Is There a Relationship Between Freezing and Executive Function In People Living with Parkinson's Disease?

A Thesis Submitted to the Committee on Graduate Studies in Partial Fulfillment of the Requirements for the Degree of Master of Science in the Faculty of Arts and Science

TRENT UNIVERSITY

Peterborough, Ontario, Canada

Psychology M.Sc. Graduate Program

January 2026

ABSTRACT

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Freezing is a debilitating phenomenon that reduces quality of life for people with Parkinson's disease (PwPD). This study tests the hypothesis that: 1) freezing is linked to executive dysfunction; 2) freezing is a global motor phenomenon, not limited to gait. We compared 14 PwPD to 16 controls. Several aspects of executive function were measured using pro- and anti-saccade tasks under gap and overlap timing conditions, where the gap effect is defined as the reduction in saccade latency associated with the removal of fixation before target presentation. As predicted, results showed larger anti-saccade gap effects in PwPD with than without FOG, and that the pro-saccade gap effect predicted FOG severity in PwPD with FOG. PwPD also demonstrated impaired performance on reaching and walking tasks designed to elicit freezing. These findings strengthen the evidence that executive dysfunction, measured by saccade tasks, is linked to freezing in PwPD.

Keywords: Parkinson's disease, freezing of upper limbs, freezing of gait, executive function, eye movements

Acknowledgements

I am deeply grateful to my thesis supervisor, Dr. Liana Brown, whose extensive knowledge, expertise, and unwavering mentorship were instrumental in the completion of this study. Her patience, wisdom, and valuable feedback have been a guiding light throughout my academic journey, profoundly shaping my growth as a researcher. I extend my thanks to Dr. Sebastien Paquette for joining my thesis committee as my second reader and providing insightful contributions that enriched this work.

My sincere appreciation goes to my lab mates, Jennifer Stevenson and Emma Pownall, for their camaraderie, support, and guidance. Their contributions made this journey rewarding and significantly contributed to my development as a researcher. To my research assistants, Alisa Pitre, Krisha Wadhwani, Rachel Smith, and Lauren Greeley, I am immensely grateful for your dedication and contributions to this project. Your hard work and commitment were vital to its success.

I am thankful to my family and loving partner for their endless support and encouragement throughout this process. Their belief in me provided the strength to persevere. Finally, I extend my deepest gratitude to the Peterborough Parkinson's Community for making this research possible. Your participation and support have been invaluable, and this work is dedicated to you.

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List of Abbreviations

Analysis of Variance (ANOVA)

Freezing of gait (FOG)

Freezing of upper limbs (FOUL)

Frontal Assessment Battery (FAB)

Hospital Anxiety and Depression Scale (HADS)

Montreal Cognitive Assessment (MOCA)

Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS)

New Freezing of Gait Questionnaire (NFOG-Q)

Parkinson's disease (PD)

People with Parkinson's disease (PwPD)

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Parkinson's disease (PD) is a neurodegenerative disorder characterized by distressing motor symptoms such as bradykinesia, postural instability, rigidity, and resting tremor (Mazzoni et al., 2012). Although motor features are a defining aspect of PD, non-motor symptoms, such as cognitive deficits can be highly debilitating (Jankovic, 2008). PD leads to the loss of dopaminergic neurons in the substantia nigra pars compacta (SNc), resulting in a widespread decrease of dopamine in the surrounding structures of the brain (Vandenbossche et al., 2013). This disruption contributes to the diverse symptoms of PD, which can have a considerable influence on quality of life (Mazzoni et al., 2012). Parkinson's affects over 10 million people worldwide, and currently, there is no known cure. Therefore, understanding the underlying mechanisms of PD is essential for managing symptoms.

One notable feature of advancing PD is freezing of gait, a symptom often described by people with Parkinson's disease (PwPD) as the sensation of their feet being glued to the ground (Bloem et al., 2004). Freezing is a troubling symptom that leads to increased falls and reduced quality of life (Kerr et al., 2010; Moore et al., 2007). While several explanations for freezing have been proposed, there is still no consensus on the underlying cause. Previous research suggests that the decline in executive function, the cognitive skills required for initiating, inhibiting, planning, and organizing behaviours, due to PD, may play a key role in freezing (Amboni et al., 2008; Kostić et al., 2012; Walton et al., 2015). Using performance on eye movement tasks as a measure of executive function, researchers have found that PwPD who experience freezing show

higher levels of executive dysfunction in comparison to PwPD who do not experience freezing (Amboni et al., 2008; Gallea et al., 2021; Nemanich & Earhart, 2016; Walton et al., 2015). Exploring the connection between executive function and freezing using saccade tasks may help elucidate the pathology of freezing.

The motivation for this study stems from the profound impact of freezing on PwPD, limiting their mobility and independence, and the lack of clarity surrounding its mechanisms. Emerging evidence suggests that freezing may not be limited to gait but could represent a broader motor phenomenon affecting upper limbs, speech, and eye movements (Ackermann et al., 1993; Heremans et al., 2019; Likitgorn et al., 2021). By focusing on executive dysfunction, assessed through saccade tasks, and comparing freezing across motor domains, this study seeks to help uncover shared mechanisms. This could lead to novel assessments for freezing, ultimately improving quality of life for PwPD. The goal of this study is to help provide greater insights into the mechanisms of freezing by using saccadic eye movements to evaluate executive function.

Parkinson's Disease

Stages, Signs and Symptoms

Parkinson's disease is highly individualized; however, five stages have been identified to help quantify disease progression (Hoehn & Yahr, 1967). In the early stages of Parkinson's disease, symptoms can be minute; finger tremors or joint stiffness may be apparent. Once the disease advances, people commonly experience resting tremors and rigidity. It becomes increasingly difficult to initiate movement; movements that are initiated will be noticeably slower than usual. Within stage 1, only unilateral impacts are present; functional impairment is low. Stage 2 can be characterized by bilateral

impairments and decreased balance. Stage 3 begins with notable unsteadiness; the disease becomes moderately disabling. Stage 4 is marked by significant disability, but the patient maintains the ability to walk. The initiation of stage 5 is confirmed when the patient becomes confined to a bed or wheelchair; they are not able to move without assistance.

The symptoms of Parkinson's disease can be divided into motor and non-motor symptoms. Primary motor symptoms include bradykinesia, postural instability, rigidity, and resting tremor (Mazzoni et al., 2012). Bradykinesia refers to slowness of movement, people experiencing bradykinesia may have difficulties initiating movements. Postural instability commonly occurs within the advanced stages of PD. This feature can be affirmed through tests that assess retropulsion and propulsion. Rigidity refers to stiffness of movement, people may show increased resistance to passive movement. Resting tremors are tremors that occur when a person is attempting to be still, they tend to occur at a frequency of 4-6 Hz (Jankovic, 2008). Additionally, PwPD may experience hypomimia, more commonly referred to as facial masking. Facial masking is often characterized by reduced eye movements (Hikosaka et al., 2000). PwPD tend to exhibit a shuffling gait with reduced arm swinging while walking (Jankovic, 2008).

Non-motor symptoms of Parkinson's disease are common and often overlooked (Jankovic, 2008). Cognitive impairment is frequently observed in PwPD (Das et al., 2016). Bradyphrenia (slowness of thought) and difficulties with word retrieval are prevalent experiences (Jankovic, 2008). Psychiatric symptoms range from depression and anxiety to fatigue and apathy. Sensory symptoms include anosmia (loss of olfactory ability), ageusia (reduced gustation), and paresthesia. PwPD often experience a reduced ability to control certain bodily functions, which can lead to symptoms such as

hypotension, constipation, sexual dysfunction, and urinary dysfunction. In addition, PwPD may experience vivid dreams, REM disorder, restless leg syndrome, and fragmented sleep.

The Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) was created to assess the disease severity and progression of Parkinson's disease (Goetz et al., 2008). The MDS-UPDRS consists of 4 parts; participants are assessed based on their non-motor experiences of daily living, motor experiences of daily living, and motor complications. The MDS-UPDRS also includes a motor examination (Part III) where the participants' motor signs and symptoms are rated as slight, mild, moderate, or severe in response to performance on specified test items. Each item is scored on a Likert scale from 0 to 4, corresponding to the severity levels (0 = normal, 1 = slight, 2 = mild, 3 = moderate, 4 = severe). The higher the total MDS-UPDRS score, the higher the severity of PD.

These symptoms and stages provide a foundation for understanding PD's impact, but freezing stands out as a particularly debilitating feature that warrants focused investigation. The variability in symptom presentation and progression underscores the need to explore specific mechanisms, such as those underlying freezing, to help develop targeted assessments.

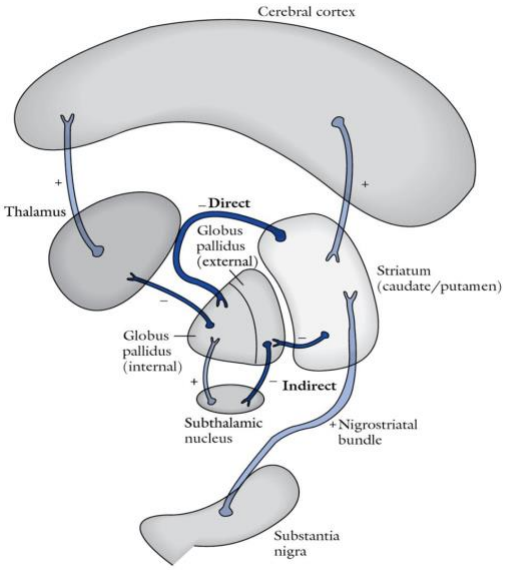
Neuropathology

The direct cause of Parkinson's disease is unknown. PD leads to a loss of dopaminergic neurons in the substantia nigra pars compacta; one of the basal ganglia nuclei (Vandenbossche et al., 2013). The basal ganglia, located at the base of the cerebrum, form a critical neural system for regulating voluntary motor control. It is

comprised of the caudate nucleus, putamen (collectively termed the striatum), globus pallidus (external segment, GPe, and internal segment, GPi), substantia nigra (pars compacta, SNc, and pars reticulata, SNr), and the subthalamic nucleus (STN) (Hikosaka et al., 2000). These structures coordinate motor function through three primary pathways: the direct, indirect, and hyperdirect pathways, each characterized by distinct anatomical connections and functional contributions to motor behaviour. These pathways are shown in Figure 1.

Figure 1

Projections of the Basal Ganglia



Note. This figure demonstrates the connections between the basal ganglia and the cerebral cortex (Banich & Compton, 2023).

The direct pathway originates in the striatum, where the caudate nucleus and putamen receive excitatory inputs from the thalamus and the cerebral cortex. These signals are transmitted to the GPi and SNr, which project inhibitory outputs to the thalamus and motor regions of the brain stem such as the superior colliculus. By reducing

inhibitory output to the thalamus, the direct pathway disinhibits thalamocortical projections, thereby facilitating the selection and initiation of purposeful voluntary movements. In PD, the degeneration of dopaminergic neurons in the substantia nigra pars compacta reduces dopamine levels in the striatum, impairing the direct pathway's ability to disinhibit thalamocortical projections (Albin et al., 1995). This disruption contributes to motor symptoms such as bradykinesia and difficulty initiating voluntary movements.

The indirect pathway also begins with striatal inputs from the thalamus and cerebral cortex but involves additional structures, including the GPe, which connects to the STN, and subsequently to the GPi and SNr. This pathway enhances inhibitory output to the thalamus, effectively suppressing unintended or competing motor actions. This mechanism ensures movement precision by preventing extraneous movements that could interfere with the intended motor plan. In PD, the loss of dopaminergic modulation in the striatum over activates the indirect pathway, leading to excessive inhibition of thalamocortical projections (Albin et al., 1995). This overactivity contributes to motor symptoms such as rigidity and difficulty suppressing unwanted movements.

The hyperdirect pathway is characterized by direct cortical projections to the STN, which in turn innervates the GPi and SNr. This pathway provides rapid inhibitory control over motor output, functioning as a brake to suppress ongoing or premature movements. By enabling swift modulation of motor activity, the hyperdirect pathway enhances the accuracy and timing of motor control, ensuring precise termination or adjustment of actions. Collectively, these pathways integrate cortical and thalamic inputs, modulating basal ganglia output to achieve coordinated motor behaviour essential for voluntary movement control. In PD, degeneration of dopaminergic neurons disrupts the

balance of excitatory input to the STN, leading to excessive STN activity and overactivation of the GPi and SNr, which impairs the pathway's ability to appropriately modulate motor control (Albin et al., 1995). This dysfunction contributes to motor symptoms such as akinesia and difficulty adjusting ongoing movements.

The disruption of these pathways provides a critical link to understanding freezing, as the impaired balance between initiation and inhibition in motor control may contribute to the episodic failures seen in freezing across motor domains. This neuropathological framework motivates our exploration of executive function, which relies on similar basal ganglia-cortical systems, as a potential driver of freezing.

Freezing

Of particular interest for this project is the debilitating type of gait dysfunction known as freezing of gait (FOG) (Jankovic, 2008). FOG has been defined as "a brief, episodic absence or marked reduction of the forward progression of the feet despite the intention to walk" (Giladi & Nieuwboer, 2008; Nutt et al., 2011). PwPD commonly describe FOG as being akin to having their feet glued to the floor (Bloem et al., 2004). The individual becomes stuck in place despite wanting and trying to move. As Parkinson's disease progresses, freezing of gait becomes more likely; approximately 50% of PwPD experience FOG (Giladi et al., 1997). Freezing episodes usually last between 3 – 30 seconds and occur more frequently in some scenarios compared to others (Nutt et al., 2011). For example, PwPD often freeze when turning or passing through narrow spaces like doorways, making these situations helpful for observing FOG in clinical settings (Cowie et al., 2012; Mancini et al., 2021). Notably, freezing is not solely the complete cessation of movement. FOG has been characterized by difficulties initiating

movement, reduced step length and amplitude, along with trembling-like leg movements in frequency bands of 3-8 Hz.

Even though the majority of literature investigates freezing of gait, there have been some reports of freezing in other coordinated movements. Freezing is not restricted to gait; similar motor blocks have been observed in upper limb movements, speech, and eye movements (Ackermann et al., 1993; Delval et al., 2017; Heremans et al., 2019; Likitgorn et al., 2021). Freezing of upper limbs (FOUL) can manifest as difficulties performing actions such as writing, stirring, or reaching for a doorhandle (Heremans et al., 2016). In experimental settings, FOUL has been observed in tapping tasks and using a freezing detection tool called the Funnel Task (Delval et al., 2017; Heremans et al., 2019). During the Funnel task, the participant simulates handwriting by making alternating up- and downstroke movements between two horizontal, symmetrical lines. The lines vary in their distance from one another, forming wider spaces, and narrower spaces (funnels). The researchers who developed this freezing detection tool claimed that the larger movements made in the wider spaces resemble walking with long strides, while smaller ones in the narrow spaces mimic taking short steps through a narrowing passage (Heremans et al., 2020). Similar to how narrow spaces can trigger FOG, the Funnel task tends to provoke similar difficulties in handwriting.

Past research has shown that during FOG, there can be the failure to produce normal amplitude in step length (Nieuwboer et al., 2001). PwPD with FOG walk with a smaller step length, reduced velocity, and have greater step length variability compared to PwPD without FOG and neurologically healthy controls (Chee et al., 2009). These characteristics of gait freezing overlap with the characteristics of upper limb freezing.

Research has demonstrated that during FOUL, there can be a decrease in movement amplitude, and an increase in variability of movement amplitude during writing tasks compared to PwPD without FOUL and controls (Heremans et al., 2016). These deficits were more pronounced in alternating-sized [large (1 cm) or small (.6 cm)] letter writing tasks. Greater overall handwriting difficulties, particularly in fluency, were observed, as indicated by higher scores on the Systematic Screening of Handwriting Difficulties test (Heremans et al., 2016). Therefore, FOUL seems to share common kinematic patterns to those of FOG, especially the reduction in movement amplitude (Heremans et al., 2016). Further exploring these common characteristics between FOG and FOUL may help provide greater insight into the underlying mechanisms of freezing.

A study conducted by Heremans et al. (2019) investigated FOUL in PwPD by utilizing the Funnel Task and examining its relationship with task demands such as speed and movement size. Additionally, they aimed to explore the correlation between FOUL and cognitive function, disease severity, and FOG. The researchers hypothesized that increasing movement speed would lead to more frequent and longer FOUL episodes. Forty-nine participants with PD and 10 controls completed the Funnel task at two subjectively defined speeds: a comfortable pace (normal funnel task) and maximum speed (fast funnel task). FOUL was defined as an interruption or absence of effective movement for at least one second, and data on movement amplitude, speed, and freezing episodes were collected. Results showed that FOUL episodes were significantly more frequent during the fast Funnel task for PwPD ($M = 2.5 \pm 4.2$ episodes per person), eliciting more freezing episodes and longer freezing times compared to the normal Funnel task ($M = 1.2 \pm 2.8$ episodes per person). The majority of freezing occurred when

writing at smaller or gradually decreasing sizes, while larger or gradually increasing sizes provoked fewer freezing episodes. The study also found that individuals with more frequent FOUL episodes had lower cognitive performance, measured using the Montreal Cognitive Assessment (MOCA). The researchers highlighted the need for further understanding of FOUL in PD to improve therapeutic strategies for managing upper limb motor impairments.

Further supporting the idea that freezing is a global motor phenomenon, not restricted to gait, is a study that explored its occurrence during speech. Freezing of speech has been observed at the initiation of speech, often presenting as a stutter (Ackermann et al., 1993). A study conducted by Ackermann et al. (1993) tested two PwPD, KBA and HWA, by having them repeat the syllable /pa/ at different speeds, both on their own and with external pacing cues. Both PwPD demonstrated smaller and slower lip movements compared to Controls. KBA's and HWA's speech was not only slower but also less coordinated, with their lip movements becoming less precise as the speed increased. The authors inferred that PwPD may experience speech "freezing" in the form of hastening (speeding up), difficulty maintaining a consistent pace, and smaller movement ranges. The study emphasized that speech freezing in PD can result in both overly fast speech and difficulty with smooth, consistent speech flow.

Additional support of freezing as a global motor phenomenon stems from a case report by Likitgorn et al. (2021) who assessed a patient with Parkinson's disease who experienced episodic "freezing of saccades", a phenomenon not previously reported in PD. The researchers wanted to address whether freezing of saccades could be a

manifestation of PD and how it relates to dopaminergic treatment. Methods included neurological and eye movement examinations, which revealed difficulty in initiating saccades, and episodes of freezing during saccadic eye movements. The freezing episodes were documented and treated with increased carbidopa-levodopa dosage. Freezing of saccades resolved with the medication adjustment, supporting the hypothesis that it was related to dopaminergic degeneration, opposed to incorrect diagnosis of PD or medication side effects. The authors interpreted these findings as evidence that eye movement abnormalities, particularly freezing of saccades, can occur in PD and may be responsive to dopamine therapy.

The combination of these findings suggest that freezing is a multifaceted phenomenon that extends beyond gait, affecting various domains such as upper limb movements, speech, and eye movements. The fact that freezing can be triggered by specific task demands and spatial constraints, and is associated with poorer cognitive performance, points to the involvement of higher-level processes, namely executive functions. Understanding how cognitive abilities contribute to freezing may provide deeper insights into its underlying mechanisms and open new avenues for intervention. This motivates our focus on saccadic eye movements as a means to probe executive function and explore the shared mechanisms of freezing.

Executive Function

Executive function is an umbrella term for the cognitive abilities that are responsible for planning, organizing, initiating, and inhibiting behaviours and is associated with the frontal cortex (Moustafa & Poletti, 2013). There are important neural connections between the striatum and the frontal cortex. It has been postulated that the

cognitive deficits PwPD experience are related to the disruption of these connections (Vandenbossche et al., 2013).

Degeneration of the basal ganglia leads to reduced dopamine levels, impairing movement control and executive functions due to disrupted connections within motor and prefrontal cortex areas (Moustafa & Poletti, 2013). Executive dysfunction can result from damage within the dorsolateral frontostriatal loop linking the basal ganglia to the cortex. Specifically, this pathway links the dorsolateral prefrontal cortex, dorsolateral caudate nucleus of the striatum, dorsomedial globus pallidus, and thalamus. All of these structures contribute to working memory, the ability to plan, the ability to switch between tasks, and the ability to inhibit behaviours. It is evident that assessing executive function can help evaluate the progression of Parkinson's disease and may help elucidate other symptoms (Dubois et al., 2000).

Building on the understanding of executive dysfunction in PD, research has explored how it impacts specific motor symptoms, such as FOG. Petrucci et al. (2021) investigated whether self-activated sensory cues, such as pressing a button to trigger a sound or mechanical ankle support, were as effective as externally triggered cues in facilitating gait initiation in PwPD with FOG. The researchers hypothesized that self-triggered cues would be less effective due to difficulties initiating movements in PwPD. They tested PwPD with FOG, older adult controls, and younger adult controls using auditory cues or a portable powered ankle-foot orthosis, a device that provided mechanical assistance to the ankle to aid walking. These cues were triggered either by the participant or an experimenter, and the researchers measured participants' anticipatory postural adjustments with force plates. Results showed that externally triggered cues

improved movement preparation (64-115% higher force generation) in PwPD and the older adult controls, but self- triggered cues did not help these groups, though younger controls showed improvement (24-25% higher force generation). The authors inferred that external cues can effectively release FOG by overcoming executive function blocks, but self-triggered cues fail due to impaired planning or multitasking in PwPD. The authors concluded that these findings highlight the challenges with home-based devices relying on self-triggering and suggest a need for new strategies, like external cues, to help PwPD move with greater ease (Petrucci et al., 2022).

To further explore the assessment of executive dysfunction, which is critical for understanding its impact on symptoms like FOG, tools such as the Frontal Assessment Battery (FAB) have proven valuable. Executive functioning can be difficult and time-consuming to assess, but the FAB, devised by Dubois et al. (2000), offers a practical solution. This tool evaluates the presence and severity of executive dysfunction affecting both motor and cognitive behaviours. The FAB is time-effective and easy to administer; it takes approximately 10 minutes to complete (Dubois et al., 2000). The FAB includes six items that assess each participant's abilities to plan, avoid distraction, and inhibit themselves. Low scores on the FAB are indicative of executive dysfunction. The FAB has been utilized extensively to assess executive function in PwPD (Das et al., 2016; Koerts et al., 2011; Lima et al., 2008). Koerts et al. (2011) used the FAB to assess executive function in 39 PwPD and 24 control participants. The UPDRS and the Hoehn and Yahr scale were used to assess disease severity. Based on the FAB, PwPD demonstrated significant impairments of executive function in comparison to the controls.

Past research demonstrates a relationship between executive function and freezing. PwPD who are experiencing executive dysfunction tend to freeze more often; this connection has been observed in gait freezing and freezing of upper limbs (Amboni et al., 2008; Gallardo et al., 2018; Heremans et al., 2019). A study conducted by Amboni et al. (2008) aimed to compare cognitive functions in PwPD with and without FOG. The researchers hypothesized that FOG is associated with cognitive deficits, particularly executive function. They predicted that PwPD with FOG would obtain lower scores on tests of executive function compared to PwPD without FOG. Twenty-eight PwPD (13 with FOG and 15 without FOG) completed the UPDRS, Mini Mental State Examination (MMSE), and various executive function tests (e.g., FAB, phonemic verbal fluency, ten-point clock test (TPCT), and Stroop test). FOG severity was measured using the Freezing of Gait Questionnaire. The results showed that PwPD with FOG performed significantly worse than PwPD without FOG on the FAB, phonemic verbal fluency, TPCT, and the Stroop test, indicating deficits in executive functioning. Correlation analyses across all participants further showed that higher FOG severity was negatively correlated with performance on tests assessing executive function, reinforcing the link between FOG and executive dysfunction. When decomposing the FAB into single subitems, sensitivity to interference and conceptualization were significantly negatively correlated with FOG scores. The authors interpreted these findings as evidence that FOG in PD is related to frontal lobe dysfunction. They inferred that freezing may be more than just a motor symptom and could involve impaired executive control over movement (Amboni et al., 2008).

Gallardo et al. (2018) investigated whether PwPD with FOG exhibit distinct neuropsychological and neuroimaging differences compared to those without FOG. The researchers hypothesized that PwPD with FOG would show greater executive dysfunction and more pronounced hypometabolism in brain regions associated with movement and cognition. They predicted that these deficits would be particularly evident in the circuits connecting the frontal lobe and the basal ganglia. The study included 17 PwPD (9 with FOG, 8 without FOG) and 6 controls. Cognitive assessments, evaluating executive functions such as sensitivity to interference, set switching, working memory, spatial construction, generative fluency, cognitive flexibility, and inhibition, along with neuroimaging, were conducted on all participants. Greater executive dysfunction was observed in the PwPD with FOG compared to PwPD without FOG, and both groups performed more poorly than controls. The study utilized fluorodeoxyglucose positron emission tomography/computed tomography to measure brain glucose metabolism across groups. The results indicated that PwPD with and without FOG exhibited significant hypometabolism in the parietal, occipital, and frontal brain regions compared to controls. PwPD with FOG showed significant hypometabolism in the motor cortex compared to PwPD without FOG. The authors interpreted these findings as evidence that FOG in PD is linked to impaired connectivity between the frontal lobe and basal ganglia, potentially contributing to movement deficits and cognitive deficits (Gallardo et al., 2018).

This research suggests the need for further exploration of the relationship between executive function and freezing. A promising avenue for further investigation involves analyzing eye movements, which have also been shown to be influenced by executive dysfunction. Eye movements require key components of executive function, such as

response initiation and inhibition. Therefore, studying how these processes interact in Parkinson's disease could provide valuable insights into the cognitive and motor difficulties experienced by individuals. Understanding how disruptions in eye movement patterns relate to executive function and freezing may open new paths for targeted assessments. The consistent link between executive dysfunction and freezing across studies provides a compelling rationale for using eye movement tasks to examine these mechanisms further.

Eye Movements

Saccades are quick, ballistic eye movements that shift the focus of the fovea from one point of interest to another (Ma et al., 2022). A saccade requires an initial movement from a point of fixation to a point of interest. The initial movement covers most or all of the distance between the fixation point and the target, followed by a smaller corrective or secondary saccade if necessary (Ma et al., 2022). Past research has demonstrated the usefulness of eye movements in exploring the functions of the basal ganglia, which are involved in the initiation and suppression of saccades (Hikosaka et al., 2000; Pretegiani & Optican, 2017). When the dopaminergic cells within the substantia nigra pars compacta are lost, an inevitable component of Parkinson's disease, striatal dopamine decreases (Pretegiani & Optican, 2017). This results in increased inhibitory output from the internal globus pallidus and the substantia nigra pars reticulata. Consequently, PwPD may experience various eye movement abnormalities such as slow, imprecise saccades and impaired initiation (Pretegiani & Optican, 2017).

Analyzing eye movements can be used to assess executive function (Leigh & Kennard, 2004). In fact, researchers have been exploring how disruptions in executive

function are linked to freezing through the analysis of eye movements (Gallea et al., 2021; Nemanich & Earhart, 2016; Walton et al., 2015). PwPD experience both gait and saccadic dysfunction (Srivastava et al., 2018). Often, people with PD experience hypometric step length and saccades. Pro-saccade and anti-saccade tasks are commonly used to assess people's eye movements and executive function simultaneously. During a pro-saccade task, participants fixate on a point and then look at a target when it appears. In an anti-saccade task, participants must inhibit the automatic reflex to look at the target and instead direct their eyes to its mirrored position. This requires both the suppression of a reflexive response to the presented target and voluntary generation of an eye movement to the mirrored position. Three brain areas are primarily responsible when completing an anti-saccade task. The dorsolateral prefrontal cortex is involved in the suppression of reflexive movement (inhibiting the urge to look at the presented stimulus). The posterior parietal cortex is responsible for generating an eye movement to the mirrored position of the stimulus, and the frontal eye field is responsible for eye movement latency. The anti-saccade task requires the executive function of inhibiting automatic responses and generating voluntary actions, making it a valuable tool for evaluating executive control (Miyake et al., 2000).

PwPD often show impaired performance on anti-saccade tasks. Walton et al. (2015) examined eye movements to explore the link between executive function and FOG in PwPD. It was hypothesized that FOG could be explained by deficits in executive function. The researchers predicted that people with FOG would show greater deficits in the anti-saccade task due to dampened cognitive control in comparison to the PwPD without FOG and the control group. Three groups of participants were recruited, PwPD

with FOG (*n*=15), PwPD without FOG (*n*=11), and controls (*n*=10). The participants completed pro-saccade and anti-saccade tasks. The researchers identified PwPD with FOG as those who exhibited freezing during the MDS-UPDRS evaluation. The results revealed that PwPD with FOG, showed significant deficits when completing anti-saccade tasks compared to PwPD without FOG and controls. This result supports the hypothesis that PwPD with FOG experience inhibitory control deficits more severely than PwPD without FOG.

Nemanich and Earhart (2016) examined the impact of FOG on executive function through the analysis of reflexive and voluntary eye movements in PwPD. The study compared PwPD with FOG to PwPD without FOG and controls. The researchers hypothesized that PwPD with FOG would exhibit executive dysfunction, demonstrated by slower eye movements and prolonged latencies during both pro-saccade and anti-saccade tasks. Twenty-six PwPD (*n* = 13 with FOG, *n* = 13 without FOG) and controls (*n* = 12) completed pro-saccade and anti-saccade tasks. The results revealed that PwPD with FOG had significantly greater saccade latencies and greater variability in saccadic velocity compared to PwPD without FOG and controls on both tasks. PwPD with FOG showed challenges in executing anti-saccades, demonstrated by the significantly greater anti-saccade response latencies compare to PwPD without FOG and controls. The researchers suggested that the difficulty in performing anti-saccades in PwPD with FOG could be due to an inability to release inhibition in the oculomotor circuit when a voluntary response to the mirrored target location is required. The researchers further inferred that FOG reflects broader motor dysfunction, affecting both gait and non-gait movements, including eye movements.

A study conducted by Gallea et al. (2021) aimed to identify predictors of FOG in PwPD, focusing on the relationship between oculomotor parameters; particularly anti-saccade latency, and the onset of FOG. Pro-saccades were not assessed in this study; anti-saccade latency was measured as the time between target appearance and saccade initiation for trials where the participant successfully inhibited the reflexive saccade, instead initiating a voluntary eye movement in the opposite direction. The researchers hypothesized that anti-saccade latency could predict FOG onset, as several brain systems involved in both gait and saccadic movements may contribute to FOG development. The mesencephalic locomotor region (MLR), located in the midbrain, and the supplementary motor area (SMA), situated in the frontal lobe, are key in gait initiation, supporting anticipatory postural adjustments before stepping (Petrucci et al., 2022; Sherman et al., 2015; Tanji, 1994). The SMA also facilitates voluntary saccade initiation. The study followed PwPD and controls over a 5-year period, assessing clinical and oculomotor data at two assessment time points: baseline and follow-up. FOG was assessed using questions that focused on walking distance, walking speed, and frequency of freezing from the Gait and Balance Scale. PwPD were assigned to FOG (score > 0) and no-FOG (score = 0) groups depending on the outcome of this assessment. It was found that higher mean anti-saccade latency at baseline predicted the eventual occurrence of FOG, with a mean anti-saccade latency value greater than 300 ms being especially discriminative. Moreover, in the FOG group, increased anti-saccade latency was associated with more severe disease progression. In this prospective 5-year study, using resting-state functional MRI, baseline analysis revealed altered connectivity between the MLR and frontal brain areas in PwPD, particularly in those who developed FOG by follow-up. The results suggest that impaired

executive function, specifically a slowed ability to suppress reflexive saccades and generate voluntary saccades, can serve as a marker for FOG onset, and may play a significant role in predicting and assessing its development (Gallea et al., 2021).

Executive functions can be effectively assessed using pro-saccade and anti-saccade tasks, with the anti-saccade task in particular providing insight into inhibitory control and cognitive flexibility. PwPD with FOG show greater impairments on anti-saccade tasks than PwPD without FOG, suggesting a relationship between executive dysfunction and FOG (Walton et al., 2015). Nemanich and Earhart (2016) found that PwPD with FOG exhibited slower eye movements and greater variability in saccadic velocity on saccade tasks, suggesting executive dysfunction affecting both gait and non-gait motor control. Supporting this, Gallea et al. (2021) found that increased anti-saccade latency predicts FOG onset and is associated with altered connectivity between the mesencephalic locomotor region and frontal cortical areas. These findings indicate that executive functions, as measured by anti-saccade performance, are closely related to FOG and may serve as valuable markers for its prediction and progression. These consistent findings across studies build a strong case for using saccade tasks to measure the executive dysfunction underlying freezing, setting the stage for examining more specific aspects, like the gap effect.

The Gap Effect

Saccade latency is strongly impacted by the presence or absence of a visual fixation (Kingstone & Klein, 1993). To maintain fixation, the viewer must actively inhibit eye movements toward other potentially interesting stimuli in their visual field. In this way, fixation serves as a form of oculomotor inhibition, requiring the suppression of

reflexive responses to maintain fixation. Removing the fixation before a target stimulus appears (gap condition) results in shorter saccade latencies than when the fixation remains while the target is presented (overlap condition). Eye movements with extremely short latencies (80-120 ms) are known as express saccades. The change in latency that results from the removal of a fixation prior to the onset of a target is known as the gap effect (Bekkering et al., 1996). The gap effect can be calculated by looking at the difference in response latencies between gap (fixation-removed) conditions and overlap (fixation-remains) conditions. It is a measure of executive function as it measures the time cost associated with needing to release from fixation when initiating a response.

PwPD with FOG exhibit increased saccadic latency and velocity variability in both pro-saccade and anti-saccade tasks. Nemanich and Earhart (2016) further demonstrated that the specific challenge in PwPD with FOG lies in executing anti-saccades, as evidenced by significantly longer anti-saccade latencies compared to PwPD without FOG and controls (Nemanich & Earhart, 2016). The researchers inferred that the impaired anti-saccade execution in PwPD with FOG may stem from a failure to release inhibition within the oculomotor circuit when they need to generate a voluntary response to the mirrored target location. Stemming from this, it could be inferred that PwPD with FOG will exhibit larger gap effects than PwPD without FOG since the size of the gap effect represents time needed to release from the fixation. To our knowledge, there is no literature exploring gap effects in PwPD with FOG versus those without FOG. By exploring gap effects in freezers and non-freezers, we may help reveal the underlying mechanisms of freezing and help to solidify the connection between freezing and executive function.

Freezing is an extremely debilitating symptom of Parkinson's disease. However, there is limited consensus on the pathology of freezing. There appears to be a multifactor, higher-level mechanism contributing to freezing, with executive function potentially playing a key role. Since eye movement evaluation can reflect executive control processes that depend on basal ganglia-cortical circuits, examining their relationship to freezing may help clarify how disruptions in these systems contribute to the initiation failures and inhibitory control deficits characteristic of freezing. Furthermore, freezing-like episodes have been observed in upper-limbs; however, it is unclear whether these occurrences are directly related to FOG. Utilizing stimuli known to induce FOG within an upper limb reaching task will further the investigation regarding whether freezing is a more global motor phenomenon, not restricted to gait.

Previous literature consistently revealing an association between executive dysfunction and freezing, coupled with evidence of freezing across multiple motor domains, motivates this study. By utilizing pro- and anti-saccade tasks to measure inhibitory control, and by introducing the gap effect to measure a person's ability to disengage, we aim to pinpoint how executive dysfunction contributes to freezing. Additionally, by designing tasks that replicate FOG-inducing conditions in both walking and reaching, we seek to support the idea of freezing as a global motor phenomenon. Therefore, the overall purpose of this work was to help provide greater insights into the mechanisms of freezing.

The objective of this study was to use the gap effect to evaluate executive function and explore its relationship with freezing. Additionally, we aimed to investigate the characteristics of FOUL and FOG using tasks designed to elicit FOG. The primary

research question was: Is the gap effect related to freezing in PwPD? We hypothesized that freezing is the result of advancing executive dysfunction. If executive function is underlying freezing, we predict that the gap effect will be larger for PwPD with FOG compared to PwPD without FOG, reflecting impaired executive control. Additionally, we predict that freezing will have a positive relationship with the gap effect, as greater executive dysfunction should correspond to more severe freezing episodes. Our second hypothesis is that freezing is a more global motor phenomenon, not just restricted to gait. We designed our study so that the reaching and walking tasks included the same inducing conditions (e.g., reversals, corners, tunnels). We predicted that conditions known to induce FOG would effectively elicit FOUL, and that we would find a relationship between subjective FOG, objective FOG, FOUL measures, and executive dysfunction observed in eye movement tasks, suggesting a shared underlying mechanism.

To test these hypotheses, two groups of participants were recruited. The experimental group consisted of PwPD at various stages of disease progression. The control group consisted of neurologically healthy participants who were sex and age-aligned with the participants in the experimental group. Participants were instructed to complete tests that assess executive function, eye movements, reaching, and walking. Parkinson's disease progression was assessed using the MDS-UPDRS motor evaluation Part III. Executive function was assessed using the Frontal Assessment Battery and pro-anti-saccade eye movement tasks with both gap and overlap timing conditions. Reaching and walking tasks that involved asking participants to perform reversals, corners, and to move through tunnels were performed and kinematic data were recorded for analysis.

Methods

The Research Ethics Board of Trent University approved this research (#29036). Written informed consent was obtained from all participants.

Participants

People with and without Parkinson's disease were invited to participate in the study. All participants needed to have normal or corrected-to-normal vision and hearing to participate. Participants could not have a current diagnosis of depression, anxiety, or dementia. The members of the control group needed to have no history of neurological dysfunction. There were no age or gender exclusions.

There were two groups of participants, controls (n=16) and PwPD (n=14). PwPD were recruited from Parkinson's support groups and physiotherapy clinics in Central East Ontario. All participants reported normal or corrected to normal vision and hearing. None of the participants reported receiving a diagnosis of depression, anxiety, or dementia. None of the participants reported a history of neurological dysfunction aside from a diagnosis of Parkinson's disease. Controls were recruited in a manner that aligned with the age and sex of the PwPD.

Project Overview

The data collection was organized into task blocks (Figure 2). Task details will be presented below. The participant completed the general questionnaires, cognitive tests, motor evaluation and the eye movement tasks sequentially; the reaching tasks and walking tasks were counterbalanced.

Figure 2

Testing Administration Order

Questionnaires	Cognitive Tests	Motor Evaluation	Eye Movement Tasks	Reaching & Walking Tasks
Health and Wellness Questionnaire	Montreal Cognitive Assessment	Unified Parkinson's Disease Rating Scale (Part III)	Pro- VS Anti-saccades	Reversals
Hospital Anxiety and Depression Scale	Frontal Assessment Battery		Overlap VS Gap	Turn
Dutch Handedness Questionnaire				Doorway/Virtual Tunnel
New Freezing of Gait Questionnaire				

Note. Both groups of participants completed all the questionnaires, evaluations, and tasks.

General Questionnaires

The following questionnaires were administered using Qualtrics (Qualtrics LLC, Provo, Utah). The participant completed a survey that asked about their overall well-being. Items included questions about the participant's age, general health, sleep, and lifestyle behaviours.

We used the Hospital Anxiety and Depression Scale (HADS) to screen for anxiety and depression (Zigmond & Snaith, 1983). There is a subscale for anxiety and a subscale

for depression; each contains seven items. Each item is scored on a scale from 0 (no problem) to 3 (severe problem); higher scores indicate higher levels of anxiety and depression. Scores above 7 on each subscale indicate that further testing for anxiety or depression is required. This scale does not screen for suicidal ideation.

The Dutch Handedness Questionnaire was used to identify the strength of the participant's left- or right-handedness (Van Strien, 2002). The questionnaire consists of 16 items. The scoring for each item ranges from 0 (left hand), 1 (both hands), to 2 (right hand). Total scores vary from 0 to 32. Scores of 0-4 indicate strong left-handedness and 28-32 indicate strong right-handedness.

Parkinson's Disease Assessments

Subjective Freezing Assessment

Freezing of gait was assessed using the New Freezing of Gait Questionnaire (NFOG-Q), developed by Nieuwboer et al. (2009). The NFOG-Q asks the participant to report on the presence, frequency, severity, and impact of any freezing episodes they experienced. In part one, the participant was asked whether they had experienced freezing episodes in the past month. The final NFOG-Q score is the sum of part two and three, higher scores indicate more severe experiences of freezing.

Motor Evaluation

The Movement Disorders Society Unified Parkinson's Disease Rating Scale, part III (Goetz et al., 2008), was used to assess motor severity and progression. This examination was video-recorded on a lab-dedicated iPhone 10 (Apple Corporation, Cupertino, CA), to allow two certified raters to assess the participant. The participant was

rated on 24 items that pertained to their motor symptoms. Each item was rated on a Likert scale of 0-4 representing normal performance to severe impairment, where severe impairment is defined as being unable to or only barely able to perform the item. The higher the MDS-UPDRS score, the greater the severity of PD. The MDS-UPDRS includes a measure of Parkinson's stage using the Hoehn & Yahr staging system (Hoehn & Yahr, 1967). The International Parkinson and Movement Disorders Society approved the use of this test for this study.

Cognitive Tests

The Montreal Cognitive Assessment (MOCA) was used to screen for dementia (Nasreddine, 2005). This assessment uses eight items to evaluate attention, concentration, memory, language skills, problem-solving abilities, and awareness of time and space. For example, some items ask the participant to name types of animals and recall words. The MOCA is scored out of 30 points. A score below 26 indicates further testing for dementia is required.

Executive Function Assessment

We used the Frontal Assessment Battery (FAB) to assess executive function (Dubois et al., 2000). The FAB uses six items to assess people's ability to plan, avoid distraction, and inhibit themselves. This test produces a single score, and lower scores indicate impaired executive function. A score of 12-13 (out of 18 total) distinguishes executive impairment from executively normal controls (Goh et al., 2019).

Eye-Movement Tasks

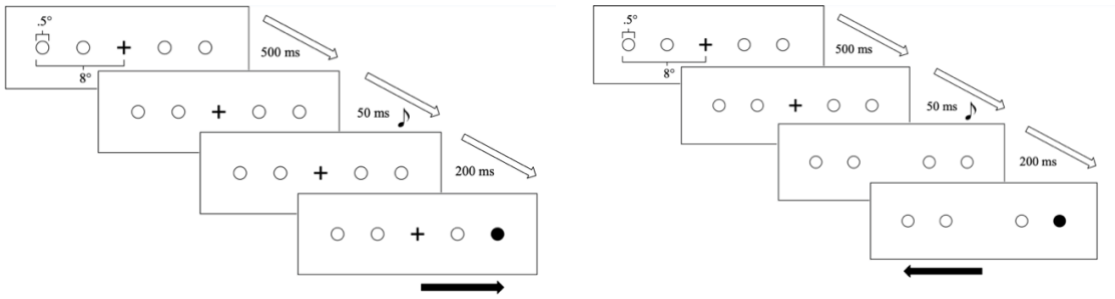
To measure the participant's eye-movements, we used an eye-tracker composed of two infrared cameras mounted on protective glasses (ViewPoint PC-60, Arrington Research Inc, Scottsdale, Arizona). The device was worn like a pair of glasses (over the participant's own prescription glasses, when necessary) and was secured to the participant's head with an adjustable strap. The task displays were presented by a personal computer (Bolen Distributing Inc., London, ON) on a 60 cm x 34 cm LCD monitor with 1920 x 1080p resolution (Hanns.G, HannStar Display Corporation, Taipei, Taiwan). To ensure consistent viewing distance, the participant was seated 57 cm away from the monitor, with their head stabilized by a chin rest (Lafayette Instrument Company, Lafayette, IN). The tasks were performed with the room lights off. The participant completed a brief one-to-two-minute calibration where the participant was instructed to look at a series of targets presented on the computer screen; this allowed us to align eye position with screen location.

The participant completed a series of eye-movement tasks designed to evaluate their ability to perform pro-saccades and anti-saccades under two counterbalanced fixation-timing conditions: gap and overlap (Antoniades et al., 2013; Bekkering et al., 1996). These conditions combined to create four eye-movement tasks: pro-saccade overlap, pro-saccade gap, anti-saccade overlap, and anti-saccade gap. Each task consisted of 12 practice trials and 20 experimental trials. The visual display for each task was composed of four unfilled black circles on a white background and a central black fixation cross (Figure 3). Targets were equally-spaced across four positions, defined relative to the fixation: left-far, left-near, right-near, right-far. Their presentation was

pseudorandomized; there was an equal number of targets presented in each position across conditions. An auditory warning tone was used to isolate the gap effect by providing a consistent alerting signal across all trials, ensuring that reduced saccade latencies were not due to a generalized warning effect from the fixation's offset.

Figure 3

Pro-Saccade Task: Overlap Condition and Anti-Saccade Task: Gap Condition



Note. This figure demonstrates the layout and timing of the pro-saccade task for the overlap condition (left) and anti-saccade task for the gap condition (right). The cross is the fixation. When the task begins, a target will appear; one of the four outlined circles will become filled.

The display and timing for the pro-saccade and anti-saccade tasks were identical. The only difference between these tasks were the instructions that the participant received. For pro-saccade tasks, the participant was instructed to look at the fixation cross, then, when the target appeared, make an eye movement to the target as quickly and accurately as possible. For the anti-saccade tasks, the participant was instructed to look at the fixation cross, then, when the target appeared, make an eye movement to the mirrored position of the target as quickly and accurately as possible. In the overlap timing condition, the fixation remained on screen while the target was presented. In the gap

timing condition, the fixation was removed 200 ms before the presentation of the target. The instructions for the pro-saccade and anti-saccade tasks in both timing conditions were the same as presented above.

Objective Freezing Assessments

Reaching Tasks

The participant was seated at a table with a height of 84 cm, and a glass top (107 cm x 183 cm). A one-way mirror was situated 28 cm above the table and an LCD monitor (LG, LG Display Corporation, Seoul, South Korea) measuring 60 cm x 33 cm was situated 25 cm above a one-way mirror. The participant's dominant arm was comfortably positioned on top of the table. The participant saw the reflected display screen through the one-way mirror. The participant could not see their own hand resting on the table. A motion tracker (Polhemus, Colchester, Vermont) was used to measure reaching movements. The motion tracker marker was attached to the tip of the participant's index finger on their dominant hand with medical tape. The motion tracker was calibrated, and the participant received continuous visual feedback on their fingertip's position on the display throughout the experiment. The participant's fingertip location was represented in the display by a green dot cursor (0.6 cm diameter). The reaching tasks were performed with the room lights off. The participant completed three reaching tasks designed to mimic the conditions that trigger FOG: reversal, corner, and tunnel (Figure 4). The same distance (15 cm) was covered for the first reaching movement in each task.

In the reversal task, the display was composed of a red start circle (1.5 cm diameter) on a static, random grey-level dot background (Figure 4A). The participant was instructed to move the green cursor to the center of the start circle. When the

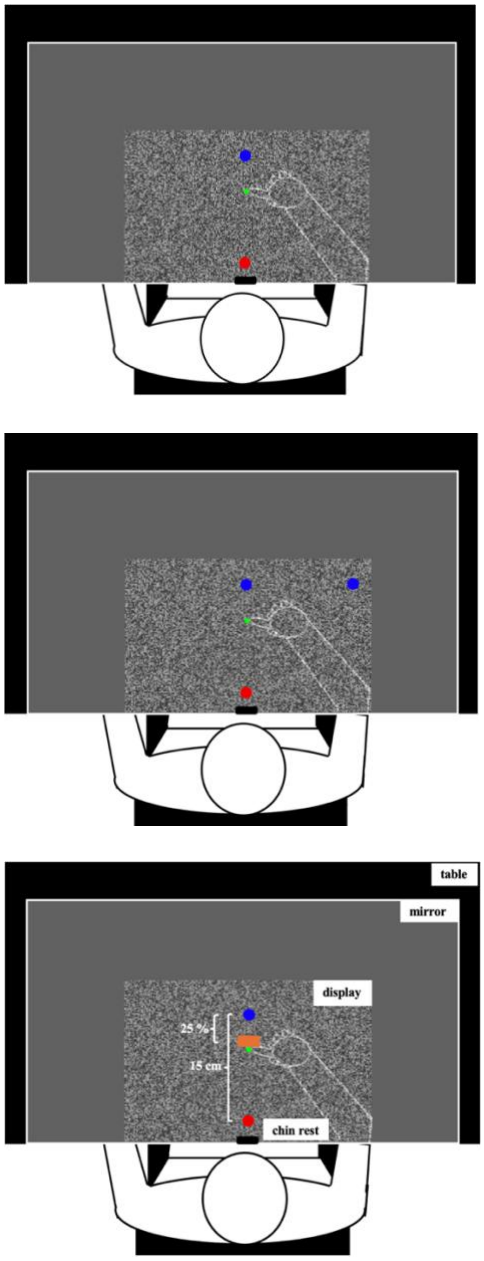
experimenter was satisfied that the participant was ready, she pressed any key on the keyboard; the target appeared immediately and the motion tracker began recording. The target was a blue circle (1.5 cm diameter) placed 15 cm in front of the start circle in depth. The participant was instructed to reach to the target as soon as it appeared and then return back to the start as quickly as possible.

The corner task used the same display features and timing (Figure 4B), except that when the keyboard was pressed, two blue circle targets appeared. One target appeared 15 cm in front of the start circle in depth, and the second appeared 15 cm to the left or right of the first target. The second target was always positioned on the side of the participant's dominant hand. The participant was instructed to reach straight out to the first target as soon as it appeared and make a 90-degree turn without stopping to continue to the second target, coming to a complete stop on the second target. They were instructed to complete this task as quickly as possible.

The tunnel task used the same display features and timing as the reversal task (Figure 4C), except that when the keyboard was pressed, the first target appeared and an orange virtual tunnel (1.6 cm high x 3.1 cm wide) appeared, at the 75% point along the straight path between the start circle and the target. The participant was instructed to reach straight out to the target by passing through the tunnel and then come to a complete stop on the target as quickly as possible. The green cursor representing their finger disappeared as it crossed the path of the orange rectangle, satisfying the criterion of passing under a tunnel. The participant completed 9 practice trials for whichever task they were assigned to complete first. Then, the participant completed 10 trials for each of the three tasks, for a total of 30 experimental reaching trials.

Figure 4

Reaching Task: Reversal, Corner, and Tunnel



Note. This figure demonstrates the layout of the reaching task. The red circle was the starting point for all tasks. The green circle represented the participant's fingertip; the participant could not see their arm and hand. Each trial began when the blue target circle appeared. A: Top. B: Center. C: Bottom. Participants could use their right or left hand for the tasks.

Walking Tasks

In the walking block, the participant completed three walking tasks. Their walking was videotaped using two iPhone 12 devices that served as lab-dedicated recording cameras (Apple Corporation, Cupertino, California). The iPhones were set up to record high-definition video (1080p Full HD, 60 Hz). Bluetooth inertial measurement units (IMUs, WitMotion, Shenzhen, Guangdong) were calibrated to acceleration with a return rate of 200 Hz (functional sampling rate of 100Hz) and acceleration data were recorded on a personal computer (Microsoft Surface 2, Redmond, Washington). The IMUs were attached to the dorsal surface of the foot, over the shoe. The participant was asked to wear dark clothing, and white markers were taped to the participant's shoulders (over the acromion), elbows (over the lateral epicondyle), hips (at the top of the iliac crest), knees (lateral to the patella), and ankles (lateral malleolus) for later kinematic analysis.

The participant completed three walking tasks designed to represent situations that trigger FOG: reversal, corner, and tunnel (Figure 5). The participant completed one practice trial for the task to which they were assigned first. Then, they completed three trials for each task, for a total of 9 experimental walking trials. The order in which the participant completed the three walking tasks (reversal, corner, tunnel) was counterbalanced and matched the order in which they completed the reaching tasks. The same distance (1.8 m) was covered for the first walking movement in each task.

In the reversal task, the participant saw a red circle (23 cm diameter) on the floor that acted as the start location. A blue target circle (23 cm diameter) was 1.8 m straight ahead of the start in depth. The participant was instructed to stand in the center of the

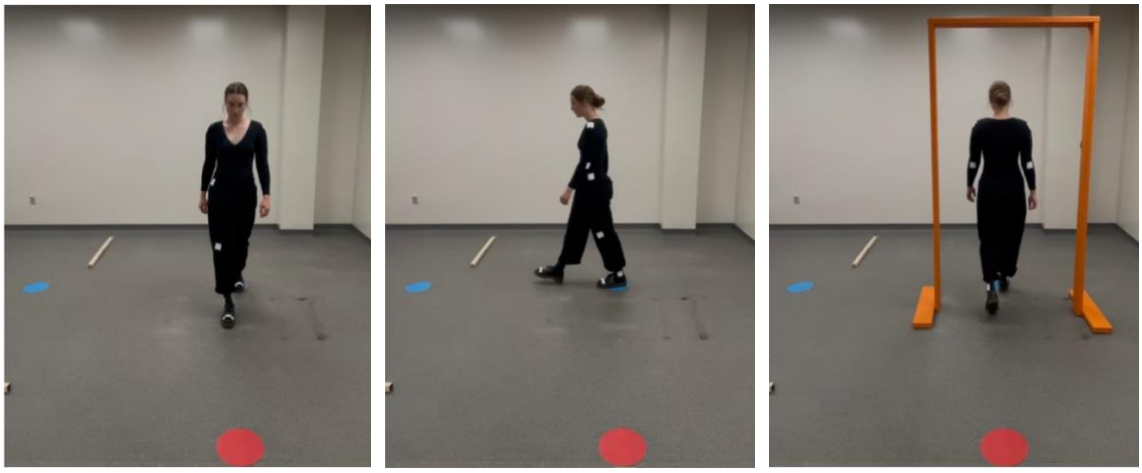
start circle, then walk from the start, out to the target and then back to the start (Figure 5A). The task began when the researcher provided a verbal “go” cue.

In the corner task, the participant saw the same start circle and target, but we also brought their attention to a second blue target circle (23 cm diameter) positioned 1.8 m to the left of target. The participant was instructed to stand in the center of the start, then walk from the start to the first target, make a 90-degree turn without stopping and continue to walk to the second target, coming to a complete stop on the second target (Figure 5B). The task began when the researcher provided a verbal “go” cue.

In the tunnel task, the participant saw the same start circle and target as for the reversal task. An orange freestanding door jamb (210 cm tall X 104 cm wide X 14 cm deep) was positioned at the 75% point between the start and target. The participant was instructed to stand in the center of the start circle, then walk from the start, pass through the orange tunnel, and come to a complete stop on the target (Figure 5C). The task began when the researcher provided a verbal “go” cue.

Figure 5

Walking Task: Reversal, Corner, and Tunnel



Note. This figure demonstrates the layout of the walking task. The red circle is the starting point for all tasks. A: Left Image. B: Center Image. C: Right Image.

Procedure

The PwPD followed their normal medication schedule during the day of testing. However, an attempt was made to manage the effects of medication by testing the participants within the same relative period of their drug cycle; appointments were scheduled 15 minutes after their last dose of medication. Consent was obtained in one of two ways. If the participant elected to begin the study by completing the questionnaires at home before their appointment, the participant read the consent form alone and was encouraged to send us any questions they had. The consent form was always completed before the online questionnaires. If the participant elected to complete the questionnaires in the lab, they completed both the consent form and the online questionnaires upon arrival at the lab. The participant was instructed to complete the questionnaires honestly

without dwelling on the questions too long. Altogether, the questionnaires took approximately 30 minutes to complete.

After the participant provided written consent, a small microphone was attached to the participant's shirt, and their natural speech was recorded for the duration of the study; this data will be analyzed at a later date.

The participant completed the FAB (10 minutes) and the MOCA (10 minutes), in this order. The participant was told that they would be asked several questions and be asked to perform several tasks: some easy and some challenging. The participant was instructed to try their best.

In the third block, the participant was assessed using a motor evaluation, Part III from the MDS-UPDRS. This block took approximately 15 minutes to complete. Two raters, each certified in administering and scoring the MDS-UPDRS, later scored the participant's performance. If there was a disagreement between raters, they would attempt to settle it by re-evaluating the participant. If an agreement was still not reached, the primary investigator assigned the final rating.

The fourth block consisted of eye-movement tests. The participant completed pro-saccade tasks and then the anti-saccade tasks, always in this order. This section took approximately 20 minutes to complete. One of the PwPD was unable to complete the eye movement testing; however, they were able to complete the reaching and walking tasks so their data was included in the data set.

In the fifth block, the participant completed reaching tasks. The order in which the participant completed the three reaching tasks matched the order of the walking tasks. The first attempt of each task was manually-guided; the experimenter took the hand of

the participant and guided them through the correct movement before allowing the practice or experimental trials to continue. The participant completed one practice trial; the practice condition was the same as the first component that the participant was assigned to complete. The participant was instructed to perform the tasks as quickly and accurately as possible. The participant completed 10 reaches in each of the three experimental tasks for a total of 30 experimental reaching trials. The reaching section took approximately 15 minutes to complete.

In the sixth block, the participant completed walking tasks. The researcher demonstrated each task to the participant as it was introduced. The participant completed one practice trial; the practice condition was the same as the first component that the participant was assigned to complete. The participant completed three walking trials in each of the three walking tasks for a total of 9 experimental walking trials. This testing took approximately 20 minutes.

After the six blocks were completed, the participant received their compensation and a debriefing sheet that revealed information about the study's hypothesis. The microphone was removed from the participant. The participant was encouraged to reach out in the future if they had any questions or concerns.

Data Processing

Eye Movement Tasks

For the eye movement tasks, the participants' response latency, eye movement time, and eye movement error were measured using the signal collected from the eye-tracking device. This signal was analyzed using a custom procedure programmed in Matlab (The Mathworks, Raleigh, NC). Each eye signal was filtered (low-pass dual

Butterworth filter with cutoff frequency = 8 Hz) and differentiated to determine eye movement velocity. Saccade initiation was defined as the first time that eye velocity exceeded 10 cm/s and termination was defined as the next sample where eye velocity fell below this criterion.

Response latency was measured as the time between target presentation and saccade initiation. Eye movement time was the time between saccade initiation and termination. Eye movement error represented the mean difference between eye movement distance covered and the target distance along the lateral (x) dimension only; positive values indicated that the participant overshot the target, negative values indicated that the participant undershot the target. Proportion correct was calculated by determining the ratio of correct eye movements for each task and condition, where a correct eye movement was defined as an eye movement made to the target (pro-saccade) or to the mirrored position of the target (anti-saccade). The gap effect was calculated by subtracting the response latency in the gap condition from the response latency in the overlap condition within each of the pro-saccade and anti-saccade conditions.

Reaching Tasks

For the reaching tasks, performance metrics for the first movement [from the start to the (first) target] were evaluated because this component was a part of every reaching task. Key metrics were obtained using the signal collected from the motion tracking device. This signal was analyzed using a custom procedure programmed in Matlab (The Mathworks, Raleigh, NC). Each signal was filtered (low-pass dual Butterworth filter with cutoff frequency = 8 Hz) and differentiated to determine reaching velocity. Acceleration was computed by differentiating the velocity signal. Reach initiation was defined as the

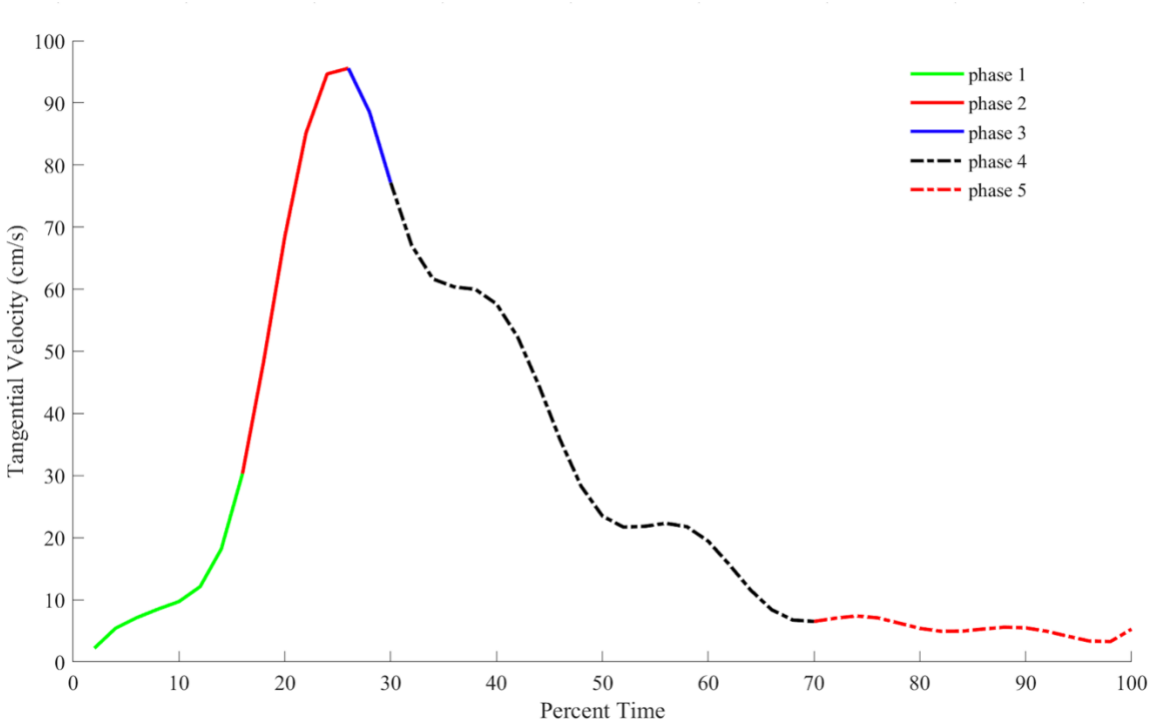
first-time velocity exceeded 3 cm/s and termination was defined as the next sample where velocity fell below this criterion. Peak velocity was defined as the maximum reaching speed that was achieved during each task (cm/s). Peak acceleration was defined as the maximum rate of change of velocity experienced during each task (cm/s^2).

Reaction time was measured as the time in milliseconds between target presentation and movement initiation. Movement time measured the time between reach initiation to reach termination. Distance covered was measured as the distance in cm covered between these times. Signed error along the depth (y) dimension, the main direction of movement, was measured as the mean difference between the fingertip location at movement termination and the target location, where positive values represent target overshoots and negative values represent undershoots. The absolute value of this measure was also determined (accuracy in depth). The standard deviation of Y error measured reaching precision in depth.

Our goal was to capture freezing behaviour and we anticipated that these behaviours may happen as participants initiated their movements and near or at the first target where participants were asked to make a transition in direction (reversal or corner). Specific phases were identified within the reaching tasks to isolate transition periods based on time (Figure 6). Five phases were of particular interest; phase 1 captured the initiation of the movement (time between movement initiation and peak acceleration), phase 2 captured the time from peak acceleration to peak velocity, phase 3 captured the time from peak velocity to peak deceleration, phase 4 captured the time from peak deceleration to the end of the first movement, phase 5 captured the time between the end of the first movement and the start of the second movement (for the reversal and corner

tasks only). Variability normalized to speed (coefficient of variation, CoV), percent time (%Time), and percent distance (%Distance) were computed to be compared across each phase and task.

Figure 6
Representative Graph of Phase Separations



Note. This graph depicts 5 specific phases defined by standard kinematic markers to isolate transition periods based on time. Phase 1 captured the time between movement initiation and peak acceleration. Phase 2 captured the time from peak acceleration to peak velocity. Phase 3 captured the time from peak velocity to peak deceleration. Phase 4 captured the time from peak deceleration to the end of the first movement. Phase 5 captured the time between the end of the first movement and the start of the second movement (for the reversal and corner tasks only). Any corrective movements made in the tunnel task were captured in phase 5.

Walking Tasks

For the walking tasks, performance metrics for the first movement [from the start to the (first) target] were evaluated because this component was a part of every walking task. Video recordings of the participant's walking task were input into a video analysis and modeling tool called Tracker (Christian et al., 2011) to extrapolate the raw timing and position data of the participant's ankle and shoulder. For this thesis, we are only presenting shoulder data to represent overall walking time, distance, and speed.

This data was analyzed using a custom procedure programmed in Matlab (The Mathworks, Raleigh, NC). Each signal was filtered and differentiated to determine walking velocity. The raw position data was transformed so the starting point was set to zero, focusing on movement relative to the start. Each signal was filtered (low-pass dual Butterworth filter with cutoff frequency = 5 Hz) and differentiated to determine walking velocity. Walking initiation was defined as the first-time velocity exceeded .3 cm/s and termination was defined as the next sample where velocity fell below this criterion. Walking time was defined as the difference in time between these two points. We also used the speed profile to identify the time the participant spent decelerating to the target. This value, percent deceleration time, was expressed as a percentage of total movement time.

Statistical Analysis

All statistical analyses were performed using IBM SPSS version 21 (IBM, Chicago, IL). This experiment was designed to compare PwPD to control participants in all scenarios; therefore, in the absence of significant group interactions, group comparisons were still performed.

Demographics

Independent-samples *t*-tests were used to compare PwPD to the control group. Demographic and clinical measures, including age, anxiety and depression scores (HADS), cognitive functioning (MOCA), executive function scores (FAB), Parkinson's motor symptom severity (MDS-UPDRS III), Hoen & Yahr stage, and subjective freezing of gait severity (NFOG-Q) were submitted to these analyses. Chi-square test of independence was used to compare the sex distribution of the two groups.

Eye Movement Tasks

We aimed to evaluate whether individuals with PD exhibit poorer eye movement performance than controls on tasks engaging executive functioning. Two performance measures, response latency (RL, in milliseconds) and proportion correct were calculated, where proportion correct is defined as the ratio of correct responses to the total number of trials.

Data were preprocessed and trimmed to ensure validity: trials with response latency (RL) < 50 ms were excluded, as this threshold reflects the minimum time for eye muscle response to visual stimuli (Antoniades et al., 2013). Trials with no eye movement (first eye movement time = 0), incorrect saccade direction (indicative of non-compliance with instructions), or eye movements exceeding 960 pixels (indicating that the participant looked at something off-screen) were also removed. For anti-saccade tasks, trials with reflexive rather than voluntary saccades were excluded to help ensure accurate assessment of inhibition. A total of 587 trials (25.26%) were removed. Response latency data, positively skewed, were log-transformed to achieve normality. Proportion correct data underwent arcsine transformation to address ceiling and floor effects (Miyake et al.,

2000). For the following analyses, if sphericity assumptions were violated, Greenhouse-Geisser-corrected F-values are reported. The measures were analyzed using 2-group (control or PwPD) by 2-task (pro-saccade or anti-saccade) by 2-timing condition (overlap or gap) mixed ANOVAs.

Additionally, we wanted to explore whether eye movement performance could predict freezing severity. First, a Pearson correlation analysis was performed to observe which questionnaire and eye movement measures had a significant relationship with freezing severity, as measured by the NFOG-Q. Next, a linear regression was performed for PwPD with freezing severity entered as the outcome variable. The details of this analysis will be provided as it is presented in the results section.

We wanted to determine whether eye movement performance could accurately categorize people as freezers or non-freezers. To achieve this, a binary logistic regression was performed for PwPD with freezing category entered as the outcome variable (based on data collected with the NFOG-Q).

Reaching Tasks

We aimed to evaluate freezing of upper limbs and compare the reaching performance of PwPD to Controls. Reaction time data, positively skewed, were log-transformed to achieve normality. Outliers were identified and removed if reaction time (RT) was less than 100 ms, as this is the minimum time required for visually presented information to influence arm and hand movements (Castiello et al., 1991; Georgopoulos et al., 1981; Paulignan et al., 1991). Trials with RT, movement time (MT) or distance travelled (Dist) exceeding three standard deviations from each participant's mean for a given task were excluded. A total of 12 trials (1.33%) were removed. For the following

analyses, if sphericity assumptions were violated, Greenhouse-Geisser-corrected F-values are reported. Performance measures were submitted to a 2-group (control or Parkinson's), by 3-task (reversal, corner, tunnel), mixed ANOVA.

Additionally, we wanted to explore whether reaching performance could predict freezing severity. First, a Pearson correlation analysis was performed to observe which questionnaire and reaching measures had a significant relationship with freezing severity, as measured by the NFOG-Q. Next, separate linear regressions were performed for PwPD within each reaching task (reversals, corner, tunnel). Freezing severity was entered as the outcome variable. The details of this analysis will be provided as it is presented in the results section.

We wanted to determine whether reaching performance could accurately categorize people as freezers or non-freezers. To achieve this, binary logistic regressions were performed for PwPD within each reaching task (reversal, corner, tunnel). Freezing category was entered as the outcome variable (based on data collected with the NFOG-Q).

Walking Tasks

We aimed to evaluate freezing of gait and compare the walking performance of PwPD to Controls. For the following analyses, if sphericity assumptions were violated, Greenhouse-Geisser-corrected F-values are reported. One participant with PD (#25) was 31 standard deviations slower than the other PwPD, due to the increased variance that was added to the PD group from this participant, they were removed from the dataset. Two performance measures, overall movement times and time spent decelerating, were

submitted to 2-group (control or Parkinson's), by 3-task (reversal, corner, tunnel), mixed ANOVAs.

Additionally, we wanted to explore whether walking performance could predict freezing severity. First, a Pearson correlation analysis was performed to observe which questionnaire and walking measures had a significant relationship with freezing severity (as measured by the NFOG-Q). Next, separate linear regressions were performed for PwPD within each walking task (reversals, corner, tunnel). Freezing severity was entered as the outcome variable.

We wanted to determine whether walking performance could accurately categorize people as freezers or non-freezers. To achieve this, binary logistic regressions were performed for PwPD within each walking task (reversal, corner, tunnel). Freezing category was entered as the outcome variable (based on data collected with the NFOG-Q).

Results

Participants

All participants were 55-82 years of age and reported normal or corrected to normal vision and hearing. Thirty participants in total were recruited to participate (16 controls and 14 PwPD; female n=14, male n= 16).

Demographic and clinical measures are presented in Table 1 for controls and Table 2 for PwPD. Continuous variables were submitted to an independent-samples t-test to compare PwPD with the control group (Table 3). Our goal was to align the PD group with the control group by age and sex. The groups did not differ in terms of sex

distribution, $\chi^2(1, N = 30) = 1.27$, $p = .261$, $\varphi = .21$ or mean age, $t(28) = -1.85$, $p = .075$, $d = -.68$. The PD group exhibited significantly higher mean depression scores (indicating greater experiences of depression), greater motor symptom severity, more advanced Hoehn & Yahr stage, and higher freezing of gait scores compared to the controls. The control group demonstrated significantly higher MOCA scores. No significant differences were observed for age, anxiety, or FAB scores.

Table 1

Control Participants Demographic Information

Participant Number	Age (years)	Sex (female/male)	Handedness (left/right)	HADS-A (z-score)	HADS-D (z-score)	MOCA (z-score)	FAB (z-score)	NFOG-Q Total	MDS-UPDRS III Total
4	73	F	R	-.84	-.55	1.21	-.41	0	0
7	65	F	R	-.84	.10	1.54	-1.09	0	0
10	71	F	R	-1.37	-1.20	1.21	.26	0	11
12	81	F	R	-.04	.43	.88	-3.79	0	7
14	61	F	R	-.84	.43	1.21	.94	0	10
16	80	M	R	.49	.76	1.21	-3.79	0	18
17	57	M	L	-.57	-.55	-.43	.26	0	0
18	55	F	R	-.57	-1.20	1.54	.94	0	0
19	67	M	R	-1.63	-.87	.55	.26	0	8
21	76	F	R	1.56	.43	-.43	-1.76	0	0
23	58	M	R	-1.10	-.55	.22	-1.76	0	2
24	57	F	R	.76	-.55	1.21	.26	0	24
26	69	M	L	-.57	-.87	1.21	-1.09	0	5
27	70	M	R	-1.63	-1.20	.55	-1.09	0	2
28	61	F	R	-.84	-.87	.55	-.41	0	1
30	62	M	R	-1.37	-1.20	.22	-3.11	0	0

Table 2

Parkinson's Participants Demographic Information

Participant Number	Age (years)	Sex (female/ male)	Hand (left/ right)	HADS-A (z-score)	HADS-D (z-score)	MOCA (z-score)	FAB (z-score)	NFOG-Q Total	MDS-UPDRS III Total	H & Y Stage
1	67	M	R	-1.38	-.46	-1.09	-1.09	0	50	2
2	69	M	R	-.90	-.22	-.43	-3.79	25	58	4
3	80	F	R	-1.38	-.94	.88	-2.44	3	28	2
5	63	M	R	-.19	-.22	.88	-1.76	18	35	2
6	67	M	R	-.67	-.46	.55	.26	4	59	2
8	70	F	R	.05	-.22	.88	-.41	18	28	2
9	67	M	R	-.43	-.70	-.43	-.41	0	43	3
11	79	F	R	-.67	-.22	-.11	-1.76	0	52	3
13	58	M	R	-.19	-1.42	1.87	.94	0	44	2
15	82	M	R	-1.38	.26	-.11	-1.09	0	29	2
20	82	M	R	-1.85	-.70	-1.75	-1.76	8	37	2
22	78	M	R	0.28	.97	-1.09	-1.76	2	59	2
25	71	F	L	-.90	-.46	.88	-1.09	24	52	3
29	72	F	R	-1.14	-.46	.55	-1.09	1	29	2

Table 3

Demographic Comparisons

Measure	Control *n*=16		PwPD *n*=14		*t*(28)	*p*	Cohen's *d*
	M	*SD*	*M*	*SD*			
Age (years)	66.4	8.3	71.8	7.4	-1.85	.075	-.68
HADS-a (z-score)	-.59	.89	-.114	1.14	-.57	.572	-.21
HADS-d (z-score)	-.47	.68	-.393	.551	-2.63	.014*	-.96
MOCA (z-score)	.78	.63	.106	.99	2.24	.033*	.82
FAB (z-score)	-.96	1.55	-1.23	1.16	.54	.595	.20
MDS-UPDRS III	5.5	7.2	43.1	12.1	-10.17	<.001*	-3.84
H & Y Stage	1.2	1.0	2.4	.6	-3.75	<.001*	-1.33
NFOG-Q Total	0	0	6.8	9.8	-2.59	.022*	-1.02

Note. Means (*M*) and standard deviations (*SD*) for each group of participants. Group comparisons after being submitted to an independent *t*-test. * Represents a significant difference between the controls and PwPD. HADS control norms (Crawford et al., 2001). HADS PD norms (Rodriguez-Blazquez et al., 2009). MOCA norms (Rossetti et al., 2011). FAB norms (Coen et al., 2016).

Eye Movement Performance

Eye movement data were collected from 29 participants (16 controls, 13 PwPD), one PD participant (#2) was unable to complete the tasks due to motor limitations.

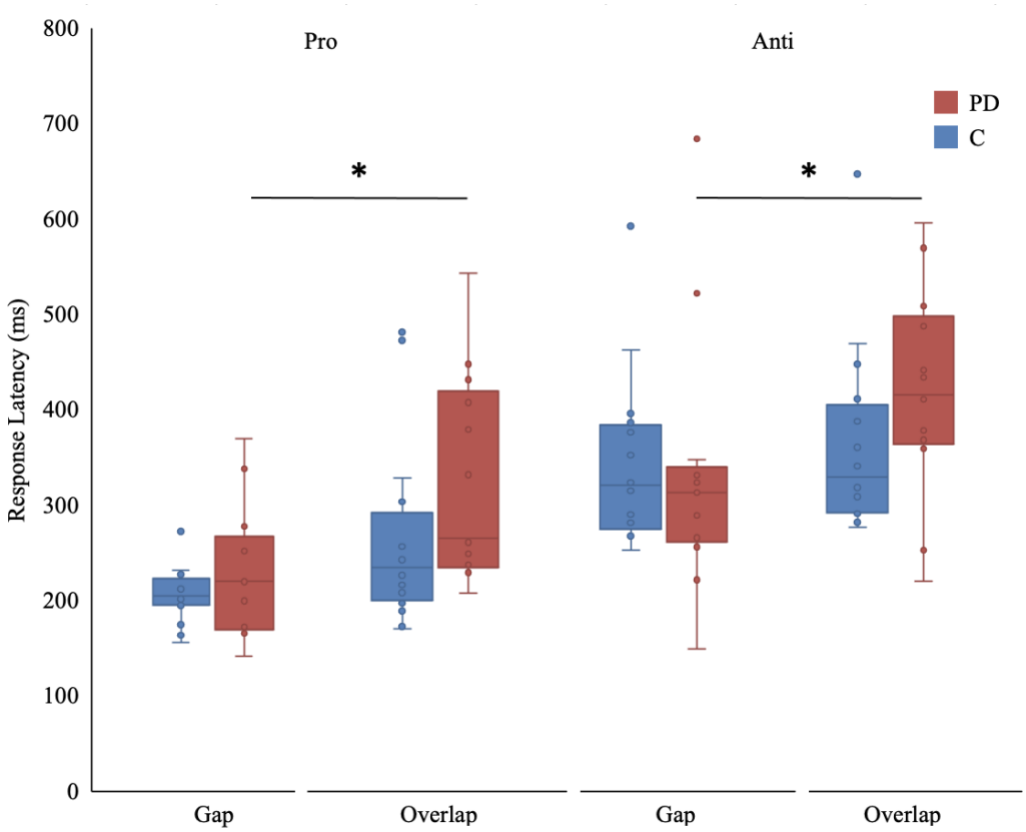
Do PwPD Perform Differently Than Controls on Eye Movement Tasks?

Response Latency. The analysis of response latency revealed no significant effect of group (p >.05). A significant main effect was found for task, response latencies were significantly faster for the pro-saccade tasks (M = 253 ms, SD = 69 ms) than for the anti-saccade tasks (M = 359 ms, SD = 89 ms), $F(1,27) = 80.46$, p<.001, $\eta^2 = .749$. A second main effect was found for timing condition, response latencies were significantly faster in the gap conditions (M = 275 ms, SD = 71 ms) compared to the overlap conditions (M = 337 ms, SD = 89 ms), $F(1,27) = 27.09$, p<.001, $\eta^2 = .501$.

A significant group by timing condition interaction was observed (Figure 7). To help decompose this interaction, we calculated the gap effect (overlap minus gap RL) for each participant across both pro- and anti-saccade conditions and submitted this measure (the gap effect) to a one-way between-subjects ANOVA with group as the only factor. The analysis revealed that PwPD (M = 88 ms, SD = 74 ms) had a significantly larger gap effects than the controls (M = 34 ms, SD = 74), $F(1,27) = 4.75$, p=.038, $\eta^2 = .15$.

Figure 7

Response Latency as a Function of Group, Task, and Timing Condition



Note. This graph shows response latency as a function of group (Parkinson's and controls), task (pro and anti-saccade), and timing condition (gap and overlap). Significant group (Parkinson's vs control) differences are indicated with asterisks (*) on the graph. The boxes represent the interquartile range (IQR), the whiskers extend to the 10th and 90th percentiles of the data, the line dividing the box represents the median, and mean scores from individual participants are overlaid.

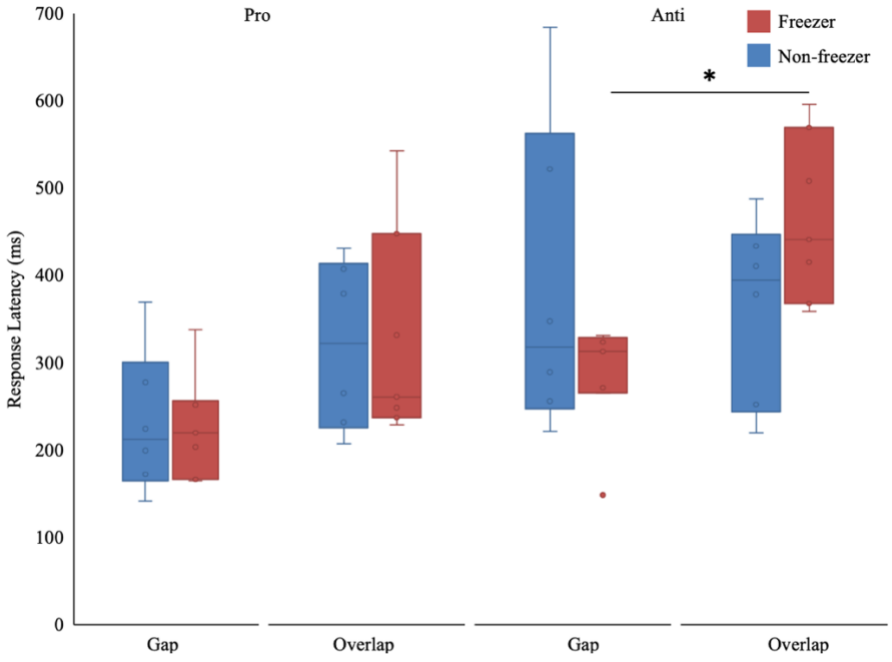
We wanted to know whether the gap effect was larger for PwPD with FOG compared to PwPD without FOG. PwPD were divided into FOG and no-FOG groups based on their answer to the first question on the NFOG-Q ("Have you experienced an

episode of freezing in the past month?"); if participants indicated yes, they were categorized as a freezer. The gap effect was submitted to a univariate ANOVA for PwPD, with group (FOG or no-FOG) as the only factor. The analysis revealed a significant group effect, PwPD with FOG exhibited significantly larger gap effects (M = 137 ms, SD = 79 ms) compared to PwPD without FOG (M = 31 ms, SD = 79 ms), $F(1,11) = 5.79$, p=.035, η^2 =.345.

The pro-saccade gap effect allowed us to measure the time cost associated with needing to release from fixation when initiating a response. The anti-saccade gap effect adds an additional aspect of the time cost associated with needing to inhibit a reflexive saccade and initiate a voluntary saccade. Therefore, to isolate the time cost of release from the time cost of both release and inhibition, we wanted to analyze the pro-saccade gap effect and the anti-saccade gap effect separately. The pro-saccade gap effect was submitted to a univariate ANOVA for PwPD, with group (FOG or no-FOG) as the only factor. The pro-gap effect for PwPD with FOG (M = 95 ms, SD = 73 ms) did not differ from PwPD without FOG (M = 85 ms, SD = 73 ms), no significant group effects were observed, $F(1,11) = .06$, p=.818, η^2 =.005. The anti-saccade gap effect was submitted to a univariate ANOVA for PwPD (see Figure 8), with group (FOG or no-FOG) as the only factor. The anti-saccade gap effect for PwPD with FOG (M = 179 ms, SD = 138 ms) was significantly larger compared to PwPD without FOG (M = -23 ms SD = 138 ms), $F(1,11) = 6.97$, p=.023, η^2 =.388.

Figure 8

Response Latency as a Function of FOG Group, Task, and Timing Condition



Note. This graph shows response latency as a function of group (freezer and non-freezer), task (pro and anti-saccade), and timing condition (gap and overlap). Significant group (freezer vs non-freezer) differences are indicated with asterisks (*) on the graph. The boxes represent the interquartile range (IQR), the whiskers extend to the 10th and 90th percentiles of the data, the line dividing the box represents the median, and mean scores from individual participants are overlaid.

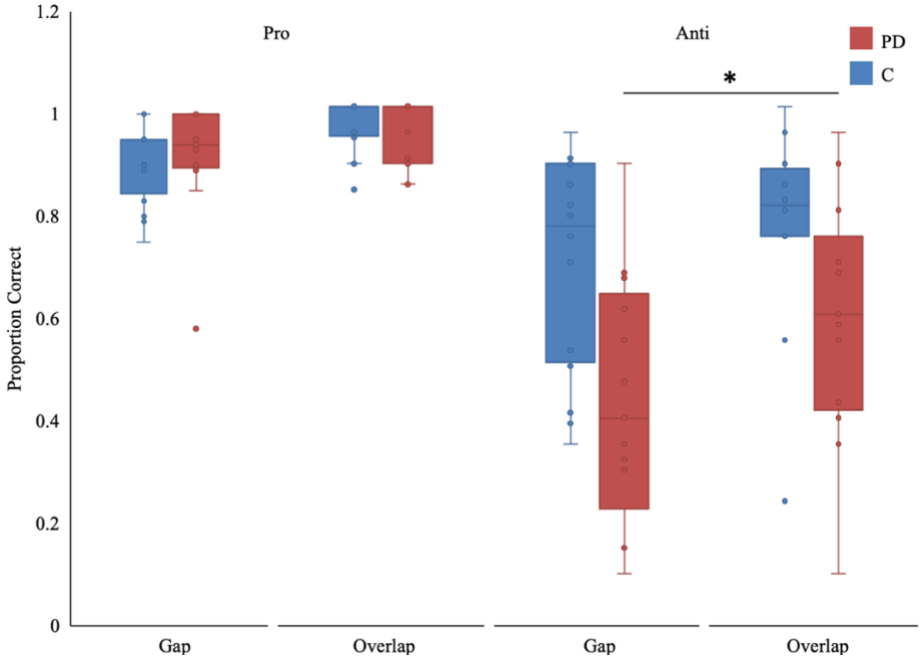
Proportion Correct. The analysis of proportion correct revealed a main effect of group, PwPD (M = 72%, SD = 10%) had a lower proportion of correct responses compared to the controls (M = 84%, SD = 10%), $F(1,27) = 11.10$, p=.003, $\eta^2 = .291$. A second main effect was observed for task, participants had a greater proportion of correct responses during the pro-saccade task (M = 94%, SD = 6%) compared to the anti-saccade task (M = 63%, SD = 20%), $F(1,27) = 73.43$, p<.001, $\eta^2 = .731$. A third main effect was

for timing condition, participants had a greater proportion of correct responses in the overlap conditions (M = 82%, SD = 10%) compared to the gap conditions (M = 74%, SD = 12%), $F(1,27) = 16.05$, $p<.001$, $\eta^2 = .373$.

A significant group by task interaction was observed (Figure 9), PwPD had a lower proportion of correct responses in the anti-saccade task (M = 52%, SD = 19%), compared to the controls (M = 74%, SD = 9%), $F(1,27) = 5.64$, $p=.025$, $\eta^2 = .173$.

Figure 9

Proportion Correct as a Function of Group, Task, and Timing Condition



Note. This graph shows proportion correct as a function of group (Parkinson's and controls), task (pro and anti-saccade), and timing condition (gap and overlap). Significant group (Parkinson's vs control) differences are indicated with asterisks (*) on the graph. The boxes represent the interquartile range (IQR), the whiskers extend to the 10th and 90th percentiles of the data, the line dividing the box represents the median, and mean scores from individual participants are overlaid.

Can Eye Movement Performance Predict Freezing Severity for PwPD?

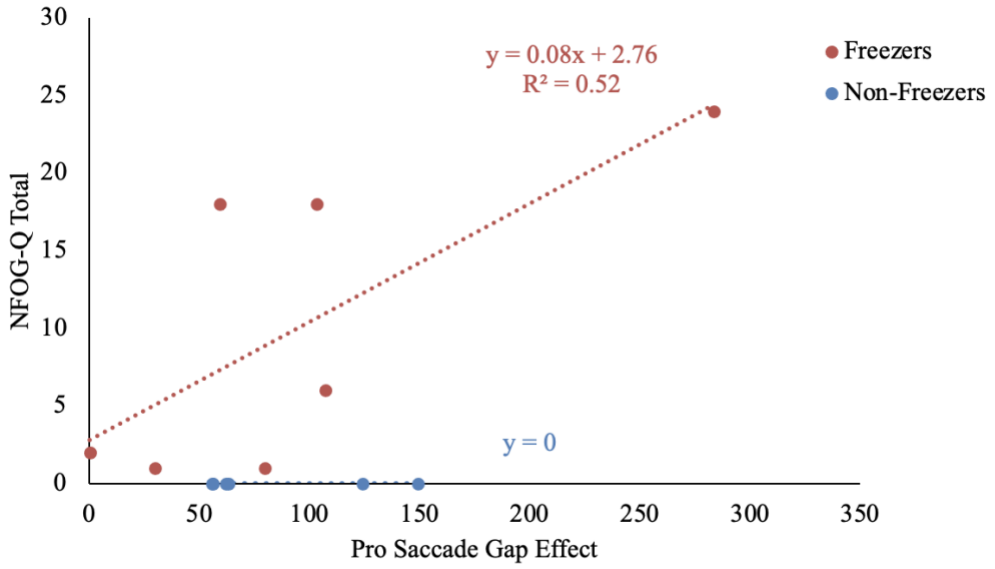
We wanted to know if performance on eye movement tasks, which measure certain elements of executive function such as response initiation and inhibition, could explain freezing severity in PwPD with FOG. We predicted that the magnitude of the gap effect would be associated with freezing severity due to executive function; individuals with larger gap effects would exhibit greater freezing severity. First, a Pearson correlation analysis was performed to observe which questionnaire and eye movement measures had a significant relationship with freezing severity (as measured by the NFOG-Q). The results revealed a significant negative correlation between subjective health rating percentage and freezing severity, $r(11) = -.65$, $p = .006$, indicating a large relationship, and a significant positive correlation between the pro-saccade gap effect and freezing severity, $r(11) = .57$, $p = .020$, indicating a large relationship. Next, a hierarchical linear regression was performed with health rating percentage entered as a level 1 covariate. Although health rating percentage was not our primary focus, we expected that PwPD with FOG would report lower health ratings based on prior literature and the correlation reported above supports this expectation; therefore, we included it as a covariate. The pro-saccade gap effect was included on the second level. Freezing severity was entered as the outcome variable.

The overall model was not significant, $F(2,10) = 2.72$, $p = .057$, accounting for 33% of the variance in freezing severity ($R^2 = .352$). For the individual predictors, health rating percentage showed a non-significant relationship with freezing severity, $t(10) = -1.668$, $p = .062$, partial $r = -.449$. The pro-saccade gap effect also demonstrated a non-significant relationship with freezing severity, $t(10) = 1.524$, $p = .080$, partial $r = .434$.

However, when the pro-saccade gap effect was entered on its own, the model was significant $F(1,11) = 5.40$, $p = .034$, accounting for 52% of the variance in freezing severity ($R^2 = .519$), see Figure 10. The pro-saccade gap effect demonstrated a significant relationship with freezing severity, $t(10) = 2.322$, $p = .034$, partial $r = .720$.

Figure 10

Pro-Saccade Gap Effect Accounts for Freezing Severity



Note. This graph depicts linear regressions for PwPD (both freezers and non-freezers); demonstrating whether performance in the pro-saccade gap task could explain freezing severity.

Can Eye Movement Performance Be Used to Categorize PwPD as Freezers or Non-freezers?

We wanted to know if performance on eye movement tasks, which measure certain elements of executive function such as response initiation and inhibition, could be

used to categorize PwPD as freezers or non-freezers. First, a Spearman's correlation analysis was performed to observe which questionnaire and eye movement measures had a significant relationship with freezing category (FOG or no-FOG; assigned using the NFOG-Q). The results revealed a significant positive correlation between the anti-saccade gap effect and freezing category, $r(11) = .619$, $p = .012$, indicating a large relationship. No other significant correlations were observed.

We ran a hierarchical binary logistic regression to categorize freezers and non-freezers using the anti-saccade gap effect. However, the results yielded perfect fit without significant predictors, indicating that our model was overfit and underpowered. Please see Appendix I.

The odds ratio told us that as the anti-saccade gap effect increased by a unit, the change in the odds of being a freezer (rather than a non-freezer) is 1.367. You're more likely to be a freezer than not if you have a larger anti-saccade gap effect. However, the anti-saccade gap effect was not a significant predictor of whether a participant was a freezer or non-freezer, b = 0.312, Wald $\chi^2(1) = .000$, p = .999.

Reaching Performance

To assess upper limb freezing in PwPD, we used three reaching tasks: reversal, corner, and tunnel to mirror conditions known to elicit freezing of gait. Using these tasks, we aimed to produce freezing-like behaviours that we could detect within the data. Reaching data were collected for 30 participants (16 control, 14 PwPD).

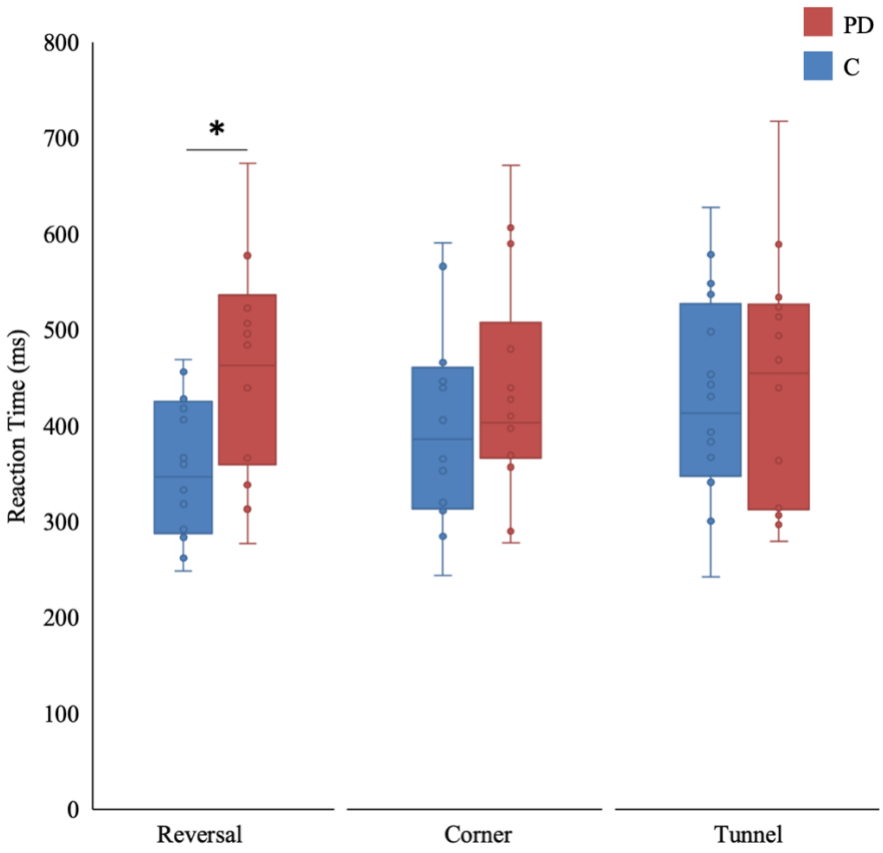
Do PwPD Perform Differently than Controls on Reaching Tasks?

Reaction Time. The analysis of reaction time revealed a significant group by task interaction $F(1,28) = 5.32$, $p = .008$, $\eta^2 = .16$, see Figure 11. We decomposed this

interaction by calculating the simple main effects of group for each level of task, which showed that PwPD (M = 456 ms, SD = 94 ms) had significantly greater reaction times than controls (M = 355 ms, SD = 94 ms) in the reversal task compared to the control group, $F(1,28) = 8.03$, $p = .008$, $\eta^2 = .223$. There were no differences between groups for the other two tasks.

Figure 11

Reaction Time as a Function of Group and Task



Note. This graph shows reaction time as a function of group (Parkinson's and controls) and task (reversal, corner, tunnel). Significant group (Parkinson's vs control) differences are indicated with asterisks (*) on the graph. The boxes represent the interquartile range (IQR), the whiskers extend to the 10th and 90th percentiles of the data, the line dividing the box represents the median, and mean scores from individual participants are overlaid.

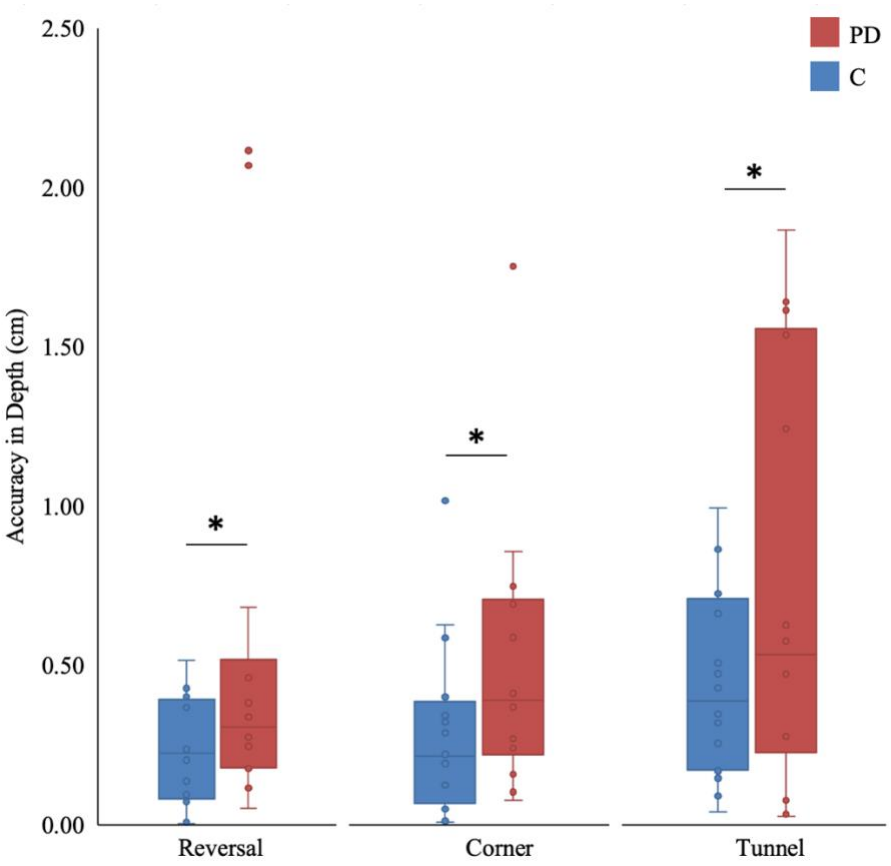
Movement Time. The analysis of movement time revealed a significant main effect of task. Movement times were greater in the tunnel task (M = 800 ms, SD =266 ms) compared to the reversal (M = 688 ms, SD = 183 ms) and corner (M = 725 ms, SD = 219 ms) tasks, $F(1,28) = 7.18$, $p = .004$, $\eta^2 = .204$. No significant main effect or interaction involving group was found.

Distance Travelled. The analysis of distance revealed a significant main effect of task. Participants undershot the target in the tunnel task (M = 14.6 cm, SD = .9 cm) in comparison to the reversal (M = 14.9 cm, SD = .6 cm) and corner (M = 14.9 cm, SD = .5 cm) tasks, $F(1,28) = 4.62$, $p = .014$, $\eta^2 = .142$. No significant main effect or interaction involving group was found.

Accuracy in Depth. The analysis of accuracy in depth revealed a significant main effect of group (see Figure 12). PwPD (M = .6 cm, SD = .4 cm) had lower accuracy than controls (M = .3 cm, SD = .4 cm) across all tasks, $F(1,28) = 4.64$, $p = .040$, $\eta^2 = .142$. A second main effect was found for task, participants had greater accuracy in the reversal (M = .4 cm, SD = .5 cm) and corner (M = .4 cm, SD = .4 cm) tasks compared to the tunnel task (M = .6 cm, SD = .5 cm), $F(1,28) = 5.37$, $p = .007$, $\eta^2 = .161$.

Figure 12

Accuracy in Depth as a Function of Group and Task



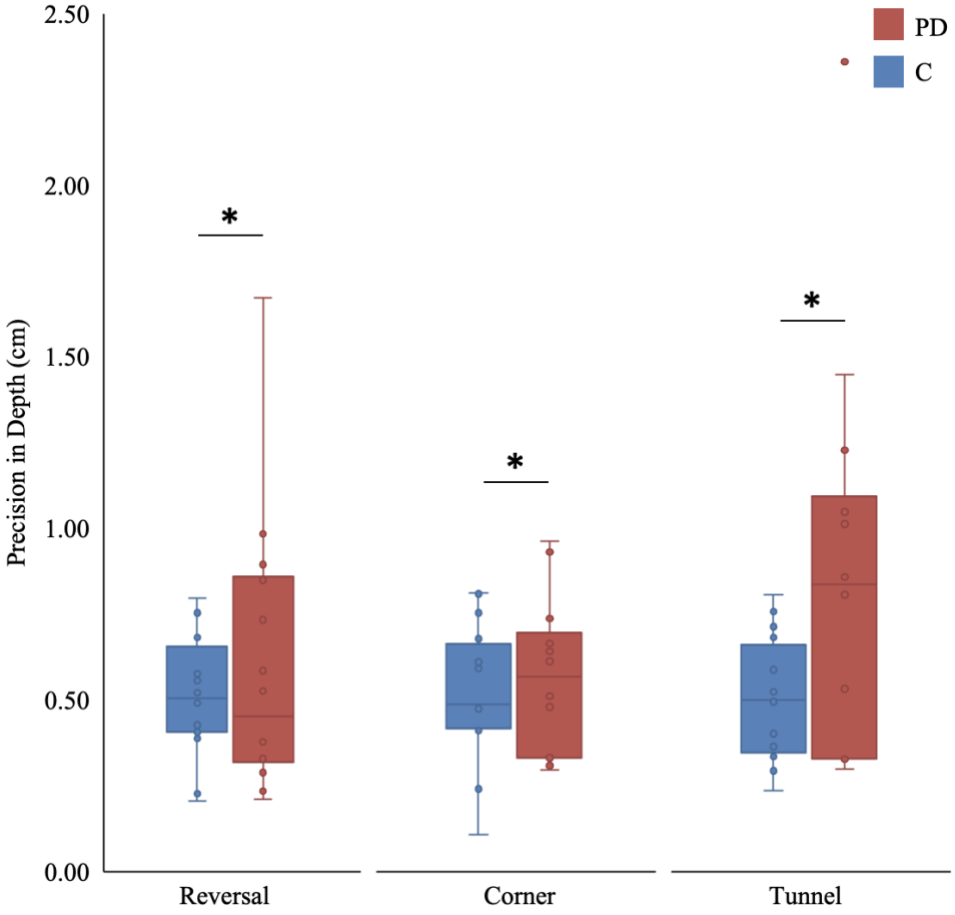
Note. This graph shows accuracy in depth as a function of group (Parkinson's and controls) and task (reversal, corner, tunnel). Significant group (Parkinson's vs control) differences are indicated with asterisks (*) on the graph. The boxes represent the interquartile range (IQR), the whiskers extend to the 10th and 90th percentiles of the data, the line dividing the box represents the median, and mean scores from individual participants are overlaid.

Precision in Depth. The analysis of precision in depth revealed a significant main effect of group. PwPD (M = .7 cm, SD = .2 cm) had lower precision than controls (M = .5 cm, SD = .2 cm) across all tasks, $F(1,28) = 5.12$, $p = .032$, $\eta^2 = .155$.

A marginal group by task interaction was found (see Figure 13). PwPD (M = .9 cm, SD = .4 cm) trended towards greater variability (lower precision) in the tunnel task compared to the controls (M = .5 cm, SD = .4 cm), $F(1,28)$ =2.71, p=.086, η^2 = .088.

Figure 13

Precision in Depth as a Function of Group and Task



Note. This graph shows precision in depth as a function of group (Parkinson's and controls) and task (reversal, corner, tunnel). Significant group (Parkinson's vs control) differences are indicated with asterisks (*) on the graph. The boxes represent the interquartile range (IQR), the whiskers extend to the 10th and 90th percentiles of the data, the line dividing the box represents the median, and mean scores from individual participants are overlaid.

Transitional Phases in the Reaching Tasks

Our goal was to capture freezing behaviour and we anticipated that these behaviours may happen as participants initiated their movements, and near or at the first target where participants were asked to make a transition in direction (reversal or corner). Specific phases were identified within the reaching tasks to isolate transition periods based on time. Initially, four phases were analyzed: phase 1 (initiation: from movement start to peak acceleration), phase 3 (transition preparation: from peak velocity to peak deceleration), phase 4 (start of transition: from peak deceleration to end of first movement), and phase 5 (transition: from end of first movement to start of second movement). Variability normalized to each participant's speed (coefficient of variation, CoV), percentage of time spent (%Time), and percentage of distance covered (%Distance) were computed for each phase and task. Phase 2 was added in post hoc for the analysis of %Distance and %Time to help solidify model findings. Phase 2 was defined as the period between peak acceleration to peak velocity.

We expected main effects of phase for every measure due to the well-documented speed profile of reaching movements. For this reason, below we report main effects or interactions involving task or group only; phase main effects will not be broken down.

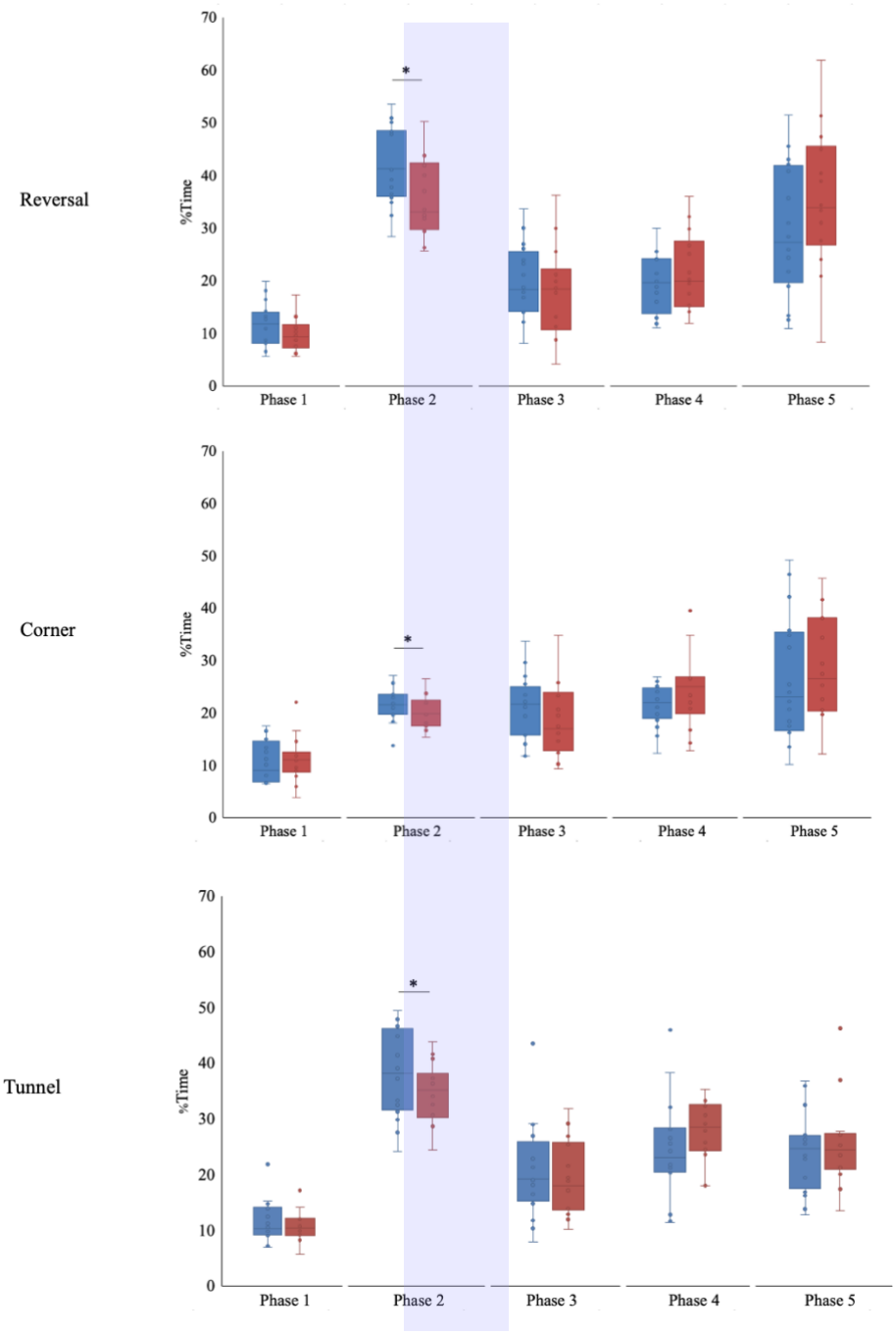
%Time. The analysis revealed a significant main effect of task, participants spent a greater percentage of time in the reversal task (M = 24%, SD = 9%) and the tunnel task (M = 23%, SD = 10%) compared to the corner task (M = 20%, SD = 8%), $F(1,28) = 167.62$, $p < .001$, $\eta^2 = .857$. A second main effect was found for phase, $F(1,28) = 62.72$, $p < .001$, $\eta^2 = .691$.

A significant task by phase interaction was observed, $F(1,28) = 13.41$, $p < .001$, $\eta^2 = .324$ (see Figure 14). We decomposed the interaction by looking at task differences within each phase. In phases 1 and 3, there were no simple main effects of task ($ps < .207$). A smaller percentage of time was spent in phase 2 for the corner task ($M = 20\%$, $SD = 3\%$) compared to the reversal task ($M = 38\%$, $SD = 7\%$) and tunnel task ($M = 36\%$, $SD = 7\%$), $F(1,28) = 124.22$, $p < .001$, $\eta^2 = .816$. A smaller percentage of time was spent in phase 4 for the tunnel task ($M = 25\%$, $SD = 8\%$) compared to the reversal task ($M = 20\%$, $SD = 6\%$) and corner task ($M = 22\%$, $SD = 6\%$), $F(1,28) = 5.23$, $p = .008$, $\eta^2 = .157$. Participants spent a greater percentage of time in phase 5, while performing the reversal task ($M = 32\%$, $SD = 13\%$) compared to the corner task ($M = 27\%$, $SD = 11\%$) and tunnel task ($M = 24\%$, $SD = 8\%$), $F(1,28) = 4.82$, $p = .018$, $\eta^2 = .147$.

Planned pairwise comparisons between groups revealed a significant main effect of group in phase 2, PwPD ($M = 29\%$, $SD = 5\%$) were spending a smaller percentage of time in phase 2 compared to the controls ($M = 33\%$, $SD = 5\%$), $F(1,28) = 4.81$, $p = .037$, $\eta^2 = .147$. We found a marginal main effect of group in phase 4, PwPD ($M = 24\%$, $SD = 4\%$) were trending towards spending a greater percentage of time in phase 4 compared to the controls ($M = 21\%$, $SD = 4\%$), $F(1,28) = 3.29$, $p = .080$, $\eta^2 = .105$. No other group effects were observed.

Figure 14

Percentage of Time Spent as a Function of Group, Task, and Phase



Note. PwPD are represented in red, controls are represented in blue. This graph shows %Time spent as function of group (Parkinson's and controls), task (reversal, corner, tunnel), and phase (1-5). Significant group (Parkinson's vs control) differences are indicated with asterisks (*) on the graph.

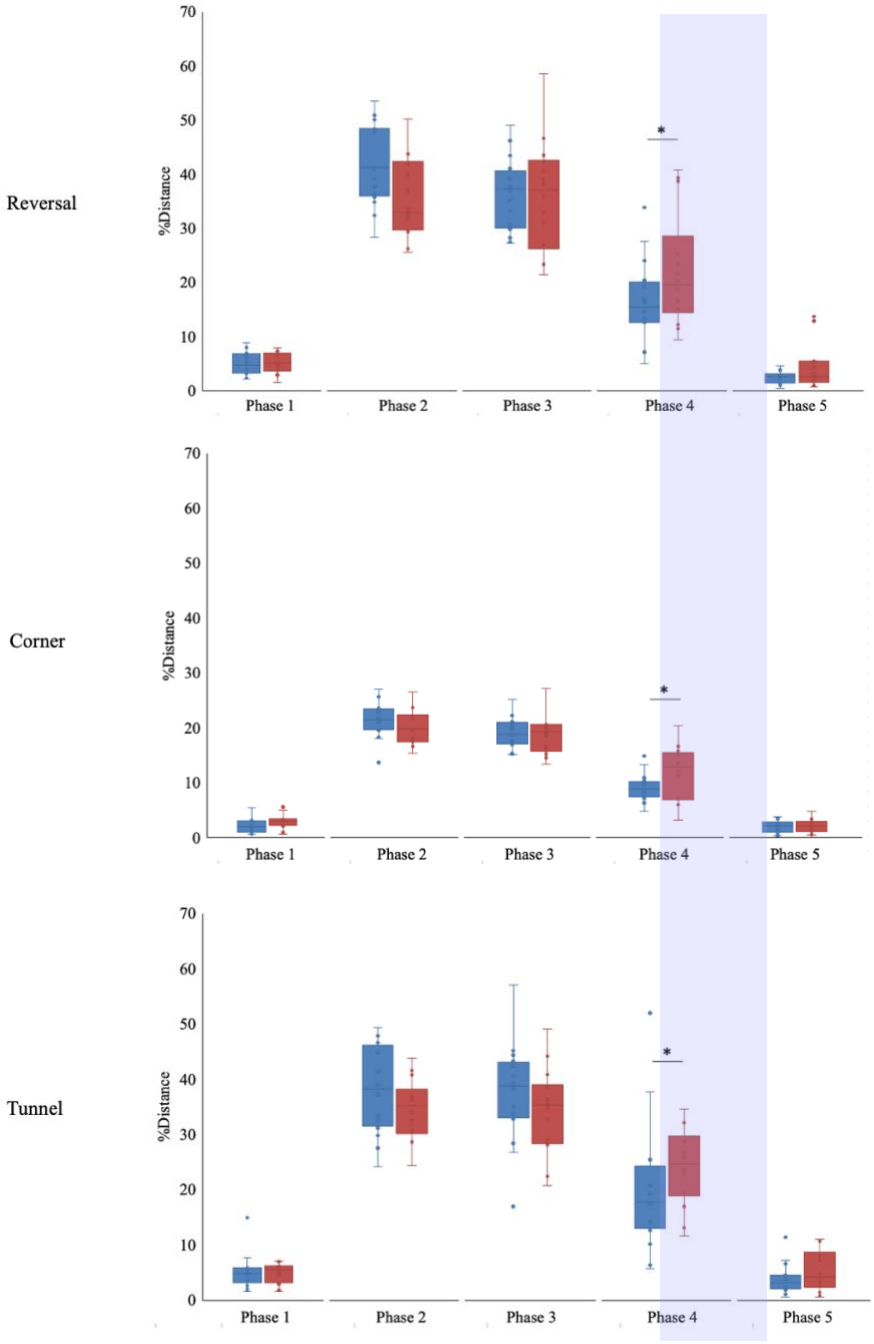
%Distance. The analysis of percentage distance revealed a significant main effect of task, participants covered a smaller percentage of distance in the corner task (M = 11%, SD = 5%) compared the reversal task (M = 20%, SD = 4%) and tunnel task (M = 20%, SD = 7%), $F(1,28) = 3051.52$, $p < .001$, $\eta^2 = .991$. A second main effect was found for phase, $F(1,28) = 325.57$, $p < .001$, $\eta^2 = .921$.

A significant group by phase interaction was observed, see Figure 15. PwPD covered a greater percentage of distance within phase 1 (M = 4.4%, SD = 1.6%), phase 4 (M = 19.1%, SD = 4.8%), and phase 5 (M = 3.8%, SD = 2.0%) in comparison to the controls: phase 1 (M = 4.1%, SD = 1.6%), phase 4 (M = 14.9%, SD = 4.8%), and phase 5 (M = 2.7%, SD = 2.0%), $F(1,28) = 3.99$, $p = .005$, $\eta^2 = .125$. PwPD covered a smaller percentage of distance in phase 2 (M = 29.4%, SD = 4.7%) and phase 3 (M = 29.0%, SD = 3.8%) compared to the controls: phase 2 (M = 33.2%, SD = 4.7%), phase 3 (M = 30.4%, SD = 3.8%), $F(1,28) = 3.99$, $p = .005$, $\eta^2 = .125$. Planned pairwise comparisons between groups revealed a significant main effect of group in phase 4, PwPD (M = 19.1%, SD = 4.8%) covered a significantly greater percentage of distance in phase 4 compared to the controls (M = 14.9%, SD = 4.8%), $F(1,28) = 3.99$, $p = .005$, $\eta^2 = .125$.

Additionally, a significant task by phase interaction was observed, $F(1,28) = 16.13$, $p < .001$, $\eta^2 = .365$. We decomposed the task by phase interaction by looking at task differences within each phase. A significant main effect of task was found in phase 1 $F(1,28) = 30.14$, $p < .001$, $\eta^2 = .518$, phase 2 $F(1,28) = 124.22$, $p < .001$, $\eta^2 = .816$, phase 3 $F(1,28) = 53.28$, $p < .001$, $\eta^2 = .656$, phase 4 $F(1,28) = 18.17$, $p < .001$, $\eta^2 = .394$, and phase 5 $F(1,28) = 10.90$, $p < .001$, $\eta^2 = .280$. A smaller proportion of distance was covered in the corner task across all phases in comparison to the other tasks.

Figure 15

Percentage of Distance Covered as a Function of Group, Task, and Phase



Note. PwPD are represented in red, controls are represented in blue. This graph shows %Distance covered as function of group (Parkinson's and controls), task (reversal, corner, tunnel), and phase (1-5). Significant group (Parkinson's vs control) differences are indicated with asterisks (*) on the graph.

CoV. The analysis of the coefficient of variation revealed that participants were significantly more variable in phase 1 (M = 73%, SD = 13%), phase 4 (M = 50%, SD = 9%), and phase 5 (M = 64%, SD = 18%) compared to phase 3 (M = 17%, SD = 2%), $F(1, 28) = 148.84$, $p < .001$, $\eta^2 = .842$. No group effects were observed.

Phase 5. We analyzed phase 5 separately because it captured any secondary corrective movements made after the first movement ended and, for the reversals and corners, included the time participants dwelled on the target, a period we considered particularly important for identifying freezing-like behaviours.

A significant main effect of task was found for the analysis of phase 5. Participants had longer movement times in the reversal task (M = 390 ms, SD = 248 ms) compared to the corner task (M = 313 ms, SD = 196 ms) and tunnel task (M = 250 ms, SD = 81 ms), $F(1,28) = 5.63$, $p = .006$, $\eta^2 = .167$. A marginal simple effect of group was observed in the reversal task. PwPD (M = 471 ms, SD = 248 ms) were trending toward greater transitional movement times in the reversal task compared to the controls (M = 308 ms, SD = 247 ms), $F(1,28) = 3.20$, $p = .085$, $\eta^2 = .102$.

Does Reaching Performance Predict Freezing Severity for PwPD?

We wanted to know if anything about reaching performance in our reversal, corner, and tunnel tasks could predict freezing severity for PwPD. First, a Pearson correlation analysis was performed to observe reaching measures had a significant relationship with freezing severity (as measured by the NFOG-Q). None of our reaching variables were correlated with freezing severity; suggesting that any further analysis would be futile.

Can Reaching Performance Be Used to Categorize PwPD as Freezers or Non-freezers?

We wanted to know if reaching performance in the reversal, corner, and tunnel tasks could be used to categorize PwPD as freezers or non-freezers. First, a Spearman's correlation analysis was performed to observe which questionnaire and reaching measures had a significant relationship with freezing category (FOG or no-FOG; assigned using the NFOG-Q). The results revealed a significant negative correlation between absolute error in depth in the reversal task and freezing category, $r(12) = -.465$, $p = .047$, indicating a moderate relationship. Additionally, we found a significant negative correlation between reaction time in the corner task and freezing category, $r(12) = -.465$, $p = .047$, indicating a moderate relationship. No other significant correlations were observed.

We ran hierarchical binary logistic regressions for each of the three reaching tasks separately to categorize freezers and non-freezers. However, the results yielded perfect fit without significant predictors, indicating that our models were overfit and underpowered. Please see Appendix J.

Walking Performance

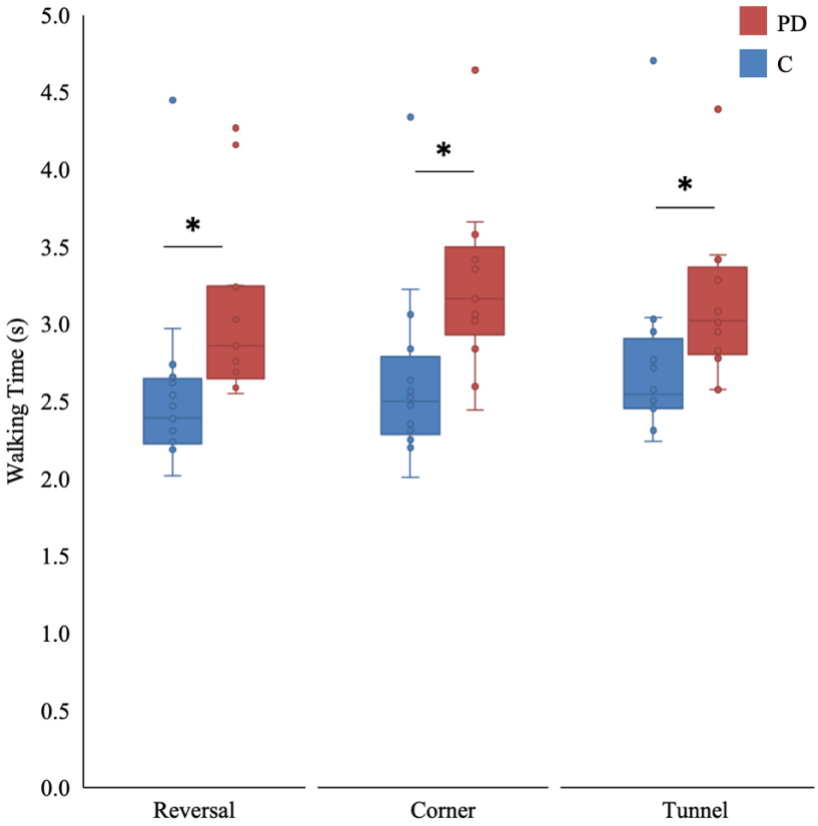
To assess freezing of gait in PwPD, we used three tasks known to elicit freezing of gait: reversal, corner and tunnel. These tasks aimed to detect freezing behaviours, primarily characterized by hesitations and gait variability. Walking data were collected for 30 participants (16 control, 14 PwPD).

Do PwPD Perform Differently than Controls on Walking Tasks?

Walking time. The analysis of walking time revealed no significant effects. However, PwPD were trending towards longer walking times (M = 3.1 s, SD = .52 s) compared to the controls (M = 2.6 s, SD = .52 s). One PwPD (#25) was notably slower than the other PwPD and is not included in the above mean (#25: M = 19.3 s); they were 31 standard deviations slower overall. Due to the increased variance that was added to the PD group from this participant, when they were removed from the dataset, a significant main effect of group was found (see Figure 16), PwPD (M = 3.1 s, SD = .52 s) were significantly slower across all walking tasks compared to the controls, (M = 2.6 s, SD = .52 s), $F(1, 27) = 6.73$, $p = .015$, $\eta^2 = .199$.

Figure 16

Walking Time as a Function of Group and Task Without Subject #25



Note. This graph shows walking time as a function of group (Parkinson's and controls) and task (reversal, corner, tunnel). Significant group (Parkinson's vs control) differences are indicated with asterisks (*) on the graph.

Percent Time in Deceleration. The analysis of percent time spent in deceleration revealed a significant main effect of task, participants spent a greater percentage of time decelerating in the reversal task (M = 55%, SD = 12%) and corner task (M = 61%, SD = 11%) compared to the tunnel task (M = 38%, SD = 13%), $F(1, 28)$ =32.39, p<.001, η^2 = .536. No group differences were observed.

Does Walking Performance Predict Freezing Severity for PwPD?

We wanted to know if anything about walking performance in our reversal, corner, and tunnel tasks could predict freezing severity for PwPD. First, a Pearson correlation analysis was performed to observe which walking measures had a significant relationship with freezing severity (as measured by the NFOG-Q). A significant positive correlation was found between corner walking time and freezing severity, $r(11) = .732$, $p = .002$, indicating a large relationship. A significant positive correlation was also found between tunnel walking time and freezing severity, $r(11) = .543$, $p = .030$, indicating a large relationship.

For the regression analyses, hierarchical linear regression models were used to predict freezing severity in PwPD. Health rating percentage was included as a level 1 covariate in all models to account for its established relationship with freezing severity and task-specific walking times were entered on level 2.

Corner. Model 1 was significant, $F(1,11) = 9.50$, $p = .005$, $R^2 = .463$, health rating percentage explained 46% of the variance in NFOG-Q. Health rating percentage demonstrated a significant relationship with freezing severity, $t(11) = -3.082$, $p = .010$, partial $r = -.681$. In model 2, the addition of corner walking time $\Delta R^2 = .089$, $p = .189$, did not significantly improve the model.

Tunnel. The only aspect of the tunnel analysis that changed was the replacement of corner walking time with tunnel walking time on level 2. In model 2, the addition of tunnel walking time $\Delta R^2 = .012$, $p = .639$, did not significantly improve the model.

Can Walking Performance Be Used to Categorize PwPD as Freezers or Non-freezers?

We wanted to know if walking performance in the reversal, corner, and tunnel tasks could be used to categorize PwPD as freezers or non-freezers. First, a Spearman's correlation analysis was performed to observe which questionnaire and reaching measures had a significant relationship with freezing category (FOG or no-FOG; assigned using the NFOG-Q). The results revealed a significant positive correlation between the percentage of time spent decelerating in the corner task and freezing category, $r(12) = .573$, $p = .016$, indicating a large relationship. Additionally, a significant negative correlation was found between the percentage of time spent decelerating in the tunnel task and freezing category, $r(12) = -.752$, $p = .001$, indicating a large relationship. No other significant correlations were observed.

We ran hierarchical binary logistic regressions for each of the three walking tasks separately to categorize freezers and non-freezers. However, the results yielded perfect fit without significant predictors, indicating that our models were overfit and underpowered. Please see Appendix K. For the corner task model, the odds ratio told us that as the percentage of time spent in deceleration increased by a unit, the change in the odds of being a freezer (rather than a non-freezer) is 1.132. You're more likely to be a freezer than not if you spend more time decelerating. However, the percentage of time spent decelerating did not significantly predict whether a participant was a freezer or non-freezer, b = .124, Wald $\chi^2(1) = 2.855$, p = .091.

Is There a Relationship Between Performance on Eye Movement, Reaching, and Walking Tasks for PwPD?

We wanted to know if performance across eye movement, reaching, and walking tasks were related. We conducted a Pearson correlation analysis to examine comparable metrics across eye movement, reaching, and walking tasks (response latencies, reaction times, movement time, and percent time spent in deceleration). The results identified two significant positive correlations, both indicating large effect sizes. First, response latencies in the express pro-saccade tasks were positively correlated with reaction times in the reaching reversal task, $r(11) = .500$, $p = .041$. Second, response latencies in the express anti-saccade task were positively correlated with reaction times in the reaching corner task, $r(11) = .522$, $p = .034$. These findings suggest that slower response latencies in express saccade eye movement tasks are associated with slower reaction times in reaching tasks designed to elicit FOUL. Lastly, we wanted to know if the gap effect was related to performance across reaching and walking tasks. The results identified four significant positive correlations, each indicating large effect sizes. The gap effect was positively correlated with walking movement time in the reversal task, $r(11) = .545$, $p = .027$, the corner task, $r(11) = .564$, $p = .022$, and the tunnel task $r(11) = .570$, $p = .021$. Additionally, the gap effect was positively correlated with percentage of time spent decelerating in the walking corner task $r(11) = .577$, $p = .009$. These results suggest that larger gap effects are associated with slower walking times and a greater percentage of time spent in deceleration in tasks designed to elicit FOG

Discussion

The purpose of this study was to use the gap effect to evaluate executive function and explore its relationship with freezing. Eye movement tasks were used to examine the executive functions of release and inhibition, demonstrating how these processes contribute to freezing in other motor tasks. Additionally, we aimed to investigate the characteristics of FOUL and FOG using tasks designed to elicit FOG. This study builds on prior research demonstrating impaired oculomotor control, upper-limb motor deficits, and gait disturbances in PD, particularly in tasks involving executive function (Bloem et al., 2004; Das et al., 2016; Mazzoni et al., 2012). Previous research has demonstrated the relationship between freezing and executive function by evaluating performance on pro- and anti-saccade tasks (Amboni et al., 2008; Gallea et al., 2021; Walton et al., 2015). Our findings indicate that PwPD exhibited significantly larger gap effects in pro- and anti-saccade tasks compared to controls, with PwPD with FOG showing greater anti-saccade gap effects than PwPD without FOG. Additionally, pro-saccade gap effects were significant predictors of FOG severity. These results suggest that executive dysfunction, as measured by the pro-saccade and anti-saccade tasks, are closely associated with FOG in PwPD, supporting their potential as objective markers for assessing FOG severity. By including gap and overlap timing conditions within pro- and anti-saccade tasks, effectively utilizing the gap effect, we were able to further support the relationship between freezing and executive function.

We assessed participant demographics and used questionnaire data to check for expected likenesses and differences between the control and PwPD groups. The two groups showed no significant differences in age or sex distribution, indicating similar

basic profile metrics. However, some notable differences between groups were observed. Consistent with the clinical profile of PD, PwPD exhibited greater motor symptom severity, more advanced Hoehn & Yahr stages, greater FOG severity, and greater experiences of depression compared to the control group (Jankovic, 2008). Additionally, the controls exhibited significantly higher MOCA scores compared to the PwPD. Among the PwPD, results from the NFOG-Q allowed categorization into freezers and non-freezers, with freezers exhibiting interesting variability in freezing severity, which proved useful for analyzing the relationship between freezing and executive dysfunction.

Executive Function and Freezing

The results of this study indicate that PwPD exhibit significantly lower performance than controls on eye-movement tests of executive function, reaching, and gait, with some measures predicting FOG severity and differentiating freezers from non-freezers, underscoring their potential to serve as valuable markers for FOG prediction and progression.

Our first hypothesis stated that freezing is the result of advancing executive dysfunction. We predicted that if executive function is underlying freezing, the gap effect would be larger for PwPD with FOG compared to PwPD without FOG. The results revealed that PwPD with FOG exhibited significantly larger gap effects compared to PwPD without FOG.

This relationship was further clarified when we separated the gap effect into pro-saccade and anti-saccade gap effects. By completing this separation, we aimed to disentangle the release component of the pro-saccade gap effect from the inhibitory control demands required during the anti-saccade gap effect. The pro-saccade gap effect

reveals the advantage gained when participants no longer need to disengage from fixation. By contrast, the anti-saccade gap effect reflects what happens when participants no longer need to release from fixation but still must inhibit the pro-saccade and generate the anti-saccade, which may be even more challenging in the gap condition without the stabilizing influence of fixation. The absence of a significant difference in the pro-saccade gap effect between PwPD with and without FOG suggests that the ability to disengage from fixation alone is relatively preserved across both groups. The anti-saccade gap effect revealed a marked difference between groups. PwPD with FOG exhibited significantly larger anti-saccade gap effects than PwPD without FOG. PwPD with FOG experienced a greater time cost when required to inhibit a reflexive response and generate a voluntary saccade under gap timing conditions. This result aligns with existing literature suggesting that PwPD, particularly those with FOG, exhibit deficits in inhibitory control and voluntary saccade generation (Gallea et al., 2021; Nemanich & Earhart, 2016; Walton et al., 2015).

The proportion correct analysis further indicated experiences of executive dysfunction in our Parkinson's participant sample. PwPD had a lower proportion of correct responses in anti-saccade tasks, particularly in gap conditions compared to the controls. Anti-saccade tasks require suppressing reflexive eye movements, a cognitively demanding process reliant on intact frontal-basal ganglia connectivity (Munoz & Everling, 2004). The reduced proportion of correct responses in PwPD suggests that these participants experienced greater difficulty inhibiting a reflexive saccade. This finding aligns with prior literature demonstrating that PwPD exhibit greater deficits in anti-saccade performance, reflecting compromised executive control (Walton et al., 2015;

Nemanich & Earhart, 2016). Additionally, the lower proportion of correct responses in the anti-saccade gap conditions may reflect reduced preparatory time for inhibiting the reflexive saccade due to the lack of fixation acting as an anchor; further highlighting executive function deficits in PwPD. These results suggest that saccade tasks, including those involving gap timing conditions, may serve as sensitive, non-invasive markers for assessing the relationship between executive dysfunction and freezing in PwPD.

Taken together, these findings suggest that while oculomotor release mechanisms (pro-saccade gap effect) may be intact, the added demand of inhibiting automatic saccadic responses (anti-saccade gap effect) reveals a significant deficit in PwPD with FOG. These deficits likely stem from the disrupted basal ganglia-thalamocortical circuits, particularly those involving the direct and indirect pathways, which impair inhibitory control and voluntary movement initiation. These findings have potential implications for understanding the neural mechanisms underlying FOG, implicating systems that are involved in both saccadic inhibition and gait regulation. Additionally, these results contribute to a growing body of evidence that FOG is not merely a motor phenomenon, but may stem from broader executive impairments (Amboni et al., 2008; Gallardo et al., 2018; Gallea et al., 2021; Nemanich & Earhart, 2016; Walton et al., 2015).

These results can be linked to the neuropathological changes in PD, particularly the degeneration of dopaminergic neurons in the substantia nigra pars compacta, which disrupts the basal ganglia's motor control circuits. The basal ganglia, including the striatum, globus pallidus, subthalamic nucleus, and substantia nigra pars compacta, regulate voluntary motor control through the direct, indirect, and hyperdirect pathways.

In PD, the loss of dopaminergic input to the striatum impairs the direct pathway's ability to disinhibit thalamocortical projections, which are critical for initiating voluntary movements, such as voluntary saccades in anti-saccade tasks (Albin et al., 1995). This impairment likely contributes to the observed difficulties in generating voluntary saccades in PwPD with FOG. Additionally, the heightened activity within the indirect pathway, resulting from reduced dopaminergic modulation, increases inhibitory output to the thalamus. This elevated inhibition further suppresses voluntary motor actions and contributes to deficits in inhibitory control (Albin et al., 1995). Such dysregulation aligns with the larger anti-saccade gap effects observed in PwPD with FOG, reflecting challenges in suppressing reflexive saccades. The hyperdirect pathway, which provides rapid inhibitory control over motor output via cortical projections to the subthalamic nucleus, may also be disrupted by excessive subthalamic nucleus activity in PD, impairing the ability to modulate ongoing movements and contributing to the executive deficits observed in the anti-saccade tasks (Albin et al., 1995)

Predicting Freezing Severity Using Eye Movement Performance

Our prediction that the gap effect would be positively correlated with FOG severity was supported. There was a significant positive correlation between the pro-saccade gap effect and FOG severity, indicating that individuals with larger gap effects experienced more severe freezing. The hierarchical linear regression analysis further supported this relationship; the pro-saccade gap effect accounted for 52% of the variance in FOG severity. These findings suggest that deficits in disengaging from visual fixation, as captured by the gap effect, are closely linked to FOG severity. This aligns with previous literature, which suggests that FOG arises from complex disruptions in neural

systems, particularly those involving the basal ganglia, frontal cortex, and their associated pathways, such as the cortico-basal ganglia-thalamo-cortical loop. These regions are critical for coordinating motor planning, execution, and modulation, as well as executive function, which are critical for gait and oculomotor control (Lewis & Barker, 2009; Nutt et al., 2011). The pro-saccade gap effect's predictive power may be reflecting shared mechanisms between oculomotor impairments (indicating executive dysfunction) and gait impairments, as both require efficient initiation and inhibition of movements (Gallea et al., 2021). Freezing may arise from difficulty releasing from a current motor state, whether that state is a sustained oculomotor fixation or a particular phase of gait. While earlier analyses indicated that only the anti-saccade gap effect differentiated freezers from non-freezers, the predictive role of the pro-saccade gap effect suggests that both pro- and anti-saccade measures may capture distinct but complementary aspects of freezing. Difficulty with inhibitory control, as reflected in the anti-saccade gap effect, may tip individuals toward developing freezing in the first place, whereas variations in motor release, indexed by the pro-saccade gap effect, may help determine the severity of freezing once it is present. Both the pro-saccade and anti-saccade gap effects therefore differ between freezers and non-freezers, but in distinct ways. This relationship further supports the potential of eye movement tasks, which assess executive function, as tools for assessing FOG severity, consistent with prior studies linking anti-saccade latency to FOG onset (Gallea et al., 2021).

Freezing as a Global Motor Phenomenon

Our second hypothesis, that freezing is a more global motor phenomenon, not just restricted to gait, was partially supported.

Reaching Performance and Freezing of Upper Limbs

The reaching tasks revealed significant differences between PwPD and controls across multiple measures, including reaction time, accuracy, and precision, along with %Time and %Distance in the transitional phases. PwPD showed greater reaction times than controls on the reversal task, suggesting they may have hesitations when initiating movements, particularly when tasks require directional changes. This finding is reminiscent of the start hesitations observed in FOG, where hesitations are common during gait transitions (Nutt et al., 2011). These findings align with prior research indicating that PwPD exhibit impairments with movement initiation under complex task demands. Such impairments are thought to arise from dysfunction within the basal ganglia, which normally help coordinate and select motor actions based on cognitive context. When dopaminergic loss disrupts this system, the basal ganglia's ability to coordinate information between frontal executive regions and motor circuits is compromised. As a result, PwPD may struggle to switch between, or initiate movements when tasks place higher demands on both cognitive control and motor execution. (Mazzoni et al., 2012; Heremans et al., 2016). The reversal task's demand for a rapid directional shift likely exacerbates these deficits, supporting the notion that FOUL may share common mechanisms with FOG.

In our tasks, PwPD showed lower accuracy and precision in depth compared to the controls. Previous studies report increased movement variability as a defining aspect of FOUL (Heremans et al., 2016). The variability shown by our PD participants may indicate the successful induction of freezing-like behaviours in an upper-limb reaching task that was designed based on conditions known to elicit FOG. At the level of analysis

presented in this thesis, we have not yet identified which specific trials participants exhibited freezing behaviours. However, the aggregate results suggest that such freezing behaviours were present. Moving forward, analyses that categorize trials according to the presence of freezing will provide more precise insights. One step in this direction is the examination of movement phases, which is discussed in the following section.

In analyzing the reaching phases, our primary interest was whether PwPD exhibited differences in reaching movements during transitional periods (at the beginning or end of the movement) compared to controls. Since PwPD are more likely to experience FOG during transitions, observing freezing-like behaviours in the transitional phases of an upper-limb reaching task may help identify instances of FOUL. However, at this stage, these observations are descriptive; only analyses that explicitly attempt to correlate FOG with FOUL or use FOUL measures to explain FOG (as will be presented in the following section), can help to formally establish a link between the two phenomena.

Analysis of the percentage of time spent in each phase revealed a marginal group by phase interaction, suggesting that PwPD may differ from controls in how they allocate time across movement phases, such as initiating, executing, and terminating reaching movements. This indicates that PwPD may spend relatively more or less time in specific phases, reflecting subtle differences in motor planning, execution, or transitions between movement states. Although this interaction did not reach conventional levels of significance, pairwise comparisons revealed meaningful differences within specific task phases that aligned with our theoretical expectations. During phase 2, a period of

acceleration, PwPD spent a smaller percentage of time compared to the controls. In phase 4, a period of deceleration and preparation for either reversing direction, turning a corner, or passing through the virtual tunnel, PwPD covered a greater percentage of distance compared to controls. These findings are indicative of movement hesitations and freezing-like behaviours during periods of transition. Together, they suggest that FOUL may manifest as increased movement variability, analogous to gait hesitations seen in FOG (Cowie et al., 2012). These results support the idea that freezing is a more global motor phenomenon, not restricted to gait alone, and that conditions known to elicit FOG also appear to trigger freezing-like behaviours in the upper limbs, potentially indicating shared mechanisms between FOG and FOUL.

Walking Performance and Freezing of Gait

One participant with PD (#25) was notably slower than the other PwPD. Due to the variance introduced by this individual, their removal from the dataset revealed a significant main effect of group on walking time. This finding highlights the heterogeneity of motor symptoms in PD, where extreme variability can obscure group differences in smaller samples (Chee et al., 2009). The task design, incorporating directional changes and spatial constraints, along with the prolonged walking times, suggests that these tasks may have successfully provoked FOG (Cowie et al., 2012). Significant correlations between walking movement times in the corner and tunnel tasks and freezing severity further support this, potentially reflecting impaired executive control over gait initiation and modulation (Gallea et al., 2021; Petrucci et al., 2022). Future analyses will aim to identify specific trials that are more likely to exhibit freezing,

allowing for more precise examination of the relationship between movement hesitations and freezing behaviours.

The hierarchical linear regression models did not show significant improvement with the addition of walking times. Health rating percentage was a consistent significant covariate, showing a significant negative correlation with FOG severity, suggesting that self-perceived health status reflects underlying motor and non-motor impairments (Giladi et al., 1997).

The Intersection of Eye Movements, Reaching, and Gait

Our final prediction, that FOUL, FOG, and executive function deficits measured using saccade tasks would be related, was partially supported. The correlation analyses between eye, hand, and walking performance revealed that slower response latencies in pro- and anti-saccade tasks were associated with slower reaction times in the reversal and corner reaching tasks, respectively, suggesting shared motor or cognitive processing deficits in PwPD. These findings align with the notion that EF and reaching impairments in PD may stem from common deficits in motor planning and initiation, potentially driven by dysfunction in the basal ganglia and frontostriatal pathways (Nutt et al., 2011). The gap timing condition saccade tasks, which isolate the time cost of disengagement required to release from visual fixation, may tap into control mechanisms similar to those in the reaching tasks. The absence of a relationship in the overlap timing conditions suggests that this disengagement process may be a key factor in understanding freezing of the upper limbs. Furthermore, the presence of relationships in both pro- and anti-saccade gap conditions indicates that initiation and inhibition are only part of the story; assessing one's ability to disengage, as captured by the gap conditions, may provide a

more complete picture. However, the lack of group differences (PwPD with FOG vs. PwPD without FOG) for the pro-saccade gap effect suggests further exploration of this relationship is needed. Notably, the pro-saccade gap effect is correlated with freezing severity, indicating that even in the absence of clear group differences, individual variability in pro-saccade gap performance may reflect the extent of freezing impairments.

The correlation analyses between eye, hand, and walking performance also revealed significant positive relationships between the gap effect and walking movement time in the reversal, corner, and tunnel tasks. Additionally, the gap effect was positively correlated with the percentage of time spent decelerating in the corner walking task. These results suggest that larger gap effects are associated both with slower walking times and a greater percentage of time spent decelerating in tasks designed to elicit FOG. This may indicate that executive dysfunction, as captured by the gap effect, may contribute to experiences of FOG. Despite the lack of consistent correlations across all three domains (eye movements, reaching, and walking), previous literature supports the notion of freezing as a multi-domain phenomenon (Gallea et al., 2021; Heremans et al., 2019; Nemanich & Earhart, 2016; Walton et al., 2015). The observed correlations between eye movement, reaching, and walking performance suggest that deficits in visuomotor integration may contribute to motor impairments in PD, warranting further investigation into the neural mechanisms of these relationships.

Strengths

This study has several strengths. The use of FOG-provoking tasks (reversal, corner, tunnel) enhanced ecological validity by mirroring real-world challenges for

PwPD. The inclusion of both gap and overlap conditions in the saccade tasks added granularity to the assessment of executive function, building on prior literature (Kingstone & Klein, 1993). Finally, the multi-domain assessment (eye movements, reaching, gait) offered a comprehensive evaluation of the motor deficits in PwPD, aligning with calls for integrative approaches to understanding freezing behaviours (Nutt et al., 2011).

Limitations

Several limitations should be considered when interpreting the findings of this study. First, the small sample size ($N = 30$) restricted statistical power and. Second, reliance on the NFOG-Q as a measure of FOG severity introduces potential recall bias and inaccuracies due to the subjective nature of the questionnaire and varying symptom awareness among participants (Nieuwboer et al., 2009). Third, the use of shoulder data for walking analysis, while practical, may have missed critical lower-limb kinematics, that could have provided deeper insights into FOG. Finally, although the reaching and walking tasks were designed to simulate FOG-provoking conditions, freezing is notoriously difficult to elicit in laboratory settings, potentially reducing the ecological and construct validity of our objective measures and the observed freezing-like behaviours. Encouragingly, the current dataset provides the opportunity to address these limitations by evaluating the ankle and accelerometer data collected in this study but not analyzed for this thesis. Future analyses are planned to examine both reaching and walking kinematics in greater detail.

Future Directions

Building on the current findings, the next steps involve both immediate and longer-term analyses. In the short term, we plan to examine movement phases in greater detail to identify specific trials in which freezing-like behaviours occur, allowing for more precise characterization of FOUL and its relationship to FOG. We will also analyse both ankle and accelerometer walking data to improve our measurements of gait impairment. Additionally, the reversal and corner tasks each involved two movements: an initial movement from the start position to target one, followed by a second movement from target one to target two. To ensure comparability across tasks, only the first movement was analyzed in this thesis. Future analyses should explore the second movements in the reversal and corner tasks for both reaching and walking, as these may reveal additional freezing-like instances not captured in this thesis. In the longer term, analyzing the speech data collected in this study may clarify our understanding of freezing, further supporting the concept of freezing as part of a global motor phenomenon. Future research should aim to replicate these findings in larger and more diverse samples to increase statistical power and generalizability.

Conclusion

This study is among the first to examine the interplay between eye movement, reaching, and gait performance in PwPD compared to controls, with a focus on the relationship between freezing and executive function. Our most notable finding was that PwPD exhibited significantly larger gap effects than controls, and that PwPD with FOG exhibited significantly larger anti-saccade gap effects than PwPD without FOG. Furthermore, the pro-saccade gap effect significantly predicted FOG severity. These

findings suggest that saccade tasks may serve as a non-invasive tool for assessing motor and executive function deficits in PwPD. This study also provides evidence of significant differences in reaching performance between PwPD and controls, particularly in reaction time, movement time, accuracy, and precision. Tasks involving directional changes and spatial constraints elicited the most pronounced differences. In addition, PwPD displayed distinct differences in gait measures in tasks designed to provoke FOG. Time spent decelerating in the corner and tunnel tasks showed promise in classifying freezers, although further analyses are needed to refine these findings.

Consistent with prior literature, these results underscore the importance of incorporating multi-domain motor assessments in the evaluation of FOG. The relationships between eye movement, reaching, and walking tasks suggest shared deficits in motor and executive function, offering promising avenues for further research. Despite its limitations, this study contributes to our understanding of the complex interplay between motor and cognitive deficits in FOG. While the relationship between eye movements, FOUL, FOG, and executive function warrants further exploration, our findings highlight the need for thorough, integrative assessments, ultimately aimed at improving outcomes for PwPD.

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Appendix A

Letter of Information & Consent Form

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Letter of Information

Project Title: Bridging the Gap: Exploring Freezing Using the Gap Effect In People Living with Parkinson's Disease
Graduate Student Investigator: Leah Steinke, B.Sc.
Faculty Investigators: Liana E. Brown, Ph.D.

0. Purpose:

The purpose of this study is to measure if and how eye movements in people living with Parkinson's Disease who experience freezing are different from people living with Parkinson's Disease who do not experience freezing.

1. Participation inclusion/exclusion criteria:

We will be recruiting two different groups of participants. The first group will consist of individuals living with Parkinson's Disease who are free from other neurological diagnoses. The second group will consist of people without Parkinson's disease. You must have normal or corrected-to-normal vision (i.e., vision that is normal with glasses or contacts), and normal or corrected-to-normal hearing. Healthy controls must be free from a history of neurological dysfunction.

2. Procedures to be followed:

All of the procedures described here have been reviewed and approved by the Trent Research Ethics Board (REB #29036). You will be asked to complete questionnaires that ask about your current health, psychological well-being, and your cognitive abilities. We will also ask you to complete several eye-movement tasks, and tasks testing your thinking skills. The eye-movement tasks will assess your ability to make a quick eye movement to a target. You will wear an eye-tracking camera that will be mounted on a set of safety glasses. You will look at targets on a computer screen and we will measure the speed and accuracy of your eye movements. You will also complete tests assessing how quickly you can generate words, switch between two tasks, and how well you can withhold a response. All of the tests will have easy components and difficult components – they are designed to challenge you and to eventually be difficult for everyone. You will be given clear instructions and an opportunity to practice each test before beginning.

3. Duration of study:

Your participation in this research will involve a single, 2 hour session.

4. a. Benefits to you:

There are no direct benefits to you . Please understand that we are not clinicians; the data we collect will not be used to inform your medical case or your treatment. We will not be able to share a summary of your performance with you. We will provide you with a report describing the outcome of the study when it is complete.

b. Benefits to society:

Vision and movement are key components of life. Our ability to care for ourselves and for our families is dependent upon our ability to move. This research may help us better understand the experiences of people living with Parkinson's Disease.

5. How the data will be used:

The researchers declare that they have no potential conflicts of interest: we will not experience any specific personal or financial gain or loss from the results of this experiment. In the future we may publish the data in a scientific journal and present it at a scientific conference. We may summarize the results in a 5-10 minute podcast and on other social media channels.

6. Voluntary participation:

Your participation is entirely voluntary. You are free to stop participating in the research at any time or to decline to answer any specific questions or perform any tasks without consequence or loss of promised compensation. You may ask questions at any time to determine whether you would like to proceed or not. We will ask you if it's OK to proceed before each test and this will serve as a reminder of your right to decline or withdraw. To withdraw from the experiment, you simply need to inform the investigator of your wish to withdraw. If you withdraw, all of your digital data will be deleted and your paper data will be shredded and discarded.

7. Statement of confidentiality:

Your participation in this research is entirely confidential. Only the person(s) in charge will have access to identifying information. To make sure that participation is confidential, individuals' data will be distinguished by a code number and only Leah Steinke and Liana Brown will have access to the materials that link names to the code. In the event that this research is published, only summaries of demographic information will be included and no personally identifying information will be disclosed. Movement tracking and reaction time data will be encrypted and stored indefinitely on a cloud storage. Deidentified data - data from which all identifying information is removed or only averages are provided - may be uploaded to a data sharing site that can be accessed by other scientists for analysis. It will not be possible for others to identify any of the participants from these data sets.

8. Discomforts and risks:

Some of the questionnaires will ask for sensitive information about your current health and behaviours. You may find these questions stressful. You are free to decline to answer any or all of these questions without consequence or loss of compensation.

The tests you will be presented with are designed to measure your strengths and weaknesses and may be challenging. This experience may be uncomfortable temporarily but challenging in an interesting way. Some individuals may find them frustrating; however, the risks involved are no more than those involved in performing your daily activities. There is a risk of falling throughout the experiment. You are, as always, free to withdraw from the study if you wish.

9. Post-experiment feedback and right to ask questions:

You will be given an opportunity to ask any questions that you may have, and all such questions or inquiries will be answered to your satisfaction. After you have finished participating, you will receive a more detailed explanation of the study and any questions that you have at that time will be answered. If you have questions in the future, you are welcome to contact Leah Steinke at leahsteinke@trentu.ca or Liana Brown at 705-748-1011 x7238 or lianabrown@trentu.ca

10. Compensation:

In return for your participation, **you will receive $20 per hour ($10 for each half-hour of participation up to $40 total). For example, if you withdraw after 40 minutes, you will receive $20.**

Action & Cognition @ Trent (ACT) Lab
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Consent Form

Project Title: Bridging the Gap: Exploring Freezing Using the Gap Effect In People Living with Parkinson's Disease
Graduate Student Investigator: Leah Steinke, B.Sc.
Faculty Investigators: Liana E. Brown, Ph.D.

I have read the letter of information and have had the nature of the study explained to me. All questions have been answered to my satisfaction. I understand that all of the procedures for this study have been reviewed and received clearance from the Research Ethics Board at Trent University, (REB #29036). If I have comments or concerns resulting from my participation that I do not feel comfortable talking about with the Faculty Investigator, I can contact the Coordinator, Research Conduct and Reporting Officer, Anna Kisiala at 705-748-1011 ext. 7896, researchintegrity@trentu.ca.
By signing below, I consent to participate in this study and acknowledge the potential risk. I understand that I may withdraw this consent at any time without penalty or loss of compensation by telling the researcher.

- ❑ I agree to be videotaped
- ❑ I agree to have my speech recorded

Participant:

_____ _____
Signature Date

_____
Print Name

Experimenter:
I certify that the informed consent procedure has been followed and that I have answered any questions from the participant above as fully as possible.

_____ _____
Signature Date

_____
Print Name

Appendix B

Hospital Anxiety and Depression Scale

Hospital Anxiety and Depression Scale (HADS)

Tick the box beside the reply that is closest to how you have been feeling in the past week.
Don't take too long over you replies: your immediate is best.

D	A		D	A	
		I feel tense or 'wound up':			**I feel as if I am slowed down:**
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite Often
3		Hardly at all		3	Very Often
		I get a sort of frightened feeling as if something awful is about to happen:			**I have lost interest in my appearance:**
	3	Very definitely and quite badly	3		Definitely
	2	Yes, but not too badly	2		I don't take as much care as I should
	1	A little, but it doesn't worry me	1		I may not take quite as much care
	0	Not at all	0		I take just as much care as ever
		I can laugh and see the funny side of things:			**I feel restless as I have to be on the move:**
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all
		Worrying thoughts go through my mind:			**I look forward with enjoyment to things:**
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time, but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all
		I feel cheerful:			**I get sudden feelings of panic:**
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Not at all
		I can sit at ease and feel relaxed:			**I can enjoy a good book or radio or TV program:**
	0	Definitely	0		Often
	1	Usually	1		Sometimes
	2	Not Often	2		Not often
	3	Not at all	3		Very seldom

Please check you have answered all the questions

Scoring:
Total score: Depression (D) _____ Anxiety (A) _____
0-7 = Normal
8-10 = Borderline abnormal (borderline case)
11-21 = Abnormal (case)

Appendix C

Dutch Handedness Questionnaire

Dutch Handedness Questionnaire (Van Strien, 2002)

Instructions: A number of activities in which you can use either your left or your right hand are specified below. Indicate which hand you usually use for these activities. Visualize the activity in question if you are not immediately sure of an answer. If you don't have a clear preference, indicate that you use both hands. For tasks that require both hands, please indicate the hand that does the primary action. For example, when unscrewing a water bottle one hand does the primary action of unscrewing, and the other hand secondary action of stabilizing/holding the bottle.

Q1 Hold scissors
- Left (1)
- Right (2)
- Both (3)

Q2 Draw
- Left (1)
- Right (2)
- Both (3)

Q3 Screw the top off bottle
- Left (1)
- Right (2)
- Both (3)

Q4 Deal cards
- Left (1)
- Right (2)
- Both (3)

Q5 Hold a toothbrush when brushing teeth
- Left (1)
- Right (2)
- Both (3)

Q6 Use a bottle opener
- Left (1)
- Right (2)
- Both (3)

Q7 Throw a ball
- Left (1)
- Right (2)
- Both (3)

Q8 Hold a hammer
- Left (1)
- Right (2)
- Both (3)

Q9 Write your name
- Left (1)
- Right (2)
- Both (3)

Q10 Hold a racket when playing tennis
- Left (1)
- Right (2)
- Both (3)

Q11 Turn a key
- Left (1)
- Right (2)
- Both (3)

Q12 Cut with a knife (without a fork)
- Left (1)
- Right (2)
- Both (3)

Q13 Stir with a spoon
- Left (1)
- Right (2)
- Both (3)

Q14 Use an eraser on paper
- Left (1)
- Right (2)
- Both (3)

Q15 Strike a match
- Left (1)
- Right (2)
- Both (3)

Q16 Open a box lid
- Left (1)
- Right (2)
- Both (3)

Appendix D

New Freezing of Gait Questionnaire

New Freezing of Gait Questionnaire

Part I – Distinction Freezer – non-Freezer, over the past month
1. **Did you experience "freezing episodes" over the past month?** *<u>Without video</u>* *Freezing is the feeling that your feet are transiently glued to the floor while trying to initiate walking, making a turn or when walking through narrow spaces or in crowded places? Sometimes it can be accompanied with trembling of the legs and small shuffling steps.* *<u>Additional instructions with video</u>* *We will watch a short video together to see the many ways in which freezing can occur. Also, look carefully for how long these episodes last, as you can expect some questions on this later. (tester points out the clock on video clip)* 0. I have not experienced such a feeling or episode over the past month 1. I have experienced such a feeling or episode over the past month ***If the answer is 1 (patient is a freezer) complete part II and III. The sum of part II and III is the final NFOG score.***

4. Very long, unable to walk for more than 30 s.
5. How frequently do you experience episodes of freezing when initiating the first step? 0. **Never** 1. **Rarely, about once a month** 2. **Not often, about once a week** 3. **Often, about once a day** 4. **Very often, more than once a day** **If the answer 1 or more go to question #6. If the answer is 0, go directly to #7.**
6. How long is your longest freezing episode when initiating the first step? **1. Very short, 1 s.** **2. Short, 2-5 s.** **3. Long, between 5 and 30 s.** **4. Very long, unable to walk for more than 30 s.**
Part III – Freezing impact on daily life
7. **How disturbing are the freezing episodes for your daily walking?**

Part II – Freezing severity

2. How frequently do you experience freezing episodes?

0. Less than once a week
1. Not often, about once a week
2. Often, about once a day
3. Very often, more than once a day

3. How frequently do you experience freezing episodes during turning?

0. **Never**
1. **Rarely, about one a month**
2. **Not often, about once a week**
3. **Often, about once a day**
4. **Very often, more than once a day**

If the answer is 1 or more go to question #4. If the answer is 0, go directly to #5.

4. How long is your longest freezing episode during turning?

1. **Very short, 1 sec**
2. **Short, 2 - 5 s.**
3. **Long, between 5 and 30 s.**

0. **Not at all** 1. **Very little** 2. **Moderately** 3. **Significantly**
8. **Do the freezing episodes cause feelings of insecurity and fear of falling?** 0. **Not at all** 1. **Very little** 2. **Moderately** 3. **Significantly**
9. Are your freezing episodes affecting your daily activities? **(Rate the impact of freezing on daily activities only. Not the impact of the disease in general)** 0. **Not at all, I continue doing things as normal** 1. **Mildly, I avoid only few daily activities** 2. **Moderately, I avoid a significant amount (about half) of daily activities** 3. **Severely, I am very restricted in carrying out most daily activities**

Appendix E

Frontal Assessment Battery

Content, instructions, and scoring of the FAB

1. Similarities (conceptualization)

"In what way are they alike?"

A banana and an orange (In the event of total failure: "they are not alike" or partial failure: "both have peel," help the patient by saying: "both a banana and an orange are..."; but credit 0 for the item; do not help the patient for the two following items)

A table and a chair

A tulip, a rose and a daisy

Score (only category responses [fruits, furniture, flowers] are considered correct)

Three correct: 3

Two correct: 2

One correct: 1

None correct: 0

2. Lexical fluency (mental flexibility)

"Say as many words as you can beginning with the letter 'S,' any words except surnames or proper nouns."

If the patient gives no response during the first 5 seconds, say: "for instance, snake." If the patient pauses 10 seconds, stimulate him by saying: "any word beginning with the letter 'S.' The time allowed is 60 seconds.

Score (word repetitions or variations [shoe, shoemaker], surnames, or proper nouns are not counted as correct responses)

More than nine words: 3

Six to nine words: 2

Three to five words: 1

Less than three words: 0

3. Motor series (programming)

"Look carefully at what I'm doing."

The examiner, seated in front of the patient, performs alone three times with his left hand the series of Luria "fist–edge–palm." "Now, with your right hand do the same series, first with me, then alone." The examiner performs the series three times with the patient, then says to him/her: "Now, do it on your own."

Score

Patient performs six correct consecutive series alone: 3

Patient performs at least three correct consecutive series alone: 2

Patient fails alone, but performs three correct consecutive series with the examiner: 1

Patient cannot perform three correct consecutive series even with the examiner: 0

4. Conflicting instructions (sensitivity to interference)

"Tap twice when I tap once."

To be sure that the patient has understood the instruction, a series of three trials is run: 1-1-1. "Tap once when I tap twice." To be sure that the patient has understood the instruction, a series of three trials is run: 2-2-2. The examiner performs the following series: 1-1-2-1-2-2-2-1-1-2.

Score

No error: 3

One or two errors: 2

More than two errors: 1

Patient taps like the examiner at least four consecutive times: 0

5. Go–No Go (inhibitory control)

"Tap once when I tap once."

To be sure that the patient has understood the instruction, a series of three trials is run: 1-1-1. "Do not tap when I tap twice." To be sure that the patient has understood the instruction, a series of three trials is run: 2-2-2. The examiner performs the following series: 1-1-2-1-2-2-2-1-1-2.

Score

No error: 3

One or two errors: 2

More than two errors: 1

Patient taps like the examiner at least four consecutive times: 0

6. Prehension behavior (environmental autonomy)

"Do not take my hands."

The examiner is seated in front of the patient. Place the patient's hands palm up on his/her knees. Without saying anything or looking at the patient, the examiner brings his/her hands close to the patient's hands and touches the palms of both the patient's hands, to see if he/she will spontaneously take them. If the patient takes the hands, the examiner will try again after asking him/her: "Now, do not take my hands."

Score

Patient does not take the examiner's hands: 3

Patient hesitates and asks what he/she has to do: 2

Patient takes the hands without hesitation: 1

Patient takes the examiner's hand even after he/she has been told not to do so: 0

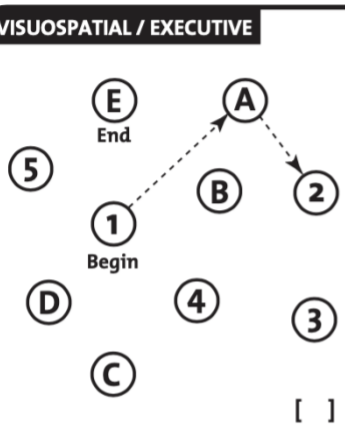
Appendix F

Montreal Cognitive Assessment

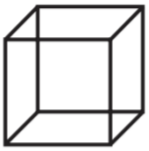
MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE — POINTS



Copy cube



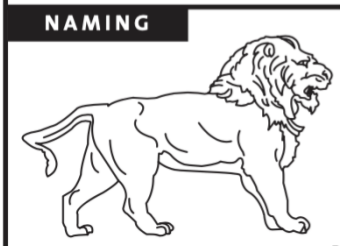
[ ] [ ]

Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands

__/5

NAMING



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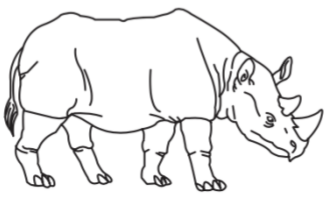

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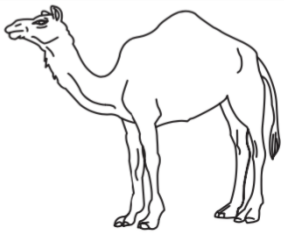

[ ]

__/3

MEMORY — Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION — Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

__/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

__/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

__/3

LANGUAGE — Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

__/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] ____ (N ≥ 11 words)

__/1

ABSTRACTION — Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

__/2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only
		[ ]	[ ]	[ ]	[ ]	[ ]	
Optional	Category cue						
	Multiple choice cue						

__/5

ORIENTATION — [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

__/6

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Normal ≥ 26 / 30

TOTAL __/30

Add 1 point if ≤ 12 yr edu

Appendix G

Unified Parkinson's Disease Rating Scale Part III

Part III: Motor Examination

Overview: This portion of the scale assesses the motor signs of PD. In administering Part III of the MDS-UPDRS the examiner should comply with the following guidelines:

At the top of the form, mark whether the patient is on medication for treating the symptoms of Parkinson's disease and, if on levodopa, the time since the last dose.

Also, if the patient is receiving medication for treating the symptoms of Parkinson's disease, mark the patient's clinical state using the following definitions:
ON is the typical functional state when patients are receiving medication and have a good response.
OFF is the typical functional state when patients have a poor response in spite of taking medications.

The investigator should "rate what you see." Admittedly, concurrent medical problems such as stroke, paralysis, arthritis, contracture, and orthopedic problems such as hip or knee replacement and scoliosis may interfere with individual items in the motor examination. In situations where it is absolutely impossible to test (e.g., amputations, plegia, limb in a cast), use the notation "**UR**" for Unable to Rate. Otherwise, rate the performance of each task as the patient performs in the context of co-morbidities.

All items must have an integer rating (no half points, no missing ratings).

Specific instructions are provided for the testing of each item. These should be followed in all instances. The investigator demonstrates while describing tasks the patient is to perform and rates function immediately thereafter. For Global Spontaneous Movement and Rest Tremor items (3.14 and 3.17), these items have been placed purposefully at the end of the scale because clinical information pertinent to the score will be obtained throughout the entire examination.

At the end of the rating, indicate if dyskinesia (chorea or dystonia) was present at the time of the examination, and if so, whether these movements interfered with the motor examination.

3a Is the patient on medication for treating the symptoms of Parkinson's disease? ☐ No ☐ Yes

3b If the patient is receiving medication for treating the symptoms of Parkinson's disease, mark the patient's clinical state using the following definitions:

☐ ON: On is the typical functional state when patients are receiving medication and have a good response.

☐ OFF: Off is the typical functional state when patients have a poor response in spite of taking medications.

3c Is the patient on levodopa ? ☐ No ☐ Yes

3.C1 If yes, minutes since last levodopa dose: _____

	SCORE
3.1 SPEECH Instructions to examiner: Listen to the patient's free-flowing speech and engage in conversation if necessary. Suggested topics: ask about the patient's work, hobbies, exercise, or how he got to the doctor's office. Evaluate volume, modulation (prosody), and clarity, including slurring, palilalia (repetition of syllables), and tachyphemia (rapid speech, running syllables together). 0: Normal: No speech problems. 1: Slight: Loss of modulation, diction, or volume, but still all words easy to understand. 2: Mild: Loss of modulation, diction, or volume, with a few words unclear, but the overall sentences easy to follow. 3: Moderate: Speech is difficult to understand to the point that some, but not most, sentences are poorly understood. 4: Severe: Most speech is difficult to understand or unintelligible.	☐
3.2 FACIAL EXPRESSION Instructions to examiner: Observe the patient sitting at rest for 10 seconds, without talking and also while talking. Observe eye-blink frequency, masked facies or loss of facial expression, spontaneous smiling, and parting of lips. 0: Normal: Normal facial expression. 1: Slight: Minimal masked facies manifested only by decreased frequency of blinking. 2: Mild: In addition to decreased eye-blink frequency, masked facies present in the lower face as well, namely fewer movements around the mouth, such as less spontaneous smiling, but lips not parted. 3: Moderate: Masked facies with lips parted some of the time when the mouth is at rest. 4: Severe: Masked facies with lips parted most of the time when the mouth is at rest.	☐

	SCORE
3.3 RIGIDITY Instructions to examiner: Rigidity is judged on slow passive movement of major joints with the patient in a relaxed position and the examiner manipulating the limbs and neck. First, test without an activation maneuver. Test and rate neck and each limb separately. For arms, test the wrist and elbow joints simultaneously. For legs, test the hip and knee joints simultaneously. If no rigidity is detected, use an activation maneuver such as tapping fingers, fist opening/closing, or heel tapping in a limb not being tested. Explain to the patient to go as limp as possible as you test for rigidity. 0: Normal: No rigidity. 1: Slight: Rigidity only detected with activation maneuver. 2: Mild: Rigidity detected without the activation maneuver, but full range of motion is easily achieved. 3: Moderate: Rigidity detected without the activation maneuver; full range of motion is achieved with effort. 4: Severe: Rigidity detected without the activation maneuver and full range of motion not achieved.	☐ Neck ☐ RUE ☐ LUE ☐ RLE ☐ LLE
3.4 FINGER TAPPING Instructions to examiner: Each hand is tested separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to tap the index finger on the thumb 10 times as quickly AND as big as possible. Rate each side separately, evaluating speed, amplitude, hesitations, halts, and decrementing amplitude. 0: Normal: No problems. 1: Slight: Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the tapping movement; b) slight slowing; c) the amplitude decrements near the end of the 10 taps. 2: Mild: Any of the following: a) 3 to 5 interruptions during tapping; b) mild slowing; c) the amplitude decrements midway in the 10-tap sequence. 3: Moderate: Any of the following: a) more than 5 interruptions during tapping or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing; c) the amplitude decrements starting after the 1st tap. 4: Severe: Cannot or can only barely perform the task because of slowing, interruptions, or decrements.	☐ R ☐ L

	SCORE
3.5 HAND MOVEMENTS Instructions to examiner: Test each hand separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to make a tight fist with the arm bent at the elbow so that the palm faces the examiner. Have the patient open the hand 10 times as fully AND as quickly as possible. If the patient fails to make a tight fist or to open the hand fully, remind him/her to do so. Rate each side separately, evaluating speed, amplitude, hesitations, halts, and decrementing amplitude. 0: Normal: No problems. 1: Slight: Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the movement; b) slight slowing; c) the amplitude decrements near the end of the task. 2: Mild: Any of the following: a) 3 to 5 interruptions during the movements; b) mild slowing; c) the amplitude decrements midway in the task. 3: Moderate: Any of the following: a) more than 5 interruptions during the movement or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing; c) the amplitude decrements starting after the 1st open-and-close sequence. 4: Severe: Cannot or can only barely perform the task because of slowing, interruptions, or decrements.	☐ R ☐ L
3.6 PRONATION-SUPINATION MOVEMENTS OF HANDS Instructions to examiner: Test each hand separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to extend the arm out in front of his/her body with the palms down, and then to turn the palm up and down alternately 10 times as fast and as fully as possible. Rate each side separately, evaluating speed, amplitude, hesitations, halts, and decrementing amplitude. 0: Normal: No problems. 1: Slight: Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the movement; b) slight slowing; c) the amplitude decrements near the end of the sequence. 2: Mild: Any of the following: a) 3 to 5 interruptions during the movements; b) mild slowing; c) the amplitude decrements midway in the sequence. 3: Moderate: Any of the following: a) more than 5 interruptions during the movement or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing; c) the amplitude decrements starting after the 1st supination-pronation sequence. 4: Severe: Cannot or can only barely perform the task because of slowing, interruptions, or decrements.	☐ R ☐ L

3.7 TOE TAPPING

SCORE

Instructions to examiner: Have the patient sit in a straight-backed chair with arms, both feet on the floor. Test each foot separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to place the heel on the ground in a comfortable position and then tap the toes 10 times as big and as fast as possible. Rate each side separately, evaluating speed, amplitude, hesitations, halts, and decrementing amplitude.

0: Normal:	No problems.
1: Slight:	Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the tapping movement; b) slight slowing; c) amplitude decrements near the end of the ten taps.
2: Mild:	Any of the following: a) 3 to 5 interruptions during the tapping movements; b) mild slowing; c) amplitude decrements midway in the task.
3: Moderate:	Any of the following: a) more than 5 interruptions during the tapping movements or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing; c) amplitude decrements after the 1st tap.
4: Severe:	Cannot or can only barely perform the task because of slowing, interruptions or decrements.

☐ R

☐ L

3.8 LEG AGILITY

Instructions to examiner: Have the patient sit in a straight-backed chair with arms. The patient should have both feet comfortably on the floor. Test each leg separately. Demonstrate the task, but do not continue to perform the task while the patient is being tested. Instruct the patient to place the foot on the ground in a comfortable position and then raise and stomp the foot on the ground 10 times as high and as fast as possible. Rate each side separately, evaluating speed, amplitude, hesitations, halts and decrementing amplitude.

0: Normal:	No problems.
1: Slight:	Any of the following: a) the regular rhythm is broken with one or two interruptions or hesitations of the movement; b) slight slowing; c) amplitude decrements near the end of the task.
2: Mild:	Any of the following: a) 3 to 5 interruptions during the movements; b) mild slowness; c) amplitude decrements midway in the task.
3: Moderate:	Any of the following: a) more than 5 interruptions during the movement or at least one longer arrest (freeze) in ongoing movement; b) moderate slowing in speed; c) amplitude decrements after the 1st tap.
4: Severe:	Cannot or can only barely perform the task because of slowing, interruptions, or decrements.

☐ R

☐ L

	SCORE
3.9 ARISING FROM CHAIR Instructions to examiner: Have the patient sit in a straight-backed chair with arms, with both feet on the floor and sitting back in the chair (if the patient is not too short). Ask the patient to cross his/her arms across the chest and then to stand up. If the patient is not successful, repeat this attempt up to a maximum of two more times. If still unsuccessful, allow the patient to move forward in the chair to arise with arms folded across the chest. Allow only one attempt in this situation. If unsuccessful, allow the patient to push off using his/her hands on the arms of the chair. Allow a maximum of three trials of pushing off. If still not successful, assist the patient to arise. After the patient stands up, observe the posture for item 3.13. 0: Normal: No problems. Able to arise quickly without hesitation. 1: Slight: Arising is slower than normal; or may need more than one attempt; or may need to move forward in the chair to arise. No need to use the arms of the chair. 2: Mild: Pushes self up from the arms of the chair without difficulty. 3: Moderate: Needs to push off, but tends to fall back; or may have to try more than one time using the arms of the chair, but can get up without help. 4: Severe: Unable to arise without help.	☐
3.10 GAIT Instructions to examiner: Testing gait is best performed by having the patient walking away from and towards the examiner so that both right and left sides of the body can be easily observed simultaneously. The patient should walk at least 10 meters (30 feet), then turn around and return to the examiner. This item measures multiple behaviors: stride amplitude, stride speed, height of foot lift, heel strike during walking, turning, and arm swing, but not freezing. Assess also for “freezing of gait” (next item 3.11) while patient is walking. Observe posture for item 3.13. 0: Normal: No problems. 1: Slight: Independent walking with minor gait impairment. 2: Mild: Independent walking but with substantial gait impairment. 3: Moderate: Requires an assistance device for safe walking (walking stick, walker) but not a person. 4: Severe: Cannot walk at all or only with another person’s assistance.	☐

	SCORE
3.11 FREEZING OF GAIT Instructions to examiner: While assessing gait, also assess for the presence of any gait freezing episodes. Observe for start hesitation and stuttering movements especially when turning and reaching the end of the task. To the extent that safety permits, patients may NOT use sensory tricks during the assessment. 0: Normal: No freezing. 1: Slight: Freezes on starting, turning, or walking through doorway with a single halt during any of these events, but then continues smoothly without freezing during straight walking. 2: Mild: Freezes on starting, turning, or walking through doorway with more than one halt during any of these activities, but continues smoothly without freezing during straight walking. 3: Moderate: Freezes once during straight walking. 4: Severe: Freezes multiple times during straight walking.	☐
3.12 POSTURAL STABILITY Instructions to examiner: The test examines the response to sudden body displacement produced by a quick, forceful pull on the shoulders while the patient is standing erect with eyes open and feet comfortably apart and parallel to each other. Test retropulsion. Stand behind the patient and instruct the patient on what is about to happen. Explain that s/he is allowed to take a step backwards to avoid falling. There should be a solid wall behind the examiner, at least 1-2 meters away to allow for the observation of the number of retropulsive steps. The first pull is an instructional demonstration and is purposely milder and not rated. The second time the shoulders are pulled briskly and forcefully towards the examiner with enough force to displace the center of gravity so that patient MUST take a step backwards. The examiner needs to be ready to catch the patient, but must stand sufficiently back so as to allow enough room for the patient to take several steps to recover independently. Do not allow the patient to flex the body abnormally forward in anticipation of the pull. Observe for the number of steps backwards or falling. Up to and including two steps for recovery is considered normal, so abnormal ratings begin with three steps. If the patient fails to understand the test, the examiner can repeat the test so that the rating is based on an assessment that the examiner feels reflects the patient's limitations rather than misunderstanding or lack of preparedness. Observe standing posture for item 3.13. 0: Normal: No problems. Recovers with one or two steps. 1: Slight: 3-5 steps, but subject recovers unaided. 2: Mild: More than 5 steps, but subject recovers unaided. 3: Moderate: Stands safely, but with absence of postural response; falls if not caught by examiner. 4: Severe: Very unstable, tends to lose balance spontaneously or with just a gentle pull on the shoulders.	☐

	SCORE
3.13 POSTURE Instructions to examiner: Posture is assessed with the patient standing erect after arising from a chair, during walking, and while being tested for postural reflexes. If you notice poor posture, tell the patient to stand up straight and see if the posture improves (see option 2 below). Rate the worst posture seen in these three observation points. Observe for flexion and side-to-side leaning. 0: Normal: No problems. 1: Slight: Not quite erect, but posture could be normal for older person. 2: Mild: Definite flexion, scoliosis or leaning to one side, but patient can correct posture to normal posture when asked to do so. 3: Moderate: Stooped posture, scoliosis or leaning to one side that cannot be corrected volitionally to a normal posture by the patient. 4: Severe: Flexion, scoliosis or leaning with extreme abnormality of posture.	☐
3.14 GLOBAL SPONTANEITY OF MOVEMENT (BODY BRADYKINESIA) Instructions to examiner: This global rating combines all observations on slowness, hesitancy, and small amplitude and poverty of movement in general, including a reduction of gesturing and of crossing the legs. This assessment is based on the examiner's global impression after observing for spontaneous gestures while sitting, and the nature of arising and walking. 0: Normal: No problems. 1: Slight: Slight global slowness and poverty of spontaneous movements. 2: Mild: Mild global slowness and poverty of spontaneous movements. 3: Moderate: Moderate global slowness and poverty of spontaneous movements. 4: Severe: Severe global slowness and poverty of spontaneous movements.	☐
3.15 POSTURAL TREMOR OF THE HANDS Instructions to examiner: All tremor, including re-emergent rest tremor, that is present in this posture is to be included in this rating. Rate each hand separately. Rate the highest amplitude seen. Instruct the patient to stretch the arms out in front of the body with palms down. The wrist should be straight and the fingers comfortably separated so that they do not touch each other. Observe this posture for 10 seconds. 0: Normal: No tremor. 1: Slight: Tremor is present but less than 1 cm in amplitude. 2: Mild: Tremor is at least 1 but less than 3 cm in amplitude. 3: Moderate: Tremor is at least 3 but less than 10 cm in amplitude. 4: Severe: Tremor is at least 10 cm in amplitude.	☐ R ☐ L

	SCORE
3.16 KINETIC TREMOR OF THE HANDS Instructions to examiner: This is tested by the finger-to-nose maneuver. With the arm starting from the outstretched position, have the patient perform at least three finger-to-nose maneuvers with each hand reaching as far as possible to touch the examiner's finger. The finger-to-nose maneuver should be performed slowly enough not to hide any tremor that could occur with very fast arm movements. Repeat with the other hand, rating each hand separately. The tremor can be present throughout the movement or as the tremor reaches either target (nose or finger). Rate the highest amplitude seen. 0: Normal: No tremor. 1: Slight: Tremor is present but less than 1 cm in amplitude. 2: Mild: Tremor is at least 1 but less than 3 cm in amplitude. 3: Moderate: Tremor is at least 3 but less than 10 cm in amplitude. 4: Severe: Tremor is at least 10 cm in amplitude.	☐ R ☐ L
3.17 REST TREMOR AMPLITUDE Instructions to examiner: This and the next item have been placed purposefully at the end of the examination to allow the rater to gather observations on rest tremor that may appear at any time during the exam, including when quietly sitting, during walking, and during activities when some body parts are moving but others are at rest. Score the maximum amplitude that is seen at any time as the final score. Rate only the amplitude and not the persistence or the intermittency of the tremor. As part of this rating, the patient should sit quietly in a chair with the hands placed on the arms of the chair (not in the lap) and the feet comfortably supported on the floor for 10 seconds with no other directives. Rest tremor is assessed separately for all four limbs and also for the lip/jaw. Rate only the maximum amplitude that is seen at any time as the final rating. Extremity ratings 0: Normal: No tremor. 1: Slight: < 1 cm in maximal amplitude. 2: Mild: ≥ 1 cm but < 3 cm in maximal amplitude. 3: Moderate: ≥ 3 cm but < 10 cm in maximal amplitude. 4: Severe: ≥ 10 cm in maximal amplitude. Lip/Jaw ratings 0: Normal: No tremor. 1: Slight: < 1 cm in maximal amplitude. 2: Mild: ≥ 1 cm but < 2 cm in maximal amplitude. 3: Moderate: ≥ 2 cm but < 3 cm in maximal amplitude. 4: Severe: ≥ 3 cm in maximal amplitude.	☐ RUE ☐ LUE ☐ RLE ☐ LLE ☐ Lip/Jaw

	SCORE
3.18 CONSTANCY OF REST TREMOR Instructions to examiner: This item receives one rating for all rest tremor and focuses on the constancy of rest tremor during the examination period when different body parts are variously at rest. It is rated purposefully at the end of the examination so that several minutes of information can be coalesced into the rating. 0: Normal: No tremor. 1: Slight: Tremor at rest is present ≤ 25% of the entire examination period. 2: Mild: Tremor at rest is present 26-50% of the entire examination period. 3: Moderate: Tremor at rest is present 51-75% of the entire examination period. 4: Severe: Tremor at rest is present > 75% of the entire examination period.	☐
DYSKINESIA IMPACT ON PART III RATINGS A. Were dyskinesias (chorea or dystonia) present during examination? ☐ No ☐ Yes B. If yes, did these movements interfere with your ratings? ☐ No ☐ Yes	
HOEHN AND YAHR STAGE 0: Asymptomatic. 1: Unilateral involvement only. 2: Bilateral involvement without impairment of balance. 3: Mild to moderate involvement; some postural instability but physically independent; needs assistance to recover from pull test. 4: Severe disability; still able to walk or stand unassisted. 5: Wheelchair bound or bedridden unless aided.	☐

Appendix H

Debriefing Form

Action & Cognition @ Trent (ACT) Lab
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Participant Feedback

Project Title: Bridging the Gap: Exploring Freezing Using the Gap Effect In People Living with Parkinson's Disease
Investigators: Leah Steinke & Liana E. Brown, Ph.D.

Purpose and Methods:

Now that you have completed the testing, we can give you a better description of the goal of the study. We typically don't reveal our hypothesis in advance so that we can be sure that participants are not trying to "help" us by behaving in a way that confirms our hypothesis.

Many people living with Parkinson's disease experience freezing. The phenomenon of freezing is poorly understood within the literature; a definitive answer regarding how and why people freeze remains to be known. The purpose of the current study is to evaluate the relationship between eye movements, executive function, and freezing. Executive functions are the thinking skills that allow us to plan and sequence tasks, follow the steps of a sequence without being distracted, track where we are as we move through the sequence, and stay motivated to finish the task. The tasks with the eye-tracker that required you to look at targets on the screen measured your executive function. The other tasks you completed, like the walking and/or reaching tasks, will be used to measure freezing behaviours. We will use statistics to determine whether executive function is predictive of freezing.

Thank you for your participation in our research. If you have questions in the future, you are welcomed to contact Leah Steinke at leahsteinke@trentu.ca, or Liana Brown at lianabrown@trentu.ca. If you have any problems or concerns as a result of your participation in this study, please contact the Coordinator, Research Conduct and Reporting Officer, Anna Kisiala at 705-748-1011 ext. 7896, researchintegrity@trentu.ca.

References:

Nemanich, & Earhart, G. M. (2016). Freezing of gait is associated with increased saccade latency and variability in Parkinson's disease. *Clinical Neurophysiology, 127*(6), 2394–2401. https://doi.org/10.1016/j.clinph.2016.03.017

If you are looking for help dealing with Parkinson's Disease, you can access resources available to you in Peterborough through the Peterborough Parkinson's Support Group website: https://www.parkinson.ca/support-groups/peterborough/

Appendix I

Eye Movement Logistic Regression

A hierarchical binary logistic regression was conducted to examine the effects of eye movement performance (measured using the anti-saccade gap effect) on the likelihood of freezing (1 = freezer, 0 = non-freezer). Three models were tested: Model 1 included background measures (age, sex, health rating percentage, UPDRS part III scores), Model 2 included only the anti-saccade gap effect, Model 3 included background measures on level 1 and anti-saccade gap on level 2. We obtained many predictors that we believed would be important to categorize our participants; therefore, we used correlations to help narrow down the number of predictors that were included in our models.

The omnibus test of model coefficients indicated that model 1, with demographic measures as the predictor, was not a significant improvement over the baseline model $\chi^2(4) = 3.816$, $p = .432$. The omnibus test of model coefficients indicated that model 2, with anti-saccade gap as the predictor, was a significant improvement over the baseline model $\chi^2(1) = 7.330$, $p = .007$. The omnibus test of model coefficients indicated that model 3, with background measures on level 1 and anti-saccade gap on level 2, was a significant improvement over the baseline model $\chi^2(1) = 14.354$, $p < .001$. Therefore, Model 3 was selected as the best-fitting model.

Model 3 achieved perfect classification accuracy, correctly classifying 100% of cases (6 non-freezers and 7 freezers). The model fit was perfect, with a -2 log-likelihood of 0.000 and a non-significant Hosmer and Lemeshow test, $\chi^2(8) = 0.000$, $p = 1.000$, suggesting potential overfitting, likely due to the small sample size ($n = 13$). The

Nagelkerke R^2 was 1.000, indicating that the model accounted for all the variance in the outcome, this may be due to overfitting. The odds ratio tells us that as the anti-saccade gap effect increased by a unit, the change in the odds of being a freezer (rather than a non-freezer) is 1.367. You're more likely to be a freezer than not if you have a larger anti-saccade gap effect. However, the anti-saccade gap effect did not significantly predict whether a participant was a freezer or non-freezer, b = 0.312, Wald $\chi^2(1) = .000$, p = .999. None of the predictors were statistically significant (all $p > .05$). The non-significant predictors suggest that these variables may not reliably distinguish between non-freezers and freezers in this sample, potentially due to limited statistical power (Table 4)

Table 4

Coefficients of Model 3: Eye Movement Performance Predicts FOG Category

Predictors	*B*(SE)	95% CI for Odds Ratio		
		Lower	Odds Ratio	Upper
Constant	333.443 (205114.230)		6.495E+144	
Age	-3.595 (2851.167)	.000	.027	-
Sex	51.681 (181008.089)	.000	2.785E+22	-
Health Rating %	.017 (.079)	.000	.497	-
UPDRS	-.067 (.068)	.000	.162	-
Anti-saccade gap	.312 (83.459)	.000	1.367	1.501E+071

Note. $R^2 = .749$ (Cox-Snell), 1.000 (Nagelkerke). Hosmer and Lemeshow $\chi^2(6) = 0.000$, p = 1.000. Model $\chi^2(5) = 17.945$, $p = .003$. No predictors were significant, all p>.05.

Appendix J

Reaching Logistic Regressions

Reversal. A hierarchical binary logistic regression was conducted to examine the effects of reaching performance in the reversal task on the likelihood of freezing (1 = freezer, 0 = non-freezer). Three models were tested: Model 1 included background measures (age, sex, health rating percentage, UPDRS part III scores, MOCA). Model 2 included reaching measures with group main effects, interactions, or significant correlations with NFOG category. RT, MT plus phase 5, accuracy in depth, precision in depth, and %Distance for the reversal task were entered on separate levels in model 2. Sex and %Distance seemed to be making the largest impact on the previous models, therefore, in an attempt to strive for parsimony, Model 3 included sex on level 1 and %Distance for all phases on level 2.

The omnibus test of model coefficients indicated that model 1, with background measures as the predictors, was not a significant improvement over the baseline model $\chi^2(5) = 3.861$, $p = .570$. The omnibus test of model coefficients indicated that model 2, with RT, MT plus phase 5, accuracy in depth, precision in depth, and %Distance for the reversal task as the predictors, was a significant improvement over the baseline model $\chi^2(5) = 13.968$, $p = .016$. The omnibus test of model coefficients indicated that model 3, with sex inputted on level 1 and %Distance on level 2, was a significant improvement over the baseline model $\chi^2(1) = 17.369$, $p = .004$. Model 3 was selected as the best-fitting model.

The model achieved perfect classification accuracy, correctly classifying 100% of cases (6 non-freezers and 8 freezers). The model fit was perfect, with a -2 log-likelihood

of 0.000 and a non-significant Hosmer and Lemeshow test, $\chi^2(8) = 0.000$, $p = 1.000$, suggesting potential overfitting, likely due to the small sample size ($n = 14$). The NagelKerke R^2 was 1.000, indicating that the model accounts for all variance in the outcome, but this is likely due to overfitting. None of the predictors were statistically significant (all $p > .05$). The non-significant predictors suggest that these variables may not reliably distinguish between non-freezers and freezers in this sample, potentially due to limited statistical power. See Table 5.

Table 5

Coefficients of Model 3: Reversal Reaching Performance Predicts FOG Category

Predictors	*B*(SE)	95% CI for Odds Ratio		
		Lower	Odds Ratio	Upper
Constant	-3733.060 (608052.272)		.000	
Sex	51.285 (8612.876)	.000	1.873E+22	-
Phase 1 - % distance covered	48.982 (8057.914)	.000	1.873E+21	-
Phase 2 - % distance covered	33.336 (5669.333)	.000	3.005E+14	-
Phase 3 - % distance covered	41.695 (6650.008)	.000	1.282E+18	-
Phase 4 - % distance covered	37.328 (6096.403)	.000	1.627E+16	-
Phase 5 - % distance covered	7.540 (1619.479)	.000	1881.571	-

Note. $R^2 = .749$ (Cox-Snell), 1.000 (Nagelkerke). Hosmer and Lemeshow $\chi^2(8) = 0.000$, $p = 1.000$. Model $\chi^2(6) = 19.121$, $p = .004$. No predictors were significant, all $p > .05$.

Corner. A hierarchical binary logistic regression was conducted to examine the effects of reaching performance in the corner task on the likelihood of freezing (1 = freezer, 0 = non-freezer). Three models were tested: Model 1 included background measures (age, sex, health rating percentage, UPDRS part III scores, MOCA). Model 2 included reaching measures with group main effects, interactions, or significant correlations with NFOG category. RT, MT plus phase 5, accuracy in depth, Precision in depth, and %Distance for the corner task were entered on separate levels in model 2. Sex, age, health rating percentage, MOCA scores and %Distance seemed to be making the largest impact on the previous models, therefore, in an attempt to strive for parsimony, Model 3 included sex, age, health rating percentage and MOCA scores on level 1 and %Distance for all phases on level 2.

The omnibus test of model coefficients indicated that model 1, with background measures as the predictors, was not a significant improvement over the baseline model $\chi^2(5) = 3.861$, $p = .570$. The omnibus test of model coefficients indicated that model 2, with RT, MT plus phase 5, accuracy in depth, Precision in depth, and %Distance for the corner task as the predictors, was not a significant improvement over the baseline model $\chi^2(5) = 9.719$, $p = .084$. The omnibus test of model coefficients indicated that model 3, with sex, age, health rating percentage and MOCA scores on level 1 and %Distance for all phases on level 2, was a significant improvement over the baseline model $\chi^2(5) = 15.966$, $p = .007$. Model 3 was selected as the best-fitting model.

The model achieved perfect classification accuracy, correctly classifying 100% of cases (6 non-freezers and 8 freezers). The model fit was perfect, with a -2 log-likelihood of 0.000 and a non-significant Hosmer and Lemeshow test, $\chi^2(8) = 0.000$, $p = 1.000$,

suggesting potential overfitting, likely due to the small sample size (n = 14). The NagelKerke R^2 was 1.000, indicating that the model accounts for all variance in the outcome, but this is likely due to overfitting. None of the predictors were statistically significant (all p >.05). The non-significant predictors suggest that these variables may not reliably distinguish between non-freezers and freezers in this sample, potentially due to limited statistical power. See Table 6.

Table 6

Coefficients of Model 3: Corner Reaching Performance Predicts FOG Category

Predictors	*B*(SE)	95% CI for Odds Ratio		
		Lower	Odds Ratio	Upper
Constant	2457.307 (2487852.989)		-	
Sex	188.023 (86861.059)	.000	4.543E+081	-
Age	-7.777 (16178.043)	.000	.000	-
Health Rating %	-8.168 (1180.881)	.000	.000	-
MOCA	-76.723 (42011.722)	.000	.000	-
Phase 1 - % distance covered	99.494 (20193.161)	.000	1.620E+043	-
Phase 2 - % distance covered	10.211 (9157.796)	.000	27196.664	-
Phase 3 - % distance covered	15.092 (7393.857)	.000	3585465.951	-
Phase 4 - % distance covered	41.220 (6663.893)	.000	7.971E+17	-
Phase 5 - % distance covered	-287.171 (46219.212)	.000	.000	-

Note. R^2 = .749 (Cox-Snell), 1.000 (Nagelkerke). Hosmer and Lemeshow $\chi^2(8) = 0.000$, p = 1.000. Model $\chi^2(9) = 19.121$, $p = .024$. No predictors were significant, all p>.05.

Tunnel. A hierarchical binary logistic regression was conducted to examine the effects of reaching performance in the tunnel task on the likelihood of freezing (1 = freezer, 0 = non-freezer). Three models were tested: Model 1 included background measures (age, sex, health rating percentage, UPDRS part III scores, MOCA). Model 2 included reaching measures with group main effects, interactions, or significant

correlations with NFOG category. Absolute Y error, standard deviation of Y error, and percentage of distance covered within all phases for the tunnel task were entered on separate levels in model 2. Age, UPDRS part III scores, MOCA scores and %Distance seemed to be making the largest impact on the previous models, therefore, in an attempt to strive for parsimony, Model 3 included age, UPDRS part III scores, MOCA scores on level 1 and %Distance for all phases on level 2.

The omnibus test of model coefficients indicated that model 1, with background measures as the predictors, was not a significant improvement over the baseline model $\chi^2(5) = 3.861$, $p = .570$. The omnibus test of model coefficients indicated that model 2, with absolute Y error, standard deviation of Y error, and percentage of distance covered within all phases for the tunnel task as the predictors, was not a significant improvement over the baseline model $\chi^2(5) = 3.087$, $p = .687$. The omnibus test of model coefficients indicated that model 3, with age, UPDRS part III scores, MOCA scores on level 1 and %Distance for all phases on level 2, was a significant improvement over the baseline model $\chi^2(5) = 17.803$, $p = .003$. Model 3 was selected as the best-fitting model.

The model achieved perfect classification accuracy, correctly classifying 100% of cases (6 non-freezers and 8 freezers). The model fit was perfect, with a -2 log-likelihood of 0.000 and a non-significant Hosmer and Lemeshow test, $\chi^2(8) = 0.000$, $p = 1.000$, suggesting potential overfitting, likely due to the small sample size ($n = 14$). The NagelKerke R^2 was 1.000, indicating that the model accounts for all variance in the outcome, but this is likely due to overfitting. None of the predictors were statistically significant (all $p > .05$). The non-significant predictors suggest that these variables may

not reliably distinguish between non-freezers and freezers in this sample, potentially due to limited statistical power. See Table 7.

Table 7

Coefficients of Model 3: Tunnel Reaching Performance Predicts FOG Category

Predictors	*B*(SE)	95% CI for Odds Ratio		
		Lower	Odds Ratio	Upper
Constant	9083.551 (826639.831)		-	
Age	55.545 (5064.323)	.000	1.327E+24	-
UPDRS III	46.967 (4366.920)	.000	2.496E+20	-
MOCA	91.849 (8416.734)	.000	7.752E+039	-
Phase 1 - % distance covered	-479.008 (43820.730)	.000	.000	-
Phase 2 - % distance covered	-101.672 (9204.501)	.000	.000	-
Phase 3 - % distance covered	-174.154 (15738.632)	.000	.000	-
Phase 4 - % distance covered	-197.981 (18024.723)	.000	.000	-
Phase 5 - % distance covered	-184.315 (16815.311)	.000	.000	-

Note. R^2 = .749 (Cox-Snell), 1.000 (Nagelkerke). Hosmer and Lemeshow $\chi^2(8) = 0.000$, p = 1.000. Model $\chi^2(8) = 19.121$, $p = .014$. No predictors were significant, all p>.05.

Appendix K

Walking Logistic Regressions

Reversal. A hierarchical binary logistic regression was conducted to examine the effects of walking performance in the reversal task on the likelihood of freezing (1 = freezer, 0 = non-freezer). Three models were tested: Model 1 included background measures (age, sex, health rating percentage, UPDRS part III scores, MOCA). Model 2 included both walking measures; movement time and percent time after peak velocity for the reversal task were entered on separate levels in model 2 (time spent decelerating on level 1, movement time on level 2). PTAVP seemed to be making the largest impact on the previous models, therefore, in an attempt to strive for parsimony, Model 3 included background measures on level 1 and time spent decelerating on level 2.

The omnibus test of model coefficients indicated that model 1, with background measures as the predictors, was not a significant improvement over the baseline model $\chi^2(5) = 3.861$, $p = .570$. The omnibus test of model coefficients indicated that model 2, with PTAVP and movement time for the reversal task as the predictors, was not a significant improvement over the baseline model $\chi^2(2) = 1.511$, $p = .470$. The omnibus test of model coefficients indicated that model 3, with background measures inputted on level 1 and PTAVP on level 2, was not significant improvement over the baseline model $\chi^2(6) = 3.984$, $p = .679$. Walking performance in the reversal task was not able to predict freezing category.

Corner. A hierarchical binary logistic regression was conducted to examine the effects of walking performance in the corner task on the likelihood of freezing (1 = freezer, 0 = non-freezer). Three models were tested: Model 1 included background

measures (age, sex, health rating percentage, UPDRS part III scores, MOCA). Model 2 included both walking measures; movement time and percent time after peak velocity for the corner task were entered on separate levels in model 2 (time spent decelerating on level 1, movement time on level 2). Time spent decelerating seemed to be making the largest impact on the previous models, therefore, in an attempt to strive for parsimony, Model 3 included background measures on level 1 and time spent decelerating on level 2.

The omnibus test of model coefficients indicated that model 1, with background measures as the predictors, was not a significant improvement over the baseline model $\chi^2(5) = 3.861$, $p = .570$. The omnibus test of model coefficients indicated that model 2, with PTAVP for the corner task as the predictor on level 1, was a significant improvement over the baseline model $\chi^2(1) = 4.925$, $p = .026$. On level 2, the contribution of movement time for the corner task was not significant $\chi^2(1) = 1.766$, $p = .184$. The omnibus test of model coefficients indicated that model 3, with background measures inputted on level 1 and PTAVP on level 2, was not significant improvement over the baseline model $\chi^2(6) = 9.040$, $p = .171$. Model 2, with time spent decelerating as the sole predictor was selected as the best-fitting model.

The model achieved strong classification accuracy, correctly classifying 71% of cases (4 non-freezers and 6 freezers). The model fit was strong, with a -2 log-likelihood of 14.196 and a non-significant Hosmer and Lemeshow test, $\chi^2(8) = 6.243$, $p = .620$. The Nagelkerke R^2 was .398, indicating that the model accounts for 40% of the variance in the outcome. The odds ratio tells us that as the percentage of time spent in deceleration increased by a unit, the change in the odds of being a freezer (rather than a non-freezer) is 1.132. You're more likely to be a freezer than not if you spend more time decelerating.

However, time spent decelerating did not significantly predict whether a participant was a freezer or non-freezer, b = .124, Wald $\chi^2(1) = 2.855$, p = .091. See Table 8.

Table 8

Coefficients of Model 2: Corner Walking Performance Predicts FOG Category

Predictors	*B*(SE)	95% CI for Odds Ratio		
		Lower	Odds Ratio	Upper
Constant	-7.363 (4.520)		.001	
Time Spent Decelerating	.124 (.073)	.980	1.132	1.307

Note. R^2 = .297 (Cox-Snell), .398(Nagelkerke). Hosmer and Lemeshow $\chi^2(8) = 6.243$, p = .620. Model $\chi^2(1) = 4.925$, p = .026. Predictor was not significant p=.091.

Tunnel. A hierarchical binary logistic regression was conducted to examine the effects of walking performance in the Tunnel task on the likelihood of freezing (1 = freezer, 0 = non-freezer). Four models were tested: Model 1 included background measures (age, sex, health rating percentage, UPDRS part III scores, MOCA). Model 2 included both walking measures; movement time and percent time after peak velocity for the tunnel task were entered on separate levels in model 2 (time spent decelerating on level 1, movement time on level 2). Time spent decelerating seemed to be making the largest impact on the previous models, therefore, in an attempt to strive for parsimony, Model 3 included background measures on level 1 and time spent decelerating on level 2.

Age, UPDRS, and time spent decelerating were making the largest impact on the previous model. Therefore, in an attempt to further simplify the model, Model 4 was created, including age and UPDRS on level 1 and time spent decelerating on level 2.

The omnibus test of model coefficients indicated that model 1, with background measures as the predictors, was not a significant improvement over the baseline model $\chi^2(5) = 3.861$, $p = .570$. The omnibus test of model coefficients indicated that model 2, with PTAVP for the tunnel task as the predictor on level 1, was a significant improvement over the baseline model $\chi^2(1) = 9.546$, $p = .002$. On level 2, the contribution of movement time for the tunnel task was not significant $\chi^2(1) = .886$, $p = .347$. The omnibus test of model coefficients indicated that model 3, with background measures inputted on level 1 and PTAVP on level 2, was a significant improvement over the baseline model $\chi^2(6) = 19.121$, $p = .004$. The omnibus test of model coefficients indicated that model 4, with age and UPDRS inputted on level 1 and PTAVP on level 2, was a significant improvement over the baseline model $\chi^2(3) = 19.121$, $p < .001$. Model 4 was selected as the best-fitting model.

The model achieved perfect classification accuracy, correctly classifying 100% of cases (6 non-freezers and 8 freezers). The model fit was perfect, with a -2 log-likelihood of 0.000 and a non-significant Hosmer and Lemeshow test, $\chi^2(8) = 0.000$, $p = 1.000$, suggesting potential overfitting, likely due to the small sample size ($n = 14$). The Nagelkerke R^2 was 1.000, indicating that the model accounts for all variance in the outcome, but this is likely due to overfitting. None of the predictors were statistically significant (all $p > .05$). The non-significant predictors suggest that these variables may

not reliably distinguish between non-freezers and freezers in this sample, potentially due to limited statistical power. See Table 9.

Table 9

Coefficients of Model 4: Tunnel Walking Performance Predicts FOG Category

Predictors	*B*(SE)	95% CI for Odds Ratio		
		Lower	Odds Ratio	Upper
Constant	3495.491 (200107.666)		-	
Age	-12.715 (750.903)	.000	.000	-
UPDRS III	-21.046 (1222.943)	.000	.000	-
Time Spent Decelerating	-41.403 (2328.395)	.000	.000	-

Note. R^2 = .749 (Cox-Snell), 1.000 (Nagelkerke). Hosmer and Lemeshow $\chi^2(7) = 0.000$, p = 1.000. Model $\chi^2(3) = 19.121$, $p<.001$. No predictors were significant, all p>.05.