2005

Parkinsonian sensory integration for balance control : time based postural effects of alterations in sensory information

Cooper, Stephanie A.

Lethbridge, Alta. : University of Lethbridge, Faculty of Arts and Science, 2005

PARKINSONIAN SENSORY INTEGRATION FOR BALANCE CONTROL: TIME BASED POSTURAL EFFECTS OF ALTERATIONS IN SENSORY INFORMATION

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B.Sc., University of Lethbridge, 2003

A Thesis
Submitted to the School of Graduate Studies
of the University of Lethbridge
in Partial Fulfillment of the
Requirements for the Degree
MASTERS OF SCIENCE

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LETHBRIDGE, ALBERTA, CANADA

DEDICATION

This thesis is dedicated to my parents – who love me fiercely and unconditionally, and who taught me the value of honesty and integrity; and to Dr. Lesley Brown – who showed me the way and who taught me how to get there.

ABSTRACT

Changes in postural stability following sensory manipulation were investigated among Parkinson's disease patients and healthy older adults. Sixteen Parkinson's disease patients (PD; mean age 68.2 ± 2.7 years) and sixteen older adults (control; mean age 67.6 ± 2.6 years) performed quiet standing trials that progressed through baseline, sensory manipulation, and reintegration. Postural control following visual deprivation was assessed following alternate removal and reinsertion of visual information. Postural recovery following sensory incongruence was assessed following the termination of visual, somatosensory, and visuo-somatosensory incongruence. PD patients' balance was disrupted following visual deprivation, and was initially disrupted when visual information was returned. PD patients' postural recovery was comparable to control subjects when sensory incongruence ended. These findings indicate that situations of visual deprivation in particular are initially disruptive for PD patients, and imply initial difficulty for sensory reorganization in these patients. Our results provide insight into environmental situations imposing greater fall risk among the parkinsonian population.

ACKNOWLEDGEMENTS

What a journey it has been! Completing this thesis could not have been possible without the advice, guidance, and encouragement from the many people I have interacted with over the last two years.

First and foremost, thank you to every research participant involved in this study, for so selflessly donating your time and energy to this project. Without your participation, this thesis could not have been possible. In particular, thank you to the Parkinson's disease patients who willingly and eagerly volunteered to participate – your strength, determination, and perseverance are truly admirable.

Thank you to Dr. Sergio Pellis and Dr. Ian Whishaw for serving as my Supervisory Committee members. Your knowledge, guidance, and insight have been invaluable. In addition, thank you to Dr. Lenora Brown for serving as my External Committee member.

Thank you to my immediate family, for listening to my ranting, for assuring me that I am, in fact, more intelligent than I believe, and for always knowing when I just needed a hug. To Pat and Rich C - for always believing that I am the third of the three smartest girls on earth, for Sunday night dinners, and for always having a near-frozen beer ready for me when I needed it most. To Nat and Di, my sisters and partners in crime - for letting me vent, for introducing me to the wonders of cable (and for canceling it when it got too distracting!), for 'Gerard nights', and for always knowing how to make me laugh. Thank you to my 'second family' – Janelle and Judi Dormaar, who always welcome me into their home, who let me cry, and who still keep inviting me back for dinner. A special thank you to Janelle, my dearest friend and third partner in crime - for truly knowing me and loving me anyway.

Thank you to all 'my girls' – Janelle, Allison, Erin, Adina, Jillr and Sarah, for all your support and encouragement over the years. Everyone should be so lucky to have such amazing friends. Thank you for convincing for me that all work and no play really *is* no fun. To Jillr and Adina - thank you for Bachelorette Mondays, Top Models Wednesdays, and for too many OJ's/Ezzie's nights to count. To Allison and Erin – thank you for your support, guidance, and friendship. Thank you to Sarah Tiede, who began as my colleague and who became one of my most treasured friends. Thank you for sharing your unique insights into life, spirituality, and motion analysis with me. Thank you for being such an amazing source of strength and guidance, and for always assuring me that honesty truly is a virtue. Thank you to Heidi Bohler, my Texan friend and fellow academic, for your guidance, encouragement, and friendship from afar. Finally, thank you to Penny VandenBerg, for debauchery-filled 'town nights', for making me laugh, and for always listening. You are a true friend.

Thank you to my colleagues, Jon Doan and Justin Kurek, for putting up with me for two years. Thank you to Jon Doan, one of the most intelligent people I know - for your enduring patience, for sharing your insight and expertise, and for always finding time to provide me with programming, editing, and stats advice. Finally, thank you for your kind words of encouragement. You have been instrumental in the completion of this thesis, and you have been an amazing colleague and friend. Thank you to Justin Kurek, for your patience and kindness. Thank you for sharing road trips, birthdays, and the 'grad school experience' with

me. Finally, thank you to Nicole Anderson, Clint Wutzke, Kendra Massie, and Sarah Tiede, for your assistance with data collection, and for 'teaching me the ropes' of the BRL.

Last, but most certainly not least, a heartfelt thank you to the person who remains the single most influential individual in my academic career – my supervisor and mentor, Dr. Lesley Brown. We have accomplished some great things over the past couple of years, and I hope you are as proud of them as I am. Thank you for your enduring support, guidance, and patience, and for knowing that I work best under deadlines! Most importantly, though – thank you for taking a chance on me and for always believing in me, even when I forgot how to. This thesis could not have been possible without you. Your influence exists in every word of this document, and for that I will always be deeply grateful.

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I. GENERAL INTRODUCTION

Balance is integral to the performance of daily activities, such as crossing the street, rising from a chair, or bending to pick up a child. Because two-thirds of total body weight is located two-thirds of the body height above the ground, the human body has been described as an inherently unstable system (Winter, 1995). Thus, the maintenance of upright posture is achieved by an intricate working relationship among the musculoskeletal system, the body's sensory systems, and the Central Nervous System. Information from peripheral muscular and sensory systems is processed and integrated by the central nervous system to provide an internal representation of the body's position with respect to the external environment (Shumway-Cook & Woollacott, 2001). Any disruption in this relationship may result in a loss of equilibrium that may cause a fall.

A concern among the elderly population is the increased fall risk that is associated with reduced postural stability (Winter, 1995; Romero & Stelmach, 2003). The mechanisms underlying reductions in postural stability in this population are theorized to be of peripheral and central origin (Shumway-Cook & Woollacott, 2001; Romero & Stelmach, 2003). Specifically, increased detection thresholds of sensory receptors and decreased muscle strength have been implicated as peripheral mechanisms contributing to deterioration in balance control (Winter, 1995; Shumway-Cook & Woollacott, 2001). In addition, reduced functional integrity of the central mechanisms responsible for the processing and integration sensory information have also been implicated in contributing to postural difficulty among the aging population (Horak & Macpherson, 1996; Romero & Stelmach, 2003). Decline in postural stability, however, is not exclusive to the aging population; on the contrary, diseases of the central nervous system are associated with postural impairment that is not related to peripheral

dysfunction beyond that associated with age. One such disease is Parkinson's disease (PD). PD is a progressive and neurodegenerative disease, which results from the death of dopamine producing cells within the midbrain of the central nervous system. Indeed, PD is associated with the highest fall rate of all neurological disorders (Stolze, Klebe, Zechlin, Baecker, Friege, & Deuschl, 2004). This high fall rate is the leading cause of physical trauma among the parkinsonian population, and is strongly associated with disease-related postural impairment (Balash, Peretz, Leibovich, Herman, Hausdorff, & Giladi, 2005). For many patients, the threat of sustaining serious fall-related injuries, combined with progressive, disease-related decline in balance control may lead to the development of fear of falling that may impose further balance threat (Adkin, Frank, & Jog, 2001). Consequently, patients may limit their participation in activities of daily living, which may cause a loss of personal independence, reduced quality of life, and in extreme cases, admission to nursing homes (Giladi, Hausdorff, & Balash, 2005).

The purpose of this thesis was to investigate the influence of sensory manipulation on postural control among patients suffering from Parkinson's disease. This thesis includes a general introduction, two independent experiments, and a general discussion. The purpose of the general introduction is to provide background into postural control and Parkinson's disease, and to provide insight into environmental situations that impose fall risk among these individuals. The first experiment investigates the influence of visual deprivation on postural control among neurologically normal older adults and among PD patients. The second experiment examines PD patients' and control subjects' capacity for postural recovery following the termination of an imposed period of sensory incongruence. The general discussion summarizes the major research findings as they relate to the current literature.

1.1. OVERVIEW

PD has been described as a progressive, neurodegenerative disorder resulting from a loss of dopamine producing neurons in the pars compacta zone of the substantia nigra, a nucleus making up part of the basal ganglia (Cote & Crutcher, 1991). The symptoms of PD typically do not begin to show until approximately 80% of dopamine producing cells within the substantia nigra are depleted, and thus, individuals may be well into disease progression at the point of diagnosis (Barbeau, 1980).

PD is one of the most common late-life neurodegenerative disorders (Tanner, Goldman, & Ross, 2002), second only to Alzheimer's disease. In the next fifty years, the prevalence of this disease is expected to triple (Tanner, et al., 2002). This age-related risk of developing PD is particularly alarming because the number of individuals who will reach the age of 65 in the next few decades is expected to increase significantly. Consequently, the number of individuals suffering from Parkinson's disease will continue to increase, adding additional burden to an already strained health care system.

1.2. PARKINSON'S DISEASE: ETIOLOGY AND PATHOPHYSIOLOGY

1.2.1 Symptoms

PD is characterized by four cardinal symptoms, including: rigidity, tremor, bradykinesia, and postural impairment (Tanner, et al., 2002). Rigidity can be described as a heightened resistance to passive limb movement, and usually predominates in the flexor muscles of the trunk and limbs (Shumway-Cook & Woollacott, 2001). Rigidity often produces functional limitations for the patient, causing difficulties in bed mobility, gait, and balance control. Bradykinesia has been described as slowness in the performance of complex voluntary movements (Purves, Augustine, Fitzpatrick, Katz, LaMantia, McNamara, &

Williams, 1997). Tremor is defined as involuntary movements occurring at a frequency of 4-6 Hz (Latash, 1998), and usually occur while a patient is at rest (resting tremor), but may also occur during the performance of a motor task (intention tremor) (Purves, et al., 1997). Finally, postural impairment can be described as unsteadiness that occurs when standing or while performing locomotor tasks (Overstall, 2001). Postural impairment is particularly prevalent with disease onset after 70 years of age (Overstall, 2001). Overall, the severity of each symptom is variable among individuals, which makes the development of a generalized PD treatment particularly difficult. Symptom severity can be a major concern for the patient, because it impedes successful performance of daily activities, thus reducing patient independence and overall quality of life.

Of particular concern is postural impairment, a symptom that intensifies with advancing disease (Bloem, van Vugt, & Beckley, 2001) and that is not alleviated by conventional levodopa treatment (Rocchi, Chiari, & Horak, 2002). Disease-related postural impairment is associated with defective basal ganglia circuitry, which causes muscle rigidity around postural joints, and which reduces patients' ability to maintain posture following external perturbations (Chong, Horak, & Woollacott, 2000; Romero & Stelmach, 2003).

1.2.2. The Basal Ganglia

PD is characterized by basal ganglia dysfunction (Cote & Crutcher, 1991). The basal ganglia are a group of five subcortical nuclei that are theorized to play a role in the sequencing, timing, and coordination of movement execution (Marsden, 1982; Kolb & Whishaw, 1996; Takakusaki, Saitoh, Harada, & Kashiwayanagi, 2004). Because the basal ganglia do not make direct connections with the motor cortex, the regulation of movement occurs via connections with the thalamus, which then directly projects to and influences the motor cortex (Cote & Crutcher, 1991). Takaksusaki and colleagues (2004) suggest that the basal ganglia play an

important role in both volitional and automatic locomotor control via their connections with both the motor cortical areas and with the brainstem. Specifically, the basal ganglia may exert influence over the initiation and termination of gait, as well as obstacle avoidance during locomotion through their interaction with the thalamico-cortical circuits (Takakusaki, Oohinata-Sugimoto, Saitoh, & Habaguchi, 2004). Moreover, the automatic control of postural muscle tone and postural reflexes may be modulated by the basal ganglia via their direct connections with the brainstem (Takakusaki, et al., 2004). Finally, Keele and Ivry (1991) suggest that a major underlying function of the basal ganglia is to generate adequate movement force production. Hyperkinetic movement disorders associated with basal ganglia dysfunction generally result in force production in excess, while hypokinetic disorders result in inadequate force production, and typically result in the reduced capacity to successfully generate movements with sufficient force (Keele & Ivry, 1991).

The source of the motor dysfunction that is characteristic of PD results from the loss of dopamine producing cells within the substantia nigra (Cote & Crutcher, 1991). Mild symptoms often manifest well before disease diagnosis, and, at the time of diagnosis, approximately 80% of dopamine producing cells have already been lost. This substantial loss of dopamine cells within the substantia nigra prevents the adequate production of dopamine, and thus results in an inability to produce normal movements (Kolb & Whishaw, 2001).

1.2.3. Direct and Indirect Pathways

The basal ganglia consist of two main neuroanatomical motor circuits, both of which function to modulate thalamic output to the motor cortex (Figure 1.1). The direct pathway is comprised of projections from the caudate and putamen to the globus pallidus internus and substantia nigra pars reticulata. A major purpose of the direct pathway is to release cortical motor neurons from tonic inhibition placed upon them by the thalamus. In other words, a

function of the direct pathway is to decrease the amount of inhibition placed upon the motor cortex, thus facilitating movement.

The indirect pathway is comprised of projections from the caudate and putamen to the globus pallidus external. Projections from the globus pallidus external are in turn sent to both the globus pallidus and to the subthalamic nucleus. The subthalamic nucleus sends additional projections to the globus pallidus internal and substantia nigra pars reticulata, and serves to increase the level of tonic inhibition placed upon cortical motor neurons. Stated simply, the indirect pathway acts to "brake" the normal function of the direct pathway.

A third circuit within the basal ganglia system acts to modulate thalamic input to the motor cortex. This circuit is comprised of dopminergic cells within the pars compacta zone of the substantia nigra and modulates output of the caudate and putamen. Neurons within the caudate and putamen project to the substantia nigra pars compacta, which in turn sends dopaminergic projections back to the caudate/putamen. The influence of dopaminergic projections to the caudate/putamen can provide excitatory inputs (mediated by D1 type dopaminergic receptors) to the globus pallidus internal. Inhibitory D2 type dopaminergic receptors also influence neuronal projections to the globus pallidus external. The antagonistic actions of the direct and indirect pathways on the output of the basal ganglia serve to produce the same effect: to decrease the inhibitory output of the basal ganglia.

Alterations to the operation of this third pathway may explain many of the motor symptoms associated with PD. The normal effects of substantia nigra pars compacta input to the caudate/putamen are excitation of the neurons projecting to the globus pallidus internal (direct pathway) and inhibition of the neurons that project to the globus pallidus external (indirect pathway). The outcome of both of these dopaminergic effects is to increase the excitability of cortical motor neurons, which is mediated by a decrease in the inhibitory output of the basal ganglia. PD-associated destruction of dopamine cells within the substantia nigra

pars compacta result in an abnormally high amount of inhibitory output of the basal ganglia, thus reducing thalamic activation of cortical motor neurons.

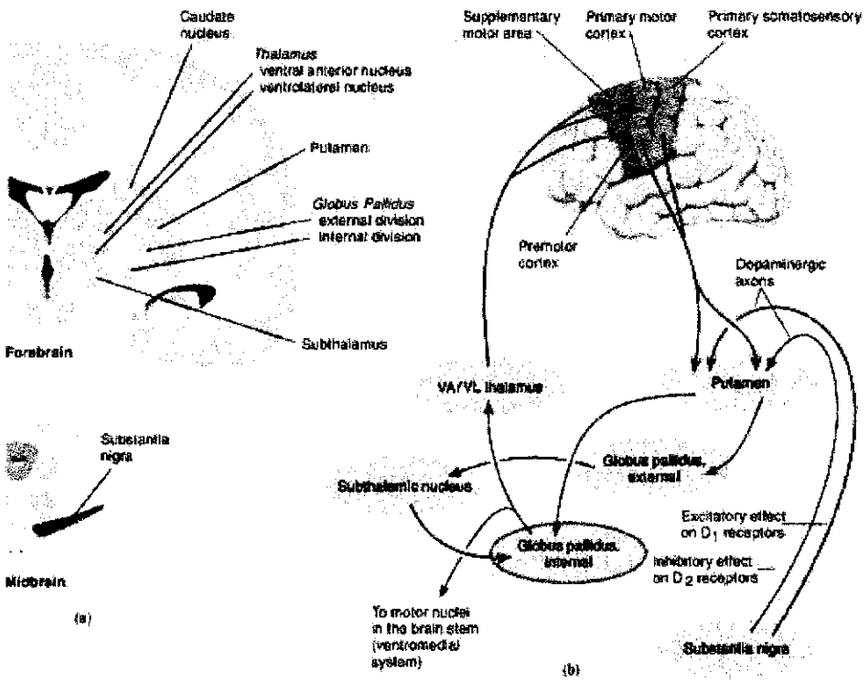

Figure 1.1: The basal ganglia and associated neuroanatomical circuitry. The basal ganglia are composed of five separate nuclei (a), including the caudate, putamen, globus pallidus (internal and external), subthalamic nucleus, and substantia nigra (pars compacta and pars reticulata). Basal ganglia activity is mediated by the release of dopamine from the substantia nigra (b), which exerts an excitatory effect on D1 receptors (black arrows) and an inhibitory effect on D2 receptors (red arrows) (http://www.driesen.com/basal_ganglia.html).

1.2.4. Etiology

Although the cause of PD is unknown, several factors have been implicated in disease onset. Two such factors include environmental factors and heredity (Tanner, et al., 2002). Environmental factors that may contribute to the development of PD include environmental toxins such as pesticides, herbicides, and industrial chemicals (Tanner & Langston, 1990). Other environmental toxins that may be associated with the risk of developing PD include trace metals, cyanide, carbon monoxide, and organic solvents (Olanow & Tatton, 1999). The theory that exposure to toxins increases the risk of developing PD originated from the

exposure of drug addicts to 1,2,3,6-methyl-phenyl, tetrahydropyridine (MPTP), which is a by-product of the illegal production of synthetic heroine (Olanow & Tatton, 1999). Drug addicts who took MPTP developed a syndrome that was clinically and pathophysiologically similar to PD (Olanow & Tatton, 1999). MPTP toxicity results from its conversion to pyridinium (MPP^+) in a reaction that is catalyzed by monooxidase type B (MAO-B) (Singer, Castagnoli, Ramsay, & Trevor, 1987). MPP^+ is then taken up by dopamine-producing neurons and becomes concentrated in the mitochondria, where it binds and inhibits NADH complex I (Tanner, et al., 2002). Blockade of NADH-I prevents oxidative phosphorylation and the production of adenosine triphosphate (ATP) (Tanner, et al., 2002). Free-radical and nitric oxide build-up also occur, which contribute to oxidative stress and cellular apoptosis (Tanner, et al., 2002).

Genetics have also been implicated as potential risk factors for the development of PD. Wood et al., (1998) report that the incidence of PD is greater in family members than in age-matched controls. Similarly, concordance rates indicated a significantly higher incidence of PD in monozygotic twins who developed the disease before the age of 50 (Tanner, Ottman, Ellenberg, & al, 1997). These findings imply that young-onset (ie onset occurring before the age of 50) PD, in particular, may have a strong genetic link.

Because the cause of PD is undetermined, disease prevention is unattainable. At present, treatment of parkinsonian symptoms is focused on returning patients to their best possible level of functionality to ensure optimal quality of life. Levodopa medication is successful as a generalized treatment for PD, often providing prolonged alleviation of tremor, rigidity, and bradykinesia (Suchowersky, 2002). Levodopa dosage must be increased, however, as symptoms become intensified with disease progression. Increased dosage often results in the development of unfavourable motor fluctuations known as dyskinesias. Levodopa is also not beneficial to reduce postural instability (Rocchi, et al., 2002; Rocchi, Chiari, Cappello,

Gross, & Horak, 2004), because it reduces tonic muscle stiffness around the ankle and hips joints without improving patients' ability to rapidly compensate for disruptions to equilibrium (Chong, et al., 2000). In addition, the development of dyskinesias can interfere with patients' postural control, and consequently may intensify parkinsonian instability (Overstall, 2001). Postural control is a biomechanically challenging task even for healthy adults, but is particularly difficult for PD patients because of enhanced rigidity, abnormal postural reflexes (Romero & Stelmach, 2003), and because of deficits in their capacity for the central integration of sensory information for postural control (Bronstein, Hood, Gretsy, & Panagi, 1990; Bronte-Stewart, Minn, Rodrigues, Buckley, & Nashner, 2002; Abbruzzese & Berardelli, 2003; Nallegowda, Singh, Handa, Khanna, Wadhwa, Yadav, Kumar, & Behari, 2004).

1.3. POSTURAL CONTROL

Postural control is defined as the process of regulating the body's position in space for the purpose of achieving an upright and stable stance (Shumway-Cook & Woollacott, 2001). As such, effective postural control requires both perception and action. 'Perception' refers to the detection and integration of sensory information to evaluate the position and motion of the body with respect to the environment. 'Action' refers to the body's ability to produce forces for controlling body position systems (Shumway-Cook & Woollacott, 2001). Thus, perception and action are dependent upon communication and interaction between the body's neural and musculoskeletal systems. Neural components of postural control include motor processes, sensory processes, and high-level integrative processes. Musculoskeletal components include joint range of motion, spinal flexibility, muscle properties, and the biomechanical relationships among body segments. Efficient communication between these systems is crucial if stability is to be maintained during the performance of daily activities. Thus, the body's systems for postural control communicate via feed-forward and feed-back

inputs to ensure that the ultimate goal of postural control is achieved: to detect and correct disruptive movements that surpass the body's stability limits to prevent an injurious fall episode.

1.3.1. The Biomechanical Basis of Postural Control

Balance is defined as the ability to maintain the body in equilibrium (Shumway-Cook & Woollacott, 2001). The human body has been described as an inherently unstable system because approximately two-thirds of the total body mass is located two-thirds of the body height above the ground (Winter, Patla, & Frank, 1990; Winter, 1995). Consequently, equilibrium control is a biomechanically challenging task. Complete balance control is achieved by regulating balance in the antero-posterior (AP) and medio-lateral (ML) directions (Winter, Prince, Stergiou, & Powell, 1993). AP balance is controlled around the ankles and is regulated by the contraction of plantarflexor (triceps surae muscle group) and dorsiflexor (tibialis anterior) muscles (Winter, et al., 1993; Winter, 1995). ML balance, on the other hand, is controlled at the hip joint and is regulated by the contraction of hip abductors and adductors (Winter, et al., 1993; Winter, Prince, Frank, Powell, & Zabjek, 1996).

Ultimately, AP and ML body movement arise because a large portion of total body mass (and thus the body's centre of mass) is located over a relatively small base of support. The influence of gravitational forces and the distribution of a large portion of total body mass above the legs present the propensity of the upper body to rotate around the hip joint (Winter, 1995). As such, the human body has been described following the model of an inverted pendulum (Winter, 1995; Winter, Patla, Prince, Ishac, & Gielo-Perczak, 1998). In this model, postural equilibrium, or balance, is maintained only when the body's centre of mass remains within the body's narrow base of support (Winter, 1995; Horak & Macpherson, 1996; (Shumway-Cook & Woollacott, 2001). Centre of mass refers to a point in space that

represents the net location of total body mass, and represents the weighted average of body segments (Winter, 1995; Shumway-Cook & Woollacott, 2001). The base of support refers to the area of the body in contact with the ground (or support surface), and is typically defined by the boundaries of the feet (Winter, 1995; Horak & Macpherson, 1996; Shumway-Cook & Woollacott, 2001).

During stance, external forces acting on the centre of mass must be of equal and opposite magnitude for postural equilibrium to be maintained (Horak & Macpherson, 1996). These external forces include the downward-acting force of gravity, and the equal and opposite ground reaction force acting under the feet (Horak & Macpherson, 1996). During quiet standing, gravitational acceleration creates a force that passes through the centre of mass, which can cause a forward movement of the centre of mass (Horak & Macpherson, 1996). Excessive forward movement of the centre of mass is prevented by the ground reaction force, which acts on the soles of the feet with a force equal and opposite to that of the force of gravity (Horak & Macpherson, 1996). Consequently, maintenance of static equilibrium is achieved.

Maintenance of postural equilibrium during quiet standing constrains movement of the centre of mass to the boundaries of the base of support (Horak & Macpherson, 1996). Centre of mass movement may occur due to movements originating from within the body, such as those caused by respiration or by the beating of the heart. Furthermore, the occurrence of continually varying muscle forces, represented by the ground reaction force, may also generate body movement (Horak & Macpherson, 1996). The point of origin of the ground reaction force is referred to as the centre of pressure, and is a theoretical point of force application. During quiet standing, the centre of pressure is usually located between the feet. The occurrence of internally-generated body movements and the ongoing variation of muscle forces generate centre of pressure movement that, if large enough, may result in centre of mass

movement (Horak & Macpherson, 1996). Thus, it is unlikely that the position of centre of mass within the base of support is ever static.

Continual variation in muscle force generates a centre of pressure movement trajectory (Horak & Macpherson, 1996) within the boundaries of the body's base of support. Winter (1995) describes the centre of pressure as a reflection of direct neural control of ankle muscle activity. Neural control of plantarflexor and invertor muscle activity produces anterior and lateral centre of pressure movement, while increased dorsiflexor and evertor muscle activity produces posterior and medial centre of pressure movement (Winter, 1995). It is important to note that centre of pressure and centre or mass, although often used interchangeably, are not synonymous; in fact, centre of pressure is independent of centre of mass (Winter, 1995). Winter (1995) describes the centre of pressure and centre of mass as being related, however, such that the position of centre of mass in relation to centre of pressure will influence centre of pressure movement, which will in turn affect centre of mass movement (Figure 1.2). For example, if the centre of mass is positioned ahead of the centre of pressure, a clockwise torque will be produced, causing clockwise angular acceleration of the body about the ankle joints. Increased activity of plantarflexor muscles will cause a forward shift in centre of pressure movement, until eventually it will lie ahead of the centre of mass. When this occurs, a counterclockwise torque will be generated, causing a counterclockwise angular acceleration of the body about the ankle joints. In this situation, the central nervous system regulates centre of pressure movement by reducing plantarflexor activity (and increasing dorsiflexor activity), thus facilitating centre of pressure movement to a position behind the centre of mass. Posterior movement of centre of pressure behind centre of mass will again create a forward angular acceleration, causing the body to move forward to its original position (Winter, 1995).

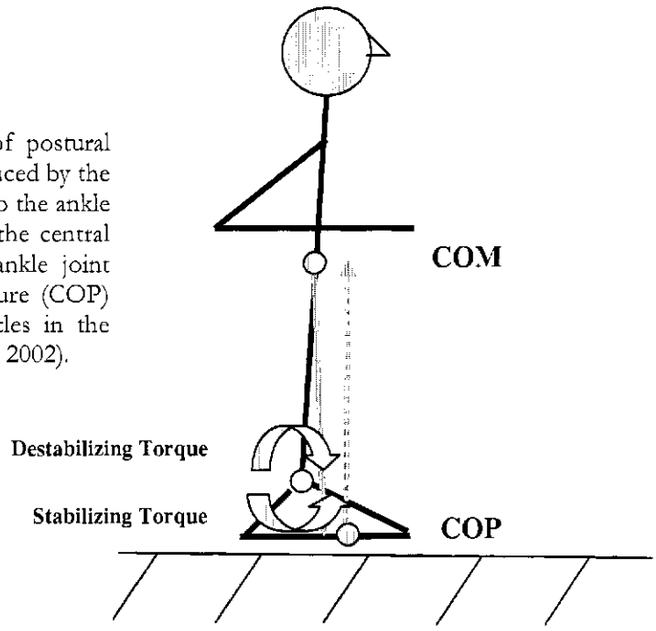

Figure 1.2. Diagram of the inverted pendulum model of postural control. During quiet standing, a destabilizing torque is produced by the downward projection of the centre of mass (COM) anterior to the ankle joint. To oppose this torque and preserve upright stance, the central nervous system generates a stabilizing torque about the ankle joint (achieved by posterior displacement of the centre of pressure (COP) behind the COM) via the activation of plantarflexor muscles in the lower leg (figure adapted from Winter et al., 1995, and Polych, 2002).

The body movement produced from the continual movement of centre of mass is commonly referred to as spontaneous sway, body sway, or simply sway (Shumway-Cook & Woollacott, 2001). Individuals who exhibit a higher degree of overall body sway during quiet standing are considered to be less stable (Patla, Winter, Frank, & al., 1990), and may be at higher risk of falling. If the centre of mass moves to within a few centimeters of, or deviates from, the boundaries of the base of support, fall probability increases (Shumway-Cook & Woollacott, 2001). In such situations, balance will be preserved only if an individual utilizes distinct movement patterns to prevent a fall (Horak & Nashner, 1986; Winter, 1995; Horak, Henry, & Shumway-Cook, 1997). These distinct movement patterns of postural recovery, also referred to as 'postural strategies', function to preserve equilibrium following external disruptions by constraining the centre of mass within the base of support (Shumway-Cook & Woollacott, 2001).

The postural strategies commonly described in the literature include the feet-in-place (ankle and/or hip) strategy and the change-in-support (stepping) strategy (Winter, 1995;

Horak & Macpherson, 1996; Shumway-Cook & Woollacott, 2001; Maki, McIlroy, & Fernie, 2003). Horak and Nashner (1986) describe the ankle strategy as being the most frequently used response during quiet standing. The ankle strategy may be used when the body sways forward, which may occur following an external perturbation such as a gentle nudge to the upper shoulders. Backward movement of the support surface creates a rotation around the ankle joint that causes an anterior shift of the centre of pressure beyond the centre of mass. The anterior shift in centre of pressure reverses centre of mass displacement and drives it backward to its original position. Consequently, forward body sway is reduced (Horak & Macpherson, 1996). The backward shift in centre of mass displacement is achieved by the sequential activation of ankle, knee, and hip extensor muscles, which rotates the body about the ankle joints, and causes relatively little movement around the hip or knee joints (Horak & Macpherson, 1996). Use of the ankle strategy is most efficient in situations involving small, slow perturbations on an even, firm surface (Horak & Macpherson, 1996), and is the strategy most commonly used by younger adults (Brown, Shumway-Cook, & Woollacott, 1999).

Situations involving rapid or large amplitude disruptions, and/or conditions which constrain or prevent ankle rotation require the use of the hip strategy (Horak & Macpherson, 1996). The hip strategy is characterized by the simultaneous bending of the trunk at the hip joints, and the counter-rotating at the neck and ankle joints caused by the sequential activation of the quadriceps muscle, the abdominal muscles, and the neck muscles (Horak & Nashner, 1986). According to Brown et al., (1999), the hip strategy is frequently used among elderly adults. In addition, elderly adults may be more inclined to employ the change-in-support strategy for the maintenance of balance. The change-in-support (stepping) strategy involves taking a step in response to very fast and/or large postural disruptions, or when there is a predominant requirement of maintaining vertical upper body orientation (Horak & Macpherson, 1996). The use of a stepping strategy may also emerge in response to small

perturbations with which individuals lack prior experience, or in situations in which individuals are not constrained to keeping their feet on the ground (Horak & Macpherson, 1996).

Effective use of postural strategies is highly dependent upon an individual's ability to adjust and modify existing motor programs according to task requirements and to environmental context. The ability to maintain equilibrium in changing environmental contexts requires the modification of motor set. Motor set can be defined as movement preparation achieved by the selection of appropriate movements and the suppression of inappropriate movements (Kropotov & Etlinger, 1999). For example, an appropriate muscle response to a platform perturbation involving backward translation involves the contraction of anterior leg muscles (tibialis anterior and rectus femoris muscles) and the suppression of posterior leg muscles (hamstring and triceps surae muscle groups) to counteract translation-induced anterior body sway (Horak & Nashner, 1986). In this situation, contraction of the posterior leg muscles would be an inappropriate response because it would impose a postural disruption beyond that induced by platform translation (Chong, et al., 2000). Conversely, a perturbation involving forward translation would require a modification of motor set to facilitate the contraction of the posterior leg muscles and the suppression of the anterior leg muscles to counteract the effects of backward sway (Horak & Nashner, 1986). The ability to rapidly modify automatic motor programs according to task demands and to environmental context is integral to an individual's ability to maintain stability in a dynamic environment. This capacity for rapid modification of motor set for postural tasks is impaired among individuals suffering from PD (Chong, Jones, & Horak, 1999), which may be even more problematic for a population already suffering from balance impairment.

1.3.2 Parkinsonian Posture

Postural impairment has been described as one of the most disabling signs of Parkinson's disease, because it is associated with a high rate of falls that often cause serious injury (Bloem, et al., 2001; Balash, et al., 2005). Epidemiologic evidence indicates that the percentage of patients who fall ranges between 38% and 68% (Hoehn & Yahr, 1967; Gray & Hildebrand, 2000; Ashburn, Stack, Pickering, & Ward, 2001; Michalowska, Krygowska-Wajs, Jedynecka, Sobieszek, & Fiszer, 2002; Wood, Bilclough, Bowron, & Walker, 2002); this is in contrast to the healthy older adult population, which is characterized by a fall rate of 30% among individuals aged 60+ years (Bloem, et al., 2001). The high rate of falling among the parkinsonian population is strongly associated with a loss of postural reflexes and increased postural impairment that are related to disease progression (Balash, et al., 2005). A high fall rate among PD patients is a concern because falls are a leading cause of physical trauma in this population; approximately 50% of PD patients fall at least twice yearly, with 1/5 of these patients suffering from bone fractures and/or intracranial hematomas (Balash, et al., 2005). For many patients, the possibility of experiencing a fall leads to the restriction of daily activities, and in some circumstances, admission to nursing homes (Giladi, et al., 2005).

1.4 SENSORY CONTRIBUTIONS TO POSTURAL CONTROL

The visual, vestibular, and somatosensory systems provide the central nervous system with information regarding the position and state of the body in relation to the external environment. Information from each type of sensory modality provides the central nervous system with an accurate internal representation of the body in space.

1.4.1 Somatosensory Inputs

The somatosensory system provides humans with the ability to monitor internal and external forces acting on the body at any moment in time (Purves, Augustine, Fitzpatrick, Katz, LaMantia, McNamara, & Williams, 1997). Information from muscle, joint, and cutaneous receptors located throughout the body's periphery provide the central nervous system with information regarding the state of the musculoskeletal system and the external environment (Horak, Nashner, & Diener, 1990). Muscle receptors include muscle spindles and golgi tendon organs, which detect changes in muscle length and muscle tension, respectively (Purves, et al., 1997). Joint receptors include Paciniform endings, ligament receptors, and free-nerve endings that are sensitive to joint movement and to stress (Shumway-Cook & Woollacott, 2001). Tactile changes in the environment and the position of the body within the environment are detected by cutneous mechanoreceptors. Several types of cutaneous mechanoreceptors exist, each detecting a different modality of sensory information. Ruffini endings respond to changes in stretch, Merkel's discs to pressure, Meissner's corpuscles to vibration and light touch, and Pacinian corpuscles to vibration (Shumway-Cook & Woollacott, 2001). The distribution of somatosensory receptors throughout the body provides the central nervous system with a wide range of information regarding the configuration of body segments in relation to each other, and with respect to the external environment (Horak & Macpherson, 1996).

1.4.2 Vestibular Inputs

The vestibular system provides a gravitoinertial frame of reference for postural control. Specifically, vestibular inputs provide the central nervous system with information regarding the position and movement of the head with respect to gravity and inertial forces (Shumway-

Cook & Woollacott, 2001). Two types of receptors respond to different aspects of head position and motion: the semicircular canals sense and respond to angular acceleration of the head, while the otolith organs sense linear position and acceleration. The semicircular canals are particularly sensitive to fast head movements, such as those that occur during slips or stumbles (Horak & Shupert, 1994). The otolith organs, on the other hand, respond primarily to slow head movements, such as those occurring during postural sway (Shumway-Cook & Woollacott, 2001).

Vestibular inputs have been implicated for the triggering of postural responses to sudden, unexpected falling (Horak & Macpherson, 1996). Experimentation with both humans and cats revealed an early activation of extensor muscles following a sudden, unexpected drop of the body from a height (Greenwood & Hopkins, 1976; Watt, 1976), an effect which was not observed in patients without vestibular function and in cats with lesioned otolith organs. The early activation of extensor muscles may function to prepare the body for impending landing following an unexpected drop (Horak & Macpherson, 1996). Conversely, vestibular inputs may not be required for the triggering of postural responses following movements of the support surface, especially when an individual is in contact with a large, stable surface (such as when standing on the ground). Patients suffering from bilateral disruption of vestibular function exhibit normal timing and patterning of muscle activation following support surface translations and rotations, although the magnitude of muscle activation may be reduced. Thus, vestibular inputs may influence the magnitude of postural responses, but are not integral for the triggering, patterning, or scaling of postural responses to surface perturbations (Horak & Macpherson, 1996).

1.4.3 Visual Inputs

Visual inputs provide information pertaining to the position and motion of the head with respect to the surrounding environment (Shumway-Cook & Woollacott, 2001). Information from both peripheral and foveal sources is included in visual inputs, although peripheral information (i.e. information from a large visual field) may be more important than foveal visual information for the control of posture (Paillard, 1987).

Visual inputs are important for the control of upright posture, but they may not be absolutely necessary. In most cases, individuals are still able to maintain their balance in conditions in which visual input is reduced or absent altogether, such as when an individual moves from a lighted to a darkened room. In such situations, a heavy reliance would likely be placed on vestibular and somatosensory inputs for the maintenance of stable posture.

The elimination of vision influences postural equilibrium in a task- and context-dependent manner (Horak & Macpherson, 1996). The removal of vision generally causes an increase in sway during quiet stance. In the original experiment that measured balance while participants closed their eyes, Romberg (1851) observed that the degree of sway was influenced by stance position. Romberg (1851) also noted that body sway appeared to increase even further in patients suffering from central or peripheral neural disorders. Similarly, alterations of visual information have been shown to reveal an increase in sway area among the elderly (Peterka & Black, 1990-1991; Redfern, Yardley, & Bronstein, 2001). Conversely, experiments in which subjects were instructed to stand as still as possible or who were anxious about falling revealed that subjects did not exhibit increased sway area following eye closure (Nashner, 1982). The magnitude of sway increase may vary according to factors such as stance posture, availability of accurate somatosensory and vestibular information, and cognitive factors such as fear of falling (Horak & Macpherson, 1996). In addition, magnitude of sway in the absence of

vision may also be related to an individual's ability to adapt motor set and compensate for the loss of vision (Horak & Macpherson, 1996).

1.4.4 Integration of Sensory Information for Postural Control

The central processing of sensory information ensures the production of a motor plan for task execution that is appropriate to the sensory environment (Allison & Jeka, 2004). Equilibrium control depends on the continual updating and prioritization of sensory information generated by the environment. The process of updating and prioritizing sensory information for postural control is referred to as sensory reweighing (Allison & Jeka, 2004). Because the centre of mass is a calculated point in space, the central nervous system can never determine its position solely from one type of sensory information. Instead, centre of mass must be determined using information conveyed from the three sensory modalities for postural control, which communicate redundant information about the position of the body relative to the external environment (Shumway-Cook & Woollacott, 2001). The redundancy of sensory inputs conveyed to the central nervous system provides a degree of flexibility for the maintenance of postural equilibrium, such that balance can be preserved when one sensory modality conveys ambiguous information, or when information from another modality becomes deprived (Horak & Macpherson, 1996; Allison & Jeka, 2004). When information from one sensory modality is incongruent to information conveyed by another, the central nervous system must resolve sensory conflict by prioritizing the remaining congruent sensory information and suppressing the inaccurate information. The central nervous system has been described as organizing sensory information in a hierarchy (Teasdale & Simoneau, 2001), such that balance control is based heavily on information conveyed by the sensory modality of 'highest priority'. If the accuracy or availability of this 'high priority' sensory input becomes compromised, the central nervous system must disregard this information and instead

reorganize the sensory hierarchy to prioritize remaining sensory information for postural control (Teasdale & Simoneau, 2001; Allison & Jeka, 2004). Moreover, when sensory information becomes available following a period of incongruence or deprivation, the central nervous system must reintegrate, or incorporate this information back into the sensory hierarchy to ensure that adjustments in postural set reflect the most current state of the sensory environment.

PD patients have difficulty adjusting to postural disruptions imposed by situations of sensory incongruence or deprivation (Bronstein, Hood, Gretsy, & Panagi, 1990; Chong, et al., 1999; Bronte-Stewart, et al., 2002; Nallegowda, et al., 2004). Results from sensory manipulation experiments indicate that PD patients experience difficulty with the reweighing of sensory inputs (Bronstein, et al., 1990; Bronte-Stewart, et al., 2002). For example, a moving-room experiment conducted by Bronstein and colleagues (1990) revealed difficulty among PD patients to adapt to successive small room movements. In that experiment, patients were examined on a stable platform during lateral linear movement of the visual surrounds. Moving the room led to increased levels of unsteadiness among PD patients. Moreover, PD patients were unable to overcome the destabilizing effects of the room motion during recurring stimulation. Current theory indicates that postural adaptation in moving-room experiments depends on a shift from primarily visual to proprioceptive control (Teasdale & Simoneau, 2001). The decrease in postural stability observed among PD patients during moving-room experiments implies a lack of adaptation, and consequently implicates a role of the basal ganglia in sensory integration (Bronstein, et al., 1990; Teasdale & Simoneau, 2001). Additional studies also indicate that postural disruptions emerge when PD patients are presented with situations of sensory incongruence (Bronte-Stewart, et al., 2002; Nallegowda, et al., 2004). These results lend support to the notion that the capacity for the suppression of incongruent sensory information is reduced among PD patients, and consequently also provide further

empirical evidence implicating a role of the basal ganglia in sensory integration for postural control.

The integrity of the central mechanisms for sensorimotor integration is generally inferred via the Sensory Organization Test (NeuroCom International, Clackamas, OR), which assesses postural control under varying sensory conditions (Nashner, 1993; Shumway-Cook & Woollacott, 2001; Allison & Jeka, 2004). The apparatus includes a movable force platform and a movable visual surround, which both move according to the magnitude of postural sway displayed by the participant. Sensory organization test protocols investigate quiet standing under varying sensory conditions, during which the availability or accuracy of sensory inputs are manipulated (Figure 1.3). A benefit of sensory organization test protocols is that they accurately assess upright standing under sensory conditions that simulate real-world situations (Nashner, 2001), and that they are not influenced by learning bias (Nashner, 1993; Paloski, Reschke, & Black, 1999).

Although sensory organization test protocols have been influential in the development of current theories regarding central contributions of sensory information for postural control, the information obtained from this protocol does not provide an assessment of changes in postural stability that occur over time. Instead, sensory organization test protocols provide a single measure of postural control that reflects stability across the entire period of perturbation, which is typically 15 or 20 seconds in duration. Although this measurement provides information regarding the overall stability of the participant across a particular period of time, it does not provide information regarding fluctuations in stability that occur within a particular time interval. For example, a participant's stability may be initially disrupted when sensory inputs are manipulated, but may stabilize within a few seconds following sensory perturbation. Thus, the single measure of stability that is provided by sensory organization test protocols may not capture this initial disruption. Consequently, the quantification of

fluctuations in postural stability within smaller intervals of time (time based assessment) may be beneficial to capture changes in stability occurring in the initial few seconds following sensory perturbation.

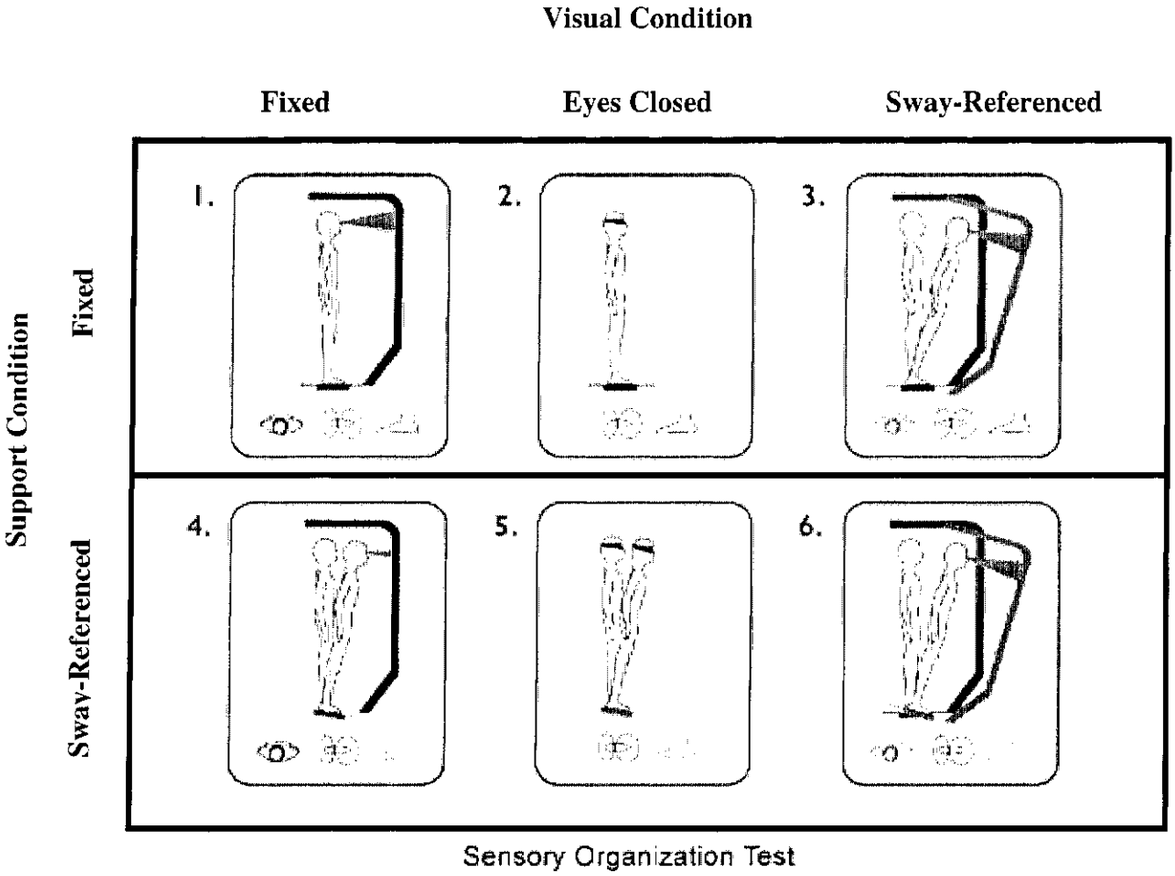

Figure 1.3. Sensory conditions of the Sensory Organization Test. Postural control is assessed under five sensory conditions. Condition 1 is considered as the 'baseline' condition, where all sensory inputs are accurate and available. Condition 2 involves visual deprivation, while Condition 3 involves a situation of visual incongruence, achieved by sway-referencing of the visual surround. Condition 4 introduces a situation of somatosensory incongruence, achieved by sway-referencing of the force platform. Condition 5 introduces a situation of visual deprivation and somatosensory incongruence, achieved by depriving the subject of visual information and by sway-referencing of the force platform. Condition 6 involves a situation of visuo-somatosensory incongruence, achieved by sway referenced movement of the force platform and visual surround (figure adapted from Allion & Jeka, 2004 and Shumway-Cook & Woollacott, 2001).

For example, if PD patients have difficulty rapidly compensating for postural disruption imposed by sensory manipulation, then an assessment of postural control across shorter time

intervals may be a useful method of exploring this possibility. Specifically, if PD patients are deficient in their ability to reorganize sensory priorities following sensory manipulation, then it is possible that the effects of sensory perturbation may not be immediate, but may be time-lagged to the onset of perturbation. In recognition of this possibility, Vuillerme and colleagues (2001) performed a time based assessment of postural control among balance-trained and balance-untrained adults following sensory manipulation. The authors' findings confirmed that the postural effects of sensory manipulation were not immediate, and that they varied according to the characteristics of the performer (Vuillerme, Teasdale, & Nougier, 2001). Consequently, these authors confirmed that the time course, or time needed to return postural sway to a magnitude that is comparable to that which occurs during full sensory availability, differed between balance-trained and balance-untrained adults, such that balance-untrained adults had a prolonged time course for postural control compared to their balance-trained counterparts.

When sensory feedback sources become available or accurate following a prolonged period of unavailability or inaccuracy, the central nervous system must update and reorganize the sensory hierarchy to accommodate this change in sensory inputs (Allison & Jeka, 2004). In addition, the ability to reintegrate sensory information following a prolonged period of incongruence or absence is also crucial for the maintenance of equilibrium (Vuillerme, et al., 2001). Thus, examining how the magnitude of postural sway changes following a manipulation of sensory information is important because it provides insight into the magnitude of postural disruption and the time course for postural compensation. For patients with PD, time based assessments of postural control following sensory perturbation will contribute additional knowledge regarding situations when PD patients may be most susceptible to a fall episode. Expansion of the current knowledge base in this domain may be important to increase patients' awareness of environmental situations impose balance threat,

and may contribute to the reduction of fall risk in this population. Moreover, investigation into the time-based characteristics of postural control among PD patients may be an important factor contributing to the development of rehabilitation strategies targeted at improving balance control in challenging sensory situations.

1.5 SUMMARY

PD is a progressive and neurodegenerative disease that imposes debilitating symptoms upon the patient, resulting in reduced independence and quality of life. Postural impairment is a concern for patients, because it is not alleviated by conventional drug therapy, and because it increases patient fall risk. Parkinsonian medications can be detrimental to balance because they reduce tonic rigidity occurring around the ankle and hip joints without improving the mechanisms underlying postural adaptation (Horak, Nutt, & Nashner, 1992; Bloem, et al., 2001). Consequently, although PD patients may experience medication-dependent relief from excessive muscle rigidity (Suchowersky, 2002), patients become more vulnerable to falls because they have difficulty maintaining equilibrium in environmental situations that impose postural disruptions.

Another factor affecting postural stability among PD patients is the central processing of peripheral sensory information (Bronte-Stewart, et al., 2002; Abbruzzese & Berardelli, 2003; Nallegowda, et al., 2004). PD-associated basal ganglia dysfunction is theorized to cause deficits in the central processing and integration of sensory information for postural control (Bronstein, et al., 1990; Bronte-Stewart, et al., 2002; Abbruzzese & Berardelli, 2003). Adequate postural control is dependent upon the ability of the central nervous system to process and integrate, or 'make sense of', afferent sensory feedback conveying the current state of equilibrium relative to the sensory environment (Allison & Jeka, 2004). The maintenance of equilibrium in dynamic sensory environments can be challenging because it requires continual

prioritization of sensory inputs for postural control, a task which can be difficult for older adults who experience age-related decline in central processing capacity. Reorganization and prioritization of sensory inputs for postural control is often more even more difficult for PD patients, who may experience deficits in central processing capacity beyond those related to age. Consequently, postural impairment may become intensified in situations involving deprivation or inaccuracy of sensory inputs.

Sensory organization protocols are useful for the assessment of postural control under various sensory conditions (Nashner, 1993; Bronte-Stewart, et al., 2002; Tsang, Wong, Fu, & Hui-Chan, 2004), and generally accepted as a reliable paradigm of measuring the capacity of the central nervous system to prioritize and reintegrate sensory information (Nashner, 1993; Bronte-Stewart, et al., 2002; Tsang, et al., 2004). Although these protocols provide insight into the magnitude of postural disruption following sensory perturbation, they do not provide a time based assessment of postural control during the perturbation period, or during the reintegration period.

1.6. OBJECTIVES OF THE THESIS

The primary objective of this thesis is to provide an in-depth examination of the influence of PD on the time course for postural control following imposed manipulations of sensory information. Two studies were conducted to address this objective. The purpose of Study 1 was to investigate the effects of visual deprivation on the time course of the reweighing and reintegration of sensory information for postural control. The purpose of Study 2 was to investigate the time course for postural recovery following the termination of imposed situations of sensory incongruence.

1.6.1. Study 1 Predictions

Based on the evidence available in the literature (Bronstein, et al., 1990; (Bronte-Stewart, et al., 2002; (Nallegowda, et al., 2004), it was predicted that visual deprivation would induce postural disruption that is more difficult to overcome for medicated Parkinson's patients than their healthy older adult counterparts. In addition, it was hypothesized that the time course for postural recalibration following the deprivation and reinsertion of visual information will be prolonged compared to healthy control subjects.

1.6.2. Study 2 Predictions

It was predicted that the termination of imposed intervals of sensory incongruence will induce postural disruptions among PD patients. Specifically, it was hypothesized that PD patients will express deficits in the reintegration of sensory information following the termination of a prolonged interval of sensory incongruence, and that this difficulty will emerge as a smaller magnitude of, and a prolonged time course for, postural recovery compared to neurologically healthy older adults.

II. STUDY 1 – PARKINSONIAN DEFICITS IN SENSORY INTEGRATION FOR POSTURAL CONTROL: TEMPORAL RESPONSE TO ALTERATIONS IN VISUAL INPUT

2.1. Introduction

Postural control is a sensorimotor process in which the central integration of visual, vestibular, and proprioceptive information conveys the current state of equilibrium to ensure on-going regulation of motor commands appropriate to the sensory experience (Allison & Jeka, 2004). The redundancy of sensory information that is conveyed to the central nervous system permits flexibility to suppress incongruent sensory information and to compensate for situations of sensory conflict and/or sensory deprivation. Sensory manipulation experiments demonstrating increased postural impairment among PD patients implicate the basal ganglia as being crucial for the integration of sensory information for postural control (Bronstein, et al., 1990; Chong, Horak, & Woollacott, 2000; Bronte-Stewart, et al., 2002; Nallegowda, et al., 2004).

Standard protocols (ie Sensory Organization Test, NeuroCom® International, Clackamas, OR) for investigating sensory contributions to postural control quantify the magnitude of deterioration in postural performance when a sensory feedback source is deprived or disrupted, either independently or in combination with other feedback sources. The foundation of this testing protocol is to assess the integrity of the central nervous system to resolve conflicts of sensory information and to compensate for situations of sensory deprivation. Although results have been influential to current theories (Bronstein, et al., 1990; Chong, et al., 2000; Bronte-Stewart, et al., 2002; Dickin & Rose, 2004), a major limitation of these protocols is that they fail to provide any information regarding the time course for postural control during the sensory manipulation interval. For example, it may be possible that

the effect of altering sensory feedback is not instantaneous, but is time-lagged from the onset of the manipulation; perhaps as a function of characteristics such as age or disease state. Recently, in recognition of this limitation, Vuillerme and colleagues (2001) explored the effect of sensory manipulation on the time course for postural control among skilled and unskilled gymnasts. Their findings confirmed that the effect of a sensory manipulation is not immediate, and that characteristics of the performer influence the time based effects of sensory manipulation. This information, currently unavailable from standard sensory organization protocols (Horak, et al., 1992; Chong, et al., 2000; Shumway-Cook & Woollacott, 2001; Bronte-Stewart, et al., 2002), provides a dimension of knowledge that will extend our current understanding of sensory contributions to postural control.

Although current theory holds that the basal ganglia contribute to sensorimotor integration for postural control (Bronstein, et al., 1990; Bronte-Stewart, et al., 2002; Nallegowda, et al., 2004), stability among PD patients is not compromised when visual information is absent (Horak, et al., 1992; Waterston, Hawken, Tanyeri, Janti, & Kennard, 1993; Bronte-Stewart, et al., 2002). Postural control is disrupted in these patients, however, if visual information is made incongruent to accurate somatosensory or vestibular feedback (Bronstein, et al., 1990; Bronte-Stewart, et al., 2002; Nallegowda, et al., 2004). These findings imply that PD patients can reweigh sensory feedback sources to prioritize accurate modalities when vision is absent, but that the presence of visual information, even if providing inaccurate feedback regarding the state of equilibrium, overrides the ability to reweigh sensory feedback sources and prioritize accurate information. Nonetheless, this continued use of visual cues, despite any incongruence, confirms that PD patients have a visual dependence for the regulation of postural control (Bronstein, et al., 1990; Nallegowda, et al., 2004) and presents the possibility that removing visual information may be initially disruptive to posture until remaining sensory inputs can be reorganized. This hypothesis has not been tested to date. Our

first purpose in this study was to compare the time course for postural control between PD patients and healthy control participants. In addition to the ability to reorganize sensory priorities following deprivation, the ability to reintegrate accurate sensory feedback following a period of deprivation or incongruence is also essential for successful postural control (Vuillerme, et al., 2001). If PD patients experience difficulty when visual information is initially deprived, then similar effects should arise if visual cues suddenly become available. The second purpose in this study was to compare how PD patients and healthy controls adapt when visual information becomes available. Because PD patients depend on visual information for postural control, but can successfully reorganize sensory priorities when visual cues are removed, we expected that the initial effects of visual manipulation during removal and reinsertion would be more severe among PD patients than among controls.

2.2. Materials & Methods

2.2.1. Participants

Thirteen participants with idiopathic Parkinson's disease (PD; M_{age} = 67.7yrs, clinical characteristics in Table 2.1) and thirteen age-matched controls (control; M_{age} = 65.1yrs) participated in this study, in accordance with the Declaration of Helsinki. All subjects were informed on the nature of the study and provided written consent for participation. Approval to conduct this study was provided by the Human Research Ethics committee of the University of Lethbridge and by the Institutional Review Board of Texas Tech University. Testing was conducted at both sites using the same equipment. Of the thirteen PD patients included in this study, nine were tested at the University of Lethbridge, and the remaining four were tested at Texas Tech University. PD patients were all taking dopaminergic medications, and were tested in their best ON (between 1 and 2 h post-medication) state, as confirmed by patient self-report and clinical measures.

Table 2.1. Clinical characteristics of Parkinson's disease patients.

Subject	Age	Disease Duration (yrs)	UPDRS (III)	Medication	Dosage (mg/day)
PD 1	54	7	16	Permax Carbidopa Comtan Amantadine Sinemet	100 200 200 100 100
PD 2	45	5	24	Carbidopa	100
PD 3	70	1	13	Requip	300
PD 4	65	1	11	Sinemet	100
PD 5	66	11	16	Sinemet Mirapex Comtan Amantadine	100 100 200 100
PD 6	66	1.5	15	Sinemet CR Mirapex	160 300
PD 7	80	5	26	Sinemet Mirapex	200 300
PD 8	57	8	5	Permax Sinement Amantadine	100 200 100
PD 9	79	10	29	Sinemet	250
PD 10	64	9	23	Sinemet Mirapex	50 300
PD 11	80	15	34	Sinemet	80
PD 12	80	5	29	Sinement CR	80
PD 13	74	1	7	Sinemet	100

2.2.2. Procedures

Postural stability was assessed using measures of static postural sway obtained from a force platform (Bertec Corporation, Columbus, OH). Subjects performed two 45-second quiet standing trials in which they stood at a self-selected stance width without footwear, and with feet equidistant from the origin of the force platform in the medio-lateral dimension. During these trials, visual information was available for the first 15 seconds of the trial (Baseline: 0 to 15 sec), was removed for the middle 15 seconds of the trial (Perturbation: 15 to

30 sec), and was made available for the final 15 sec of the trial (Reintegration: 30 to 45 sec). Visual information was manipulated using liquid crystal vision-occlusion goggles (PLATO®, Translucent Technologies, Toronto, ON), which provide a near instantaneous (< 3ms) alteration in lens opacity between clear and occluded without any alteration in light intensity. During each trial, the goggles were open for the baseline interval (0 to 15 sec), were closed for the perturbation interval (15 to 30 sec), and were re-opened for the reintegration interval (30 to 45 sec) of the balance trial.

2.2.3. Data Analysis

Forceplate data were collected at a sampling frequency of 600Hz (National Instruments 16-bit A/D board; LabView software). Forceplate data were filtered using a 4th order Butterworth dual pass digital filter at a cut-off frequency of 5 Hz using a custom written algorithm (Matlab, The MathWorks, Natick MA USA). Co-ordinates for the medio-lateral (x) and antero-posterior (y) positions of the centre of pressure relative to the forceplate origin were then calculated for the assessment of spontaneous postural sway. Postural control was quantified as Elliptical Sway Area, which represents the area of an ellipse that encompasses the points of the centre of pressure path (Sokal & Rohlf, 1981).

The time course for postural control following visual deprivation and re-insertion was determined by dividing the 45 sec test trial into 9 equal 5 sec time bins and calculating the elliptical sway area for each bin. The immediate effect of the visual perturbation was investigated by comparing elliptical sway area obtained from the time bin prior to, and following, the removal (ie Bin 3 vs Bin 4) or the reinsertion (ie. Bin 6 vs Bin 7) of visual information. The time course for postural control during sensory reweighing in the absence of visual information was determined by comparing elliptical sway area across Bin 4 to Bin 6. The time course for reintegration of visual information was determined by comparing elliptical

sway area across Bin 7 to Bin 9. The effectiveness of sensory reweighing and reintegration was assessed by determining whether elliptical sway area values from the extended deprivation state (Bin 6) and the extended re-insertion state (Bin 9) approximated baseline levels (Bin 3).

The possibility for time-dependent changes in baseline elliptical sway area values (Bins 1-3) independent of visual manipulation was determined using a one-way Repeated Measures Analysis of Variance (RM ANOVA) across the first three time bins (Bins 1-3). A separate test was conducted for each group. We used separate GROUP X BIN Repeated Measures Analyses of Covariance (RM ANCOVA) to (1) assess the immediate effect of visual deprivation and the time course for the reweighing of sensory information in the absence of visual information, and (2) to assess the immediate effect of reinserting visual information and the time course for the reweighing of sensory information when visual information became available. The immediate effect of visual deprivation and the time course for reweighing sensory information in the absence of vision was compared between groups using a GROUP X BIN RM ANCOVA across time bins 3 through 6. The immediate effect of re-inserting visual information and the time course for reweighing sensory information when vision becomes available was determined using a GROUP X BIN RM ANCOVA across time bins 6 through 9. For both tests, UPDRS (III) score was used as a covariate. Paired samples t-tests were conducted to assess within-groups differences following significant interactions (alpha = .05).

2.3. Results

There were no significant effects for BIN across the baseline interval among control or PD ($p > .05$). A significant main effect for BIN did emerge across bins 3-6 ($F = 5.70$; $p = .005$). Moreover, a significant BIN X GROUP effect confirmed that the effect of visual deprivation differed between control and PD patients ($F = 3.47$; $p = .03$). Post-hoc comparisons revealed that significant differences in elliptical sway area emerged between Bins

3 and 4 for both groups (Control: $t(12) = -2.69$; $p = .02$, PD: $t(12) = -3.55$; $p = .004$), and that elliptical sway area in the extended deprivation state (Bin 6) was not significantly different from initial deprivation levels (Bin 4). However, reductions in elliptical sway area across the deprivation period (Bins 4-6) brought elliptical sway area at Bin 6 among control to a level that was not significantly different from baseline (Bin 3), while elliptical sway area among PD did not return to baseline levels (Bin 3_{PD} vs Bin 6_{PD}: $t(12) = -2.68$; $p = .020$). These results are illustrated in Figure 2.1.

There was no effect for BIN across the visual reintegration period (Bins 6-9: $p > .05$). Moreover, the effect of providing visual feedback after a prolonged absence did not differ between PD and control ($p > .05$). Finally, paired sample t-tests confirmed that there were no significant differences in ESA between Bin 9 and Bin 3 for either group ($p > .05$).

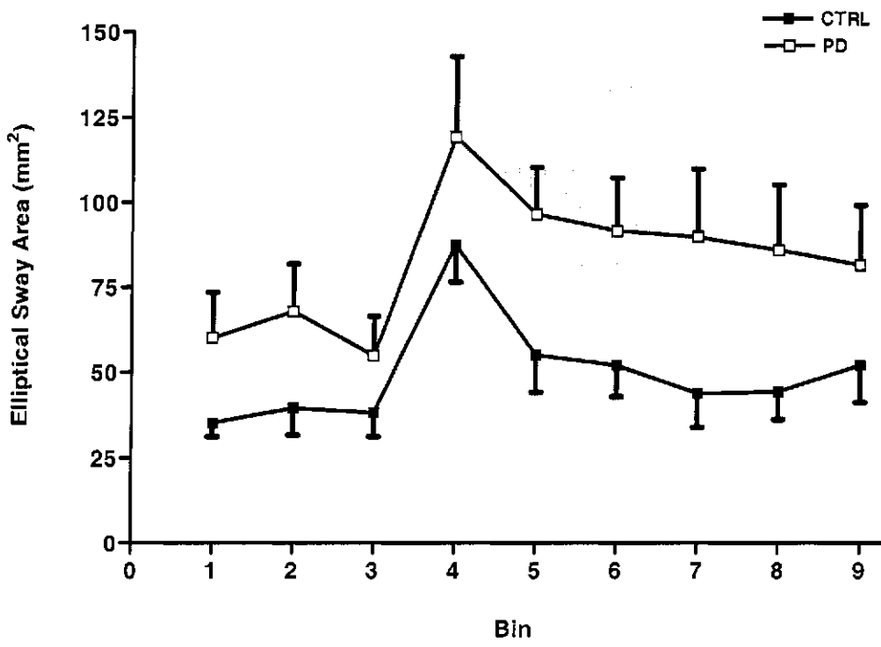

Figure 2.1. Time course of sway area following visual deprivation and reinsertion.
Values represent mean ± SE. Shaded area indicates interval of visual deprivation. Elliptical sway area among PD patients is represented by open boxes, and among control participants by closed boxes. Each time bin represents a 5 sec portion of the 45 sec balance trial. Stability among PD patients and control subjects was disrupted by visual deprivation, but this disruption was sustained among PD patients only. Stability among PD patients was initially disrupted when visual information was reinserted.

2.4. Discussion

The first purpose of this study was to compare the time course of postural control between PD patients and healthy control subjects immediately following the removal of visual information. Like control subjects, PD patients showed significant increases in sway area immediate to visual deprivation. However, contrary to our expectations, the magnitude of increase in postural sway following this sensory perturbation was comparable between groups, with control showing a 118% increase and PD showing a 128% increase over baseline elliptical sway area values immediate to visual deprivation. Furthermore, like control subjects, PD patients did not show a significant reduction from initial deprivation levels (Bin 4) by the extended deprivation interval (Bin 6). However, unlike control participants, sway in the extended deprivation state (Bin 6) among the PD patients remained significantly higher than baseline values. These results suggest that although both groups were equally affected by the onset of visual cue deprivation, the long-term effect of removing visual cues was more disruptive to postural control for PD patients than for control subjects. The inference we draw from this finding is that PD patients have initial difficulty with the reorganization of sensory inputs when visual information is deprived. This interpretation is in apparent contradiction with findings published by Bronte-Stewart and colleagues (2002), who forwarded that postural control among PD patients was not compromised when visual information is deprived. However, due to methodological differences between our study and that of Bronte-Stewart and colleagues', we suggest that our findings extend, rather than contradict, this previous work. Specifically, Bronte-Stewart et al. (2002), present an assessment of postural control during trials in which vision was removed when participants closed their eyes. Our study assessed the effect of visual deprivation by removing visual cues using computer-controlled liquid crystal goggles that did not require eye closure. Rougier (2003)

suggested that eyelid closure during upright standing increases excitatory drive to postural muscles and enhances muscle tone. Established links between increased activation of the musculature relevant to the regulation of upright standing and a reduction in postural sway (Winter, et al., 1998; Carpenter, Frank, & Silcher, 1999; Brown, Polych, & Doan, under review) confirm that increased muscle tone can serve to preserve postural control. That this effect was mediated by eyelid closure is supported by Rougier's (2003) suggestion that brainstem circuits exert control over muscles that regulate eyelid closure. Specifically, levator palpebrae muscle fibres travel through the oculomotor nerve, which in turn may interact with the mesencephalic and paramedian pontine reticular formations of the brainstem via connections with the oculomotor nuclei (Rougier, 2003). These brainstem regions are also thought to exert control over descending pathways and influence the activity of motor neurons providing innervation to axial postural muscles (Sapper, 2000). Through this mechanism, the action of eye closure may partially reduce postural sway resulting from deprivation of visual information and, consequently, provide justification why the results presented in this study differ from those published previously (Bronte-Stewart, et al., 2002).

The second purpose of this study was to determine the time course of postural control between PD patients and healthy control subjects following the re-insertion of visual information. Our findings indicate that Parkinson's disease patients expressed initial difficulty with the reintegration of visual information for postural control. Specifically, postural sway among PD patients did not initially decrease when visual information was reintroduced (Bin 6 vs Bin 7). Interestingly, similar to PD patients, control subjects did not show significant reductions in sway area when visual information became available. However, postural sway among control participants had already reduced to baseline levels by the end of period of visual deprivation (Bin 3 vs Bin 6) thereby removing the need for any further improvement in stability. Postural sway among PD patients, on the contrary, was significantly higher than

baseline at the end of visual deprivation (Bin 6), and did not immediately deviate from this level when visual information was made available. This finding implies a deficit associated with the demands of reintegrating visual information that results from basal ganglia dysfunction and is not alleviated by levodopa therapy. A similar concept has been forwarded by Bronstein and colleagues (1990), who suggested a role for the basal ganglia in postural adjustment under novel sensory environments. These authors proposed that postural adjustment in novel sensory conditions is dependent upon effective reweighing of sensorimotor loops. Consequently, compromised postural control among PD patients in situations of visual incongruence may emerge because patients cannot de-emphasize the influence of the visuopostural loop. Based on the findings of this study, we suggest that the sustained increase in postural sway among PD patients emerged as a result of central deficits with the reorganization of sensory information for postural control.

Overall, our results indicate a persistent, Parkinson's disease-associated dependence on visual information for posture that could not be captured without (1) a protocol that permitted manipulation of visual information without eye closure, or (2) a time based analysis of postural control. We suggest that this apparent visual dependence may be driven by deficits in central integration of sensory information necessary for the maintenance of stability. When visual information is absent, the central nervous system should reorganize the sensory hierarchy to prioritize remaining sensory input and adjust posture accordingly. PD patients, however, exhibited a more persistent increase in postural sway when visual information was deprived. This finding implies that PD patients were unable to prioritize remaining sensory input to adjust posture. Moreover, the gradual reduction in postural sway following reintroduction of visual feedback may indicate inherent deficits in patients' ability to quickly (< 5 sec) reintegrate visual information when it becomes available following a prolonged absence. This difficulty

with initial postural adjustment may implicate the basal ganglia as a critical structure for the reorganization of sensory inputs following visual manipulation.

2.6. Conclusion

Regardless of the underlying mechanisms, our results indicate that Parkinson's patients express inherent deficits of sensorimotor integration when visual information is absent. This finding may be particularly important for patients to consider should they encounter daily situations in which the availability of visual cues becomes compromised, such as when moving from a lighted to a darkened room. Increasing patients' awareness of disease-related integrative deficits may be an important method to reduce fall risk in this population.

III. STUDY 2 - PARKINSONIAN CAPACITY FOR POSTURAL RECOVERY FOLLOWING THE TERMINATION OF SENSORY INCONGRUENCE

3.1 Introduction

For body equilibrium to be maintained, the central nervous system must process and integrate sensory feedback to generate a set of motor commands that are appropriate to the sensory environment (Balasubramaniam & Wing, 2002; Allison & Jeka, 2004). The redundancy of sensory inputs conveyed to the central nervous system allows flexibility to disregard incongruent sensory information and to prioritize accurate sensory inputs without compromising postural control if the sensory environment is altered (Shumway-Cook & Woollacott, 2001; Allison & Jeka, 2004). For example, to maintain balance while standing on a moving walkway, visual flow created by walkway motion conveys the message that the body is moving, while vestibular and somatosensory information indicate that the body is stationary. For balance to be preserved in this situation, the central nervous system must disregard erroneous visual information implying body motion, and prioritize accurate vestibular and somatosensory information.

Clinical evidence derived from balance assessment paradigms incorporating computerized dynamic posturography indicates that postural control among patients with PD is readily compromised when sensory feedback sources convey incongruent information. For example, Bronte-Stewart and colleagues (2002) demonstrated disrupted postural control among PD patients when somatosensory information was incongruent with vestibular information. Similarly, Nallegowda and colleagues (2004) noted that situations of visual and visuo-somatosensory incongruence induced postural disruptions of greater magnitude among PD patients compared to control subjects. Taken together, these results indicate that PD patients may express difficulty with the suppression of incongruent sensory information and

with the prioritization of accurate feedback sources to ensure that stability is maintained (Bronte-Stewart, et al., 2002; Nallegowda, et al., 2004). These findings provide empirical support for the current theory implicating the basal ganglia as being crucial for the integration of sensory information for postural control (Bronstein, et al., 1990; Bronte-Stewart, et al., 2002; Nallegowda, et al., 2004).

It stands to reason that if postural control is initially disrupted when sensory inputs become incongruent, then a similar effect may occur when sensory incongruence ends. For example, if patients are unable to quickly readjust sensory priorities to reflect the most current state of the sensory environment, then postural disruption may continue even when sensory conflict is no longer present. In addition, if PD patients are compromised in their capacity to reintegrate accurate sensory inputs, then postural recovery may be time-lagged to the termination of sensory incongruence. A similar delay in postural recovery following sensory reintegration has been identified between balance-trained and balance-untrained adults (Vuillerme, et al., 2001), and among PD patients in situations of visual deprivation (Brown, Cooper, Doan, Dickin, Pellis, Whishaw, & Suchowersky, under review). Whether a similar delay in postural recovery exists when sensory incongruence ends remains to be explored as a possible deficit of PD. The purpose of this study was to investigate the time course for postural control following the termination of an imposed period of sensory incongruence among PD patients. We assessed postural control of medicated PD patients and neurologically normal older adults during standing trials that progressed through baseline quiet standing, sensory manipulation, and reintegration. This paradigm provided a qualitative assessment of the magnitude of postural recovery and the time course for postural recovery experienced by PD patients following brief visual, somatosensory, or visuo-somatosensory perceptual incongruencies. Based on previous evidence (Bronstein, et al., 1990; Bronte-Stewart, et al., 2002; Nallegowda, et al., 2004; Brown, et al., under review), we suggest that the

magnitude of postural recovery following sensory manipulation will be smaller among PD patients, and that they will express a prolonged time course for sensory reintegration compared to healthy older adults. An expanded understanding of the time course for sensory reintegration for postural control may help tailor mobility strategies and rehabilitation therapies for PD patients, and consequently be beneficial for the maintenance of optimal quality of life.

3.2. Materials & Methods

3.2.1. Participants

Seven participants with idiopathic Parkinson's disease (PD; M_{age} = 63.6 ± 5.2 yrs, clinical characteristics in Table 3.1) and seven age-matched older adults (control; M_{age} = 63.8 ± 4.9 yrs) participated in this study. All subjects were informed on the nature of the study prior to providing written consent for participation. Ethics approval for this study was provided by the Institutional Review Board of Texas Tech University. All PD patients were taking dopaminergic medications, and were tested in their best ON (between 1 and 2 h post-medication) state, confirmed via patient self-report and clinical measures. PD patients and control subjects were recruited from the surrounding community and from the local university.

3.2.2. Equipment

Postural stability was assessed using computerized dynamic posturography (CDP), conducted on a SMART Balance Master (SMART-BM)(NeuroCom International, Clackamas, OR) using DATA software version 2.1. The SMART-BM is comprised of a 36 cm x 36 cm forceplate enclosed on three sides by a visual surround room. The platform and visual surround were coupled to servo-motors that facilitated sway-referenced rotational movement in the antero-posterior plane. A separate computer and analog-to-digital board (DAQPad-6020E – National Instruments, Austin, TX) were used to collect load cell and potentiometer

signals from the forceplate, visual surround room, and a synchronization pulse from the SMART-BM.

Table 3.1. Clinical characteristics of Parkinson's disease patients.

Patient	Age	Disease Duration (yrs)	UPDRS (III)	Medication	Dosage (mg/day)
PD01	63	1.5	15	Requip	3.75
PD02	82	5.5	21	Carbidopa	100
PD03	54	8.5	16	Permax Carbidopa Comtan Amantadine Sinemet	1 200 200 100 100
PD04	45	5.5	24	Carbidopa	100
PD05	70	1.0	13	Requip	5
PD06	66	10.0	26	Sinemet Requip	25 3
PD07	65	4.0	11	Sinemet	100

3.2.3. Procedures

Participants were fitted with an upper-body harness and positioned on the force platform according to manufacturer specifications based on participant height. Participants were asked to stand as still as possible while directing their gaze straight ahead.

Three sensory conditions were included in this study. The conditions selected for this study represent three testing conditions of the Sensory Organization Test (Nashner, 1993) that create sensory incongruence. Each condition included either a disruption of visual information, achieved by sway-referenced movement of the visual surround, a disruption of

somatosensory information, achieved by sway-referenced rotation of the force platform, or both, achieved by sway-referenced rotation of the force platform and sway-referenced movement of the visual surround. The three test conditions included in this study were: a) sway referenced room with eyes open (SOT3), referred to hereafter as EOR, b) sway referenced floor with eyes open (SOT4), referred to hereafter as EOF, and c) sway referenced room and sway referenced floor with eyes open (SOT6), referred to hereafter as EOFR. An outline of the imposed sensory conditions are available in Figure 3.1.

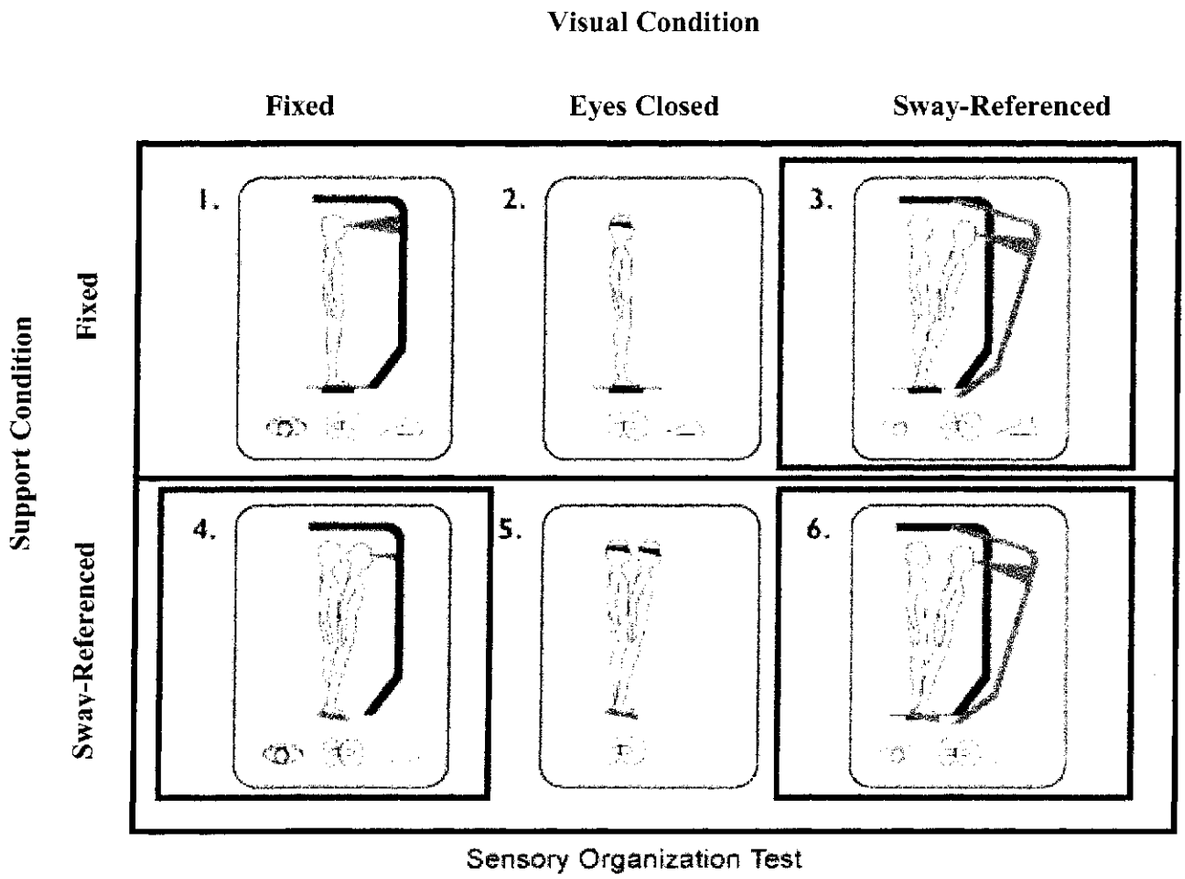

Figure 3.1. Sensory conditions of the Sensory Organization Test. We assessed postural control during Conditions 3, 4, and 6. Condition 3 (EOR) involved sway-referenced movement of the visual surround; Condition 4 (EOF) involved sway-referenced movement of the force platform; Condition 6 (EOFR) involved sway-referenced movement of the force platform and visual surround (figure adapted from Allison & Jeka, 2004 and Shumway-Cook & Woollacott, 2001).

Each trial lasted a total of 45 seconds, and was divided into three equal 15 second time intervals that differed based on the availability of sensory information. Participants had full sensory availability during the initial (baseline) 15 seconds and the final (reintegration) 15 seconds of each test trial; the middle 15 seconds consisted of the perturbation interval, during which sensory incongruencies were present. Participants were blinded to the testing conditions, and were not given any information regarding commencement of sensory manipulation. All participants performed three trials on each of the three balance conditions in a block randomized order, with a five minute rest period between blocks.

3.2.4. Data Analysis

Data were sampled at 1000Hz over a 45 second duration and stored off-line for analysis. Force platform data were filtered using a dual pass zero-phase Butterworth filter with a cutoff frequency of 4 Hz (Matlab, Mathworks Inc, Natick MA). Postural stability was determined using an Equilibrium Quotient (NeuroCom International, Clackamas OR), which provides a measure of the maximum AP centre of mass angle measured as a percentage of the theoretical maximum sway an individual can tolerate before losing balance (Bronte-Stewart, et al., 2002). Measurement of equilibrium quotient is common in clinical practice and is standard to sensory organization protocols. Moreover, assessment of equilibrium quotient over time has been shown to be consistent and unaffected by learning bias (Coogler & Wolf, 1992; Nashner, 1993; Paloski, et al., 1999). Equilibrium quotient (expressed as a percent score) was calculated off-line using the following algorithm:

$$\%EQ = \frac{12.5° - (\theta\max - \theta\min)}{12.5°} \times 100,$$

where 12.5° is the normal range of antero-posterior sway,
Θmax is the maximum excursion of the centre of mass, and
Θmin is the minimum excursion of the centre of mass in the antero-posterior direction (Bronte-Stewart et al., 2002)).

Equilibrium quotient scores were calculated across the baseline interval (Base; 0 msec – 15000 msec), across the perturbation interval (Pert; 15001 msec – 30000 msec), and across the reintegration interval (R; 30001 – 45000 msec). To assess postural behaviour during the reintegration interval, equilibrium quotient scores were calculated across five separate 3 sec time intervals commencing when the perturbation interval ended: Reintegration Bin 1 (R1): 30001 – 33000 msec; Reintegration Bin 2 (R2): 330001 – 36000 msec, Reintegration Bin 3 (R3): 36001 msec – 39000 msec, Reintegration Bin 4 (R4): 39001 msec – 42000 msec, and Reintegration Bin 5 (R5): 42001 msec – 45000 msec. Similar to Vuillerme and colleague's (2001) study, we restricted our analysis of postural recovery to time bin intervals R1 and R2. To assess postural recovery during these selected time intervals, absolute (EQ_{ABS}) and relative improvements (EQ_{REL}) in equilibrium quotient score following perturbation were determined. Absolute recovery of postural stability at R1 was determined as the change in equilibrium quotient score calculated between the minimum equilibrium quotient score (ie maximum instability) during the perturbation interval and the baseline interval. Relative recovery of lost stability was determined to assess bin-specific postural recovery, and was expressed as the percentage of stability recovered relative to the total stability lost using the following algorithm:

$$EQ_{REL}\,(\%) = \frac{EQR(n) - EQR(n-1)}{EQ_{ABS}} \text{ x } 100\%,$$

where n = Equilibrium Quotient score at R1,
n-1 = Equilibrium quotient score at Pert,
EQ_{ABS} = change in equilibrium quotient score calculated between the minimum Equilibrium Quotient score during perturbation and the baseline EQ score.

3.2.5. Statistical Analysis

Unpaired samples t-tests were conducted to assess between groups differences in the magnitude of postural recovery at time bins R1 and R2 following each sensory manipulation. Unpaired samples t-tests were also conducted to assess between groups differences in relative postural recovery at time bins R1 and R2 following each sensory manipulation (alpha = .05).

3.3. Results

Time series data for each sensory perturbation are provided in Figure 3.2(A.), Figure 3.3(A.), and Figure 3.4(A.) to indicate the effect of sensory perturbation on PD and control subjects. The effect of sensory perturbation on postural control is already documented (Bronte-Stewart, et al., 2002; (Nallegowda, et al., 2004); our analyses are restricted to the reintegration period.

3.3.1 EOR

Unpaired samples t-tests conducted on absolute recovery revealed a significant difference between control subjects and PD. Specifically, the magnitude of absolute recovery among PD patients at time bin R1 was greater than control subjects (t = -2.67; p = .021; Figure 3.2B). There was no significant between groups difference in absolute recovery at R2. Independent

samples t-tests conducted for relative postural recovery indicated that control participants and PD did not differ in relative postural recovery at R1, with both groups showing near-complete postural recovery within this time interval ($t = 0.10$; $p > .05$, $control_{relR1} = 95.5 \pm 9.6\%$; $PD_{relR1} = 94.3 \pm 9.6$; Figure 3.2C). No differences in relative postural recovery emerged between groups at bin R2 ($p > .05$).

3.3.2. EOF

Unpaired samples t-tests conducted for absolute postural recovery did not reveal any significant between groups differences in postural recovery at either R1 or R2 ($p > .05$), indicating that the magnitude of postural recovery did not differ between control participants and PD (Figure 3.3B). No significant between groups differences emerged for relative postural recovery at either R1 or R2, indicating that relative recovery did not differ between control subjects and PD ($p > .05$; Figure 3.3C).

3.3.3. EOFR

No significant differences in the magnitude of absolute recovery emerged between CTRL and PD subjects at either R1 or R2 ($p > .05$; Figure 3.4B). Moreover, there were no between groups differences in relative postural recovery at either R1 or R2 ($p > .05$; Figure 3.4C).

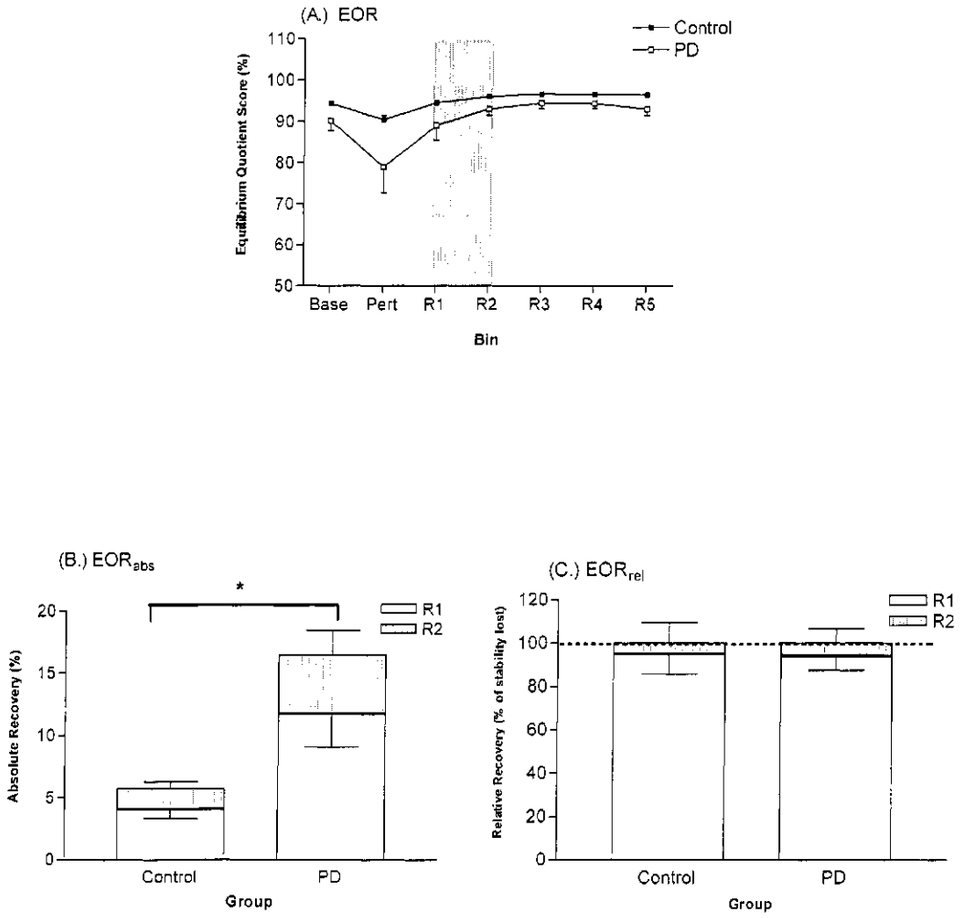

Figure 3.2. Time series data (A), absolute (B), and relative recovery (C) of postural stability among PD patients and control participants. Time series data (A) represent fluctuations in stability in both groups across the duration of the 45sec balance trial. Values are expressed as means ± SE. Shaded region indicates time bins of interest across which absolute and relative recovery were compared between groups. (B) represents absolute recovery of postural stability across time bins R1 (open portion of bars) and R2 (shaded portion of bars), measured as the absolute magnitude of improvement in equilibrium quotient score following termination of visual incongruence. (C) represents relative recovery of postural stability across R1 and R2 following the termination of visual incongruence. Relative recovery was measured as the percentage of stability recovered at R1 and R2 relative to stability lost during the interval of visual incongruence.

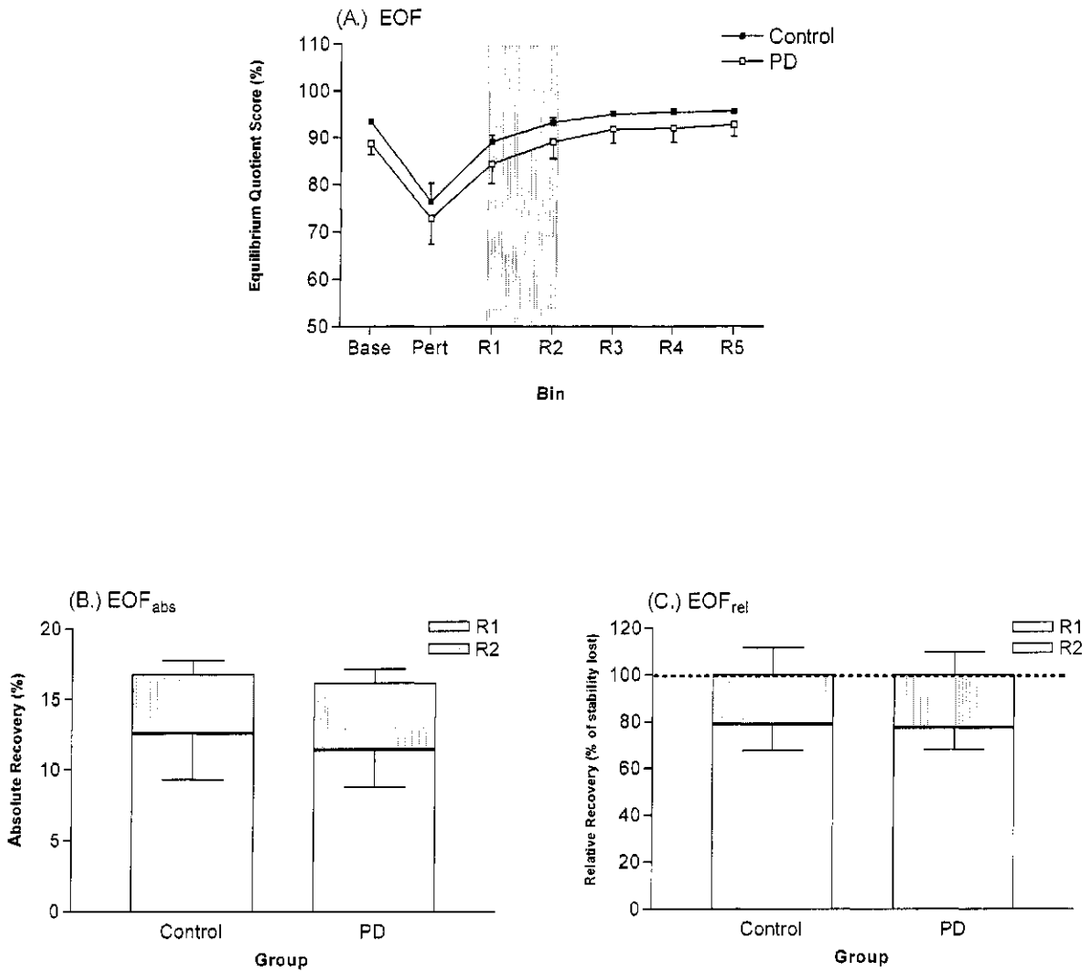

Figure 3.3. Time series data (A), absolute (B), and relative recovery (C) of postural stability among PD patients and control participants. Time series data (A) represent fluctuations in stability in both groups across the duration of the 45sec balance trial. Values are expressed as means ± SE. Shaded region indicates time bins of interest across which absolute and relative recovery were compared between groups. (B) represents absolute recovery of postural stability across time bins R1 (open portion of bars) and R2 (shaded portion of bars), measured as the absolute magnitude of improvement in equilibrium quotient score following termination of somatosensory incongruence. (C) represents relative recovery of postural stability across R1 and R2 following the termination of visual incongruence. Relative recovery was measured as the percentage of stability recovered at R1 and R2 relative to stability lost during the interval of somatosensory incongruence.

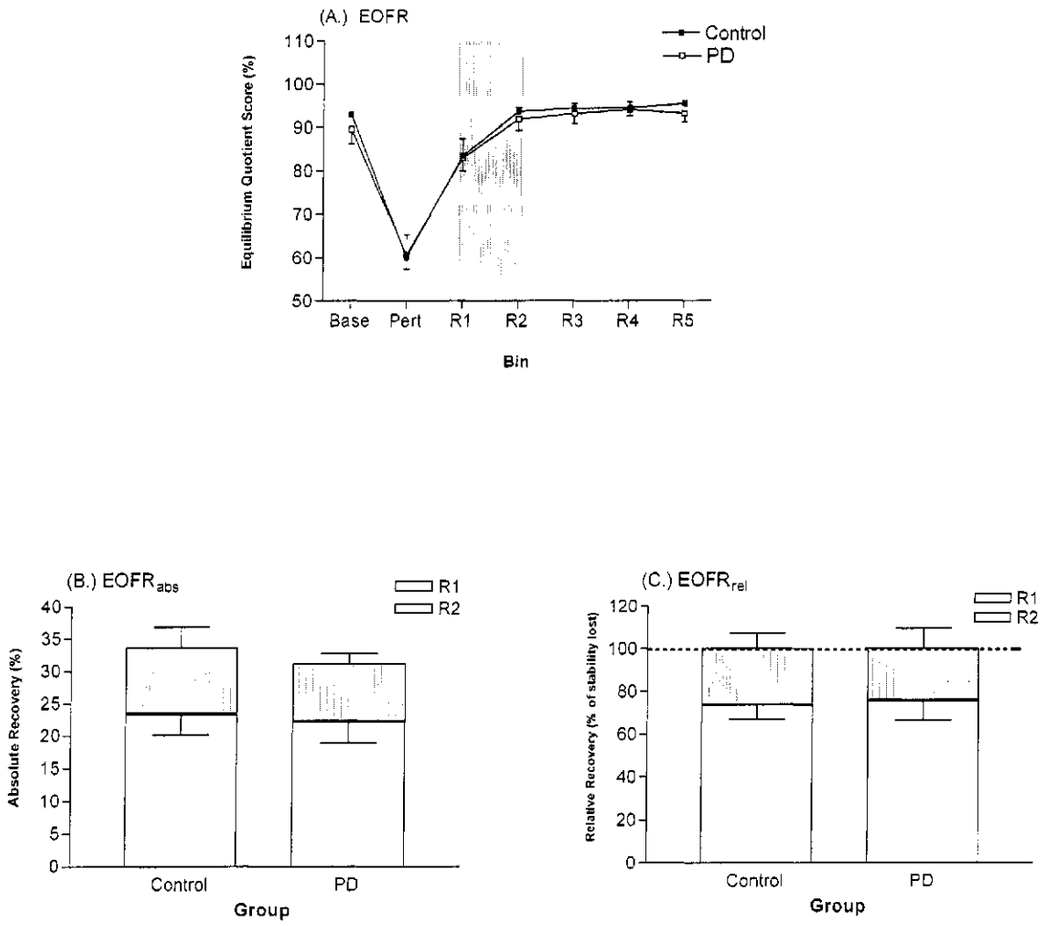

Figure 3.4. Time series data (A), absolute (B), and relative recovery (C) of postural stability among PD patients and control participants. Time series data (A) represent fluctuations in stability in both groups across the duration of the 45sec balance trial. Values are expressed as means ± SE. Shaded region indicates time bins of interest across which absolute and relative recovery were compared between groups. (B) represents absolute recovery of postural stability across time bins R1 (open portion of bars) and R2 (shaded portion of bars), measured as the absolute magnitude of improvement in equilibrium quotient score following termination of visuo-somatosensory incongruence. (C) represents relative recovery of postural stability across R1 and R2 following the termination of visual incongruence. Relative recovery was measured as the percentage of stability recovered at R1 and R2 relative to stability lost during the interval of visuo-somatosensory incongruence.

3.4. Discussion

The purpose of this study was to investigate the time course for postural control following the termination of an imposed period of sensory incongruence. We assessed postural recovery across two separate time intervals between Parkinson's disease patients and

age matched neurologically normal older adults. Overall, our results indicate that PD patients showed patterns of postural recovery that were similar to control subjects. These findings suggest that the PD patients involved in this study did not show deficits in postural recovery when situations of sensory incongruence end and imply that these patients did not experience deficits in sensory reintegration for postural control.

Based on recent evidence displaying postural disruption among PD patients during periods of sensory incongruence (Bronte-Stewart, et al., 2002; Nallegowda, et al., 2004), our hypothesis for this study was that PD patients would show continued postural disruption when sensory incongruence ends. The rationale behind this hypothesis was that if PD patients express deficits in the reorganization of sensory information when sensory information is incongruent, then correcting the inaccuracy could be disruptive because it also requires a reconfiguration of the postural control system (Vuillerme, et al., 2001). Contrary our expectation, we did not observe any differences in the relative magnitude of postural recovery between PD patients and control subjects following any of the sensory manipulations imposed in this study. In fact, PD patients and control subjects showed similar patterns of recovery when the period of sensory incongruence was terminated. Specifically, both groups demonstrated improvement in postural recovery during the first time bin interval in each sensory condition ($PD(R1)_{EOR}$ = 95%, $control(R1)_{EOR}$ = 93%; $PD(R1)_{EOF}$ = 78%, $control(R1)_{EOF}$ = 79%; $PD(R1)_{EOFR}$ = 76%, $control(R1)_{EOFR}$ = 74%), and both groups achieved complete postural recovery during the second time bin interval in each testing condition ($PD(R2)_{EOR}$ = 5%, $control(R2)_{EOR}$ = 7%; $PD(R2)_{EOF}$ = 12%, $control(R2)_{EOF}$ = 11%; $PD(R2)_{EOFR}$ = 24%, $control(R2)_{EOFR}$ = 26%). An interesting finding was that a difference did emerge between groups in magnitude of absolute recovery at R1 for SOT1. Specifically, the PD group exhibited a greater magnitude of absolute recovery at R1 compared with control subjects (PD_{R1abs} = 12%; $control_{R1abs}$ = 4%). This finding indicates that PD patients were able

to recover from a greater magnitude of postural disruption within the same time period as control subjects. Moreover, these results confirm that PD patients, like control subjects, showed complete postural recovery within a 6 second time interval.

Collectively, the results of this study indicate a similar time course for postural recovery between PD patients and control subjects when periods of sensory incongruence are terminated. This finding implies that PD patients retain the ability to reintegrate congruent sensory information for postural control. This implication is surprising for several reasons. First, previous experiments revealed that situations of sensory incongruence induced postural disruptions among PD patients beyond those observed among control participants (Bronstein, et al., 1990; Bronte-Stewart, et al., 2002). These postural disruptions were suggested to reflect deficits in sensory reweighing for postural control (Bronstein, et al., 1990; Bronte-Stewart, et al., 2002). Based on this evidence, we expected that parkinsonian deficits in sensory integration would extend to the process of sensory reintegration, which also requires reorganization of the postural control system (Vuillerme, et al., 2001).

The absence of any differences between control participants and PD subjects may reflect the demographics of the patient population included in this study. One possibility is that disease duration may differentially influence the central integration of sensory information for postural control among PD patients. A similar explanation was forwarded by Smiley-Oyen and colleagues (2002), who observed that early-stage PD patients, like control subjects, were able to improve postural control following only one trial of somatosensory incongruence. The authors suggested that early-stage PD patients retained their ability to de-emphasize erroneous somatosensory information and maintain postural control by instead prioritizing congruent visual and vestibular inputs (Smiley-Oyen, Cheng, Latt, & Redfern, 2002). In the current study, the mean disease duration among PD patients was shorter than the patients included in Smiley-Oyen and colleagues' (2002) study. Consequently, it remains possible that the apparent

retention of the capacity for sensory reintegration for postural control among the patients included in the current study was related to their early-stage disease state. Indeed, Klawans and Topel (1974) suggested that postural difficulties generally begin to emerge in patients with a more advanced disease state. Thus, it must be acknowledged that although our findings present promising insight regarding patients' ability to recover from postural disruption following periods of sensory incongruence, these findings may not be generalized across the parkinsonian population as a whole. It stands to reason that disease progression to mid- and late-stage PD could induce progressive decline in the capacity for the central integration of sensory information for postural control, and thus provides foundation for further exploration.

Following the findings of Bronte-Stewart and colleagues (2002), it is also possible that PD patients may respond differently during sensory reintegration. For example, Bronte-Stewart and colleagues (2002) observed a differential effect of sensory manipulation among PD patients included in their study. Specifically, these authors noted two groups of PD patients who were differentially affected by sensory manipulation: one group whose postural control was not disrupted following any sensory manipulation, and another group who was particularly disrupted when somatosensory information was incongruent. The authors noted that the differences in postural disruption between these groups were not related to age, disease duration, or disease severity. This finding implies the existence of subpopulations of patients who express vastly dissimilar patterns of postural behaviour during periods of sensory incongruence. Therefore, these patients may also exhibit diverse patterns of postural recovery when sensory feedback becomes congruent. It is possible that some of the patients included in the current study comprised a similar subset of patients whose posture is not disrupted by sensory incongruence. Therefore, future work incorporating a larger sample of PD patients should explore this possibility.

The work presented in this study provides preliminary insight into the postural behaviour

of PD patients during the process of sensory reintegration. Although we have incorporated the use of a standardized and widely accepted method of postural assessment (Dickin, Brown, & Doan, in press), future work should incorporate an analysis of postural control across shorter time bin intervals to address the possibility that group differences in the onset of postural recovery may exist. For example, it is possible that the onset of postural recovery occurs earlier for control subjects than for PD patients, but that this difference could not be captured across the time interval used in this study. In addition, the use of time-series analyses (ie stabilogram diffusion analysis (Mitchell, Collins, De Luca, Burrows, & Lipsitz, 1995)) to assess postural recovery during sensory reintegration may provide deeper insight into postural behaviour expressed by PD patients when sensory incongruence ends.

3.5. Conclusion

The PD patients included in this study displayed a time course for complete postural recovery that was comparable to control subjects. This finding implies that PD patients' capacity for the reintegration of sensory inputs for postural control following the termination of sensory incongruence was maintained, and provides positive insight regarding patients' ability to recover from postural disruption induced by situations of sensory incongruence. Nonetheless, continued research aimed at investigating reintegrative capacity among patients varying in disease state may provide valuable information regarding the stage of disease progression at which deficits in sensory integration for postural control emerge. Moreover, educating patients about environmental situations that impose balance threat may be an important method to assist patients in developing strategies to minimize fall risk.

IV. GENERAL DISCUSSION

This thesis investigated the influence of Parkinson's disease on the time course for postural control following imposed sensory manipulations. Two studies were conducted to investigate postural behaviour among PD patients and age-matched neurologically healthy older adults following situations of sensory deprivation and sensory incongruence. Study 1 examined the effects of visual deprivation on the time course for postural control among PD patients and among control participants. Study 2 explored the time course for postural recovery among PD patients and control participants following the termination of an imposed period of sensory incongruence. In both studies, participants performed quiet standing trials that progressed through baseline quiet standing, sensory manipulation, and reintegration.

4.1. The Influence of PD on Postural Behaviour Following Visual Deprivation

The first study in this thesis investigated the time course for postural control among PD patients and control subjects following an imposed period of visual deprivation. We chose to investigate the specific effects of visual deprivation because it is well documented that PD patients express visual dependence for postural control (Bronstein, et al., 1990; Nallegowda, et al., 2004). This visual dependence is proposed to result from deficits in the central integrative processes necessary for the preservation of balance when the availability of sensory information becomes compromised. Specifically, disruptions to postural control among PD patients become apparent because of defective sensory reweighing processes that facilitate balance control in situations of visual deprivation. Because the basal ganglia have been implicated as making a crucial contribution to sensorimotor integration for postural control (Bronstein, et al., 1990; Bronte-Stewart, et al., 2002; Abbruzzese & Berardelli, 2003; Nallegowda, et al., 2004), we expected that an imposed period of visual deprivation would

induce greater postural disruption among PD patients compared to control subjects. Although the results from Study 1 did not reveal differences in the magnitude of disruption following visual deprivation between groups, they did confirm the disruptive effect of visual deprivation on postural control among both groups. Interestingly, the disruptive postural effect of visual deprivation among PD patients was sustained across the duration of the deprivation period. In contrast, control subjects were able to improve postural stability across the deprivation period, such that stability in the extended deprivation state approximated baseline stability. This finding indicates that PD patients, in contrast to control subjects, had initial difficulty with the reorganization of sensory inputs for postural control when visual information is deprived. In addition, this reduced capacity for sensory reorganization when visual information is deprived may be related to parkinsonian deficits in sensory integration for postural control.

Perhaps the most compelling finding from Study 1 was that, contrary to control participants, PD patients were unable to quickly improve postural control despite the renewed availability of visual information. Although patients were able to achieve baseline stability by the end of the balance trial, they were unable to do so as quickly as control subjects. This result indicates that PD patients experienced difficulty in the reintegration and utilization of visual information to improve balance control. A similar explanation was forwarded by Bronstein and colleagues (1990), who suggested a role for the basal ganglia in postural recalibration in novel sensory environments. These authors suggested that the preservation of equilibrium in novel sensory contexts depends on effective reweighing of sensorimotor loops. The process of sensory reintegration requires that previously unavailable or incongruent sensory information is reintegrated into the sensory hierarchy, and that sensory priorities are subsequently reorganized to reflect the most current state of the sensory environment. The consequence of ineffective sensory reorganization processes in situations of visual deprivation

may emerge because patients experience difficulty rapidly de-emphasizing, and later re-emphasizing, the contribution of the visuopostural loop. Moreover, the sustained disruption in postural control when visual information was made available following prolonged absence may reflect perpetual central reorganizational deficits that are associated with basal ganglia dysfunction. Overall, the findings from Study 1 provide additional evidence to substantiate the notion of basal ganglia contributions to sensory integration for postural control (Bronstein, et al., 1990; Chong, et al., 1999; Teasdale & Simoneau, 2001; Bronte-Stewart, et al., 2002).

4.2. The Influence of PD on Postural Behaviour Following Sensory Incongruence

The second study in this thesis examined postural control among PD patients and control subjects following situations of imposed sensory incongruence. Specifically, we sought to investigate the time course for postural recovery following the termination of imposed periods of visual, somatosensory, and visuo-somatosensory incongruencies. We expected the results of this study to reveal differences in postural recovery between PD patients and control subjects following the termination of sensory incongruence. Our results revealed that, contrary to our expectation, PD patients demonstrated postural recovery that was comparable to control participants, regardless of the sensory manipulation imposed. Specifically, like control subjects, PD patients retained their ability to recover from postural disruption induced by sensory incongruence, and that, interestingly, they were able to do so within the same time interval as control subjects. Overall, the results from Study 2 indicate that PD patients not only retained their ability to recover from postural disruption induced by sensory incongruence, but that they were able to do so within the same time period as control subjects. The results derived from this study suggest that PD patients and control subjects exhibit a similar time course for postural recovery following the termination of imposed situations of sensory incongruence. This finding implies that, among these patients, the functional capacity

of the basal ganglia to reintegrate congruent sensory information for postural control following a prolonged period of incongruence was preserved.

The measures used to quantify postural control in this thesis are different between Study 1 and Study 2. Our measurement of postural stability in Study 1 was elliptical sway area, which quantified the area of an ellipse that captured 95% of the centre of pressure movement area. By using this measure, we were able to capture centre of pressure movement in the antero-posterior and medio-lateral dimensions. As a result, we were able to quantify the area of postural sway occurring in two dimensions. To quantify postural stability in Study 2, we used equilibrium quotient score, which quantifies centre of mass movement in the antero-posterior dimension. Equilibrium quotient score is the standardized measure that is used in sensory organization test protocols applied in clinical settings (Bronte-Stewart et al., 2002; Nashner 1993; Allison & Jeka, 2004), and as such, our use of this measure conformed to the parameters of the protocol.

Although elliptical sway area and equilibrium score quantify the displacement of two different variables (i.e. centre of pressure versus centre of mass), they are related because of the biomechanical relationship between centre of pressure and centre of mass. Specifically, centre of pressure and centre of mass are related such that displacement of the centre of pressure influences displacement of the centre of mass. For example, if centre of pressure position moves far enough ahead (i.e. anteriorly) of the centre of mass, the centre of mass will also move in the anterior direction. If the centre of mass moves too far anteriorly, however, centre of pressure will move posteriorly until it is located behind the centre of mass. This posterior displacement of the centre of pressure behind the centre of mass will cause posterior displacement of the centre of mass to its original position (Winter, 1995). Consequently, fluctuations in the location of the centre of pressure relative to the centre of mass function to constrain the centre of mass within the body's base of support. Because of this biomechanical

relationship, both elliptical sway area and equilibrium quotient score are acceptable measures to quantify postural sway. Specifically, centre of pressure movement influences centre of mass movement, such that the magnitude of centre of pressure movement induces a greater magnitude of centre of mass movement. Consequently, a lower equilibrium quotient score in Study 2 indicated a greater magnitude in centre of mass movement, which can be inferred to result from a greater magnitude in centre of pressure movement. We performed a post hoc correlation between elliptical sway area and equilibrium quotient score to confirm that the documented relationship between centre of pressure and centre of mass movement was upheld for the results presented in this thesis. A significant relationship between these variables did emerge, such that decreases equilibrium quotient score were significantly correlated with increases in elliptical sway area. This relationship provides justification for our use of measures in these experiments.

4.3. Postural Stability Following Sensory Deprivation Versus Sensory Incongruence

Perhaps the most compelling finding in this thesis was that the detrimental postural effects induced by visual deprivation were sustained among PD patients even when visual information was made available. In contrast, postural control among PD patients was not disrupted following the termination of a prolonged period of visual incongruence. Although the mediating factor for this difference may be disease duration, further explanation of the mechanisms underlying this difference is warranted.

One possibility is that situations of sensory incongruence were not as disruptive to postural control among PD because some accurate sensory information was still available. Similar explanations have been reported by Smiley-Oyen and colleagues (2002), and by Nallegowda and colleagues (2004). Smiley-Oyen and colleagues (2002) recognized that although somatosensory incongruence generated by muscle vibration does disrupt a large

portion of somatosensory inputs that regulate upright stance, PD patients may have been able to utilize accurate inputs conveyed from joint receptors and cutaneous inputs to improve their postural control. Likewise, Nallegowda and colleagues (2004) observed that postural control among PD patients was not disrupted following somatosensory incongruence. In light of this finding, the authors suggested that patients may have been able to preserve balance by utilizing accurate somatosensory inputs received from gravitoreceptors located in the kidneys and other large organs (Mittelstaedt, 1996; Dietz, 1998).

An alternate explanation for our findings is that the effect of sensory deprivation is disruptive among later-stage PD patients because the task of completely suppressing a sensory modality is more demanding than the task of extracting the accurate information from inaccurate information (Horak & Macpherson, 1996). Perhaps the condition of visual deprivation induced disruption among later-stage PD patients because it introduced an additional step in the integrative process. Specifically, if a role of the basal ganglia is to extract and utilize sensory information that is consistent with the internal model of the body position, then perhaps the task of extracting meaningful sensory inputs and subsequently suppressing deprived inputs is beyond the functional capacity of the basal ganglia in later-stage patients. Likewise, the sustained disruption of postural control when previously-deprived visual information is made available occurs because the dysfunctional basal ganglia has exceeded its capacity for further sensory integration. Whether the occurrence of this sustained postural disruption is specific to the termination of imposed periods of visual deprivation provides foundation for further investigation. Moreover, whether reintegrative difficulties following prolonged periods of sensory deprivation are exclusive to later-stage PD patients also warrants further exploration.

A third possibility for our findings in Study 1 may be related to differences in basal ganglia processing occurring following sensory manipulation. Specifically, because the basal

ganglia are responsible for continually evaluating the availability and quality of sensory inputs, then it is possible that situations of visual deprivation disrupt this evaluation process. For example, when visual information is deprived for long enough, the basal ganglia may eventually stop 'checking', or evaluating sensory inputs. The basal ganglia may evaluate sensory inputs initially following visual deprivation, but will not extract any meaningful visual information because visual inputs are not available. Consequently, if visual information is deprived for a prolonged period of time, the basal ganglia may stop its evaluation of visual information altogether. Or, alternatively, the basal ganglia may continue to 'check' for visual information, but it may not do so as frequently. This possibility may explain the initial, but not sustained disruption in postural control among PD patients when visual information was reinserted. Moreover, this hypothesis may also provide explanation for PD patients' ability to recover stability when visual incongruence, or sensory incongruence in general, ended. It is possible that, while evaluating sensory information during the period of sensory incongruence, the basal ganglia was still able to extract a small amount of meaningful sensory information. Consequently, the frequency at which the basal ganglia evaluated sensory inputs may not have changed. This possibility may provide explanation for PD patients' ability to recover postural stability in the same time period as control subjects when sensory incongruence ended.

PD patients' ability to recover balance when sensory incongruence ends may also be driven by the activity of alternate motor loops, such as those acting through brainstem structures such as the pedunculopontine nucleus. There is anatomical evidence to indicate that the pedunculopontine nucleus makes connections with the basal ganglia (Lee, Rinne, & Marsden, 2000), and thus it may be possible that the activation of these connections (in lieu of a faulty basal ganglia) facilitates postural recovery when sensory incongruence ends. Finally, it may be possible that patients' ability to recover balance following the termination of sensory incongruence was driven by attentional processes. Specifically, there is evidence to indicate

that by directing attention to the performance of motor tasks, patients are able to bypass faulty basal ganglia motor loops to facilitate successful task performance (Morris, Iansek, Matyas, & Summers, 1996; Morris, Iansek, Smithson, & Huxham, 2000). By directing attention to maintaining balance, postural control shifts from an automatic motor task (controlled by the dysfunctional basal ganglia) to a voluntary task (controlled primarily by higher cortical structures such as the premotor cortex and the supplementary motor area) (Wise, 1985). Consequently, by directing attention to staying balanced, patients were able to recover stability in the same time period as control subjects. This possibility provides foundation for further exploration.

4.4. Contribution of the Sensory Hierarchy to Postural Control

The collective results from this thesis, while providing insight into the postural behaviour PD patients during and following alterations in sensory information, also support the theory of the existence of a sensory hierarchy for postural control. The theory of sensory reweighing, introduced by Nashner and colleagues (1982) describes the process by which postural control is maintained when the sensory environment changes. Specifically, the central nervous system organizes sensory information in a hierarchy, such that postural control is primarily achieved by prioritizing sensory information conveyed by the sensory priority given 'highest priority' (Teasdale, Stelmach, Breunig, & Meeuwsen, 1991). In addition, Bronte-Stewart and colleagues (2002) have suggested that the priority, or weight, given to each sensory modality may vary among individuals. For example, whereas visual information may be the highest priority sensory modality among some individuals, somatosensory information may be allocated highest priority in others. As a consequence, individual differences in sensory weighting may differentially affect balance control following disruptions in sensory information. Our findings from Study 2, in particular, provide empirical evidence to support

this theory. Specifically, we observed that PD patients were more disrupted by visual incongruence than control subjects. This greater disruption was reflected by the significant difference in magnitude of absolute recovery between PD patients and control subjects, and may imply that PD patients allocated higher priority to visual information for balance control, and consequently became more disrupted when visual inputs became incongruent. We did not observe any differences in the magnitude of absolute recovery that emerged between groups following the termination of somatosensory, or visuo-somatosensory incongruence. This finding may indicate that both groups showed similar weighting of sensory inputs in these situations, and thus were similarly affected when these inputs became incongruent.

4.5. Implications for PD Patients

All PD patients who participated in this thesis were dopamine dependent, and were testing during their best reported ON state. We did not investigate the influence of sensory manipulation on the time course for postural control among non-medicated patients or among patients employing surgical interventions as their primary method of treatment. Furthermore, we did not restrict our analysis to PD patients categorized according to disease state. When considering these demographics, we cannot generalize our findings across the parkinsonian population as a whole. Our results do, however, provide groundwork for future research in this domain.

We restricted our analysis to medicated patients only because we believe that investigating postural control in the ON state best represents patients' behaviour during the performance of activities of daily living. Assessing postural control following sensory manipulation when patients are in their OFF state may provide valuable insight into postural disruptions that may occur if patients experience a 'wearing off' effect (Suchowersky, 2002), or when they are approaching the completion of a medication cycle. Although summary

measures of postural stability (ie postural sway area) occasionally indicate that non-medicated PD patients are more stable compared to their medicated state, (Rocchi, et al., 2002; Rocchi, et al., 2004), the evidence regarding postural behaviour among non-medicated patients following sensory manipulation is controversial. Specifically, results from some studies revealed that situations of sensory incongruence induced postural disruptions among non-medicated PD patients (Bronstein, et al., 1990; Bronte-Stewart, et al., 2002; Nallegowda, et al., 2004), while others have shown postural disruption among non-medicated PD patients following sensory deprivation as well (Nallegowda, et al., 2004). In contrast, there is also evidence to suggest that postural control among non-medicated PD patients is not disrupted following sensory perturbation of any kind (Horak, et al., 1992; Waterston, et al., 1993). In particular, Horak and colleagues (1992) noted that non-medicated PD patients displayed postural sway following sensory manipulation that was smaller than older adult control subjects, thus implying that deficits in sensory integration for postural control were non-existent among these patients. Consequently, the inconsistent evidence regarding the postural effects of sensory manipulation on non-medicated PD patients provides foundation for further research. Future studies should be aimed at clarifying the effects of sensory manipulation on postural control among these patients, and at providing further insight into the time-based postural behaviour of non-medicated patients following sensory manipulation.

Results from a series of studies conducted by Rocchi and colleagues (2002; 2004) indicate that patients receiving deep brain stimulation of the subthalamic nucleus and of the globus pallidus internal display decreased postural impairment compared to their medication-only state, and compared to older adult control subjects. From these results, the authors suggested that deep brain stimulation may improve postural stability by influencing the integration of somatosensory information, thereby improving kinesthetic control of the centre of mass. While the specific actions of deep brain stimulation are still unclear, the results of Rocchi and

colleagues' (2002; 2004) studies provide foundation for further exploration. Specifically, if deep brain stimulation does aid in the integration of somatosensory information for postural control, then it is possible that this effect may be beneficial for postural recovery following the reinsertion of congruent sensory information. Moreover, it might be possible that deep brain stimulation generates a general, rather than modality-specific, influence on sensory integration for postural control. This implication is particularly important for patients currently receiving DBS as a treatment method, because these patients generally experience severe postural impairment. Consequently, further research targeted at exploring potential influences of deep brain stimulation on sensory integration for postural control is warranted.

A recent study conducted by Bronte-Stewart and colleagues (2002) highlighted the existence of subsets of PD patients whose postural control was differentially affected by sensory manipulation. In that study, the authors observed the existence of a patient group who expressed postural disruption beyond that associated with PD. Although these authors did not provide explanation for the mechanisms underlying postural disruption in this specific patient group, it is possible that intensified postural disruption could be mediated by cognitive factors such as fear of falling. Fear of falling has been widely accepted as a factor mediating balance performance among both elderly (Adkin, Frank, & Jog, 2003), and young adults (Brown & Frank, 1997; Adkin, Frank, Carpenter, & Peysar, 2000; Carpenter, Frank, Silcher, & Peysar, 2001), and has also been identified as a factor mediating balance performance among PD patients (Adkin, et al., 2003). For example, older adults who identify with having a fear of falling exhibit larger amplitude of postural sway when visual information is deprived compared to elderly adults who do not report being fearful of falling (Maki, Holliday, & Topper, 1991; Maki, Holliday, & Topper, 1994). In addition, fear of falling generated by introducing significant postural threat has been shown to influence balance control among younger adults during quiet standing, and when responding to an unexpected external perturbation to posture

(Brown & Frank, 1997; Adkin, et al., 2000; Carpenter, et al., 2001). Adkin and colleagues (2003) recently showed that PD patients who displayed postural impairment also reported lower confidence in their balance abilities. What remains unknown, however, is whether fear of falling exacerbates postural instability that is related to the parkinsonian disease process. Furthermore, potential influences of fear of falling on sensory organization for postural control remain unexplored among the parkinsonian population. Although Adkin and colleagues (2003) incorporated the use of balance tasks to assess postural stability among PD patients, they did acknowledge that these balance tasks were relatively simple. Consequently, the assessment of postural control among PD patients who identify with fear of falling using balance tasks that impose challenge to the sensory systems may provide insight into potential mediating effects of fear of falling on sensory integration for postural control in this population.

Finally, Bronte-Stewart and colleagues (2002) have shown that PD patients who received pallidotomy to alleviate parkinsonian symptoms displayed reduced postural impairment following combined visual deprivation and somatosensory incongruence compared to their pre-surgery stability scores. Moreover, this improvement in postural stability following sensory manipulation was maintained at 6 and 12 months post-surgery. The authors suggested that, in contrast to medication, pallidotomy may be beneficial to completely correct abnormalities in sensory organization for postural control following sensory manipulation. Specifically, pallidotomy may act to improve sensory integration processes by normalizing irregular neuronal firing patterns in the pallido-thalamocortical and pallido-pedunculopontine-thalamocortical pathways (Vitek & Giroux, 2000), thus releasing downstream nuclei from the inhibitory commands that generate movement difficulties. This correction of sensory organizational abnormalities may improve patients' ability to recover from postural disruptions imposed during periods of sensory manipulation, and following the

termination of sensory manipulation. Consequently, this possibility also provides justification for further study.

Because we did not restrict our analysis to patients categorized by disease state, future studies should be directed at investigating the possibility that sensory organizational processes for postural control are influenced by disease duration. Klawans and Topel (1974) suggested that postural impairment emerges in patients with more advanced disease state. If postural impairment in these patients is caused by deficient sensory organizational processes, then it is possible that a relationship between disease duration and measures of postural stability following sensory manipulation exists. Although we did not explore this possibility in this thesis, it provides foundation for further investigation.

4.6. Future Research

The existence of subject heterogeneity and diverse treatment methods provide vast opportunity for ongoing investigation of the sensory organizational processes that regulate postural control among individuals suffering from PD. Bronte-Stewart and colleagues' (2002) identification of subsets of patients whose postural responses greatly differ during sensory incongruence present the possibility that these patients may also show differential postural recovery when periods of sensory incongruence end. In addition, the existence of patients who employ different treatment strategies warrants future research, because the underlying physiological actions of these treatments (ie medication versus DBS versus surgery) may influence the sensory organizational processes for postural control among PD patients. However, future research should also maintain a strong focus on providing patients with rehabilitation strategies for balance control that can be utilized in the home, and in a social setting. For example, the incorporation of regular exercise regimes tailored specifically to target balance control may be an effective rehabilitative strategy for PD patients. In addition,

the organization of exercise classes developed exclusively for PD patients may be useful not only to improve balance control, but also to return a social aspect to the daily lives of patients.

Recent evidence indicates that elderly adults who actively participate in balance activities targeted to challenge the sensory systems express improvements in balance performance (Ledin, Kronhed, Moller, Moller, Odkvist, & Olsson, 1991; Hu & Woollacott, 1994; Rose & Clark, 2000). For example, Tsang and colleagues (2004) noted that elderly individuals who regularly practiced Tai Chi displayed balance performance that was comparable to young adults, even in altered sensory conditions. In contrast, balance performance among elderly non-Tai Chi practitioners was significantly reduced. From these results, the authors concluded that practicing Tai Chi improved balance control among elderly adults in situations when sensory information was reduced or conflicting.

Although there is evidence to suggest that exercise programs combining resistance and balance training are beneficial to improve postural control among PD patients (Hirsch, Toole, Maitland, & Rider, 2003; Lun, Pullan, Labelle, Adams, & Suchowersky, 2005), the effects of exercises that challenge the sensory systems among PD patients are unknown. However, evidence derived from similar studies conducted on elderly adults indicates that regular practice of exercises that challenge the sensory systems are beneficial to improve balance control (Tsang, et al., 2004) in these individuals. Thus, it is possible that the incorporation of a balance training regime that emphasizes sensory challenge may also be beneficial to enhance postural control among PD patients. Because PD patients suffer from balance impairments beyond those associated with the aging process (Romero & Stelmach, 2003), emphasis should be placed on developing rehabilitation strategies that target sensory organization processes in this population.

4.7. Research Applications

The results of this thesis indicate that postural control among PD patients is disrupted following situations of sensory manipulation. Patients' capacity to quickly recover from postural disruption following the reinsertion of previously deprived or incongruent sensory inputs may depend on factors such as disease duration and disease severity. Nonetheless, the main purpose of this thesis was to provide an in-depth assessment of postural control among PD patients following the imposed manipulations of sensory information. Our results provide insight that is relevant to daily life, because they present clinicians, patients, and their caregivers with information regarding environmental conditions that may impose threat to balance among PD patients. The collective results of Study 1 indicate that PD patients express difficulty recovering from postural disruption induced by visual deprivation. Furthermore, this postural disruption is initially sustained among PD patients even when visual information becomes available. Consequently, the results of Study 1 provide insight into a specific sensory situation that is disruptive to balance among PD subjects in particular.

The results from Study 2 present promising preliminary evidence regarding patients' ability to recover from postural disruption induced by situations of sensory incongruence. However, we must caution that the results from this study cannot be generalized across the parkinsonian population in its entirety. Specifically, the disease state of the patients included in Study 2 may provide explanation for patients' ability to recover from postural disruptions induced by sensory manipulation. Nonetheless, our findings in this study do imply that patients PD do not express deficits in postural recovery when congruent sensory information becomes available. Moreover, our findings extend the current knowledge regarding the time-based postural behaviour among PD patients following the termination of imposed sensory conflict.

4.8. Limitations

The results of Study 1 may be limited by subject heterogeneity. Specifically, we did not control for disease severity. There is evidence to indicate that disease severity may differentially affect postural behaviour among PD patients following sensory manipulation. For example, Waterston and colleagues (1993) observed differences in stability between PD patients who differed in disease severity. Specifically, patients suffering from a more severe disease state exhibited greater postural disruption following an external perturbation to balance compared to patients suffering from lower disease severity and compared to control subjects. This finding presents the possibility that differences in disease severity among the patients included in this thesis may have influenced the outcome of our results. We suggest that patients suffering from greater disease severity should express greater disruptions in postural control during sensory organization for postural control that are related to more advanced basal ganglia degeneration. This prediction provides foundation for exploration in this domain.

The results of Study 2 may also be limited by sample number, because a total of 7 PD patients participated in this study. Although other studies have incorporated similar PD participant numbers (Rocchi, et al., 2002; Rocchi, et al., 2004), we suggest that future studies should incorporate a larger sample size to further increase statistical power. In addition, the results of Study 2 could be limited in that mean disease duration of PD participants was relatively low. Consequently, the results obtained from this study should not be generalized to patients suffering from more advanced disease states. Indeed, Smiley-Oyen and colleagues (2002) observed that, like control subjects, early-stage PD patients were able to improve balance following only one trial of somatosensory incongruence. Thus, it remains possible that the early disease state of the patients included in Study 2 influenced the outcome of this

investigation. Consequently, future investigation should be targeted at elucidating differences in sensory organizational capacity among patients varying in disease state.

Finally, the results of Study 1 and Study 2 are limited because the length of the time bin intervals within which postural behaviour was analyzed may have been too long, and thus may not have been sensitive enough to reveal differences in postural recovery between groups. Specifically, it is possible that onset of postural recovery during the sensory reweighing and reintegration processes may differ between groups, but that these differences could not be detected given the time intervals used in this study. Future work in this area should incorporate measurement of postural behaviour across smaller time intervals (ie < 3 sec), as well as a measure that reflects the time point at which postural recovery occurs. Moreover, future studies could incorporate the use of time series analysis (Mitchell, et al., 1995; (Peterka & Loughlin, 2004) of postural control to gain a deeper understanding of the physiological mechanisms underlying postural impairment among PD patients.

4.9. Conclusions

The results of Study 1 indicate that environmental situations involving a deprivation of visual information induce sustained postural disruptions that are difficult for PD patients to overcome. When visual information was deprived, postural control among PD patients and control subjects was disrupted. Unlike control subjects, PD patients were unable to recover from postural disruption across the duration of the deprivation interval. Contrary to control subjects, postural stability among PD patients in the extended deprivation state remained substantially worse than baseline levels of stability. Furthermore, postural control among PD patients was initially disrupted even following the reintroduction of visual information. The inference we draw from these findings is that parkinsonian deficits in the central integration of sensory inputs for postural control detrimentally influenced patients' stability following visual

deprivation. We suggest that these central deficits manifested as a reduced ability of patients to rapidly reprioritize sensory inputs when visual information became deprived, and as a reduced ability to reintegrate visual inputs when the interval of visual deprivation was terminated.

The results of Study 2 indicate that PD patients retained their ability to recover from postural disruption induced by situations of sensory incongruence. Specifically, when situations of sensory incongruence were terminated, PD patients exhibited magnitudes of relative postural recovery that were comparable to control subjects. Moreover, PD patients were able to recover from postural disruption within the same time period as control subjects. Consequently, our findings in Study 2 indicate that PD patients express a time course for postural control that is similar to healthy, age-matched older adults of similar age. This result implies that, among these patients, the sensory organizational processes for sensory reintegration were maintained.

Collectively, our results indicate that patients suffering from Parkinson's disease are susceptible to postural disruptions induced by deprived or altered sensory conditions, and that their ability to recover from such disruptions may depend on the type of sensory manipulation imposed. Specifically, it is possible that situations of sensory deprivation are fundamentally more disruptive to balance control compared to situations of sensory incongruence, and that the faulty basal ganglia induce difficulty among patients to quickly recovery from instability. The results of this thesis indicate that situations of visual deprivation impose a particularly disruptive effect on postural control among PD patients. In such conditions, PD patients express an initial disruption in postural recovery following visual deprivation compared to control participants. Interestingly, however, PD patients retain their capacity for postural recovery following the termination of imposed intervals of sensory incongruence. Moreover, it may also be possible that PD patients' capacity for sensory integration may depend on individual characteristics such as disease state. As a result, continued research targeted at

investigating the capacity for sensory integration among PD patients varying in disease state may provide valuable insight regarding the stage of disease progression at which integrative deficits emerge. Moreover, our results provide insight into the contribution of sensory information to balance control. Although equilibrium control is physically achieved the actions of the musculoskeletal system, these actions are mediated by the activity of the central nervous system based on information conveyed by the sensory systems (Allison & Jeka, 2004). Consequently, the functional integrity of the basal ganglia to process, integrate, and 'make sense of' sensory information conveying body position is necessary for the generation of motor plans for the musculoskeletal system to implement. Our results indicate that PD-associated deficits in this functional integrity do generate postural difficulties in specific sensory contexts. Finally, our results provide information regarding environmental situations that impose balance threat among individuals suffering from PD, and thus provide preliminary evidence that may be useful for the development of rehabilitative strategies to minimize fall risk in this population.

REFERENCES

Abbruzzese, G., & Berardelli, A. (2003). Sensorimotor integration in movement disorders. Movement Disorders, 18, 231-240.

Adkin, A. L., Frank, J. S., Carpenter, M. G., & Peysar, G. W. (2000). Postural control is scaled to the level of postural threat. Gait and Posture, 12, 87-93.

Adkin, A. L., Frank, J. S., & Jog, M. S. (2003). Fear of falling and postural control in Parkinson's disease. Movement Disorders, 18, 496-502.

Allison, L., & Jeka, J. J. (2004). Multisensory integration: Resolving ambiguities for human postural control. In (G. Calvert), Handbook of multisensory processes. Cambridge, MA: MIT Press. 785-797.

Ashburn, A., Stack, E., Pickering, R. M., & Ward, C. D. (2001). A community-dwelling sample of people with Parkinson's disease: characteristics of fallers and non-fallers. Age Ageing, 30, 47-52.

Balash, Y., Peretz, C., Leibovich, G., Herman, T., Hausdorff, J. M., & Giladi, N. (2005). Falls in outpatients with Parkinson's disease: Frequency, impact, and identifying factors. Journal of Neurology, Epub.

Balasubramaniam, R., & Wing, A. M. (2002). The dynamics of standing balance. Trends in Cognitive Science, 6, 531-536.

Barbeau, A. (1980). Biomechanical aging in Parkinson's disease. In (L. Amadocci, A. N. Davison, & P. Antuono), Aging of the Brain and Dementia. New York: Raven. 275-285.

Bloem, B. R., van Vugt, J. P. P., & Beckley, D. J. (2001). Postural instability and falls in Parkinson's disease. In (E. Ruzicka, M. Hallett, & J. Jankovic), Gait disorders. Advances in Neurology. Philadelphia: Lippincott Williams & Wilkins. 209-223.

Bronstein, A. M., Hood, J. D., Gretsy, M. A., & Panagi, C. (1990). Visual control of balance in cerebellar and parkinsonian syndromes. Brain, 113, 767-779.

Bronte-Stewart, H. M., Minn, A. Y., Rodrigues, J., Buckley, E. L., & Nashner, L. M. (2002). Postural instability in idiopathic Parkinson's disease: the role of medication and unilateral pallidotomy. Brain, 125, 2100-2114.

Brown, L. A., Cooper, S. A., Doan, J. B., Dickin, D. C., Pellis, S. M., Whishaw, I. Q., & Suchowersky, O. (under review). Parkinsonian deficits in sensory integration for postural control: Temporal response to changes in visual input. Neuroscience Letters.

Brown, L. A., & Frank, J. S. (1997). Postural compensations to the potential consequences of instability: Kinematics. Gait and Posture, 6, 89-97.

Brown, L. A., Polych, M. A., & Doan, D. B. (under review). The effects of anxiety on regulation of upright standing among younger and older adults. Gait and Posture.

Brown, L. A., Shumway-Cook, A., & Woollacott, M. H. (1999). Attentional demands and postural recovery: The effects of aging. The Journals of Gerontology Series A: Medical Sciences, 54, M165-M171.

Carpenter, M. G., Frank, J. S., & Silcher, C. P. (1999). Surface height effects on postural control: a hypothesis for a stiffness strategy for stance. Journal of Vestibular Research, 9, 277-286.

Carpenter, M. G., Frank, J. S., Silcher, C. P., & Peysar, G. W. (2001). The influence of postural threat on the control of upright stance. Experimental Brain Research, 138, 210-8.

Chong, R. K. Y., Horak, F. B., & Woollacott, M. H. (2000). Parkinson's disease impairs the ability to change set quickly. Journal of the Neurological Sciences, 175, 57-70.

Chong, R. K. Y., Jones, C. L., & Horak, F. B. (1999). Postural set for balance control is normal in Alzheimer's but not in Parkinson's disease. The Journals of Gerontology Series A: Medical Sciences, 54, M129-M135.

Coogler, C. E., & Wolf, S. (1992). Consistency of postural responses in elderly individuals. In (M. Woollacott, & F. Horak), Posture and gait: control mechanisms, Vol. II. Eugene, OR: University of Oregon Books. 239-242.

Cote, L., & Crutcher, M. D. (1991). The basal ganglia. In (E. R. Kandel, J. H. Schwartz, & T. M. Jessel), Principles of neural science. New York: Elsevier. 647-660.

Dickin, D. C., Brown, L. A., & Doan, J. B. (in press). Age differences in the time course of postural control during sensory perturbations. Age and Ageing.

Dickin, D. C., & Rose, D. J. (2004). Sensory organization abilities during upright stance in late-onset Alzheimer's-type dementia. Experimental Aging Research, 30, 373-390.

Dietz, V. (1998). Evidence for load receptor contribution to the control of posture and locomotion. Neuroscience Biobehavioral Reviews, 22, 495-499.

Giladi, N., Hausdorff, J., & Balash, Y. (2005). Episodic and continuous gait disturbance in Parkinson's disease. In (J. M. Hausdorff, & N. B. Alexander), Evaluation and management of gait disorders. Marcel Dekker Inc.

Gray, P., & Hildebrand, K. (2000). Fall risk factors in Parkinson's disease. Journal of Neuroscience Nursing, 32, 222-8.

Greenwood, R., & Hopkins, A. (1976). Muscle responses during sudden falls in man. Journal of Physiology (London), 254, 507-518.

Hirsch, M. A., Toole, T., Maitland, C. G., & Rider, R. A. (2003). The effects of balance training and high-intensity resistance training on persons with idiopathic Parkinson's disease. Archives of Physical Medicine and Rehabilitation, 84, 1109-1117.

Hoehn, M. M., & Yahr, M. D. (1967). Parkinsonism: onset, progression and mortality. Neurology, 17, 427-42.

Horak, F. B., Henry, S. M., & Shumway-Cook, A. (1997). Postural perturbations: new insights for treatment of balance disorders. Physical Therapy, 77, 517-33.

Horak, F. B., & Macpherson, J. M. (1996). Postural orientation and equilibrium. In (L. B. Powell, & J. T. Shepherd), Exercise: regulation and integration of multiple systems. Oxford, NY: APS. 255-292.

Horak, F. B., & Nashner, L. M. (1986). Central programming of postural movements: Adaptation to altered support-surface configurations. Journal of Neurophysiology, 55, 1369-1381.

Horak, F. B., Nashner, L. M., & Diener, H. C. (1990). Postural strategies associated with somatosensory and vestibular loss. Experimental Brain Research, 82, 167-177.

Horak, F. B., Nutt, J. F., & Nashner, L. M. (1992). Postural inflexibility in parkinsonian subjects. Journal of the Neurological Sciences, 111, 46-58.

Horak, F. B., & Shupert, C. (1994). The role of the vestibular system in postural control. In (S. Herdman), Vestibular rehabilitation. New York: FA Davis. 22-46.

Hu, M. H., & Woollacott, M. H. (1994). Multisensory training of standing balance in older adults: Postural stability and one-leg stance. The Journals of Gerontology Series A: Medical Science, 49, M52-M61.

Keele, S. W., & Ivry, R. (1991). Does the cerebellum provide a common computation for diverse tasks? A timing hypothesis. In (A. Diamond), The development and neural bases of higher cognitive functions. Annals of the New York academy of sciences. New York: New York Academy of Sciences. 197-211.

Klawans, J. L., & Topel, J. L. (1974). Parkinsonism as a falling sickness. Journal of the American Medical Association, 230, 1555-1557.

Kolb, B., & Whishaw, I. Q. (1996). Organization of the motor system. In (B. Kolb, & I. Q. Whishaw), Fundamentals of human neuropsychology. New York, NY: W.H. Freeman & Company. 120-144.

Kolb, B., & Whishaw, I. Q. (2001). How does the brain produce movement? In (W. I. Kolb B), An introduction to brain and behaviour. New York: Worth Publishers. 354-397.

Kropotov, J. D., & Etlinger, S. C. (1999). Selection of actions in the basal ganglia-thalamocortical circuits: Review and model. International Journal of Psychophysiology, 31, 197-217.

Latash, M. L. (1998). The basal ganglia. In (M. L. Latash), Neurophysiological basis of movement. Champaign, IL: Human Kinetics. 139-144.

Ledin, T., Kronhed, A. C., Moller, C., Moller, N., Odkvist, L. M., & Olsson, B. (1991). Effects of balance training in elderly evaluated by clinical tests and dynamic posturography. Journal of Vestibular Research, 1, 129-138.

Lee, M. S., Rinne, J. O., & Marsden, C. D. (2000). The pedunculopontine nucleus: Its role in the genesis of movement disorders. Yonsei Medical Journal, 41, 167-184.

Lun, V., Pullan, N., Labelle, N., Adams, C., & Suchowersky, O. (2005). Comparison of the effects of a self-supervised home exercise program with a physiotherapist-supervised exercise program on the motor symptoms of Parkinson's disease. Movement Disorders, Epub.

Maki, B. E., Holliday, P. J., & Topper, A. K. (1991). Fear of falling and postural performance in the elderly. The Journals of Gerontology Series A: Medical Sciences, 46, M123-M131.

Maki, B. E., Holliday, P. J., & Topper, A. K. (1994). A prospective study of postural balance and risk of falling in ambulatory and independent elderly population. The Journals of Gerontology Series A: Medical Sciences, 49, M72-M84.

Maki, B. E., McIlroy, W. E., & Fernie, G. R. (2003). Change-in-support reactions for balance recovery. IEEE Engineering in Medicine and Biology Magazine, 22, 20-26.

Marsden, C. D. (1982). The mysterious motor function of the basal ganglia: The Robert Wartenberg lecture. Neurology, 32, 514-539.

Michalowska, M., Krygowska-Wajs, A., Jedynecka, U., Sobieszek, A., & Fiszer, U. (2002). Analysis of causes for falls in people with Parkinson's disease. Neurologia I Neurochirurgia Polska, 36, 57-68.

Mitchell, S. L., Collins, J. J., De Luca, C. J., Burrows, A., & Lipsitz, L. A. (1995). Open-loop and closed-loop postural control mechanisms in Parkinson's disease: increased mediolateral activity during quiet standing. Neuroscience Letters, 197, 133-136.

Mittelstaedt, H. (1996). Somatic graviception. Biological Psychology, 42, 53-74.

Morris, M., Iansek, R., Smithson, F., & Huxham, F. (2000). Postural instability in Parkinson's disease: A comparison with and without a concurrent task. Gait and Posture, 12, 205-216.

Morris, M. E., Iansek, R., Matyas, T. A., & Summers, J. J. (1996). Stride length regulation in Parkinson's disease: Normalisation strategies and underlying mechanisms. Brain, 119, 551-568.

Nallegowda, M., Singh, U., Handa, G., Khanna, M., Wadhwa, S., Yadav, S. L., Kumar, G., & Behari, M. (2004). Role of sensory input and muscle strength in maintenance of balance, gait, and posture in Parkinson's disease: A pilot study. American Journal of Physical Medicine and Rehabilitation, 83, 898-908.

Nashner, L. M. (1982). Adaptation of human movement to altered environments. Trends in Neuroscience, 5, 358-361.

Nashner, L. M. (1993). Computerized dynamic posturography. In (G. Jacobson, C. Newman, & J. Kartush), Handbook of balance function and testing. Mosby Year Book. 280-307.

Nashner, L. M. (2001). Computerized dynamic posturography. In (J. A. Goebel), Practical management of the dizzy patient. Philadelphia, PA: Lippincott Williams & Wilkins. 143-170.

Nashner, L. M., Black, F. O., & Wall, C. I. (1982). Adaptation to altered support and visual conditions during stance: Patients with vestibular deficits. The Journal of Neuroscience, 2, 536-544.

Olanow, C. W., & Tatton, W. G. (1999). Etiology and pathogenesis of Parkinson's disease. Annual Review of Neuroscience, 22, 123-144.

Overstall, P. W. (2001). Motor problems. In (J. R. Playfer, & J. V. Hindle), Parkinson's disease in the older patient. London, England: Arnold. 184-199.

Paillard, J. (1987). Cognitive versus sensorimotor encoding of spatial information. In (P. Ellen, & C. Thinus-Blanc), Cognitive processes and spatial orientation in animal and man: Neurophysiology and developmental aspects. Hague: Martinus Nijhoff. 43-77.

Peterka, R. J., & Black, F. O. (1990-1991). Age-related changes in human posture control: Sensory organization tests. Journal of Vestibular Research, 1, 73-85.

Peterka, R. J., & Loughlin, P. J. (2004). Dynamic regulation of sensorimotor integration in human postural control. Journal of Neurophysiology, 91, 410-23.

Purves, D., Augustine, G. J., Fitzpatrick, D., Katz, L. C., LaMantia, A.-S., McNamara, J. O., & Williams, S. M. (1997). Modulation of movement by the basal ganglia and cerebellum. In (D. Purves, G. J. Augustine, D. Fitzpatrick, L. C. Katz, A.-S. LaMantia, J. O. McNamara, & S. M. Williams), Neuroscience. Sunderland, MA: Sinauer Associates, Inc. 329-344.

Purves, D., Augustine, G. J., Fitzpatrick, D., Katz, L. C., LaMantia, A.-S., McNamara, J. O., & Williams, S. M. (1997). The somatic sensory system. In (D. Purves, G. J. Augustine, D. Fitzpatrick, L. C. Katz, A.-S. LaMantia, J. O. McNamara, & S. M. Williams), Neuroscience. Sunderland, MA: Sinauer Associates. 189-207.

Redfern, M. S., Yardley, L., & Bronstein, A. M. (2001). Visual influences on balance. Anxiety Disorders, 15, 81-94.

Rocchi, L., Chiari, L., Cappello, A., Gross, A., & Horak, F. B. (2004). Comparison between subthalamic nucleus and globus pallidus internus stimulation for postural performance in Parkinson's disease. Gait and Posture, 19, 172-83.

Rocchi, L., Chiari, L., & Horak, F. B. (2002). Effects of deep brain stimulation and levodopa on postural sway in Parkinson's disease. Journal of Neurology, Neurosurgery, & Psychiatry, 73, 267-274.

Romberg, M. H. (1851). Lehrbuch der mercenkrankheiten des menschen. Berlin: Duncker.

Romero, D. H., & Stelmach, G. E. (2003). Changes in postural control with aging and Parkinson's disease. IEEE Engineering in Medicine and Biology Magazine, 2, 27-31.

Rose, D. J., & Clark, S. (2000). Can the control of bodily orientation be significantly improved in a group of older adults with a history of falls? Journal of the American Geriatrics Society, 48, 275-282.

Rougier, P. (2003). The influence of having the eyelids open or closed on undisturbed postural control. Neuroscience Research, 47, 73-83.

Sapper, C. B. (2000). Brain stem modulation of sensation, movement and consciousness. In (E. R. Kandel, J. H. Schwartz, & T. M. Jessel), Principles of Neural Science. New York, NY: McGraw-Hill. 889-909.

Shumway-Cook, A., & Woollacott, M. H. (2001). Motor Control: Theory and practical applications. Baltimore, MA: Lippincott Williams Wilkins. 614.

Singer, T. P., Castagnoli, N., Jr., Ramsay, R. R., & Trevor, A. J. (1987). Biochemical events in the development of parkinsonism induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine. Journal of Neurochemistry, 49, 1-8.

Smiley-Oyen, A. L., Cheng, H.-Y. K., Latt, D. L., & Redfern, M. L. (2002). Adaptation of vibration-induced postural sway in individuals with Parkinson's disease. Gait and Posture, 16, 188-197.

Sokal, R. R., & Rohlf, F. J. (1981). Biometry: The principles of and Practice of Statistics in Biological Research. New York, NY: Freeman.

Stolze, H., Klebe, S., Zechlin, C., Baecker, C., Friege, L., & Deuschl, G. (2004). Falls in frequent neurological diseases: Prevalence, risk factors and aetiology. Journal of Neurology, 251, 79-84.

Suchowersky, O. (2002). Parkinson's disease. Current neurology and neuroscience reports, 2, 310-316.

Takakusaki, K., Oohinata-Sugimoto, J., Saitoh, K., & Habaguchi, T. (2004). Role of basal ganglia-brainstem systems in the control of postural muscle tone and locomotion. Progress in Brain Research, 143, 231-7.

Takakusaki, K., Saitoh, K., Harada, H., & Kashiwayanagi, M. (2004). Role of basal ganglia-brainstem pathways in the control of motor behaviors. Neuroscience Research, 50, 137-51.

Tanner, C. M., Goldman, S. M., & Ross, G. W. (2002). Etiology of Parkinson's disease. In (T. E. Jankovic JJ), Parkinson's disease and movement disorders. Philadelphia: Lippincott Williams & Wilkins. 90-100.

Tanner, C. M., & Langston, J. W. (1990). Do environmental toxins cause Parkinson's disease? A critical review. Neurology, 40, 17-30.

Tanner, C. M., Ottman, R., Ellenberg, J. H., & al, e. (1997). Parkinson's disease (PD) concordance in elderly male monozygotic (MZ) and dizygotic (DZ) twins. Neurology, 48, 333.

Teasdale, N., & Simoneau, M. (2001). Attentional demands for postural control: The effects of aging and sensory reintegration. Gait and Posture, 14, 203-210.

Teasdale, N., Stelmach, G. E., Breunig, A., & Meeuwsen, H. J. (1991). Age differences in visual sensory integration. Experimental Brain Research, 85, 691-696.

Tsang, W. W., Wong, V. S., Fu, S. N., & Hui-Chan, C. W. (2004). Tai chi improves standing balance control under reduced or conflicting sensory conditions. Archives of Physical Medicine and Rehabilitation, 85, 129-137.

Vitek, J. L., & Giroux, M. (2000). Physiology of hypokinetic and hyperkinetic movements disorders: Model for dyskinesia. Annals of Neurology, 47, S131-S140.

Vuillerme, N., Teasdale, N., & Nougier, V. (2001). The effect of expertise in gymnastics on proprioceptive sensory integration in human subjects. Neuroscience Letters, 311, 73-76.

Waterston, J. A., Hawken, M. B., Tanyeri, S., Janti, P., & Kennard, C. (1993). Influence of sensory manipulation on postural control in Parkinson's disease. Journal of Neurology, Neurosurgery, and Psychiatry, 56, 1276-1281.

Watt, D. G. D. (1976). Responses of cats to sudden falls: An otolith-originating reflex assisting landing. Journal of Neurophysiology, 39, 257-265.

Winter, D. A. (1995). Human balance and posture control during standing and walking. Gait and Posture, 3, 193-214.

Winter, D. A., Patla, A. E., & Frank, J. S. (1990). Assessment of balance control in humans. Medical Progress Through Technology, 16, 31-51.

Winter, D. A., Patla, A. E., Prince, F., Ishac, M., & Gielo-Perczak, K. (1998). Stiffness control of balance in quiet standing. Journal of Neurophysiology, 80, 1211-1221.

Winter, D. A., Prince, F., Frank, J. S., Powell, C., & Zabjek, K. F. (1996). Unified theory regarding A/P and M/L balance in quiet stance. Journal of Neurophysiology, 75, 2334-2343.

Winter, D. A., Prince, F., Stergiou, P., & Powell, C. (1993). Medial-lateral and anterior-posterior motor responses associated with with centre of pressure changes in quiet standing. Neuroscience Research Communications, 12, 141-148.

Wise, S. P. (1985). The primate premotor cortex: past, present, and preparatory. Annual Review of Neuroscience, 8, 1-19.

Wood, B. H., Bilclough, J. A., Bowron, A., & Walker, R. W. (2002). Incidence and prediction of falls in Parkinson's disease: a prospective multidisciplinary study. Journal of Neurology, Neurosurgery, and Psychiatry, 72, 721-5.