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Contributions of Vision to Gait Improvement and Perceptual Impairment in Parkinson's Disease

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CONTRIBUTIONS OF VISION TO GAIT IMPROVEMENT AND PERCEPTUAL IMPAIRMENT IN PARKINSON'S DISEASE

by

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CHAPTER 1

INTRODUCTION

1.1 Introduction

The overall purpose of this thesis was to investigate how vision contributes to gait impairment in Parkinson's disease (PD). This was achieved by manipulating visual feedback in the form of step cues, but also from a perceptual standpoint to evaluate how visual perception might contribute to gait impairment. Combining visual feedback aids in perpetually demanding conditions facilitated a greater understanding of the deficits associated with gait in PD. Also, a number of visual cues were examined to determine the viability of these cues in improving the abnormal gait patterns demonstrated by these individuals with PD, including freezing of gait (FOG) and the less severe shuffling step pattern. The visual cues that were tested included ground lines, and a laser device that presented lines in both a forward, and reverse optic flow pattern. The goal was to gain a better understanding of the causes and perceptual mechanisms underlying the gait experienced by individuals with PD and the cues that can lead to an improvement and increased quality of life.

A combination of varying degrees of symptoms commonly observed in PD such as tremor, rigidity, akinesia, bradykinesia and postural instability usually translate into the gait impairment observed within individuals with PD. However, there remains inconclusive evidence regarding why the gait of individuals with PD can be improved through the use of visual cues, as well as the mechanisms behind FOG.

Maintenance of a functional gait pattern is a prerequisite for normal aging. A loss of independence and overall quality of life is usually the result of the extreme forms of gait disorders that can occur in elderly individuals. These abnormal gait patterns are even more common in those individuals with PD (Azulay et al., 1999; Azulay, Mesure, & Blin, 2006; Bloem, Hausdorff, Visser, & Giladi, 2004; G. N. Lewis, Byblow, & Walt, 2000; Moore, Peretz, & Giladi, 2007). A lack of physical activity is also a contributing factor to the secondary health issues that arise in PD and can lead to both gait impairments and a decline in quality of life.

Although extensive research has been completed examining the influence of visual cues on abnormal gait patterns of individuals with PD, the mechanisms behind the observed improvements remain poorly understood. Even less knowledge exists regarding the cause of freezing of gait (FOG) and how it might be prevented through the use of these same visual strategies. By performing comparisons between healthy individuals, non-FOG individuals with PD, and individuals with PD who experience FOG, increased understanding in the area of vision contribution and inhibition in gait in PD may be gained.

Section 1.2 of this thesis examined PD in more depth, and the gait impairments common in PD was discussed in Section 1.3. Section 1.4 discussed specific gait issues such as FOG and provided the reasons for investigating the potential benefits of visual cues on preventing freezing episodes and the rationale for investigating the use of visual cues in PD was explained in section 1.5. Lastly, section 1.6 outlined the organization of this thesis and presented the research questions and hypotheses.

1.2 General introduction to idiopathic Parkinson's disease

Parkinson's disease is a debilitating and slowly progressing neurodegenerative disease (Leung & Mok, 2005). The prevalence of idiopathic PD increases greatly with age. It has been found to be extremely rare in those under the age of 45, with the prevalence peaking at an estimated 2% of individuals over the age of 85 (Ben-Shlomo & Sieradzan, 1995). The main symptoms of PD have been well-documented and include tremor; rigidity; akinesia, which is an overall absence of movement; bradykinesia, which is a slowness of movement; and postural instability (Bodis-Wollner, 2003; Guttman, Kish, & Furukawa, 2003; Schenkman et al., 1989).

Parkinson's disease is the most common disorder involving the region of the brain known as the basal ganglia. The basal ganglia refers to the combination of the caudate nucleus, putamen, globus pallidus, subthalamic nucleus, and substantia nigra (Nolte, 2002). These structures are responsible for many things including the integration of sensory and motor processes required for effective movement control. The basal ganglia are constantly informed about most aspects of cortical function and provide feedback loops to both the cerebral cortex and thalamus (Middleton & Strick, 2000). The principal circuit of the basal ganglia is a loop that starts with projections from a section of the cerebral cortex to the basal ganglia and then returns to the same part of the cortex by way of the thalamus. A primary function of the basal ganglia is the inhibition of the thalamus (Nolte, 2002). The thalamus normally has excitatory projections on the cortex and therefore its selective inhibition by the basal ganglia is integral to proper neurological function and motor control. The specific area that the basal ganglia projects to is the ventrolateral thalamus. This part of the thalamus is thought to project mostly to a single cortical area, the primary motor cortex. Therefore the basal ganglia loops function largely in the domain of motor control (Middleton & Strick, 2000). Recent research however has pointed towards the existence of additional projections from the basal ganglia traveling to other areas of the cortex including subdivisions of the premotor, oculomotor, prefrontal, and inferotemporal cortex (Middleton & Strick, 2000). These projections also travel through the thalamus to these distinct cortical areas. This information suggests that in addition to its role in motor control, the basal ganglia may have an even greater role in the influence of human behaviour. In another recent study researchers used positron emission tomography while measuring the ability of individuals with PD to perform planning and spatial memory tasks. They demonstrated that certain projections in the basal ganglia project to the prefrontal cortex and are responsible for spatial memory (Owen, Doyon, Dagher, Sadikot, & Evans, 1998). Therefore, the basal ganglia likely have a large influence on many aspects of movement. By increasing the understanding of the mechanisms behind gait impairments in PD and how these deficits may be overcome will lead to a greater understanding of the specific role of the basal ganglia in movement control.

In PD there is a marked loss of the dopaminergic neurons in the basal ganglia, which leads to the common symptoms observed in individuals affected with PD. As previously mentioned, the symptoms usually involve some combination of tremor, rigidity, akinesia, bradykinesia, and postural instability. The tremor that tends to persist in PD is a resting tremor that is characterized by a "pill-rolling" movement involving the hands (Nolte, 2002). These tremors tend to become less noticeable during voluntary movement and worsen during times of mental or emotional stress (Nolte, 2002). Also, research has indicated that certain individuals with PD might experience an action tremor which occurs specifically during movement (Guttman et al., 2003). This type of tremor is likely to exert a greater influence on gait as compared to the more common resting tremor. The rigidity observed in PD is attributed to increased muscle tone in muscles affected by the disease. However, strength and reflexes are not especially affected in the aforementioned muscles (Nolte, 2002). There are two types of rigidity that occur in PD. The first is called plastic and may be uniform throughout a range of movements, while the other is called cog-wheel rigidity and may be interrupted by a series of brief relaxations (Nolte, 2002). Currently, definitive reasons are not yet known for the presence of one form of rigidity over the other. Lastly, the akinesia common in PD is demonstrated by observations such as a decreased arm movement during gait, decreased rate of blinking, difficulty with voluntary movement, and a lack of facial expressions (Nolte, 2002).

1.2.1 Other motor and non-motor symptoms of Parkinson's disease

In addition to the primary symptoms of PD; tremor, rigidity, akinesia, bradykinesia and postural disturbances, there are a number of other symptoms that individuals with PD encounter. These additional features of PD can be grouped into categories consisting of motor and non-motor symptoms.

Motor symptoms of PD can be widespread and numerous. They tend to be initially unilateral or at least asymmetrical as the disease begins on one side of the basal ganglia before eventually progressing to both sides of the brain (Ben-Shlomo & Sieradzan, 1995). Therefore, symptoms at first appear on only the opposite side of the body from the side of the damage in the basal ganglia. Resting tremor appears in up to 80% of individuals with PD but is usually not the first sign of the disease (Ben-Shlomo & Sieradzan, 1995). In addition to rigidity and akinesia, postural instability can occur which leads to an increased risk of loss of balance and falls and a decreased quality of life (Bloem, Grimbergen, Cramer, Willemsen, & Zwinderman, 2001). Jacobs and Horak (2006) found that individuals with PD have a decreased compensatory stepping ability. This means that they are less able to react to postural disturbances and therefore are less able to deal with disturbances in balance and prevent falls as compared to healthy individuals. Motor symptoms beyond the cardinal features of PD can be grouped into gait and postural disturbances, impaired motor coordination, speech and swallowing difficulties, and other symptoms. Gait impairments are another common feature in PD and will be discussed in detail in Section 1.3.

Disturbances of speech and swallowing are a common occurrence within individuals with PD. A monotone voice and decreased volume of speech tends to occur in PD along with a frequent inability to swallow that is termed dysphagia. This impaired ability to swallow often leads to drooling. Oral festination in PD is also fairly common and includes a tendency to increase the rate of speech and lose the normal amplitude (Moreau et al., 2007). Micrographia is also often present in PD and involves small handwriting that continually decreases in size during the course of a sentence (Guttman et al., 2003; Nolte, 2002). Another primary motor symptom that is observed in PD is increased fatigue.

In addition to the previously described impairments in motor function that are common in PD, there are a number of non-motor symptoms including an impairment in cognition, vision, sleep, autonomic function, behaviour, and sexual function that can be observed within individuals with PD (Bodis-Wollner, 2003; Uc et al., 2006). Impairments in cognition are fairly common in PD and have recently been suggested to be at least partly caused by the depletion of dopaminergic neurons in the substantia nigra and striatum that has been observed by use of fMRI, and the disruptive influence that this neuronal loss can have on the feedback loops between the striatum and the frontal cortex (S. J. Lewis, Dove, Robbins, Barker, & Owen, 2003). Depression is also commonly found to be linked with PD, and often can be elicited fairly early in the course of the disease (Levin & Katzen, 2005). Uc et al. observed a deficit in driving ability among individuals with PD and suggested that the navigational errors and decrease in safety while driving was associated more with impairments in cognition and visual function rather than motor symptom severity (Uc et al., 2007). These non-motor impairments can be just as debilitating as the commonly observed motor symptoms observed in PD and have a tremendous effect on the quality of life of the individual. Recent evidence has even suggested that in some cases the genetic mutation that is linked with early-onset PD can lead to cognitive impairment well before dopaminergic neuronal loss occurs (Zhu et al., 2007). Therefore, consideration of the implications of these non-motor symptoms is essential when devising a treatment plan or considering causes of gait impairment in individuals with PD.

1.2.2 Possible causes: Environmental and genetic factors

Possible risk factors for the development of Parkinson's disease have been studied extensively throughout the last number of years. Research into the area of genetic factors have proved inconclusive and family studies suggest that the risk for a secondary case of PD within the immediate family is no greater than for a control population (Ben-Shlomo & Sieradzan, 1995). However, several genetic forms of PD have recently been discovered and are currently being researched. A study of twins suggests that genetic factors play a role in the development of early onset PD, but have no influence on later onset idiopathic PD (Tanner et al., 1999). Also, evidence is beginning to lead to the thought that the degenerative process that occurs in PD might be similar to that found in the rare hereditary forms of degenerative parkinsonisms (Guttman et al., 2003). An abnormality in the function of a cellular level system that is partly responsible for the degradation of damages proteins has been suggested to be linked to these hereditary forms (Mouradian, 2002). This has led to the thought that PD might be caused by either the presence of a toxic protein that is left free to cause damage because of the abnormality of the previously mentioned system, or because this system begins to selectively damage dopaminergic neurons (Guttman et al., 2003).

A number of environmental agents have been found have a part in the development of PD. Neurotoxic factors such as carbon monoxide, manganese, mercury, pesticides such as paraquat, and 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) can lead to the neurological damage consistent in PD (Ben-Shlomo & Sieradzan, 1995). A sudden case of severe early onset PD in a number of young individuals that had recently injected themselves with a “synthetic heroin” that had been contaminated with MPTP led to the discovery that MPTP is selectively toxic to dopaminergic neurons in the substantia nigra (Nolte, 2002). Exposure to infective factors such as intrauterine influenza, herpes simplex, and encephalitis lethargica have also been linked with later development of PD; however, research in this area remains incomplete (Ben-Shlomo & Sieradzan, 1995). Also, a number of lifestyle factors such as diet, head injury, vitamin intake, and smoking have been thought to play a role in the incidence of PD. However, confounding factors lead to problematic research into this area and therefore inconclusive results.

1.2.3 Treatment options in Parkinson's disease

There are several different areas of treatment options available to individuals with PD that are designed to treat and manage the disease including drug therapy, surgical intervention, and different forms of physical therapy. Medicinal treatment is the most widely used in the fight against the disease and there are a number of different types of drugs used by themselves, or in combination with other drugs (Table 1.1).

Levodopa is one of the primary drugs utilized by individuals with PD. It is the amine precursor of dopamine and metabolizes to dopamine in specific cells that contain dopa-decarboxylase (Guttman et al., 2003; Leung & Mok, 2005). Dopamine is not able to cross the blood-brain barrier, but administration of levodopa restores a degree of the cortical activity that is suppressed by the excessive inhibition of the thalamus that is observed in PD (Nolte, 2002). It is combined with a peripheral dopa-decarboxylase inhibitor in order to allow as much levodopa as possible to reach the areas where it can be used, into the widely used drug Sinemet and is effective in combating bradykinesia, rigidity and some tremor (Ben-Shlomo & Sieradzan, 1995; Leung & Mok, 2005). All individuals with PD will eventually over the course of the disease require levodopa treatment (Leung & Mok, 2005). Initially, a small dose such as three to four administrations is effective in relieving symptoms. However with time, a greater amount of the drug is required to produce the same desired effects (Ben-Shlomo & Sieradzan, 1995). Long term administration of levodopa is associated with motor complications such as dyskinesia and motor fluctuations and therefore the current recommendation is to avoid high doses if possible in order to prevent these side effects from occurring (Ben-Shlomo & Sieradzan, 1995; Leung & Mok, 2005). It has been reported that motor complications occur with long term use of levodopa in 30% to 50% of patients after 2 to 5 years of treatment and in 80% to 100% after 10 years of treatment (Poewe, 1994). Therefore young onset individuals that develop PD have an increased chance of experiencing adverse motor effects as they are subject to an increased number of years of levodopa therapy. Currently, levodopa is the most effective medicinal treatment administered to combat PD.

Many other types of drugs are also used either by themselves, or in combination with other drugs to treat PD. Anticholinergics have been found to have mild beneficial effects on cardinal features of PD such as rigidity and bradykinesia (Leung & Mok, 2005). Amantadine promotes the release of dopamine and can be used both in early stages PD before levodopa, and in advanced stages in order to curb dyskinetic movements (Guttman et al., 2003; Leung & Mok, 2005). Dopamine agonists tend to be administered in combination levodopa in the treatment of motor complications in PD (Leung & Mok, 2005). These drugs stimulate the release of dopamine by acting directly on dopamine receptors and therefore have an advantage over levodopa as they do not need to be metabolized into dopamine and might possibly avoid unwanted side effects (Leung & Mok, 2005). Both MAO and COMT inhibitors act by inhibiting the enzymes that are responsible for degrading dopamine and thereby allow for increased availability (Ben-Shlomo & Sieradzan, 1995; Leung & Mok, 2005).

A number of negative effects are associated with many of the medicinal interventions designed to treat symptoms of PD. Many of the drugs are responsible for a degree of cognitive dysfunction which can contribute to the gait impairments observed in PD. Despite the fact that these drugs are designed to improve the day to day life of those with PD, they actually may be associated with some of the gait impairments that they are indirectly attempting to alleviate. Confusion and attention demands are important issues to consider when evaluating gait impairments, as will be examined in this thesis.

Table 1.1
Drugs used to treat Parkinson's disease (Guttman et al., 2003)

Drug or drug class	Mechanism of action	Side effects	Specific drugs
Anticholinergics	Block acetylcholine receptors	Dry mouth, dry eyes, urinary retention	Trihexyphenidyl, Benztropine, Ethopropazine
Amantadine	Blocks NMDA receptors and acetylcholine receptors and promotes release of dopamine	Cognitive dysfunction, peripheral edema, skin rash	Amantadine
L-dopa	Metabolism to dopamine in cells that contain dopa-decarboxylase	Nausea, hypotension, hallucinations	L-dopa/carbidopa, L-dopa/benserazide, Sinemet CR
Dopamine agonists	Directly stimulate dopamine receptors	Nausea, hypotension, hallucinations	Bromocriptine, Pergolide, Ropinirole, Pramipexole
Monoamine oxidase (MAO) inhibitors	Block MAO-B receptors to reduce dopamine metabolism	Nausea, dizziness, sleep disorder	Selegiline
Catechol O-methlytransferase (COMT) inhibitors	Block peripheral COMT activity to improve L-dopa pharmacokinetics	L-dopa-related side-effect exacerbation, diarrhea, urine discolouration	Entacapone

There are a number of different surgical interventions that have proved to be effective in the treatment of PD. Lesion-producing procedures that eliminate the site of the brain deemed to be causing tremors have been used for a number of years. However, such procedures are not effective in improving the slowness of movement that is experienced in PD (Ben-Shlomo & Sieradzan, 1995). Deep brain stimulation (DBS) has been gaining in popularity and has been shown to be effective in treating cases in which pharmacological therapy has become less effective due to a wearing off of the medication or increased occurrence of negative side effects. In DBS, a pacemaker is implanted into the brain which electrically stimulates the appropriate sites. Possible sites include the subthalamic nucleus, ventral intermediate thalamus, and globus pallidus. However, DBS of the subthalamic nucleus has been shown to be most effective in improving all of the cardinal features of PD (Leung & Mok, 2005). The abnormal firing of the subthalamic nucleus is believed to lead to many of the symptoms observed in PD and DBS can inhibit neuronal firing via activation of inhibitory GABAergic fibres (Leung & Mok, 2005). Advantages of DBS over other surgical techniques includes the adjustable settings of stimulator frequency and intensity, no lesion is created, and there is a potential for bilateral improvement (Guttman et al., 2003). DBS is not without inherent risk and eligible candidates are usually required to be under the age of 70 and without cognitive dysfunction (Leung & Mok, 2005).

Another surgical technique that currently remains in the experiment stages is the implantation of dopaminergic neurons into different areas affected by PD. The goal is to replace the degenerated neurons in the basal ganglia with healthy dopamine producing neurons in order to deter the progression of PD and possibly improve symptoms of the disease. However, problems remain in the maintenance of the implanted neurons as the development of dystonia and dyskinesia has been found in some patients at 3 years post surgery (Leung & Mok, 2005). More clinical studies are required to test the long-term viability of transplantation surgery in the treatment of PD.

Different forms of physical therapy are becoming more popular in the treatment of PD by those who wish to avoid invasive surgeries and minimize the use of drugs which often lead to negative side effects (Johnson & Almeida, 2007). There is currently little research examining potential benefits of physiotherapy, speech therapy, and tai chi in PD. However, preliminary data in these areas suggest that it is worthwhile for further investigation into alternative therapies as a supplementation to the more traditional treatments.

1.3 Gait impairments in Parkinson's disease

An impaired gait pattern is a hallmark symptom of PD and has been well documented (G. N. Lewis et al., 2000; Schubert, Prokop, Brocke, & Berger, 2005; van Wegen et al., 2006). Individuals with PD tend to display a shuffling gait pattern with a decreased stride length and a reduced overall velocity. Cadence may be normal in comparison with healthy individuals, but is elevated in relation to their own velocity (G. N. Lewis et al., 2000). Gait deficits are persistent in PD despite optimal drug management and have been found to be associated with reduced independence and safety (Rochester et al., 2007). The side of the body affected by PD usually tends to display a decrease in arm swing during gait (van Wegen et al., 2006). Other properties of gait in PD have also been observed to be asymmetric such as the timing of swing durations

(Yogev, Plotnik, Peretz, Giladi, & Hausdorff, 2007). Individuals with PD often experience difficulty in making turns and require several short, rigid, and shuffling steps to make a turn instead of the fluid turning motion that is used by healthy individuals. Individuals with PD also experience a reduced ground clearance as well as a decreased joint range of motion (Morris, Huxham, McGinley, & Iansek, 2001). Another feature of parkinsonian gait is festination which entails a combination of a stooped posture, poor balance and short steps leading to an increased chance of falling forward. These gait impairments have been said to be exacerbated during the performance of additional tasks while simultaneously walking. The impaired dual-task performance has been said to occur because the need to concentrate on walking and other tasks exceeds the individuals available attentional resources (Bloem et al., 2001; Rochester et al., 2007). Interventions such as physiotherapy have been suggested for the management of the gait impairments observed in PD (Schenkman et al., 1989). However, the development of a successful rehabilitation strategy to combat common symptoms of parkinsonian gait such as decreased step length has been unsuccessful due to the inadequate understanding of the pathogenesis of the gait disturbances in PD (Morris, Iansek, Matyas, & Summers, 1996). The most severe gait disorder that occurs in some individuals with PD is called Freezing of Gait (FOG) and will be discussed in detail in Section 1.4

1.4 Freezing of gait in Parkinson's disease

Freezing of Gait (FOG) is an extreme form of gait disorder that is experienced in PD and is perhaps one of the most debilitating symptoms associated with PD. It is characterized by a sudden and transient inability to either initiate or maintain a normal gait pattern. Individuals with PD who experience FOG describe a freezing episode as feeling that their feet are "glued" to the ground (Iansek, Huxham, & McGinley, 2006). FOG can also occur upon the confrontation with an obstacle or a narrowing of space such as a doorway (Bloem et al., 2004). The incidence of individuals with PD who experience freezing of gait has been found to be very low in young onset PD, but can rise to anywhere from 20% to 60% in advanced cases that have been subjected to a prolonged exposure to dopaminergic treatment (Giladi et al., 2001). This leads to the question of whether the FOG that develops in these individuals is due to prolonged exposure to this medicinal treatment or the continued neuronal degeneration that occurs in a progressive neurodegenerative condition.

It has been reported that individuals with PD affected with FOG walk differently than other individuals with PD, even in between freezing episodes (Hausdorff et al., 2003). Nieuwboer et al. reported gait changes such as an impaired step length and greater stride to stride variability in these individuals just prior to a freezing episode and they suggested that freezing is caused by both an inability to walk with a normal stride length and an unregulated cadence (Nieuwboer et al., 2001). When observing an individual before a FOG episode when walking has already been initiated, their cadence appears to increase as their stride length shortens before the onset of the freezing episode. Hausdorff et al. compared the gait of individuals with PD with and without FOG and reported that individuals with PD who experience FOG have a higher stride-to-stride variability prior to a freeze occurrence when compared to those without FOG (Hausdorff et al., 2003). These observations lead to the notion that FOG might be an extreme form of loss of gait rhythm. However, to date the exact cause of FOG episodes is unknown.

FOG that is experienced by individuals with PD while "on" their normal medication tends to be short-lived, typically lasting less than one minute before the subject is able to resume movement (Schaafsma et al., 2003). This suggests that with time they are able to find an alternate, more conscious motor pathway to regulate their stepping pattern and overcome the freezing episode. This limited duration FOG is quite different than that seen in some individuals with PD who have abstained from medication. In these individuals the freezing episodes can last much longer, and at times will continue until medication has been taken and is integrated into their system. This type of FOG appears to be caused by the lack of dopamine in the central nervous system, as once medication becomes functional active the FOG tends to disappear.

A number of methods have been suggested in an attempt to prevent or lessen the severity of FOG episodes within individuals with PD. Gurevich et al. tested the effects of injecting botulinum toxin into the calf muscles of participants who experience FOG. The results obtained failed to show any therapeutic benefit of the prevention of freezing through the use of this treatment (Gurevich, Peretz, Moore, Weizmann, & Giladi, 2007). Another study attempted to determine the effects that caffeine might have on the prevention of FOG. Kitagawa et al. hypothesized that the properties of caffeine that cause an increase in locomotor behaviour and stimulate locomotion might have a beneficial effect on FOG (Kitagawa, Houzen, & Tashiro, 2007). It was reported that small doses of caffeine might improve the inability of heel-off at gait initiation in certain individuals; however, additional research is required to validate these findings (Kitagawa et al., 2007).

The visual cues that have been observed to improve and normalize the gait of individuals with PD have not been extensively tested on those who experience FOG. Kompoliti et al. tested a laser beam stick as a visual cue in an attempt to determine if FOG can be overcome through the same type of cue that has beneficial effects on parkinsonian gait (Kompoliti, Goetz, Leurgans, Morrissey, & Siegel, 2000). It was determined that the provided visual cue did not have an effect on the number of freezing episodes (Kompoliti et al., 2000). However, no other gait variables besides the number of freezing episodes were measured which makes it difficult to assert that an improvement in FOG cannot be obtained through the use of visual cues.

1.5 Visual cues in PD

Visual cues have been shown to have a beneficial effect on gait in healthy populations and an even more pronounced effect in the PD population (G. N. Lewis et al., 2000; Morris et al., 1996). The ability to maintain a steady gait rhythm and a stable walking pattern consisting of minimal changes from one stride to the next has been shown to be impaired in PD (Frenkel-Toledo et al., 2005). It has been argued that individuals with PD have a deficit in the internal regulation of stride length and therefore require external visual cues to bypass a faulty basal ganglia regulatory mechanism and invoke a more cortically driven and conscious mode of motor control pathway (G. N. Lewis et al., 2000; Morris et al., 1996).

Visual cues have been shown to be the most effective type of external cue in gait normalization in PD. Ground lines are the most commonly used form of visual cue in PD. Most often, transverse lines are placed on the ground and participants are instructed to touch their heel to the lines in succession as they walk through the environment. When these lines approximate normal healthy step length, there are a number of studies that have shown a dramatic improvement in the gait of individuals with PD with the use of ground lines as visual step cues (Azulay et al., 1999; G. N. Lewis et al., 2000; Morris et al., 1996; Suteerawattananon, Morris, Etnyre, Jankovic, & Protas, 2004; van Wegen et al., 2006). Morris et al. provided visual cues in the form of cardboard ground lines that were placed at a distance equivalent to the step length for each individual with PD's age, sex and height matched control. An irregular gait pattern was found in the participants with PD at baseline, but when the visual cues were employed, step length improved as well as velocity and cadence (Morris et al., 1996). From these results they determined that individuals with PD do not lose the ability to generate a normal stepping pattern, but instead are required to focus their attention on gait to achieve this goal (Morris et al., 1996). Azulay et al. also provided visual cues as external stepping targets to individuals with PD (Azulay et al., 1999). Gait irregularities were also found in the PD group at baseline levels, and it was determined that gait was normalized with the use of ground lines as visual cues. Stroboscopic lighting was employed that masked the movement of the lines during gait, and therefore suppressed the perceived motion of the stripes. In this case, the previously mentioned improvement in gait found within individuals with PD disappeared confirming that movement of the ground lines is required for a normalization of gait pattern to occur (Azulay et al., 1999). It was therefore suggested that optic flow must be the critical underlying factor driving the improvement in gait with use of visual cues (Azulay et al., 1999). Lewis et al utilized three-dimensional kinematic analysis, along with kinetic and electromyographic gait analysis to determine that both taped step length markers and a light device mounted on the subject are effective in improving the gait of individuals with PD to levels observed in a healthy controls (G. N. Lewis et al., 2000). Therefore, the abnormal gait of individuals with PD can be significantly improved through the use of external visual cues in the form of ground lines, although the mechanism driving this improvement needs to be better understood.

Other types of external cues have also been shown to be effective in normalizing the abnormal gait pattern observed in PD. Auditory cues such as a metronome can improve step length and normalize cadence in certain individuals. It has been suggested that metronome stimulation can also significantly reduce the time and number of steps required by individuals with PD to complete a walking course as compared to when walking the same course without the use of any type of cue (Enzensberger, Oberlander, & Stecker, 1997). Suteerawattananon et al. supplied individuals with PD with an auditory cue consisting of a metronome beat that was 25% faster than the subject's fastest gait speed (Suteerawattananon et al., 2004). Participants were instructed to take each step in cue with the beating of the metronome. The use of the auditory cue resulted in an increase in gait velocity due to an increased cadence (Suteerawattananon et al., 2004). A small increase in step length above that found in the uncued condition that did not reach significance was also found, which indicates that auditory cues are not as effective as visual cues in normalizing the gait pattern of individuals with PD. However, other studies have shown that step length can also be improved with use of auditory cues. Rochester et al. attempted to evaluate the influence of auditory rhythmic cues during gait while simultaneously completing a cognitively challenging task (Rochester et al., 2005). A significant increase in mean step length (19%) was found with use of the auditory cue while performing a dual-motor task (Rochester et al., 2005). Nieuwboer et al. also found an improvement in overall gait performance when individuals with PD were trained over a period of 3 weeks with auditory cues that were delivered via a metronome beat in an earpiece (Nieuwboer et al., 2007). Despite the apparent beneficial effect that auditory cueing can have on gait improvement and normalization in PD, there is also the potential for increased variability with auditory cues (Almeida, Frank, Roy, Patla, & Jog, 2007). Therefore, visual cues have been shown to be an overall more effective and reliable cue.

Along with the beneficial effects that external cues can have on the gait of individuals with PD, there are also a number of drawbacks to the use of currently tested visual and auditory cues. Firstly, it is important to note that the use of external visual cues require an increased attentional focus. A number of studies have demonstrated that individuals with PD have a difficulty in focusing on multiple stimuli at the same time, especially in time-constrained stressful situations (Bartels et al., 2003; Okuma, 2006; Schaafsma et al., 2003). Negative changes in movement have also been found to occur during activities that require a shift in attentional resources, which may occur while using external cues to modulate gait (Almeida, Wishart, & Lee, 2003; Giladi et al., 1992). Therefore, although improvements in gait have been demonstrated in the laboratory environment with use of visual and auditory cues, there is the possibility that the types of cues tested might not have the same beneficial effect when used outside of the home or laboratory. More testing is required to determine if when attentional demands are increased, the external cues will lead to a decrease in gait performance instead of the designed improvement. Another drawback to the currently used form of visual cue is the fact that ground lines are not able to be used outside of the home or lab environment. A more portable device that provides the same type of visual cue and can be utilized in more situations and environments has the potential to be valuable to individuals with PD.

1.6 Research questions and hypotheses

The main research questions to be examined in this thesis are:

1. How do visual cues lead to the improvement in gait observed within individuals with PD and does a reverse optic flow device lead to similar improvements to those observed with the typical optic flow provided by the use of ground lines?
2. How does perception of space affect the gait of individuals with PD who experience FOG?
3. Are visual cues able to prevent FOG episodes and improve the gait prior to the potential freezing episode?

The main hypotheses of this thesis are as follows:

1. The reverse optic flow device will lead to similar improvements in gait performance suggesting that this improvement is due to the increased attentional focus on gait caused by the visual cue.
2. Individuals with PD who experience FOG have a decreased ability to accurately perceive special constraints.
3. Visual cues will improve the gait of individuals with PD who experience FOG prior to a potential freezing episode.

Chapters 2, 3, and 4 each explore one of the research questions and will attempt to gain a more holistic understanding of the gait abnormalities experienced in PD and the potential improvements that might be gained through the use of ambulatory aids in the form of visual cues. Chapter 5 provides the summary of the findings and discusses the clinical significance of the obtained results.

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CHAPTER 2

CONTRIBUTIONS OF OPTIC FLOW TO GAIT IN PARKINSON'S DISEASE

2.1 Abstract

Research has documented the improvements in gait in PD that can be gained through the use of external visual step cues. The present study evaluated the effect of ground lines and a reverse optic flow laser device on the gait of individuals with PD. Two separate groups: 22 PD participants "On" dopaminergic medication and 12 healthy age-matched controls participated in this experiment. Participants walked on a computerized carpet in four conditions; i) self-paced walk, ii) ground lines, iii) laser lines, iv) laser lines in a dark environment. Measures of step length, cadence, and velocity indicated that individuals with PD were able to improve their gait to levels comparable to those of healthy individuals with use of both the ground lines and the laser device as visual step cues. Interestingly, individuals with PD exhibited increased within-trial step length variability, and an increased time spent in double support across all conditions. The use of the laser device also led to a further increase in these two variables across both groups. These results suggest the gait observed with use of visual cues is due to the focus of attention on a more conscious gait pattern provided by both cue types. The increased variability may be attributed to the lack of ability to effectively pre-plan step patterns, as the visual cue from the laser device was only presented one step at a time.

2.1.1 Introduction

Walking difficulties commonly observed in PD are an important limiting factor for independence and quality of life. Abnormal gait is a hallmark symptom of individuals with PD. One of the well-documented primary characteristics of this gait pattern is a smaller than normal step length (Lewis, Byblow, & Walt, 2000; Morris, Iansek, Matyas, & Summers, 1996; van Wegen et al., 2006). This reduced step length is a primary determinant of the decrease in movement and mobility that affects many who suffer from PD. Short shuffling steps result from the decreased step length and lead to an increased risk of falls and an overall loss of independence (Schenkman, 1992). Step cues in the form of lines on the ground have been shown to improve step length in PD, as well as normalize gait (Azulay et al., 1999; Lewis et al., 2000; Morris et al., 1996). Other types of sensory cueing, such as auditory cues, have also been shown to be effective in improving the mobility of individuals with varying severities of PD in home-based clinical trials (Nieuwboer et al., 2007). In all of these studies, the mechanisms by which this improvement is found remains poorly understood. By analyzing the difference in gait improvements observed with the traditional ground lines as compared to step lines presented from a reverse optic flow laser line device, insight towards the possible mechanisms that drive this beneficial effect on the gait of individuals with PD might be gained. It is currently unknown whether attention or visual flow drives this improvement. The aim of this experiment was to evaluate the gait observed in Parkinson's disease (PD) and to determine if ambulatory aides in the form of external visual cues can improve certain gait variables.

2.1.2 Role of vision in gait

Vision is the one of the main sensory inputs utilized during gait. When walking, vision provides a large amount of sensory information including object location, as well as body position in relation to those objects in the environment. A number of studies have shown that in the absence of visual information, the movement of that person becomes increasingly inaccurate and variable (Adamovich, Berkinblit, Hening, Sage, & Poizner, 2001; Almeida et al., 2005). These studies also demonstrated that individuals with PD are more reliant on visual information in order to make accurate movements in comparison to healthy populations. Adamovich et al. tested pointing accuracy and found that individuals with PD become much less accurate as compared to healthy individuals in trials in which visual information was removed (Adamovich et al., 2001). Almeida et al. measured the locomotion and target accuracy of individuals with PD in a task in which they were required to travel to a target under a number of different conditions which manipulated the availability of sensory feedback (Almeida et al., 2005). They found that in the absence of vision, both individuals with PD and healthy subjects employ similar adaptations that appear to be aimed at increasing safety while ambulating in a dark environment. Both groups walked at slower velocities with a smaller step length, a wider base of support, and spent an increased amount of time in double support (Almeida et al., 2005). Together, these studies suggest that vision acts as the primary source of sensory information required for accurate movement in disorders like PD, in order to overcome basal ganglia degeneration.

There is also evidence that suggests that proprioceptive information can be utilized in the absence of vision to assist in the maintenance of movement accuracy.

Lebold et al. found that healthy individuals, as well as individuals with PD on dopaminergic medication, were able to ambulate remembered distances in a condition in which visual information was removed similar to that observed in conditions in which visual information was available (Lebold & Almeida, 2006). In this experiment individuals with PD that had abstained from dopaminergic medication were compared to individuals with PD on medication, as well as healthy individuals. Results demonstrated that individuals with PD removed from dopaminergic medication were less accurate in distance accuracy as compared to the other groups. The researchers concluded that without any dopaminergic supplementation, the individuals with PD did not have the benefit of a functioning basal ganglia and therefore were thought to be lacking the ability to integrate proprioceptive information (Lebold & Almeida, 2006). Individuals with PD on medication and healthy control subjects were more accurate than individuals with PD off medication in conditions that allowed proprioceptive cues but prevented visual information from being utilized (Lebold & Almeida, 2006). However, a condition in which proprioceptive cues were removed through the use of a wheelchair demonstrated no significant differences between all three groups, suggesting that proprioceptive information contributes to spatial-movement production.

The integration of several different sources of sensory information is necessary during movement. However, when vision is available it appears to be relied upon to guide movement performance.

2.1.3 Visual cues are possibly focusing attention on step length

It has been hypothesized that external visual cues may act to focus an individuals' attention on the step they are taking (Morris et al., 1996). External cues are located in the environment and can be used to target step accuracy or gait timing. Individuals with PD are able to improve their step length and normalize their cadence when they are asked to focus on each step by making heel contact with transverse lines in succession that are placed on the ground in front of them. In healthy populations, gait appears to be an automatic function in which people do not consciously think about each step in order to maintain a normal gait pattern, which is in stark contrast to individuals with PD. However, when they are no longer forced to rely on internal regulation for maintenance of their gait pattern, but instead can rely on these external visual cues, the gait pattern of individuals with PD has improved to levels consistent to that observed in age-matched healthy populations (Lewis et al., 2000; Morris et al., 1996).

It has also been shown that training using an attentional strategy in which individuals with PD were asked to develop a mental picture of the goal stride size can be effective in improving gait (Morris et al., 1996). When these people consciously focused on walking with the imagined stride size, it was found that they were able to improve step length and maintain a normal cadence without the use of the normal visual cues. This beneficial effect had a lasting effect as it was found that the normalized gait pattern remained for at least 2 hours after the training had been completed (Morris et al., 1996). The authors proposed that the cues, whether visual or imagined, draw the attention of the individuals with PD, therefore invoking a more conscious motor control pathway and bypassing the basal ganglia, which is affected in PD (Morris et al., 1996). This information seems to point to the improvement in gait being derived from the individuals with PD being forced to consciously focus their attention on each step. Therefore, the type of cue presented should not be a factor in whether an improvement in gait is observed. The presence of any type of information which will focus attention on their step pattern should improve gait close to a level regularly seen in individuals of comparable age.

2.1.4 Perceived optic flow during gait

During gait, information as to the whereabouts of objects in the environment and body position in relation to those objects is presented to the individual in the form of optic flow. This optic flow is induced on the retina and contains all the information regarding the kinematics of gait, such as speed and direction of movement (Gibson, 1958). Optic flow has been shown to have a direct influence on locomotion. Prokop et al. demonstrated that healthy participants would slow their gait when the optic flow information provided was accelerated, and would speed up when the optic flow was slowed (Prokop, Schubert, & Berger, 1997). Varraine et al. also manipulated the rate of perceived optic flow in order to monitor the effect it would have on gait velocity. A slight increase of velocity was found with an increase in optic flow speed which was reported to indicate that an irreducible part of propulsive forces are driven by optic flow and cannot be controlled voluntarily (Varraine, Bonnard, & Pailhous, 2002). It has also been demonstrated that in the absence of optic flow information, individuals with PD experience a decreased stride length and overall gait velocity (Schubert, Prokop, Brocke, & Berger, 2005). Visual cues such as ground lines give an additional source of optic flow information during gait. This increase in optic flow information received by the participant can be thought of as a potential reason for the improvement in gait observed in individuals with PD with the use of visual cues. Therefore, it is necessary to determine whether visual cues solely focus attention or are a more salient cue that is directly relevant to gait.

2.1.5 Laser device provides reverse optic flow

Typically, the optic flow information received travels in an oncoming direction as a person moves through the environment. In contrast to the optic flow normally received during gait, the laser device used as a visual step cue in this experiment was provided in a reverse optic flow direction. The line was initially projected directly in front of the participants' feet, and then preceded to move in a forward direction away from the individual as they were walking. Therefore, this visual cue was traveling in an opposite direction as compared to the direction of optic flow that was simultaneously being received from other objects in the environment. This might be expected to induce a certain degree of distraction or increase in attention demand in the individual as this visual cue is drastically different from other visual cues that have been utilized in the past in an attempt to improve the gait of individuals with PD. In contrast, if the laser only directs attention towards the feet then we would expect an improvement similar to that observed with use of the ground lines. To our knowledge, the effect of presenting a visual cue in a reverse optic flow direction has yet to be examined.

2.1.6 Specific Aims

The aim of this experiment was to determine the method by which visual cues in the form of step lines have the ability to regulate the gait of individuals with PD. If the visual cues from the reverse optic flow laser device provide a benefit similar to that of the ground lines, then it can be postulated that the improvement observed with these cues is due to the ability of the cues to focus the individuals' attention on their gait pattern. However, if the reverse optic flow device does not lead to similar improvement in gait pattern as the ground lines, it would appear that individuals with PD require cues that not only focus attention on their gait pattern, but also provide an additional source of optic flow in order to normalize gait.

2.1.7 Hypothesis

H_O: Individuals with PD will demonstrate a similar gait pattern in the baseline, ground lines, laser, and laser dark conditions.

H_1: Individuals with PD will regulate their gait with the use of the reverse optic flow device to a level similarly observed when using ground lines as step cues, as well as levels seen in a baseline walk in healthy age matched controls.

2.2 Method

2.2.1 Participants

Each participant was informed about the requirements of the study and signed institutionally approved consents. Twenty-two individuals with idiopathic PD (mean age 69.7 +/- 7.2 yrs, range 56-79 yrs, 14 men, 8 women, mean height 169.9cm +/- 7.2) and 11 healthy control subjects (mean age 69 +/- 8.4 yrs, range 60-82 yrs, 6 men, 5 women, mean height 172.3cm +/- 10.4) participated in this study. The 22 individuals with PD were recruited from the database of the Movement Disorders Research and Rehabilitation Centre at Wilfrid Laurier University in Waterloo, Ontario. The individuals with PD used in this study were of varying severity of PD symptoms with mean Unified Parkinson's Disease Rating Scale (UPDRS) motor scores of 30.81 +/- 6.45, range 21.5-41 while "on" dopaminergic medication. Individuals with PD were tested while on their medication in order to increase the external validity of the findings. All patients tested had clinically typical PD which had been diagnosed by at least one movement disorder specialist and were responsive to anti-parkinsonian medication. The 11 healthy control participants were mostly spouses of the individuals with PD.

Subjects were excluded from testing if they had a past history of neurological conditions other than PD or orthopedic or visual disturbances that severely impaired walking ability. Individuals with PD were also excluded if they were diagnosed with dementia or if they had dyskinesias which would alter an individual's gait. Table 3.1 summarizes the participant characteristics for each group. There were no significant differences between groups for any of the variables described.

Table 2.1
Characteristics of the two groups

Group	Age- M (yrs)	Age- SD (yrs)	Height- M (cm)	Height- SD (cm)	UPDRS- M (score)	UPDRS-SD (score)	Gender
PD	69.73	7.26	169.95	7.22	30.81	6.45	14 male, 8 female
HC	69.00	8.39	172.26	10.40	n/a	n/a	7 male, 5 female

Note: M denotes mean; *SD* denotes standard deviation

2.2.2 Experiment set-up and data collection

The room used for data collection was a laboratory measuring approximately 9.5m X 6m. Data was collected on a GAITRite® carpet (GAITRite®, CIR System, Inc., Clifton, NJ, USA) which is a 4.6m long and 0.95m wide carpet containing thousands of sensors that send information received from the participants' footsteps to an attached computer (Fig. 2.1). A researcher walked alongside the participant at all times throughout the testing in order to maintain the safety of the participant during each trial. An additional black carpet made out of a thin cloth material with white horizontal lines 3 cm wide spaced at 65 cm intervals was placed over top of the GAITRite carpet in the second condition. This carpet was designed so as to not impede the normal functioning of any of the sensors in the GAITRite® carpet (Fig 2.2). A laser line projector device, which attached to the participant's waist by use of a belt, was used for the last two conditions (Fig. 2.3). This device projected a roughly 1 cm wide transverse LED laser line onto the ground ahead of the participant. The initial projection was approximately 10cm in front of the participants and then moved in the forward direction ahead of the participant. The individual was instructed to touch their toe to the laser line when it reached its furthest point and continued to walk down the length of the carpet repeating this procedure in sequence with the movement of the laser. The laser device was attached by a belt to each participant's waistline and the constant angle in which the laser was set to a maximum projection distance that was based on the height of each individual, and therefore an average step length. The device projected the visual cue in a reverse optic flow direction which is opposite to the normal optic flow received during gait. Each participant initially completed the baseline walk condition, and then the other three conditions in a randomized order.

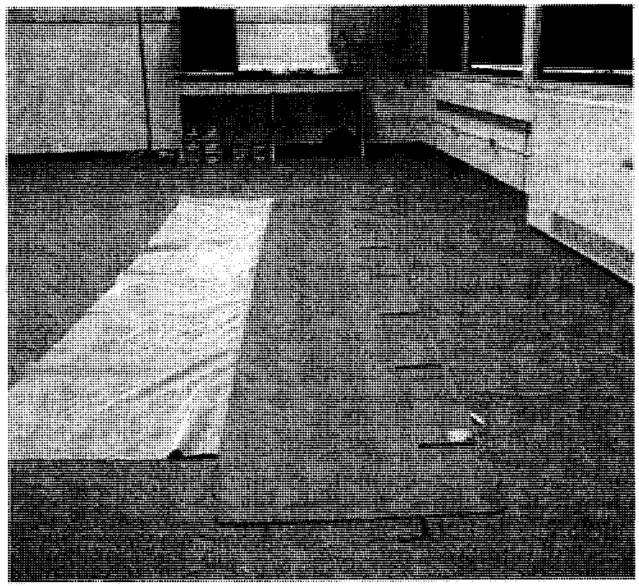

Figure 2.1 GAITRite® Carpet

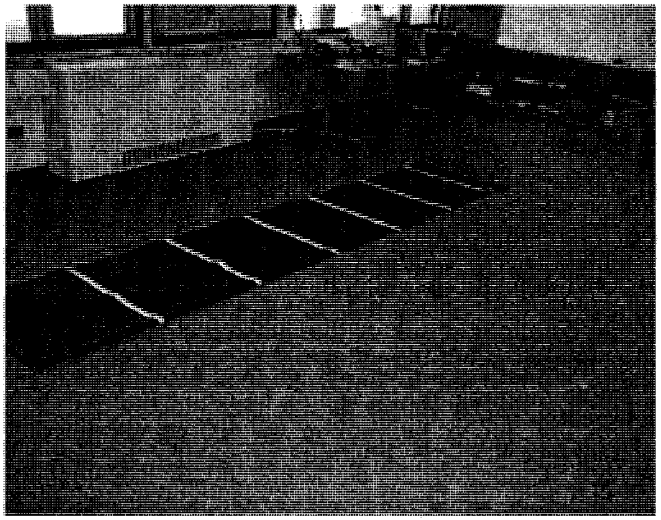

Figure 2.2 Ground lines

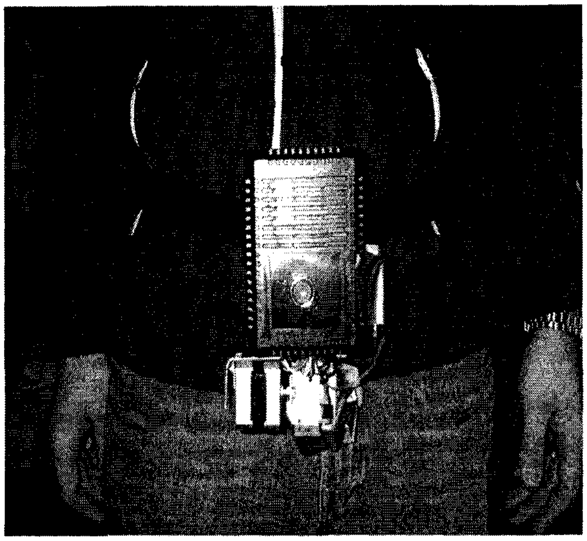

Figure 2.3 Laser device

2.2.3 Procedure

Participants walked the length of the GAITRite carpet under four different conditions for 5 trials each. Participants began by completing condition 1, and then proceeded to complete the other three conditions in a randomized order. The reasoning behind this order was to obtain a measurement of each participant's baseline gait before completing the remaining conditions. The four conditions examined in this study were:

i) A Self-paced walk condition in which the participants were required to walk at a self-selected pace across the GAITRite carpet.

ii) A Lines on ground condition in which a carpet with horizontal lines placed 65cm apart was placed over top of the GAITRite carpet. Lines of this interval were chosen as this distance is equal to a normal step length of a person of average height. Participants were instructed to touch each line with their heel consecutively as they proceeded through the trial.

iii) A Laser condition in which the laser line projector was used by the participant. The laser was set at a speed of one cycle per second, as this was deemed to be an appropriate speed in order to be able to follow the laser as accurately as possible.

iv) A Laser dark condition in which the laser line projector was used in a completely dark environment in order to remove the participant's vision of all other surroundings. This condition was employed in order to determine if limiting the amount of distractions in the environment would make it easier to for participants to focus on the laser lines and therefore maximize gait improvement.

2.2.4 Data analysis and statistics

The four conditions in this protocol allowed for the analysis of whether the direction of optic flow has an effect on the gait improvements observed when individuals with PD are supplied with a visual step cue. There were two independent groups in this experiment; individuals with PD (PD) and healthy control participants (HC). The primary dependant variables analyzed were the gait velocity (cm/s), walking cadence (steps/min), mean step length (cm), within-trial variability of step length (cm) and double support time (s).

Step length is defined as the distance that separates heel contact of one foot to the heel contact of the next foot during gait. The GAITRite® carpet measured each individual's step length along the horizontal axis joining geometric heel centre of one foot to the geometric heel centre of the other foot (Systems, 2000). The reason for including step length in the primary analysis is based on previous observations that step length becomes significantly altered in parkinsonian gait. Therefore, combined with the potential benefits in step length elicited by visual cues which have been discussed, step length analyses was a key measurement.

Double support time is a temporal characteristic of gait and can be used to provide information regarding an individual's stability while walking. It can be defined as the sum of initial double support, which is the time when both legs are in contact with the ground, and the terminal double support which refers to the start of contact with the contralateral leg to the ground to the loss of contact to the ground of the ipsilateral leg (Perry, 1992). Individuals with PD tend to spend an increased amount of time in double support as compared to healthy individuals, because altering gait in this manner means they will spend less time in single support and enable better accommodation to various environmental perturbations during walking (Winter, Patla, Frank, & Walt, 1990).

Within-trial variability of step length was also analyzed in this experiment. This variable examines the changes in the size of step length maintained by a participant throughout a trial and is measure in cm.

Results were analyzed using the STATISTICA computerized statistical package using a mixed model 2 groups X 4 conditions X 5 trials ANOVA. Additionally, in order to analyze gait adaptations based on conditions solely in the PD group a 4 conditions X 5 trials analysis was completed on the PD group. A p level of 0.05 was employed throughout the analyses. In order to determine where the significant differences found in the ANOVA's occurred, Tukey's Honest Significant Difference (HSD) post hoc procedure was employed.

2.3 Results

2.3.1 PD group has decreased velocity, cadence and step length

Overall, individuals with PD were found to walk with a decreased velocity, cadence, as well as a shorter step length compared to the HC group. A main effect of group when examining velocity was observed in which the controls had an average gait that was roughly 10 cm/s faster than the individuals with PD ($F_{(1,31)} = 10.89$, $p < 0.003$) (Fig. 2.4). Also, a trend reaching significance was evident when examining the cadence between these two groups as individuals with PD walked with fewer number of steps per minute (94.14 steps/min in PD, 101.21 steps/min in HC) as compared to the HC group ($F_{(1,31)} = 3.88$, $p = 0.058$) (Fig. 2.5). The analysis of groups also found that individuals with PD took steps that were roughly 13 cm smaller on average as compared to the HC group. A main effect of group when analyzing step length was found ($F_{(1,31)} = 12.24$, $p < 0.002$; Fig. 2.6). The combined effect of the cadence and shorter step length lead to the aforementioned decreased gait velocity which is a hindrance prevalent in PD (Table 2.2).

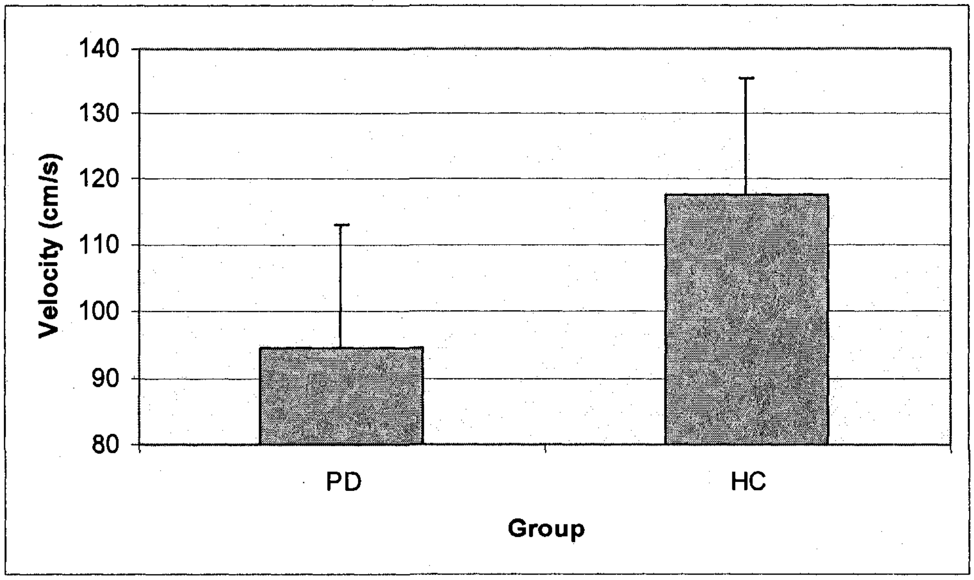

Figure 2.4 Comparison of velocity in PD and HC groups

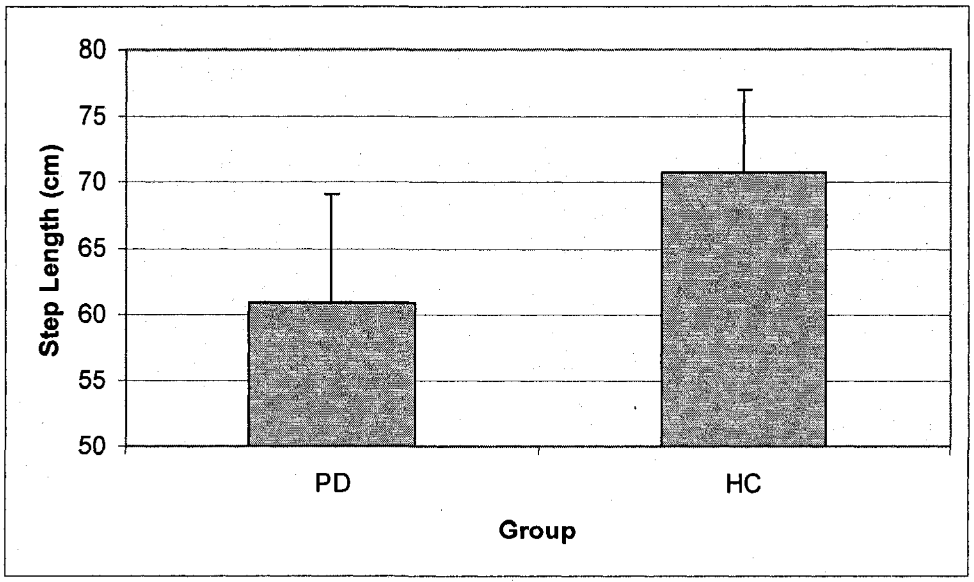

Figure 2.5 Comparison of step length in PD and HC groups

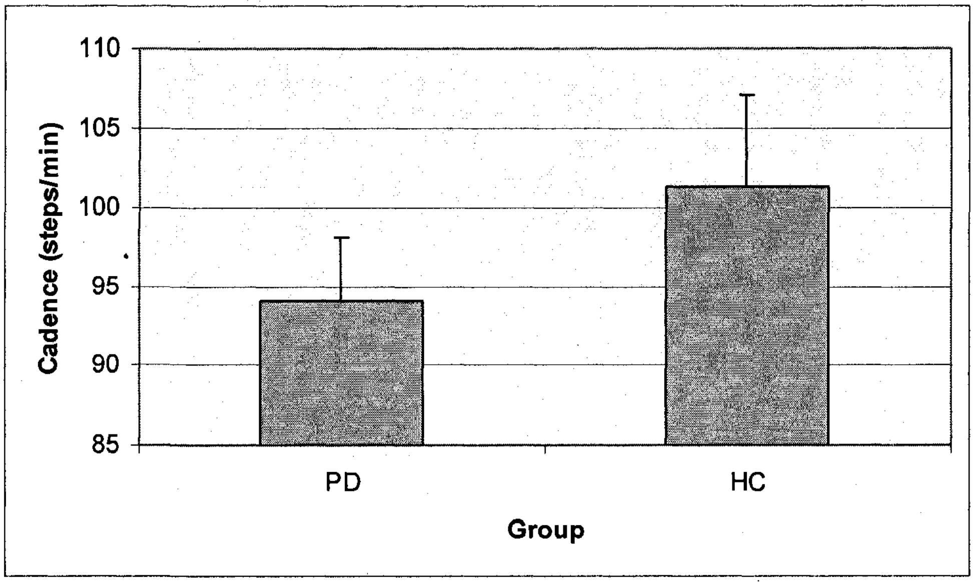

Figure 2.6 Comparison of cadence in PD and HC groups

Table 2.2
Velocity (cm/s), cadence (steps/min) and step length (cm) between groups

Group	Velocity (M)	Velocity (SD)	Cadence (M)	Cadence (SD)	Step Length (M)	Step Length (SD)
PD	94.58	18.35	94.14	4.03	60.96	8.06
HC	117.44	17.91	101.32	5.80	70.68	6.27

Note: M denotes mean; *SD* denotes standard deviation

2.3.2 Analysis of step length in PD and HC groups throughout different conditions

The analysis of step length revealed a significant interaction ($F_{(3,93)} = 3.17$, $p < 0.0279$, Fig.2.7). As expected, post hoc analysis confirmed that individuals with PD took significantly shorter steps at baseline (54.79 cm in PD, 65.58 in HC) as compared to the HC group ($p < 0.0019$) (Table 2.3). Both the ground lines ($p < 0.001$) as well as the laser device ($p < 0.0032$) were effective in significantly improving the step length of individuals with PD above baseline levels. The Ground condition was the only condition in which step length was normalized in the PD group to levels comparable to that seen in the HC group. The Laser condition produced a step length in the PD group comparable to that observed in the HC group in the Baseline condition. The reason for the disparity between PD and HC in the Laser condition was caused by the production of an even greater step length by the HC group with use of the laser device. The Laser Dark condition in which the participant's vision was restricted so that only the laser beam was visible did not significantly alter the step length taken in either of the two groups as compared to baseline.

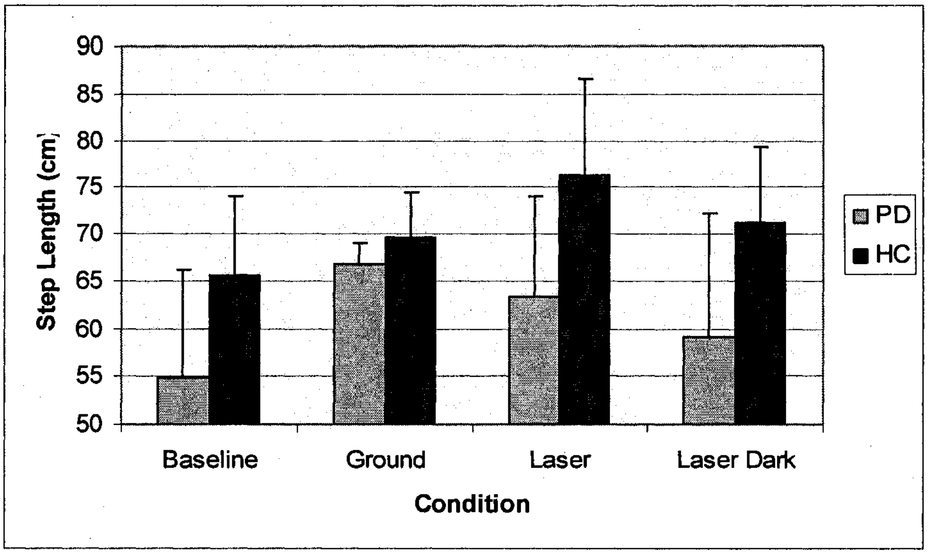

Figure 2.7 Analysis of step length reveals an interaction of group and condition

Table 2.3
Step length (cm) by group and condition

Group – Condition	Mean	SD
PD – Baseline	54.79[1-3]	11.35
HC – Baseline	65.58[3,4]	8.38
PD – Ground	66.76[1]	2.20
HC – Ground	69.68	4.78
PD – Laser	63.28[2,5]	10.85
HC – Laser	76.24[4,5]	10.42
PD – Laser Dark	59.02[6]	13.21
HC - Laser Dark	71.24[6]	8.06

1-6 Significant differences between the groups and conditions were determined by Tukey's HSD.

2.3.3 Analysis of velocity and cadence throughout conditions

The analysis of velocity in the PD group by itself revealed a significant main effect of condition ($F_{(3,63)} = 4.29$, $p < 0.008$) (Figure 2.8). Post hoc analysis revealed that individuals with PD walked at significantly different speeds in the baseline condition as compared to the laser dark condition ($p < 0.025$) and the ground condition against the laser dark condition ($p < 0.015$) (Table 3.4). Individuals with PD did not significantly alter their gait velocity between the baseline, ground and laser conditions.

Analysis of cadence also revealed a significant main effect of condition ($F_{(3,63)} = 15.52$, $p < 0.001$) (Figure 2.9). Post hoc analysis demonstrated that individuals with PD walked with a significantly increased number of steps per minute in the baseline condition as compared to the ground condition ($p < 0.001$), the laser condition ($p < 0.001$), as well as the laser dark condition ($p < 0.001$) (Table 3.4).

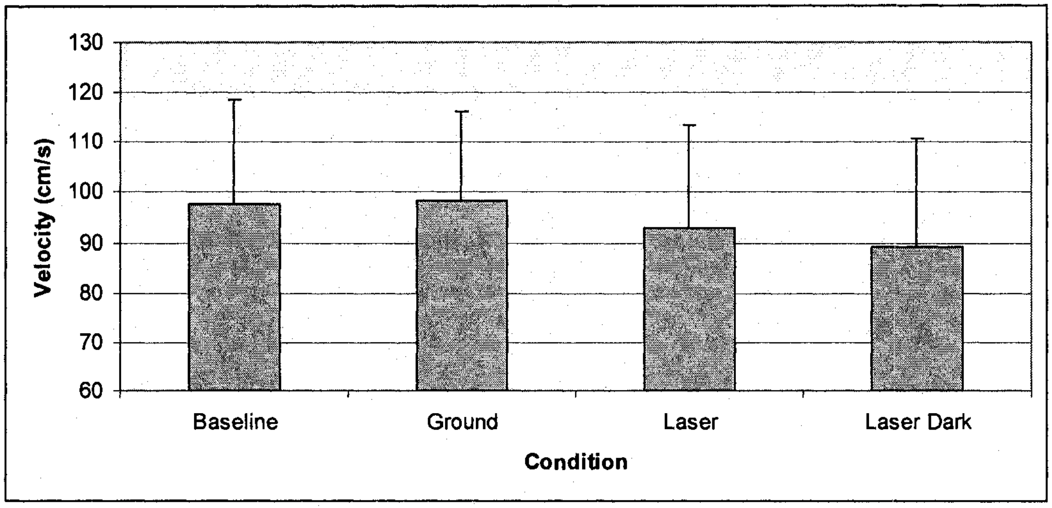

Figure 2.8 Comparison of velocity in PD group

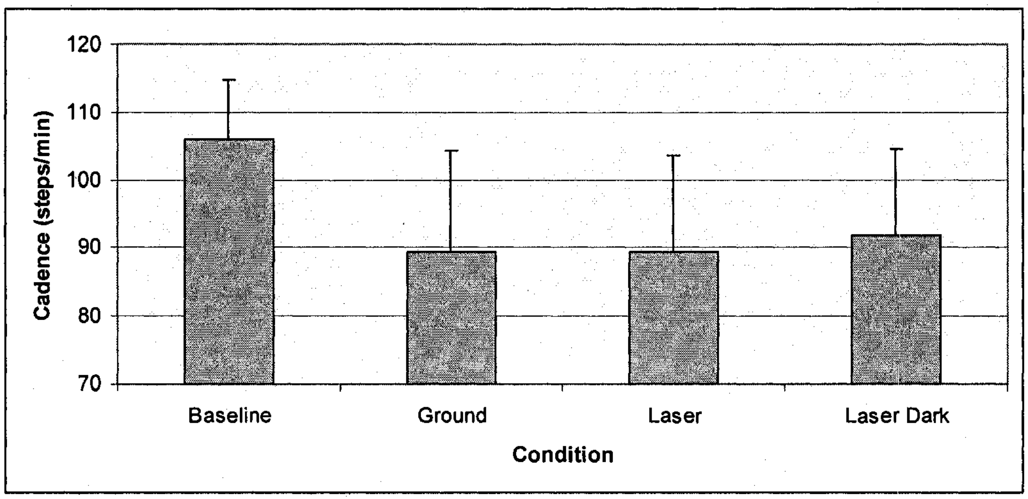

Figure 2.9 Comparison of cadence in PD group

Table 2.4
Velocity (cm/s) and cadence (steps/min) in PD group

	Baseline	Ground	Laser	Laser Dark
Velocity – M	97.80[1]	98.35[2]	92.96	89.22[1,2]
Velocity – SD	20.77	17.81	20.54	21.50
Cadence – M	106.03[1-3]	89.27[1]	89.46[2]	91.79[3]
Cadence - SD	8.91	15.02	14.04	12.82

Note: M denotes mean; *SD* denotes standard deviation
1-3 Significant differences between the conditions were determined by Tukey's HSD.

2.3.4 Within-trial variability of step length

Analysis of the variability observed in the size of steps taken by individuals with PD and healthy participants, a main effect of group was evident. The PD group was significantly more variable with respect to their step length across conditions as compared to the HC group ($F_{(1,31)} = 8.68$, $p < 0.006$) (Fig. 2.10). The means and standard deviations of the two groups are displayed in Table 2.5.

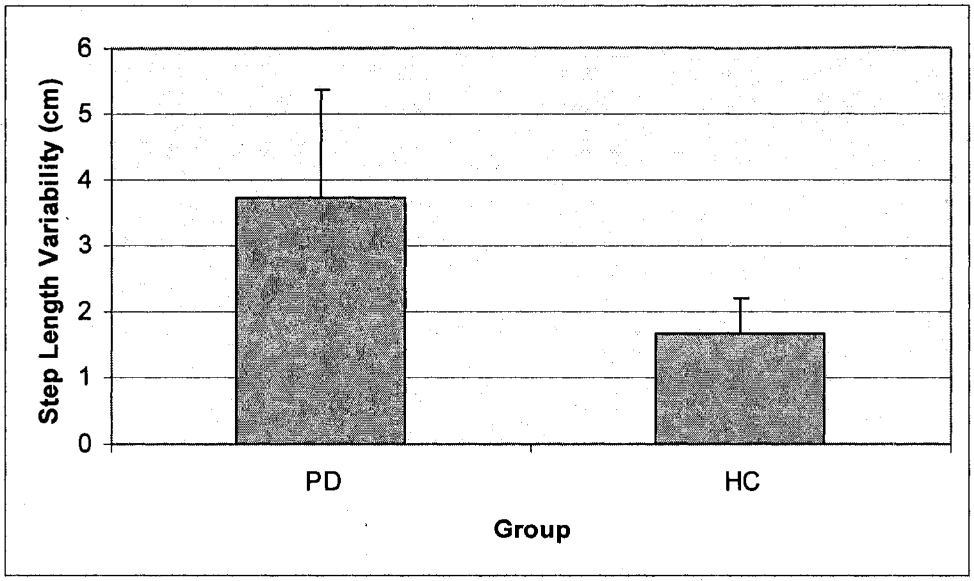

Figure 2.10 Variability of step length group comparison

Table 2.5
Step length variability (cm) by group

Group	Mean	SD
PD	3.74	1.64
HC	1.66	0.56

2.3.5 Double support time

The amount of time spent in double support during the walking trials varied depending on condition. The analysis of the double support time of all participants revealed a significant main effect of condition ($F_{(3,93)} = 3.78$, $p < 0.014$) (Fig. 2.11). Double support time was not significantly altered from the baseline condition in any of the three conditions. However, post hoc analysis confirmed that all participants spend significantly less time in double support in the ground lines condition as compared to both while using the laser device with full vision ($p < 0.029$) and in the absence of visual information ($p < 0.033$) (Table 2.6).

The 4 condition X 5 trial analysis of solely the PD group also revealed a main effect of condition for the amount of time spent in double support ($F_{(3,63)} = 4.83$, $p < 0.0073$) (Figure 2.12). Post hoc analysis revealed that individuals with PD spent significantly more time in double support when using the laser line device as compared to the baseline walk condition ($p < 0.023$).

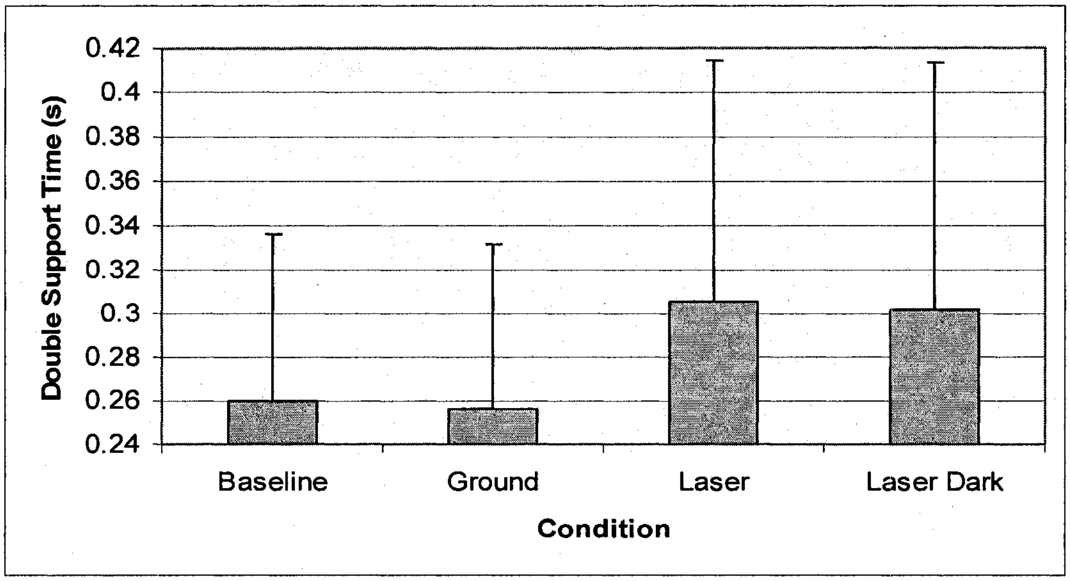

Figure 2.11 Comparison of time spent in double support in all participants across conditions

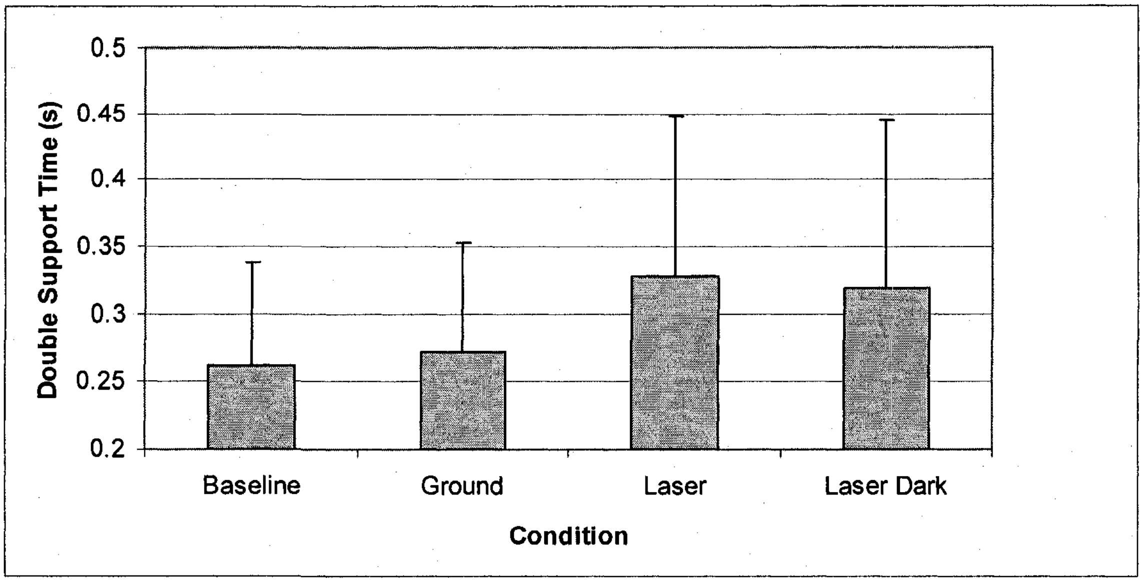

Figure 2.12 Comparison of time spent in double support across condition in PD group

Table 2.6
Double support time (s) across group and condition

Group – Condition	Mean	SD
Combined - Baseline	0.260	0.077
PD – Baseline	0.262[1]	0.077
Combined – Ground	0.265[2,3]	0.076
PD – Ground	0.271	0.081
Combined – Laser	0.306[2]	0.109
PD – Laser	0.328[3]	0.121
Combined – Laser Dark	0.302[3]	0.112
PD - Laser Dark	0.319[1]	0.127

1-3 Significant differences between the groups and conditions were determined by Tukey's HSD.

2.4 Discussion

The current experiment investigated the mechanisms by which visual cues guiding step length are able to improve the gait of individuals with PD. We hypothesized that individuals with PD would be able to regulate their gait with the use of the reverse optic flow device to a level similarly observed when using ground lines as step cues, as well as levels seen in a baseline walk in healthy age matched controls. The results of the experiment supported the hypothesis that the visual cues are effective in focusing the individuals' attention on their gait, which may be invoking a more conscious mode of control that bypasses the impaired basal ganglia in PD. The reverse optic flow laser device provided similar benefits of gait to that observed with use of ground lines when used by individuals with PD. However, the increased within-trial step length variability which appeared in trials while using the laser device as compared to other conditions seems to suggest that the reverse optic flow lead to some degree of confusion while attempting to use the laser lines as a target. An alternative explanation to this might be that individuals are more consciously controlling their gait pattern. Thereby instead of the automatic step length generation observed during self-paced gait, a more conscious control of gait is being used in which only the next step is being planned, possibly leading to this increased variability.

2.4.1 Gait pattern becoming normalized with use of reverse optic flow device

This experiment demonstrated that individuals with PD were able to normalize their gait pattern with use of the laser device. Their gait velocity did not significantly change with use of the laser as compared to baseline while cadence significantly decreased. The maintenance of a regular gait velocity while at the same time removing the short shuffling steps from their gait pattern was due to the significant increase in step length observed with use of the laser device as compared to the baseline condition. These gait alterations are similar to those elicited with the use of ground lines as a visual cue for individuals with PD, which have been demonstrated in a number of previous studies (Azulay et al., 1999; Lewis et al., 2000; Morris et al., 1996). The direction of optic flow perceived by the participant was altered with use of the device as compared to direction perceived with ground lines. The optic flow perceived with ground lines travels in an oncoming direction, which is standard to the information perceived from objects while traveling through a normal environment. The laser device gives optic flow in a forward direction that travels away from the participant. The fact that the improvement in gait was still evident lends to the belief that the benefit obtained from visual cues can be solely attributed to the increased focus of attention that is directed to each step through the use of these visual cues. As previously reported by Morris et al, this demonstrates that motor control mechanisms for gait are intact in PD and a these individuals are able to return to a normal gait pattern under the appropriate conditions (Morris, Iansek, Matyas, & Summers, 1994).

2.4.2 Gait becomes more variable with laser device

Another interesting finding in this experiment was that an increased variability in gait performance was associated with use of the reverse optic flow laser device. Within-trial variability in step length was greater overall in the PD group as compared to the healthy control participants. More interestingly however was the finding that individuals with PD spent a significantly increased amount of time in the double support phase in the laser condition as compared to their self-paced walk. Although the device appears to be normalizing their gait cycle as observed through the increased step length and slower cadence, it is also increasing their double support time, which may be an indicator of unsteady gait (Almeida, Frank, Roy, Patla, & Jog, 2007). A possible reason for this increased double support time is that the reverse optic flow information which is being presented to these individuals by the laser is causing some confusion in the integration of visual information with their motor commands to target their steps, therefore leading to a slightly more unsteady gait cycle. The alternative to this argument is that the increased double support time may also indicate an increase in voluntary or more cortical control of gait. During automatic unconscious gait, each step is planned well ahead of time and barring sudden changes an increased time in double support is not required. However, when each step is consciously controlled and planned only one step prior, an increase in double support time is a possible result. Nevertheless, this drawback has the potential to be improved with additional practice using the laser device. With a certain amount of practice, individuals might learn to focus their attention on the step targets given by the laser while ignoring the conflicting optic flow information given from the laser, which contradicts the regular optic flow received in sequence from the environment. This might be different than the instantaneous improvement derived from the ground lines because stepping pattern can be planned ahead of time when using the ground lines, however cannot be pre-planned when using the laser as the visual cue is only given one step at a time.

2.4.3 Attention appears to be main factor in benefit of gait derived from visual cue

The improvement in gait observed in individuals with PD with the use of visual cues as step targets appear to be attributed to the increased attentional focus placed on each individual step by the cue which leads the participant to discretely plan each step. It has been suggested that individuals with PD lack the ability to unconsciously regulate their gait pattern as effectively as healthy individuals (Rochester et al., 2005; Rochester et al., 2007). Visual cues such as ground lines are argued to improve gait by forcing a more conscious mode of motor control in the regulation of gait thereby overcoming a faulty basal ganglia (Lewis et al., 2000). This experiment demonstrated consistent results with other work examining the effects of visual cues on gait in PD, and more conclusively affirmed that the benefits observed with visual cues are due to individuals with PD being forced to focus their attention on their gait pattern. The conflicting information that was received from the reverse optic flow was not able to negate the improvement received from the use of visual cues during gait. Had this occurred, it would be feasible to suggest that improvements derived from visual cues such as ground lines are at least partly due to the optic flow received from these cues, and not solely because of the increased attentional focus on the gait pattern. However, the trend of gait pattern normalization observed within individuals with PD suggests that a more conscious motor control pathway in the regulation of gait has the ability to overcome the gait deficits and abnormalities prevalent in PD.

The decreased performance observed in the Laser dark condition in which visual information other than the laser was removed, as compared to the Laser condition in full vision might lead to an alternative suggestion. If purely attention can be attributed to the improvement in gait observed with the use of external visual cues, then a condition in which solely the cues are visible, as was the case in the Laser dark condition, the gait improvement should be maximized. However, it has been argued that the lack of proprioceptive ability in individuals with PD creates a need to consistently maintain visual information regarding the position of the limbs (Almeida et al., 2005; Jacobs & Horak, 2006). In the absence of this visual information and therefore reliance on proprioception for this information, the result might be a decrease in movement accuracy.

2.4.4 Clinical implications

The knowledge received from the findings of this chapter is that individuals with PD have an inability to internally monitor gait effectively. When their attention is focused on each step though the use of external visual cues, they become able to normalize their gait pattern and improve to a degree similar to that observed in healthy aged matched individuals. Optic flow does not appear to be a critical component of these visual cues as the laser device that projected visual cues in a reverse optic flow direction did not result in a complete removal of the benefits observed from the visual cues. Hence, identifying specific and transferable methods of drawing a person's attention to each step may be a critically important goal for rehabilitation interventions in PD.

2.4.5 Limitations

Although the current experiment demonstrated an improvement in gait with use of the reverse optic flow laser device, the attachment of the device to the participant may have been a limitation. The device was attached around the individual's waist by the use of a leather adjustable belt. Due to the lengthwise size of the device, it rested on each person differently because of the variation in proportional dimensions of each participant. It was able to rest perfectly flat on a person with a smaller waist circumference, while it was angled when worn by a person with a larger waist. This may have caused some variation in the projection distance on the ground of the laser as the angle of which the laser is moving could be slightly skewed, which would therefore not denote a comparable target step length based on height for each participant. To compensate for this possible limitation, the angle was monitored for each individual in order to make the length of the projection as close to constant for each trial, relative to the height of the person. However, this may have not been completely accurate and allows for some possible error.

Another potential limitation in this experiment was also caused by the point of attachment of the device. Since the device was attached to the participant's waist, those individuals with a high degree of torso movement caused the laser to move slightly from side to side during gait. This caused some difficulty in certain participant when attempting to follow the laser in a straight path down the GAITRite® carpet, and therefore may have led to some of the gait variability observed. This was not an issue with each individual and did not appear to be a cause for concern in those with a smaller degree of torso movement. A wider laser projection line may have been more effective as this would provide a greater degree of visual information, even in those individuals in which torso movement caused a slight change in the direction of laser projection.

The difference in the width of the laser line projected from the device and the ground line may have been a limitation in the study. The laser LED was approximately 1 cm wide and was smaller than the 3 cm wide ground line. This may have had a part in the differences observed between these two conditions.

2.4.6 Conclusion

This experiment demonstrated the effects of different types of visual cues on the gait of individuals with PD. Both the ground lines as well as the reverse optic flow laser device were effective in improving the gait of individuals with PD to levels comparable to that observed in healthy aged matched individuals. Devices that draw attention to gait improvement are most important to those individuals with PD who suffer from extreme gait disabilities such as freezing. The increased time spent in double support observed in the PD group with use of the laser device can be partly attributed the reverse optic flow causing some confusion during gait, as well as possibly design flaws of the device.

The next chapter will examine individuals with PD who experience a gait disorder called Freezing of Gait (FOG). Their gait will be monitored throughout situations which normally lead to FOG episodes. Also the presence of visual cues will be examined for their potential benefits of gait improvements in these individuals.

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CHAPTER 3

EFFECT OF SPACE PERCEPTION ON FREEZING OF GAIT IN PARKINSON'S DISEASE

3.1 Abstract

Research has implicated lack of perceived space to be a direct cause of freezing of gait (FOG), yet currently there is a limited understanding of the cause of these FOG episodes in confined spaces. The present study evaluated the gait pattern alterations caused by varying sizes of upcoming doorways. The effect of approaching doorways of narrow, normal, and wide dimensions was evaluated in three separate groups: 15 individuals with PD who experience FOG; 16 non-FOG individuals with PD; and 16 healthy age-matched controls. Participants walked on a computerized carpet leading up to the three varying sizes of upcoming space for a total of fifteen trials. The measurement of step length indicated that the FOG group was most affected by the narrow doorway and were the only group to alter their step length based on doorway size. Also, an increased within-trial step length variability was found in the FOG group in the narrow doorway condition. The non-FOG individuals with PD walked at levels comparable to the healthy participants in the normal and wide doorway conditions. However, base of support measurements indicated that these individuals reverted to a similar gait pattern to that observed in the FOG group in the narrow doorway condition. Therefore, it appears that there might be a certain physiological distinction between the PD observed in those experiencing FOG and the non-FOG individuals with PD.

3.1.1 Introduction

An impaired gait pattern is a hallmark symptom of PD and has been well documented (Lewis, Byblow, & Walt, 2000; Schubert, Prokop, Brocke, & Berger, 2005; van Wegen et al., 2006). Freezing is a factor observed in PD that can especially lead to gait difficulties. Recent evidence has supported "freezing" or the temporary inability to execute a voluntary movement as a fifth cardinal symptom of Parkinson's disease (Giladi, Kao, & Fahn, 1997). Freezing is believed to occur because of the co-contraction of agonist-antagonist pairs of muscles and is considered one of the more serious impairments of PD, as it may lead to falls and severe loss of independent functioning. Episodes of FOG are characterized by a sudden inability to begin or continue walking (Iansek, Huxham, & McGinley, 2006). Individuals experiencing FOG describe the phenomenon as feeling that their feet “are glued to the ground” and observation of an episode reveals a complete absence of leg movement or a trembling of the lower legs and feet (Iansek et al., 2006). These freezing episodes lead to decreased mobility and a loss of independence, as the vast majority of those experiencing FOG are forced into the use of some type of assisted walking device during the course of their lifetime. FOG episodes are typically experienced while turning, in stressful time-constrained situations, and upon entrance into and through confined spaces such as doorways (Bartels et al., 2003; Okuma, 2006; Schaafsma et al., 2003). It is well documented that these confined spaces lead to FOG episodes and therefore dramatic changes to the individual’s gait while attempting to travel through this area (Bartels et al., 2003; Okuma, 2006; Schaafsma et al., 2003). The cause of FOG occurrences while traveling through smaller spaces currently is poorly understood. A comparison of the gait alterations undergone by individuals while walking in conditions which manipulate the amount of space could possibly lead to greater understanding in the area of FOG. The aim of this experiment was to determine the effect the size of the doorway, and therefore the amount of perceived space, has on one's gait prior to reaching the doorway of individuals with PD both experiencing freezing of gait (FOG) and with gait abnormalities absent of FOG.

3.1.2 Freezing of gait in confined spaces

Many individuals with PD when asked questions regarding their mindset when traveling up to and through confined spaces reported that they "feel" too large to pass through the space, even though they know that doorways are designed large enough for them to easily pass through (Lee & Harris, 1999). Also, to our current knowledge there is no information depicting whether an alteration in gait occurs in anticipation of the confined space. This has the potential to be an important finding as it would provide information as to whether the perception of approaching limited space is partly responsible for the upcoming FOG episode. By the examination of the gait preceding a confined space of individuals with PD who experience FOG, as well as individuals with PD afflicted with gait disturbances other than FOG, and healthy individuals, it may be possible to determine whether anticipatory gait responses have a role in triggering FOG episodes.

3.1.3 Mental aspects of FOG

Traditionally FOG has been viewed as a motor system disorder in which movements become frozen for a period of time due to a variety of causes. However, recent evidence has supported the theory that mental conditions might have an important role in FOG. The inability of pharmacological interventions that are common in PD such as dopaminergic medication to overcome FOG episodes to the same effect that they improve other motor symptoms commonly disabled in PD, contributes to the thought that FOG likely has a different pathophysiology (Giladi, Huber-Mahlin, Herman, & Hausdorff, 2007). Also, a number of recent studies have suggested a potential link between mental aspects such as anxiety, depression and panic with FOG (Giladi et al., 2007; Lieberman, 2006). However, Giladi et al. examined a number of individuals with higher level gait disorders and found that FOG was not associated with either anxiety or depression, thereby suggesting that FOG is not provoked by the affective state (Giladi et al., 2007). Based on findings from Chapter 2, it is possible that attention may also play a factor in FOG due to the apparent role that attentional focus can have on improving gait impairment in PD. A difference remains in the way information is processed between individuals with PD experiencing FOG and individuals with PD who experience gait disorders absent of FOG and healthy individuals that as of yet has not been determined.

3.1.4 Brain structure possibly affected in FOG

In between freezing episodes, the gait observed within individuals with PD who experience FOG does not appear to be different from subjects who are not afflicted with freezing episodes. However, an increased stride-to-stride variability in FOG individuals has been reported when compared to individuals with PD who do not experience FOG while completing a 20 m stand up and go walking task (Hausdorff et al., 2003). Hausdorff et al demonstrated that the ability to regulate the stride to stride fluctuations during gait is severely impaired within individuals with PD who experience FOG, as compared to other individuals with PD. They also identified alterations in the gait of subjects with PD who experience FOG in between freezing episodes and that diminished gait stability was common in these subjects (Hausdorff et al., 2003). A central gait timing disorder has been identified and has been suggested to be linked to freezing (Almeida, Frank, Roy, Patla, & Jog, 2007). This mechanism has been hypothesized to be controlled by the brainstem, cerebellar and spinal regions with overriding control by the frontal motor cortices (Hausdorff et al., 2003). This information along with the demonstration that the gait of individuals with PD experiencing FOG is affected differently by upcoming confined space would assist in the understanding of the neuro-anatomical regions diseased within individuals with PD affected with FOG.

3.1.5 The role of perception of space in FOG

It was demonstrated that individuals with PD have an intact neural circuitry involved in the updating spatial location information, and therefore their perception of spatial location is comparable to healthy individuals through the examination of saccadic eye movements towards a sequence of targets (Gurvich, Georgiou-Karistianis, Fitzgerald, Millist, & White, 2007). Researchers found that individuals with PD produced an increased percentage of express and anticipatory saccades as compared to healthy participants but had a preserved spatial working memory during single and two-step memory-guided tasks (Gurvich et al., 2007). However, there is a possibility that individuals with PD who experience FOG are differently affected by space perception as compared to those with PD with gait disorders absent of FOG and healthy individuals.

Lee et al. found that individuals with PD who responded yes to the question "Have you ever had problems walking through narrow spaces?" were also likely to be subject to difficulties with freezing (Lee & Harris, 1999). Individuals with PD have been shown to have difficulty with the integration of visual and spatial memory in adapting to their environment. At times they have problems in the navigation through tight spaces such as doorways and in traveling around obstacles without running into them (Lee & Harris, 1999). Middleton et al. hypothesized that the visuospatial problems associated with PD are caused in part by the compromised functional basal ganglia loops (Middleton & Strick, 2000). However, to our knowledge there has been no work clarifying the anatomical differences between the basal ganglia damage observed within individuals with PD who experience FOG as opposed to individuals with PD not afflicted by FOG. Therefore, by evaluating whether space influences both groups similarly, some insight might be gained into the structure or loop whose damage leads to FOG in PD.

3.1.6 Specific aims

The aim of this experiment was to investigate the effects of altering the size of an upcoming doorway, and therefore the amount of perceived space, has on the gait of individuals with PD that experience FOG episodes in contrast to individuals with PD with other less severe gait disabilities prior to reaching the doorway.

3.1.7 Hypothesis

Ho: Individuals with PD experiencing FOG will not alter their gait in conditions in which a smaller space will be required to travel through as compared to conditions in which a larger space is provided. The step length, base of support, and within-trial step length variability will not be significantly altered in these participants between conditions. Also, there will be no difference in any of the gait variables between the three conditions.

H_1: Individuals with PD experiencing FOG will alter their gait in conditions where they will be experiencing a smaller space that they will be required to ambulate through as compared to conditions in which a larger space is provided in anticipation of a possible FOG episode. Also, the gait of individuals with PD absent of FOG episodes and healthy control subjects will remain consistent while walking throughout conditions with varying size of doorways. The step length, base of support, and step length variability will only significantly altered between conditions in individuals with PD who experience FOG. As well, gait variables will be significantly different between the three conditions.

3.2 Method

3.2.1 Participants

Each participant was informed about the requirements of the study and signed institutionally approved consents. The comparison of gait between 15 individuals with PD experiencing FOG and 16 individuals with PD absent of FOG, through three different conditions was completed. These individuals with PD absent of FOG had all been diagnosed with other gait abnormalities that would score on a UPDRS test by a movement disorder specialist as not having completely normal gait. All 31 of the individuals with PD involved in this study were recruited from the database of the Movement Disorders Research and Rehabilitation Center at Wilfrid Laurier University in Waterloo, Ontario. Each participant was tested while "on" their medication for a minimum of 1 hour in order to increase the external validity of the findings. However, criteria were used to verify that individuals in the FOG group were experiencing episodes of freezing at the time of test. Before the experiment began, each individual with PD who experiences FOG performed a standard timed up and go test (TUG). This test began with the patient seated in a chair and upon a go signal they proceeded to stand and walk to a marker on the ground three meters from the chair. Once they reached this marker, they turned around and proceeded back to the chair and sat down. The gait of these individuals during this test was observed by a movement disorder specialist and if any FOG indicators were observed such as abnormal steps, festination of gait involving shuffling steps, or mid-stride hesitation, then the normal testing procedure commenced. If FOG indicators were absent, the patient underwent a 30 minute break in order for the amount of medication active in their system to continue to diminish. This procedure was repeated until a FOG episode was observed in the TUG test. All patients that were tested had clinically typical PD which had been diagnosed by at least one movement disorder specialist. Also, each participant was responsive to anti-parkinsonian medication. Sixteen healthy control subjects also participated in the study. These individuals were mostly spouses or relatives of the PD participants.

Subjects were excluded from testing if they had a past history of neurological conditions other than PD, or orthopedic or visual disturbances that severely impair walking ability. Participants were also excluded if they had been diagnosed with dementia or if they had dyskinesias which would alter an individual's gait.

Table 3.1 summarizes the participant characteristics for each group. There were no significant differences between groups for any of the variables described.

Table 3.1
Characteristics of the three groups

Group	Age- M (yrs)	Age- SD (yrs)	Height- M (cm)	Height- SD (cm)	UPDRS- M (score)	UPDRS-SD (score)	Gender
Freezers	72.4	6.79	172.51	8.15	32.8	7.34	13 male, 2 female
Shufflers	72.19	6.23	170.66	9.69	28.81	6.35	10 male, 6 female
Controls	70.75	5.98	167.96	7.53	n/a	n/a	6 male, 10 female

Note: M denotes mean; *SD* denotes standard deviation

3.2.2 Experiment set-up and data collection

The room that was used for data collection is a laboratory containing a doorway that leads out into an empty hallway. The lighting in both the laboratory and the hallway was maintained at a consistent brightness. Data was collected on a *GAITRite®* carpet (*GAITRite®*, CIR System, Inc., Clifton, NJ, USA) which is a 3.96m long X 0.79m wide carpet containing thousands of sensors that send information received from the participants' footsteps to an attached computer. A researcher walked alongside the participant at all times throughout the testing in order to maintain the safety of the participant during each trial.

3.2.3 Procedure

Participants walked the length of the *GAITRite®* carpet under three different conditions for five trials each. They began each trial two metres before the start of the *GAITRite®* carpet to ensure that the initiation of gait was not recorded. The three conditions examined in this study were:

i) Narrow doorway condition in which the participant walked normally across the *GAITRite®* carpet through a smaller than normal ($3/4^{th}$ size) doorway; (0.675m wide X 2.1m high).
ii) Normal doorway condition in which the participant walked normally across the *GAITRite®* carpet through a normal sized doorway (0.9m wide X 2.1m high).
iii) Wide doorway condition in which the participant walked normally across the *GAITRite®* carpet through a double sized doorway (1.8m wide X 2.1m high).

3.2.4 Data analysis and statistics

The three conditions in this protocol allowed for the analysis of whether the size of doorway is the contributing factor in the alteration of gait and freezing of gait experienced while traveling through confined spaces such as a doorway. Solely spatiotemporal characteristics of the individuals' gait preceding the doorway was analyzed in order to determine the effect of the doorway on gait leading up to the narrowed space. Any foot falls at, or after the doorway were excluded from analysis in this experiment.

There were three independent groups in this experiment; individuals with PD experiencing FOG (Freezers), those with PD experiencing gait abnormalities absent of FOG (Shufflers) who were at optimal medication levels, and healthy control subjects (Controls). The primary dependant variables analyzed were gait velocity (cm/s), mean step length (cm) which is equal to the length of a toe off to the opposite foot heel contact, base of support (cm), cadence (steps/min), time spent in double support (s), and the within-trial step length variability. Results were analyzed by the STATISTICA computerized statistical package using a mixed model 3 groups X 3 conditions X 5 trials ANOVA. In order to determine where the significant differences found in the ANOVA's occurred, Tukey's Honest Significant Difference (HSD) post hoc procedure was employed.

3.3 Results

3.3.1 Freezers walk slower as compared to the shufflers and controls

Individuals who experience FOG were found to walk significantly slower on average as compared to the two other groups as demonstrated by a main effect of group ($F_{(2,44)} = 10.90$, $p < 0.001$) (Figure 3.1). Post hoc analysis confirmed that the Freezers walked at a significantly slower velocity as compared to both Shufflers (20.3% decrease, $p = 0.012$) and Controls (28.3 % decrease, $p < 0.001$) (Table 3.2). There was no significant interaction of velocity observed with condition.

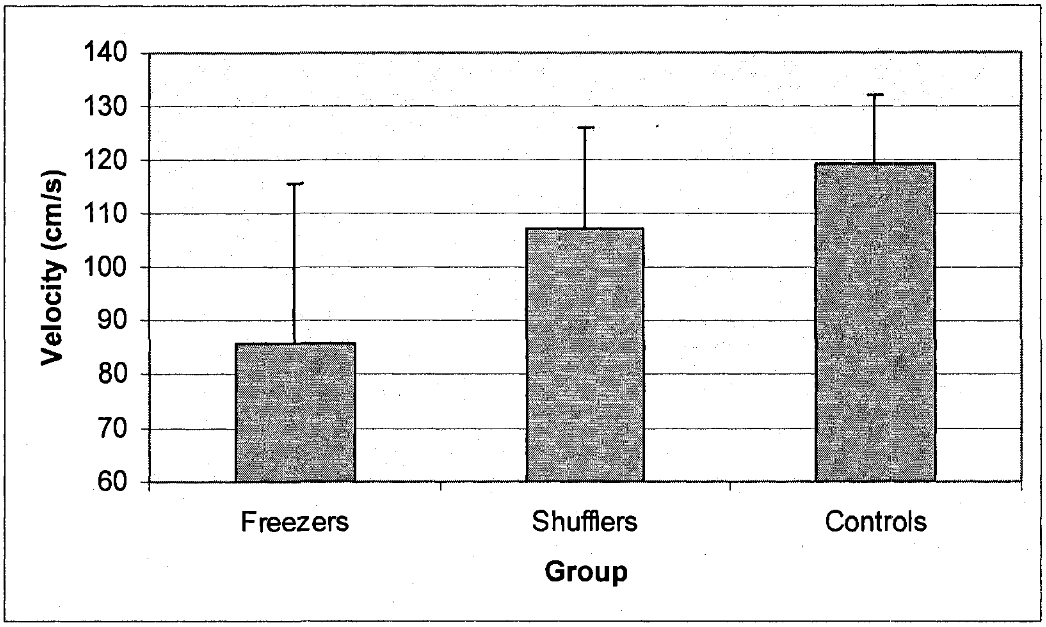

Figure 3.1 Comparison of velocity between the three groups

Table 3.2
Velocity (cm/s) by group

Group	Mean	SD
Freezers	85.50[1,2]	29.95
Shufflers	107.25[1]	18.80
Controls	119.26[2]	12.81

1,2 Significant differences between the groups were determined by Tukey's HSD.

3.3.2 The effect of size of doorway on step length

It was observed that Freezers had a significantly smaller step length as compared to both Shufflers and Controls. This was evident from the observed main effect of group ($F_{(2,44)} = 13.11$, $p < 0.001$) (Fig. 3.2). Post hoc analysis confirmed that Freezers had a significantly smaller step length as compared to the Shufflers ($p < 0.011$) and Controls ($p < 0.001$), while shufflers did not differ from Controls (Table 3.3). The narrow doorway condition caused all participants to take smaller steps leading up to the doorway as compared to the normal and wide doorway conditions as indicated by a significant main effect of condition ($F_{(2,88)} = 22.32$, $p < 0.001$) (Fig. 3.3). In the Narrow doorway condition participants significantly decreased their step length as compared to the Normal ($p < 0.002$) and Wide ($p < 0.001$) doorway conditions (Table 3.4).

Additionally, a significant interaction was found when comparing group and condition ($F_{(4,88)} = 2.73$, $p < 0.034$) (Fig. 3.4). The Narrow doorway affected the step length of Freezers the most of any of the three groups. This was confirmed through post hoc analysis in which the narrow doorway caused the Freezers to shorten their steps as compared to the normal doorway by 8.4% ($p < 0.005$) and wide doorway by 12.7% ($p < 0.001$) (Table 3.5). The other two groups did not significantly alter their steps in respect to the different sizes of doorways they were approaching.

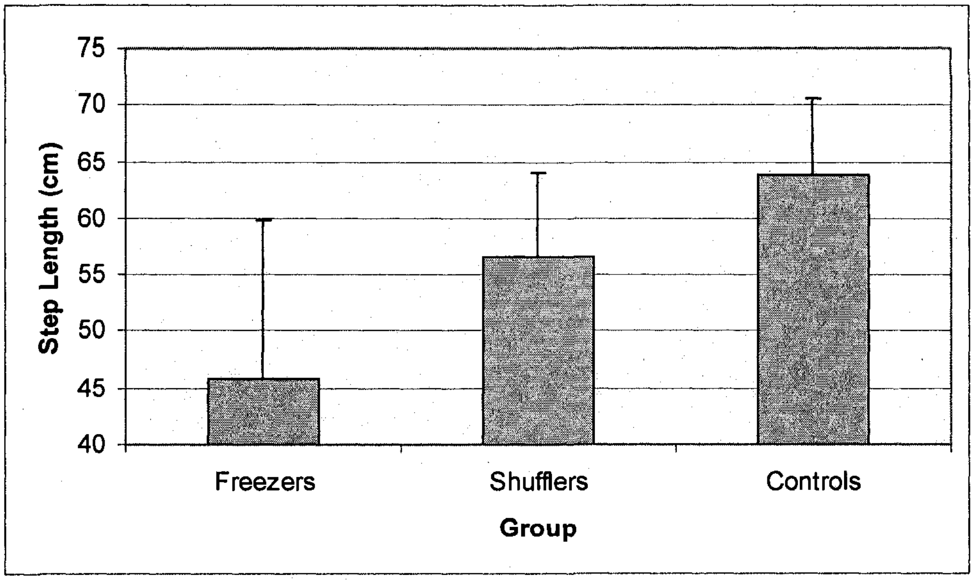

Figure 3.2 Comparison of mean step length between groups

Table 3.3
Step length (cm) by group

Group	Mean	SD
Freezers	45.89[1,2]	13.92
Shufflers	56.64[1]	7.42
Controls	63.86[2]	6.79

1,2 Significant differences between the groups were determined by Tukey's HSD.

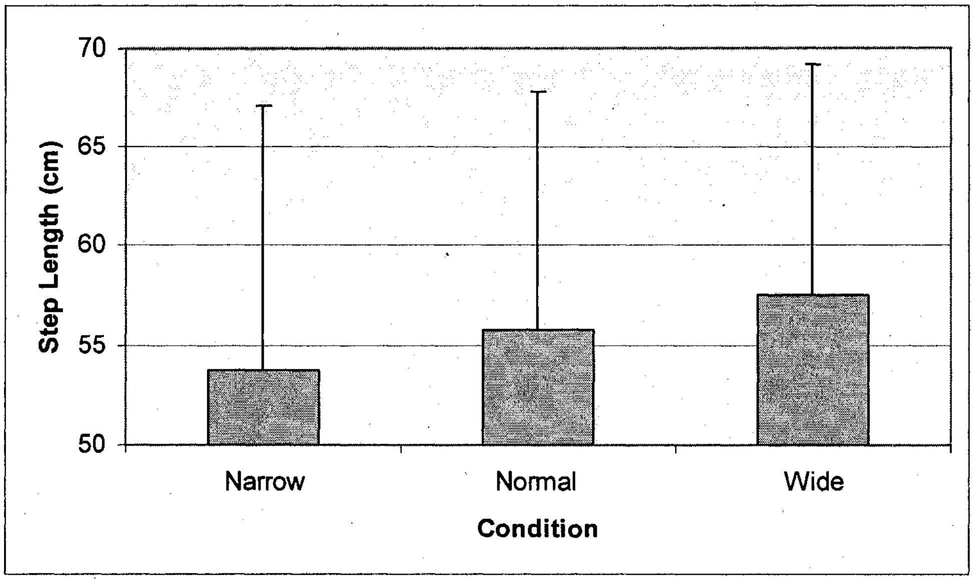

Figure 3.3 Step length is significantly affected by condition

Table 3.4
Step length (cm) by condition

Group	Mean	SD
Narrow	53.78[1,2]	13.26
Normal	55.77[1]	11.98
Wide	57.44[2]	11.70

1,2 Significant differences between the conditions were determined by Tukey's HSD.

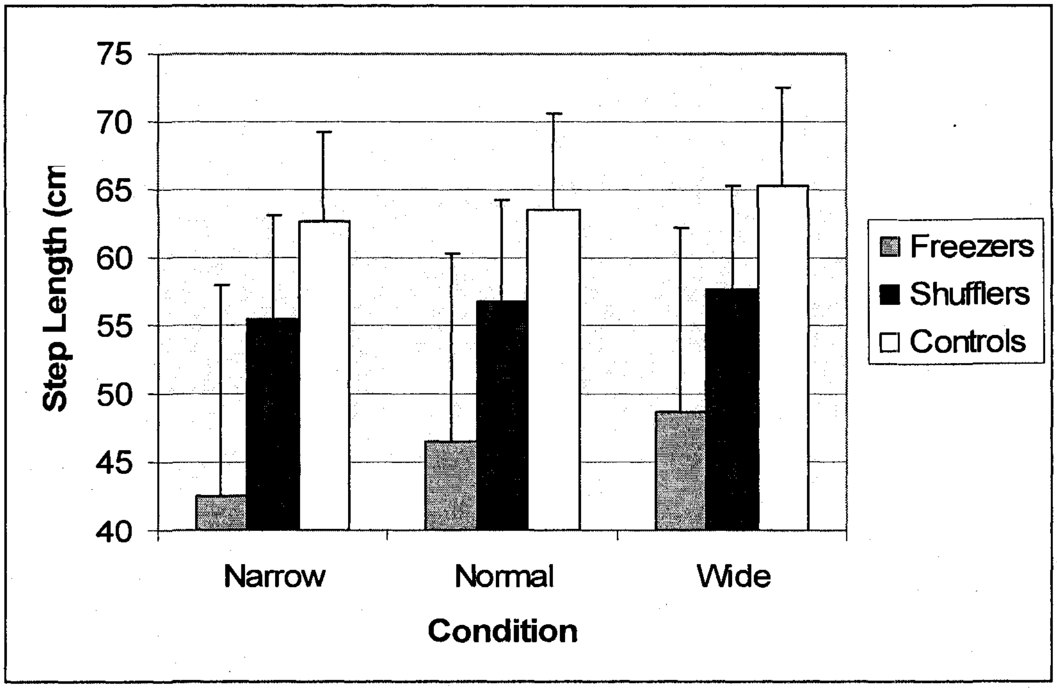

Figure 3.4 Changes in step length over the three conditions in Freezers, Shufflers and Controls

Table 3.5
Step length (cm) by group and condition

Group – Condition	Mean	SD
Freezers – Narrow	42.53[1-4]	15.41
Freezers – Normal	46.41[1,5,6]	13.91
Freezers – Wide	48.73[2,7,8]	13.45
Shufflers – Narrow	55.40[3,9]	7.72
Shufflers - Normal	56.81[5,10]	7.47
Shufflers – Wide	57.72[7,11]	7.58
Controls – Narrow	62.71[4,9]	6.60
Controls – Normal	63.51[6,10]	7.15
Controls - Wide	65.35[8,11]	7.11

1-11 Significant differences between the groups and conditions were determined by Tukey's HSD.

3.3.3 Time spent in double support

A trend reaching significance was found between groups when examining the amount of time individuals spent in the double support phase of the gait cycle ($F_{(2,44)} = 3.13$, $p < 0.054$) (Figure 3.5). Individuals with PD experiencing FOG spent a greater, albeit non-significant amount of time in double support as compared to both the non-FOG individuals with PD as well as the healthy control subjects. Again, there was no significant interaction of double support found when examining condition.

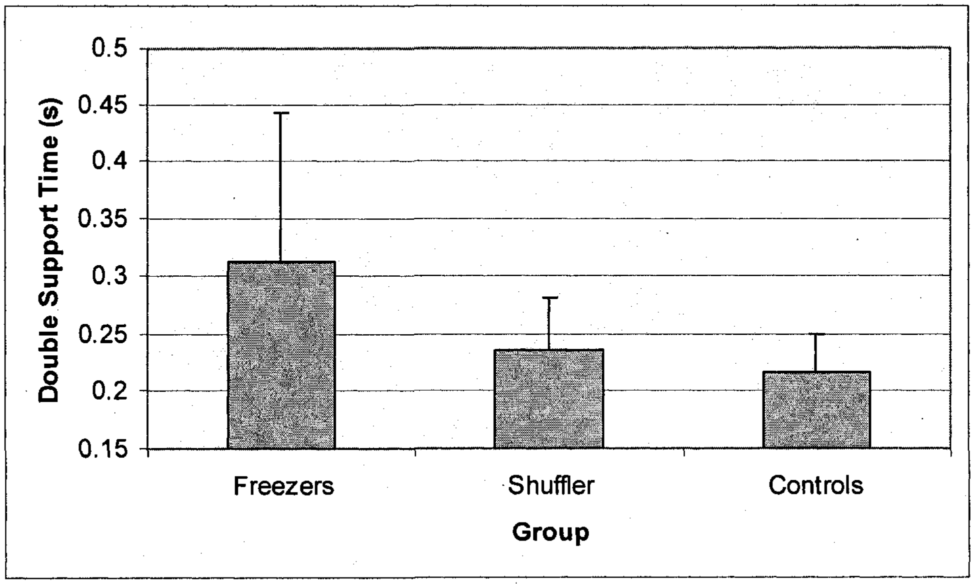

Figure 3.5 Comparison of double support time between groups

3.3.4 Base of support changes dependant on condition

In this experiment certain groups were found to alter their base of support based on the condition that was presented (Figure 3.6). A significant interaction of group and condition was found when analyzing base of support ($F_{(4,88)} = 3.96$, $p < 0.053$) (Fig. 3.6). Base of support did not significantly change with condition in either the Freezers or Controls. Also, it was found that throughout the three conditions the Freezers had a significantly larger base of support (on average 29.6% larger) as compared to Controls ($p < 0.001$) (Table 3.6). The Freezer's base of support was found to be consistently the widest and the Controls the narrowest. In the wide doorway condition Shufflers were found to behave like Controls and with respect to base of support and had a significantly smaller base of support as compared to Freezers ($p <0.001$). In the Normal doorway they behaved differently than both groups. However, when confronted with the narrow doorway condition, their base of support became similar to that observed in the Freezers in the same condition and differed significantly from the control group ($p < 0.001$).

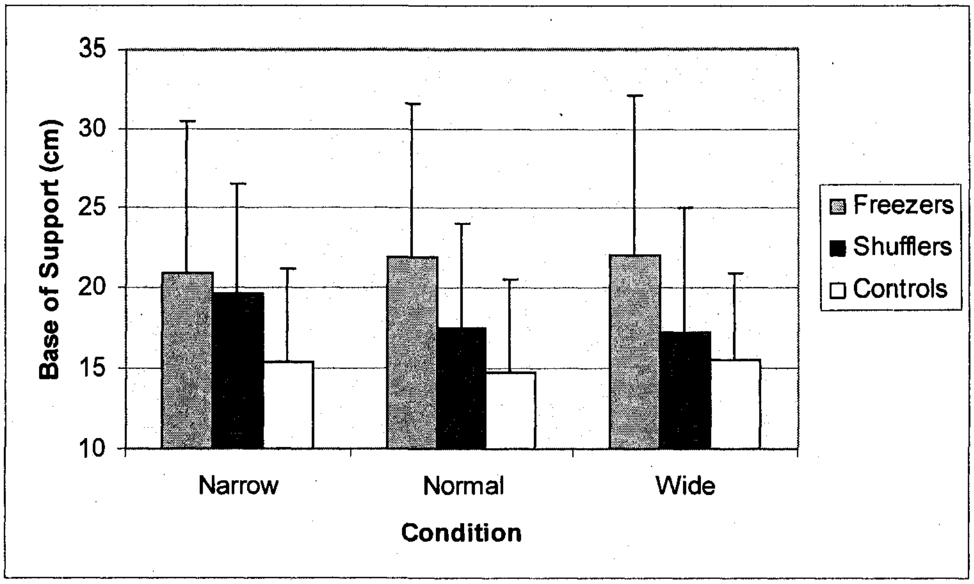

Figure 3.6 Base of support alterations across conditions

Table 3.6
Base of support (cm) by group and condition

Group – Condition	Mean	SD
Freezers – Narrow	20.84^{6}	9.68
Freezers – Normal	$21.90^{3,4}$	9.68
Freezers – Wide	$22.02^{2,7}$	10.11
Shufflers – Narrow	19.59^{1}	6.95
Shufflers - Normal	$17.56^{3,5}$	6.50
Shufflers – Wide	17.30^{2}	7.65
Controls – Narrow	$15.37^{1,6}$	5.72
Controls – Normal	$14.76^{3,4}$	5.71
Controls – Wide	15.49^{7}	5.35

1- 7 Significant differences between the groups and conditions were determined by Tukey's HSD.

3.3.5 Step length variability

When comparing individuals with PD and controls for the amount of step-to-step variability in step length, a main effect of group was found ($F_{(2,44)} = 7.79$, $p < 0.002$) (Fig. 3.7). Post hoc analysis confirmed that Freezers had significantly greater step length variability as compared to both Shufflers ($p < 0.014$) and Controls ($p < 0.002$) (Table 3.7).

A trend reaching towards significance was also found when examining each specific condition and group ($F_{(4,88)} = 2.08$, $p < 0.091$) (Fig.3.8). This appears to demonstrate that only Freezers were negatively affected by the Narrow doorway and became increasingly variable in the length of each step. Shufflers and Controls had a decreased variability in all conditions as compared to the Freezers and conditions did not have an effect on either of these two groups. However, these results are faced with increased scrutiny as a significant interaction was not found.

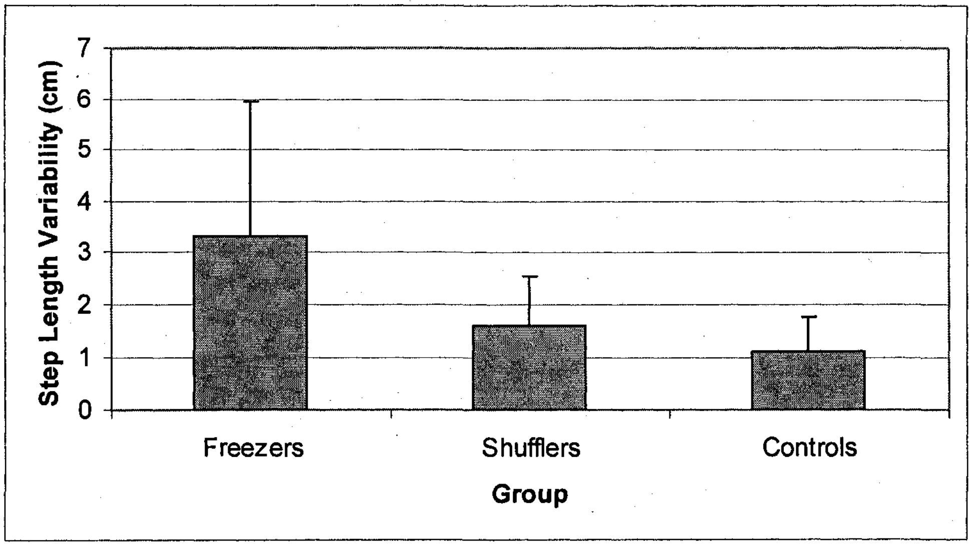

Figure 3.7 Step length variability increased in Freezers

Table 3.7
Step length variability (cm) between groups

Group	Mean	SD
Freezers	3.34[1,2]	2.63
Shufflers	1.61[1]	0.95
Controls	1.14[2]	0.64

1,2 Significant differences between the groups were determined by Tukey's HSD.

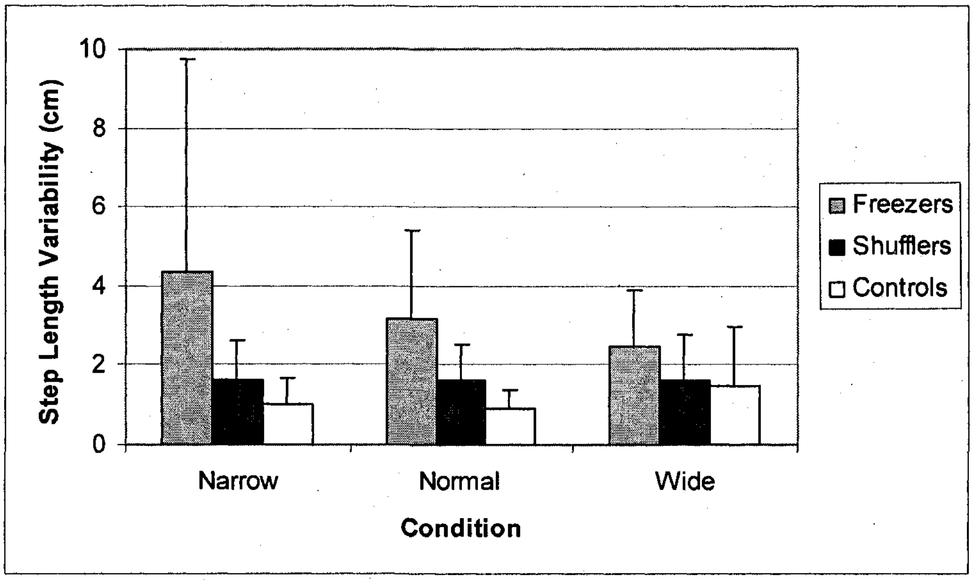

Figure 3.8 Trend reaching significance in step length variability for group X condition

3.4 Discussion

This experiment investigated the potential effects that perception of space has on the gait of individuals with PD who experience FOG, those with gait abnormalities absent of FOG, and healthy age matched participants. The results supported the hypothesis in that an upcoming confined space was found to only affect the gait of those with FOG. Solely individuals with PD experiencing FOG were found to alter their gait pattern in respect to the upcoming narrow doorway in comparison to the normal and wide doorways. The gait of the FOG individuals was also significantly more variable overall as compared to the other two groups. In the normal and wide doorways the gait of Shufflers appeared to be similar to that observed in Controls, in the narrow doorway condition it appeared to be more closely related to the gait of Freezers.

3.4.1 Step length is affected by doorway size solely in FOG group

When approaching a narrow doorway, individuals with PD who experience FOG were shown to exhibit changes in their gait pattern which were not evident in other individuals with PD or healthy participants when ambulating in a similar situation. The FOG group significantly shortened their steps when traveling towards the narrow doorway as compared to both the normal sized and wide doorways, while the step lengths of all other participants were not significantly influenced by the conditions. The manipulation of the amount of space through which the participant was required to travel evidently led to changes in the gait pattern of individuals with PD who experience FOG. The ability to accurately perceive the amount of space, and therefore a certain degree of visuospatial ability, is more greatly affected in those individuals with PD who are subject to FOG. It is has been reported that there are two major pathways of visual information in the cortex. The ventral stream projects from the striate cortex to the inferior temporal lobe and is responsible for the processing of object identity, while the stream responsible for the "where" in visual cognition is the dorsal stream which projects from the striate cortex to the superior posterior parietal cortex and codes the location of objects in space (Brandt, Shpritz, Munro, Marsh, & Rosenblatt, 2005). The caudate nucleus is the message receiving striatum of the basal ganglia that degenerates throughout the course of PD and receives significant input from the posterior parietal cortex (Brandt et al., 2005). Therefore it has been suggested that primary neuronal loss in the caudate nucleus may result in retrograde degeneration of parietal association areas that are critical to the ability to accurately estimate your location in relation to objects in the environment during movement (Brandt et al., 2005; Butters, Soeldner, & Fedio, 1972). Due to the different gait responses observed between the individuals with PD who experienced FOG and those with gait abnormalities absent of FOG in response to the narrow upcoming doorway, it is suggested that the difference between these two groups of individuals with PD may be partly caused from the degree of degeneration that has occurred in the caudate nucleus. It is important to note that relatively few neurons in the caudate nucleus respond to movement and positions, and instead are thought to be involved more prominently in cognitive functions (Nolte, 2002). The loop from the association cortex through the caudate nucleus, and back to the prefrontal cortex implies that damage to the caudate would result in findings similar to those that occur with prefrontal damage such as changes in personality, affect, motivation and cognition (Nolte, 2002). However, it is possible that the neurons in the caudate that do respond to movement are damaged in individuals with PD who experience FOG and this appears to lead to the gait abnormalities observed in space constrained situations observed solely within individuals with PD subject to FOG.

An alternative based on base of support data is that Shufflers exhibit similar behaviour to Freezers when demands are increased in situations such as experienced in the narrow doorway condition. The support base used by individuals when walking in this experiment were somewhat expected. As the gait abnormalities experienced by participants worsened, the base of support size became larger as it would appear individuals used a wide base of support as a security mechanism to prevent from loss of balance, falls or freezing episodes. However, Freezers were expected to decrease their base of support in the Narrow condition. Their decreased ability to properly perceive the amount of upcoming space and therefore accurately monitor their body position in order to ambulate through this doorway would be expected to lead to an over-compensation in this situation, and therefore a smaller base of support. This was not the case as Freezers did not significantly adjust their base of support within the three conditions and in fact the Shufflers were the only group to use a larger, albeit non-significant base of support in the Narrow condition as compared to the other two conditions.

3.4.2 Individuals with PD experiencing FOG have increased gait instability

As expected based on previous research examining FOG, these individuals experienced an increase in gait variability and instability. Upon the analysis of the three groups, increased step length variability and a trend towards an increased time spent in double support was observed in the FOG group as compared to the non-FOG individuals with PD and healthy control participants. They also exhibited an increased base of support as compared to Shufflers in the Normal and Wide doorway conditions, and a larger base of support across all three conditions when compared to Controls. The increased step length variability is indicative of an unstable gait pattern, or based on results obtained in the previous chapter are an unnecessary attempt at voluntary control of gait. The individuals were not maintaining a normal stride during the trials, but instead were altering the distance of each step which might lead to an increased risk of falls.

A trend was observed with regards to the amount of time spent in double support between the three groups which indicated that Freezers might be spending more time in the double support phase of the gait cycle. This suggests that individuals with PD experiencing FOG tend towards a pattern of remaining in the double support phase for an extended period of time. This tendency might be used to compensate for the decreased stability and therefore fear of falling due to a potential freezing episode.

3.4.3 Clinical implications

The new information from the findings of this experiment is that the step length and within-trial step length variability of individuals with PD who experience FOG is altered when traveling towards a situation in which a FOG episode is a likely outcome. Other individuals with PD experiencing gait abnormalities absent of FOG were found to be mostly unaffected by confined spaces, as was the case with healthy individuals. The exception to this was the base of support results that demonstrated that non-FOG individuals with PD increased their base of support when confronted with the narrow doorway. The inability of individuals with PD experiencing FOG to maintain a normal gait pattern in the presence of upcoming confined spaces or other obstacles should be studied more intensively in order to determine the viability of treatment options that might attempt to improve gait and prevent freezing episodes in these individuals.

A treatment program may include the use of visual or auditory cues, and anticipatory strategies that have been shown effective in improving the abnormal gait pattern observed within individuals with PD (Azulay et al., 1999; Lewis et al., 2000; Morris, Iansek, Matyas, & Summers, 1996). Visual cues such as step lines as targets may focus their attention on each step, thereby distracting the individual from the upcoming doorway, summoning the return of a normalized gait pattern. Auditory cues in the form of a metronome might also regulate gait in these situations as they have been shown to be effective in a number of studies involving individuals with PD (Rochester et al., 2005; Willems et al., 2006). However, recent studies suggest that gait may become more variable with auditory timing cues (Almeida et al., 2007). The anticipatory strategies prior to reaching the doorway may include some type of visualization in which they focus on their body traveling through the doorway instead of the thought normally experienced in these situations of possibly bumping into the doorway. Further research is required to more properly understand the neural mechanisms behind FOG and to test the viability of treatment programs in improving the gait of individuals with PD experiencing FOG.

3.4.4 Limitations

Although the current experiment identified gait alterations in individuals with PD experiencing FOG upon the lead up to a confined space in the form of a narrow doorway, the relatively few steps monitored may have been a limitation. Due to the size of the

GAITRite® carpet, it was only possible to monitor the 4-6 steps prior to reaching the doorway, depending on the height, and therefore step length, of the individual. Therefore, a longer carpet would be useful in order to measure the gait of participants for a longer amount of time and from an increased distance back from the doorway in order to receive a more complete understanding of the underlying mechanisms of FOG. Another limitation of this study was the use of only one size of narrow doorway. An effort was to allow should clearance through the doorway although in certain cases experienced in everyday life such as traveling through a closing elevator door, the opening could be much smaller. The transition through an even smaller space might lead to more conclusive results. The narrow doorway used in this experiment was 0.675m wide, and was still easily maneuvered in most cases. An opening in which a body position manipulation, such as turning sideways, is required may lead to an even greater effect of the gait of individuals with PD experiencing FOG. Also, the use of a cognitively challenging task while walking through a confined space may give insight into the area of dual-task processing and FOG, an area that which has shown to frequently lead to freezing episodes (Giladi & Hausdorff, 2006).

3.4.5 Conclusion

This experiment demonstrated the effects of upcoming confined spaces on individuals with PD experiencing FOG. The gait of these individuals approaching the doorway was found to become altered when approaching a decreased amount of perceived space. This demonstrated a potential physiological distinction between individuals with PD experiencing FOG, and those with gait abnormalities absent of FOG.

The next chapter will examine the effects of different types of visual cues of FOG and their potential effect of normalizing the gait pattern of individuals with PD who experience FOG. Cues in the form of step lines and an optic flow laser device will be utilized.

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CHAPTER 4

INFLUENCE OF DIFFERENT VISUAL CUES ON FREEZING OF GAIT IN PARKINSON'S DISEASE

4.1 Abstract

The improvement in gait derived through the use of visual cues in PD has been well documented. However, research examining the possible beneficial effect these cues might provide to individuals with PD who experience FOG remains incomplete. The present study evaluated the use of visual cues on the gait approaching an enclosed area in three separate groups: 15 individuals with PD who experience FOG, 16 non-FOG individuals with PD, and 16 healthy age-matched controls. Participants walked on a computerized carpet leading up to the narrow doorway in a self-paced walk condition, with the use of ground lines as a visual cue, and with the use of a laser device as a visual cue, for a total of fifteen trials. The measurement of step length indicated that individuals with PD who experience FOG were only able to improve their gait with the use of ground lines as a visual step cue. The laser device produced an increased within trial step length variability as well as an increased amount of time spent in double support. Therefore it appears that visual cues are able to improve the gait of individuals with an impaired visuospatial perception, but a sufficient amount of time to maintain a preplanned step pattern is required.

4.1.1 Introduction

Research has well documented the improvement in gait individuals with PD experience with use of external visual cues (Azulay, Mesure, & Blin, 2006; Lewis, Byblow, & Walt, 2000; Morris, Iansek, Matyas, & Summers, 1996; Rochester et al., 2005). However, little research has been completed regarding the possible influence of these visual cues in the prevention of freezing of gait (FOG) and maintenance of a normal gait pattern. The use of visual cues is especially important for individuals with PD who experience FOG as they can possibly use visual manipulations, such as aiming their foot for a location in front of them, to overcome FOG episodes. The previous chapter examined the gait of these individuals as they approached an enclosed space which might normally induce a FOG episode. Results indicated that individuals with PD who experience FOG negatively alter their gait pattern when approaching a narrow doorway, perhaps because of an impaired ability to effectively perceive spatial locations. This experiment will test the gait of participants as they approach a narrow doorway, and therefore a situation in which FOG is common, both in a baseline condition and while using visual cues in an attempt to regulate their gait pattern. This will attempt to determine the viability of external visual cues in focusing attentional resources on gait and preventing the gait disabilities experienced in FOG. The aim of this experiment was to determine the influence of visual attention on the prevention of FOG and maintenance of a normal gait pattern while ambulating in a situation which would regularly induce a freezing episode.

4.1.2 Common observations in FOG

FOG has been noted to occur often upon the confrontation with an obstacle or a narrowing of space such as a doorway (Bloem, Hausdorff, Visser, & Giladi, 2004). Individuals with PD who experience FOG at times show normal gait once the first step is initiated. This lends to the thought that FOG may be associated with a defect in the neuronal mechanisms that are specifically involved in the self-initiated transition from standing still to dynamic movement (Lyoo et al., 2007). A question remains as to whether this FOG observed at initiation has the same underlying cause as the FOG being examined in this experiment that occurs during gait. There are differing opinions of the cause of FOG episodes. In chapter 3 it was suggested that the occurrence of FOG in only certain individuals with PD is dependant on the degree of degeneration experienced in the caudate nucleus. Other studies have suggested that abnormal activation of the mesocortical dopaminergic system and ventral striatum may be related to the pathophysiology of FOG (Kitagawa, Houzen, & Tashiro, 2007). However, to date there remains contradicting evidence as of the underlying cause or mechanics of freezing episodes.

FOG that occurs when an individuals with PD is "off" their medication has been treated with varying degrees of success through medicinal intervention, whereas FOG that occurs when "on" medication does not respond to medicinal treatment. Therefore, a different pathophysiology between a number of different FOG subtypes has been suggested (Kompoliti, Goetz, Leurgans, Morrissey, & Siegel, 2000; Schaafsma et al., 2003). A FOG episode consists of an absence of movement in which it appears as if the individual's feet are suddenly and inexplicably glued to the floor. This has been noted to typically last less than one minute and movement usually recommences within a few seconds (Bartels et al., 2003). Giladi et al reported that the presence of FOG as a symptom in an individual with PD predisposes that person to faster cognitive and functional decline (Giladi, Huber-Mahlin, Herman, & Hausdorff, 2007). Therefore, the occurrence of FOG is thought of as one of the most severe symptoms that occur in PD. A method by which freezing episodes can be prevented and normal gait maintained would be extremely beneficial to individuals with PD who are commonly affected by FOG. Further study is required to devise methods to prevent the cognitive and functional declines observed in individuals with PD who experience FOG.

4.1.3 What is known about the visual cues which lead to a gait improvement in PD

As previously mentioned, a number of studies have shown that visual cues lead to an improvement in the gait of individuals with PD (Azulay et al., 2006; Lewis et al., 2000; Morris et al., 1996; Rochester et al., 2005). It has been suggested that enhancing the visual signals in the environment may aid in cortical processing which in turn activates neurological circuits, allowing for the reinstatement of more normal gait through these visual cues (Davidsdottir, Cronin-Golomb, & Lee, 2005). Along with this, the suggestion has been made that individuals with PD lack the ability to unconsciously regulate their gait pattern as effectively as healthy individual (Rochester et al., 2005; Rochester et al., 2007). Visual cues such as ground lines were said to improve gait due by forcing a more conscious motor control pathway in the regulation of gait thereby overcoming a faulty basal ganglia (Lewis et al., 2000). In chapter 2, the results obtained suggest that increased attentional focus is specifically responsible for bypassing the basal ganglia and regulating gait in individuals with PD when using ground lines as visual step cues. A visual cue device has been developed which uses a laser beam stick as a visual cue in an attempt to overcome freezing (Kompoliti et al., 2000). Kompoliti et al. had individuals with PD who experience FOG walk on a 60 foot track with the use of different types of visual cues and measured the number of observed freezing episodes. They determined no effect of FOG episode prevention with use of these cues but did not measure any other gait variables of the participants while walking (Kompoliti et al., 2000). Therefore, as of yet research is incomplete as to whether the gait observed in PD patients who are subject to FOG episodes can be improved before a potential freezing episode with the use of these external visual cues.

4.1.4 Specific aims

The aim of this experiment was to manipulate the presence and type of visual cue in a situation leading up to an enclosed space that tends to induce gait abnormalities such as FOG, in order to determine the potential benefit of these cues. Improvement and normalization of gait with the use of visual cues above that observed in the baseline condition will help evaluate that FOG can be at least partially prevented. A laser line device that presents visual cues in the form of regular optic flow will also be presented to participants in order to test the viability of a more portable form of visual cue as compared to the traditional ground lines, and therefore more functionally efficient in the prevention of FOG.

4.1.5 Hypothesis

H_0: Individuals with PD experiencing FOG will not be influenced by visual cues and these visual cues will not improve or normalize the gait of individuals with FOG. There will be no differences observed between the three groups.

H_1: Individuals with PD experiencing FOG will improve their gait with the use of visual cues above that seen in the baseline condition to levels comparable of that observed in the non-FOG individuals with PD and healthy participants. Also, the laser line device will demonstrate improvements in the gait of individuals with PD experiencing FOG to similar levels observed with the ground lines.

4.2 Method

4.2.1 Participants

Each participant was informed about the requirements of the study and signed institutionally approved consents. The comparison of gait between 15 individuals with PD experiencing FOG and 16 individuals with PD absent of FOG, throughout 5 different conditions was completed. All 31 of the individuals with PD involved in this study were recruited from the database of the Movement Disorders Research and Rehabilitation Center at Wilfrid Laurier University in Waterloo, Ontario. Each participant was tested while "on" their medication for a minimum of one hour in order to increase the external validity of the findings. However, criteria were developed to verify that individuals in the FOG group were currently experiencing this disorder while on their normal medication. Before the experiment began, each individual with PD who experience FOG performed a standard timed up and go test (TUG). This test began with the patient seated in a chair and upon a go signal they proceeded to stand and walk to a marker on the ground three meters from the chair. Once they reached this marker, they turned around and proceeded back to the chair and sat down. The gait of these individuals during this test was observed by a movement disorder specialist and if any FOG indicators were observed such as abnormal steps, festination of gait involving shuffling steps, or mid-stride hesitation, then the normal testing procedure commenced. If FOG indicators were absent, the patient underwent a 30 minute break in order for the amount of medication active in their system to continue to diminish, therefore leading to a greater chance of FOG occurring. This procedure was repeated until a FOG episode was observed in the TUG test.All patients that were tested had clinically typical PD which had been diagnosed by at least one movement disorder specialist. Also, each participant was responsive to anti-parkinsonian medication. Sixteen healthy control subjects also participated in the study. These individuals were mostly spouses or relatives of the PD participants.

Subjects were excluded from testing if they had a past history of neurological conditions other than PD, or orthopedic or visual disturbances that might severely impair walking ability. Participants were also excluded if they had been diagnosed with dementia or if they had dyskinesias which would alter an individual's gait.

Table 3.1 summarizes the participant characteristics for each group. There were no significant differences between groups for any of the variables described.

Table 4.1
Characteristics of the three groups

Group	Age- M (yrs)	Age- SD (yrs)	Height- M (cm)	Height- SD (cm)	UPDRS- M (score)	UPDRS-SD (score)	Gender
Freezers	72.4	6.79	172.51	8.15	32.8	7.34	13 male, 2 female
Shufflers	72.19	6.23	170.66	9.69	28.81	6.35	10 male, 6 female
Controls	70.75	5.98	167.96	7.53	n/a	n/a	6 male, 10 female

Note: M denotes mean; *SD* denotes standard deviation

4.2.2 Experiment set-up and data collection

The room that was used for data collection is a laboratory containing a doorway that leads out into an empty hallway. The lighting in both the laboratory and the hallway was maintained at a consistent brightness. Data was collected on a *GAITRite®* carpet (*GAITRite®*, CIR System, Inc., Clifton, NJ, USA) which is a 3.96m long X 0.79m wide carpet containing thousands of sensors that send information received from the participants' footsteps to an attached computer. A researcher walked alongside the participant at all times throughout the testing in order to maintain the safety of the participant during each trial.

4.2.3 Procedure

Participants walked the length of the *GAITRit®e* carpet under three different conditions for five trials each. They began each trial two metres before the start of the *GAITRite®* carpet to ensure that the initiation of gait was not recorded. The three conditions that were examined in this study are:

i) Narrow doorway condition in which the participant walked normally across the *GAITRite®* carpet through a smaller than normal ($3/4^{th}$ size) doorway; (0.675m wide X 2.1m high). In all three conditions the participant was required to walk towards the narrow doorway.

ii) Ground lines condition in which the participant walked across the *GAITRite®* carpet while making consecutive heel contacts on ground lines provided by a black overlay placed on top of the GAITRite® carpet. This black overlay was made out of a thin clothe material with white horizontal lines 3 cm wide spaced at

65 cm intervals. It was designed as to not impede the normal functioning of any of the sensors in the GAITRite® carpet

iii) Laser condition in which the participant walked across the *GAITRite®* carpet while making consecutive heel contacts on lines on the ground provided by a laser line device, through a smaller than normal sized doorway ($3/4^{th}$ size) doorway; (0.675m wide X 2.1m high). This device projected a roughly 1 cm wide transverse LED laser line onto the ground ahead of the participant. The initial projection was approximately 65 cm in front of the participants and then moved in the direction towards the participant, therefore traveling in a optic flow direction consistent to that obtained from other objects in the environment. The individual was instructed to touch their toe to the laser line when it was at its furthest point and continued to walk down the length of the carpet repeating this procedure in sequence with the movement of the laser. The laser device was attached by a belt to each participant's waistline and the constant angle in which the laser was set to led to a maximum projection distance that was based on the height of each individual, and therefore an average step length.

4.2.4 Data analysis and statistics

The three conditions in this protocol allowed for the analysis of whether additional visual cues in the form of either ground lines or laser lines, can possibly prevent the impaired gait experienced by individuals with PD experiencing FOG as they approach a situation that regularly induced FOG episodes. Only the individuals' gait preceding the doorway was analyzed in order to determine the effect these visual cues have on gait prior to a possible FOG episode. Any foot falls at, or after the doorway were excluded from analysis in this experiment.

There were three independent groups in this experiment; individuals with PD experiencing FOG (Freezers), those with PD experiencing gait abnormalities absent of FOG (Shufflers) who were at optimal medication levels, and healthy control subjects (Controls). The primary dependant variables analyzed were gait velocity (cm/s), walking cadence (steps/min), mean step length (cm) which is equal to the length of a toe off to the opposite foot heel contact, step width (cm), time spent in double support (s), and the within trial step length variability. Results were analyzed by the STATISTICA computerized statistical package using a mixed model 3 groups X 3 conditions X 5 trials ANOVA. In order to determine where the significant differences found in the ANOVA's occurred, Tukey's Honest Significant Difference (HSD) post hoc procedure was employed.

4.3 Results

4.3.1 Velocity of gait is affected by group and condition

Analysis of the velocity of the Freezers, Shufflers and Controls revealed a main effect of group ($F_{(2,44)} = 10.12$, $p < 0.001$) (Fig. 4.1). Post hoc analysis confirmed that Freezers ($\bar{X} = 76.49$ cm/s, $SD = 25.87$) walked significantly slower as compared to the Shufflers ($\bar{X} = 93.04$ cm/s, $SD = 12.42$) ($p < 0.037$) and the Controls ($\bar{X} = 105.56$ cm/s, $SD = 13.15$) ($p < 0.001$) (Table 4.2). There was no significant difference found in the walking velocity of the Shufflers as compared to the Control group.

A significant interaction was found between group and condition ($F_{(4,88)} = 2.52$, $p < 0.0465$) (Fig. 4.2). Post hoc analysis determined the existence of a number of significant differences within this interaction. In contrast to self paced walking through the narrow doorway without visual cues ($\bar{X}$ = 78.91 cm/s, *SD* = 32.6), Freezers significantly decrease their gait velocity when laser visual cues are available ($\bar{X}$ = 59.13 cm/s, *SD* = 25.98) ($p < 0.008$) but do not significantly alter gait velocity when ground lines are provided ($\bar{X}$ = 97.43 cm/s, *SD* = 25.27). In contrast to the self-paced walking through the narrow door ($\bar{X}$ = 105.59 cm/s, *SD* = 18.67), Shufflers were also found to show no increase in gait velocity when using ground lines ($\bar{X}$ = 99.36 cm/s, *SD* = 12.89) but a similar significant decrease with use of the laser device ($\bar{X}$ = 74.16 cm/s, *SD* = 20.68) ($p < 0.001$). Healthy control participants displayed the same pattern as observed with Shufflers, as their self-paced walk through the narrow doorway ($\bar{X}$ = 119.02 cm/s, *SD* = 11.96) was significantly faster than observed when using the laser ($\bar{X}$ = 86.86 cm/s, *SD* = 22.98) ($p < 0.001$) and not significantly different from the ground lines condition ($\bar{X}$ = 110.79 cm/s, *SD* = 12.83) (Table 4.3). Overall, all participants decreased their gait velocity when using the laser device. It is also important to note that Freezers were most affected by the narrow doorway and walked significantly slower as compared to both Shufflers ($p < 0.001$) and Controls ($p < 0.001$). The gait velocity of the Shufflers during self-paced walk through the narrow doorway was not significantly different from the Controls. With use of visual cues the significant difference found between the Freezers and the Shufflers disappeared. This is evident as there was no significant difference between the two groups when either ground lines or the laser line device was employed. However, there remains a significant difference gait velocity in Freezers compared to Controls in both of these conditions as Freezers walked slower in the Ground ($p < 0.001$) and Laser ($p < 0.001$) conditions.

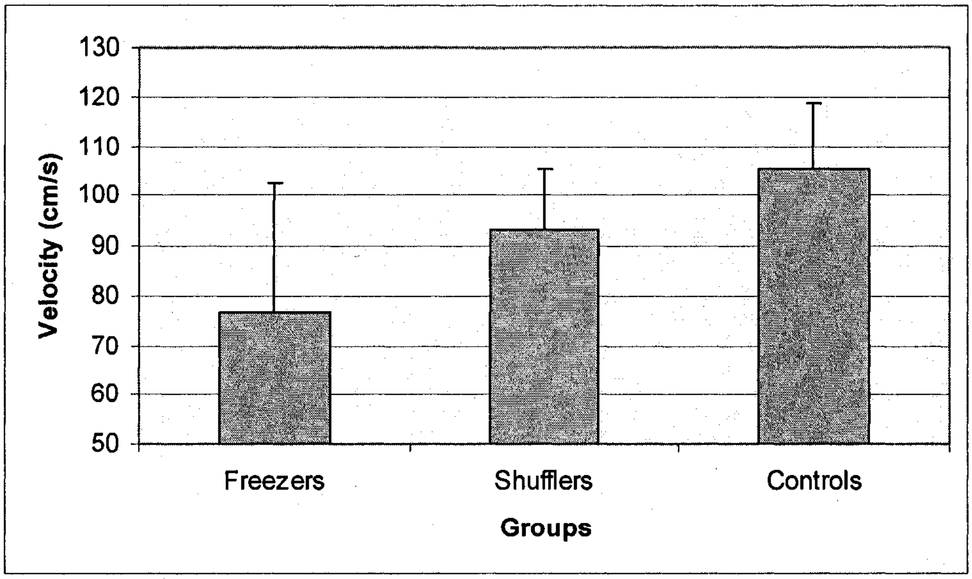

Figure 4.1 Comparison of velocity of the three groups

Table 4.2
Velocity (cm/s) by group

Group	Mean	SD
Freezers	76.49[1,2]	25.87
Shufflers	93.04[1]	12.42
Controls	105.56[2]	13.15

1,2 Significant differences between the groups were determined by Tukey's HSD.

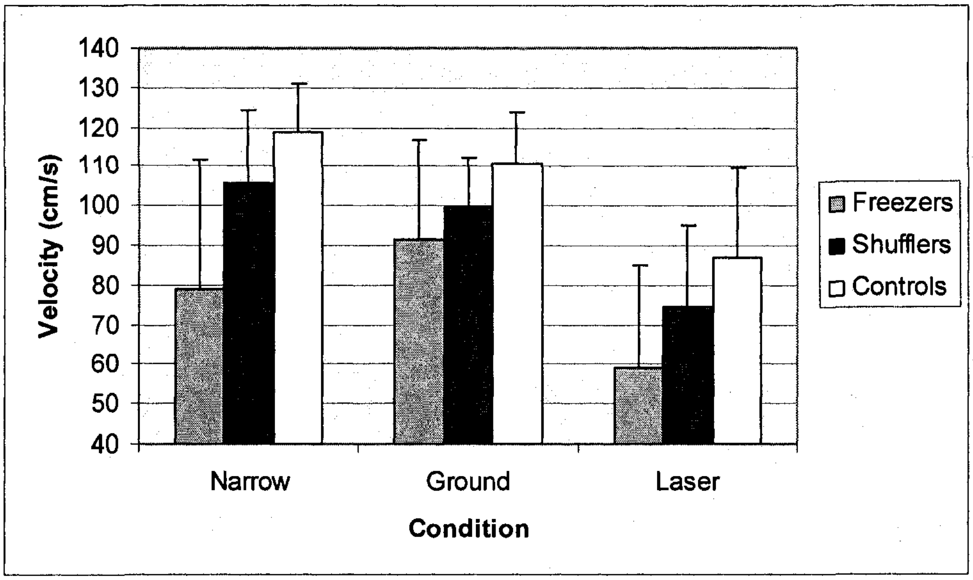

Figure 4.2 Examination of velocity reveals an interaction of group and condition

Table 4.3
Velocity (cm/s) by group and condition

Group – Condition	Mean	SD
Freezers – Narrow	78.91[1-3]	32.6
Freezers – Ground	97.43[4]	25.27
Freezers – Laser	59.13[1,6]	25.98
Shufflers – Narrow	105.59[2]	18.67
Shufflers – Ground	99.36	12.89
Shufflers – Laser	74.16[2]	20.68
Controls – Narrow	119.02[3,5]	11.96
Controls – Ground	110.79[4]	12.83
Controls – Laser	86.86[5,6]	22.98

1-6 Significant differences between the groups and conditions were determined by Tukey's HSD

4.3.2 Freezers take significantly shorter steps in narrow doorway condition

As expected, there was a significant difference in the mean step lengths when comparing the three groups. A main effect of group was found ($F_{(2,44)} = 17.48$, $p < 0.001$) and post hoc analysis confirmed that Freezers ($\bar{X}$ = 50.95 cm, SD = 11.09) took significantly shorter steps as compared to both Shufflers ($\bar{X}$ = 61.27 cm, SD = 5.28) ($p < 0.002$) and Controls ($\bar{X}$ = 67.18 cm, SD = 5.53) ($p < 0.001$) (Fig. 4.3) (Table 4.4). The step length of the Shufflers did not significantly differ from that observed in the healthy participants.

This was superseded by a significant interaction between group and condition ($F(4,88) = 14.65$, $p < 0.001$) (Fig. 4.4). Post hoc analysis confirmed a number of key differences. Freezers ($\bar{X}$ = 42.53 cm, SD = 15.4) had a significantly shorter step length in the Narrow doorway condition as compared to Shufflers ($\bar{X}$ = 55.4 cm, SD = 7.72) ($p < 0.001$) and Controls ($\bar{X}$ = 62.71 cm, SD = 6.6) ($p < 0.001$). This effect was also found in the Laser condition where the Freezers group step length ($\bar{X}$ = 44.18 cm, SD = 17.68) was again significantly smaller than both Shufflers ($\bar{X}$ = 61.65 cm, SD = 9.47) ($p < 0.001$) and Controls ($\bar{X}$ = 71.84 cm, SD = 10.29) ($p < 0.001$). Importantly, there was no difference in the step lengths of the three respective groups when they were using ground lines as a visual step cue. Freezers experienced a significant increase in step length in the ground line condition ($\bar{X}$ = 66.15 cm, SD = 2.86) as compared to both the Narrow ($p < 0.001$) and Laser ($p < 0.001$) conditions. There was also a significant increase in step length observed in Shufflers in the Ground condition ($\bar{X}$ = 66.75 cm, SD = 1.07) as compared to the Narrow condition ($p < 0.001$) (Table 4.5). It is also worth noting that neither Freezers nor Shufflers revealed any significant improvements in step length with the laser device above the self-paced walk through the narrow doorway. However, healthy controls did exhibit an increased step length in the laser condition as compared to the narrow doorway condition ($p < 0.015$).

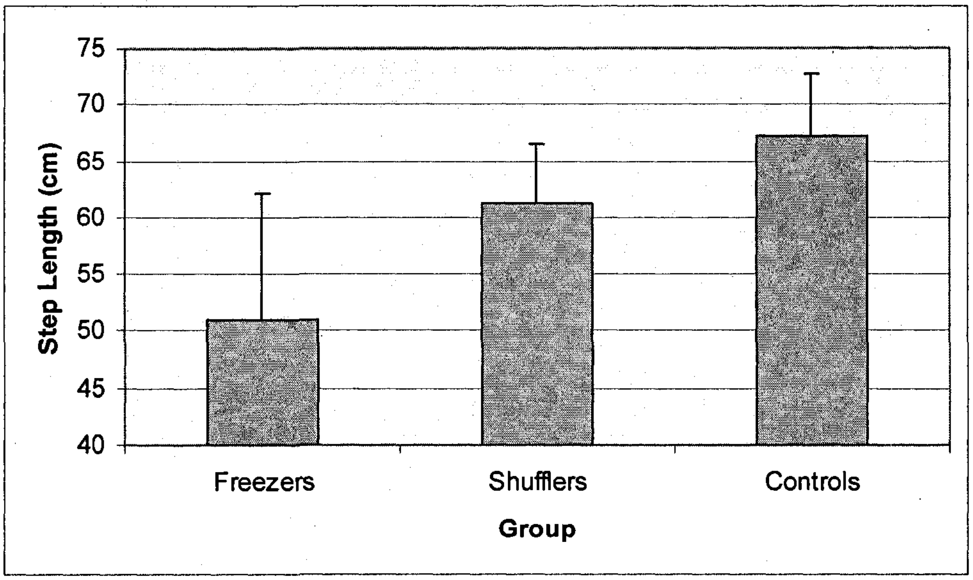

Figure 4.3 Comparison of groups revealed a difference in step lengths

Table 4.4
Step length (cm) by group

Group	Mean	SD
Freezers	50.95[1,2]	11.09
Shufflers	61.27[1]	5.28
Controls	67.18[2]	5.53

1,2 Significant differences between the groups were determined by Tukey's HSD.

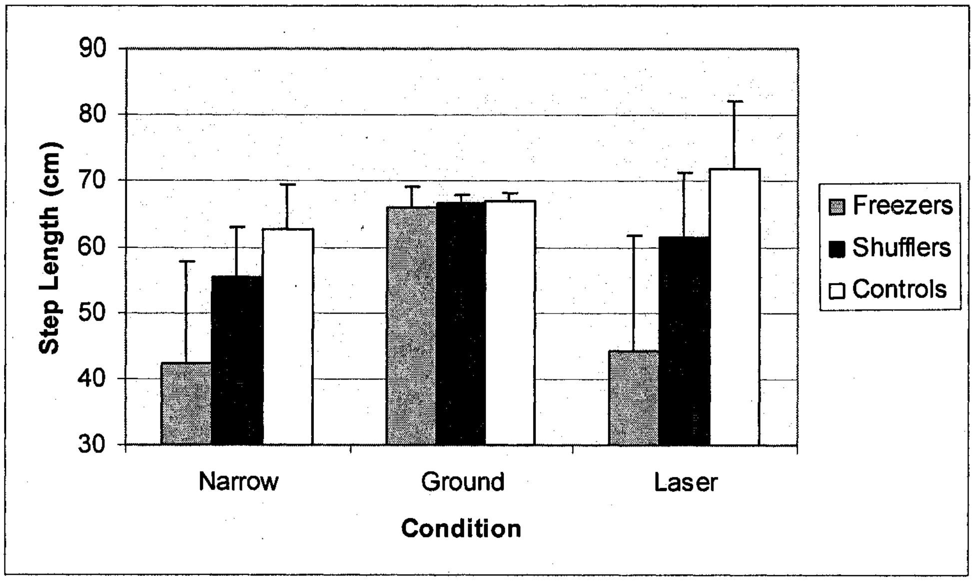

Figure 4.4 Significant interaction of group and condition in step length

Table 4.5
Step length (cm) by group and condition

Group – Condition	Mean	SD
Freezers – Narrow	42.53[1-3]	15.4
Freezers – Ground	66.15[1,5]	2.86
Freezers – Laser	44.18[5-7]	17.68
Shufflers – Narrow	55.4[2,4]	7.72
Shufflers – Ground	66.75[4]	1.07
Shufflers – Laser	61.65[6]	9.47
Controls – Narrow	62.71[3,8]	6.6
Controls – Ground	66.98	1.26
Controls – Laser	71.84[7,8]	10.29

1-8 Significant differences between the groups and conditions were determined by Tukey's HSD

4.3.3 Effect of visual cues on cadence

Examination of cadence revealed a main effect of condition ($F_{(2,88)} = 98.29$, $p < 0.001$) (Fig. 4.5). Post hoc analysis confirmed that all participants significantly decreased their number of steps per minute in the Laser condition ($\bar{X}$ = 75.54 steps/min, *SD* = 16.95) as compared to both the Ground ($\bar{X}$ = 90.5 steps/min, *SD* = 15.85) ($p < 0.001$) and Narrow ($\bar{X}$ = 112.67 steps/min, *SD* = 14.0) ($p < 0.001$) conditions (Table 4.6). Cadence was also significantly decreased when participants used ground lines as a visual step cue as compared to the baseline walk through the narrow door.

A significant interaction for cadence across group and condition, was found ($F_{(4,88)} = 3.85$, $p < 0.007$) (Fig. 4.6). Post hoc analysis indicated that the cadence of Freezers did not significantly differ within each condition from Shufflers. However, Freezers ($\bar{X}$ = 80.6 steps/min, *SD* = 20.85) in comparison to Controls ($\bar{X}$ = 99.12 steps/min, *SD* = 10.64) significantly decreased their cadence in the Ground condition ($p < 0.018$). Freezers also significantly decreased their cadence from the levels observed in the self-paced walk through the narrow doorway ($\bar{X}$ = 109.78 steps/min, *SD* = 21.47) in both the Ground ($p < 0.001$) and Laser conditions ($\bar{X}$ = 81.17 steps/min, *SD* = 17.36) ($p < 0.001$) (Table 4.7). As well, Shufflers displayed a significantly decreased cadence in both the Ground and Laser condition as compared to the self-paced walk through the narrow doorway ($p < 0.001$). The same pattern was evident in the healthy participants as their cadence was lower in the Ground ($p < 0.036$) and the Laser ($P < 0.001$) conditions as compared to the Narrow condition.

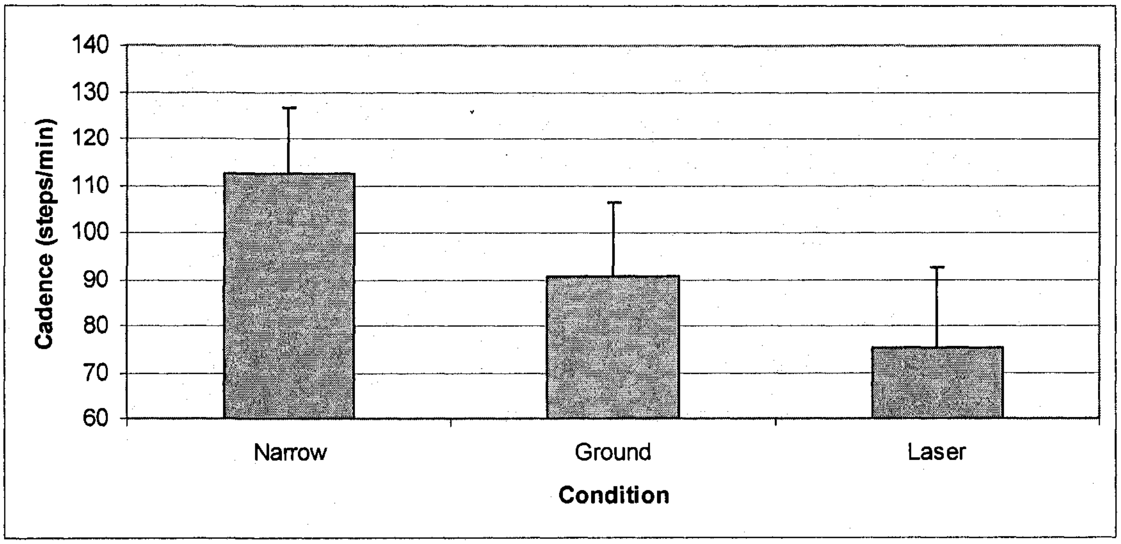

Figure 4.5 Cadence significantly differs across conditions

Table 4.6
Cadence (steps/min) by condition

Condition	Mean	SD
Narrow	112.67[1,2]	14.0
Ground	90.5[1,3]	15.85
Laser	75.54[2,3]	16.95

1-3 Significant differences between the conditions were determined by Tukey's HSD.

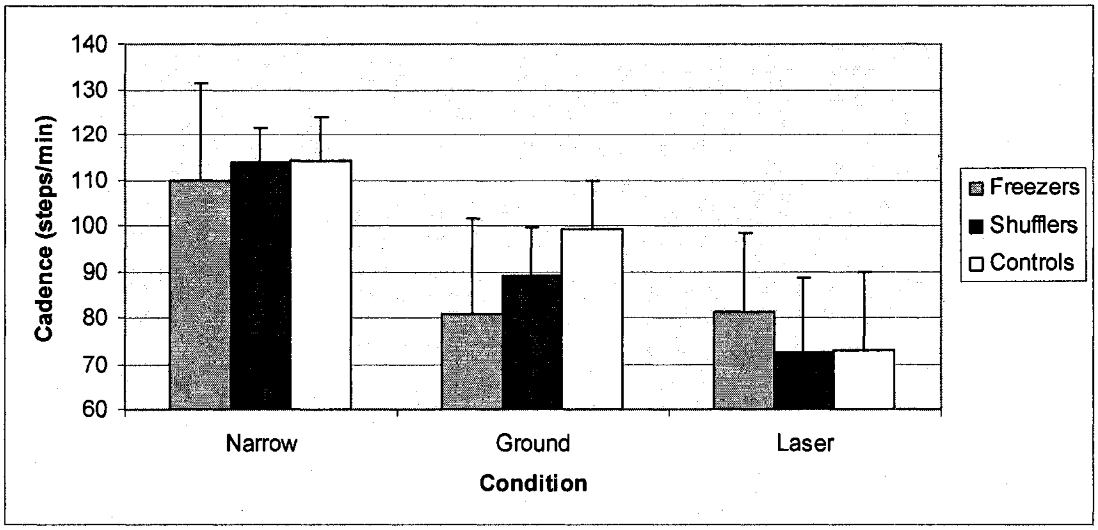

Figure 4.6 Cadence displays an interaction of group and condition

Table 4.7
Cadence (steps/min) by group and condition

Group – Condition	Mean	SD
Freezers – Narrow	109.78[2,4]	21.47
Freezers – Ground	80.6[1,2]	20.85
Freezers – Laser	81.17[4]	17.36
Shufflers – Narrow	113.87[3,5]	7.89
Shufflers – Ground	89.18[3]	10.47
Shufflers – Laser	72.5[5]	16.14
Controls – Narrow	114.17[6,7]	9.86
Controls – Ground	99.12[1,6]	10.64
Controls – Laser	72.94[7]	17.05

1-7 Significant differences between the groups and conditions were determined by Tukey's HSD

4.3.4 Freezers have increased step length variability

A main effect of group was found when examining within trial step-to-step variability of step length ($F_{(2,44)} = 7.20$, $p < 0.002$) (Fig. 4.7). Post hoc analysis revealed that Freezers ($\bar{X}$ = 3.79 cm, *SD* = 2.48) were significantly more variable as compared to the Control group ($\bar{X}$ = 1.60 cm, *SD* = 0.74) ($p < 0.002$). A trend almost reaching significance was also found showing that the step length of Freezers was slightly more variable as compared to Shufflers ($\bar{X}$ = 2.43 cm, *SD* = 1.19) ($p < 0.062$) (Table 4.8). A main effect of condition was also identified ($F_{(2,88)} = 16.62$, $p < 0.001$) (Fig. 4.8). Post hoc analysis revealed that participants had significantly greater step length variability in the Laser condition ($\bar{X}$ = 4.02 cm, *SD* = 2.77) as compared to both the Narrow ($\bar{X}$ = 2.28 cm, *SD* = 3.38) ($p < 0.001$) and Ground condition ($\bar{X}$ = 1.46 cm, *SD* = 0.95) ($p < 0.001$) (Table 4.9). There were no significant interactions between group and condition identified with regards to within trial step length variability.

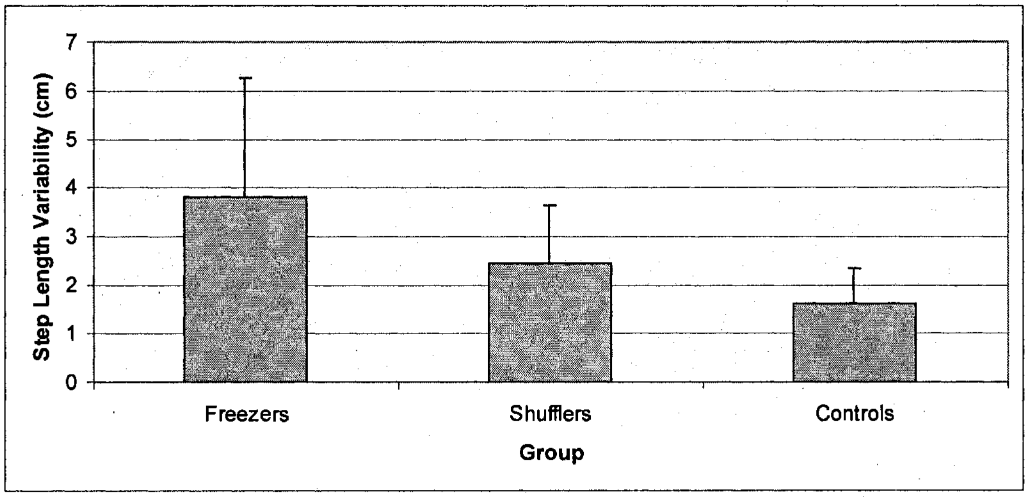

Figure 4.7 Freezers have increased step length variability

Table 4.8

Step length variability (cm) by group

Group	Mean	SD
Freezers	3.79[1]	2.48
Shuffler	2.43	1.19
Controls	1.60[1]	0.74

1 Significant difference between the groups was determined by Tukey's HSD.

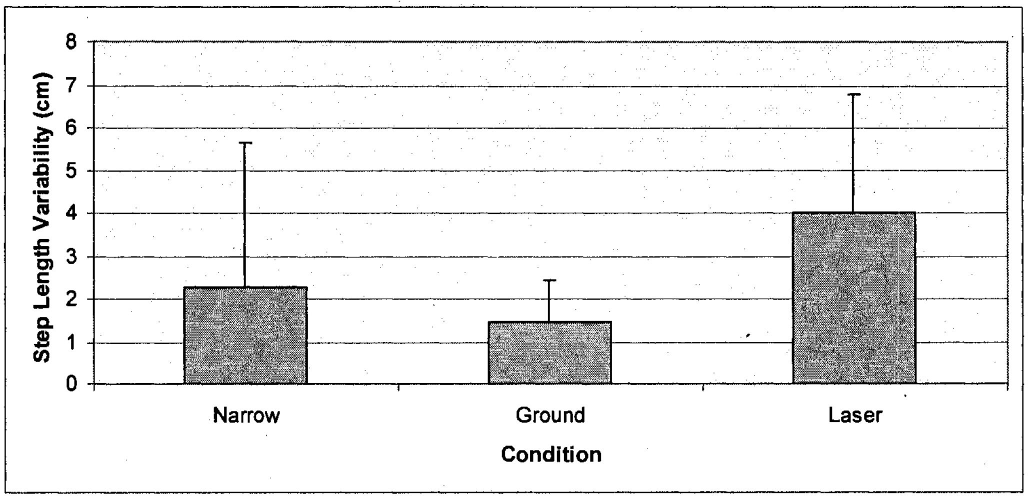

Figure 4.8 Laser condition elicits increased step length variability in participants

Table 4.9
Step length variability (cm) by condition

Condition	Mean	SD
Narrow	2.28[1]	3.38
Ground	1.46[2]	0.95
Laser	4.02[1,2]	2.77

1,2 Significant differences between the conditions were determined by Tukey's HSD.

4.3.5 Time spent in double support differs among groups and conditions

The amount of time that individuals spent in the double support phase of the gait cycle differed significantly. A main effect of group was found when comparing double support ($F(2,44) = 3.76$, $p < 0.031$) (Fig. 4.9). Post hoc analysis confirmed that Freezers ($\bar{X} = 0.52$ s, $SD = 0.46$) spent significantly more time in double support as compared to Controls ($\bar{X} = 0.27$ s, $SD = 0.06$) ($p < 0.036$) (Table 4.10). The time Shufflers spent in double support did not differ significantly as compared to the other two groups.

A main effect of condition was also found ($F_{(2,88)} = 4.32$, $p < 0.016$), which after post hoc analysis confirmed that all participants spent an increased amount of time double support in the Laser condition ($\bar{X} = 0.46$ s, $SD = 0.27$) as compared to the Ground condition ($\bar{X} = 0.31$ s, $SD = 0.19$) ($p \leq 0.022$) (Fig.4.10). A trend almost reaching significance was observed that suggested that all participants also spent more time in double support in the Laser condition as compared to the Narrow condition ($\bar{X} = 0.33$ s, $SD = 0.53$) ($p < 0.058$) (Table 4.11).

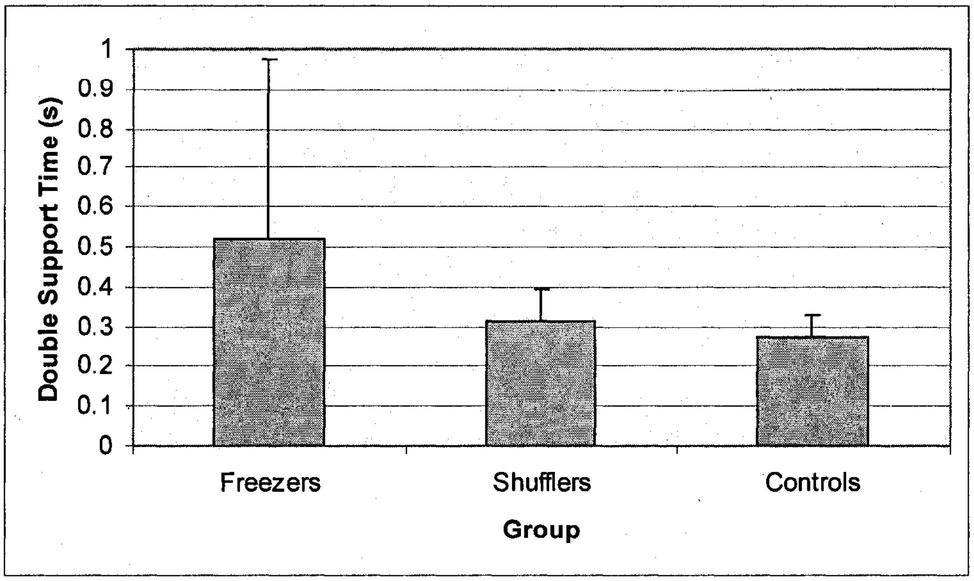

Figure 4.9 Main effect of group apparent when examining double support time

Table 4.10
Double support time (s) by group

Group	Mean	SD
Freezers	0.52[1]	0.46
Shufflers	0.31	0.08
Controls	0.27[1]	0.06

1 Significant difference between the groups was determined by Tukey's HSD.

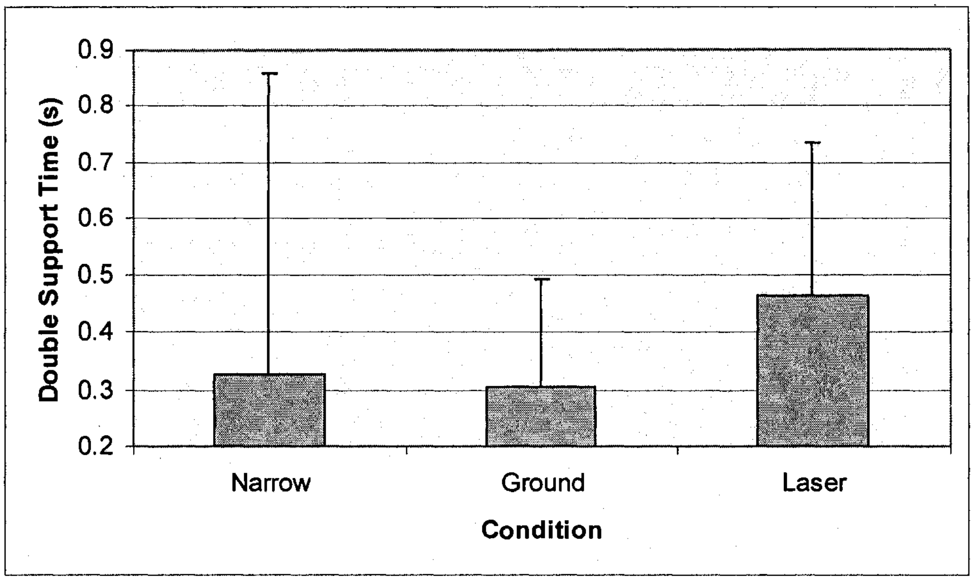

Figure 4.10 Laser demonstrates an increased double support time

Table 4.11

Double support time (s) by condition

Condition	Mean	SD
Narrow	0.33	0.53
Ground	0.31[1]	0.19
Laser	0.46[1]	0.27

1 Significant difference between the conditions was determined by Tukey's HSD.

4.4 Discussion

This experiment investigated the influence of external visual cues on improving the gait of individuals with PD who experience FOG in a narrowed doorway situation that might normally lead to an FOG episode. Overall, the results supported the hypothesis that these individuals were able to improve and normalize some characteristics of gait to levels comparable to that seen in non-FOG individuals with PD and healthy control participants with use of ground lines. The laser line device was not as effective and the same level of gait improvement was not evident when it was used as the source of visual cue.

4.4.1 Ground lines effective in normalizing gait of individuals with PD experiencing FOG

A number of key results leads to the indication that ground lines effectively improve the gait of those experiencing FOG leading up to an obstacle which would normally induce an FOG episode. Most importantly, the ground lines were found to lead to a significant improvement in step length as compared to the steps recorded in the absence of any type of visual cue. This increased step length when coupled with the significantly decreased cadence led to the statistically similar velocity observed in the Freezers between the Narrow and Ground conditions meaning that they were likely using a more stable and safe gait pattern. The short shuffling steps which are common in PD and even more debilitating in individuals who experience FOG are being replaced through the use of ground lines by a more normalized gait pattern which is increasing similar to that observed in the control participants. This same improvement was not found with use of the laser line device as the external visual cue. They continued to take shorter steps and their gait velocity decreased as a result of their decreased cadence. The reason for this difference in gait performance in respect to the type of visual cue is as of yet unknown.

It was hypothesized that if visual step cues had the ability to improve the gait of individuals with PD subject to FOG episodes, then the type of cue presented would be inconsequential. However, this was not the case as the benefits of the ground lines disappeared with use of the laser device. The laser visual cue was presented in an optic flow pattern that is in the same direction to the optic flow information received from the environment in which the initial projection was in front of their feet, and then scanned forwards, stopping at a step length distance relative to the participants' height. It is possible that the additional optic flow information of the laser device was a hindrance to these individuals with PD who experience FOG. It has been well documented that an overload of environmental stimuli can lead to gait abnormalities in patients with PD, especially those with documented FOG episodes (Nieuwboer et al., 2004; Okuma, 2006; Schaafsma et al., 2003). Instead of leading to an improvement in gait, the laser device which presented a visual cue in sequence with additional optic flow information may require more attentional resources than the individuals with PD experiencing FOG have at their disposal. Therefore the gait in these participants returned to levels observed without the benefit of any visual cues.

4.4.2 Increasingly unstable gait demonstrated in those with FOG and with use of laser

The laser line device led to an increased amount of time spent in double support and within trial step length variability as compared to the ground lines and narrow doorway conditions. These results could indicate two things which are that participants have experienced an increase in instability, or that they are exhibiting a greater attempt to control their gait pattern. This information coincides with the results previously mentioned which demonstrated that an increased number of visual cues, and therefore external information that requires attention, leads to an increasingly unstable gait pattern. The ground lines demonstrated no significant change in any of the gait stability variables as compared to the narrow doorway condition. The main differences between these two conditions were that with ground lines they had ample time to devise a step pattern before reaching the ground lines. However, with the laser participants faced a time constraint as they were forced to only plan one step at a time in sequence with the presentation of each laser line. Also, the laser presented an additional form of optic flow information and this may be what is leading to an increasingly unstable gait pattern and therefore an increased risk of loss of balance and falls when used by individuals with PD who experience FOG.

4.4.3 Improvement in gait and prevention of FOG dependant on visual cue type

In chapter 2 it was found that individuals with PD when presented with visual cues were able to normalize their gait pattern as long as the cues focused their attention on their step pattern. The type of cue presented to the participants was found to be primarily inconsequential in the observed gait improvement. However, in this experiment it was found that those individuals with PD who experience FOG are more selective in the type of cue presented. Dynamic visual cues presented in an optic flow pattern were not successful in improving the gait of Freezers. Therefore, it appears that when faced with a situation with an upcoming decreased amount of perceived space, a type of visual cue that can be examined further ahead of time is required in order for gait to be improved. An increase in attention and therefore conscious control of gait is no longer sufficient, but instead pre-planned conscious control is required in those individuals with gait disabilities for improvement to be observed. This information should be utilized while attempting to devise a method to prevent FOG episodes in these individuals with PD.

4.4.4 Clinical implications

The new information from these results of this experiment is that visual cues are able to improve the abnormal gait observed within individuals with PD who experience FOG prior to a possible freezing episode. More importantly however, is the fact that this gait improvement is dependant on the type of visual cue presented to the individual. This information is imperative when developing strategies that attempt to prevent freezing episodes and regulate gait disabilities in these individuals. The thought that additional optic flow might lead to normalization of gait was shown to be flawed as the increased attentional demands from the laser device decreased gait performance to levels comparable to those observed at baseline. More work is necessary to realize hopes of developing an effective visual cue in the prevention of FOG that is portable and might be used outside of the laboratory and home environment.

4.4.5 Limitations

As mentioned in chapter 3, the relatively few steps that were able to be recorded on the lead up to the narrow doorway. It was again only possible to monitor the 4-6 steps prior to reaching the doorway, depending on the height, and therefore step length, of the individual. Again, a longer carpet would be useful in order to measure the gait of participants for a longer amount of time and from an increased distance back from the doorway in order to receive a more complete understanding of the underlying mechanisms of FOG and potential benefits derived from the use of visual cues.

The attachment of the laser device might again be leading to the increased variability in gait observed in participants when using the device for step cues. The lengthwise size of the device caused it to rest differently on each participant depending on waist dimensions and may cause some variation in the projection distance of the laser. The angle was again monitored with each individual in order to make the length of the laser projection as close to constant for each trial relative to the height of the person. A large amount of torso movement might also be responsible for the increase in gait variability observed with use of the laser device as this would cause the line to be projected side to side with each step instead of completely straight ahead. Future work in this area should employ the use of a device that uses both a more stable attachment and a wider laser line.

4.4.6 Conclusion

This experiment demonstrated the effects of different forms of visual step cues on the gait of individuals with PD who experience FOG. It was demonstrated that ground lines are effective in improving the gait of these participants in preceding a situation which would normally induce a freezing episode and therefore decreased gait performance. A portable laser device that projects visual cues in sequence with optic flow was found to be ineffective in these same individuals, which leads to the conclusion that an increased amount of information was causing a decrease in gait performance. The consistent performance with both cues that was observed in the individuals with PD experiencing gait abnormalities absent of FOG implies that they are better equipped to deal with increased attentional demands as compared to Freezers.

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CHAPTER 5

GRAND DISCUSSION

5.1 Introduction

The overall purpose of this thesis was to investigate how vision contributes to gait in Parkinson's disease (PD), with the secondary objective of gaining a greater understanding of the mechanisms that potentiate freezing of gait (FOG). Determining such mechanisms might help develop a greater appreciation of how vision might be involved in circumventing basal ganglia dysfunction. A number of visual cues were examined to determine the viability of these cues in improving abnormal gait patterns demonstrated by these individuals with PD, including FOG and the less severe shuffling step pattern. Impairments in gait are common in PD and often have a detrimental effect on the quality of life of these individuals. Therefore, this thesis aimed to gain knowledge into the mechanisms behind these gait impairments and the driving factor behind the beneficial effects observed from the use of visual cues. The experiments described in chapters 2, 3, and 4 were constructed to address these issues. Chapter 2 evaluated how visual cues help improve gait performance in PD, while chapter 3 examined how vision might contribute perceptually to gait impairments such as FOG. Chapter 4 evaluated the effects of visual cues on gait in a condition that has been found to negatively affect gait performance. This chapter will summarize the major findings from the previous chapters.

5.2 Individuals with PD require conscious control of gait

Chapter 2 examined the effect of visual cues on gait of individuals with PD as compared to healthy control participants. The overall goal was to determine whether gait improvement observed with use of visual cues is caused by focusing attention on gait, or through the additional sensory feedback available with the optic flow provided by the ground lines. In the ground line condition, visual step cues provided normal optic flow (i.e. optic flow in the same direction as the optic flow received from other objects in the environment). In contrast, the laser device projected visual cues in a reverse optic flow direction, opposite to the regular optic flow received from the environment. Therefore, it was predicted that if both conditions (ground lines and reverse optic flow) produced increased step length and velocity, while also normalizing cadence then the results would suggest that gait improvements should be attributed to anything that causes an increased attentional focus on producing discrete steps. Alternatively, if the laser device did not lead to similar improvements, then the regular optic flow received from the cues is imperative to the gait improvement observed in PD with use of visual step cues.

The results obtained in chapter 2 provided evidence suggesting that the gait disabilities common in PD can be regulated with use of visual cues by focusing attention on gait. Specifically, an improvement in step length and a normalization of cadence with respect to velocity was observed with use of visual cues in both the ground lines and laser lines conditions. The ground lines that have been found to improve gait in a number of other studies also led to an increase in step length and a more normal cadence with respect to velocity (Azulay, Mesure, & Blin, 2006; Lewis, Byblow, & Walt, 2000; Morris, Iansek, Matyas, & Summers, 1996; Nieuwboer et al., 2007). These results supported the hypothesis that the demonstrated benefit in gait obtained through the use of visual cues is due to gait becoming a more conscious endeavor. Gait is normally an autonomic function that requires the focus of limited attentional resources. However, individuals with PD seem to lack the ability to automatically regulate their gait pattern. This was supported by the data showing a decreased step length and elevated cadence with respect to velocity during a self-paced baseline walk. Both the ground lines and the reverse optic flow laser device were able to improve the gait of individuals with PD. The fact that visual cues from the device led to gait normalization similar to that observed when ground lines were employed, despite the lack of a regular optic flow pattern, demonstrates that focusing attention on gait can lead to an improvement in those individuals that are unable to unconsciously regulate gait. The same gait improvement was not found when the laser device was employed in an otherwise dark environment. If an increased attentional focus was the sole cause of the improvement observed with use of visual cues, then improvements should be maximized in a condition in which this cue was the only attentional requirement. This was not the case, and therefore it might be argued that the cues also are focusing attention on the position of the limbs, thereby improving the sense of proprioception that may possibly be damaged in PD (Almeida et al., 2005; Jacobs & Horak, 2006). It is most important to note that both of these theories reach the conclusion that individuals with PD require conscious control of their gait pattern in order to overcome the gait deficits which are prevalent in PD. The distinction between these two theories is that one points to attention as the key while the other maintains that the increase in attention is not enough to drive the improvement, but instead the heightened attention must lead to an increase in proprioceptive feedback.

5.3 Individuals with PD experiencing FOG differently perceive space

The experiment described in chapter 3 examined the individuals with PD affected with the more extreme disorder, FOG. Non-FOG individuals with PD that are affected with less severe gait impairments as well as healthy participants were tested in addition to those experiencing FOG in a number of conditions that altered the size of an upcoming doorway. The obtained results suggested that FOG individuals alter characteristics of their gait when approaching a narrow doorway in a different pattern than that observed in other participants. Their step length becomes significantly shorter and they experience an increased within-trial variability of step length. The non-FOG individuals experience gait alterations to a lesser degree than that observed in the FOG group; their base of support is narrower than the FOG group in the normal and wide doorway conditions but is increased to a level observed in the FOG group when traveling towards the narrow doorway. Healthy participants did not experience any significant alterations in gait variables with regards to doorway condition.

Hence, the manipulation of the size of an upcoming doorway and therefore different amounts of perceived future space, evidently led to changes in the gait pattern of individuals with PD who experience FOG. The ability to accurately perceive the amount of space, and therefore a certain degree of visuospatial ability, appears to be more greatly affected in those individuals with PD who are subject to FOG. This suggests an important perceptual difference between the PD observed within those who experience FOG and non-FOG individuals with PD. The degree of damage of the caudate nucleus might play an important role in this disparity. The caudate nucleus is part of the basal ganglia acting as the striatal receptor receiving significant input from the posterior parietal cortex (Brandt, Shpritz, Munro, Marsh, & Rosenblatt, 2005). The posterior parietal cortex processes sensory information regarding where objects are located in space in relation to body position and codes the location of these objects (Brandt et al., 2005). Therefore, increased damage to the caudate nucleus in PD could negatively affect a person's ability to accurately perceive upcoming space and manipulate movement effectively. This may be an important mechanism that leads to possible FOG episodes.

5.4 Effect of visual cues on FOG

In chapter 4, an effort was made to combine the two major perspectives evaluated in chapters 2 and 3. The experiment described in chapter 4 examined the effect of visual cues on gait leading up to an enclosed space. Visual cues were presented in the form of ground lines, as well as through a laser device which provided regular optic flow cues, similar to the direction of flow received from the ground lines discussed in chapter 2. In this chapter, the direction of optic flow was found to be inconsequential to gait improvement. In order to approximate normal optic flow, the laser device was presented in the direction of traditional optic flow in order to determine the influence of visual cues in potentially stressful situations (i.e. the narrow doorway). Individuals with PD who experience FOG were tested in order to determine if these cues could improve gait disabilities that would normally occur when traveling towards a narrow doorway. Kompoliti et al. also examined the effects of visual cues on FOG, however only measured the occurrence of FOG episodes during a normal walk (Kompoliti, Goetz, Leurgans, Morrissey, & Siegel, 2000). The current experiment analyzed other aspects of gait such as step length, velocity, cadence, double support time, and within-trial step length variability.

The results of obtained from this experiment demonstrated that with use of the ground lines, individuals with PD who experience FOG were able to improve many gait characteristics to levels observed in the non-FOG individuals with PD, and healthy participants. The same improvement was not evident with use of the laser device where gait actually became more variable while using the laser as a visual step cue. This suggests that in situations in which the amount of upcoming space is limited, gait improvement caused by visual cues is type dependant. Ground lines provide a more stable visual cue that more easily fit into the context of the surrounding environment and can be observed well ahead of time. Chapter 2 demonstrated that as long as attention is focused on gait pattern, an improvement was evident. Testing this same idea leading up to a narrow doorway shows that when traveling up to and through an enclosed space, a visual cue that can be examined further ahead of time is required in order for gait to be improved. This suggests that the visual information and optic flow received from the cue must be continuous. An increase in attention and therefore conscious control of gait is no longer sufficient to improve gait. Instead pre-planned conscious control may be required in those individuals with gait disabilities for improvements to be observed. Another possible reason for the decrease in performance with the laser device was that the upcoming doorway required some attentional focus. This may have caused the individual with PD experiencing FOG to exceed their attentional capacity. This overload has a negative effect on gait in PD and therefore may be causing the decrease in performance with use of the laser device._ This increase in attentional demands is also possibly heightening the difficulty to use the enhanced proprioceptive signals derived through use of the cues, as the narrow doorway is demanding attentional resources that could otherwise be allotted gait pattern alterations.

Results obtained in chapter 4 also suggested that the regular direction of optic flow provided by the laser device was not as effective in improving gait as the reverse optic flow provided by the device described in chapter 2. However, this difference may have been caused by the upcoming narrow doorway as the reverse optic flow was tested in a situation without any spatial constraints. Therefore, both directions of optic flow may elicit similar results when tested under identical circumstances.

5.5 Conclusion

The results of this thesis provide evidence that the gait improvement observed in individuals with PD through the use of visual cues can be mainly attributed to the focus of attention on gait, thereby forcing more conscious control on the regulation of gait. Results obtained showing that visual cues are not effective in a dark environment point towards the role of visual cues in increasing our attentiveness to proprioceptive information, including the location and methods by which the lower limbs are moving through space. Also, it was demonstrated that individuals with PD who experience FOG are differently affected by enclosed spaces when compared to non-FOG individuals with PD. This suggests that differing degrees of neurological damage might be an indicator of the presence of FOG in PD. Also, these results demonstrated that in the case of traveling through an enclosed space, vision may have a negative effect on gait in those experiencing FOG. It appears that at a certain level of attentional demands, confined spaces or obstacles in the environment cause a perceptual impairment and overrule the focus on proprioception that is normally obtained through the use of visual cues. Another key finding was that the most effective type of visual cue in the improvement of gait impairments in PD are transverse ground lines. Visual cues in the form of laser lines were not able to improve gait in PD to levels observed with use of the ground lines. The laser lines led to a gait improvement in situations without any additional attentional demands. However, in stressful situations, such as when traveling towards a narrowed space, the ground lines were the only type of visual cue found to be consistently effective in the maintenance of a normal gait pattern. Lastly, visual cues that allow for a pre-planned step pattern were shown to be capable of improving the gait disabilities observed in individuals with PD who experience FOG leading up to a possible FOG episode. Future visual aid devices should be designed in order to decrease the amount of required last second planning and instead allow for pre-planning of future movements.

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