subjects were asked to do whatever came naturally to recover their balance. As discussed earlier, subjects held a handlebar during all trials in order to minimize upper extremity movement and
subjects were asked not to try not to use their arms. Prior to the trials commencing, subjects
looked at the marker straight ahead and counted backward aloud by three’s from a number
provided by the experimenter. Counting backwards was used as a distraction task in order to
maximize the unpredictability of the upcoming perturbations. Subjects were instructed to count
backwards until the trial was over. Subjects were not instructed as to any specific behaviour
during these twelve trials, but did hold the handlebar behind their backs in order to minimize
movements of the upper extremities and limit upper extremity reactions as lower extremity
reactions were the focus of this study.

3.4.3 Cued Stepping Trials

During the next two sets of trials, subjects started each trial in the standardized foot
position. They were instructed to step as quickly as possible to the targets placed on the floor as
soon as they were cued by either the light or the platform motion. Step distances were marked
on the floor (30 cm forward and 20 cm backward). These distances were selected as they
represent average step distances in healthy adults to equivalent perturbations as those used in the
constrained stepping trials (McIlroy and Maki, 1996). Step distances during cued trials were
standardized for all PD patients in order to compare timing of stepping responses across groups.
Subjects practiced stepping prior to commencement of the trials until they were able to step to
the target while looking straight ahead with either foot. Subjects were not told which foot to step
with in any of the cued trials.

3.4.3.1 Light Cued

During the first of the two series of trials, stepping was cued with forward or backward
light cues. A cue light (LCD display) was placed at eye level, straight ahead of the subjects and
either the top row (step forward) or the bottom row (step backwards) of lights illuminated after trial commencement. A total of six randomized light cued trials (three forwards, three backward) were completed.

3.4.3.2 Perturbation Cued

Following the light cued trials, a second set of cued stepping trials was completed (called constrained stepping trials). Subjects were again asked to step as quickly as possible to one of the targets after the cue. However during this series, the cue was either forward or backward platform motion. The platform moved at three different amplitudes (see Table 4). Subjects were instructed that the platform motion would direct their step direction. Subjects practiced stepping to the targets again prior to commencement of this series. A series of twelve trials was completed (nine backwards translations, three forward translations)

3.5 Data Analysis

3.5.1 Trials

Control subjects completed a total of 136 trials (4 subjects) in the three task conditions examined. PD patients completed a total of 122 trials in the OFF condition (4 subjects) and another 110 trials in the ON condition. Please see Appendix B1-3 for protocol details. Out of the total, trials were omitted from analysis for the following reasons:

- If they were not backward perturbations (of perturbation trials), or forward oriented cues (light cued)
- Second waveform omitted for control subjects in order that only like waveforms were compared between the two groups
If onset of reaction occurred later than 600 ms after the onset of platform acceleration or light cue, in order to remove trials in which a reaction occurred only in response to the platform deceleration.

- Trials in which no step occurred were not analysed

- In PD patients, a small number of trials (one large unconstrained and one small unconstrained) in which the first step was a very small step in the wrong direction were also omitted

- For between group analysis, only large constrained trials were analysed in the PD patients as control subjects did not complete small or medium sized perturbations

3.5.2 Post-processing of Data

The timing points of interest for this study were onset of platform acceleration, onset of stepping reaction, time to peak APA, time to foot off and time to foot contact (see Figure 3). Onset of reaction was determined as the point when ML COP excursion exceeded 4 mm beyond the starting COP position. This lateral excursion of the COP has been used in previous studies as a reliable marker for the onset of stepping behaviour (McIlroy and Maki, 1999). Peak APA was the maximum lateral COP position under the swing foot prior to foot off. Foot off was the point at which less than one percent of body weight was under the swing foot and foot contact was taken as the point at which body weight under the swing foot returned to more than one percent. Centre of mass displacement values were calculated by double integrating the shear forces from perturbation onset up to these timing points. Figures 3 and 4 provide an illustration of the temporal and spatial parameters measured in the data analysis.
Figure 3: Illustration of temporal and spatial parameters reported in results, including vertical force changes, COP and COM displacement. Subject stepped forward with right foot (light cued task condition). Timing points marked are (1) onset of light cue, (2) onset of step, (3) time of peak APA prior to foot off, (4) time of foot off, and (5) time to foot contact. COM displacement noted to point of foot contact: COM calculation accuracy drifts after this point and is therefore removed.
Figure 4: Illustration of spatial parameters measured during stepping trials. In this trial, subject took one step with the right foot. AP1 is the AP step length of the first step and ML1 is the ML step length of the first step. Foot position was always marked from the reflective marker on the fifth metatarsal head.
Kinematic analysis was completed by manually coding all of the stepping trials to determine the number of and type of steps taken, step direction, forceplates stepped on, other body movements and the spatial coordinates of the feet prior to and after each step. Visual coding of foot position using the position of the fifth metatarsal reflective marker relative to the grid marked on the platform has been found to be a simple and reliable method (accurate within 1 cm) in previous studies in the lab (McIlroy and Maki, 1996). These coordinates were used to determine anteroposterior step length and mediolateral step length. Occurrence of stepping was confirmed between kinematic and ground reaction force data. Stability margins during stepping responses were characterized by examining the AP COM at FC (relative to starting position) as it related to the new stability limits (BOS). This measurement was taken as the relative AP COM at FC/AP Step Length of the first step (in percent) and labeled COMPT. This measurement provides an indication as to how close subjects were to their new stability limits at the end of the first step.

Data analysed in this study were limited to that gathered during backward perturbations and forward oriented volitional stepping responses. The rationale for this specific focus was based on two factors. First, previous studies focussing on compensatory stepping have suggested the occurrence of multiple stepping in forward directed steps, as opposed to backward steps, was more likely to be the result of instability as opposed to a control strategy (Luchies et al., 1994). Second, it was necessary to keep the number of perturbation trials to a minimum for the PD patients. The need to test multiple amplitudes of backward perturbations permitted the use of only a limited number of forward perturbations primarily to ensure stimulus unpredictability. In the present study, the comparison of the control of compensatory stepping responses with that of
Volitional stepping was of interest, and therefore, analysis of backward perturbations and therefore forward oriented stepping responses was considered most appropriate.

3.5.3 Statistical Analysis of Data

Unless otherwise noted, all comparisons of PD patients versus control subjects were made with PD patients OFF medication. Analysis of modifiability of stepping responses was also made with PD patients off medication. Secondary analysis, evaluating the influence of medication, was achieved by within patient comparisons made possible by having patients off medication for a standardized (twelve hour) period and testing OFF medication prior to being tested ON medication. All statistical analysis was performed using the SAS statistical analysis software package (Version 6.0. SAS Institute Inc. Cary, North Carolina). For all tests the significance level was set at p<0.05. Data are presented as mean ± standard error (except frequency counts). Error bars on figures represent standard error (SE) throughout.

3.5.3.1 Incidence of Multiple Stepping

Stepping trials in which more than one step occurred in response to the perturbations or light cue were analysed to determine incidence of multiple stepping. Chi square analysis was completed for non-parametric analysis of frequency of multiple stepping data across groups (PD off vs. control group) and across medication (ON vs. OFF. PD patients, constrained and unconstrained tasks separately). Continuity adjusted Chi-square values were taken secondary to some cell counts representing less than 5% of the overall count.
3.5.3.2 Spatial and Temporal Characteristics of Stepping Responses

Two-way analyses of variance (ANOVA) were completed on all dependent spatial and temporal variables (time to onset, time to peak APA, time to FO, time to FC, APA amplitude, step length, COMPT). For comparisons between groups two factors (group[between subject] and tasks[within-subject]) were tested since patients were only compared in the OFF state. Comparisons within the PD population were also contrasted using a repeated measures ANOVA. In such ANOVAs the main effects were task (within-subject), medication (within-subject) and perturbation amplitude (within-subject). A priori contrasts were conducted to test the specific experimental hypotheses (e.g. timing values would not decrease with increasing perturbation magnitude). Post hoc multiple comparison analyses were completed using Scheffé's post hoc test, for all other comparisons.
Chapter 4.0 Results

4.1 Baseline Measures

There was no difference between groups in the AP or ML average COP position prior to onset of trials (AP $F_{1,6}=1.95, p=0.2$, ML $F_{1,6}=0.2, p=0.7$), nor was there a significant effect of task on this position (AP $F_{1,6}=1.3, p=0.3$, ML $F_{1,6}=0.04, p=0.96$). Both groups behaved similarly across tasks as well, as there was not significant interaction between group and task. Prior to commencement of platform trials, PD patients’ BOS was traced in patients’ preferred stance position and in the standardized stance position. When comparing the dimensions of these two positions, it was found that PD patients preferred to stand in a narrower stance position than the standardized position (preferred $38.5\pm 1.8$ cm. standardized $43.6\pm 0.7$ cm. paired $t=3.9, p=0.03$). There was no statistical difference in BOS length or in the distance between the heels in the two positions.

4.2 Perturbation Induced Instability: PD Patients versus Controls

PD patients demonstrated an increased frequency of multiple stepping in response to the backward perturbations in contrast to the control group (91.7% vs. 16.7%), when these perturbations were the most novel and unpredictable (unconstrained trials, off medication) ($X^2_{11}=10.74, p=0.001$). All PD patients behaved similarly, with three of four patients taking multiple steps during 100% of trials and one patient taking multiple steps 75% of the time. In contrast, two control patients never took multiple steps, and the other two did so 33.3% of the time. It is noteworthy that there were no incidents of multiple stepping in response to the light cues in any subject (PD or control).
A complimentary measure of instability used in the present study was the stability margin measured as the relative position of AP COM at foot contact (see Figure 5). The PD patients executed initial stepping responses in which the COM was closer to the new limits of their BOS (COMPT PD 52.29 ± 4.94% Ctrl 37.64 ± 3.59 %), when compared with age-matched controls. These results approached statistical significance (COMPT $F_{1,6}=5.42$, $p=0.06$). There was also a significant difference between tasks (Co 52.1 ± 4.08%, Li 16.17 ± 1.6%, Un 66.28 ± 3.62%); $F_{2,16}=21.61$, $p=0.0002$). During unconstrained trials, the centre of mass was closest to the new base of support boundaries; COMPT was smallest during the light cued trials (see Figure 5) for both PD and control subject groups. When tasks were compared using multiple comparison analysis, all tasks were found to be different from one another (Scheffé $p<0.05$).

Importantly, there was no statistically significant interaction between the task (light-cued, constrained and unconstrained) and group (PD versus controls) for COMPT ($F_{2,11}=0.16$, $p=0.86$). The differences between PD and control subjects were consistent across the task conditions as highlighted in Figure 5. Noteworthy is the fact the PD subjects, during unconstrained trials, featured the narrowest distance between the limits of the BOS and the position of the COM at foot-contact (Figure 5).

When PD patients were reviewed individually, all PD patients stepped with larger excursions of their COM relative to their new stability limits compared with individual data for the control group for all task conditions (see Figure 6). There was some variation in the task effects in the four PD subjects. In three of four patients, the position of the COM was closest to the stability limits in the unconstrained trials, whereas in one subject it was closest during the constrained trials. However, the COM was always farthest from the stability limits in the light cued trials (3/3 subjects).
In summary, PD patients demonstrated increased incidence of multiple stepping in response to platform perturbations, coupled with COM excursions that were closer to their new stability limits at the end of the first step. This was most evident during unconstrained task conditions.

4.3 Timing of the Stepping Response: PD Patients versus Control Subjects

The second main hypothesis, that PD patients would be slower to execute compensatory stepping responses, was characterized by latency to onset, as well as timing of step execution (time to peak APA, time to FO, time to FC). There was a significant effect of task on all timing parameters across groups (see Figure 7). (onset $F_{2,11}=22.2$, $p=0.0001$, APA $F_{2,11}=213.59$, $p=0.0001$, FO $F_{2,11}=121.89$, $p=0.0001$, FC $F_{2,11}=190.51$, $p=0.0001$). Step execution in light cued trials was always slower than in unconstrained trials and responses in constrained trials were always fastest. This occurred for both PD and control subjects. Multiple comparison analysis revealed that, at onset, the task effects arose from differences between light cued and constrained trials, as well as unconstrained and constrained trials (Scheffé, $p<0.05$). In contrast, although there was a 30 ms mean difference in onset latency between unconstrained and light cued stepping trials, there was no statistically significant difference in onset latency of the stepping responses between these tasks.

When the timing of stepping responses was compared between the PD patients and the control group, it was found that PD patients were significantly slower in the execution of the stepping responses when considering all task conditions. (APA $F_{1,6}=7.89$, $p=0.03$, FO $F_{1,6}=19.59$, $p=0.004$, FC $F_{1,6}=14.21$, $p=0.009$) but not in the latency to onset ($F_{1,6}=0.01$, $p=0.93$).

Important to the present study was the fact that such group differences between PD and control subjects arose from differences in the light-cued trials but not the unconstrained stepping
PD Patients' COM at FC Is Closer to Their New Stability Limits

Unconstrained

Light Cued

Constrained

Figure 5: Relative AP COM excursion as it relates to the AP step length (new stability limits) in PD patients and control subjects, for each of the three tasks. Groups differences were largest during unconstrained task conditions. Both groups displayed similar task effects.
Figure 6: Task affected the relative excursion of the COM/stability limits (COMPT) similarly in PD patients and control subjects. In three of the four patients and controls, COMPT was always longest during unconstrained trials. In all subjects, COM was always furthest from the stability limits during light cued trials. Standard error was very small for control subjects 2 and 4.
trials (highlighted by interaction between task and group on time to peak APA \(F_{2,11}=18.07, p=0.0003\), time to FO \(F_{2,11}=18.01, p=0.0003\) and time to FC \(F_{2,11}=29.77, p=0.0001\)). The differences between groups in timing at foot-contact was highlighted by responses that were 300 ms more rapid for the control group as opposed to PD patients for the light-cued trials (see Figure 7). In contrast to the experimental hypothesis, PD patients were actually 30 ms faster to onset of stepping and 15 ms faster in step execution (time to foot-contact) than the control group in unconstrained stepping trials. Similarly they were only 55 ms slower in time to foot-contact for constrained stepping. In order to determine that group observations were consistent across individual PD patients, data were examined on an individual patient basis. All subjects demonstrated similar task effects on the timing of step execution, with light cued trials being slowest and constrained trials being fastest (see Figures 8 and 9). Individually, all PD patients were as fast in executing compensatory stepping responses in the unconstrained conditions as the control subjects, whereas they were always slower in executing volitional steps to light cues (see Figures 8 and 9).

To confirm that timing characteristics were not influenced by specific phase duration differences, the duration of each phase of the stepping reactions (APA duration, unloading duration, swing duration) were also compared across groups. As step length influences swing phase duration, swing phase velocity was calculated and compared. As was found in timing of step execution, when all task conditions were considered, PD patients stepped with longer APA duration, and longer unloading time but not a slower swing velocity than the control subjects (APA \(F_{1,6}=5.2, p=0.06\), Unload \(F_{1,6}=8.1, p=0.03\), Swing velocity \(F_{1,6}=2.8, p=0.2\)). Again, group differences observed in the duration of the step execution arose from differences in the light cued task condition, as evidenced by significant group vs. task interaction (APA duration \(F_{2,11}=3.7\).
Unloading duration $F_{2,11}=6.7, p=0.01$). Light cued trials were highlighted by 130 ms differences in APA duration between the groups and 140 ms differences in unloading duration. In contrast, during unconstrained trials, PD patients exhibited APAs that were only 40 ms longer than those of the controls and were actually 10 ms faster in unloading their limb than their control counterparts. Of interest, PD patients did exhibit APAs more frequently than the control subjects during these unconstrained trials (PD 75% vs. Ctrl 25%. $X^2_{1,1}=4.2, p=0.04$).

While PD patients appear to be slower in executing cued volitional stepping responses they were able to generate rapid stepping when engaged by induced instability. During these novel platform perturbations, PD patients were able to step as quickly as their age-matched controls.

4.4 Response Modifiability to Amplitude of Perturbation: within PD Patients

The third main hypothesis related to the ability of PD patients to modify the temporal and spatial parameters of their stepping responses when perturbation characteristics changed unpredictably. Timing and spatial characteristics of the stepping responses were compared between the three magnitudes of perturbation during the constrained trials (OFF medication). During the perturbation cued constrained stepping trials, PD patients increased the speed of execution (time to peak APA, time to FO and time to FC) of stepping responses to increasing magnitude of perturbations (see Figure 10). These decreased times to execution were found to be significant using a priori contrasts (APA $F_{1,6}=7.6, p=0.03$, FO $F_{1,6}=11.12, p=0.02$, FC $F_{1,6}=20.63, p=0.004$). In contrast, perturbation size did not have a significant effect on the latency to onset ($F_{1,6}=2.96, p=0.14$) of stepping reactions in the constrained stepping trials.

When examining the effect of perturbation size on the timing of step execution, it was found that three of the four patients behaved in the same manner (see Figure 11), increasing the
Figure 7: PD patients are slower to execute stepping reactions than age-matched controls during light cued trials. The slowed stepping execution was not seen during compensatory stepping responses, particularly during the unconstrained trials. Onset latency was not different between groups during any task.
Figure 8: All four PD patients demonstrated similar task effects on the timing of step execution, with constrained trials always being fastest and light cued trials always being slowest (Patient 1 did not complete light cued trials).
Figure 9: All four control subjects also demonstrated similar task effects on the timing of step execution with constrained trials always being fastest and light cued trials always being slowest.
speed of step execution when perturbation size increased. Patient 2 increased execution speed from medium to large perturbations, but actually decreased his speed between small and medium perturbations. It is noteworthy that when this patient was reviewed ON medication, he behaved like the other patients and demonstrated a consistent increase in execution speed with increasing perturbation size.

During the constrained stepping trials, perturbation size was also found to influence step length and COMPT. AP step length was shortest in response to the small perturbations (sm 24.51 ± 2.41 cm, me 28.03 ± 2.71 cm, lg 30.57 ± 2.41 cm). These step length differences were statistically significant (Stepap $F_{2,6}=8.11, p=0.02$). The position of the COM with respect to the new base of support limits was smaller in response to the small magnitude perturbations and increased in response to the large perturbations (sm 20.97 ± 2.87%, me 41.07 ± 5.32%, lg 57.06 ± 7.13%, $F_{2,6}=25.02, p=0.001$). Multiple comparison analysis revealed that step length differences were secondary to differences between small and large size perturbations (Scheffé, $p<0.05$). Differences in the position of the COM with respect to the new base of support were secondary to differences between all three sizes (Scheffé, $p<0.05$).

When reviewing results on an individual basis, spatial parameter findings tended to be more variable between subjects. When examining the effect of perturbation size, it was found that two of the four patients increased step length with increasing perturbation size (see Figure 12). One patient did increase their step length from small to medium sized perturbations, but then step length decreased (slightly) when comparing between medium and large magnitudes. The fourth patient increased step length from medium to large perturbations, but the step length in the small perturbation trials was actually the largest. These two patients demonstrated more consistent increases in step length with increasing perturbation size when examined ON
medication. In contrast, all patients’ AP COM at foot contact approached their new stability limits with increasing perturbation size (see Figure 13).
PD Patients Modify Timing of Stepping Reactions

Figure 10: During the constrained task conditions (perturbation cued stepping), PD patients increased the speed of their stepping responses as perturbation magnitude increased. These findings were statistically significant (APA p=0.03, FO p=0.02, FC p=0.004). In contrast, perturbation magnitude did not affect onset latency (p=0.14).
Figure 11: During constrained stepping trials, three of the four PD patients demonstrated similar responses to changes in perturbation size, decreasing the time of step execution (APA, FO, FC) as perturbation magnitude increased. Onset latency did not change with magnitude changes. PD patient 2 decreased time of step execution between medium and large magnitudes of perturbations but was faster responding to the small sized perturbations compared with the medium sized ones. Absence of a SE bar for PD patient 4 at FC was secondary to a missing value at FC only, as the patient's foot landed off the forceplates.
Figure 12: During constrained stepping trials, two of the four PD patients demonstrated increasing step length with increasing perturbation size when OFF medication. Patient 1 increased step length between small and medium perturbations but not to large. Patient 4 decreased step length between small and medium sized perturbations and then increased it slightly to large perturbations.
Figure 13: During constrained stepping trials, the position of the AP COM approached the new stability limits with increasing magnitudes of perturbation. This effect was consistent in all four PD patients.
4.4 Spatial Characteristics of Stepping Responses: PD Patients versus Control Subjects

In order to address the observation of increased perturbation-induced instability in the absence of significant differences in timing between PD patients and control subjects, as well as intact modifiability of stepping responses during compensatory stepping in the PD patients, the spatial characteristics of the stepping responses were further examined. Specifically focusing on the initial step as well as the characteristics of multiple stepping, the present analysis focuses on group differences across the three task conditions, when PD patients were OFF medication.

In addition to the noted difference in COMPT, discussed in section 4.1, there was also an important group difference featuring the PD patients' tendency to step with shorter steps, when compared with age-matched controls. As anticipated, there were mean differences in AP step length across task conditions (Un 25.57 \pm 1.67 \text{cm}, Li 29.01 \pm 1.34 \text{cm}, Co 31.02 \pm 1.57 \text{cm}), but these differences were not significant ($F_{2,11} = 1.96, p=0.19$). The tendency for PD patients to step with shorter AP step lengths occurred primarily in the responses to unconstrained task conditions. Mean differences in responses to unconstrained trials in AP step length (PD 21.01 \pm 1.55 \text{cm}, Ctrl 29.74 \pm 2.33 \text{cm}) were large and statistically significant ($F_{1,6} = 6.51, p=0.04$). This contrasted limited differences between groups when comparing between light cued ($F_{1,6} =1.54, p=0.27$) or constrained ($F_{1,6} =0.05, p=0.83$) stepping conditions (see Figure 14).

As a group, constrained trials were always associated with the longest steps and unconstrained with the shortest. this effect was consistent when subjects were examined individually (see Figure 15). In three of the four PD patients, AP step length was the longest during constrained trials and the shortest during unconstrained. In the fourth PD patient
constrained step length was actually 3 cm shorter than during unconstrained responses. In all PD patients the step lengths to unconstrained trials were shorter than light-cued trials (Figure 15).

In contrast to differences in AP step length there were no such differences in the ML step length on the individual step (PD 1.49 ± 0.42 cm, Ctrl 2.44 ± 0.53 cm) (F_{1,6} = 0.78, p = 0.41). Similarly there were no differences in the mediolateral APA COP excursions between PD patients and the control subjects (PD 2.60 ± 0.34 cm, Ctrl 3.0 ± 0.47 cm, F_{1,6} = 0.00, p = 0.99, see Figure 16).

As anticipated, there was a significant difference in APA amplitude, expressed as both COP and COM excursions when comparing across tasks (see Figure 16), with the largest APAs during the light cued condition, followed by constrained and then unconstrained trials (COP \( F_{2,11} = 10.58, p = 0.003 \), COM \( F_{2,11} = 52.74, p = 0.0001 \)). Multiple comparison analysis revealed that all three tasks were significantly different from one another (Scheffé \( p < 0.05 \)). APA amplitude differences, expressed as the mediolateral excursion of the COM at foot off, were statistically significant comparing between groups (PD 1.02 ± 0.28 cm, Ctrl 0.53 ± 0.17 cm, \( F_{1,6} = 8.75, p = 0.03 \)). Importantly, these differences between PD and control subjects were associated with light-cued stepping (mean difference 2 cm), as evidenced by a significant task-group interaction (\( F_{2,11} = 8.5, p = 0.006 \)). PD patients executed much larger APAs (as measured by ML COM excursion) in the light cued trials compared to the controls. In contrast, there was little difference between the ML COP/COM comparing between PD and controls when considering constrained and unconstrained task conditions (see Figure 16).

Results to this point have focused on the temporal and spatial characteristics of the first step during volitional and compensatory stepping responses in the PD patients and controls. Multiple stepping responses during the unconstrained trials were also reviewed in both groups to
examine the spatial characteristics of the second steps during these trials. This review focused on the placement of the second step and the leg with which the subjects stepped.

Typically, when control subjects took multiple steps it involved stepping with the same foot as the first step (100% of trials involving multiple stepping). This second step returned the foot back close to the starting position in the AP direction, but was also placed in a more lateral position (see Figure 17). Of the trials with multiple steps, PD patients stepped with the same foot during 23.1% of the trials but with the opposite foot during 76.9% of the trials. When stepping with the same foot, PD patients exhibited similar patterns as the control subjects, returning towards their starting AP position but with a lateral component to the step (see Figure 18). It is noteworthy, however, that during these trials, PD patients’ first steps were 20 cm shorter than those of the controls. In contrast, when PD patients’ second step was with their opposite foot, it was a second small AP step with very little change in the ML position (relative to the starting foot position) (see Figure 18). Again, these steps were much shorter than those of the control subjects as well as compared to stepping responses in PD patients in which only one step was taken to recover stability ("none" in Figure 18).

Overall, PD patients took shorter steps than the age-matched control subjects, specifically during unconstrained task conditions. These shorter steps appear to be associated with the increased incidence of multiple stepping seen in the PD patients and two patterns of multiple stepping have emerged from the results.

### 4.4.1 Influence of Medication: within PD Patients

To address the secondary question of the influence of medication, the prevalence of multiple stepping was contrasted within PD patients comparing ON and OFF states. PD patients were
PD Patients Take Shorter First Steps than Controls

Unconstrained

Light Cued

Constrained

Figure 14: PD patients tended to take shorter first steps than control subjects during unconstrained and light cued stepping trials. This difference was corrected during large sized constrained stepping trials.
Figure 15: PD patients 1-3 demonstrated similar task effects on step length, with shortest steps during unconstrained task conditions and longest steps during constrained trials. Patient 4 stepped with the shortest steps in response to the constrained task conditions. Patient 1 did not complete light cued trials. Step length between tasks was more variable in control subjects.
Effect of Group on APA Amplitude
Unconstrained Trials

Light Cued Trials

Constrained Trials

Figure 16: Group differences in ML COM at FO arose primarily from differences during the light cued task condition. Positive COM is in stabilizing direction (towards stance side)
Figure 17: During unconstrained compensatory stepping trials, control subjects executed compensatory stepping reactions with only one step (none) in 10/12 trials and these steps were on average large AP oriented steps with no ML component. In contrast, during the 2/12 trials, in which the control subjects took more than one step so as to recover balance, they took the second step with the same foot as the first (same) on both occasions. During these two trials, the first step continued to have a large AP component, but also a ML component. In the second step, the subjects took a large backward step, close to their AP starting position, but even further laterally.
Multiple Step Characteristics-PD Patients

Figure 18: During unconstrained compensatory stepping trials, PD patients executed compensatory stepping reactions with only one step (none) in 1/14 trials; this step was a large AP oriented step with no ML component. In contrast, during 3/13 trials in which the PD patients took more than one step so as to recover balance, they took the second step with the same foot as the first (same). During these three trials, the first step had a large AP component, although 20 cm shorter than control subjects, but also had a significant ML component. In the second step, the subjects took a large backward step, close to their AP starting position, but even further laterally. During 10/13 multiple stepping trials, PD patients took the first step with one foot and the second with the other (opposite). During these trials, both steps were short AP oriented steps, compared with control subjects and with PD patients’ single steps, and both steps had small ML components in opposite directions. The starting position is different for the two steps as all subjects stood in a standardized foot position with heels placed 11% of their height apart. Heel width distance is illustrated here as the average, based on average height.
more likely to take multiple steps in the unconstrained conditions when in the OFF state as opposed to the ON state (OFF 91.7%, ON 18.2%, $X^2_{11}=9.81$, $p=0.002$). In contrast, there was no effect of medication during the constrained stepping trials when patients were told to step in response to the perturbation (OFF 23.7%, ON 13.5%, $X^2_{11}=0.70$, $p=0.40$).

In addition, PD patients tended to be slightly faster to respond and execute steps when on PD medication; these results, however, were not statistically significant (onset $F_{1,8}=3.39$, $p=0.16$, APA $F_{1,8}=1.41$, $p=0.32$, FO $F_{1,8}=1.77$, $p=0.28$, FC $F_{1,8}=1.77$, $p=0.28$). There was no significant interaction between task conditions and medication, although at onset and foot contact, differences approached statistical significance (Figure 19: onset $F_{2,4}=6.06$, $p=0.06$, APA $F_{2,4}=0.91$, $p=0.47$, FO $F_{2,4}=3.29$, $p=0.14$, FC $F_{2,4}=5.93$, $p=0.06$). This was highlighted by the observation that the influence of medication was largest in light cued trials for all four measures (onset, peak APA, foot off and foot contact). In fact, during unconstrained stepping trials, PD patients were actually slower when ON medication than when OFF.

There were also no significant effects of medication on AP step length or COMPT (step length $F_{1,8}=2.86$, $p=0.19$, COMPT $F_{1,8}=2.58$, $p=0.21$), although there was a general trend of an increased step length (4 cm), coupled with a decrease in COMPT (7.5%) when PD patients were ON medication. There was, however, a significant difference in the mean APA amplitude, as expressed by ML COP excursion (OFF 3.24 ±0.3 vs. ON 4.02± 0.35 cm, $F_{1,8}=14.21$, $p=0.03$), but not in the resultant mediolateral COM excursion at foot off (OFF 1.36± 0.24 vs. ON 1.27 ±0.21 cm, $F_{1,8}=0.03$, $p=0.87$) between the OFF and ON medication states. There was no interaction between the effect of task and the effect of medication on any of the spatial parameters discussed ($p>0.80$).
With regard to the modifiability of the response, PD medication did not affect the relationship between perturbation size and speed of execution of stepping (Onset $F_{1.3} = 0.00$, $p=0.97$ Peak $F_{1.3} = 2.41$, $p=0.22$, FO $F_{1.3} = 2.28$, $p=0.22$, FC $F_{1.3} = 3.12$, $p=0.18$; nor was there any significant interaction between medication and perturbation size (Onset $F_{2.6} = 0.79$, $p=0.50$. Peak $F_{2.6} = 0.54$, $p=0.61$, FO $F_{2.6} = 0.90$, $p=0.45$, FC $F_{2.6} = 1.12$, $p=0.39$). Medication also did not influence the modifiability of the spatial parameters of stepping (step length $F_{1.3} = 2.67$, $p=0.20$; COMPT $F_{1.3} = 0.82$, $p=0.43$; ML COP $F_{1.3} = 1.83$, $p=0.27$), except for the change in relative ML COM at foot off (OFF =1.3 ± 0.3 cm, ON=1.06 ± 0.2cm, $F_{1.3} = 5.96$, $p=0.09$). There was no evidence of interaction between effect of size and effect of medication ($p$'s $>0.18$)

PD medication did not significantly change the temporal and spatial characteristics (analysed up to foot contact of the first step) of the compensatory stepping responses in the PD patients, although there was a general trend toward faster, larger responses when ON medication. Medication also appeared to have a preferential effect on cued volitional responses compared to compensatory responses. Despite this finding, PD patients did execute compensatory stepping responses with a decreased incidence of multiple stepping when on PD medication.
Figure 19: PD patients tended to step more quickly when ON PD medication than when OFF, but these differences arose from faster responses during light cued volitional stepping trials.
Table 5: Summary of Results:

<table>
<thead>
<tr>
<th>Factor</th>
<th>Summary of Results</th>
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<tbody>
<tr>
<td><strong>Group</strong></td>
<td>PD patients demonstrated increased incidence of multiple stepping</td>
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<tr>
<td></td>
<td>PD patients’ COM was closer to their stability limits of their first step than the control subjects</td>
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<tr>
<td></td>
<td>PD patients stepped with shorter first steps than control subjects, particularly during compensatory stepping trials</td>
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<tr>
<td></td>
<td>PD patients were not slower than control subjects in executing compensatory stepping responses</td>
</tr>
<tr>
<td></td>
<td>PD patients were able to modify the temporal and spatial characteristics of their stepping responses to changes in perturbation magnitude</td>
</tr>
<tr>
<td><strong>Task</strong></td>
<td>Responses in light cued trials were always slower. These task differences were more pronounced in the PD group</td>
</tr>
<tr>
<td></td>
<td>In PD patients, shortest steps were taken during unconstrained trials, and COM was closest to the stability limits during these trials</td>
</tr>
<tr>
<td><strong>Medication</strong></td>
<td>PD patients responded with fewer multiple stepping reactions when ON medication</td>
</tr>
<tr>
<td></td>
<td>Medication had little effect on the temporal and spatial characteristics of the first steps of compensatory stepping responses</td>
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Chapter 5.0 Discussion

5.1 Discussion of Study Findings

The purpose of this study was to determine if PD patients demonstrated impairments in the execution of their compensatory stepping responses and to explore the consequences of such impairments on their postural stability. It was hypothesized that PD patients would demonstrate increased postural instability, as measured by increased incidence of multiple stepping. As well, PD patients would be slower to execute stepping responses and they would have difficulty modifying these responses to changes in perturbation characteristics.

In this study, PD patients reacted to the most novel, unpredictable perturbations by taking multiple steps 92% of the time. When taking multiple steps, PD patients' COM was closer to their new limits of stability at foot contact of the first step than the control group, as well as compared to their own steps during constrained trials, suggesting that such high incidence of multiple stepping is an indicator of the increased instability and therefore falls risk in this population. Although PD patients were slower to execute volitional stepping responses, the timing of their compensatory stepping responses was not different from that of the controls. They did, however, take smaller steps than control subjects. As well, they were able to modify their stepping reactions (temporal and spatial parameters) to the changing magnitudes of perturbation during the constrained stepping trials.

5.1.1 Frequency of Multiple Stepping

PD patients demonstrated a dramatic increase in the incidence of multiple stepping when compared to age-matched controls, supporting the first hypothesis. Literature in the past
McIlroy and Maki. 1996) has suggested that such increased incidence of multiple stepping, particularly in forward oriented steps, can be seen as an indicator of postural instability. However, there remains some controversy over the interpretation of the occurrence of multiple steps taken in response to applied perturbations. Some have argued that such stepping reflects a strategy to improve stability rather than being a consequence of dyscontrol (Luchies et al., 1994). In Luchies’ study, the authors hypothesized that older adults took multiple, fast, short steps in response to backward pulls as a strategy choice. However, in the present study, there appears to be some evidence to support the view that such multiple stepping may be the consequence of disrupted control of balance reactions: (1) absence of multiple stepping during light cued and constrained task conditions, (2) decreased incidence of multiple stepping when on PD medication, and (3) COM excursion approaching stability limits during multiple stepping reactions.

PD patients were able to decrease the incidence of multiple stepping during the perturbation cued, constrained stepping trials, even though the perturbation parameters were identical to those in the unconstrained trials. It would appear that prior instruction to step to the target and hold the position, combined with a perturbation stimulus, provided an external cue that PD patients were able to use to take larger steps that appear to increase their postural stability. These findings are similar to those of Burleigh-Jacobs and colleagues (Burleigh-Jacobs et al., 1997) who found that characteristics of PD patients’ stepping responses more closely resembled those of controls subjects when cued to step by a perturbation. They hypothesized that these external sensory triggers (Burleigh-Jacobs et al., 1997; Horak and Frank, 1993) allowed for the engagement of an appropriate stepping responses without involving the impaired basal ganglia pathways. In volitional stepping and during gait, PD patients have shown improvements in their
stepping behaviour with visual and auditory or verbal cues (Behrmann et al., 1998; Hanakawa et al., 1999; Thaut et al., 1996). It is possible that similar mechanisms are available to PD patients during the cued stepping reactions such as those described above. It is unclear, however, whether such external stimuli would be beneficial in the execution of a response to a truly unpredictable perturbation. There is also the possibility that the instruction to step to the target provided the PD patients with an implicit instruction to limit their response to one step. These perturbations were, however, of the same magnitude and unpredictability as those in the unconstrained condition and it is important to note that the PD patients were able to regain stability with only one step in over 75% of the perturbation cued trials. It is also noteworthy that in 23.5% of perturbation cued trials PD patients took more than one step, despite any explicit or implicit instruction or cue. Order of tasks may also have impacted on the incidence of multiple stepping in the constrained trials. Constrained trials were always presented after unconstrained trials in order to ensure that unconstrained trials were the most novel. Previous studies by Maki and colleagues (Maki et al., 1999) have demonstrated that repeated blocks of trials similar to those presented in the present study may reduce multiple stepping by over 40%. Although the two blocks of trials (unconstrained and constrained) were not identical (see Appendix B), perturbation characteristics were similar and may have enabled learning to affect the responses during the second set (constrained trials).

PD patients also demonstrated decreased incidence of multiple stepping when ON PD medication, although never comparable to the level seen in the control group. This decrease occurred only during the novel unconstrained trials and not during constrained trials. The fact that there was no influence on constrained trials supports work by Burleigh-Jacobs and colleagues (1997) who also reported that medication did not affect the sensory triggered
responses and only affected volitional (not perturbation cued) responses. However, it does not account for why medication would influence the unconstrained trials. One possible explanation is that changes in multiple stepping arise due to the order of the trials rather than due to medication. In order to ascertain that the unconstrained trials were the most novel, unpredictable perturbations, they were always presented first to all subjects. However, when looking at the effect of medication, the second time the unconstrained trials were presented, there was opportunity for learning and they were no longer the most novel trials. As mentioned previously, incidence of multiple stepping has been shown to decrease significantly with repeated blocks of trials (Maki et al., 1999). The potential importance of testing the initial trials (most novel) is confounded by the challenges of conducting within-patient analysis of the effect of medication (e.g. ON/OFF paradigms).

In light of these findings of increased incidence of multiple stepping and the effects of cues and potential influence of medications, a complimentary measure of instability used in the present study was the stability margin measured as the relative position of the AP COM at foot contact relative to the new BOS. During the unconstrained trials, PD patients' high incidence of multiple stepping was coupled with an AP COM excursion that was closer to their new stability limits, when compared to other tasks as well as to the control group. The approximation of the COM excursion to their limits of stability in the unconstrained task condition, provides further evidence for the postural instability seen in the PD population and the use of incidence of multiple stepping as an indicator of such instability. If PD patients are choosing to trade off stability in order to take faster steps in this task condition, they are in effect increasing their risk of falling as they have demonstrated difficulty in controlling the spatial and temporal parameters of stepping, as is outlined in this study.
As well, during the constrained stepping trials, when patients were cued to a step distance and to step to recover balance secondary to the perturbation, their COM excursion as a factor of their new BOS was considerably smaller compared to the unconstrained trials, even though perturbation parameters were identical to those causing stepping reactions in the unconstrained trials. If cued by a perturbation and with verbal and visual cues, they appeared to be able to adjust the relationship of their COM excursion to their step length and to the perturbation characteristics in order to efficiently recover balance with only one step. In the present study, this appears to have been accomplished by primarily increasing step length (9 cm) while the relative AP COM excursion increased by 2 cm (13%) during constrained trials. It would appear that these external sensory cues can be utilized to compensate for the compromised control that is evident during unconstrained stepping. These findings are similar to what is often clinically described of PD patients during gait. Particularly prior to falling, PD patients are often seen to be trying to “catch up with their COM” during their classic festinating gait pattern (Parkinson, 1817). Although PD patients were found to have intact abilities to modify spatial and temporal characteristics of stepping to changing magnitudes of perturbation, one could argue that this inability to maintain their COM within a margin of stability is an impairment in scaling of reaction parameters, such as step length and COM excursion, appropriately. This limitation was most evident in the task condition with the least amount of prior planning (cueing) suggesting patients are able to adapt responses to improve control when provided some additional ability to plan and to rely on cues.
5.1.2 Timing of stepping responses

When tasks were pooled, PD patients were slower to execute their stepping responses compared with the age-matched controls, although they were not slower to onset (latency). Analysis of the interaction of group effects and task effects revealed that the group differences arose primarily from slower responses to light cues in the PD population as well as a small decrease in execution speed during constrained trials. PD patients were not slower than the control subjects during the unconstrained task conditions in which PD patients exhibited increased incidence of multiple stepping. These findings do not support the second hypothesis. Slowed step execution speed during cued volitional stepping found in the present study is similar to findings of Lee and colleagues (1995) who found that PD patients demonstrated single leg lifts with increased time to peak APA and to lift-off. As well, Burleigh-Jacobs and colleagues (1997) found that when PD patients stepped volitionally or to a cutaneous cue, both the time to peak APA and to foot-off were increased compared to controls. When patients were cued to step with small platform perturbations, they found that they were able to decrease their time to peak APA but could not generate the force required to decrease time to foot-off. In the present study, during the constrained task conditions, PD patients were told to step when the platform moved and were given a target distance. Again, although PD patients stepped more slowly than the controls: these differences were not statistically significant until foot contact. Comparable findings (of slowed time to foot off) to those of Burleigh-Jacobs and colleagues were not seen. The unpredictability of perturbation direction and magnitude as well as the size of the perturbations themselves in the present study would likely account for the differences in findings.
Most noteworthy, however is the finding that PD patients did not behave differently from control subjects in the timing of step execution when patients stepped so as to recover balance during the most novel task conditions. Again, compared to previous studies, experimental paradigm differences would likely account for the different results found. In the present study, platform perturbations evoking stepping reactions were large, and unpredictable in terms of direction, magnitude and timing of onset. Subjects were not given any specific instructions other than to behave naturally so as to recover balance. It is apparent that despite difficulty in stepping quickly during volitional or cued stepping task, PD patients are able to execute fast compensatory stepping reactions when sensory information arising from the induced instability cues them. The increased postural instability seen cannot, therefore, be accounted for simply by slowed step execution or increased time to onset to reaction.

5.1.3 Modifiability of Stepping Responses

PD patients did increase the speed of their stepping response by decreasing the time to peak AP, time to foot off and time to foot contact in the perturbation cued constrained stepping trials, rejecting the third hypothesis. These findings appear in contrast to those seen studying scaling of fixed support strategies. (though it should be noted that these studies examined scaling of responses to changes in platform displacement and not acceleration). Both Beckley and colleagues (1993) and Horak and colleagues (1996) have found that PD patients have difficulty scaling their FS strategies. Beckley and colleagues (1993) found that when the size of the perturbation was changed (4 to 10 degree platform rotation), PD patients were unable to scale the size of their long latency, posturally stabilizing, response (as measured by EMG amplitude) to the changing perturbation, even when the change in perturbation size was predictable. They
found that PD patients consistently generated undersized long latency responses to all perturbations.

Horak and colleagues (1996) also had somewhat different findings than those of Beckley. They found that PD patients could, in fact, scale their FS strategies when perturbations were altered by changing the velocity of the perturbation. In these instances, they felt PD patients could use the sensorimotor feedback of the altered velocity to scale their response. When the amplitude (displacement) was altered (acceleration and velocity remaining constant), however, PD patients had more difficulty scaling their postural response, particularly to larger sized displacements (above 3.6 cm). They concluded that PD patients were unable to use prediction to scale their postural responses in these instances, as they had to begin their response prior to the full displacement of perturbation being known. PD patients were therefore thought to have difficulty changing central set. Alternatively, it could be argued that with such long, slow perturbations, PD patients were unable to predict the deceleration characteristics of the perturbation, as opposed to the final displacement, causing the impairment seen. Unpredictability of response characteristics, particularly acceleration and deceleration may be key components to determining if the ability to modify or scale responses on-line is impaired, as opposed to an impairment in prior planning, particularly in instances when perturbation characteristics can be predicted.

PD patients in our study had no difficulty modifying the speed of their response to match changing magnitudes of perturbation, although these changes were unpredictable. These findings may suggest that change in support reactions, such as compensatory stepping responses seen in our study, may be controlled similarly as the FS strategies studied by Beckley, et al (1993) and Horak, et al (1996), at least in modifying behaviour in response to changes in
perturbation velocity or acceleration. However, a number of other factors must first be considered. In the present study, patients were presented with randomized perturbations of three magnitudes and two directions. No prior knowledge of direction or magnitude was given. As well, three levels of magnitude were randomly presented in order to better characterize the relationship between the perturbation magnitude and the response characteristics. Beckley and colleagues (1993) presented a combination of blocked trials and randomized trials and altered the delivery order between patients, thus ensuring unpredictability of the perturbation magnitude. They limited their perturbation magnitudes to two and rotations were in only one direction, however, thus limiting the inferences that can be made in the ability to scale. In contrast, Horak and colleagues (1996) presented multiple levels of perturbation (five or more in each set), but all presentations were made in blocks of trials. As well, perturbations were always presented in one direction (posterior) and in an increasing order of magnitude (either velocity/acceleration or amplitude). These perturbation sizes were, therefore, predictable to the patients. It is possible that by presenting perturbations that are predictable, one is testing the patient’s ability to prior plan and execute compensatory responses, as well as their capacity to learn rather than their ability to scale reactive balance strategies “on-line” to changing perturbation characteristics. Studies of impairments in predictive control of posture and volitional movement have demonstrated that PD patients have significant difficulty in this domain. Furthermore, in the present study, perturbation magnitude at large size perturbations was the same as that used to evoke compensatory stepping responses in the healthy controls and PD patients. In previous studies, perturbation magnitude, coupled with predictability may not sufficiently threaten the postural stability of the PD patient to engage the system to scale responses appropriately.
As well, both Beckley and colleagues (1993) and Horak and colleagues (1996) measured responses and scaling of responses with integrated EMG and/or rates of change of torque about the ankle joint, whereas this study considered speed of execution of the stepping movement using centre of pressure and vertical force measures. Using torque values and rates of change of torque, these findings should be comparable, however, as speed of execution of the response is a result of changes in muscle force and torque. IEMG findings, alone, may not be comparable to speed of execution, as other factors such as muscle recruitment patterns or rigidity may play a role other than EMG amplitude of specific muscles measured in determining response velocity.

PD patients were also able to modify the spatial characteristics of their stepping responses, further supporting an intact ability to scale responses. Step length and COMPT (AP COM excursion over new stability limits) increased with increasing magnitudes of perturbation, although not always significantly. In contrast, APA amplitude decreased with increasing magnitudes of perturbation. This decrease was expected in light of findings by McIlroy and Maki (1993b) that in healthy adults, APAs are absent in response to the most novel perturbations, presumably in order to decrease the time necessary to respond.

PD patients do appear to be able to execute fast compensatory stepping reactions and modify the temporal and spatial characteristics of their stepping behaviour to changing magnitudes of perturbation. Despite these abilities, however, they executed compensatory stepping responses with significantly higher incidence of multiple stepping, coupled with increased excursion of their COM towards their stability limits during the first steps of these multiple stepping reactions. In light of these findings, further examination of the spatial characteristics of the stepping responses were reviewed in order to gain a better understanding of the relationship between multiple stepping and increased instability.
5.1.4 Spatial Characteristics of Stepping: PD Patients versus Control Subjects

As noted, it is presently argued that the occurrence of increased multiple stepping in PD patients arises due to dyscontrol associated with the planning and/or execution of the compensatory stepping reaction rather than as a preferred response strategy. This is supported by several observations detailed below, including shorter step lengths and poorly coupled foot placement with COM excursion in PD patients compared with control subjects, as well as spatial patterns of the multiple stepping responses themselves.

PD patients tended to take shorter first steps than their age-matched controls. Step length differences, however, were dependent on task with the most pronounced differences seen in the unconstrained and light cued trials. Most interestingly, although stepping in unconstrained trials was evoked by large platform perturbations, PD patients’ stepping responses were, in fact, shortest during these trials. During these unconstrained trials, shorter steps were accompanied by a dramatic increase in multiple stepping while there was no multiple stepping during the light cued trials. During the unconstrained trials, PD patients’ short steps were coupled with an AP COM excursion that was closer to their new stability limits, when compared to other tasks as well as to the control group. If patients were ‘choosing’ short, multiple steps, they were certainly doing so at the expense of stability by completing first steps with COM excursions approaching their stability limits. Given PD patients’ impairments in controlling even volitional stepping, as evidenced by shorter than targeted steps during light cued trials in this study, such a tradeoff could certainly increase risk of instability and falls in this population. It is unlikely that PD patients’ step length was limited by a limitation in available range of motion in the lower extremities. Gross examination of range of motion did not reveal any restrictions at the ankle,
knee or hip level. As well, as noted below, PD patients were able to increase their step length when cued, demonstrating available range of motion.

As well, during the constrained stepping trials, when patients were cued to a step distance and to step to recover balance secondary to the perturbation, their step length increased and their COM excursion as it related to their new stability limits was considerably smaller compared to the unconstrained trials, even though perturbation parameters were identical to those causing stepping reactions in the unconstrained trials. If cued by a perturbation with verbal and visual cues, they appeared to be able to adjust the relationship of their COM excursion to their step length in order to efficiently recover balance with only one step. It would appear that these external sensory cues can be utilized to compensate for the compromised control that is evident during unconstrained stepping. Furthermore, during light cued trials, patients took shorter steps than control subjects even though they were cued to step to a specific target, and these short steps were accompanied by a smaller COM excursion as well. In these trials, PD patients were always able to maintain their position with only one step. It would appear that in cued volitional stepping, PD patients utilized a strategy to maintain stability, taking smaller than cued steps to do so.

Evidence of changes in predictive control could be inferred from response characteristics of the APAs. The subjects presently tested did reveal evidence of APAs prior to voluntary and perturbation cued stepping. The amplitude of the responses varied, as seen in previous studies, across the task conditions. PD patients did have larger APA amplitudes compared to controls (when APAs are represented by ML COM excursion at FO) during light cued trials. Lee and colleagues (1995) demonstrated similar findings in the mild to moderately affected PD patients. They found these patients to have larger amplitudes in their APAs prior to volitional leg lifts; but
the APAs did not appear to provide the stability necessary to hold single-leg stance in the patient group. APAs prior to stepping evoked or cued by perturbations were comparable to control subjects. Typically, responses, if present, were small in amplitude and short in duration (McIlroy and Maki, 1993b). As in control subjects, such APAs do not appear to provide significant benefits to the control of lateral stability (McIlroy and Maki, 1999).

The consequence of inadequate APAs during perturbation evoked stepping can be lateral instability to anteroposterior directed perturbations. In the present study, ML step length of the first steps was not different between PD patients and control subjects. In contrast to the controls subjects, when taking multiple steps in response to backward unconstrained translations, PD patients took second steps with the opposite foot in the majority of multiple stepping trials (76.9%). This second step, however, was also very small and final AP displacement of the PD subjects after two steps continued to be much shorter than controls. During these stepping trials, there was minimal ML involvement in the second step as well. From these findings, it is apparent that although PD patients can execute fast reactions, during the most novel conditions, their ability to execute large enough steps so as to recover AP stability is significantly compromised. Despite taking multiple steps, they continue to fail to couple their AP step length with AP COM excursion. Also of interest is the pattern of stepping of the other three multiple stepping responses. During these steps, PD patients and control subjects alike took steps with the same leg as the first step, but with large backward components as well as significant ML components. Stepping in the opposite direction on the second step may be a response to the deceleration of the platform perturbation or it may simply be a correction for an initial "over-reaction" in stepping. This second possibility appears unlikely given that PD patients took significantly shorter steps on the first step but continued to step backward on the second step.
when compared to control subjects. Such lateral components of stepping might suggest that PD patients require multiple steps to regain lateral stability in the face of AP oriented perturbations. These findings are similar to those of McIlroy and Maki (1996) who found that healthy elderly subjects also took laterally oriented steps in over 30% of their multiple stepping responses. In the present study, the control subjects executed second steps with an increased lateral component during all of their trials with multiple steps. This inability to maintain lateral stability may also be one reason PD patients take multiple steps when perturbed and likely contributes to their postural instability.

Medication did not affect most temporal or spatial parameters. Previous studies have demonstrated similar findings (Bloem et al., 1996; Burleigh-Jacobs et al., 1997; Horak et al., 1996). From these results, the majority of the effects of medication appear to be limited to control of volitional stepping. Such findings remain striking considering that levodopa is the primary course of treatment for PD patients, while impairments in postural stability are often a limiting factor in patients' continued independence and safety within the community.

5.2 Mechanisms of Postural Dyscontrol in PD

The mechanisms responsible for the postural dyscontrol seen in the PD population remain unclear. What causes the postural instability seen in PD patients, as measured by multiple stepping, coupled with COM excursions approaching their stability limits? Why are PD patients slower to execute steps volitionally or to cutaneous cues of some kind, but are able to step quickly when their stability is threatened? It is evident from perturbation trials that they are able to increase their execution speed and they are not slower to onset of the reaction (latency) than their age-matched controls. There are several factors that have been proposed: 1) bradykinesia, 2) peripheral stiffness or co-contraction, 3) reduced strength, or 4) changes in attentional
capacity. If bradykinesia is the root of the impairments seen, then it would follow that PD medication should improve the temporal and spatial impairments seen as it does affect bradykinesia positively (Lang and Lozano, 1998b). In fact, in the present study, light cued steps are most affected by medication, whereas medication administration had little effect on the temporal and spatial characteristics of the perturbation cued and perturbation evoked steps. Similarly, Burleigh-Jacobs and colleagues (1997) found that PD medications improved stepping responses in the volitional and cutaneous cued stepping, but not in the perturbation cued stepping. Alternatively, increased stiffness or co-contraction may account for the rigidity seen in PD patients and this rigidity may play a role in their impaired control. If inability to elicit a fast agonist contraction secondary to increased co-contraction were a significant contributor to the impaired compensatory stepping reactions, it might also impact on the ability to generate the force required to step with sufficient amplitude so as to recover stability. The findings of this study (e.g. shorter step length) would support this concept. Decreased force generation capacity may also simply be an issue of strength. There is some evidence to suggest that PD patients may have muscle strength impairments (Koller and Kase, 1986). One gait study in healthy older adults demonstrated a relationship between ankle plantarflexor power and the shortened step length seen in the older adults compared to young healthy subjects (Judge et al., 1996); it is possible that such deficits in strength and power may impact on compensatory stepping responses as well. Studies have demonstrated that at least some of the dyscontrol seen in the FS strategies may be accounted for by the stooped posture that PD patients exhibit (Bloem et al., 1999). In the present study, however, PD patients AP COP position was not anterior to that of control subjects during any tasks. In fact, during the unconstrained trials, PD patients pre-task position was actually more upright than that of the control subjects. As well, deficits in
attentional capacity available to PD patients when they are perturbed may play a role. There is a growing body of literature (Brown et al., 1999), (McIlroy et al., 1999b) supporting the use of such resources in the control of stability. PD patients, particularly in later stages of the disease process, have definite and significant cognitive impairments (Owen et al., 1993; Stam et al., 1993) that could impact on attention. Based on findings on the UPDRS, three of the four subjects in this study would fall into the akinetic-rigid subgroup of PD patients. Only one subject had significant tremor as a primary symptom compared to bradykinesia and rigidity. All four patients were in the early to middle stages of the disease process and did not have any significant cognitive impairments, although most complained of some memory deficits. Given these findings, it is possible that a complex combination of rigidity, attentional deficits and bradykinesia could contribute to the impairments seen in the present subjects. At this time, it remains unknown which of these mechanisms are involved in the dyscontrol of compensatory stepping reactions in PD patients.

Important to the discussion of the potential mechanisms of dyscontrol is the finding that the fundamental problem of hypometric stepping responses seen in the present study is not an isolated finding. Similar deficits of distance control have been demonstrated in gait studies of PD patients, as well as in the reaching literature and in the control of eye movements and saccades in the PD population. PD patients have been shown to walk volitionally with a decreased gait speed and stride length (Knuttson, 1972; Morris and Iansek, 1997; Morris et al., 1994). When gait speed is increased in the PD population, it is accomplished by increasing cadence, but not stride length as in the control subjects (Morris et al., 1994). PD patients appeared to be unable to increase their stride length in order to increase walking speed. In this paradigm, PD patients were also able to increase their stride length to increase gait speed when
given visual targets for stepping (Morris et al., 1994; Morris et al., 1996). PD patients have also been shown to make more errors of amplitude during pointing to target tasks during which the arm trajectory (but not target) is not visible (Flash et al., 1992). Moreover, voluntary saccadic eye movements of PD patients have also been shown to be impaired. The literature suggests that voluntary saccadic eye movements of PD patients may be hypometric in nature (White et al., 1988), (Briand et al., 1999), as well as demonstrating impaired saccadic gain to a predictive paradigm, undershooting targets at low frequency and overshooting at high frequency (O'Sullivan et al., 1997). Furthermore, deep brain stimulation of GPi has been shown to improve these impaired saccades (Straube et al., 1998). Such similarities in the impairments seen in the control of both volitional and reactive movement, as well as movement control of the upper limb, lower limb and also oculomotor control in the PD population lend important insight into determining the mechanisms responsible for the impaired control of posture and movement in Parkinson's disease.

The findings of this study do support the role of the basal ganglia in the control of compensatory stepping reactions. It is also apparent that non-dopaminergic systems may be involved as PD patients did not demonstrate significant changes in the characteristics of their compensatory stepping reactions when on medication. These findings are at least in part similar to those seen in the control of fixed support strategies (Bloem et al., 1996; Horak et al., 1996). This would lead one to believe that CIS strategies and FS strategies may be controlled, in part, by similar mechanisms or centres. As well, some centres may be involved in controlling step length in both compensatory and volitional stepping, but alternate pathways or inputs appear to be available to PD patients when provided with the appropriate cues in order to bypass the affected areas. These findings are in line with recent suggestions that initiation and scaling of
CIS strategies are controlled by the same transcortical and subcortical pathways thought to be involved in the control of FS strategies (Maki and McIlroy, 1997).

5.3 Limitations of the Study

5.3.1 Sample Size

The sample size in this study was small (n=4). Secondary to the nature of the perturbations and the overall length of the study day, subjects were carefully screened and inclusion criteria were tightly set to ensure that experimental testing would be a positive experience for all subjects. The small sample size made it difficult to generalize the results to the larger PD population; however, as the subjects were all at very similar stages of disease progression (see Table 3), results may apply to PD patients with similar levels of physical impairment. This generalization is made more difficult by the fact that many possible mechanisms of the apparent dyscontrol of compensatory stepping in the PD patient may exist. As patients of similar overall physical impairment (staging) may vary considerably in terms of which symptoms are most prevalent (i.e. rigidity vs. bradykinesia), the effects of these symptoms on postural control may also vary considerably. Further study of a larger sample size and/or wider range of impairment levels will be necessary to confirm the findings of this preliminary study. It is noteworthy, however, that even with a small sample size of PD patients at a relatively mild stage in the disease process, the present study did find significant impairments in their control of compensatory stepping reactions and postural stability.
5.3.2 Medication/Order of Presentation

All subjects arrived for testing at least twelve hours off medication and were re-tested 45 minutes to one hour after taking their medication. Although these are accepted values in the literature for off/on testing of PD patients, effect of medication may still vary from patient to patient. Thus, patients may not have all been equally "off" medication or in similar "on" states when tested.

More importantly, as has been noted earlier in this thesis, secondary to the medication requirement for the study, patients were all exposed to the sets of trials in the same order and the effect of learning must be considered for all results discussed. This effect is probably most significant when reviewing incidence of multiple stepping between unconstrained and constrained trials as well as any other comparisons between these two tasks (step length, COM excursion, etc). In order to decrease the effect of learning as a factor when comparing multiple stepping between the two tasks, results were pooled for off and on medication. It was considered that by doing so, the effect of learning would be balanced between the two tasks as the second (ON) run of the unconstrained trials would also be affected by prior learning. As well, subjects practiced stepping to the targets until they could do so without looking in order to eliminate a learning effect during the series of trials itself (for light cued and constrained trials).

Regardless of effect of learning or medication, PD patients had significantly increased incidences of multiple stepping during the most novel, unpredictable unconstrained trials at the beginning of testing compared to age matched controls. These results would not be affected by learning any differently than the control group and are strong indicators of the dyscontrol seen in the PD patients in response to the most unpredictable perturbations.
5.3.3 Visual Cues

As discussed previously, PD patients appear to require external (visual/verbal and perturbation) cues in order to take effective and efficient compensatory steps in response to perturbations. It is important to note that the effect seen may have been limited by the visual cues of the floor set-up itself that were always available to subjects. The floor was marked as a grid in order to perform kinematic analysis and these markings may have assisted PD patients more than controls in executing balance responses. Hanakawa and colleagues (1999) have demonstrated in treadmill studies that PD patients can make effective use of horizontal line cues on the treadmill to take larger steps; similar effects could be possible with our set-up, especially during forward oriented stepping. Subjects were asked to look straight ahead at a target for all trials (i.e. not at their feet), but subjects’ gaze was difficult to control once each trial began. However, it is important to note that this effect may have assisted PD patients in behaving more like controls and thus did not add to any effect seen, but rather may have decreased it.

5.3.4 Level of Arousal/Anxiety

There is also the possibility that level of arousal or anxiety may affect postural control and responses observed in platform studies. Evidence suggests that increased arousal or anxiety may increase static postural sway (Maki and McIlroy, 1996a); it is therefore possible that similar effects occur during dynamic tasks. Of note in this study, it was observed that 3/4 PD patients were able to move about on the platform with minimal freezing, even if arrests in movement were observed while subjects moved around the laboratory environment. Levels of arousal and anxiety during testing may be measured in the future to capture between and within subject changes.
5.4 Clinical Implications of Study Findings

The findings presented here may provide some preliminary insight into the assessment and treatment of balance dysfunction in the PD population. It is apparent from these results that PD patients have profound impairments in executing compensatory stepping reactions but may be able to utilize cues to effectively bypass impaired CNS areas in order to execute an efficient compensatory stepping reaction when perturbed. Clinically, this information may be utilized in the development of assessment tools and treatment protocols for balance training in this population, by demonstrating the importance of compensatory stepping in the recovery of stability. When assessing balance in the neurological population, compensatory stepping has traditionally been seen as a “protective” reaction of last resort (Nashner, 1989; Shumway-Cook and Horak, 1989 as cited in Horak et al., 1989b; Shumway-Cook and Woollacott, 1995). The results of the present study support the thinking that CIS strategies are key components of balance recovery and may be significantly compromised in the PD population. Compensatory stepping and the ability to execute large, fast, appropriate stepping responses should, therefore, be carefully considered when assessing balance responses in the PD patient. It would appear that PD patients should be trained to step quickly and with large steps when perturbed and to use environmental cues to assist whenever possible in the execution of volitional, as well as compensatory stepping. Previous studies have found that PD patients can utilize cues to increase step length during gait (Behrman et al., 1998; Hanakawa et al., 1999; Thaut et al., 1996), perhaps similar mechanisms may be utilized in balance training. Compensatory stepping reactions are, however, much faster than volitional stepping and the present study reveals important differences between light cued and perturbation evoked reactions. The capacity to
prior plan (and rely on cues) may be an insurmountable limitation in the execution of compensatory reactions to truly novel perturbations making understanding of such control from voluntary or perturbation-cued stepping difficult.

5.5 Future Directions

The results of this work lead to important future studies that would enable us to further understand the role of the basal ganglia in the control of balance and posture, as well as balance control and treatment in the PD population. It would be important to test a broader spectrum of PD patients with possibly a smaller subset of the tests performed here. One could then map the findings across the stages of the disease course itself. Such a study would provide further support of the preliminary findings cited here and determine if disease progression correlated to more pronounced impairments in the control of compensatory stepping.

It may also be possible to test PD patients who have received deep brain stimulators in either GPi or STN for the control of their hypokinetic symptoms. Although these surgeries are accepted standard (GPi) or experimental (STN) methods of PD treatment (Hallett et al., 2000), little information on the effect these surgeries have on postural control and gait, beyond clinical UPDRS scores, is available. A study involving patients with implanted stimulators would also allow for randomizing the order of testing between OFF and ON among patients. As well, as many studies including this one, have found that levodopa may have limited effect on the control of balance in this population. Laboratory testing of balance and movement control in the stimulator population may validate some of the clinical findings of the effectiveness of these devices in controlling PD symptoms including balance dysfunction.
In the present study, postural instability appeared to be related to an inability to execute large steps and impaired coupling of the COM excursion with this step length, causing PD patients to approach their static stability limits when responding. Recent evidence (Maki and McIlroy, 1999) has suggested that dynamic stability, as seen in any perturbation-response paradigm, is best modeled by taking into account both the “static” stability margins depicted with COM displacement, as well as the “dynamic” stability margins described with the velocity of this COM displacement. It would therefore be of interest to determine if PD patients’ instability can be further explained with this dynamic model.

Furthermore, it would be important to determine if the external sensory cues that appear to assist PD patients in executing cued stepping reactions that maintain postural stability can be accessed during unpredictable perturbation settings. Further study of the effects of subtle environmental cues (gridmarks on floors, etc) during novel, unconstrained task conditions may assist in resolving this question.

5.6 Conclusions and Summary

As a result of work described in these chapters, it is possible to make a number of conclusions:

- Even at mild to moderate stages of disability (Hoehn and Yahr 2.5-3), PD patients are posturally unstable, demonstrating dramatic increases in the incidence of multiple stepping in response to novel perturbations, as compared to age-matched controls.
• This postural instability appears to be due, in part, to execution of shorter steps and step lengths that are poorly coupled to AP COM excursion during compensatory stepping responses.

• Despite difficulty in executing fast compensatory stepping responses of appropriate size, PD patients do appear to be able to modify their stepping responses when perturbation characteristics change unexpectedly.

• PD medication does not appear to impact compensatory stepping responses significantly and thus current pharmacological treatment may not be sufficient in treating balance impairment and gait disorders in this population.

The impairments seen in PD patients' execution of compensatory stepping responses to the most novel perturbations, coupled with the ability to modify these responses when provided with external sensory cues provides an interesting insight into the possible neural control of compensatory stepping responses. From this preliminary study of a small sample of mild-moderate PD patients, it is apparent that the basal ganglia may be crucial structures in the pathway involved in the processing and execution of compensatory stepping responses to unpredictable and novel perturbations. Lesions in the basal ganglia, as seen in PD, produce profound impairments in the execution of such responses, as paralleled by the postural instability seen in PD patients during activities of daily living, limiting their independence and safety in the community.
Chapter 6.0 References


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Chapter 7.0 Appendices

7.1 Appendix A: Clinical information form and informed consent form

CLINICAL INFORMATION FORM
POSTURAL BALANCE STUDY

Objectives: Researchers and clinicians are searching for an understanding of what causes falls in the elderly in order to develop techniques to prevent falls. This study is aimed at providing further understanding of how balance is controlled.

Procedures: To test your balance, you will be asked to stand on a special platform that is controlled to move in different directions. During each platform movement, muscle activity in muscles of the legs will be measured by electrodes (small metal disks) that are taped to the surface of your skin. During the test, you will stand on special plates that will measure the forces at your feet. You may, during different parts of the study, be required to wear a blindfold and to stand on a piece of foam rubber. The balance tests will be videotaped, for analysis purposes only, and at no time will your name ever be associated with these pictures. In addition to the balance testing, a number of simple tests will be performed to assess your vision, reaction time, skin sensation and flexibility, and you will be asked to fill out a questionnaire regarding your medical history and lifestyle. One visit, lasting 3 hours, will be required. We will ask that you not take your Parkinson's medication when you wake up the morning of the test, and delay taking the medication until we have completed a portion of the testing. At that point you will be able to take your usual medication, rest for a short period (45-60 minutes) and then complete further balance testing.

All information that is gathered during the study will remain strictly confidential, and at no time will your name be associated with this information. You will be paid a total of $25 to reimburse you for your time and travel expenses.

Benefits: This study will not provide any direct benefit to you, but the information may aid in the understanding of falling in the elderly and in people with Parkinson's disease and the treatment of elderly individuals who are at risk of falling.

Risks: There is a very small chance that you may fall and injure yourself during the balance tests. However, safety handrails are mounted on the balance platform, within easy reach, and the experimenter will always stand closely behind you during each test, so that he/she can catch you if necessary. You will also be guarded closely when walking around the lab and during all other testing to ensure your safety. We have tested over 300 subjects using similar types of balance tests, and no one has ever fallen or sustained an injury.

Contact Person: Evelyn Heung, 480-5858
I voluntarily enter this study, the details of which have been explained to me by one of the researchers.

I understand that the researchers will be asking me questions concerning my health and lifestyle. This information will remain confidential and I will be free to refuse to reply to any question that I am unwilling to answer. The researcher explained that he/she will measure my height, weight, vision, strength, flexibility, skin and joint sensation, and leg dimensions. He/she has explained that none of these tests and measurements will involve any discomfort or risk. I understand that I will delay taking my Parkinson's medication on the morning of the test until after a portion of the balance testing has been completed.

I have been shown the platform on which I will stand, in order to test my balance. The researcher has stood on the platform and shown me how it moves. I understand that there is a chance that I might fall and sustain an injury during these tests; however, I have examined the safety precautions that will be taken and am satisfied that these precautions are adequate.

Small sensors may be taped to the surface of my skin to monitor the activity of my muscles. Other sensors may be taped to my limbs or body to measure motion. The plates on which I will stand during the tests will measure the forces on my feet.

The researcher has told me that I will be required to close my eyes and wear a blindfold at different times during the experiment. I have also been informed that I will be required to stand on a foam-rubber surface, at different points in the experiment. I have been told by the researcher that this will not cause any discomfort or risk to me.

Video tapes will be recorded during the tests. I understand that these visual materials will be used for analysis purposes only and my name will never be associated with these pictures.
I understand that I am free to ask questions and to withdraw from this study at any time. I also understand that, if I feel uncomfortable or unsteady on the platform, I may ask the researcher to stop it immediately. In addition, I realize that my withdrawal will not prejudice my rights to receive normal medical treatment.

I understand that this study will require one visit lasting 3 hours. To reimburse me for my time and travel expenses, I will be paid $25.

Contact person: Evelyn Heung, 480-5858

I have read and understood the entire consent form.

Signature of volunteer ________________________________

Name of volunteer ________________________________

Signature of witness ________________________________

Name of witness ________________________________

Date ________________________________
7.2.1 Appendix B1:
Parkinson’s Protocol-Experiment 1 –Subjects 2,3 and 4
Complete entire series of tests x 1, take meds, rest for 30–45 mins repeat platform tests rounds 2–4
*Prep: EMG-TA and GM bilat.
PEAK-toe, 5MT, LM, heel, knee, grtr troch, T10, C7, acromion, head*

<table>
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<tr>
<th>ITEM #</th>
<th>Balance Task</th>
<th>Task Cond</th>
<th>Directns</th>
<th>Waveforms</th>
<th>Magnitudes</th>
<th>#</th>
<th>RPT</th>
<th>Total Trials</th>
<th>Total Time</th>
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<td>30 mins</td>
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<td>30 mins</td>
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<tr>
<td>2</td>
<td>ROUND 1: Spontaneous Sway</td>
<td>EO Bar Stand still</td>
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<td>1.0 min</td>
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<td></td>
<td>Two-foot stance</td>
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<tr>
<td>3</td>
<td>Two-foot stance</td>
<td>EO, b. Stand still</td>
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<td>Time required for Round 1</td>
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<td>2.0 mins</td>
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<tr>
<td>4-15</td>
<td>ROUND 2: Compensatory Stepping, unconstrained</td>
<td>EO, b. D</td>
<td>2 (f,b)</td>
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<td>15 mins</td>
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<td></td>
<td>Rest Break-check EMG/PEAK, instruct for next round, demo light cue</td>
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<td>10 mins</td>
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<tr>
<td>10-21</td>
<td>ROUND 3: Voluntary Step-Light Cued-Step as quickly as possible</td>
<td>EO, b</td>
<td>2</td>
<td>N/a</td>
<td>N/a</td>
<td>3</td>
<td>6</td>
<td></td>
<td>8 mins</td>
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<td></td>
<td>Rest Break-instructions for next round</td>
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<tr>
<td>22-33</td>
<td>ROUND 4: Voluntary Step-Perturbation Cued-step as quickly as possible</td>
<td>EO, b</td>
<td>2 (3:1 b-f)</td>
<td></td>
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<td>15 mins</td>
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<td></td>
<td>Rest Break-Take medication</td>
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<td>Time required-tasks only</td>
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<td></td>
<td>55 mins</td>
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<td></td>
<td>Time required-including set-up, breaks-for Platform Testingx2</td>
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<td>3-3.5 hrs</td>
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<td>Clean-up-with subject</td>
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<td>15 mins</td>
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</table>

EO-eyes open, EC-eyes closed, b-hold bar behind, D-distraction task (serial 3’s)
7.2.2 Appendix B2:
Parkinson's Protocol—Experiment 1—Subject 1
Complete entire series of tests x 1, take meds, rest for 30-45 mins, repeat round 3
Prep: EMG-TA and GM bilat., PEAK-toe, 5MT, LM, heel, knee, grtr troch, T10, C7, acromion, head

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<th>Waveforms</th>
<th>Magnitudes</th>
<th># Reps</th>
<th>Total Time</th>
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<td>30 mins</td>
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<td></td>
<td>Time required for prelims</td>
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<td></td>
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<td>30 mins</td>
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<tr>
<td>2</td>
<td>ROUND 1: Spontaneous Sway</td>
<td>EO</td>
<td></td>
<td></td>
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<td>1</td>
<td>1.0 min</td>
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<tr>
<td></td>
<td>Two-foot stance</td>
<td>Bar</td>
<td>Stand still</td>
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<td></td>
<td>1</td>
<td>1.0 mins</td>
</tr>
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<td>3</td>
<td>Two-foot stance</td>
<td>EC, b.</td>
<td>Stand still</td>
<td></td>
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<td>1</td>
<td>1.0 mins</td>
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<tr>
<td></td>
<td>Time required for Round 1</td>
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<td>2.0 mins</td>
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<tr>
<td>4-15</td>
<td>ROUND 2: Compensatory Stepping, unconstrained</td>
<td>EO, b.</td>
<td>D</td>
<td>2 (f.b)</td>
<td>1</td>
<td>2</td>
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<td></td>
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<td></td>
<td></td>
<td>25 mins</td>
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<td>16-35</td>
<td>ROUND 3: Voluntary Step-Perturbation Cued-step as quickly as possible</td>
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<td>2 (3:1 b/f)</td>
<td>1</td>
<td>3</td>
<td>5</td>
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<tr>
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<td>Time required—tasks only</td>
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<tr>
<td></td>
<td>Clean-up—with subject</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15 mins</td>
</tr>
</tbody>
</table>

EO-eyes open, EC-eyes closed, b-hold bar behind, D-distraction task (serial 3's)
7.2.3 Appendix B3: Experimental Protocol-Healthy Elderly Control Subjects (MRC MD2 Protocol)

<table>
<thead>
<tr>
<th>ROUND 1: SPONTANEOUS SWAY TESTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Eyes open</td>
</tr>
<tr>
<td>2 Eyes closed, blindfold</td>
</tr>
<tr>
<td>3 Serial 7's</td>
</tr>
<tr>
<td>4 Backward recall (40 bpm)</td>
</tr>
<tr>
<td>5 Eyes open to eyes closed transition</td>
</tr>
<tr>
<td>6 Eyes open, stand on foam</td>
</tr>
<tr>
<td>7 Eyes closed, blindfold, stand on foam</td>
</tr>
<tr>
<td>8 Lean forward</td>
</tr>
<tr>
<td>9 Lean backward</td>
</tr>
<tr>
<td>10 Lean left</td>
</tr>
<tr>
<td>11 Lean right</td>
</tr>
<tr>
<td>12 FICSIT-5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUND 2: COMPENSATORY STEPPING - UNCONSTRAINED</th>
</tr>
</thead>
<tbody>
<tr>
<td>13-32 Eyes open, 4 directions, serial 3s, hold handlebar, 4 waveforms, 2 amplitudes (small and large)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUND 3: MARCH RESPONSES-UNCONSTRAINED</th>
</tr>
</thead>
<tbody>
<tr>
<td>33-41 Eyes open, 4 directions, no distraction, hold handlebar</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUND 4: COMPENSATORY FS STRATEGY-TRY NOT TO STEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>42-57 Eyes open, 4 directions, no distraction, hold handlebar</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUND 5: PSEUDORANDOM PERTURBATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>58-60 Eyes open, serial 3s, 3 directions (ap, ml, diagonal), masking noise distraction, hold handlebar</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUND 6: VOLUNTARY SWAY + COMPENSATORY FS STRATEGY-TRY NOT TO STEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>61-68 Eyes open, hold handlebar, 2 directions</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUND 7-1ST HALF-LIGHT CUED STEPPING</th>
</tr>
</thead>
<tbody>
<tr>
<td>69-72 Eyes open, 2 directions, right foot</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUND 8-PERTURBATION CUED STEPPING</th>
</tr>
</thead>
<tbody>
<tr>
<td>73-78 Eyes open, 2 directions, 1 amplitude (large)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUND 9-2ND HALF-LIGHT CUED STEPPING</th>
</tr>
</thead>
<tbody>
<tr>
<td>79-82 Eyes open, 2 directions</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUND 10-1ST HALF-LIGHT CUED GRASPING</th>
</tr>
</thead>
<tbody>
<tr>
<td>83-85 Hand rail in front, arms at sides, 1 direction</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUND 11-PERTURBATION CUED GRASPING</th>
</tr>
</thead>
<tbody>
<tr>
<td>86-91 Hand rail in front, arms at sides, 2 directions</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUND 12-2ND HALF-LIGHT CUED GRASPING</th>
</tr>
</thead>
<tbody>
<tr>
<td>92-94 Hand rail in front, arms at sides, 1 direction</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUND 13: PREFERRED SIT TO STAND</th>
</tr>
</thead>
<tbody>
<tr>
<td>95-97</td>
</tr>
</tbody>
</table>