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The relationship between motor planning and freezing of gait in Parkinson's disease

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The research presented here reflects part of the requirements for the Master's degree in Kinesiology, partially completed by the first author from Wilfrid Laurier University.

ABSTRACT

Objective To examine how a cued change in motor plan influences Parkinson's disease (PD) patients with freezing of gait (FOG) (PD FOG; n=10), compared with those without FOG (PD non-FOG; n=10) and healthy controls (n=10).

Methods Participants walked through a doorway in three experimental conditions: no cue; cue before gait initiation; and cue after gait initiation. The light cue was presented at the end of the pathway and signified that individuals must walk to the cue, turn around and return to starting position.

Results Step-to-step variability (a known precursor to FOG) revealed a significant main effect of group (F2,27=32.83, p<0.001), where PD FOG walked with greater step length variability than PD non-FOG and the control group. A significant interaction (F4,54=3.035, p=0.025) demonstrated that only the PD FOG group was most variable when the cue was present before gait initiation.

Conclusion This study concludes that motor planning deficits affect gait, specifically in individuals who experience FOG. This may have important implications for the design of therapeutic interventions in PD FOG.

INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder that is characterised by a lack of dopamine producing cells in the substantia nigra compacta of the basal ganglia. The cardinal symptoms of PD include but are not limited to: bradykinesia (slowness of movement), akinesia (absence of movement), postural instability, tremor and rigidity. Freezing of gait (FOG) is argued by some to be a fifth cardinal symptom distinguished by the sudden inability to initiate or continue walking.[1] FOG is identified as one of the major contributors to a decreased quality of life in PD and has been increasing over the years appearing in about 53% of patients with PD in the advanced stages of the disease; however, the pathophysiology is still poorly understood.[2][4]

Several studies have investigated the physiological mechanisms associated with FOG. FOG is typically considered a motor impairment; however, recent research suggests that declining executive function and deficits in perception may also contribute to FOG.[5][7] One study examined the executive function of PD patients and found worse performance in patients with FOG regardless of disease severity.[8] Spatial perceptual deficits have also been shown to interrupt the initial online movement sequence in patients with FOG.[9] However, given that freezing occurs when turning, manoeuvring through a crowded area and even when a change in gait is prompted by the closing of an elevator door, it is important to consider how motor planning might be associated with FOG. Somewhat related, individuals with Parkinson's disease who exhibit freezing also have difficulty shifting attention when performing online modification of a complex motor sequence.[10] Although gait is typically controlled fairly automatically, when gait requires more conscious control (such as when planning of an upcoming event is necessary), impairments may be more readily identified.

In order to evaluate how gait may be influenced by the requirement to plan an upcoming movement while walking, three groups of participants were required to walk through a narrow doorway with the possibility of being cued to turn around and walk back. By manipulating when the cue prompted this switch, it would be possible to uncover whether gait is influenced by the need to plan the switch during walking (in contrast to prior to walking). The aim was to determine if and when the requirement to plan an upcoming change in walking would influence gait and trigger a freezing episode within individuals with PD who experienced FOG (PD FOG) compared with PD non FOG and healthy control participants.

METHODS

Participants

The study involved 20 participants with PD (10 PD FOG, 10 PD non FOG) and 10 healthy, age matched control participants (table 1). All participants were recruited from the database at the Sun Life Financial Movement Disorders Research and Rehabilitation Centre at Wilfrid Laurier University. All participants with Parkinson's disease were tested approximately 1 h after taking their anti Parkinson's medication. Participants in the PD FOG group were classified based on their self report of FOG. The participants must have scored one or higher on question 14 of the Unified Parkinson's Disease Rating Scale (UPDRS II), which addresses whether the freezing phenomenon was experienced at the time of enrolment as a research participant. An interview was also conducted by a clinician to confirm FOG in these patients at the time of the test. All participants with PD were confirmed by a movement disorder neurologist and were excluded if they were previously diagnosed with dementia (severe loss of cognitive ability). The non FOG PD group had no self report of freezing

Table 1 Patient demographics

Group	Age (p=0.437)	Age range	Years since diagnosis (p=0.03)	UDPRS (p=0.003)	Gender	N
PD FOG	72.2 (7.4)	60 81	9.8 (5.5)	33.9 (5.9)	8 M, 2 F	10
PD non FOG	68.7 (10.3)	53 83	5.3 (3.5)	23.5 (7.6)	5 M, 5 F	10
Control	65.8 (7.8)	55 77	NA	NA	4 M, 6 F	10
Total	69.4 (8.7)	53 83	7.6 (5.0)	28.7(8.5)	17 M 13 F	30

F, female; M, male; UPDRS, Unified Parkinson's disease rating scale, motor score.
Mean (SD); p values denote differences between PD FOG and PD non FOG.

experiences in their case history and scored at least 1 (out of 4) on the gait portion of the UPDRS (motor section III). Each participant was informed of the requirements of the study and signed an approved informed consent, according to the declara tion of Helsinki (*BMJ* 1991;**302**:1194).

Apparatus

The study contained a metal framed double doorway leading into an empty hallway. The lighting in both the laboratory and the hallway was maintained at a consistent brightness. Data were collected on a *GAITRite*® carpet (*GAITRite*®, CIR System, Inc., Clifton, New Jersey, USA) which contains sensors that send information from the participants' footsteps to an attached computer. Additionally, a MAG LITE® operated as the light cue and was present at the end of the carpet to indicate when a change in motor plan is required. A researcher walked with all participants for safety reasons.

Procedure

Participants walked the length of a *GAITRite*® carpet (26 feet) as it was positioned through a narrow doorway. Three randomised conditions with six (randomised) trials were preformed for each participant. Trials commenced with the participant sitting with eyes closed, 2 m before the start of a *GAITRite*® carpet. This ensured that characteristics of gait initiation were not recorded. The participants were instructed to open their eyes and walk the length of the carpet (figure 1). If the light cue was present, participants were instructed to turn around on the carpet at the location of the light cue. Alternatively, when no light cue was presented, participants were to walk straight off the carpet. The three experimental conditions were: (1) no light cue condition (NLC): baseline control condition where participants were instructed to continue walking off the carpet resulting in no change in motor plan; (2) light cue after gait initiation (LCA): the target light illuminated at the end of the carpet (2 feet after the doorway) as the participant walked down the *GAITRite*® carpet. The light cue was always illuminated in the same spot, and the light cue was standardised by having two, four or six steps between when the light cue illuminated to the relative turning point. (3) Light cue before gait initiation (LCB) began with the target light illuminating prior to the participants' gait initiation and was present throughout the entire trial. The presence of a narrow doorway ($^3/_4$ size of normal: 0.675 m wide×2.1 m high) was incorporated to help induce a freezing episode.

Gait parameters analysed

The dependent variables used in the experiment were velocity (cm/s), step length (cm), time in double support phase (% of gait cycle, where both feet are in contact with the ground) and step to step length variability (within trial SD). According to previous work by our group, we specifically analysed gait data prior to the doorway[9] and before any turn could have been initiated. Furthermore, observable freezes were determined by individuals

being in double support phase longer than 1 s, which was accounted for by using video analysis in conjunction with double support phase data derived from the *GAITRite*® software system.

Statistical analysis

The results were analysed using STATISTICA 8 using a mixed model of three groups (PD FOG, PD non FOG and controls)× three conditions (NLC, LCA, LCB) analysis of variance (ANOVA). To determine significant differences between groups within the ANOVA, Tukey's Honest Significant Difference post hoc analysis procedure was conducted. Observational data were collected to determine the frequency of freezes within each
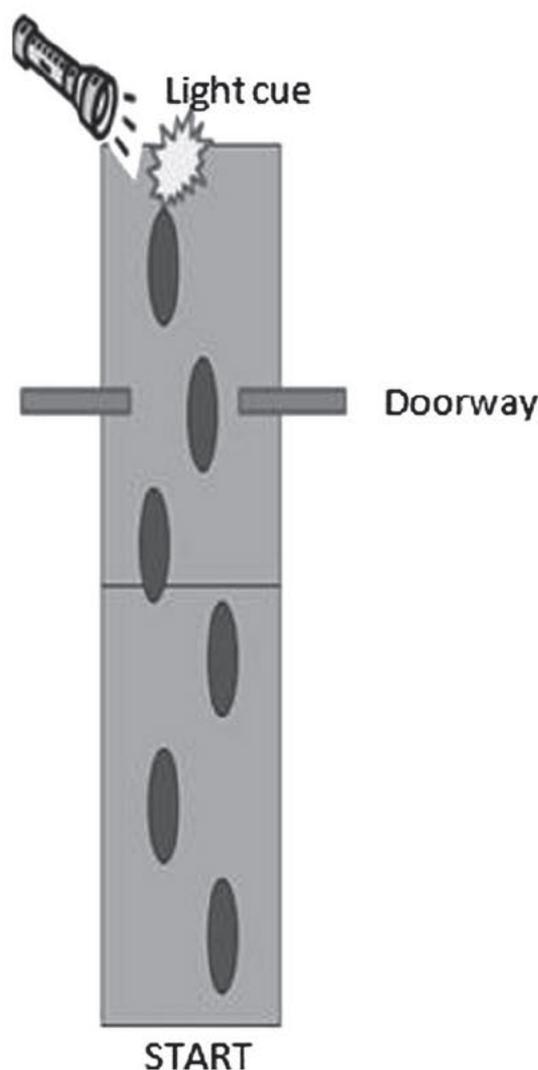

Figure 1 Experimental setup. Participants began at the 'start' and walked through a narrow doorway. Light cue could have occurred while at the start position or just prior to the doorway.

condition. χ^2 tests were conducted to determine significance between the conditions.

RESULTS
Patient demographics
No significant differences in age were evident between groups (see table 1), although an independent t test illustrated a signif icant difference in years since diagnosis between PD patients who experienced FOG (9.8 years, SD=5.49) and PD patients who do not (5.3 years, SD=3.30) (t_{18}=2.22, p=0.03).

Gait velocity
PD FOG had significantly slower velocity (85.09 cm/s, SD=37.38) on average compared with the PD non FOG group (126.98 cm/s, SD=14.02) and the control group (148.79 cm/s, SD=17.16) ($F_{2,27}$=18.419, p<0.05). Post hoc analysis revealed that the PD FOG group walked significantly slower than both the PD non FOG (32% decrease, p=0.0016) and control group (42.8% decrease, p<0.01). In contrast, no significant differences were identified between the control and PD group. There was no significant difference between conditions for gait velocity.

Step length
A significant main effect of group was found between the PD FOG (44.78 cm, SD=17.64), PD non FOG (68.03 cm, SD=8.77) and control group (74.83 cm, SD=9.42) ($F_{2,27}$=16.32, p<0.01). Post hoc analysis confirmed that participants who experience FOG have significantly smaller step lengths than both the PD and control group. The PD non FOG group did not significantly differ from the control group with respect to step length. A significant interaction between group and condition illustrates that PD FOG had significantly smaller step lengths compared with the control and PD non FOG group when the light cue was present before gait initiation ($F_{4,54}$=2.56, p<0.05).

Double support phase
It was observed that the PD FOG group (0.498% GC, SD=0.517) spends significantly more time in double support phase compared with PD non FOG (0.248% GC, SD=0.066, p=0.0017) and healthy controls (0.243% GC, SD=0.163, p<0.0014) ($F_{2, 27}$=10.318, p<0.05). The PD non FOG group and the healthy control group did not differ significantly from one another.

Step-to-step variability
When comparing groups, a main effect was identified ($F_{2,27}$=32.83, p<0.001). Post hoc analysis revealed that PD FOG had significantly more variability in their step length (5.54 cm, SD=4.536) when compared with PD non FOG (3.05 cm, SD=1.877, p<0.001) and healthy controls (2.90 cm, SD=1.782, p<0.001). No significant differences were found between the PD and the healthy control group.

Interesting to note is the main effect of condition (figure 2). In the light cue before gait initiation condition (4.58 cm), partici pants had significantly more variability in their step length when compared with the no light cue condition (3.52 cm) and the light cue after initiation condition (3.38 cm) ($F_{2,54}$=11.267, p<0.001). Post hoc analysis confirmed that when the light cue was present before gait initiation, participants had more vari ability than both the no light condition (p=0.001) and when the light cue was present after gait initiation (p<0.001).

A significant interaction of step length variability was also found when comparing group and condition ($F_{4,54}$=3.035, p=0.025) (figure 3). This interaction is driven by the PD FOG group, in which the group had significantly higher variability
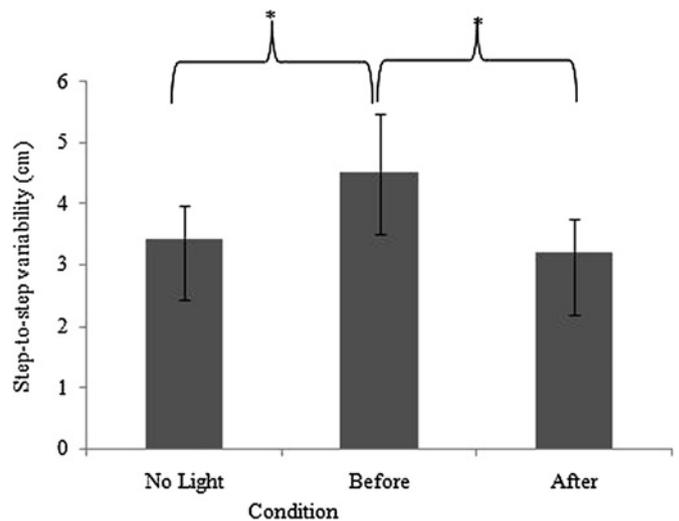

Figure 2 Within trial step-to-step variability across conditions in PD FOG, PD non-FOG and healthy controls.

when the light cue was present before initiation of gait condi tion (7.03 cm) than both no light cue (4.83 cm) and light cue after initiation condition (4.77 cm). Post hoc analysis confirmed that the PD FOG group differed significantly from both the PD non FOG and control group when comparing between no light cue and light cue after initiation conditions. The results indicate that the PD FOG group was significantly more variable when the light cue was present after gait initiation than the other groups, and neither the PD non FOG group nor the healthy control group differed significantly in variability as a result of a light cue condition.

Frequency of freezing episodes
The frequency of freezing episodes within the PD FOG group was obtained by observing each trial through video recordings. A χ^2 analysis demonstrated a significant group effect between conditions (χ^2=10.059, DF=2, p<0.01). Upon further exami nation, a χ^2 analysis confirmed that the condition in which the light cue was present after gait initiation (47.5%) had signifi cantly higher number of freezing episodes than no light cue
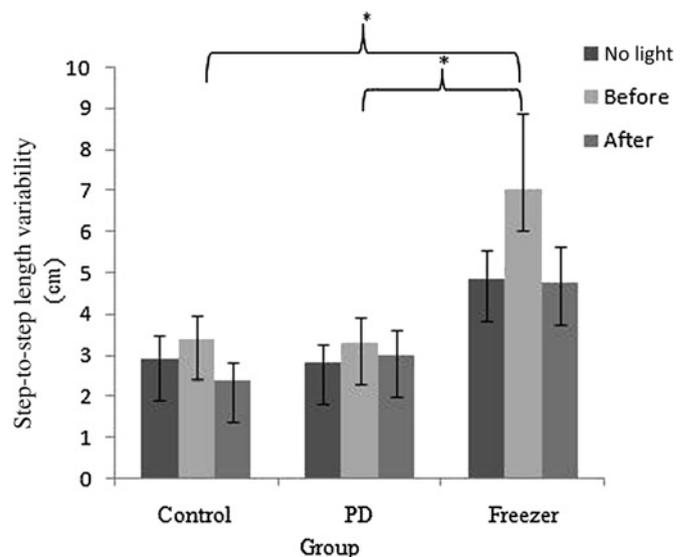

Figure 3 Within trial step-to-step variability interaction between groups and conditions.

(16.4%, $\chi^2=9.935$, p<0.002) and light cue before initiation (35.8%, $\chi^2=4.308$, p<0.05). In addition, having no light cue elicited significantly less freezes than when the light cue was present before initiation ($\chi^2=5.876$, p<0.02).

DISCUSSION

The primary objective of the study was to evaluate how gait might be influenced by a cued change in motor planning in PD FOG (compared with PD non FOG and healthy controls). Outcome measures included: step to step variability, step length, velocity and double support time. The observable freeze frequency in conjunction with the previously mentioned gait parameters demonstrated that cognitively altering a gait pattern with an additional attentional focus may have detrimental effects on gait in PD FOG.

This is the first study to show that freezers exhibit changes in gait parameters with an alteration of a movement plan. The current study found increased step to step length variability within the PD FOG group, and was more profound when the light cue was present before gait initiation, suggesting that gait adjustments were made in order to pass through the doorway safely. It is important to note that freezers were the only group to illustrate this effect, demonstrating that increasing cognitive demands may have a negative effect on gait in PD FOG patients. The results support the notion that when gait becomes abnormal and less automatic, gait asymmetry may rely on cognitive input and attention.[11] The use of an intentional switch cue allowed for further testing of the hypothesis since responding to a switch cue requires intentional control (requiring prefrontal activation) to initiate new motor set.[12 14] If this were the case, then we would expect greater interruptions of move ment and more freezes when the light cue is present after gait initiation. Interestingly, increased step length variability and an increased number of freezes were evident when the light cue was present before and after gait initiation conditions compared with no light cue condition. Most observable freezes when the light cue was present after gait initiation condition occurred after the light cue was presented, suggesting that an unexpected change in the outcome or goal of a movement plan in PD FOG may also elicit freezing. These findings support Almeida et al in 2003, in which individuals with PD were unable to separate plans of action, which may be related to attention shifting deficits when transferring between different motor sets.[10 14 17]

The results provide evidence that FOG may be influenced by difficulty in processing a voluntary switch within a movement task through executive function decline. Increased time in double support phase, step to step variability, decreased velocity, step length and observed freezing episodes during the light cue conditions all support the implication that individuals with FOG alter their gait in response to a shift in attention while switching movement tasks and may trigger FOG episodes.

PD patients were tested in their 'ON' state of medication as mentioned earlier to get an accurate understanding of the potential effects during their everyday activities. Although this may be a potential limitation to the study, previous research indicates that FOG may be typically unresponsive to medica tion.[18] Future studies may include patients in their 'OFF' state to get an understanding of basal ganglia contributions to FOG in attentionally demanding situations. It is also important to consider that our PD FOG group was slightly older (although not significantly), with longer disease duration and higher motor severity as determined by the UPDRS. Thus, it is possible that advanced disease, or other differences between groups such as

cognitive decline, depression and anxiety, might account for the performance differences between groups. While it was not the focus of this study to address these issues, future research should be directed at examining these potential influences more thor oughly. The fact remains that the number of freezes, decrease in step length and an increased variability of step length were all specifically influenced by condition in only the PD FOG group. Overall, the motor planning required to switch between motor sets is an important factor that needs to be considered, since there is potential to develop new treatment strategies for individuals with PD FOG.

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