

AN INVESTIGATION OF GAIT AND GAZE IN PARKINSON'S DISEASE
THROUGH A CLUTTERED ENVIRONMENT

by

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ABSTRACT

The overall purpose of the current thesis was to investigate how visual behaviours in cluttered environments might affect gait in Parkinson's disease (PD). Freezing of gait (FOG) is one of the most debilitating symptoms of PD, involving the sudden inability to initiate or continue walking. While several FOG triggers have been previously investigated, clutter has been anecdotally reported as a FOG trigger but has not yet been verified in laboratory settings. It is also important to recognize the link between the visual system and walking behaviours, and hence it is critical to consider if impaired eye movements may influence gait behaviour. While some eye movement abnormalities have been identified in PD, investigations have not yet been conducted regarding how eye movements during locomotion may influence gait disturbances in PD. Thus, the three articles within this thesis attempted to answer the following research questions:

- ❖ Does the location of clutter with respect to a travel path provoke gait disturbances (i.e. freezing of gait) in PD?
- ❖ Are eye movement behaviours in PD-FOG different from healthy individuals?
- ❖ Are eye movements linked to gait behaviours in PD-FOG?

The first article examines how gaze behaviours influence gait in healthy older adults when walking through a cluttered environment with clutter located close to (direct) or far from (indirect) the travel path. Direct clutter was found to induce a more conservative gait pattern characterized by reduced step length and velocity, and increased step width. Gaze analyses revealed a predominant end goal fixation when clutter was located far from the path, suggesting a feedforward strategy for control of gait. However, when clutter was located close to the path, individuals fixated the travel path for the first half of the path, and then the end goal for the remainder. It seems that older adults started with an on-line feedback processing method to collect information about the rest of the path, and then switched to feedforward control when enough feedback about the approaching environment was collected. Gait

patterns in direct clutter also revealed a more cautious behaviour characterized by decreased step length and velocity, and increased step width.

The subsequent chapter investigates how gait behaviours are influenced in PD when walking through cluttered environments. In order to investigate the role of clutter as a freeze-provoking situation, three groups were analyzed: healthy age-matched control participants, Parkinson's disease patients without FOG, and Parkinson's disease patients with FOG. Participants walked through an environment with clutter close to the path (direct) or far from the path (indirect). FOG was qualitatively assessed through video recordings and confirmed quantitatively with kinematic data. Freezing episodes only occurred in PD-FOG participants in direct clutter, and consistently occurred at the narrowest section of the path. The PD-FOG group significantly increased variability of both step length and step time in direct clutter, whereas the other two groups maintained the same variability as in indirect clutter. Thus, it appears that clutter has a significant effect on gait in PD-FOG. Although this finding may be attributed to different theories of FOG (attentional, perceptual), this study argues that perceptual mechanisms most thoroughly explain these results. Overall, clutter was defined as a FOG trigger and the importance of gaining an understanding of how clutter provokes FOG was identified.

The final article attempts to address a fundamental question of the current thesis regarding how eye movements may influence gait behaviours in PD patients with FOG. This investigation may allow for a better understanding of how clutter acts as a FOG trigger. These aims were accomplished by manipulating the location of clutter with respect to the path which altered both the visual and physical complexity of the environment. Eye movements and walking behaviours were compared between healthy age-matched control participants and PD patients with FOG (PD-FOG). While healthy individuals demonstrated feedforward control with minimal gait alterations regardless of clutter location, PD-FOG appeared to be dependent on closed-loop feedback in both clutter conditions and exhibited drastic gait changes when clutter was located close to the path. It was proposed that the observed increases in gait variability may be an attempt to increase proprioceptive sensory information, while increases in the number of fixations, mean fixation durations, and number of areas fixated, may be an attempt to heighten

the amount of novel visual sensory information. The resultant increase in the overall amount of incoming sensory information may be suggestive of an inaccurate perception of environmental threat. While attentional mechanisms were suggested to have considerable affects on FOG, a perceptual mechanism was thought to best represent the findings, and was discussed as the root of the FOG phenomenon. Further, significant changes in gaze behaviours when in direct clutter revealed that gaze is an important measure to consider in this patient population. In the current study, gaze measures revealed that clutter may be a trigger for FOG not just because it confines space, but also because of the high amount of visual stimulation that is associated with realistic clutter. This finding provides directions for future research regarding the incorporation of eye movement measures in FOG studies.

The unique combination of gait and gaze measures in the current study has allowed for a confirmation of clutter as a FOG trigger. Further, gaze behaviours in PD-FOG differ from healthy individuals, revealing that PD-FOG are more reliant on sensory feedback from the environment. Finally, it is concluded that gaze behaviours significantly contribute to gait disturbances in PD, suggesting avenues for further research of eye movements in other freeze-provoking environments.

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CHAPTER 1

INTRODUCTION

A REVIEW OF PARKINSON'S DISEASE

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the cardinal symptoms of akinesia, bradykinesia, tremor and postural instability (Gelb, Oliver & Gilman, 1995). Symptoms of Parkinson's disease begin asymmetrically and gradually progress to both limbs. These symptoms result from a lack of a neurotransmitter called dopamine, in the basal ganglia of the brain. As the disease progresses, individuals gradually lose their independence as it becomes increasingly difficult to perform activities of daily living. Although there are dopamine replacement medications which help relieve or reduce symptoms in the early stages of the disease, individuals respond less to these medications as the disease progresses. Currently, there is no cure for Parkinson's disease.

Many of the previously listed symptoms of PD greatly affect an individual's ability to walk safely and independently through an environment. Individuals with PD exhibit a slow, unsteady, short-stepped gait pattern with stooped posture (Morris, Iansek, Matyas, & Summers, 1996). The step length of PD patients has been found to range from 49.2 to 64.0 cm, compared to a step length of 57.1 to 70.7 cm found in healthy non-neurologically impaired older adults (Almeida & Lebold, 2010). This unsteady gait pattern predisposes individuals to falls and imbalances. In a group of 109 PD patients, 68.7% reported experiencing a fall over the course of one year (Wood, Bilclough, Bowron, & Walker, 2002).

Oculomotor Characteristics

In addition to gait impairments, differences in oculomotor functioning have also been found in PD. DeJong and Jones (1971) were one of the first groups to investigate eye movements in patients with PD. Participants completed a gaze shifting task between two visual targets while electrooculography was used to evaluate timing and coordination of eye patterns. It was found that eye patterns were similar to

healthy control participants; however, PD patients took about twice as long to complete a gaze shifting cycle. The authors proposed that this delay was due to a slower initiation of gaze shift and/or hypometric gaze shifts which necessitated PD patients to perform multiple smaller gaze shifts to reach the target. These proposals were confirmed by later groups which found delayed initiation of gaze shifts (Corin, Elizan, & Bender, 1972) and hypometric eye movements (Shibasaki, Tsuji, & Kuroiwa, 1979). The multiple saccades that correct for hypometria are termed gaze shift fragmentation. In an effort to characterize gaze shift fragmentation, Kimmig, Haufmann, Mergner and Lucking (2002) recorded eye movements during memory guided and visually guided horizontal gaze shifts. It was concluded that gaze shift fragmentation is a physiological phenomenon stemming from strong inhibition over cortico-striatal loops through the basal ganglia. This inhibition results in weak driving signals to pre-oculomotor structures like the superior colliculus. Weak driving signals then cause hypometric saccades, but do not impede the ability to perform corrective saccades in order to successfully reach the target. While these investigations reveal gaze behaviours during stationary tasks, eye tracking studies during locomotion have not been conducted in PD. This is of particular importance since an increased number of hypometric eye movements may influence the acquisition and quality of visual information. Since it is well-established that PD patients are excessively reliant on visual information (Vaillancourt, Slifkin, & Newell, 2001), investigating eye movements during locomotion may assist in understanding how visual behaviours influence gait disturbances in PD.

Reflexive saccades seem to be intact in PD, whereas voluntary saccades are compromised (van Koningsbruggen, Pender, Machado, & Rafal, 2009; Joti, Kulashekhar, Behari, & Murthy, 2007). In a target-switching task, researchers investigated the ability of PD patients to inhibit an eye movement or to change a partially prepared eye movement (Joti, Kulashekhar, Behari, & Murthy, 2007). PD patients took significantly longer than healthy control participants to redirect their gaze, leading to the conclusion that the ability to change or cancel a voluntary saccade is deficient in PD. This behaviour is especially concerning during locomotion in environments of high visual complexity. Since PD patients are known

to be overly susceptible to peripheral visual distracters, the inability to change a saccade to an environmental distraction may prevent safe locomotion. Furthermore, it has been well-established that vision has an integral role in guiding stepping behaviours (Patla, 1997). Thus, if patients are unable to transfer gaze to relevant environmental features, stepping behaviours may become impaired, potentially resulting in severe gait disturbances such as freezing of gait.

Freezing of Gait

One of the most debilitating symptoms of PD is freezing of gait (FOG) which is experienced by 7% of patients in the early stages of PD and up to 60% of patients in the more advanced stages of the disease (Bartels, Balash, Gurevich, Schaafsma, Hausdorff, & Giladi, 2003). FOG is defined as the sudden inability to continue walking despite the intent to maintain locomotion. It is one of the most important aspects of PD to study since it is the source of severe frustration, anxiety and disability. Falls and freezing have also been found to be highly correlated (Bloem, Hausdorff, Visser, & Giladi, 2004). Previous investigations have identified specific situations that reliably provoke FOG. Some of these triggers are turning, initiating gait, and walking through a confined space. Individuals also report that FOG episodes most commonly occur in areas of high visual complexity within their own homes (i.e. a small, crowded living room) (Morris, Iansek & Galna, 2008). Freezing episodes may commonly occur in the home because objects in the home may confine the space, or object location may necessitate turning, both of which are known to provoke freezing episodes. The identification of freeze-provoking environments has encouraged researchers to analyze these environments to determine why FOG occurs, why it occurs in some patients and not others, and what mechanisms underlie this phenomenon. Additionally, the debate regarding why FOG occurs when patients are on and off medications, raises many potential implications of the basal ganglia. Thus, while gaining a better understanding of FOG will help clinicians assist patients, the study of FOG also has the potential of providing researchers with critical information regarding the impaired neural connections which result from PD and the many evolving roles of the basal ganglia.

Trigger: Navigating through a narrow space

Navigating through narrow spaces such as doorways, small closets, or crowded spaces is one of the most commonly stated triggers of FOG and is especially reflected in a cluttered environment. Deviations from healthy control participants are even seen in individuals with PD who do not experience FOG. When approaching a doorway, individuals with PD (without FOG) exhibited stronger veering and central deviation at the doorway than healthy control participants (D'Souza, Smith, Harris, & Ewins, 2008). Additionally, the veering consistently occurred in the direction opposite to the side of greater motor severity. Veering has been previously associated with impaired perceptions of one's egocentric midline in left-side affected PD patients (Davidsdottir, Wagenaar, Young & Cronin-Golomb, 2008). When investigating individuals with FOG passing through doorways of different widths, it was found that narrower doorways elicited a greater number of freezing episodes (Cowie, Limousin, Peters, Zrinzo, Hariz, & Day, 2009). In agreement with previous works, this research study also found that gait parameters (step time, step length) decreased during the approach towards the doorway. Almeida and Lebold (2010) investigated gait behaviours when approaching doorways of different widths (wide, normal, narrow) in three groups of participants: PD with FOG, PD without FOG, and non-neurologically impaired individuals. The PD-FOG group was the only group to significantly decrease their already smaller step length when approaching the narrow doorway. Also, the PD-FOG group always had the widest base of support regardless of the door condition and was the only group to increase step length variability in the narrow and normal doorway width conditions (in comparison to the wide doorway condition). Consistent findings of freezing episodes in narrow spaces have even led to an identification of 'apparent hesitation in tight quarters' as a specific type of freezing (Schaafsma, Balash, Gurevich, Bartels, Hausdorff et al., 2003). In cluttered environments, narrow spaces are commonly created by two objects in close proximity to each other. It will be important to compare behaviours in narrow spaces and cluttered environments to explore whether clutter simply replicates a narrow space, or if there are additional characteristics of clutter which contribute to gait disturbances.

Freezing of gait theories

Although there have been several FOG theories proposed, this review will consider three of the most widely accepted. These theories attribute FOG to impaired sensory-perceptual function, a deficit to closed-loop feedback control, or attentional impairments.

Sensory-perceptual deficit

Freezing of gait has been argued to result from sensory deficits. Impaired proprioception, sensory integration, and vision (contrast sensitivity, colour discrimination) are related to dysfunctional basal ganglia which are known to have roles in sensory integration and sensory gating (Morris, Iansek & Galna, 2008; Kaji, Urushihara, Murase & Shimazu, 2005). Perceptual deficits have also been identified as a non-motor symptom of PD (Harris, Atkinson, Fowler, Lee, & Nithi, 2002; Bodis-Wollner, 2003) and include impaired depth perception, spatial perception, and size perception. Of particular interest, Ballanger, Gil, Audiffren and Desmurget (2007) found that deficits in a reaction time task resulted from perceptual deficits involving the inability to extract relevant features of the stimulus. This impairment may be especially important to consider during locomotion in environments with multiple complex visual features. Perceptions are created from sensory information, thus deficits in either or both of these functions can critically affect a person's ability to move through an environment. Impaired processing or gating of incoming sensory information may lead to inaccurate perceptions of feedback from the environment. Recent studies have investigated functional gait in PD and have suggested that gait adjustments prior to a freeze may result from a sensory-perceptual deficit that is especially pronounced in individuals who experience FOG (Almeida & Lebold, 2010). It is possible that inaccurate perceptions of door width, object size, and object distance may result from sensory deficits such as reduced contrast sensitivity and impaired oculomotor functioning. Investigating eye movements during locomotion is an important next step in FOG literature as it may reveal what visual information is being processed and how perceptions are influenced by the visual information acquired.

Deficit to closed-loop feedback motor control

The ability to use sensory information to guide movement is described as a closed-loop feedback model of motor control. Previous studies have found that the ability to integrate sensory information into appropriate motor output is impaired in individuals with PD (Labyt, et al., 2003; Lewis & Byblow, 2002). To investigate this deficit, Almeida et al. (2005) manipulated visual and proprioceptive input during locomotion toward a target in PD. It was found that PD and healthy control participants performed most accurately when both vision and proprioception were available. PD participants moved to the target less accurately when in the 'off' phase of medication. Thus, it was proposed that the basal ganglia may have a specific role in the integration of proprioceptive feedback with motor output in order to improve the planning and control of movement. FOG has been linked to the inability to use visual information to effectively guide motor actions (Cowie, Limousin, Peters & Day, 2010). Investigating eye movements and walking behaviours together may reveal how patients acquire and use visual information to guide motor output, potentially allowing for inferences to be made regarding the functioning of closed-loop feedback in PD patients with FOG.

Attentional deficits

Previous findings that external cues (visual, auditory) can assist Parkinson's disease patients regulate stride lengths and prevent freezing episodes (Morris et al., 1996; Lebold & Almeida, 2011) has led researchers to propose that a reduced amount of attention allocated to gait may result in FOG. The inability to divide attention or a reduced overall attentional capacity is most evident through dual-tasking paradigms. In these studies, it has been found that when asked to simultaneously perform a cognitive and a motor task, healthy older adults prioritized walking over the cognitive task whereas freezers divided attention equally between the two tasks, resulting in greater gait deficits (Bloem, Grimbergen, van Dijk et al., 2006). In individuals with PD who experience FOG (PD-FOG), dual-tasking has been found to provoke FOG episodes (Bloem, Hausdorff, Visser & Giladi, 2004). Further, studies have found that

teaching patients to use an attentional strategy during walking can reduce freezing and help individuals overcome freezing episodes (Morris et al., 1996). When individuals are in novel, complex environments with multiple distracters, the ability to adapt to higher attentional demands becomes of utmost importance to ensure safe locomotion.

LOCOMOTION THROUGH COMPLEX ENVIRONMENTS

Ambulation, or locomotion through the environment, is one of the most common and necessary activities of daily living. Environments of high visual and physical complexity are common and often include activities which involve balance control such as stepping around obstacles and changing one's travel path. Navigating through complex environments requires continuous assessment and organization of information from multiple senses. As the following section describes, the flexibility of the locomotor system is compromised with the aging process. Despite the higher incidence of falls during locomotion, few adaptive locomotion studies have been conducted with PD patients, thus providing a major research gap to be filled.

Characteristics of Older Adults

While the ability to adapt walking characteristics in a challenging environment is generally intact in healthy young adults, performance has been found to decline in older adults (Weerdesteyn, Nienhuis & Duysens, 2005; Reed, Lowrey & Vallis, 2006). In an investigation of obstacle avoidance, Weerdesteyn, Nienhuis and Duysens (2005) had participants walk on a treadmill and avoid an obstacle which was lowered at different stages of the gait cycle. Older adults had significantly lower obstacle avoidance success rates and reaction times than younger adults. When splitting the group of older adult participants into four sub-groups by age, it was found that age was a successful predictor of success rate, reaction time, and toe distances. The significance of these findings was replicated in an obstacle course paradigm by Reed, Lowrey and Vallis (2006). Mid-old and old-old aged adults were required to step over, duck under, or step around foam obstacles on the path. Increased age had significant effects on obstacle

navigation as evidenced by a greater number of obstacle contacts in the mid-old adults, and an even higher number of contacts in old-old adults. A decreased ability of older adults to navigate complex environments is of great concern when one considers the overall reduced dynamic balance and visual abilities that are characteristic of the aging process (Lord, Clark & Webster, 1991; Delbaere et al., 2010). These factors all contribute to a higher incidence of falls in elderly populations. Furthermore, it has been found that falls most frequently occur during locomotion (Prince, Corriveau, Herbert & Winter, 1997). With these findings, it becomes clear that locomotion through complex environments is an important area of research, with many potential real-world implications including the development of safer environments for older adults.

Gerin-LaJoie, Richards and McFayden (2006) investigated how young and old adults walk down a path while navigating around a stationary or moving mannequin. In some trials, participants had to concurrently listen to auditory messages in order to answer related questions after the trial. Results showed that older adults increased their personal space (distance from the mannequin) more than younger adults. Most importantly, the increased information processing demands of the environment and task affected the motor and cognitive performance of older adults to a greater extent than in younger adults. Therefore, environments that impose greater motor and cognitive demands (i.e. a cluttered environment) may impede gait and balance performance. Thus, it is important to investigate such scenarios in older adults and individuals with movement disorders.

While previous studies have used obstacle courses to investigate the abilities of older individuals to adjust to different environments, the applicability of such obstacle courses to the real world is questionable. What has yet to be investigated is a more real-life scenario with common objects (i.e. tables, chairs, computers) as opposed to cylindrical objects (Reed, Lowrey & Vallis, 2006). As a result, the current study attempted to create a more realistic environment by using objects commonly found in homes and offices. Since eye movements reveal areas of interest in an environment, the utilization of common objects in the current study is an important consideration in order to allow for a study of realistic eye movements in a natural setting.

Characteristics of Parkinson's disease

The known challenges that a complex environment poses on locomotion in older populations begs the question of how these environments influence special populations with gait impairments. Additionally, it has been suggested that the basal ganglia, which are implicated in PD, may contribute to adaptive locomotion (Mizumori, Puryear & Martig, 2009). However, only a few studies have investigated this important topic. As previously described, upon approaching a narrow doorway, individuals with PD adapt to the environment by decreasing step length and velocity, and increasing double support time (Almeida & Lebold, 2010; Cowie, Limousin, Peters & Day, 2010). It has also been found that dropping an obstacle on a treadmill can elicit FOG episodes in individuals with PD who have a history of FOG (Snijders, Weerdesteyn, Hagen, Duysens, Giladi & Bloem, 2010). However, these studies all used a single-constraint design which may not be an accurate reflection of constraints encountered on a daily basis. With the known changes to gait patterns observed in single-constraint paradigms, it may be interesting to determine if similar gait alterations are found in more complex environments.

SIGNIFICANCE OF EYE MOVEMENTS DURING LOCOMOTION

The visual system is essential for predictive and proactive behaviours during locomotion. Previous research has identified a top-down approach during turning and adaptive locomotion, in which the eyes move first, followed by the head, trunk, and then legs (Hollands, Patla & Vickers, 2002). These findings confirm that our eyes are our first defence against falls and moving objects in our surroundings. It has been firmly established that the aging process is accompanied by a decline in the overall functioning of the visual system. Additionally, significant correlations between declines in oculomotor functions (saccade peak velocity, saccade delay time, smooth pursuit) and gait and balance measures have been found, revealing the intricate relationship between vision and locomotion (Kerber, Ishiyama & Baloh, 2005). Exploring the relationship between oculomotor function, locomotion, and the aging process is an important endeavour and may provide a better understanding of how vision guides locomotion.

Eye tracking investigations with younger adults have allowed for the identification of common gaze patterns. Patla and Vickers (2003) studied locomotion in young adults through a simple pathway with clearly identified visual footfall targets. A dominant ‘travel gaze fixation’ was observed, in which individuals maintained a stable gaze that travelled at the speed of the whole moving body (Patla & Vickers, 2003). This type of behaviour was preferred since it is suggested to optimize the acquisition of optic flow information from the environment. Optic flow is generated from the motion of a person in relation to objects in the environment, and can be used to guide steps. The less dominant fixation pattern was termed ‘target fixation’, in which participants tended to fixate targets 2 steps ahead of their present location. This study provides a first look into the possible gaze behaviours that may be observed in the current study. It will be interesting to determine whether participants can rely primarily on optic flow (via travel gaze fixation) when navigating through a more complex environment with multiple objects.

Previous eye tracking studies involving goal-oriented tasks such as crossing an intersection (Geruschat et al., 2003) and driving (Land and Lee, 1994), have revealed that healthy individuals fixate on task-relevant areas that assist in the planning of future actions. For instance, Marigold and Patla (2007) discovered that, when young adults crossed a path with varying terrain complexity (i.e. tilted, slippery, rocky surfaces), fixations were made to highly task-relevant areas such as future foot targets. Fixations were also made to areas which would maximize the amount of information that could be used to guide safe stepping behaviours (i.e. between changes of surface on the pathway). Finally, participants seemed to sequentially sample upcoming terrain in small sections, which is suggestive of an on-line feedback utilization of visual information. Comparing these behaviours to those of individuals with Parkinson’s disease may shed some light on whether PD patients are able to effectively use visual information to guide safe locomotion. An investigation by Chapman and Hollands (2006) found that older adults who were at high risk for falls used a premature gaze transfer strategy when navigating a path with multiple obstacles. Consequently, it was concluded that older adults who were at high risk of falls sacrificed the execution of ongoing movements for the prioritization of future steps. This behaviour may be related to falls in older adults.

Despite the current knowledge that older adults are more challenged by complex environments, to our knowledge, similar studies have not yet been conducted in individuals with Parkinson's disease. This is particularly disconcerting since individuals with PD have been found to be excessively reliant upon visual information during stationary and dynamic tasks (Vaillancourt, Slifkin, & Newell, 2001).

THESIS OBJECTIVES

The main objective of the current thesis was to evaluate the influence of cluttered environments on gait and gaze in individuals with Parkinson's disease. The following three chapters contain separate analyses of the large data set collected in an attempt to achieve this objective.

The first chapter aims to describe the influence of eye movements on walking characteristics in healthy older adults during locomotion through a cluttered environment. This investigation was necessary since locomotion through a realistically cluttered environment has not been reported in the literature. An investigation of gaze variables provides a novel aspect of the experiment which will provide a baseline for future research in special populations.

In the second chapter, a comparison of gait characteristics between PD patients with a history of FOG, PD patients without a history of FOG, and healthy age-matched control participants in cluttered environments was conducted. The objectives of this chapter were to evaluate clutter as a freeze-provoking environment and examine how gait results relate to previously described theories of FOG.

The third chapter investigates both gait and gaze measures in PD patients with FOG. This chapter attempted to answer the following questions: i) Are eye movement behaviours in PD-FOG different from healthy individuals, and ii) Are eye movements linked to gait outcomes in PD-FOG. This is the first study to collect eye movement data during a locomotor task in PD patients, and will hopefully provide interesting findings regarding how vision is used during locomotion in PD.

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CHAPTER 2*

INFLUENCE OF A CLUTTERED ENVIRONMENT ON GAIT AND GAZE IN HEALTHY OLDER ADULTS

ABSTRACT

When walking around obstacles, older adults adopt a more conservative stepping pattern and transfer gaze away from targets earlier than younger adults. This gaze behaviour has been associated with decreased stepping accuracy which may be especially dangerous in cluttered environments. Thus, the current study evaluated how walking patterns and eye movements of older adults are influenced by clutter. Participants ($n=16$) walked down a 7-m pathway with clutter objects adjacent to the walking path (direct condition) or at the perimeter of the room (indirect condition). Gaze data was collected from 6 participants. Analysis of participant location (body location) through the path revealed how gaze patterns changed in each path section. Three areas of interest (AOI) (end goal, travel path, clutter) were identified to explore which features were most frequently fixated. Participants walked significantly slower, with smaller steps and a wider base of support in direct clutter. An interaction between Condition, Body Location, and AOI ($F_{(6,96)} = 6.25$, $p=0.00001$) revealed that participants only fixated the end goal in indirect clutter, but fixated both the end goal and travel path in direct clutter. An interaction of Condition by Body Location by Fixation Location was also found ($F_{(9,128)}=2.09$, $p<0.04$), revealing that participants looked 2 steps ahead when fixating the travel path. While single-obstacle studies have identified travel path fixations as feedforward control, the current study suggests that travel path fixations in a complex environment reflect on-line control. These results show that clutter located close to a path influences gait and gaze in older adults.

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1. Introduction

In order to walk safely and efficiently through a cluttered environment, it is necessary to collect details about the location of objects in the environment and adjust movements accordingly. As individuals get older, declines in balance and stability along with decreased sensitivities of sensory receptors¹ make navigating around obstacles more difficult². Older adults decrease velocity, step length and cadence when circumventing multiple obstacles^{2,3}. It has been suggested that clutter challenges the limits of stability of older adults and places them at a higher risk of falls, although it has been recommended to extend these interpretations to more complex environments. Previous obstacle avoidance studies have used unrealistic obstacles (i.e. foam cylinders, boxes)^{4,5} which may not provide accurate representations of real-life gait behaviours due to differences in perceived environmental threat. It is therefore necessary to determine how clutter simulated with items common in the real world will affect gait.

While investigations of gait provide an understanding of how individuals navigate through clutter, it is also known that vision is critical for guiding walking in complex environments. A temporal relationship between eye movements and stepping patterns has been established in several studies^{6,7,8}. In a target stepping task, Patla and Vickers (2003) found that participants' eyes either moved at the same speed as the body (travel fixation), or fixated on the targets (target fixation), with travel fixation being the most common behaviour. Most interestingly, when individuals fixated targets, they consistently fixated 2 steps ahead. This type of behaviour has been argued to represent the use of visual information in a feedforward manner to plan future movements. In the current study, multiple objects may require a switch in the use of visual information. A target stepping task is of relatively low difficulty since all targets provide similar visual information. Conversely, cluttered environments contain objects of high visual complexity (multiple colours, shapes and contrasts). This difference may result in a switch to on-line control in order to increase sensory feedback.

Investigations of gait and gaze have also been conducted with obstacle avoidance tasks. Chapman and Hollands (2007) demonstrated that when challenged with a single raised obstacle, older adults prematurely shifted gaze from one target to another which was associated with decreased stepping accuracy. Paquette and Vallis (2010) found that prior to, and during, circumvention of a single obstacle younger adults maintained a stable gaze focused on the wall ahead which may be representative of feedforward control. Conversely, older adults spent more time gazing at the ground, which may indicate an attempt to retrieve focused sensory feedback. These studies provoke interest into the potential link between eye movements and stepping behaviours in a more physically demanding cluttered environment.

While clutter can be manipulated in several ways (i.e. colour, size, contrast, threat), the current study solely investigated the location of clutter with respect to the travel path. It was hypothesized that when clutter confines the path, gaze behaviours may reveal a switch to feedback control due to the higher visual complexity within the line of sight. The purpose of this study was to determine if differences in gait and gaze behaviours exist when individuals walk through a path with clutter items located at the perimeter of the room, and a path where clutter items are directly adjacent to the path.

2. Methodology

2.1. Participants

This study involved 16 healthy older adults recruited from the healthy elderly database at the Sun Life Movement Disorders Research & Rehabilitation Centre at Wilfrid Laurier University (*Table 1*). This group of participants acted as a control group in a larger data set involving locomotion through clutter in Parkinson's disease. Participants were excluded from the study if they had severe vision or hearing problems.

2.2. Materials

Three-dimensional gait data was collected using the Optotrak motion capture system (NDI, Waterloo, Ontario, Canada). Three markers (big toe, anterior foot, heel) were placed on each foot.

Digital video camera recordings were used to estimate participant location through the path to allow for an analysis of how gaze behaviours changed throughout the path. Environmental clutter was simulated with objects typical of everyday life (*Figure 1*). The same cluttered design was used for each participant (i.e. the same objects were placed in the same orientation and location).

Gaze data was collected from a sub-set of participants with the Mobile Eye (ASL, Bedford, USA). This device is a light-weight pair of glasses which is connected to a video recorder worn as a pouch around the participant's waist. Data was collected at a frequency of 30 Hz. Due to technical difficulties with the equipment, data was lost from one participant. Therefore, analysis was conducted on gaze data from 5 participants in total.

2.3. Protocol

Participants signed institutionally approved consent forms and were instrumented with Optotrak markers and the Mobile Eye (subset population). After participants became comfortable with the equipment, the researcher demonstrated the task. Participants were instructed to walk to the end of the path, at which point they were told to 'remain standing here until the researcher tells you to return to the start'. No specific target was provided in order to prevent a constant fixation of the target. Participants walked outside of the pathway to return to the start position. Participants were asked to walk down the 7m path at their self-selected pace under two different clutter conditions: i) indirect clutter and ii) direct clutter. Indirect clutter involved clutter at the perimeter of the room and not directly surrounding the walking pathway (*Figure 1a*). The direct clutter condition involved the same objects, but the clutter items surrounded the walking pathway (*Figure 1b*). The path was maintained at a minimum width of 0.675 metres which simulates the width of a narrow doorway¹². Five trials per condition were completed in blocks, resulting in a total of 10 trials. Conditions were blocked and randomized per participant.

2.4. Data Analysis

Although the entire path was 7 metres in length, variables were calculated over a 4-metre distance, as this was the area of richest data (*Figure 1*). Since it was important to evaluate changes in gaze while individuals walked, the path was divided into 4 sections, each 1-metre in length.

Gait variables investigated were velocity (m/s), step length (m), step width (m), and cadence (steps/min), step time variability. Coefficient of variation was calculated for step length and step width, by dividing the standard deviation of all steps within a trial, by the mean of those steps. This value was then multiplied by 100. To assess for a potential learning effect, the STATISTICA computerized statistical package was used to conduct a 2 (condition) by 5 (trial) repeated measures ANOVA on gait variables.

Frame-by-frame video analysis of gaze data was conducted in INTERACT (Mangold International, Germany). Since it was important to determine changes in gaze variables as individuals walked through the path, the following levels were included in the analysis: Condition (2), Area of Interest (AOI) (3), Body Location (4), and Fixation Location (4). Three AOIs were identified (end goal, travel path, clutter). The four path sections were used to define four levels of body and fixation location. This allowed for a description of which section was fixated when participants were in a specific section. Gaze variables included: mean number of fixations for each AOI, mean fixation duration, and percentage of time spent fixating each AOI. A fixation was defined as a stabilization of gaze on the same point for a minimum of 100 ms (3 frames)¹³. To investigate if gaze behaviour differed through the pathway, the percentage of fixation time was also analyzed for each path section. A three-way ANOVA (Condition by AOI by Body Location) was used to analyze the percentage of fixation time. To determine which sections of the travel path were fixated when in each section, a three-way ANOVA (Condition by Body Location by Fixation Location) was conducted on the duration of time spent fixating each section of the path, summed over the five trials. This sum allowed us to focus on fixations that occurred only in the travel path AOI, which may not have been present in each trial. Thus, the significance of this variable

may have been lost if a mean had been calculated instead of a sum. Tukey's Honest Significant Difference (HSD) post-hoc procedure was employed in order to determine where significant differences found in the ANOVA's occurred.

3. Results

3.1. Participant demographics

The mean age of participants was 72.06 (+/- 7.51). The mean height of participants was 169.70 (+/- 9.60) (*Table 1*).

3.2. Gait variables

3.2.1. Kinematic variables

Significant main effects of clutter condition were observed for step length ($F_{(1,15)} = 25.43$, $p < 0.001$), step width ($F_{(1,15)} = 35.25$, $p < 0.0001$) velocity ($F_{(1,15)} = 18.47$, $p < 0.001$), and cadence ($F_{(1,15)} = 13.99$, $p < 0.01$) (*Table 2*). In direct clutter, participants had significantly smaller step lengths, wider base of support, slower velocity, and decreased cadence.

3.2.2. Measures of variability

Significant main effects of clutter condition were found for step length coefficient of variation ($F_{(1,15)} = 13.82$, $p < 0.01$) and step time variability ($F_{(1,15)} = 8.06$, $p < 0.05$), in which participants had significantly more variable step length and step times in the direct clutter condition (*Table 2*). No significant effect of clutter was found for step width variability.

3.3. Gaze variables

3.3.1. Mean number of fixations

Participants had a significantly higher number of fixations in the direct clutter condition (5.48 +/- 1.05) than the indirect clutter condition (2.25 +/- 1.49) (paired t-test, $p < 0.02$).

3.3.2. Percentage of fixation time per area of interest

A main effect of Area of Interest (AOI) was found ($F_{(2,72)}=267.91$, $p<0.0001$), in which the end goal was fixated significantly more than the travel path and clutter, and the travel path was fixated more than the clutter. A significant Condition by Path section by AOI interaction was also found ($F_{(6,72)}=14.98$, $p<0.0001$) (*Figure 2*). Post-hoc analysis revealed that participants fixated the end goal significantly more than the other AOIs, regardless of location in the path in indirect clutter. Conversely, in direct clutter, participants mainly fixated the travel path when in the first half of the path. When in the second half of the path, participants fixated the end goal significantly more than both the travel path and end goal.

3.3.3. Duration of travel path fixations on each path section throughout locomotion

Significant main effects of Condition ($F_{(1,128)}=45.19$, $p<0.0001$), Body location ($F_{(3,128)}=9.69$, $p<0.00009$), and Fixation location ($F_{(3,128)}=20.63$, $p<0.0001$) were found. Most importantly, a significant three-way interaction of Condition by Body location by Fixation location was found ($F_{(9,128)}=4.45$, $p<0.00005$) (*Figure 3*). Tukey's post-hoc analysis revealed that the travel path was rarely fixated in indirect clutter. However, in direct clutter, when located in the first section, participants equally fixated the third and fourth sections. When located in the second section, participants fixated the last section significantly more than the other three sections. When located in the last two sections of the path, the travel path was rarely fixated. Finally, the first two sections of the path were rarely fixated on in direct clutter, regardless of location in the path.

4. Discussion

Since single-obstacle and target stepping studies have identified that older adults might use a different form of control than younger adults, older adults may be at greater risk of injuries or falls when walking in environments with multiple obstacles. With the well-established relationship between stepping patterns and eye movements, this study sought to investigate how gait and gaze behaviours are

affected by clutter location. Older adults adopted a more cautious gait pattern when surrounded by direct clutter. While older adults primarily fixated the end goal when clutter was indirect, they fixated both the travel path and end goal in direct clutter. Additionally, no learning effects were found across any of the variables.

4.1. Older adults adopt a more cautious stepping pattern when walking through direct clutter

As found in previous obstacle avoidance studies, the current study found that gait through a more challenging environment (direct clutter) was characterized by reduced step length, increased step width, and decreased velocity^{9,10,15}. The magnitude of change in step length was 6cm which replicates that of a dual-tasking study by Gerin-Lajoie et al. (2006). In this study, older adults circumvented an obstacle while concurrently attending to auditory messages. In this study, participants answered questions about the audio messages after the trial. Older adults adopted a more cautious gait pattern (slower velocity, shorter step length) and were more inaccurate than younger adults at answering questions, indicating that older adults had greater problems dividing attention. In the current study, it is possible that a similar conflict between attending to the clutter versus the walking task may have resulted in a conservative gait pattern. The finding of a redirection of gaze to the travel path may reflect online processing, demonstrating that participants attempted to increase the amount of visual feedback and were thus attending to the clutter. Gerin-Lajoie et al. (2006) also suggested that a decreased velocity may reflect a strategy to gain more time to assess the situation. Although step width variability was not reported in this study, increased step width variability was found in the current study and may reflect an attempt to increase the amount of time the central nervous system has to process information⁹. Finally, step width variability has been identified as one of the most important indicators of instability and falls risk^{16,17}. These gait changes identified in the direct clutter condition are of great concern and reflect the need for such paradigms to be included in falls risk assessments.

4.2. Older adults change gaze behaviours when walking through direct clutter

This is the first study to investigate eye movements in older adults through a cluttered environment. We found that participants fixated the end goal in indirect clutter, which has been previously defined as ‘travel gaze fixation’⁹. This fixation pattern optimizes the acquisition of optic flow and self-motion information and involves individuals maintaining a stable gaze that moves in the same direction and speed of locomotion. When individuals walked in direct clutter, the end goal and travel path were fixated equally. In target stepping tasks and single-obstacle clearance studies, fixating the travel path has been defined as ‘target fixation’. In agreement with Patla and Vickers (2003), the current study found that when individuals looked at the travel path, they fixated a location that was approximately 2 steps ahead which was identified as feedforward control. However, an environment with multiple objects of different colours, shapes and contrasts increases the visual complexity of the environment. Thus, fixating the travel path in a highly complex cluttered environment may actually reflect feedback control in which sensory information is acquired and used to plan future movements.

An interesting change in fixation pattern was observed in the direct clutter condition. With direct clutter, participants fixated the travel path when walking in the first two sections. As previously suggested, this behaviour reflects an online feedback control mechanism. After the midpoint of the path, participants switched fixations to the end goal, representing a change to feedforward control. It is hypothesized that this switch may have occurred at this point for a couple of reasons. First, the narrowest section of the path was located at the midpoint of the path. After passing this point, the environmental threat may have decreased, thus allowing for a switch to a gaze location which would rely primarily on optic flow information. Alternatively, after passing the midpoint, there were only 3 metres left of the path. To fixate the last two sections of the path would most likely require a change of head position towards the floor. Therefore, the more practical adjustment would be to look straight ahead at the end goal.

The findings of the current study are consistent with those of Paquette and Vallis (2010). In a comparison of kinematic and gaze variables between younger and older adults as they circumvented a single obstacle, it was found that older adults spent more time looking at the ground, whereas younger adults spent more time gazing straight ahead at the obstacle or the wall. Older adults also navigated the path with significantly reduced step length and velocity, and larger step width. Paquette and Vallis (2010) suggest that looking at the path indicated increased scanning of the environment which may provide the central nervous system with more time to process visual information. Interestingly, a similar conclusion was made in the current study. When objects were far from the path, participants relied on optic flow (travel gaze fixation) by looking straight ahead. However, when challenged with multiple objects, participants could not just rely on optic flow to complete the task. Fixating the travel path represents a conscious attempt to obtain more focused information about the upcoming path, with the goal of planning future movements.

5. Conclusions

This study has demonstrated that cluttered environments provoke gait adjustments in older adults such as an increased step width and step length variability. Since such changes have been linked to increased falls risk, it is suggested that cluttered environments are potentially dangerous for older adults. Given the common occurrence of cluttered environments, future research regarding falls prevention programs is warranted. Furthermore, the gaze data collected in this study suggests that older adults use visual information in an online manner in cluttered environments, as supported by the increased amount of travel path fixation. Future research should be conducted with younger adults in realistically cluttered environments to determine specific gait and gaze changes that may be associated with aging.

6. Acknowledgments

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Table 1: Participant demographics

Participant	Age (years)	Height (cm)	Gender
1	56	182.88	M
2	66	170.18	M
3	77	154.94	F
4	75	165.10	F
5	85	177.8	M
6	70	167.64	F
7	76	154.94	F
8	70	160.02	F
9	68	162.56	F
10	79	170.18	M
11*	74	175.26	M
12*	60	182.88	M
13*	69	182.88	M
14	80	177.80	M
15*	78	170.18	M
16*	70	160.02	F
MEAN	72.6 +/- 7.51	169.70 +/- 9.60	9M, 7F

*Gaze data collected from participant

Table 2: Mean and standard deviation for each gait measure

Gait measure	Indirect clutter Mean (Std. Dev)	Direct clutter Mean (Std. Dev)	<i>P</i> values
Step length (m)	0.68 (0.094)	0.62 (0.090)	p<0.00
Step length CV	4.86 (6.036)	11.05 (12.95)	p<0.00
Step width (m)	0.090 (0.021)	0.12 (0.037)	p<0.00
Step width CV	71.80 (22.31)	78.79 (19.28)	p>0.10
Step time CV	0.021 (0.021)	0.029 (0.025)	p<0.02
Cadence (steps/min)	114.29 (7.83)	110.66 (9.51)	p<0.00
Velocity (m/s)	1.25 (0.20)	1.076 (0.15)	p<0.00

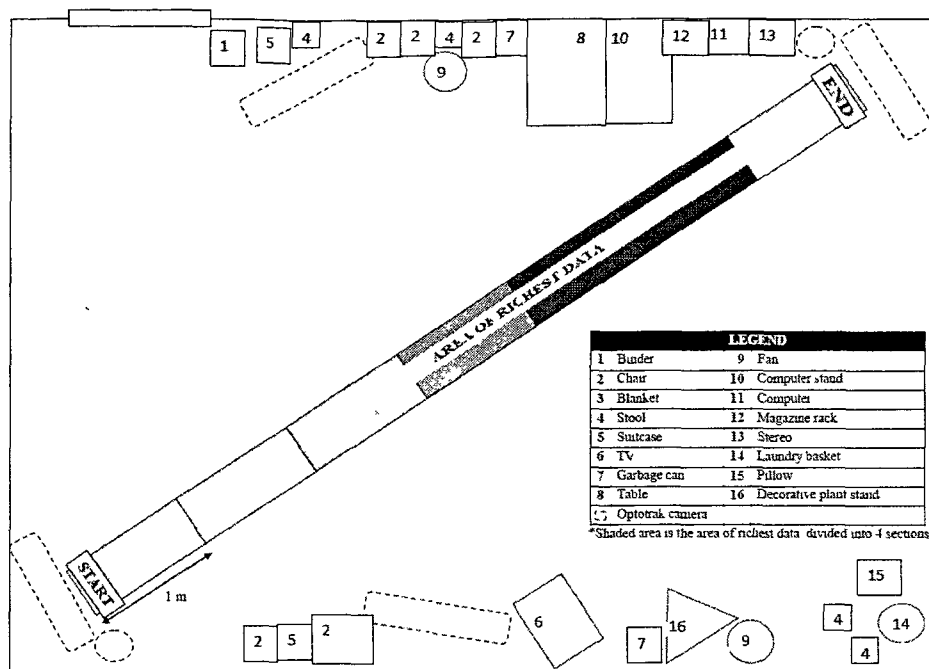


Figure 1a: Indirect clutter - items located at perimeter of room

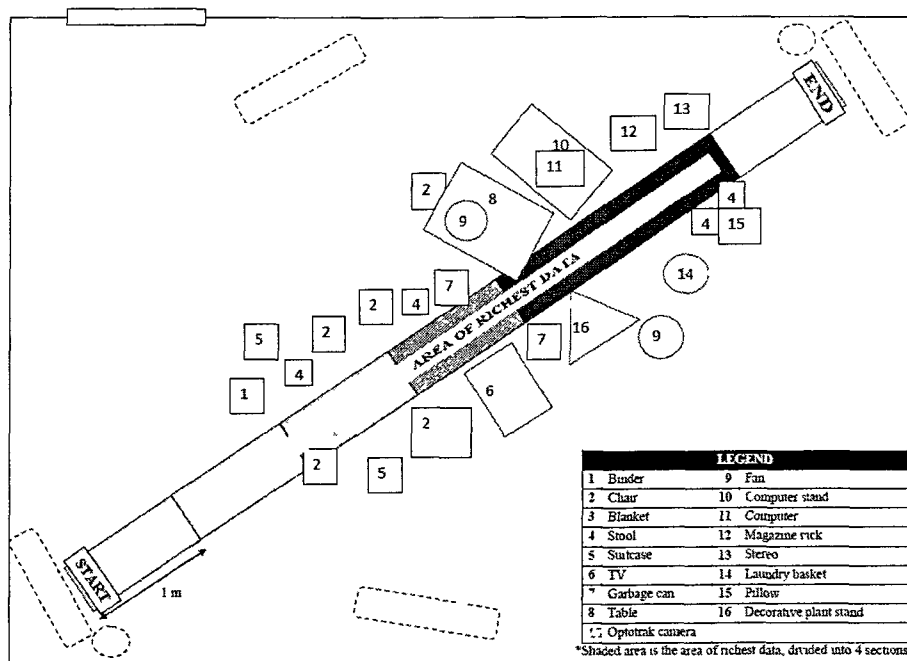


Figure 1b: Direct clutter - items located directly adjacent to the path

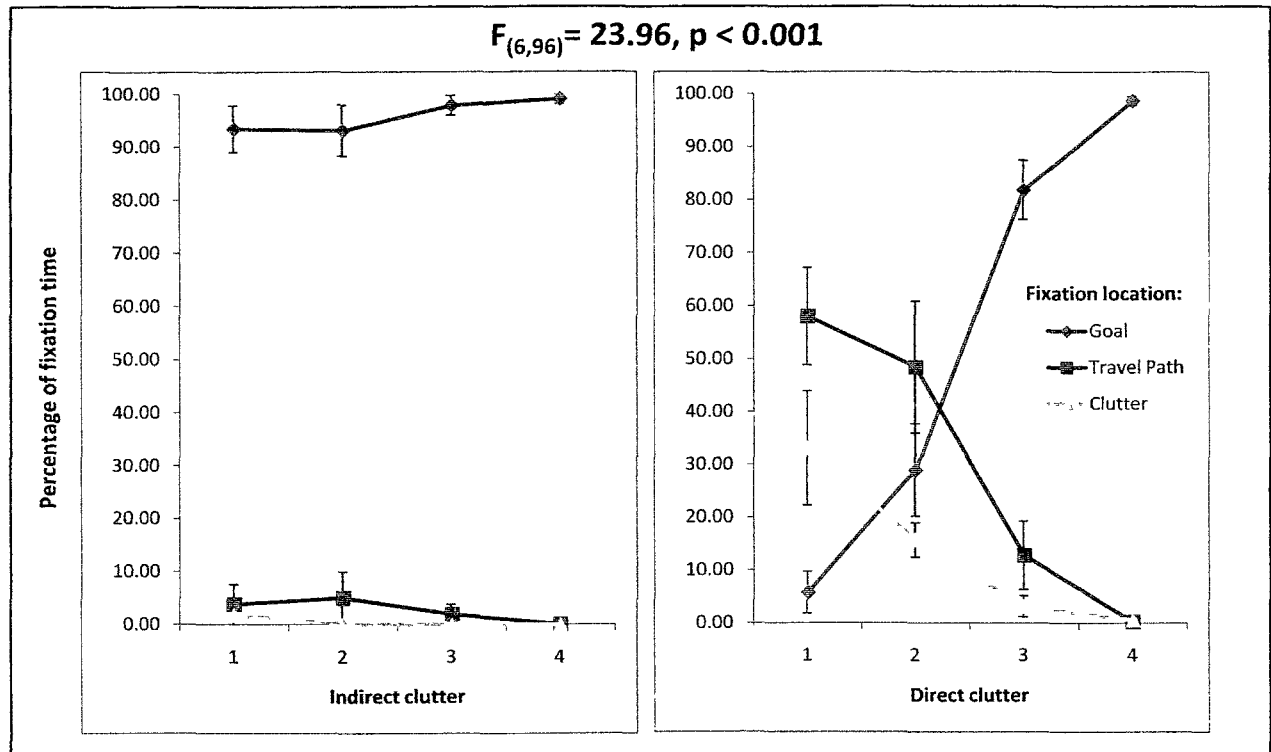


Figure 2: Percentage of Fixation Time – In direct clutter, participants fixated the travel path during the first half of the path, and the end goal during the second half of the path. In indirect clutter, participants fixated the end goal regardless of where they were located in the path.

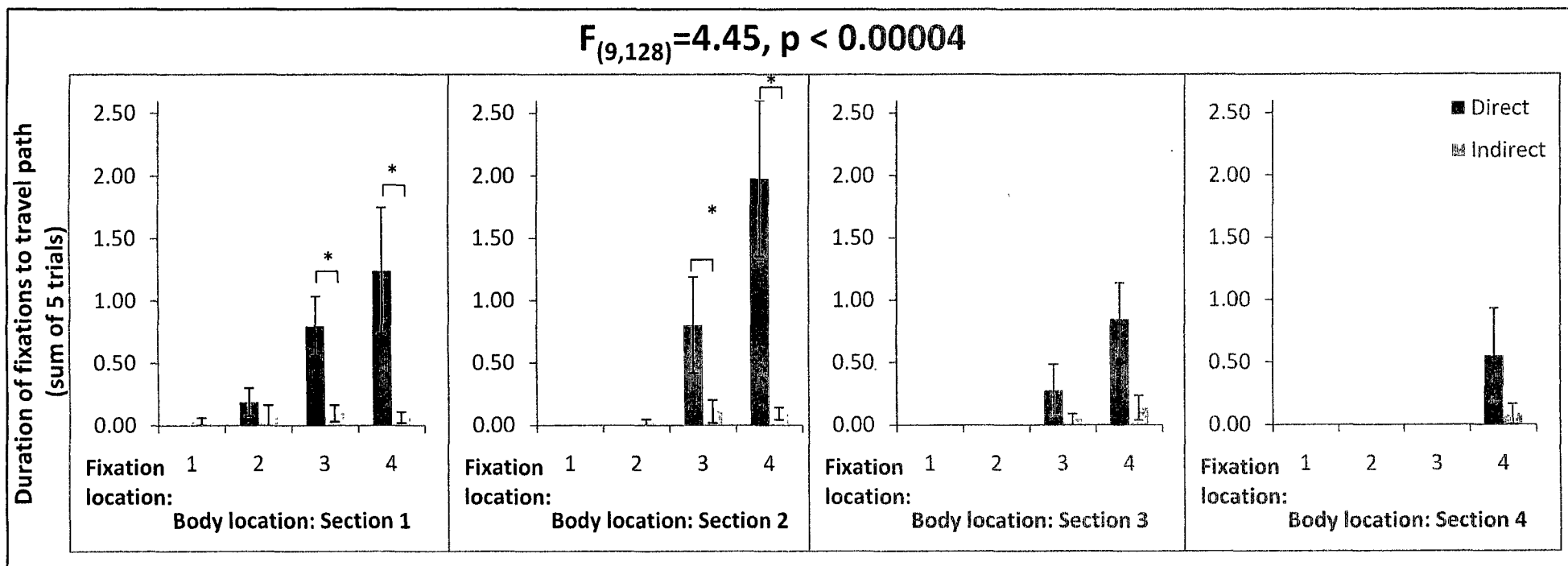


Figure 3: Duration of fixation per section of the travel path – In direct clutter, when participants were located in the first section, they fixated the last two sections equally. When participants were in the second section, they fixated the last section. When participants were in the last two sections, they rarely fixated the travel path. In indirect clutter, the travel path was rarely fixated.

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CHAPTER 3

INFLUENCE OF A CLUTTERED ENVIRONMENT ON GAIT IN PARKINSON'S DISEASE

ABSTRACT

Although freezing of gait (FOG) has been anecdotally reported to occur in busy, cluttered environments in the home^{1,2}, how clutter specifically influences characteristics of gait in Parkinson's disease (PD) has not been studied. The current study investigated gait through an environment with clutter located either directly adjacent to the path (direct clutter) or at the perimeter of the room (indirect clutter). This study was driven by the hypothesis that PD-FOG may have greater perceptions of threat regarding the location of clutter to the path. Ten PD patients without FOG, 12 PD patients with FOG, and 16 healthy age-matched control participants walked down a 7-m path in direct or indirect clutter. All groups had significantly smaller steps in the direct condition than the indirect condition; but more importantly, PD-FOG had significantly smaller steps than both groups across conditions ($F_{(2,34)}=4.75$, $p<0.02$). While groups performed with similar variability of both step time and step length in indirect clutter, only the PD-FOG group significantly increased both variability measures in direct clutter ($F_{(2,34)}=4.54$, $p<0.02$; $F_{(2,29)}=7.53$, $p<0.003$). Both the healthy control and PD non-FOG groups had similar (low) cadence in the direct condition compared to the indirect condition, PD-FOG had a higher cadence ($F_{(2,34)}=4.12$, $p<0.02$). FOG episodes were only observed during the direct condition, and consistently occurred at the narrowest section of the path. While all groups were influenced by direct clutter, only PD-FOG adopted a significantly more cautious gait pattern. Findings are discussed from both attentional and sensory-perceptual perspectives.

INTRODUCTION

One of the most debilitating symptoms of Parkinson's disease (PD) is freezing of gait (FOG) which is defined as the sudden inability to initiate or continue walking. Freezing is not experienced by all PD patients, and tends to occur in later stages of disease progression³. However, the underlying mechanism of FOG remains unknown. FOG often occurs in situations involving dual-tasking, turning, and walking through a narrow space⁴. Previous studies of FOG triggers have identified that spatial and temporal gait patterns change prior to a FOG episode⁵. Spatial parameters such as step length and velocity have been found to decrease before a freezing episode, while temporal parameters are characterized by excessively increased cadence and step time variability⁶. These variables are believed to be indicative of on-line perceptual processing⁷, an impaired ability to integrate sensory and motor information⁸, or a reduced amount of attention to gait⁹. Altering the proximity of clutter to a travel path manipulates the perceptual and attentional demands of the environment, potentially due to changes in perceived threat. Consequently, the current study may reveal how perception and attention contribute to gait disturbances.

A number of mechanisms have been proposed to explain FOG. Researchers have proposed that an inability to control timing may contribute to the FOG phenomenon, as observed through the increased gait variability and increased cadence prior to a freezing episode⁶. In a cluttered environment with multiple obstacles, it may be necessary to adjust step timing in order to efficiently manoeuvre around objects. Therefore, a cluttered environment may provide a means to effectively draw out timing deficits in individuals with PD-FOG.

It has been well-established that well-learned movement plans such as walking become less automatic in PD, resulting in an increased attentional focus on stepping movements^{8,10,11}. Studies have found that gait performance declines when asked to perform mental and motor tasks concurrently¹¹, meaning that patients either have a limited attentional capacity, or are less able to divide attentional

resources. An attentional mechanism is important to consider in the current study, since clutter items are visually stimulating and may result in the division of attentional resources. The current study uses the same number and type of clutter items in each condition, in an attempt to create similar attentional demands in both conditions. If gait performance is similar in both conditions, an attentional mechanism may explain the findings since attentional requirements are similar between conditions, whereas perceptual requirements change drastically. However, if greater gait changes are observed when clutter is located close to the path, it may be more likely that a perceived confinement of space is a greater contributor to FOG than an attentional deficit.

Thus, a perceptual processing deficit is another important mechanism of FOG to consider. Previous research has identified that perceptual deficits are common in PD, in which individuals misjudge distances between objects and the rate at which objects move in the environment¹². However, it is unclear whether these impairments result from sensory-perceptual processing deficits or from a more cognitive perceptual problem. Additionally, when approaching a narrow doorway, only individuals with FOG adjusted gait patterns despite the knowledge that they would be able to fit through the doorway^{7,13}. A cluttered path often involves random narrowing and widening of the path, which may be perceived as more threatening by individuals with FOG.

Since clutter located close to a walking path is both physically and visually complex, an investigation of gait through a cluttered environment may assist in further investigating previously proposed theories of FOG. Thus, the purpose of the current study was to compare gait adjustments in a cluttered environment between healthy age-matched control participants, and PD patients with and without FOG. Additionally, the current study aimed to explore sensory, perceptual and attentional contributions to freezing of gait.

METHODOLOGY

Participants

This study involved 16 healthy age-matched control participants, 10 individuals with Parkinson's disease without freezing of gait (PD non-FOG), and 12 individuals with Parkinson's disease with freezing of gait (PD-FOG) (*Table 1*). Patients were included in the PD-FOG group if they had previously self-reported experiencing FOG episodes. Additionally, a movement disorder specialist confirmed the presence of FOG in the patient assessment completed prior to participation in the study. This assessment included a physical walking assessment involving a timed-up-and-go test, a walk through a narrow doorway, and 360° turns in clockwise and counter-clockwise directions to confirm the presence of FOG. No significant differences in UPDRS score, age, or height were found between groups ($p>0.30$). Participants were recruited from the patient or older adult databases at the Sun Life Movement Disorders Research & Rehabilitation Centre at Wilfrid Laurier University. This group of participants was taken from a larger data set investigating eye movements during locomotion through clutter in Parkinson's disease. Participants were excluded from the study if they had severe vision or hearing problems.

Materials

Three-dimensional gait data was collected using the Optotrak motion capture system (NDI, Waterloo, Ontario, Canada). Three infrared markers were placed on each foot with 1 marker on each of three foot locations: big toe, anterior foot, and heel. A digital video camera was used to record all trials from a posterior view, aimed at the lower limbs. Video recordings were used to qualitatively identify FOG episodes. Environmental clutter was simulated with objects typical of everyday life (*Figure 1*). The same cluttered design was used for each participant (i.e. the same objects were placed in the same orientation and location).

Protocol

Upon arrival, participants signed consent forms and were instrumented with infrared markers. Participants were asked to walk for several minutes prior to testing to ensure their personal comfort. The researcher then demonstrated the task. When the researcher reached the end of the path, participants were instructed to, 'please remain standing here until the researcher tells you to return to the starting position'. Participants walked outside of the pathway to return to the start position. Participants walked down a 7m path at their normal pace under two clutter conditions distinguished by location of clutter: i) indirect clutter and ii) direct clutter. Indirect clutter involved objects located at the perimeter of the room and not directly surrounding the walking pathway (*Figure 1a*). The direct clutter condition involved the same objects, but they surrounded the walking pathway (*Figure 1b*). Despite the presence of direct clutter, the pathway was maintained at a minimum width of 0.675 metres to simulate the width of a narrow doorway⁷. Five trials per condition were completed, resulting in a total of 10 trials. Trials were block randomized, thus some participants started with the 5 trials of indirect clutter, while other participants started with the 5 trials of direct clutter. A researcher walked alongside (and slightly behind) participants who usually used a mobility aide during locomotion, if necessary.

Data analysis

All variables were calculated over a 4-m distance (3rd to 6th metres), since the richest data was collected in this area (*Figure 1*). The gait variables investigated were gait velocity (m/s), step length (m), step length variability, step width (m), step width variability, step time variability and cadence (steps/min). Coefficient of variation was calculated for step length and step width, by dividing the standard deviation of all steps within a trial, by the mean of those steps. This value was then multiplied by 100. To assess for a potential learning effect, the STATISTICA computerized statistical package was used to conduct a 3 (group) by 2 (condition) by 5 (trial) repeated measures ANOVA on all gait variables. Tukey's Honest Significant Difference (HSD) post-hoc procedure was employed in order to determine where significant differences found in the ANOVA's occurred.

RESULTS

Freezing of gait episodes

A freezing episode was defined as the apparent inability to initiate or continue locomotion¹³, and was quantitatively defined from the kinematic data as a 1-second cessation of movement in the direction of progression¹⁴. Five of the 12 PD-FOG participants froze during the direct clutter trials, resulting in a total of 23 freezing episodes. Within these 5 participants, episodes occurred across 14 of the potential 25 direct trials (56% of the trials). A researcher walked through the path with four of these five participants to ensure safety. FOG most commonly occurred at the narrowest point in the path, which was surrounded by a tall, partially transparent decorative plant stand, as well as the corner of a table (*Figure 1b*).

Step length

Significant main effects of Group ($F_{(2,34)}=28.95$, $p<0.0001$) and Condition ($F_{(1,34)}=73.77$, $p<0.0001$) were found. A significant interaction between Group and Condition was also found ($F_{(2,34)}=4.75$, $p<0.02$) (*Figure 2*). Tukey's post-hoc analysis revealed that each group significantly decreased step length in the direct clutter condition. Furthermore, PD-FOG had significantly smaller step lengths than both the PD non-FOG and healthy control groups in both conditions.

Step length variability

Significant main effects of Group ($F_{(2,29)}=9.07$, $p<0.001$) and Condition ($F_{(2,29)}=34.19$, $p<0.0001$) were found for step length variability. A significant interaction between Group and Condition was found ($F_{(2,29)}=7.53$, $p<0.003$). Tukey's post-hoc analysis revealed that the PD-FOG group had significantly higher step length variability than the other two groups in the direct condition. However, the PD-FOG group did not exhibit significantly different step length variability from the other two groups in the indirect condition.

Step width

A significant main effect of Condition ($F_{(1,34)}=17.63$, $p<0.0002$) was found for step width, in which participants significantly increased step width in the direct clutter condition.

Step width variability

A significant main effect of Group ($F_{(2,34)}=11.78$, $p<0.0002$) was found for step width coefficient of variation (CV). Tukey's post-hoc analysis revealed that the Healthy control and PD non-FOG groups had similar variation of step width, whereas PD-FOG had significantly lower step width CV than both groups.

Velocity

Significant main effects of Group ($F_{(2,34)}=32.60$, $p<0.0001$) and Condition ($F_{(1,34)}=48.97$, $p<0.0001$) were found for velocity. Tukey's post-hoc analysis revealed that healthy control participants walked significantly faster than both PD groups, and PD non-FOG walked significantly faster than PD-FOG. Overall, participants walked faster in the indirect clutter condition than in the direct clutter condition.

Step time variability

Significant main effects of Group ($F_{(2,34)}=11.06$, $p<0.0002$) and Condition ($F_{(1,34)}=20.02$, $p<0.0001$) were found for step time variability. A significant interaction between Group and Condition was found ($F_{(2,34)}=4.54$, $p<0.02$) (*Figure 3*). Tukey's post-hoc analysis revealed that the PD-FOG group was the only group to significantly increase step time variability in the clutter condition. All groups performed similarly in the indirect clutter condition.

Cadence

A significant interaction between Group and Condition was found for cadence ($F_{(2,34)}=4.12$, $p<0.03$) (*Figure 4*). Healthy control participants and PD non-FOG decreased cadence in the direct clutter condition, whereas PD-FOG participants increased cadence in direct clutter.

DISCUSSION

Cluttered environments have been anecdotally reported as challenging for individuals with FOG^{1,2}, yet how or why gait is influenced by clutter has not been described in the literature. Investigations of this nature are warranted since cluttered environments provide an experimental situation which may provoke FOG episodes, thus allowing for a better understanding of FOG. The overall objective of the current study was to evaluate the influence of a cluttered environment on gait in PD patients with and without FOG, and healthy age-matched participants. Further, the study aimed to identify specific gait adaptations in the PD-FOG group that may lead to a better understanding of FOG. Analyses revealed that a learning effect was not present in any of the groups. Interestingly, freezing consistently occurred at the narrowest section of the path. While PD-FOG performed similarly to other groups in indirect clutter, PD-FOG was the only group to have greater step time and step length variability in direct clutter. Thus, while all groups demonstrated changes to gait when in the direct condition, PD-FOG were the most significantly influenced by clutter located close to the path.

Although previous studies have identified that FOG is difficult to elicit in a laboratory setting (most likely due to heightened arousal and focus on performance)⁵, the current study design provoked FOG in 5 of 12 PD-FOG participants. Qualitative and quantitative analyses revealed that FOG episodes were consistently elicited at the narrowest section of the path. This finding is reflective of previous studies which have found that narrowing a space and/or adding random obstacles provokes FOG episodes^{2,5}. Several reasons may explain the occurrence of freezing episodes at this location. First, the location of freezing in the current study coincided with the location of the most fragile obstacle on the

path, which may reflect an increased perceived threat of the environment. A previous investigation of fragile and solid obstacles found that subjects increased toe clearance, hip vertical velocity and vertical hip position when stepping over a fragile obstacle¹⁶. The potential for fragile objects to contribute to FOG should be taken into consideration when planning environments for individuals with PD. Second, this location appears to occur at the midpoint of the cluttered area. Thus, it is possible that the distance to this location may have contributed to freezing. It has been previously reported that PD is associated with slower cognitive processing as well as reduced visual working memory¹⁷. Therefore, this position may have been the point at which memory capacity was reached, thus triggering freezing episodes. Future studies should manipulate the location of objects which frequently provoke freezing episodes in order to determine whether distance to a challenging area is an important factor for FOG. Finally, 4 of the 5 PD-FOG participants who experience freezing episodes walked through the path with a researcher (alongside and slightly behind) for safety. It is possible that the movement and location of the researcher may have influenced the occurrence of freezing episodes. Since this location was the narrowest point of the path, the researcher had to adjust the support strategy used by moving directly behind the individual instead of alongside the participant. This may have affected the participant's perception of safety, triggering fear and panic which have been previously related to FOG¹⁸. However, freezing episodes occurred even in the last trials of the direct condition. Thus, familiarity (which may reduce fear) did not improve participant susceptibility to freezing at this location.

In support of previous observations that freezing is characterized by gait asymmetry and a loss of bilateral coordination^{6,19}, timing deficits were only found in the PD-FOG group. Specifically, PD-FOG increased cadence in the more challenging condition (direct clutter), whereas all other groups decreased cadence. These findings agree with previous studies which have suggested that an inability to control cadence may be an important contributor to the FOG phenomenon^{20,21,22}. PD-FOG also increased step time variability which has been suggested to represent a shift to a more conscious control of gait²³. Since PD-FOG performed with similar step time variability as other groups in the indirect clutter condition, the

switch to online control manifests as a direct impact of clutter in close proximity to the path. Potential contributions to this apparent timing deficit are discussed in the remainder of this paper.

A timing deficit may reflect an attentional impairment, which has been previously suggested as a potential mechanism for FOG^{5, 9, 24}. Previous dual-tasking paradigms have also found that PD-FOG participants increased walking cadence while performing a dual task, whereas PD non-FOG and Controls decreased cadence²². Additionally, Morris (1996) found that gait was improved when PD patients were trained to use an attentional strategy during gait. Thus, it has been proposed that PD patients may have diminished attentional resources. In the present study, gait became significantly impaired in the PD-FOG group when clutter was located close to the path. It is suggested that the presence of clutter may have acted in a similar manner as a dual-task in which available attentional resources were divided between walking and the visual inspection of the clutter. It is also possible that clutter simply distracted the PD-FOG participants from performing the motor task. Despite these potential explanations, attention does not fully explain the results of the study. If an attentional deficit was the major contributing factor to FOG, FOG episodes should have occurred throughout the entire cluttered path. Instead, FOG always occurred within the same narrow section of the path. While attention may have been drawn to this location due to the potential danger, this interpretation would involve other contributions such as a sensory-perceptual deficit. Thus, it is proposed that other contributions to FOG must exist in addition to an attentional deficit.

A sensory-perceptual impairment may also explain the timing deficits observed in PD-FOG. In an investigation with healthy age-matched participants, and PD patients with and without FOG, Almeida and Lebold (2010) found that only PD patients with FOG significantly altered gait variables (decreased step length, increased STV, increased step length variability) prior to reaching a narrow doorway. It was proposed that PD patients with FOG changed gait patterns in accordance to how they perceived the environment. In the current study, the direct clutter condition involved objects directly surrounding a pathway of varying width. Since FOG episodes consistently occurred at the narrowest point in the

pathway, it is suggested that PD-FOG incorrectly perceived the width of the path or the size of their body, resulting in FOG. Spatial neglect has been previously identified in PD and is commonly attributed to spatial perception deficits^{25,26}. Although spatial perception deficits could account for the findings of the current study, it remains unclear as to whether the perceptual deficit originates from an inability to process and perceive incoming sensory information, or from a purely perceptual processing cognitive deficit. Future studies should incorporate baseline perceptual judgement tasks as well as cognitive function assessments to assist in distinguishing the origin of perceptual deficits in PD-FOG.

The current study was the first to investigate locomotion through a cluttered environment in individuals with PD who experience FOG. The major finding that individuals with FOG adopt an even more cautious gait pattern than individuals with PD who do not experience FOG, qualifies the importance of identifying cluttered environments as a trigger for FOG. With the common occurrence of cluttered environments in activities of daily living, it becomes important to ensure that patients have appropriate supports when navigating such environments. Importantly, this research has the potential to be translated into environmental design and infrastructure planning which will help create safer environments for individuals with Parkinson's disease. Further investigations should be conducted regarding perceptual processing in PD patients with FOG. Specifically, it is important to determine if perceptual deficits result from a disconnect between incoming sensory information and perception of such information, or from a more cognitive source of perceptual dysfunction. Future studies of perceptual function in PD may assist in understanding the origins of FOG.

Table 1: Participant characteristics

Group	Age	Height	Gender (M:F)	UPDRS
	Mean (Std. Dev.)	Mean (Std. Dev.)		Mean (Std. Dev.)
Healthy	72.06 (7.51)	169.70 (9.60)	9M:7F	---
PD non-FOG	72.3 (9.79)	172.21 (8.96)	7M:3F	33.40 (10.44)
PD-FOG	76.3 (5.76)	169.76 (10.77)	9M:3F	36.12 (8.86)

Table 2: Mean and standard deviation for each gait measure

Gait measure	Group	Indirect Mean (SD)	Direct Mean (SD)	p value	Healthy vs PD non-FOG	Healthy vs PD-FOG	PD non-FOG vs PD-FOG			
					Indirect	Direct	Indirect	Direct	Indirect	Direct
Step length (m)	Healthy	0.68 (0.094)	0.62 (0.090)	p < 0.02						
	PD non-FOG	0.60 (0.088)	0.52 (0.11)	p < 0.01	n s	n s	p < 0.001	p < 0.001	p < 0.01	p < 0.001
	PD-FOG	0.44 (0.095)	0.32 (0.13)	p < 0.001						
Step length CV	Healthy	4.86 (6.04)	11.05 (12.95)	n.s.						
	PD non-FOG	5.57 (2.61)	16.81 (15.90)	n.s.	n s	n.s.	n.s.	n.s.	n.s.	n s
	PD-FOG	8.48 (4.81)	39.22 (50.72)	n.s.						
Step width (m)	Healthy	0.089 (0.021)	0.12 (0.037)	n s						
	PD	0.094 (0.02)	0.10 (0.024)	n s	n s	n s	n s	n s	n s	n s
	PD-FOG	0.10 (0.03)	0.11 (0.063)	n s						
Step width CV	Healthy	71.80 (22.31)	78.79 (19.28)	n.s.						
	PD non-FOG	69.51 (16.92)	80.46 (20.21)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
	PD-FOG	53.83 (18.21)	55.40 (21.37)	n.s.						
Step time CV	Healthy	0.021 (0.020)	0.029 (0.025)	n s						
	PD non-FOG	0.020 (0.009)	0.038 (0.034)	n s	n s	n s	n s	p < 0.001	n s	p < 0.004
	PD-FOG	0.033 (0.020)	0.078 (0.090)	p < 0.001						
Cadence (steps/min)	Healthy	114.29 (7.83)	110.66 (9.51)	n.s.						
	PD non-FOG	109.90 (8.43)	105.70 (10.59)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
	PD-FOG	110.82 (11.51)	117.72 (23.58)	n.s.						
Velocity (m/s)	Healthy	1.25 (0.20)	1.08 (0.15)	n s						
	PD non-FOG	1.06 (0.20)	0.89 (0.20)	n s	n s	n s	n s	n s	n s	n s
	PD-FOG	0.73 (0.28)	0.51 (0.23)	n s						

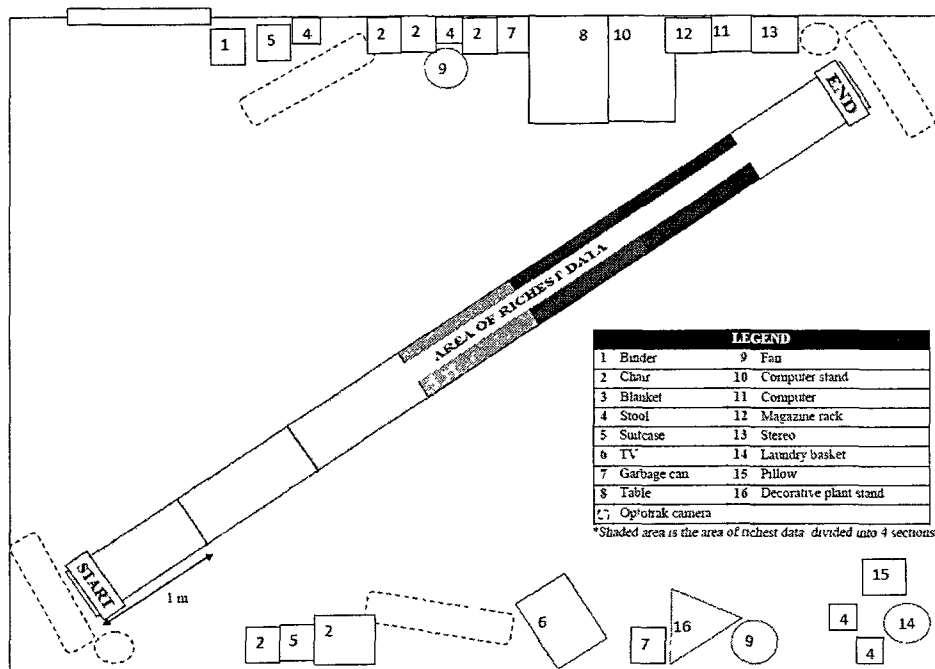


Figure 1a - Indirect condition: All objects located at the perimeter of the room

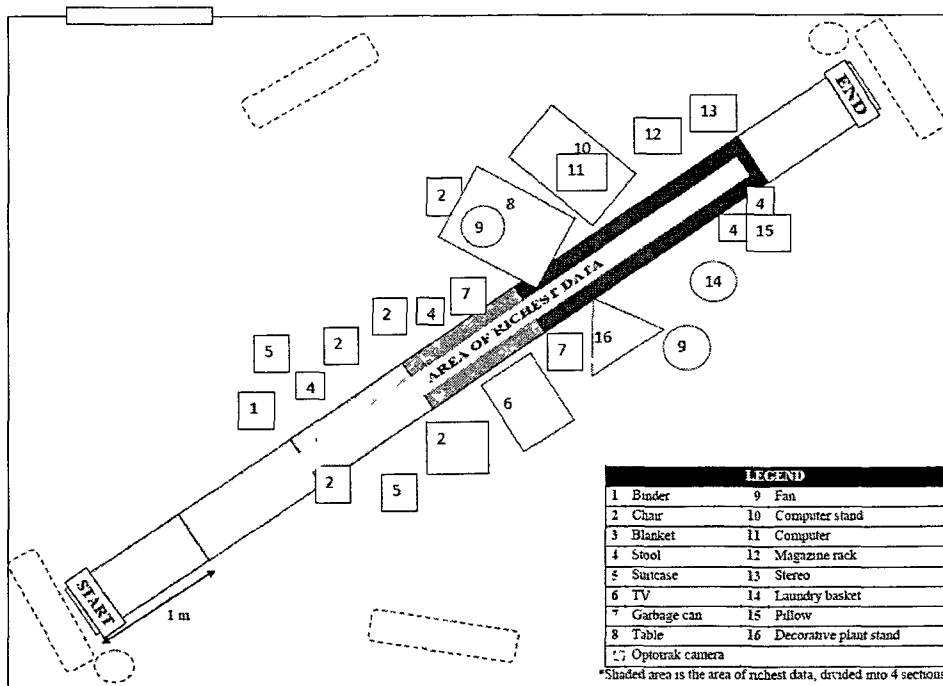


Figure 1b - Direct condition: All objects located in close proximity to the travel path

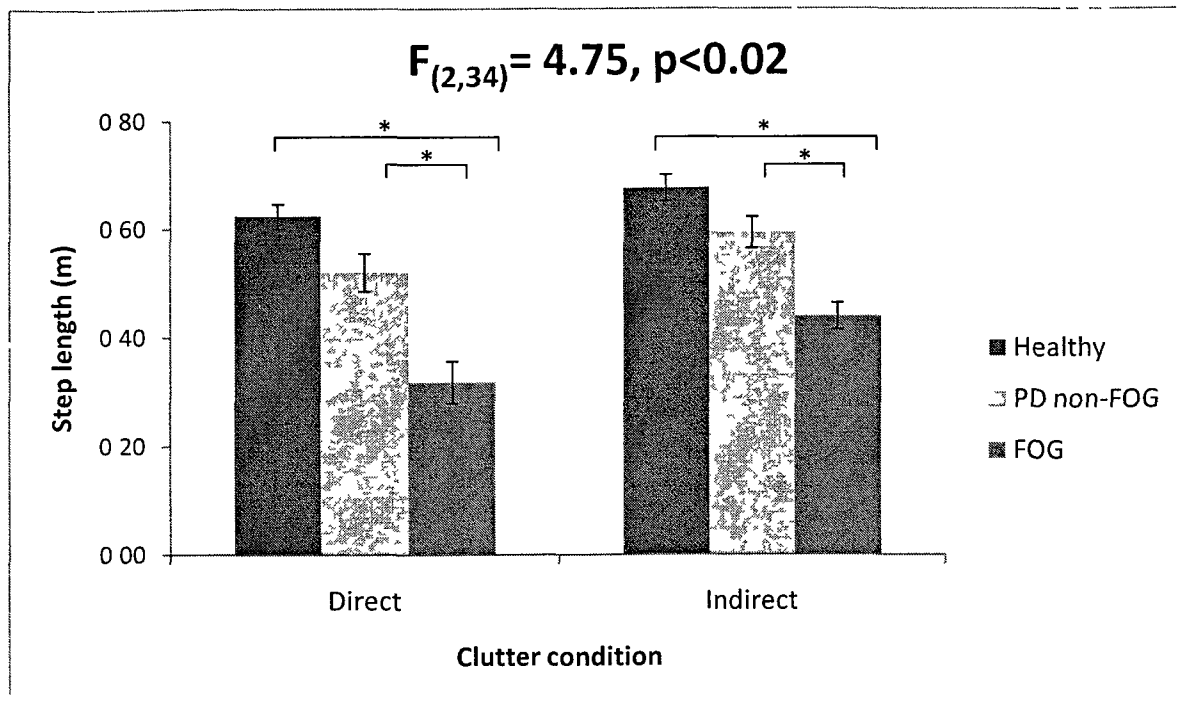


Figure 2 – Step length: A significant Group by Condition interaction revealed that PD-FOG had significantly smaller steps than PD non-FOG and healthy control participants in both conditions

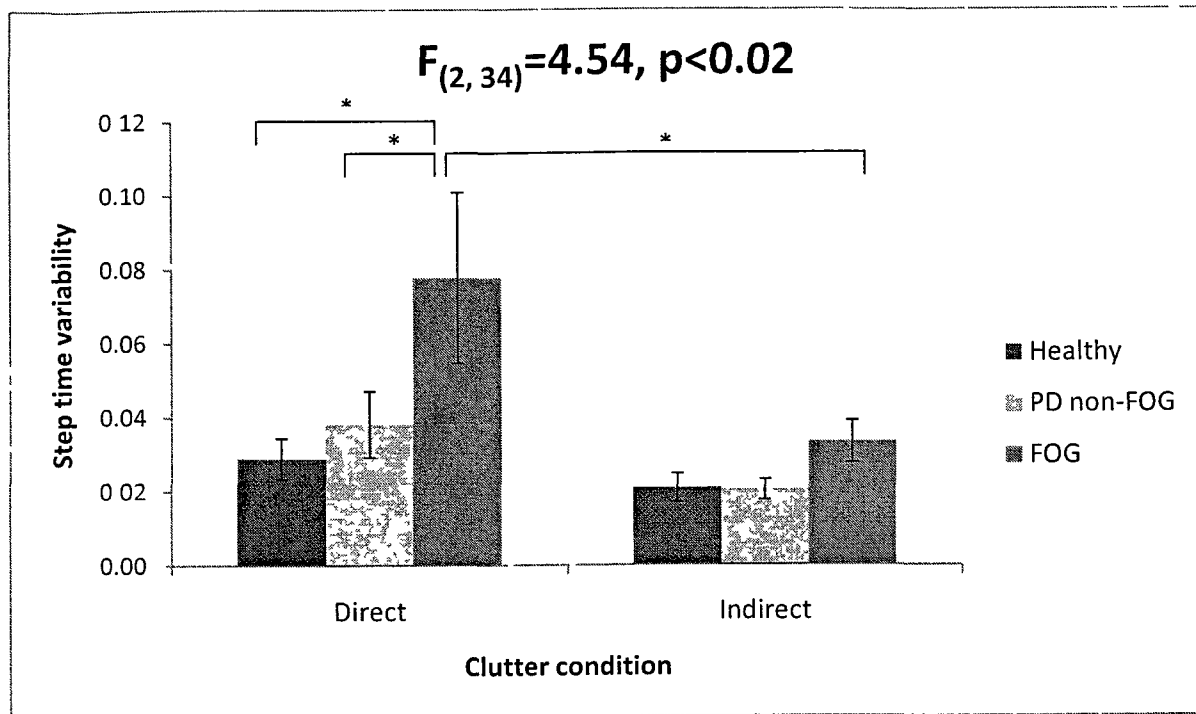


Figure 3 – Step time variability: A significant Group by Condition interaction revealed that all groups performed with similar step time variability in the indirect condition. Only the PD-FOG group had significantly higher step time variability in the direct condition.

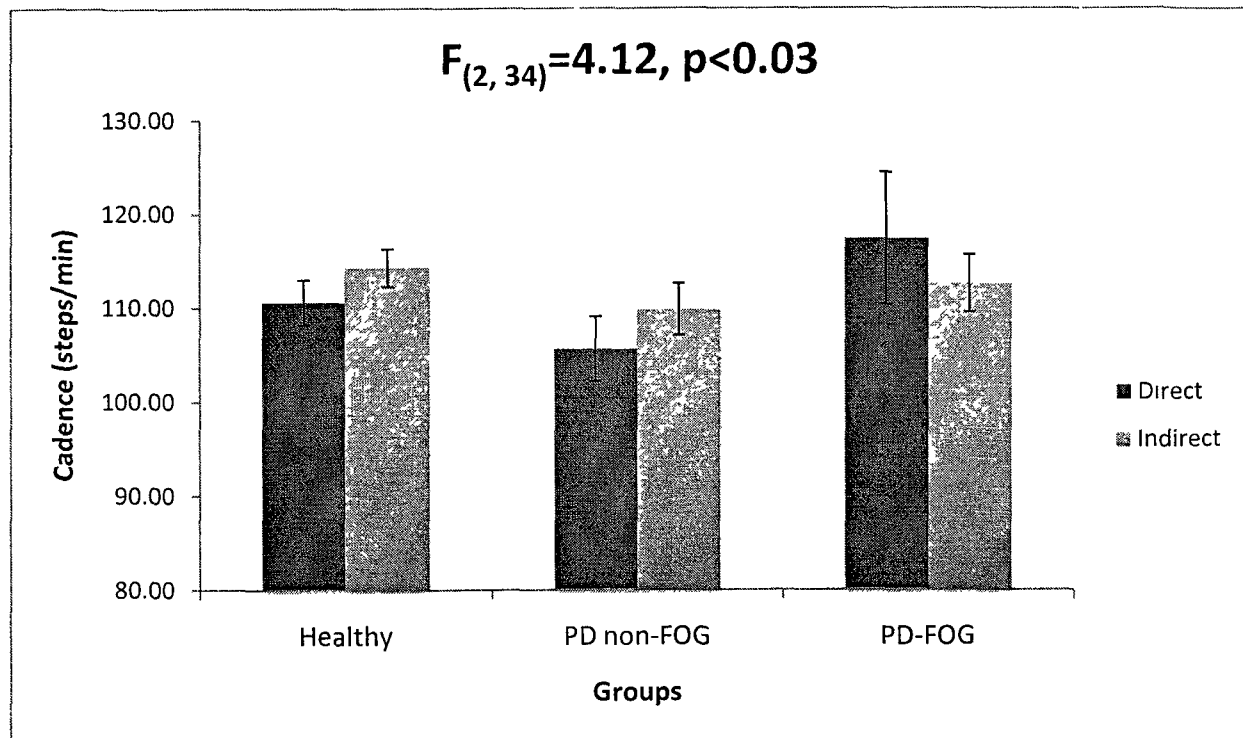


Figure 4 – Cadence: A significant Group by Condition interaction. A trend revealed that healthy and PD non-FOG decreased cadence from indirect to direct clutter, whereas PD-FOG increased cadence from indirect to direct clutter.

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CHAPTER 4

THE INFLUENCE OF A CLUTTERED ENVIRONMENT ON GAIT AND GAZE IN PARKINSON'S DISEASE PATIENTS WITH FREEZING OF GAIT

ABSTRACT

In Parkinson's disease (PD), visual feedback is critical for preventing and overcoming freezing of gait (FOG), especially in complex environments (i.e. clutter) with high visual stimulation. An investigation of eye movements during locomotion may reveal how visual feedback is acquired and used by PD patients with FOG, thus allowing for a better understanding of the FOG phenomenon. The purpose of the current study was to investigate how eye movements are linked to gait in PD and to examine how a complex cluttered environment provokes FOG. This study aimed at gaining a better understanding of the underlying mechanisms of FOG by manipulating the location of clutter relative to a travel path. Participants ($n=27$) walked 7-m through a path with clutter located adjacent to the walking path (direct) or at the perimeter of the room (indirect). Three areas of interest (AOI) (end goal, travel path, clutter) were identified to explore which features were most frequently fixated. Healthy control participants fixated the end goal in indirect clutter, and both the end goal and travel path in direct clutter ($F_{(6,144)}=2.18, p<0.05$). Conversely, PD-FOG fixated the end goal and travel path in indirect clutter, and the end goal, travel path, and clutter in direct clutter ($F_{(6,144)}=2.18, p<0.05$). PD-FOG and healthy control participants performed with similar variability in both step length and step time in indirect clutter ($F_{(1,22)}=13.80, p<0.01$; $F_{(1,25)}=7.49, p<0.02$), however, in direct clutter the PD-FOG group significantly increased gait variability. Findings reveal that PD-FOG altered both gait and gaze variables which may demonstrate an attempt to increase incoming sensory information when clutter was located close to the path. Visual and kinematic findings converge to reveal both attentional and perceptual contributions to FOG, although it is suggested that perceptual mechanisms may be greater in cluttered environments.

INTRODUCTION

Freezing of gait (FOG) is one of the most debilitating symptoms of Parkinson's disease (PD) and is commonly triggered during gait initiation, turning, walking through a confined space, and dual-tasking (Rahman et al., 2008). In addition to these triggers, cluttered environments have been anecdotally reported to provoke freezing (Snijders et al., 2008), although studies have not yet quantitatively assessed FOG in cluttered environments. The challenge of cluttered environments may result from high visual complexity (Morris et al., 2008) and/or the combination of multiple FOG triggers (i.e. turning, narrow spaces) in one environment. Consequently, an investigation of eye movements and walking characteristics through clutter provides an interesting opportunity to study FOG and may yield new information to the ongoing debate about the underlying mechanisms of FOG. More specifically, manipulating the proximity of clutter to a travel path alters the attentional and perceptual demands of the environment through changes in perceived threat of the environment. Therefore, investigating how gait parameters change as a result of different environmental demands may help identify contributions of attentional and/or perceptual mechanisms to the FOG phenomenon.

An attentional mechanism argues that FOG results from a decreased attentional capacity, and a reduced amount of attention to gait due to the presence of FOG triggers (i.e. a dual task, a turn) (Plotnik et al., 2009; Yogev et al., 2005). In dual-tasking paradigms, it has been found that when asked to simultaneously perform a cognitive and a motor task, healthy older adults prioritized walking over the cognitive task whereas freezers divided attention equally between the two tasks, resulting in greater gait deficits (Bloem et al., 2006). In individuals with PD who experience FOG (PD-FOG), dual-tasking has been found to provoke FOG episodes (Bloem et al., 2004). Attentional mechanisms are important to consider in the current study because the highly stimulating nature of clutter may draw attention away from locomotion, resulting in gait disturbances.

A sensory-perceptual mechanism is also important to consider in the current study. While previous research has identified that PD patients have deficits to the perception of their body and/or the environment, the only study which has linked perceptual deficits to FOG was recently conducted by Almeida and Lebold (2010). In this study, locomotion through narrow, normal and wide doorways was investigated. The PD-FOG group was the only group to exhibit significant gait changes (decreased step length, increased step time variability, increased step length variability) prior to the doorway. An altered perception of the door was suggested to be responsible for the observed gait adaptations. In the current study, the width of the path created by clutter objects may be incorrectly perceived by PD-FOG participants. By investigating gait and qualitatively assessing where FOG occurs throughout the path, it may be possible to suggest which mechanism is the primary contributor to FOG in a cluttered environment.

While an investigation of gait alone may allow inferences to be drawn about attentional and perceptual contributions to FOG, an evaluation of eye movements during locomotion may strengthen these findings. Although previous studies have identified that vision has an important role in guiding locomotion (Patla, 1997), investigations of gaze during locomotion have not yet been conducted in PD. Stationary investigations of eye movements have reported that PD have fragmented gaze shifts and hypometric saccades, both of which may affect the ability of patients to acquire and use visual information (Corin et al., 1972; Kimmig et al., 2002). Since cluttered environments are highly stimulating and may require complex visual processing, an investigation of eye movements during locomotion is an important aspect of this study. Further, eye movements may reveal which areas of the environment participants pay more attention to during locomotion. Previous studies have also identified that investigating eye movements may assist in understanding perceptual strategies used by individuals (Pelz and Canosa, 2001). Thus, an investigation of eye movements may reveal potential contributions to FOG.

The use of a cluttered environment is an important and necessary next step in FOG literature. It is essential to identify freeze-provoking environments for the safety of patients as well as to gain a better

understanding of the FOG phenomenon. Further, since gait disturbances are common in PD, the current study investigated eye movements during locomotion in order to determine specific gaze behaviours which may contribute to gait deficits. Overall, the current study aimed to provide examine how clutter provokes FOG, to explore the potential link between vision and gait disturbances in PD, and to evaluate which theories most thoroughly describe FOG in a cluttered environment.

METHODOLOGY

Participants

This study involved 16 healthy age-matched control participants and 11 PD patients who were confirmed to experience FOG (*Table 1*). Participants were recruited from the patient and healthy age-matched control participant databases at the Sun Life Financial Movement Disorders Research and Rehabilitation Centre at Wilfrid Laurier University in Waterloo, Canada. All patients had been previously diagnosed with PD by a movement disorder neurologist and had previously self-reported experiencing FOG episodes. Additionally, a movement disorder specialist confirmed the presence of FOG in the patient assessment completed prior to participation in the study. This assessment included a physical walking assessment involving a timed-up-and-go test, a walk through a narrow doorway, and 360° turns in clockwise and counter-clockwise directions to confirm the presence of FOG. A Snellen eye chart was used to confirm that all participants had a minimum visual acuity of 20/50. All participants were informed about the experimental protocol and signed institutionally approved consent forms. No significant differences were found in age ($t_{(26)} = -1.64$, $p > 0.11$) or height ($t_{(26)} = -0.39$, $p > 0.70$) between groups.

Materials

Three-dimensional gait data was collected from all participants using the Optotrak motion capture system (NDI, Waterloo, Ontario, Canada). Three infrared markers were placed on each foot with 1 marker on each of three foot locations: ventral aspect of big toe, middle-anterior aspect of the foot, and

middle of the calcaneus. A digital video camera was used to record the lower limbs from a posterior view. These recordings were used to estimate participant location in the path as well as to qualitatively assess FOG episodes. The camera was located at the beginning of the path and collected data from the start to the end of the path.

Due to unavailability of equipment, gaze data was collected from a subset of participants (8 healthy; 6 PD-FOG) with the Mobile Eye (ASL, Bedford, USA). This device is a light-weight pair of glasses which is connected to a video recorder worn as a pouch around the participant's waist. Due to technical difficulties, data could only be analyzed for 5 of the healthy older adults and 4 of the PD patients.

Environmental clutter was simulated with objects typical of everyday life. These objects included a variety of chairs, a computer, books, a fan, pillow, table, decorative plant stand, television, garbage cans, stools, stereo, and magazine rack. (*Figure 1*). The same cluttered design was used for each participant (i.e. the same objects were placed in the same orientation and location).

Protocol

Participants remained on all medications for the study. Upon arrival, participants signed institutionally-approved consent forms and were instrumented with the infrared markers and the Mobile Eye (subset of participants). Participants were asked to walk for several minutes prior to testing to ensure their personal comfort. The researcher then demonstrated the task. When at the end of the path, participants were instructed that when they reached this point, 'please remain standing here until the researcher tells you to return to the starting position'. Participants walked outside of the pathway to return to the start position. No specific target was given in order to prevent a constant fixation of the target. Participants walked down the 7-m path at their normal pace under two different clutter conditions: i) indirect clutter and ii) direct clutter. Indirect clutter involved clutter at the perimeter of the room and not directly surrounding the walking pathway. The direct clutter condition involved the same objects, but

the clutter items surrounded the walking pathway. Despite the presence of direct clutter, the pathway was maintained at a minimum width of 0.675 metres. This width simulated the width of a narrow doorway (Almeida and Lebold, 2010). Five trials per condition were completed, resulting in a total of 10 trials. Trials were block randomized, thus some participants started with the 5 trials of indirect clutter, while other participants started with the 5 trials of direct clutter.

Data Analysis

Although the entire path was 7 metres in length, variables were calculated over a 4-metre distance, as this was the area of richest data (*Figure 1*). Since it was important to evaluate changes in gaze while individuals walked, this area was divided into 4 sections (each 1-metre in length), accordingly referred to as sections 1, 2, 3, and 4.

The gait dependent variables investigated were gait velocity (m/s), step length (m), step width (m), step time variability, and cadence (steps/min). Coefficient of variation was calculated for step length and step width, by dividing the standard deviation of all steps within a trial, by the mean of those steps. This value was then multiplied by 100. To assess for a potential learning effect, the STATISTICA computerized statistical package was used to conduct a 2 (group) by 2 (clutter condition) by 5 (trial) repeated measures ANOVA on all gait variables.

Frame-by-frame video analysis of gaze data was conducted in INTERACT (Mangold International, Germany). Since it was important to determine changes in gaze variables as individuals walked through the path, the following levels were included in the analysis: Condition (2), Area of Interest (AOI) (3), and Path Section (4). Three AOIs were identified (end goal, travel path, clutter). Clutter was coded when the fixation point was located on a clutter object or on the edge of the path since both are attempts at defining clutter location. The four, 1-m path sections were used to define the four levels of Path Section, allowing for a description of which AOI was fixated when participants were in a specific part of the path. Gaze variables included: mean number of fixations of each AOI, mean fixation duration (normalized to walking velocity), and percentage of time spent fixating each AOI. A fixation

was defined as a stabilization of gaze on the same point for a minimum of 100 ms (3 frames) (Patla and Vickers, 1997). To investigate if gaze behaviour differed through the pathway, the percentage of fixation time was also analyzed for each path section. To investigate if gaze behaviour differed throughout the pathway, the variables were analyzed per each of the four path sections. The STATISTICA computerized statistical package was used to conduct a 2 (group) by 2 (condition) by 3 (AOI) by 4 (path section) factorial ANOVA on each gaze variable. Tukey's Honest Significant Difference (HSD) post-hoc procedure was employed in order to determine where significant differences found in the ANOVA's occurred.

RESULTS

Gaze variables

Mean number of fixations

Significant main effects of Group ($F_{(1,144)}=8.51$, $p<0.005$) and Condition ($F_{(1,144)}=18.46$, $p<0.00003$) were found. A three-way interaction of group by condition by area of interest was found to be significant ($F_{(2,144)}=3.69$, $p<0.03$) (*Figure 2*). Tukey's post-hoc analysis revealed that in the direct clutter condition, PD-FOG had a significantly higher number of fixations on clutter than controls. In the indirect clutter condition, PD-FOG had a significantly higher number of fixations on the travel path than controls. Comparing between conditions, healthy control participants increased the number of fixations of the travel path in direct clutter, whereas PD-FOG increased the number of fixations of the clutter.

Mean duration of fixations

A significant three-way interaction was found between Group, Condition and AOI ($F_{(2,144)}=4.38$, $p<0.02$) (*Figure 3*). Tukey's post-hoc analysis revealed that the mean duration of fixation was significantly greater for the end goal than the other two AOIs in the indirect condition for both groups. In the direct condition, both groups equally fixated each AOI. However, while healthy control participants did not

change their duration of fixations significantly between conditions, PD-FOG fixated each AOI significantly longer in the direct condition than in the indirect condition.

Percentage of fixation time per area of interest

A significant main effect of area of interest was found ($F_{(2,144)}=54.19, p<0.0001$). A significant four-way interaction of Group by Condition by Path Section by AOI ($F_{(6,144)}=2.18, p<0.05$) was also found (*Figure 4*). Tukey's post-hoc analysis revealed that in the indirect condition, healthy control participants fixated the end goal for the entire path, however, PD-FOG fixated both the end goal and travel path when in the first 3 sections, and primarily fixated the end goal in the fourth section. In the direct condition, when in sections 1 and 2, there were no significant differences in the percentage of time that healthy control participants spent on the three AOIs. However, in sections 3 and 4, healthy control participants primarily fixated the end goal, with minimal time spent fixating the travel path and clutter. In the direct condition, PD-FOG equally fixated all AOIs while in each section of the path.

Gait variables

Spatial kinematic measures

A significant interaction between Group and Condition ($F_{(1,25)}=7.63, p<0.02$) was found for step length. Tukey's post-hoc analysis revealed that PD-FOG had significantly smaller step lengths in both conditions, and both groups significantly decreased step lengths in direct clutter. A main effect of Group ($F_{(1,25)}=4.16, p>0.05$) approached significance, in which the step length variability (CV) was higher in the PD-FOG group than the healthy control group.

No significant differences between groups were found for step width. However, a main effect of Condition ($F_{(1,25)}=19.25, p<0.0002$) revealed that participants increased step width in the direct clutter condition. A significant main effect of Group ($F_{(1,25)}=16.50, p<0.0005$) was found for step width

variability (CV), in which healthy control participants had significantly higher step width variability than PD-FOG participants.

Temporal kinematic measures

A significant interaction between Group and Condition ($F_{(1,25)}=7.49$, $p<0.02$) was found for step time variability (*Figure 5*). Tukey's post-hoc analysis revealed that PD-FOG and healthy control participants have similar step time variability in the indirect clutter condition. However, while healthy control participants maintained similar step time variability in the direct clutter condition, PD-FOG significantly increased step time variability.

A significant Group by Condition interaction was also found for cadence ($F_{(1,25)}=5.42$, $p<0.03$). The healthy control group decreased cadence with direct clutter, whereas the PD-FOG group increased cadence.

Qualitative analysis of FOG episodes

Freezing episodes were qualitatively identified from video recordings, and then quantitatively confirmed through kinematic data. A FOG episode was defined as the apparent inability to initiate or continue locomotion (Schaafsma et al., 2003), and was quantitatively defined from the kinematic data as a 1-second cessation of movement in the direction of progression (Almeida, Wishart & Lee, 2002). FOG episodes were elicited from 5 of the PD-FOG participants and only occurred during the direct clutter condition. A researcher walked through the path with four of these five participants to ensure safety. Both gaze and gait data was collected from 1 of the 5 participants. A total of 23 FOG episodes were elicited. FOG most commonly occurred at the narrowest point in the path. Additionally, this location was the middle of the cluttered area and was surrounded by a tall, partially transparent decorative plant stand, as well as the corner of a table (*Figure 1*).

DISCUSSION

Although patients have anecdotally reported the freeze-provoking nature of cluttered environments, quantitative investigations of FOG through clutter had not been previously conducted. In the current study, eye movements provided critical information regarding how visual feedback was acquired and used while walking through clutter. Further, eye movement analysis revealed which areas of the environment were considered important by participants. By collecting both eye movements and kinematic measurements, the current study aimed to (i) describe gaze behaviours in PD-FOG during locomotion, (ii) determine how clutter influences walking characteristics and FOG, and (iii) evaluate how findings relate to previously described theories of FOG. Results revealed that PD-FOG used a different fixation pattern (characterized by fixations of all areas of interest, and increased number of fixations) than healthy control participants, which may represent a dependence on visual feedback from the environment. FOG episodes were elicited in 5 of the 12 PD-FOG participants, verifying that cluttered environments provoke FOG. Finally, in direct clutter, gait of PD-FOG was significantly more influenced than that of healthy control participants.

PD-FOG use feedback control and are distracted by clutter located close to the travel path

PD-FOG exhibited different gaze patterns from healthy control participants in both clutter conditions. While healthy control participants fixated the end goal in indirect clutter, they fixated the end goal and travel path equally in the direct clutter condition. Conversely, PD-FOG fixated the end goal and travel path in indirect clutter, and fixated all three areas of interest (end goal, travel path, clutter) equally in direct clutter. These behaviours can be interpreted in several ways. First, fixation of the end goal can be argued to represent feedforward motor control, in which individuals rely on an internal movement plan to guide actions. Fixation of the travel path and clutter may represent an on-line feedback strategy, involving the acquisition and use of sensory information to guide future movements. Although it is recognized that feedback and feedforward strategies for motor control are not mutually exclusive, identifying different areas of interest in the environment allowed for a general

understanding of how PD-FOG may use visual information differently than healthy older adults. While healthy control participants switched to feedback control only in direct clutter, PD-FOG used feedback control in both conditions. Interestingly, imaging studies have identified that the basal ganglia have an important role in feedforward control. Thus, the malfunctioning basal ganglia in PD may contribute to an increased reliance on sensory feedback.

Furthermore, fixations can be interpreted with respect to the relevance of the fixated area to the primary task of walking through the path. In this context, the end goal and travel path were relevant to the primary task because they involved fixations of potential targets, whereas clutter objects were irrelevant because they did not involve future stepping targets. Thus, it appears that PD-FOG were distracted by the clutter, whereas healthy control participants were able to focus on features relevant to the task to help guide future actions. This is supported by several findings that PD patients are more susceptible to be distracted by irrelevant items in the visual scene (McDowell and Harris, 1997; Lee et al., 2010). As a result of fixating environmental distracters (clutter), PD-FOG participants transferred irrelevant visual information into spatial working memory. Unfortunately, this problem is exacerbated by a smaller working memory capacity which is characteristic of PD (Lee et al., 2010). Thus, storing irrelevant information is more problematic in PD-FOG because of a limited capacity of working memory. A fully occupied working memory may be reflected in gait patterns of PD patients (i.e. slowing down) to allow for further processing. Ultimately, this deficit could result in severe gait impairments such as FOG.

Influence of a cluttered environment on gait

While healthy control participants adopted a more cautious gait pattern by decreasing step length and velocity during locomotion in direct clutter, decreases in step length were more severe in PD-FOG. Interestingly, decrements to step length in PD were accompanied by increases in both step time variability and cadence. In contrast, healthy control participants did not change step time variability and cadence actually decreased in direct clutter. Changes to these temporal values have been argued to reflect internal

timing deficits or general asymmetries to gait. However, PD patients performed similarly to healthy control participants in the indirect condition, revealing that altered gait timing found in PD-FOG may result from the location of clutter close to the path. Increases in step time variability and cadence have also been suggested to reflect a switch to a more conscious control over gait patterns (Almeida et al., 2005). In a directly cluttered environment, PD patients may be inclined to carefully assess every step in order to ensure safety. These step-to-step adjustments would be quantitatively interpreted as decreases in step length and more variable step lengths. This type of behaviour would be indicative of increased perceived threat of the environment, which will be discussed in the next section.

Exploring the mechanisms which link the use of vision to impaired gait in PD-FOG

The current study was the first to simultaneously record eye movements and walking behaviours during locomotion in individuals with PD. An investigation of this nature was necessary in order to describe how visual information was used to guide locomotion in this population. The previous sections have outlined how behaviours are different in PD-FOG and healthy groups. As described in the following section, a common goal of increasing the overall amount of incoming sensory information was found in both the visual and kinematic data. Potential mechanisms underlying this behaviour are discussed in this section.

In the analysis of eye movements, PD-FOG increased the number of fixations and the mean duration of fixations when walking through direct clutter. In a previous study involving visual target identification amongst multiple distracters, researchers determined that increases in these two gaze variables indicated an attempt to increase the amount of time available to process sensory information (Vlaskamp and Hooge, 2005). The results from the current study support this previous hypothesis, in that participants slowed their walking velocity in direct clutter, increasing visual processing time. However, the current study employed a more complex environment with a greater variety of distracters. It is suggested that increases in visual and kinematic variables represents an attempt to increase novel visual

information due to the highly stimulating environment. The greater amount of information may also result in decreased velocity which allows for more time to process this information. In addition to gaze changes, the increased step time variability in the PD-FOG group may also reflect an attempt to increase the amount of incoming sensory information (Almeida et al., 2005). More specifically, an adjustment in the timing of steps throughout a path reflects on-line control of movement and provides novel proprioceptive information to the central nervous system. Overall, it appears that PD-FOG attempt to increase sensory inputs when challenged with walking through a cluttered environment.

From this finding, it then becomes important to address the question of why PD-FOG increased incoming sensory information when clutter was in close proximity to the travel path. An attentional mechanism may explain the increased number of fixations to clutter objects in the room when clutter was located close to the path. Clutter may have distracted participants, thus reducing the amount of attention allocated to walking. However, if objects simply distracted participants, then fixations of clutter would have been found in the indirect clutter condition as well. Therefore, it is suggested that participants attended to clutter objects because of an increased perceived environmental threat associated with clutter location. An increased amount of attention allocated to clutter may have reduced the amount of attention to walking patterns, resulting in FOG.

Impaired perceptual abilities may also explain the findings of the current study. In the direct clutter condition, clutter narrowed the walking path, simulating a narrow corridor which is a known FOG trigger. Almeida and Lebold (2010) discussed their finding of decreased step length, and increased cadence and step time variability which occurred upon approach of a narrow doorway as an indicator of increased on-line perceptual processing. Further, impaired perception of space in PD has been previously described in the literature. In a large-scale questionnaire study about spatial perception, Lee and Harris (1999) found that PD patients are aware of changes in perception. These deficits were discussed in relation to inaccurate perception of self (i.e. perception of own body image) and inaccurate perception of the extrapersonal space (i.e. perception of environment). In the current study, these impaired perceptions

may have contributed to the consistent occurrence of FOG episodes at the narrowest section of the path. An interesting relationship between the side of motor symptom severity and perception has also been found. Lee et al. (2001b) had participants make perceptual judgements about whether they would fit through a doorway positioned at near or far distances. It was found that the Left-PD (LPD) group overestimated door width, whereas the Right-PD (RPD) group underestimated door width. The authors proposed that LPD patients may have a compressed representation of the world, whereas RPD patients may have a compressed representation of self. Although the current study did not distinguish between left and right-side affected PD, it becomes apparent that an altered perception of self or the environment is a plausible explanation for our findings. Further, we suggest that these findings may relate specifically to FOG.

Conclusions

This study has demonstrated that clutter located close to a travel path may provoke FOG in individuals with Parkinson's disease who experience FOG, confirming the importance of reducing cluttered environments in areas frequented by individuals with Parkinson's disease. This information can be used in future infrastructure planning to reduce FOG-related falls in PD patients. Further research should investigate other characteristics of cluttered environments (i.e. colours, fragility, contrasts of objects) to gain a better understanding of how clutter provokes FOG.

Importantly, this study has found that gaze behaviours of PD-FOG are different from healthy individuals. Gaze behaviours of individuals with PD-FOG were characterized by a reliance on on-line feedback control regardless of where clutter was located, whereas in healthy control participants this strategy was only utilized when clutter was close to the path. Previous studies have identified that eye movement training can improve gaze control in a related movement disorder, progressive supranuclear palsy (Zampieri and DiFabio, 2009). Similar eye movement training programs may be employed to encourage PD-FOG to generate more efficient gaze patterns.

Although attentional contributions are important to consider with respect to FOG, it is suggested that greater contributions to FOG may arise from perceptual impairments. Perceptual deficits may have

resulted in a change in visual and stepping behaviours to increase the amount of sensory feedback from the environment. However, this may have led to sensory overload, which has been previously identified as a potential cause of FOG (Morris, Iansek & Galna, 2008). Future research studies using a sensory loading paradigm should be conducted in order to further delineate sensory processing impairments in PD-FOG.

Table 1 – Participant characteristics (all participants)

Group	Age	Height	Gender (M:F)	UPDRS
	Mean (Std. Dev.)	Mean (Std. Dev.)		Mean (Std. Dev.)
Healthy	72.06 (7.50)	171.29 (9.99)	9M:7F	36.13 (8.88)
PD-FOG	76.33 (5.76)	169.76 (10.77)	9M:3F	

Table 2 – Eye tracker participant characteristics

Group	Age	Height	Gender (M:F)	UPDRS
	Mean (Std. Dev.)	Mean (Std. Dev.)		Mean (Std. Dev.)
Healthy	70.60 (7.33)	180.84 (4.17)	4M:1F	38.38 (3.94)
PD-FOG	75.75 (6.13)	177.80 (8.03)	4M	

Table 3 – Mean and stand deviation for each gait measure

Gait measure	Group	Indirect	Direct	P values	Healthy vs. PD-FOG	
		Mean (SD)	Mean (SD)		Indirect	Direct
Step length (m)	Healthy	0.68 (0.094)	0.62 (0.09)	p < 0.02	p < 0.001	p < 0.001
	PD-FOG	0.44 (0.095)	0.32 (0.13)	p < 0.001		
Step length CV	Healthy	4.86 (6.036)	11.05 (12.95)	n.s.	n.s.	p < 0.001
	PD-FOG	8.48 (4.81)	39.22 (50.72)	p < 0.001		
Step width (m)	Healthy	0.089 (0.021)	0.12 (0.036)	n.s.	n.s.	n.s.
	PD-FOG	0.098 (0.028)	0.11 (0.063)	n.s.		
Step width CV	Healthy	71.80 (22.31)	78.79 (19.28)	n.s.	n.s.	n.s.
	PD-FOG	53.83 (18.21)	55.40 (21.37)	n.s.		
Step time CV	Healthy	0.021 (0.020)	0.029 (0.025)	n.s.	n.s.	p < 0.001
	PD-FOG	0.033 (0.020)	0.078 (0.090)	p < 0.002		
Cadence (steps/min)	Healthy	114.29 (7.83)	110.66 (9.51)	n.s.	n.s.	n.s.
	PD-FOG	110.82 (11.51)	117.72 (23.58)	n.s.		
Velocity (m/s)	Healthy	1.25 (0.20)	1.08 (0.15)	n.s.	n.s.	n.s.
	PD-FOG	0.73 (0.28)	0.51 (0.23)	n.s.		

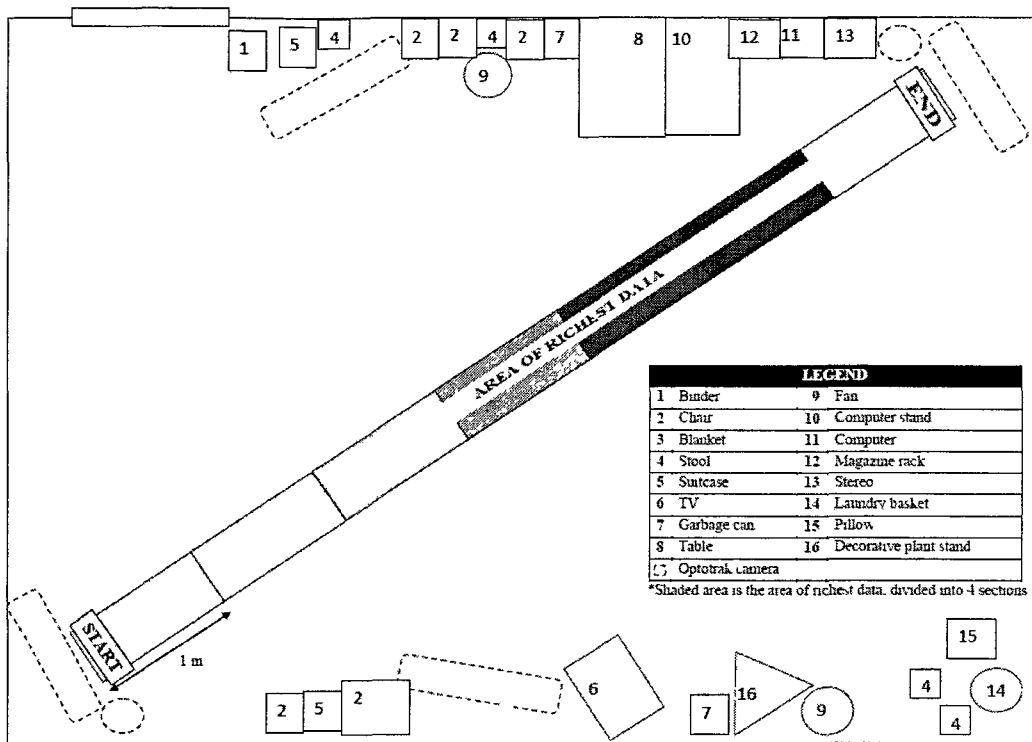


Figure 1a: Indirect clutter – All clutter items located at the perimeter of the room

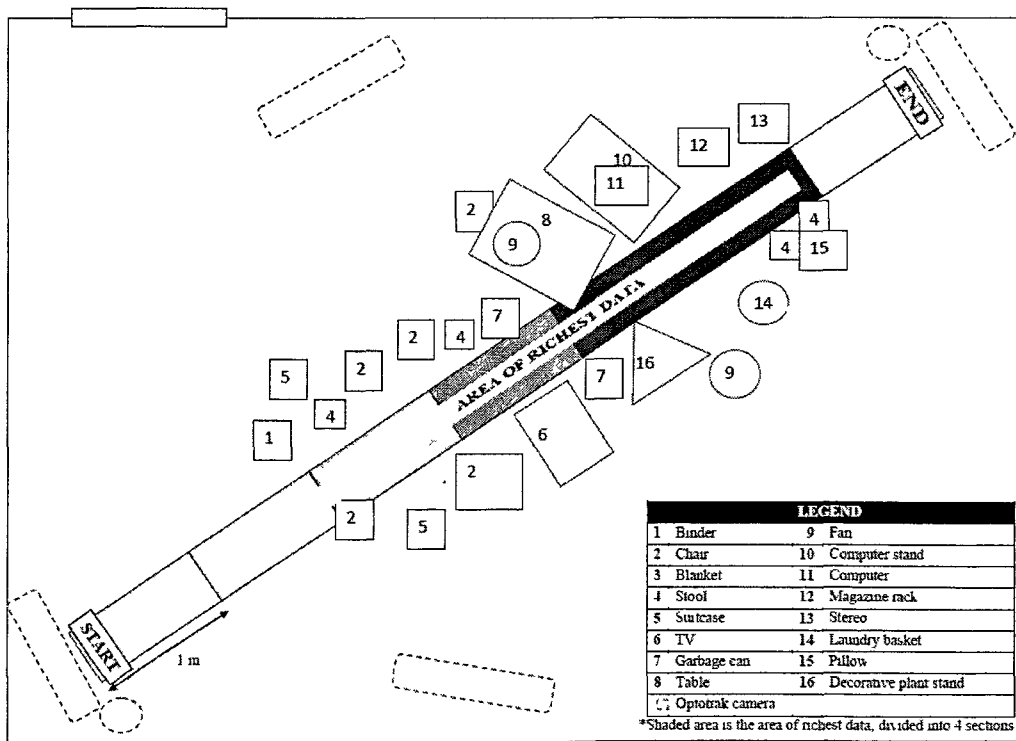


Figure 1b: Direct clutter – All clutter items located in close proximity to the path

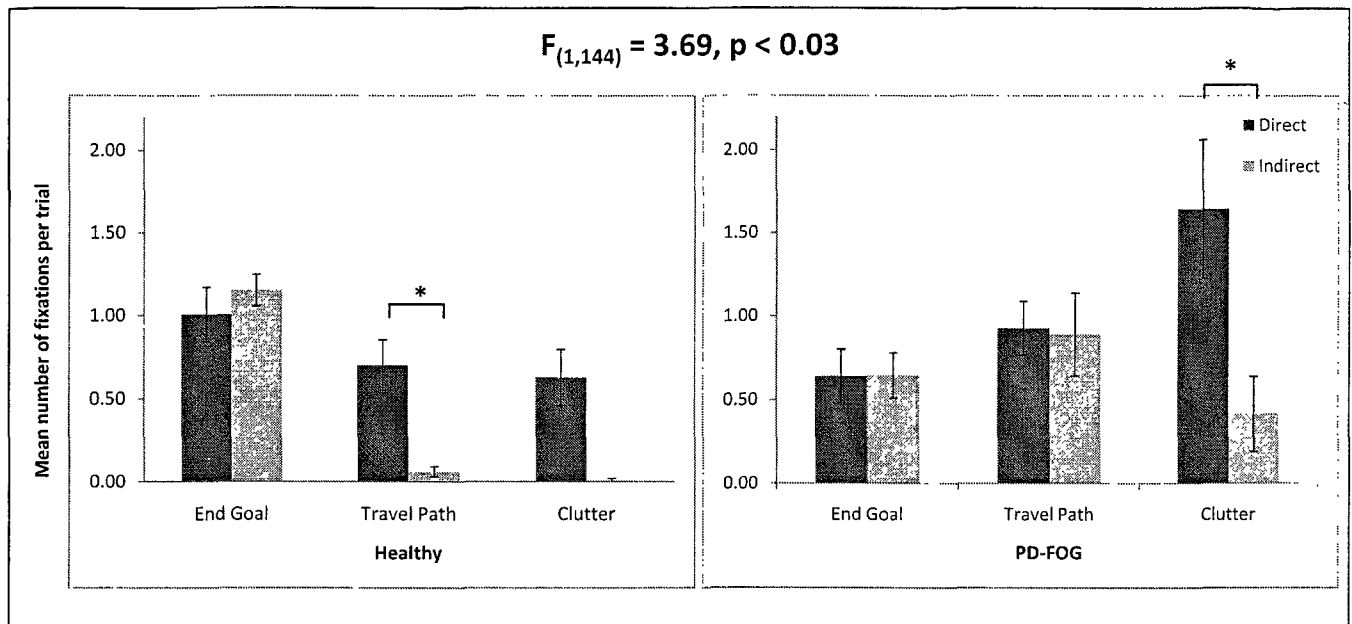


Figure 2: Interaction (Group by Condition by Area of Interest) for mean number of fixations per trial: When compared to Indirect clutter, in the Direct clutter condition healthy participants significantly increased number of fixations to the travel path, whereas PD-FOG significantly increased number of fixations to the clutter.

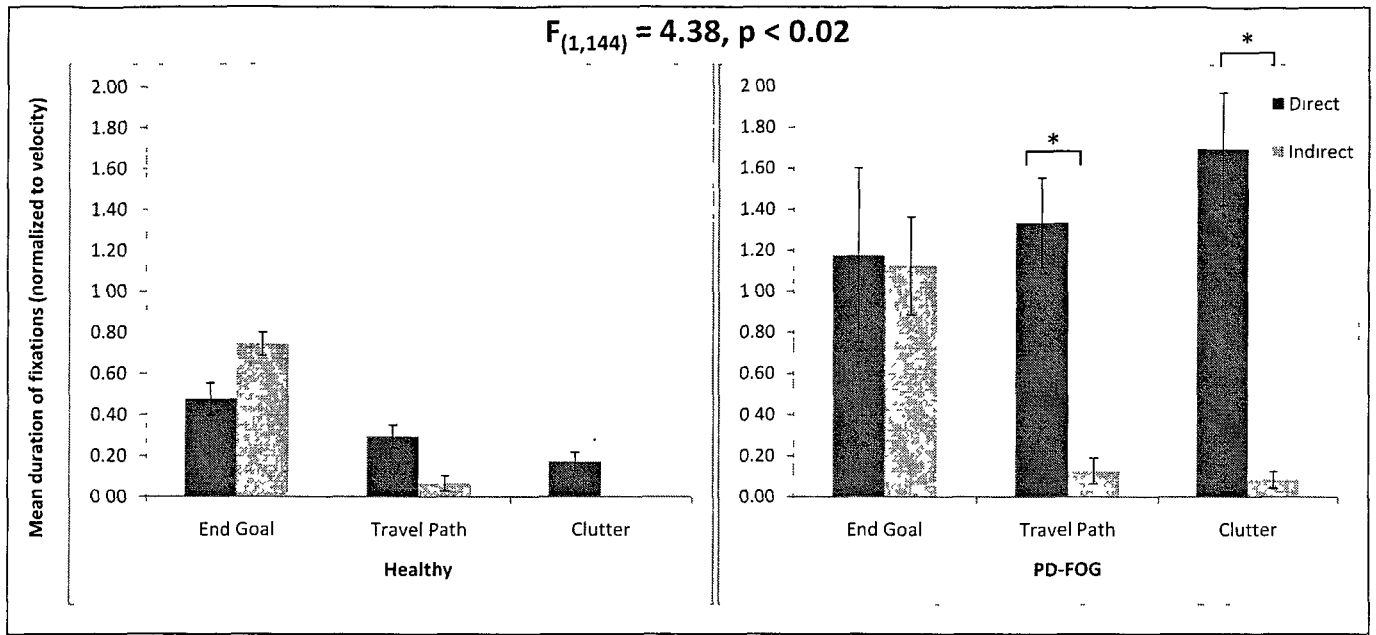


Figure 3: Interaction (Group by Condition by Area of Interest) for mean fixation duration (normalized to velocity): Tukey's post-hoc analysis revealed that healthy participants did not change mean fixation durations to each AOI between conditions, whereas PD-FOG significantly increased mean fixation duration to both the travel path and clutter in the Direct condition.

$F_{(6,144)} = 2.18, p < 0.05$

HEALTHY

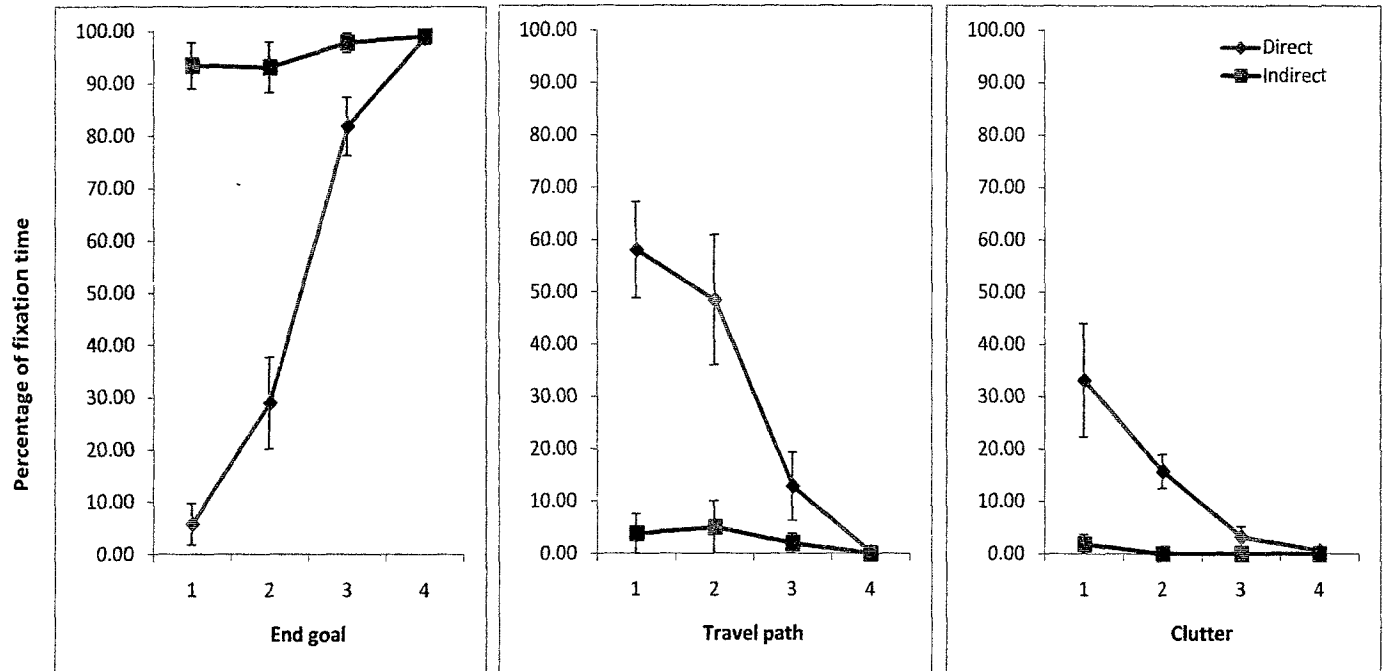


Figure 4a: Interaction (Group by Condition by Area of Interest by Path Section) for percentage of fixation time; Healthy participants: In indirect clutter, the end goal was fixated throughout the path, whereas in direct clutter, the travel path was fixated for the first two sections, then the end goal was fixated for the last two sections.

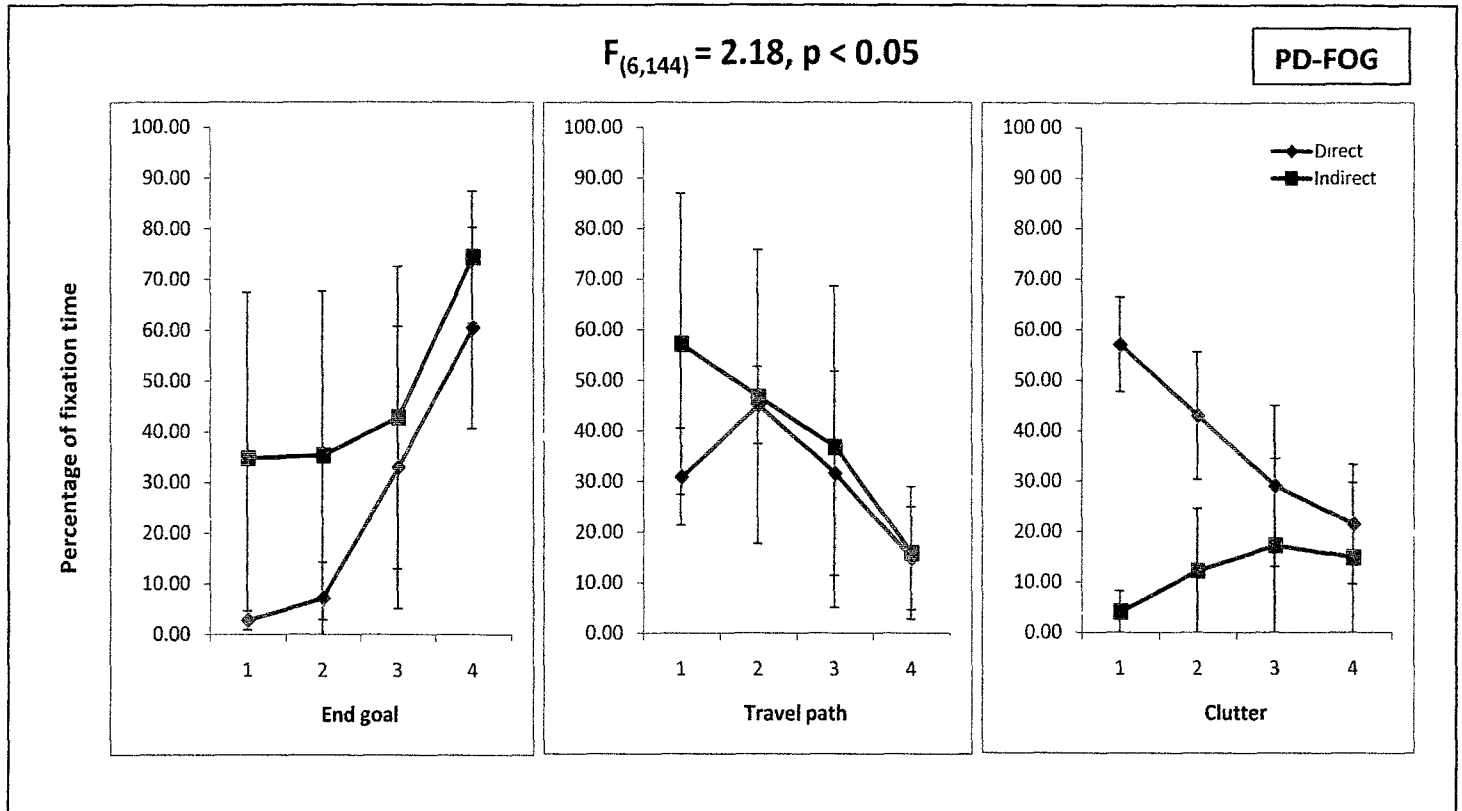


Figure 4b: Interaction (Group by Condition by Area of Interest by Path Section) for percentage of fixation time; PD-FOG participants: In indirect clutter, the end goal and travel path were fixated equally throughout the entire path. In direct clutter, all areas of interest were fixated equally throughout the entire path, although a trend is observed where the clutter and travel path were most fixated in the first two sections of the path.

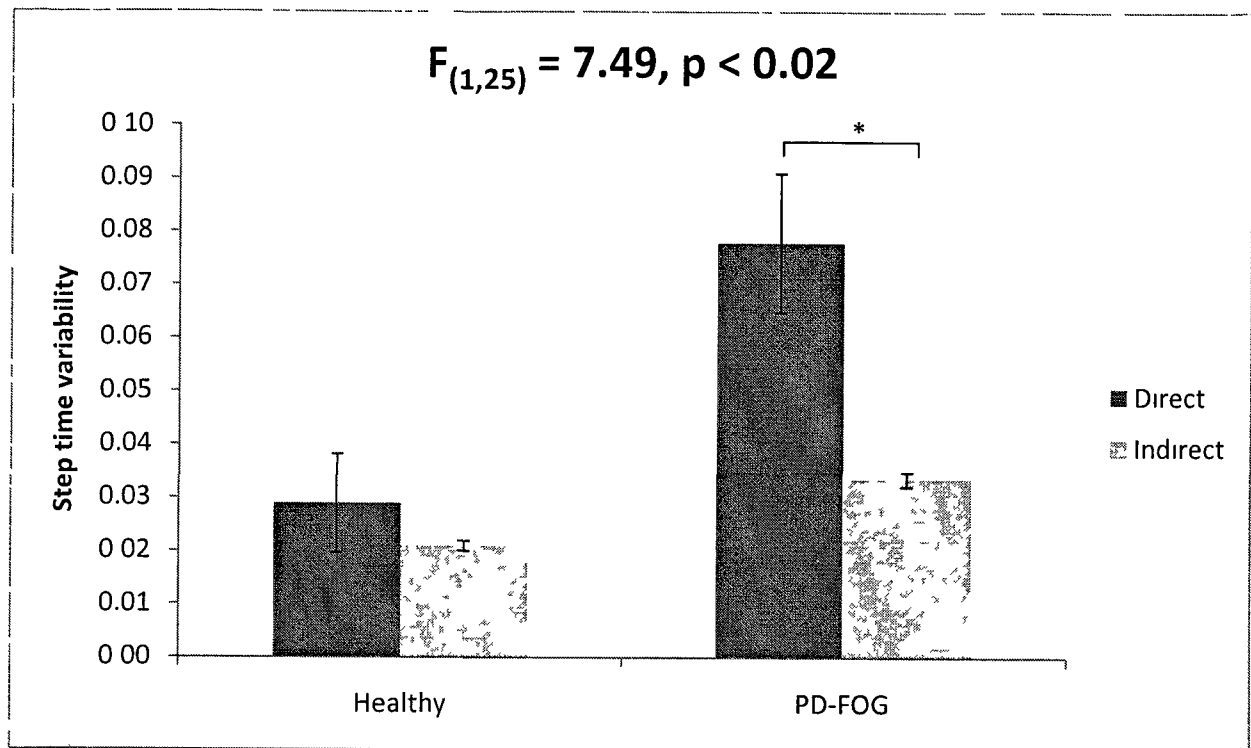


Figure 5: Interaction (Group by Condition) for step time variability: Both groups performed with similar step time variability in the Indirect condition. Only the PD-FOG group significantly increased step time variability in the Direct condition.

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CHAPTER 5

GENERAL DISCUSSION

The overall objective of this thesis was to investigate the influence of cluttered environments on the relationship between eye movements and stepping behaviours during locomotion in individuals with Parkinson's disease (PD). Since locomotion through a realistically cluttered environment in a healthy population had not been described in the literature, chapter two investigated how gaze behaviours in a cluttered environment might influence gait in healthy older adults. It was found that gait adaptations and an increased use of feedback control occurred when clutter was located close to the path. Interestingly, older adults were able to collect sensory feedback and switch from a feedback mode of control to feedforward. It was hypothesized that even greater differences in eye and stepping adjustments would be found in PD patients. Chapter three compared gait variables during locomotion through clutter between three groups of participants: healthy age-matched control participants, PD patients without freezing of gait (FOG), and PD patients with FOG. While healthy control participants and PD non-FOG participants performed with similar gait variability in both conditions, it was found that only the PD-FOG participants increased gait variability in direct clutter. It was suggested that gait disturbances in PD may be related to an increased perceived threat of the environment, which is reflected in gait variability. Finally, chapter four investigated how visual behaviours in cluttered environments might affect walking behaviours in PD-FOG. This investigation attempted to examine how eye behaviours might be related to gait, with the aim of understanding severe gait disturbances in PD-FOG. With these aims, comparisons were made between PD patients with FOG and healthy age-matched control participants. The purpose of this final chapter of general discussion is to examine the major findings of the preceding chapters. Given the novelty of this study of combining two sets of data (eye movements and gait) in PD patients, the first discussion point focuses on how visual information was used by PD-FOG patients. A discussion of how cluttered environments provoke FOG follows, and connections are made between FOG and potential perceptual contributions. Finally, a sensory-perceptual model for FOG is proposed to help describe the

findings of this thesis. Limitations and areas of future research are then discussed, in hopes of spurring more discussion in this important area of research.

Acquisition and use of visual information is different in PD-FOG

This thesis was the first to investigate eye movements during locomotion in Parkinson's disease. In agreement with previous stationary eye tracking studies, PD patients exhibited gaze shift fragmentation (characterized by a greater number of fixations) as well as hypometric eye movements (characterized by longer fixation durations). This investigation has revealed how the use of feedback and feedforward control in Parkinson's disease patients with FOG is different from a healthy population. As discussed in Chapters 2 and 4, gaze data was analyzed according to fixations of three areas: the end goal, travel path, and clutter. Although it is recognized that feedback and feedforward strategies for motor control are not mutually exclusive, identifying different areas of interest in the environment allowed for a general understanding of how PD-FOG may use visual information differently than healthy older adults. Fixations of the end goal represented feedforward control in which individuals relied on an internal movement plan instead of sensory feedback from the environment (Seidler, Noll & Thiers, 2004). Although previous single-obstacle studies have argued that fixations of the travel path also reflect feedforward control (Patla & Vickers, 2003), the current study incorporated multiple objects of different colours, shapes, and contrasts, effectively increasing the physical and visual complexity of the environment. Thus, fixating sections of the travel path slightly ahead of the body in a complex cluttered environment is argued to represent feedback control which uses sensory feedback to guide movements (Seidler, Noll & Thiers, 2004). Using these definitions, it was found that different gaze strategies were used by healthy and PD-FOG groups.

In healthy participants, feedforward control was used in indirect clutter, whereas in direct clutter, they attempted to switch from feedback control in the first half of the path to feedforward control in the second half of the path. As described in chapter two, this interpretation is supported by the higher

percentage of fixations directed at the travel path in the first half of the path, then at the end goal for the remainder of the path. In chapter four, although fixations of the travel path increased in direct clutter, no significant differences were found in step time variability or mean fixation duration between conditions in the healthy participants. Although healthy individuals increased the percentage of time spent fixating the travel path, the mean duration of fixation did not increase. This represents a cautious gaze pattern in which fixations of the travel path were only used to check or confirm the preconceived motor plan.

Interestingly, the gaze strategy of healthy participants in the more challenging direct condition closely resembles the gaze strategy employed by PD-FOG in the less challenging indirect condition. As reported in chapter four, this strategy was characterized by fixations of the end goal and travel path, while maintaining similar variability of step time as healthy control participants. However, while a switch occurred between fixations of the travel path and the end goal in healthy control participants, PD-FOG maintained fixations of both locations throughout the entire path. Thus, it is suggested that in indirect clutter, PD-FOG used feedback control in a similar manner as healthy participants with the goal of confirming a preconceived motor plan. However, the gaze strategy of PD-FOG differs from healthy participants in that PD-FOG continued to require a confirmation of the motor plan throughout the entire pathway as opposed to only in the first half of the path. This behaviour may reflect a difference in perceived environmental threat between the two groups. Since the behaviour of the PD-FOG group is more cautious, it appears that they had a perception of higher environmental threat than the healthy control participants. Unfortunately, perceived environmental threat was not specifically tested (i.e. by administering a qualitative scale), thus our data can only be used to make inferences regarding this point. Nevertheless, these findings demonstrate that PD-FOG utilized a different gaze strategy during locomotion than healthy participants, even in an environment with minimal threat.

Differences in gaze strategies between groups were even more pronounced in direct clutter, during which PD-FOG fixated the end goal, travel path and clutter equally. Additionally, increased step time variability was found in PD-FOG, confirming that sensory feedback from the environment may have

been used to make on-line adjustments to stepping patterns. Since fixations of the travel path and clutter both represent feedback control, PD-FOG relied on sensory feedback more than a preconceived motor plan (feedforward). As a result, it is suggested that the location of objects in a room relative to a path is an important consideration during locomotion. Comparing this behaviour to that of the healthy control group reveals the possibility that PD-FOG may have a lower threshold of perceived threat, in which an environment of lower threat will trigger a switch in motor control. More pointedly, perhaps the healthy control participants did not find the direct clutter condition very challenging. However, if healthy individuals were challenged with an even more complex task such as walking on slippery ice, this greater amount of threat may trigger a switch to feedback control, similar to what was observed in the PD-FOG group.

The differences in gaze strategies observed between groups even in the baseline condition of indirect clutter, demonstrates that PD-FOG are generally more reliant on sensory feedback. The gaze behaviour of PD-FOG in indirect clutter reveals that patients are more cautious and take more time to confirm a motor plan than healthy participants. The drastic changes to gaze fixations observed in direct clutter provoke discussion regarding why PD-FOG change gaze patterns to rely more on sensory feedback.

First, as discussed in chapter four, it is possible that clutter located close to the pathway distracted PD-FOG participants, therefore resulting in the observed increase in percentage of fixation time spent fixating clutter. Previous studies have found that PD patients are more susceptible to peripheral visual distracters in the environment (Lee, Cowan, Vogel, Rolan, Valle-Inclán et al., 2010). However, if clutter objects only served to distract gaze, it would be expected that fixations of clutter were of short duration. Interestingly, the mean duration of clutter fixation was significantly higher in direct clutter (when compared to indirect). We suggest a few possible reasons to explain why PD-FOG participants fixated clutter. First, it is possible that clutter objects were used as timing cues. Previous research has found that visual cues can regulate gait patterns (Azulay, Mesure & Blin, 2006) and prevent and overcome FOG

episodes (Rahman, Griffin, Quinn & Jahanshahi, 2008). Secondly, previous studies have identified that PD-FOG may be related to cognitive deficits (Snijders, Nijkrake, Bakker, Munneke, Wind et al., 2008). Thus, perhaps clutter is fixated because individuals are not able to select an appropriate response. Unfortunately, the current study did not include cognitive measurements to determine whether cognitive deficits contributed to our findings.

Another explanation for the apparent dependence on feedback comes from imaging studies which have revealed that anatomical structures may also contribute to the inability of PD patients to use feed-forward motor control (Seidler, Noll & Thiers, 2004). Feed-forward motor control involves brain areas which function in movement planning and force control, such as the left primary motor cortex, premotor cortex, and basal ganglia. Feedback motor control involves brain areas that contribute during tasks of high difficulty, such as the ipsilateral motor cortex and cerebellum. Impairment of the basal ganglia due to reduced dopamine availability is known to be the cause of PD.

It is important to consider how the characteristic eye behaviours of PD (slower and smaller saccades) might contribute to the current study's findings. Hollands et al. (1996) found that even when stepping targets were removed on a pathway, participants still continued to fixate the remembered target locations in consecutive trials. This may suggest that the behaviours seen in the current study may have been a result of reflexive saccades, instead of focused meaningful fixations on areas of interest to the participant. Alternatively, the differences in gaze behaviours elicited by PD-FOG in the direct condition may actually have resulted from the highly complex visual information collected through the greater number of fixations of the entire environment. Future studies should attempt to investigate the specific contribution of oculomotor deficiencies in PD-FOG on locomotion.

Overall, this study has found that PD-FOG are more reliant on sensory feedback regardless of clutter location. In direct clutter, PD-FOG incorporated sensory feedback to adjust steps, while healthy participants continued to rely on a preconceived motor plan. Spending more time fixating objects in the

environment reveals that clutter located close to the path may divide a patient's attention, with less attention to gait than in indirect clutter. FOG episodes, which were elicited only in the direct condition, may result from this lack of attention. Alternatively, fixating multiple areas of the environment may also reflect a need to extract more information from the environment to form a perceptual judgement about the task. Thus, a deficit to the processing of perceptual information may result in FOG. These potential contributions to FOG are discussed in the next section which focuses on how clutter may provoke FOG episodes.

Location of clutter close to a path provokes FOG episodes

A fundamental question of the current thesis was whether clutter would elicit FOG episodes in an experimental setting. Patients have previously reported that cluttered environments provoke FOG (Snijders, Nijkrake, Bakker, Munneke, Wind et al., 2008), however, these anecdotal reports had not been quantitatively or qualitatively verified in laboratory settings. Furthermore, characteristics of clutter which induce FOG have not been identified. As such, chapter three sought to investigate gait adjustments in PD patients with FOG. There are many characteristics of clutter that may influence FOG (colour, contrast, size, perceived environmental threat). For the purpose of this preliminary study of locomotion through clutter, clutter location was manipulated by placing items either close to the path or at the perimeter of the room.

FOG episodes were only observed in the direct clutter condition, indicating that the proximity of clutter to a path is an important characteristic to consider in PD-FOG. Additionally, all FOG episodes occurred at the narrowest section of the path. This finding can have several possible interpretations. First, FOG may have occurred at this location because of the specific objects surrounding the area. The narrow section of the path was confined by the corner of a table on the left side and a semi-transparent decorative plant stand on the right side. Based on a previous study which found that subjects increased toe clearance, hip vertical velocity and vertical hip position when stepping over a fragile obstacle, objects

in the current study may have been perceived as more fragile or dangerous, thus resulting in FOG (Patla, Rietdyk, Martin, & Prentice, 1996). It is most likely that healthy participants made similar judgements regarding object fragility, yet gait adjustments and disturbances were not observed in this group. Thus, it is suggested that PD-FOG make similar judgements, yet respond differently. Understanding why PD-FOG responded differently will provide further insight to the FOG phenomenon.

A second interpretation of these results is that the width of the path may have been perceived differently by PD-FOG participants. This is supported by the consistent occurrence of freezing episodes at the narrowest point of the path. As discussed in previous studies investigating perception in PD, participants may have over- or under-estimated the width of the door (Lee et al., 2001). Lee and Harris (1999) found that perceptual difficulties may differ between PD patients with greater left-side motor severity (LPD) and right-side motor severity (RPD). When making perceptual judgements about whether they could fit through a doorway, it was found that LPD underestimated door width (compressed representation of world) while RPD overestimated door width (compressed representation of self) (Lee et al., 2001). Although the current study did not analyze data according to side of motor severity, it is possible that perceptual impairments may have resulted in incorrect perceptions of path width, and consequently, FOG. Perceptual contributions to FOG have been previously discussed in the literature (Almeida & Lebold, 2010; Cowie et al., 2010). Almeida and Lebold (2010) proposed that these gait changes observed upon approach of a narrow doorway reflected on-line perceptual processing which may interfere with motor planning and result in FOG. Additionally, an inaccurate perception of door width may reflect impaired perception of one's own body and the ability to fit through the doorway. In other words, individuals may have employed an egocentric frame of reference during locomotion, in which individuals identify environmental features with reference to their own body location. Employing this type of frame of reference may be detrimental to locomotion in PD, since it has been previously found that PD have an altered egocentric capacity (Davidsdottir et al., 2008).

While a perceptual impairment is a probable explanation for FOG, it may appear that clutter is just an example of a confined, narrow space. However, the gaze data collected in the current study suggests that clutter not only confines space, but also presents a complex visual scene which may interfere with sensory and perceptual processing. As described in chapter four, when confronted with clutter located close to the travel path, PD-FOG increased the number of fixations, duration of fixations, and the number of areas attended to in the environment. Thus, while clutter objects may confine the path, higher visual stimulation may actually add to the demands of the walking task.

In order to better probe the question of whether clutter is just an example of a confined space, we compared our results for step length CV to the results of a previous study conducted in our laboratory which investigated gait measures upon approach to narrow, normal and wide doorways. Almeida and Lebold (2010) found that step length CV of the narrow doorway (0.118, +/- 0.129) was significantly greater than the wide doorway (0.06 +/- 0.048) ($p < 0.004$). This resulted in a percent change in step length CV of approximately 46.78%. In the current thesis, we found that the step length CV of the direct condition (0.392 +/- 50.71) was significantly greater than that of the indirect condition (0.0848 +/- 4.81), resulting in a percent change of step length CV of approximately 64.43%. It is important to note that the PD-FOG groups of both studies were comparable (36.12 vs. 32.80), where a difference of 7 points is considered significant. Although we cannot draw firm conclusions based on these two separate studies, the greater difference in percent change of step length CV between conditions suggests that clutter is not just a confinement of space, and provides additional challenges to locomotion. The observation of FOG episodes in the current study and not in the Almeida and Lebold (2010) study, also supports this suggestion. To better answer the question of whether clutter is more than a confined space, both possibilities (confined space and higher visual stimulation) should be investigated separately in future research. It is already known that narrow spaces provoke freezing; thus, future research should investigate eye movements while walking through simple and complex visual scenes which do not

confine space. If complex visual scenes with high visual stimulation are found to trigger FOG, then perhaps the combination of the two triggers is really what makes clutter a freeze-provoking environment.

In conclusion, the current study has provided a first look into clutter as an environment which provokes FOG. Cluttered environments not only stress the locomotor system, but seem to constrain visual processing, although future research should be conducted to explore the influence of complex visual scenes on FOG.

Proposing a sensory-perceptual model of FOG

A central aim of this thesis was to gain a better understanding of FOG and provoke further discussion regarding its underlying mechanisms. Our findings suggest a strong connection between FOG and how participants used visual information to guide locomotion. When PD-FOG were confronted with direct clutter, they made more fixations to clutter objects, thus increasing the amount of visual stimulation. PD-FOG also increased proprioceptive inputs by making on-line gait adjustments. As described by Morris, Iansek and Galna (2008), the basal ganglia integrate sensorimotor information, allowing for the prioritization of stimuli. However, when the basal ganglia are not functioning properly (such as in Parkinson's disease), the increased stimulation overloads the sensory system, which is proposed to result in FOG. These impairments point to a sensory-perceptual deficit as the mechanism that causes individuals to increase the amount of incoming sensory information. This proposal is illustrated in Figure 1. In sum, FOG may be rooted in a sensory-perceptual impairment, which leads to inappropriate response selection involving an attempt to increase the amount of novel sensory feedback. Previous research groups have identified that PD patients may have a reduced capacity for processing sensory information (Kaji, Urushihara, Murase et al., 2005). Furthermore, several sensory functions of the basal ganglia have been suggested, including the role as a gate-keeper for sensory inputs at various levels (Kaji & Murase, 2001), a role in integrating sensory information with motor output (Almeida, Frank, Roy, Jenkins, Spaulding et al., 2005; Morris, Iansek & Galna, 2008), and a role in sensory

perception (Brown, Schneider & Lidsky, 1997). Consequently, impairment to the sensory functions of the basal ganglia may lead to gait deficits (Kaji & Murase, 2001). Therefore, as originally suggested by Morris et al. (2008), this increase in multiple sensory stimuli may result in an overload of the sensory system, and ultimately, FOG. While it is recognized that there may be several influences (i.e. attention, cognition) that occur throughout this process, the novelty of this model lies in the recognition of a sensory-perceptual deficit as the underlying mechanism of these subsequent errors.

Since changes to gait behaviours were only observed in the PD-FOG group, we are assured that the origin of FOG occurs prior to the stage of attempting to increase sensory information (Figure 1). Therefore, we will discuss how the differences in PD patients which led to FOG may result from: a) lack of awareness of perceptual impairment, therefore inappropriate response selection, b) difference in extent of perceptual impairment, or c) similar perceptual impairment, but inappropriate response selection (increasing sensory feedback).

a) Lack of awareness of a perceptual impairment

As described in the previous section, Lee and Harris (1999) found that PD patients were aware of their perceptual difficulties. However, PD patients with FOG were either not identified within their patient population, or were not included. The difference in perception could therefore be the lack of awareness of a perceptual difficulty. If these were the case, patients may select an inappropriate sensory or motor response resulting in the observed precursors to FOG as identified in our model. A follow up investigation of the Lee and Harris (1999) study could be conducted with a PD-FOG population to determine if this awareness, or lack thereof, exists.

b) Difference in the extent of perceptual impairment

Perceptual impairments have been clearly identified as a non-motor symptom of PD. In an imaging study, Pereira et al. (2009) correlated gray matter density with performance on three neuropsychological tests that evaluated visuospatial and visuoperceptual function. Significant

correlations were found between decreased gray matter density in specific parts of the brain and poor visuospatial and visuoperceptual functioning. This study revealed that perceptual impairments have a neuroanatomical basis in PD. Several perceptual studies with PD patients have also identified perceptual deficits of optic flow speed (Young, Wagenaar, Lin, Chou, Davidsdottir et al., 2010), size (Harris, Atkinson, Lee, Nithi, & Fowler, 2003), and depth (Maschke, Gomez, Tuite, Pickett & Konczak, 2006). However, the previously described perceptual deficits have only been identified in PD patients without FOG. This leaves us with the question: Do PD patients without FOG have different impairments to perception than PD patients with FOG?

A few studies have been conducted with PD patients who experience FOG. Lee (2001) investigated Parkinson's disease patients with greater left-side motor severity (LPD) and Parkinson's disease patients with greater right-side motor severity (RPD), with 2 PD-FOG patients in each of these groups. While LPD patients seemed to perceive the environment to be smaller than actuality, RPD patients perceived the doorway to be larger than actuality. Due to this small sample size of PD-FOG participants, Lee et al. (2001) recommended that further research on perception with respect to FOG be conducted with more sensitive measures to detect FOG and perceptual differences. In 2010, Cowie et al. investigated locomotion through, and perception of, narrow, normal and wide doorways. Although PD patients were thought to have a perceptual distortion of space, differences in the perception task were not found between PD-FOG patients and healthy age-matched control participants. However, as noted in a previous discussion, participants gained experience with the doorway prior to making perceptual judgements. This may have improved their performance on the perceptual judgement task. It becomes clear that further studies comparing perceptual abilities of PD patients with and without FOG are necessary.

Finally, with the known links between vision and perception, it is recognized that the current study should be conducted to include a group of PD participants without FOG. This is especially warranted given the strong differences in gaze patterns seen between healthy participants and PD-FOG. Such an analysis would allow for further distinction between potential visuoperceptual

differences in PD non-FOG and PD-FOG groups. Additionally, since differences between LPD and RPD have been identified, it would be important to analyse data according to side of greater PD symptom severity.

c) Similar perceptual impairment, but inappropriate response selection

Due to the lack of research comparing perceptual impairments between groups of PD patients with and without FOG, it may also be possible that there is no difference in perception between these groups. Thus, the final potential stage for error is in selecting a correct response. Perhaps, PD non-FOG patients are better able to control motor responses and respond with minimal changes to gait timing. Conversely, PD-FOG patients may select the inappropriate response by varying their gait cycles, consequently increasing the amount of incoming novel sensory information. In a recent study, Vandebossche et al. (2011) investigated executive functioning in PD patients with and without FOG as well as a control group of healthy age-matched participants. Impairment of conflict resolution, or response selection, was the only specific executive function associated with FOG. Future studies with basic response selection tasks with PD patients with and without FOG may assist in answering this question regarding an impairment of appropriate response selection.

The proposed model for FOG can also be applied to other known freeze-provoking scenarios. For example, turning requires accurate judgements of distance and space. As described by Lee and Harris (1999), patients have reported difficulties in perceiving distance and space. Thus, when approaching a turn, patients may incorrectly perceive the distance to the turning axis, thus resulting in sudden alterations of gait at the turning axis. Further, similar to the current study, confined spaces may be incorrectly perceived as being smaller than they actually are. This inaccurate perception may lead to gait changes and result in FOG. An especially puzzling aspect of FOG is that it is sometimes reported to occur in wide, open spaces (Rahman, Griffin, Quinn & Jahanshahi, 2008). Although freezing in open spaces usually occurs in PD patients with high severity, this is not always the case. The proposed model can explain this occurrence by suggesting that individuals who freeze in open spaces may have a greater

impairment to the perception of their own body, as opposed to the perception of the environment. Further, as described by Lee and Harris (1999), Parkinson's disease patients with greater left-side motor severity (LPD) are more impaired at perceiving the environment, while Parkinson's disease patients with greater right-side motor severity (RPD) are more impaired at perceiving themselves. Since an open environment presumably does not contain any threatening or overly stimulating features, it would be interesting to investigate if individuals who are prone to freezing in open environments are more likely to be RPD patients. While we have proposed theoretical applications of this model to other FOG triggers, future research must be conducted to further explore the applicability of the model.

Conclusion

As the first study to explore the relationship between gaze behaviour and gait patterns during locomotion in Parkinson's disease, the current thesis revealed that PD-FOG used on-line feedback control as opposed to feedforward control to guide locomotion through a complex environment. This study was also the first to attempt to verify anecdotal reports of clutter as a FOG trigger and discovered that clutter located close to a travel path provoked freezing episodes. Finally, gait and gaze variables both revealed attempts at increasing sensory feedback which is suggested to be associated with an inaccurate perception of the environment. Thus, the current thesis lends support to previous suggestions of perceptual deficits as the primary contributor to FOG. Future work should focus on developing a better understanding of perceptual deficits in PD and how they may contribute to gait disturbances. Investigations of eye movements in other freeze-provoking environments will also assist in developing a better understanding of FOG.

Future Directions

The current thesis has discovered that individuals with PD who experience FOG rely heavily on sensory feedback during locomotion through a complex environment, instead of a preconceived motor plan. However, since this study did not investigate eye movements in individuals with Parkinson's disease who do not experience FOG, these findings cannot be specifically attributed to the presence of FOG. Future studies should include a group of Parkinson's disease patients without FOG in order to help distinguish whether these behaviours are specific to the disease or to the FOG symptom.

Qualitative analysis of FOG also revealed that freezing episodes occurred in 5 of 11 PD-FOG participants. Thus, this study has confirmed that cluttered environments do provoke FOG episodes. Future studies investigating different types of clutter characteristics (colour, contrast, size of objects) should be conducted to determine whether these characteristics also influence the occurrence of FOG. Additionally, a similar investigation conducted with patients in the 'off' state of medication may reveal basal ganglia contributions to FOG, locomotion, and eye movements in PD.

Finally, the combination of gaze and gait findings revealed attempts at increasing the overall amount of sensory feedback. This behaviour was suggested to reveal perceptual impairments as the root of the FOG phenomenon. However, the current study lacked perceptual measurements to specifically investigate perceptual impairments. We conclude that perception is a very important aspect of PD to consider. Future studies should incorporate baseline perceptual measures such as perceptual judgement tasks, depth perception, and rod and frame tasks. Correlations between performance on these measures and FOG may help support or refute a perceptual model for FOG.

Recommendations

Since this thesis has found that clutter located close to a path may provoke freezing episodes, the following recommendations are made with respect to infrastructure planning:

- Environments frequented by PD-FOG should be cleared of hazardous, unnecessary objects
- Open spaces should be a priority when planning environments for PD patients
- Areas should be removed of items with high, complex visual stimulation as they may serve to distract PD patients
- Avoid including fragile objects close to a walking path

Additionally, if a sensory-perceptual impairment underlies freezing of gait, it may be important to take the following steps in an attempt to offset this impairment:

- Increase patient awareness of perceptual impairments
- Teach perceptual strategies to PD patients (i.e. recognizing and compensating for impairments)
 - Understanding that they may consistently perceive areas to be smaller than actuality
- Encourage patients to take their time when navigating cluttered environments
 - Patients should not start walking until they have assessed the entire area and are comfortable with their perceptions of the path

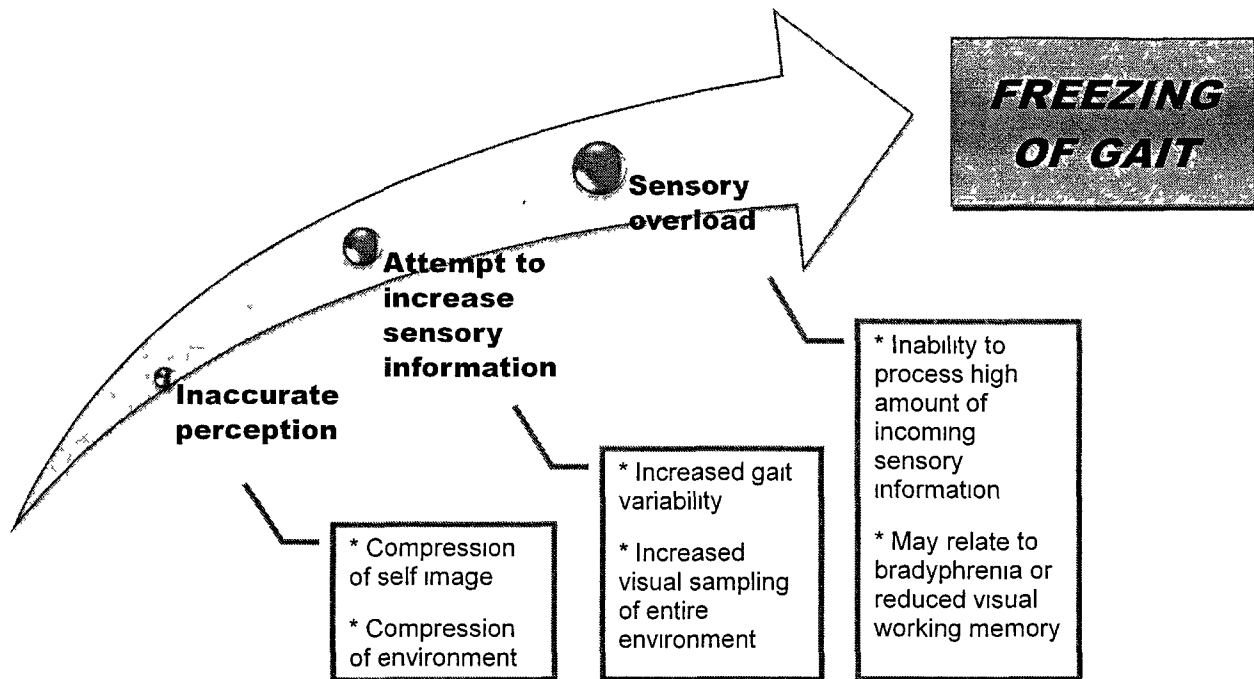


Figure 1: Proposing a sensory-perceptual model of freezing of gait

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