Summer 7-9-2024

Treadmill Walking with Concurrently Controlled Speed and Cadence in People with Parkinson's Disease

Rebecca Ban

ACCEPTANCE

This dissertation, TREADMILL WALKING WITH CONCURRENTLY CONTROLLED SPEED AND CADENCE IN PEOPLE WITH PARKINSON'S DISEASE, by REBECCA BAN, was prepared under the direction of the candidate's Dissertation Advisory Committee. It is accepted by the committee members in partial fulfillment of the requirements for the degree, Doctor of Philosophy, in the College of Education & Human Development, Georgia State University.

The Dissertation Advisory Committee and the student's Department Chairperson, as representatives of the faculty, certify that this dissertation has met all standards of excellence and scholarship as determined by the faculty.

_____
Feng Yang, PhD
Committee Chair

_____
Chris Ingalls, PhD
Committee Member

_____
Jeff Otis, PhD
Committee Member

_____
Pey-Shan Wen, PhD
Committee Member

_____
Date

_____
Jianhua Wu, PhD
Chairperson, Department of Kinesiology & Health

_____
Paul Alberto, PhD
Dean, College of Education & Human Development

AUTHOR'S STATEMENT

By presenting this dissertation as a partial fulfillment of the requirements for the advanced degree from Georgia State University, I agree that the library of Georgia State University shall make it available for inspection and circulation in accordance with its regulations governing materials of this type. I agree that permission to quote, to copy from, or to publish this dissertation may be granted by the professor under whose direction it was written, by the College of Education & Human Development's Director of Graduate Studies, or by me. Such quoting, copying, or publishing must be solely for scholarly purposes and will not involve potential financial gain. It is understood that any copying from or publication of this dissertation which involves potential financial gain will not be allowed without my written permission.

_____

REBECCA BAN

NOTICE TO BORROWERS

All dissertations deposited in the Georgia State University library must be used in accordance with the stipulations prescribed by the author in the preceding statement. The author of this dissertation is:

Rebecca Jane Ban
Department of Kinesiology & Health
College of Education & Human Development
Georgia State University

The director of this dissertation is:

Dr. Feng Yang
Department of Kinesiology & Health
College of Education & Human Development
Georgia State University
Atlanta, GA 30303

CURRICULUM VITAE

Rebecca Ban

ADDRESS: 125 Decatur Street NW
Atlanta, GA 30303

EDUCATION:

Ph.D.	2024	Georgia State University Kinesiology
M.S.	2016	Georgia State University Exercise Science
B.S.	2006	Appalachian State University Athletic Training

PROFESSIONAL EXPERIENCE:

2016-2024	Graduate Teaching Assistant Graduate Research Assistant Georgia State University

PRESENTATIONS AND PUBLICATIONS:

PRESENTATIONS

Ban, R., Simpkins, C., Yang, F. (August 2022). *Acute effect of an intervention to improve ankle dorsiflexion on landing biomechanics.*
North American Congress on Biomechanics, Ottawa, Canada.

Ban, R., Yang, F. (2020, August). *Acute effect of an intervention to improve ankle dorsiflexion among individuals who display medial knee displacement.*
American Society of Biomechanics, Virtual.

Ban, R., Cain MS., Linens, SW., Wong, B., Goerger, B. (2017, June). *Abdominal hollowing and a single leg balance task in subjects with and without anterior cruciate ligament reconstruction.*
National Athletic Trainers' Association Annual Symposium, Houston, Texas.

PUBLICATIONS

Ban, R., Ahn, J., Simpkins, C., Lazarus, J., Yang, F. (2024). *Dynamic gait stability in people with mild to moderate Parkinson's disease.*
Clinical Biomechanics, 118: 106316.

Ahn, J., Ban, R., Simpkins, C., Yang, F. (2024). *Android obesity could be associated with a higher fall risk than gynoid obesity following a standing-slip: a simulation-based biomechanical analysis.*
Journal of Biomechanics, 164: 111962.

Simpkins, C., Ahn J, Buehler, R., Ban, R., Wells, M., Yang, F. (2023). *Commingling effects of anterior load and walking surface on dynamic gait stability in young adults.*
Journal of Applied Biomechanics, 40(1): 66-72.

Ban, R., Yang, F. (2022). *Acute effect of an intervention to improve ankle dorsiflexion among individuals who display medial knee displacement.*
Clinical Biomechanics, 95: 105637.

Yang, F., Ban, R., Yang F. (2022). *Anterior load carriage increases the risk of falls following a slip in gait.*
Safety Science, 145: 105489.

Cain, MS., Ban, RJ., Chen, YP., Geil, MD., Goerger, GM., Linens, SW. (2020). *Four-week ankle-rehabilitation programs in adolescent athletes with chronic ankle instability.*
Journal of Athletic Training, 55: 801-810.

PROFESSIONAL SOCIETIES AND ORGANIZATIONS

2023-present	American Society of Biomechanics
2007-present	National Athletic Trainers' Association Certification
2013-present	State of Georgia Athletic Training Licensure

TREADMILL WALKING WITH CONCURRENTLY CONTROLLED SPEED AND CADENCE IN PEOPLE WITH PARKINSON'S DISEASE

by

REBECCA BAN

Under the Direction of Dr. Feng Yang

ABSTRACT

Gait and stability impairments are common symptoms of Parkinson's disease (PD) that can lead to a loss of mobility, increased fall risk, and a decreased quality of life. Rhythmic auditory cueing has commonly been used to improve gait speed by increasing cadence without modulating step length. However, most of the current rhythmic auditory cueing-based training modalities only control the speed and people with PD may just increase their step frequency without changing the stride length to walk faster. The increased cadence could be problematic for people with PD who may have already experienced high cadence and short steps, like in the shuffling gait. Given the interrelations between gait speed, step length, and cadence, investigating the effects of gait interventions that control speed and cadence simultaneously may be warranted. The primary purpose of this randomized controlled pilot study was to examine the acute effects of a treadmill walking intervention, which manipulates the step length and gait speed concurrently, on gait quality in people with PD. Thirty-two participants diagnosed with PD

(age: 67.13 ± 6.23 years) were randomly assigned to a 30-minute treadmill walking intervention that controlled speed and cadence (the advanced group) or only speed (the regular group). Before, in the middle of, and after the intervention, stride length (primary outcome), speed, cadence, and other spatiotemporal gait parameters (secondary) and dynamic gait stability (tertiary outcome), were assessed during overground walking and compared between groups over sessions. The results suggest the advanced treadmill intervention increases stride length (p = 0.04), gait speed (p = 0.05), double leg stance time (p = 0.04), and vertical ground reaction force (p = 0.04) more than the regular treadmill intervention. The two intervention regimes seem to show little differences in altering the single leg stance time, anteroposterior ground reaction force and impulse, or dynamic gait stability. The findings of this study could provide a foundation for designing effective interventions to improve gait and stability for this population. More studies are needed to investigate the best dosage and long-term and retention effects of the advanced treadmill gait training for people with PD's gait quality.

INDEX WORDS: Parkinson's disease, gait speed, cadence, stride length, treadmill training, stability

TREADMILL WALKING WITH CONCURRENTLY CONTROLLED SPEED AND CADENCE IN PEOPLE WITH PARKINSON'S DISEASE

by

REBECCA BAN

A Dissertation

Presented in Partial Fulfillment of Requirements for the

Degree of

Doctor of Philosophy

in

Kinesiology

in

Department of Kinesiology & Health

in

the College of Education & Human Development

Georgia State University

Atlanta, GA
2024

ACKNOWLEDGMENTS

I would first like to express my deepest gratitude to my advisor, Dr. Feng Yang for taking me on as a doctoral student and his support and guidance throughout my PhD journey. I am extremely grateful for his ideas, feedback, encouragement, and the tools he provided me to complete this project.

I am sincerely appreciative for my dissertation committee members: Dr. Pey-Shan Wen, Dr. Brett Wong, Dr. Jeff Otis, Dr. Chris Ingalls, and Dr. Jianhua Wu. Their contributions enriched the quality of this dissertation and I am truly grateful for their time, insights, and constructive feedback.

A special thanks to all members of the biomechanics lab, specifically Caroline Simpkins and Wendy Ahn. I could not have done this without you.

I would also like to express my gratitude to my family for their unwavering support throughout my academic journey. Their encouragement, understanding, and belief in my abilities have been invaluable.

I am grateful to Georgia State University for their generous financial support through the Dissertation Grant to fund this study, and I'm honored to have received this award. This funding played a pivotal role in facilitating the completion of this study.

Finally, I would like to offer a heartfelt thank you to all of the participants. This study was possible because of you.

Table of Contents

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

BOS: Base of support

CI: Confidence interval

COM: Center of mass

FSR: Feasible stability region

GRF: Ground reaction force

H&Y: Hoehn and Yahr Scale

LO: Liftoff

MoCA: Montreal cognitive assessment

PD: Parkinson's disease

PDQ-8: Parkinson's Disease Questionnaire - 8

PwPD: People with Parkinson's disease

TD: Touchdown

1 THE PROBLEM

1.1 Introduction

Parkinson's disease (PD) is a progressive neurological disorder that affects approximately 9 million people worldwide (Owais and Siddique, 2023). Although the cause remains unknown, PD is defined by the progressive loss or degeneration of dopamine-producing neurons in the brain, which can lead to a variety of symptoms such as motor dysfunction, postural instability, and gait impairments. These can contribute to a loss of mobility, increased risk of falls, and reduced quality of life (Adkin et al., 2003; Bloem et al., 2001). The most common primary treatment for PD involves using pharmacological management, levodopa, to restore depleted dopamine levels. However, dopaminergic treatment has not only been shown to gradually diminish over time but can also cause severe motor-related side effects (Galna et al., 2015; Lewitt, 2008; Rascol et al., 2000; Thanvi et al., 2007). Further, postural stability does not respond well to these medications, and they can be ineffective at improving gait impairments, both cardinal symptoms of PD (Curtze et al., 2015; Sethi, 2008). Therefore, non-pharmacologic treatment is warranted as a supplemental therapy to levodopa for people with PD (PwPD).

Bradykinesia is associated with gait impairments in PwPD, which manifest as reduced gait speed, decreased step length, and increased cadence, resulting in shuffling steps (Morris et al., 1994). Slower gait speeds are associated with increased fall risk, and gait training has primarily focused on increasing walking speed (Verghese et al., 2009). Because gait speed is determined by step length and cadence, PwPD could increase their gait speed by lengthening their step, increasing their cadence, or both. PwPD have displayed difficulty in regulating stride length and typically increase cadence as a strategy to increase gait speed (Morris et al., 1994). As a result, PwPD may exhibit a cadence already within the normal range or higher than healthy

counterparts (Hollman et al., 2011). Therefore, when attempting to increase gait speed, it is important for PwPD to increase step length while maintaining, or even reducing cadence, as a strategy.

PwPD commonly demonstrate a loss of automaticity and rhythmicity of their movements (Koshimori and Thaut, 2018). Rhythmic auditory stimulation (RAS) is an external cue, typically a metronome, that helps PwPD facilitate initiating and/or maintaining motor activity by synchronizing their movements with external rhythmic cues through an innate internal timing process (Thaut et al., 2015). The cyclic nature of RAS can help PwPD synchronize ground contact when walking and control variability in musculoskeletal activation patterns (Ford et al., 2010; Koshimori and Thaut, 2018).

The use of RAS during treadmill training has demonstrated increases in gait speed and step length, but findings are inconsistent (Howe et al., 2003; Morris et al., 1994; Murgia et al., 2018; Nieuwboer et al., 2007; Thaut et al., 2019). Interventions have used faster tempos, in which the beat of the metronome depends on a person's cadence, to increase gait speed. Because cueing faster tempos intends to alter cadence, gait speed can be increased without increasing step length. Increasing the step length may be more critical for PwPD, and using an RAS with a tempo at or above baseline may lead to even shorter steps (Morris et al., 1994; Morris et al., 1996). It has recently been demonstrated that a slower RAS frequency can increase step length during treadmill walking in PwPD (Chawla et al., 2020). With a steady rhythm, PwPD can anticipate their next walking step and possibly replace their dysfunctional internal timing regulation (Forte et al., 2021). Using a RAS tempo slower than the baseline cadence may be a more effective method for managing cadence and increasing step length to increase gait speed.

Like gait impairments, postural stability does not respond well to anti-Parkinsonian medication, and exercise interventions are necessary to improve postural instability and reduce falls in PwPD (Bronte-Stewart et al., 2002). Most treadmill training with RAS research focuses on gait speed, while few studies have evaluated the effect of gait training with RAS on postural stability. It has been suggested that the use of rhythmic auditory and visual stimulation during gait training improves balance function, indicating that gait training with RAS has the potential to reduce fall risk (Harro et al., 2014; Song et al., 2015).

While there is some evidence that RAS with treadmill training can improve gait velocity and step length, it is unknown if simultaneously modulating gait speed and cadence is more effective in managing cadence to increase step length and gait speed compared to only modulating gait speed. Further, increasing step length can increase the time spent in the single leg stance phase, which might indicate an improvement in dynamic balance, leading to a reduction in fall risk while walking. It has been demonstrated that a single session of treadmill walking can elicit longer steps and faster walking (Bello et al., 2008; Pohl et al., 2003). Hence, this study aims to explore if simultaneously modulating speed and cadence during treadmill training can deliver more immediate benefits than controlling speed alone in PwPD.

1.2 Research Questions

This project aimed to answer the following questions:

1. Does modulating speed and cadence concurrently (advanced treadmill intervention) elicit a greater improvement in stride length compared to controlling speed alone (regular treadmill intervention) in a single treadmill session in PwPD?
2. How does the advanced treadmill intervention affect spatiotemporal and kinetic gait parameters relative to regular treadmill intervention?

3. Does the advanced treadmill intervention improve dynamic gait stability more than the regular treadmill intervention in a single session of treadmill walking in PwPD?

Correspondingly, the following hypotheses were tested:

1. The advanced treadmill intervention group would display a significantly larger increase in stride length compared to the regular treadmill intervention group following the training.
2. The advanced intervention group exhibits more improvements in the spatiotemporal and kinetic gait parameters compared to the regular intervention group.
3. The advanced treadmill intervention group would show a higher increase in dynamic gait stability than the regular treadmill intervention group from the pre-intervention to the post-intervention assessment.

1.3 Purpose

The overall purpose of this pilot, single-session, randomized controlled trial was to examine how the advanced treadmill intervention improves gait functions relative to the regular treadmill intervention in PwPD. Specifically, three aims were pursued: (1) to explore if a treadmill intervention that simultaneously modulates cadence using RAS and speed immediately improves stride length compared to a treadmill intervention that only controls gait speed; (2) to examine how a treadmill intervention that concurrently controls cadence and speed immediately affects spatiotemporal gait parameters compared to a regular intervention that only controls speed, and (3) to investigate if a treadmill intervention that simultaneously modulates cadence using RAS and gait speed immediately improves dynamic gait stability compared to a treadmill intervention that only manipulates speed.

1.4 Significance of the Study

To our knowledge, this was the first acute study that will simultaneously control speed and cadence as an intervention to improve gait characteristics in PwPD. The effects of two different treadmill interventions on spatiotemporal gait characteristics and dynamic gait stability were examined. Given that gait and postural impairments are common and devastating symptoms of PD, it is vital to determine the most effective treatments that help PwPD improve their walking and reduce their risk of falls. With improved gait, PwPD would have better mobility, reduced fall risk, and increased quality of life. This study is clinically and socioeconomically impactful.

1.5 Delimitations and Limitations

Delimitations

This study was limited to people with a clinician-confirmed PD diagnosis and a disability level characterized by the Hoehn and Yahr (H&Y) stage between 1 and 3. To control the heterogeneity of the participants, the age was restricted to 50 years and over. Due to the nature of the interventions, only those who could walk on a treadmill for at least 30 minutes without using a walking aid were recruited. Additionally, this project excluded anyone with self-reported uncontrolled cardiorespiratory or metabolic disease, other neurologic disorders that affect walking, and visual and communication impairments. These delimitations may reduce the generalizability of this study.

Limitations

This study is not without limitations. It was difficult to recruit an equal number of male and female participants, as men are 1.5 times more likely to develop PD than women. This could

dampen the generalizability of our findings of both sexes. Due to the specific inclusion criteria related to the age range and assistive device use, the findings of this project may not be generalizable to PwPD in other age ranges and disability levels. Because this treadmill training intervention is based on previous studies, it is unknown if this protocol is optimal. Given that the intervention took place inside a lab, it remains unknown how the findings would transfer to everyday living conditions. Fatigue, footwear, sensorimotor function impairments, quality of sleep, hydration, nutrition, and the time of day of testing were not controlled. Lastly, because this study assessed the acute effects of a single-session treadmill intervention, it is unclear what the long-term training effect would be and how long the effects would last.

1.6 Overview of the Study

Gait and postural impairments are prevalent and debilitating symptoms for PwPD that can limit their ability to perform daily tasks, cause injury, and compromise their quality of life. PwPD typically display decreased walking speed, shortened step length, and an increased cadence resulting in shuffled gait. External auditory cueing is commonly used in conjunction with gait rehabilitation and has been shown to improve gait quality through rhythmic entrainment. Specifically, external auditory cueing, typically a metronome, has commonly been used at a tempo faster than baseline to increase walking speed on a treadmill. This may cause PwPD to take even shorter steps to increase speed. It may be more beneficial to use a slower cadence to increase step length for increasing gait speed. Therefore, this project adopted a randomized controlled design to explore if simultaneously controlling cadence and gait speed (or the advanced treadmill intervention) is acutely more effective at improving the stride length and other gait characteristics than controlling gait speed alone (or the regular treadmill intervention). Thirty PwPD were enrolled in this study. They were randomly assigned into one of the two groups:

advanced intervention or regular intervention. Participants in the advanced group completed a single session of a treadmill walking intervention in which speed and cadence were manipulated. The regular training group completed a single session of treadmill walking where the speed alone was controlled. Gait parameters included stride length (primary outcome), cadence, gait velocity, single leg stance time, double leg stance time, peak vertical ground reaction force (GRF), peak anterior and posterior GRFs, braking and propulsive impulses, and rate of loading (secondary outcomes). In addition, dynamic gait stability (tertiary outcome) was examined. The three categories of outcome measurements were collected during overground walking and were compared between groups over sessions to test the three hypotheses, respectively. The findings of this project may provide insight into the reaction of PwPD to the manipulated gait and furnish a new foundation to design effective interventions to improve gait characteristics for this population.

2 REVIEW OF THE LITERATURE

2.1 Overview and Relevance of Parkinson's Disease

Parkinson's disease (PD) is a progressive neurodegenerative disorder that was first identified by James Parkinson in 1817 under the term "shaky palsy" (Parkinson, 2002). From 1990 to 2015, the number of people with PD (PwPD) increased by 118% to over 6.2 million, making it the fastest growing neurological disorder and the leading cause of disability worldwide (Dorsey et al., 2018; Rocca, 2018). The incidence of PD increases with age and rises sharply around age 65, where men are 1.5 times more likely to develop PD than women (Moisan et al., 2016; Van Den Eeden et al., 2003). Given the increase in longevity and the aging population, the number of people with PD is projected to exceed 12 million worldwide by 2040 (Dorsey and Bloem, 2018; Goldman, 2014; Scheperjans et al., 2015). Though non-infectious, some scientists consider PD a pandemic as it is experiencing exponential growth, no one is immune, and PD is increasing in every major region of the world (Morens et al., 2009).

While the cause of PD remains unknown, there is sufficient evidence that genetic variability and environmental risk factors are associated with developing the disease (Betarbet et al., 2000; Blauwendraat et al., 2019). The α-synuclein gene (*SNCA*) was the first gene to be associated with the development of PD in 1997 (Polymeropoulos et al., 1997). Since then, more than 20 gene loci have been associated with PD (Blauwendraat et al., 2019). Pesticide exposure, as a potential risk factor, was raised in the 1980s after the discovery of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), which caused irreversible parkinsonism in patients (Langston et al., 1983). It has been demonstrated that long-term exposure to pesticides can cause parkinsonism, and it is hypothesized that exposure to these environmental factors produces oxidative stress, which aids in neural degeneration (Betarbet et al., 2000; Jenner and Olanow, 1998).

The cardinal signs of PD relate to motor dysfunction, including tremors at rest, bradykinesia, rigidity, and postural impairments (Rajput et al., 1991; Wirdefeldt et al., 2011). Although historically considered a motor disease, non-motor manifestations, including sensory symptoms (pain, tingling), anxiety, depression, hypotension, sleep disturbances, and cognitive impairments, have been recognized (Chaudhuri and Schapira, 2009; Gallagher et al., 2010; Jankovic, 2008). It is now known that the above motor dysfunctions occur as a result of a loss of dopaminergic neurons of the pars compacta of the substantia nigra leading to loss of dopamine in the striatum of the brain and the development of neuronal Lewy Bodies in the neurons that are still alive (Wirdefeldt et al., 2011). Symptoms do not develop until about 50-60% of the nigral neurons are lost, 80-85% of the dopamine content of the striatum is depleted, and the reduction of dopamine results in decreased automatic control of movement (Kalia and Lang, 2016; Michel et al., 2016; Postuma et al., 2010; Wu and Hallett, 2008).

Currently, only clinical criteria are used to diagnose PD, including resting tremors, rigidity, bradykinesia, and postural impairments, as no standardized biomarker or neuroimaging finding confirms its presence (Li and Le, 2020). Because these motor symptoms can also be present in other neurodegenerative disorders, PD diagnosis can be challenging. It is postulated that neurologists have a misdiagnosis rate of 24%, while movement disorders specialists have a misdiagnosis rate of 8% (Jankovic et al., 2000; Rajput et al., 1991).

Due to the amount of motor and non-motor symptoms, PwPD have higher medical care needs, miss work or lose the ability to work, and can require paid and/or unpaid care partners, creating both direct and indirect economic burdens (Whetten-Goldstein et al., 1997). As of 2017, it was estimated that one million people were diagnosed with PD in the United States, with an approximate economic cost of $51.9 billion (Yang et al., 2020). Further, research suggests that

motor and non-motor symptoms of PD negatively impact the health-related quality of life (Crispino et al., 2020).

Though PD is the fastest growing neurological disorder in the world, there is neither a clinical biomarker for early detection nor a cure available. Both motor and non-motor related symptoms are experienced by PwPD and can reduce health-related quality of life and cause an economic burden, extending beyond the patient to society at large. Therefore, it is important to identify treatment options to help patients maintain independence and quality of life while living with PD.

2.2 Clinical Motor Symptoms of Parkinson's Disease

As mentioned previously, common clinical motor symptoms of PD include resting tremors, bradykinesia, rigidity, and postural impairments, which all contribute to impaired walking and functional mobility (Boonstra et al., 2008; Miller-Patterson et al., 2018; Morris, 2000; Plotnik and Hausdorff, 2008; Takakusaki et al., 2008). Bradykinesia refers to slowing movement and is a hallmark of basal ganglia disorders (Berardelli et al., 2001). The basal ganglia refer to a group of structures located beneath the cortex of the brain called the subcortical nuclei and are responsible for the coordination of movement (among other functions). The basal ganglia generate internal cues to facilitate the initiation of movement sequences and enable appropriate motor function execution, along with inhibiting unwanted movements (Muthukrishnan et al., 2019).

The prevailing model of basal ganglia function consists of two circuits, the direct and indirect pathways, originating from distinct striatal medium spiny neurons (MSNs) and projecting to different output structures. It is hypothesized the direct pathway promotes movement by direct inhibitory projections to the globus pallidus internus (GPi), while the indirect pathway is thought to inhibit movement projecting to the GPi through globus pallidus externus (PGe) and

subthalamic nucleus (Calabresi et al., 2014). In PwPD, striatal dopaminergic depletion leads to increased GPi inhibition of the output structures. This leads to deficiencies in the execution of movement, resulting in bradykinesia, a cardinal motor symptom of PD (Boonstra et al., 2008; Cunnington et al., 1995; Debaere et al., 2003; Georgiou et al., 1993; Muthukrishnan et al., 2019).

Gait manifestations of bradykinesia include a reduced gait speed, shuffling when walking, dragging one or both feet while walking, and freezing (muscles are immobile for a period of time). Gait hypokinesia is related to decreased stride height and length, reduced stride frequency, and extended double limb support (Kang et al., 2019). Gait disturbances are one of the most incapacitating symptoms of PD. PwPD tend to walk slower, with a shorter step and a higher cadence compared to healthy counterparts (Canning et al., 2006; Morris, 2000; Morris et al., 1996). Further, PwPD may also present with stooped and forward-flexed posture, reduced arm swing, gait instability, falls, and increased stride-to-stride variability (Bello et al., 2010; Boonstra et al., 2008; Hausdorff et al., 1998; Murray et al., 1978). Results from 190 patients with PD demonstrated gait difficulties and postural instability as the main determinants of poor quality of life (Muslimovic et al., 2008). Because it can result in the loss of independence and quality of life, efforts must be dedicated to improving options for treating gait impairments in PwPD.

2.3 Treatment for Improving Gait Function in Parkinson's Disease

Clinically, there are two types of treatment for PD: surgery (deep brain stimulation) and medication. Deep brain stimulation (DBS) of the subthalamic nucleus (STN) or the GPi is an established treatment for advanced-stage PD and involves an electrode being implanted to provide continuous high-frequency electrical stimulation (Habets et al., 2018). Stimulation of the STN has been shown to consistently improve stride length but with no effects on stride time or stride variability, while stimulation of the GPi has been shown to improve gait velocity without any

significant improvement in stride length (Pötter-Nerger and Volkmann, 2013). Although DBS improves some motor symptoms of PD, it is not without adverse effects. Postoperative worsening of gait and increased risk of falls have been reported (Pötter-Nerger and Volkmann, 2013).

The most common treatment for PD involves the attempt to restore depleted dopamine levels in the basal ganglia. Because dopamine does not cross the blood brain barrier, dopamine cannot simply be administered to a patient. Instead, patients can be given a precursor to dopamine, called levodopa. Levodopa can cross the blood brain barrier and is used by the brain to synthesize more dopamine. Although levodopa does not halt the neurodegeneration that occurs in PD, it has been shown to improve some gait characteristics in PwPD. Improvements in stride length, gait speed, and double support time variability have been shown to improve with levodopa, but it may not significantly impact cadence (Rochester et al., 2011). Unfortunately, the effect of dopaminergic treatment gradually diminishes over time, and motor control symptoms become resistant to pharmacological therapy (Galna et al., 2015). Further, levodopa can cause severe side effects termed Levodopa-induced dyskinesias (LIDs), including involuntary, erratic, writhing body movements (Lewitt, 2008; Rascol et al., 2000; Thanvi et al., 2007). Along with dyskinesias, other motor fluctuations, such as wearing-off, delayed/no *on*-phase, and freezing effects, can also occur in response to levodopa (Jankovic et al., 2000; Mehrholz et al., 2015). The longer a PwPD spends on levodopa, the more common LID becomes. It is possible for PwPD to progress to a stage of treatment that involves managing the dosage of levodopa to control the trade-off between the original Parkinsonian symptoms and LID (Rajput et al., 1991).

Among non-pharmacological therapies for PD, exercise has become increasingly popular. A link between exercise and PD was first reported in 1992 when researchers documented that exercise in adulthood significantly reduced the risk of developing PD for the rest of their life

(Sasco et al., 1992). Further, more recent studies have indicated that exercise may provide not only a neuroprotective effect but also attenuate PD symptoms (Hirsch and Farley, 2009). Either as a complement to clinical treatment or alternative therapy, a meta-analysis and systematic review of 14 studies report exercise improves both motor and non-motor symptoms of PD by enhancing the plasticity of motor-related structures (Goodwin et al., 2008). Clinical studies have examined various types of exercise, such as aerobic exercise, gait training, resistance training, and complementary exercises like tango and yoga, on symptoms of PD (Alberts and Rosenfeldt, 2020; Cheung et al., 2018; Feng et al., 2020; Herman et al., 2009; Holmes and Hackney, 2017; Saltychev et al., 2016; Wu et al., 2017).

2.4 Exercise-based Interventions for Improving Giat Function

Aerobic Exercise Training

Aerobic exercise training is considered one of the best ways to improve health throughout a person's lifetime (Voss et al., 2011). Previous data have indicated that stationary cycling improves aerobic ability and cognitive function in those with early-stage PD (Duchesne et al., 2015; Nadeau et al., 2016). Fourteen participants with mild to moderate PD who completed 12 sets of 30-minute low-resistance interval training on a recumbent bike displayed improvements in disease severity, functional mobility, upper extremity movement, and cognitive function (Uygur et al., 2017). Aerobic exercise has also been suggested as the most effective method in reducing depression in PwPD compared to other physical activities like Qigong and Tai Chi (Wu et al., 2017). In a separate study, participants with PD completed a 12-week aerobic training program on a stationary bike and displayed increases in gait velocity and cadence but not step length (Nadeau et al., 2016).

In addition, aerobic exercise training has been associated with improving motor learning capacity in daily activities through increased plasticity of motor-related structures (Duchesne et al., 2016). Further, a single session of moderately intense (60-70% of VO_{2max}) aerobic cycling was effective at promoting motor skills consolidation (motor memory formation) in participants with PD (Steib et al., 2018). Aerobic exercise training is a popular therapy that positively affects motor function, disease severity, and depression but has not been beneficial in improving step length during gait.

Resistance Training

Resistance training is another exercise that involves repetitive movements to increase muscular strength. Multiple systematic reviews and meta-analyses have reported that resistance training has a positive effect on muscle strength, motor function, endurance, mobility, and motor symptoms in PD (Brienesse and Emerson, 2013; Feng et al., 2020; Lima et al., 2013; Saltychev et al., 2016). Further, in a randomized controlled trial in which participants completed two resistance training sessions a week for 12 weeks, PwPD improved sleep quality based on the Pittsburgh Sleep Quality Index (Silva-Batista et al., 2017). In a different study following a 12-week high intensity eccentric resistance training program, participants with mild to moderate PD exhibited improvements in muscular strength, clinical measures of bradykinesia, and quality of life (Dibble et al., 2009). Participants also displayed an increase in gait velocity, but it was unclear how the cadence and step length changed in response to the training (Dibble et al., 2009). Because both step length and cadence can affect the gait speed, it is vital to check how exactly these two factors were modified by the training and their impact on the gait velocity.

Complementary Exercise

Mind-body exercise programs such as Tango, Qigong, Tai Chi, and yoga have been studied in the PD population. These slow aerobic exercises have the potential to relax the body and mind. Tango is a partnered ballroom dance in which dancers must focus on their coordination, body movements, and stepping strategies. Due to the emotional, physical, and social aspects, tango could improve the quality of life, body self-efficacy, and activities of daily life in PwPD (Albani et al., 2019; Feng et al., 2020; Holmes and Hackney, 2017; Koch et al., 2016; Wells and Yang, 2021). A Bayesian network meta-analysis reported that tango is the most effective exercise to increase functional mobility in PwPD compared to Qigong, Tai Chi, resistance training, and yoga (Tang et al., 2019). After completing 20 sessions of a 1-hour Tango class over 10 weeks, PwPD displayed improvements in balance, functional reach, and gait velocity during the 6-minute walk test, but the cadence and step length were not examined (Hackney and Earhart, 2010).

Qigong originated from conventional Chinese medicine and is a type of exercise that incorporates movement, meditation, and breathing patterns to control the flow of Qi, a meridian system in the body (Tsang et al., 2002). Similarly, Tai Chi involves a series of dance-like movements linked together in a slow and continuous sequence. Prior studies have reported that both Qigong and Tai Chi may improve balance, postural stability, and sleep disorders in PwPD (Chen et al., 2016; Kim et al., 2014). For example, after a 6-month Qigong intervention, PwPD reported better sleep, balance, and an increase in gait velocity in the 6-minute walk test and Timed-Up-and-Go test (Xiao and Zhuang, 2016). In a separate 10-week study consisting of Qigong exercises five times a week, PwPD displayed improvements in balance, hand-eye coordination, and gait velocity during the Timed-Up-and-Go test (Liu et al., 2016). Even though it is encouraging

that both studies reported increases in gait velocity, neither measured cadence nor step length; therefore, the cause of the increased gait velocity was undetermined. While multiple studies have demonstrated the positive effect Tai Chi has on balance, cognitive function, psychological well-being, and sleep disorders, no improvements in gait impairments have been reported.

Yoga has been increasingly used to integrate breathing with postures and movement. Yoga also consists of stretching, improving flexibility and strength (Tran et al., 2001). In a 12-week study, PwPD improved motor and cognitive functions after the yoga-based training program (Cheung et al., 2018). Similar to Tai Chi-related studies, the evidence supporting the effect of yoga on gait impairments is lacking.

Additionally, dance-based exercise (Simpkins and Yang, 2023) and whole-body vibration training (Yang, 2020) have recently been applied to PwPD to improve their balance and gait functions with promising results.

Treadmill Training

Bradykinesia can cause common gait impairments in PwPD, which manifest as reduced gait speed, decreased step length, and increased cadence, resulting in shuffling steps (Morris et al., 1994). Further, slower gait speeds are associated with increased fall risk (Kyrdalen et al., 2019), and as such, gait training has primarily focused on increasing walking speed (Verghese et al., 2009). Numerous studies have reported an increase in gait speed after a treadmill training intervention for PwPD (Cakit et al., 2007; Canning et al., 2008; Pelosin et al., 2007; Skidmore et al., 2008).

Treadmill training has also been established as an effective treatment program to improve step length in PwPD (Herman et al., 2009; Mehrholz et al., 2015). However, studies that report increases in gait speed and step length do not always describe cadence (Canning et al., 2008;

Frazzitta et al., 2009; Herman et al., 2009; Pohl et al., 2003). Compared with healthy counterparts, PwPD displayed difficulty in regulating stride length and increased cadence as a compensatory strategy to maintain speed (Morris et al., 1994). Because gait speed is determined by step length and cadence, PwPD could increase their gait speed by lengthening their step, increasing their cadence, or both.

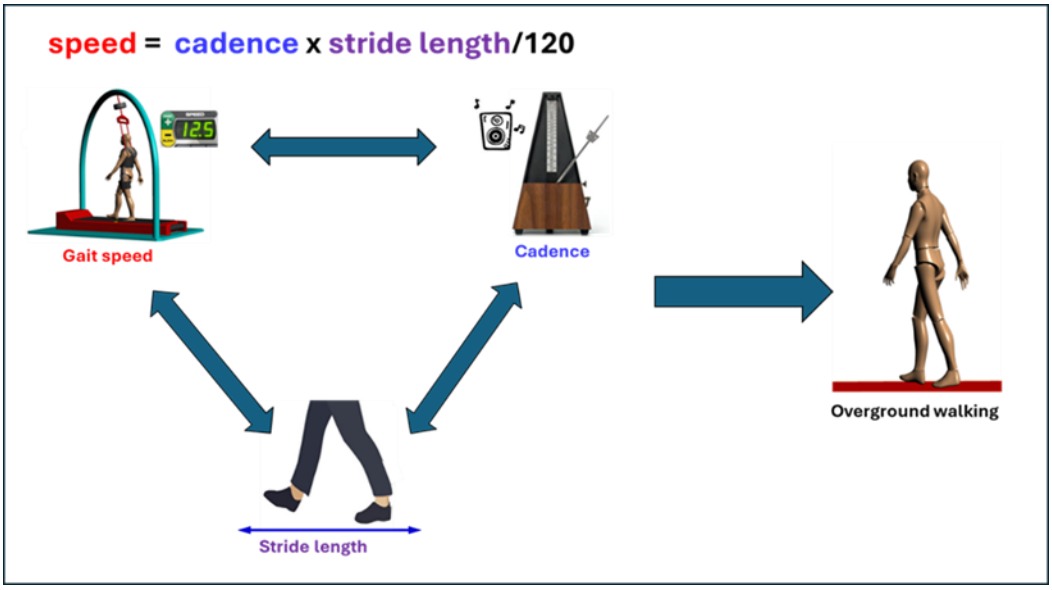


Figure 2.1 Interrelations between gait speed, cadence, and stride length, as defined by the mathematical equation. While a person is walking on a treadmill, the gait speed can be precisely controlled. Additionally, a metronome is usually used to modulate the cadence of the trainee. Given the strict mathematical relationships among gait speed, cadence, and stride length (shown as the equation), the stride length would be controlled. This provides us with a more advanced paradigm to train PwPD to force them to walk at the desired stride length, gait speed, and cadence. The training on the treadmill may improve the gait quality of PwPD on the ground.

It has been shown that PwPD increase cadence to increase gait speed despite cadence being already within the normal range or higher than healthy counterparts (Hollman et al., 2011). In an 8-week training program in which the treadmill speed gradually increased, PwPD displayed significant increases in gait speed and cadence (Protas et al., 2005). Though participants also increased their step length, these results were not statistically significant, indicating that increases

in gait speed more likely came from taking more steps rather than longer steps (Protas et al., 2005). Similarly, in a 5-week treadmill training program that adopted a constant treadmill walking velocity but a progressively prolonged training session duration, PwPD increased their gait speed, step length, and cadence (Bello et al., 2013). Therefore, it would be equally important to control the cadence and step length for a gait training program targeting PwPD. A training strategy that addresses both cadence and step length may lead to a better gait outcome. The interrelations between the three fundamental gait parameters (stride length, cadence, and gait speed), as indicated in Figure 2.1, make such training paradigms possible.

2.5 Rhythmic Auditory Stimulation

Striatal dopamine loss is present in PwPD and results in a reduced transfer of information to the basal ganglia, which leads to a diminished ability to detect movement cues (Muthukrishnan et al., 2019; Redgrave et al., 2010). This may worsen movement selection and sequencing resulting in gait impairments, as PwPD may be unable to execute movement successfully due to the lack of proprioceptive information (Muthukrishnan et al., 2019; Weiss et al., 2020). Cueing can serve as a stimulus to bypass the impaired internal timing present in PwPD (Ashoori et al., 2015). Cueing is defined as a mechanism of applying a spatial or temporal stimulus to facilitate initiating or maintaining motor activity and has been suggested to help with the initiation, amplitude, and timing of movement (Ashoori et al., 2015; Ginis et al., 2018; Nieuwboer et al., 2007). Auditory and visual cues are the most widely used to improve gait in PwPD. Most auditory cues are delivered as rhythmic auditory stimulation (RAS) using a metronome.

RAS is not a new concept and has been used during overground and treadmill gait training for over 20 years (Frazzitta et al., 2009; Harro et al., 2014; Murgia et al., 2018; Thaut et al.,

1996). Although the loss of automaticity and rhythmicity of movements is present, it seems PwPD are still able to synchronize their movements with external rhythmic cues through an innate internal timing process, referred to as rhythmic entrainment (Thaut et al., 2015). This process is thought to depend on the interaction of several structures of the subcortico-thalamo-cortical network, including cerebellum, basal ganglia, pre-supplementary and supplementary motor areas (Thaut et al., 1999). All of these areas are negatively affected by PD and contribute to the loss of normal rhythmic gait. Sound can increase a motor neuron's excitability, aiding in anticipatory motor control patterns in the brain and spinal cord and reducing the time for a muscle to activate a motor command (Forte et al., 2021). Brain imaging studies report rhythm perception can change the auditory-motor network (Koshimori and Thaut, 2018). The cyclic nature of RAS can help PwPD synchronize ground contact when walking and control variability in musculoskeletal activation patterns (Ford et al., 2010; Koshimori and Thaut, 2018).

RAS and Gait Training

Like gait training without RAS, the use of RAS during gait training has demonstrated increases in gait speed and step length, but findings are inconsistent (Howe et al., 2003; Morris et al., 1994; Murgia et al., 2018; Nieuwboer et al., 2007; Thaut et al., 2019). These interventions have used faster tempos, where the beats per minute (BPM) of the metronome or music depends on a person's cadence. A strategy of maintaining a step cadence that matches or exceeds a person's baseline value can be adopted to adjust the gait speed (Arias and Cudeiro, 2008; Ashoori et al., 2015; McIntosh et al., 1997). Because cueing faster tempos intends to alter cadence, gait speed can be increased without increasing step length. As mentioned above, increasing step length may be more critical for PwPD, and using RAS at a tempo at or above baseline may lead to even shorter steps (Morris et al., 1994; Morris et al., 1996).

It has recently been documented that a slower RAS frequency can increase step length during treadmill walking (Chawla et al., 2020). When walking at a tempo of 85% of baseline cadence, PwPD lengthened their average step length from 0.56 m to 0.61 m (Hoppe et al., 2020). RAS can help create predictable temporal (cadence) synchronization patterns between sensory input and motor output, making the anticipation of movement possible for PwPD. With a steady internal rhythm, PwPD can anticipate their next walking step and possibly replace their dysfunctional internal timing regulation (Forte et al., 2021). Among the limited gait training involving RAS, most of them adopted a faster tempo to increase gait speed to the detriment of cadence. Using a RAS tempo slower than baseline cadence may be a more effective method for increasing step length and possibly managing cadence, as a strategy to increase gait speed.

2.6 Falls in Parkinson's Disease

Postural instability is one of the cardinal signs of PD and is a very common and challenging symptom that can lead to falls. With an incidence rate of 40% - 70%, fall prevention is an urgent need for PwPD as falls can lead to physical injury, restrained mobility, and impaired ability to perform daily activities (Ashburn et al., 2008; Bloem et al., 2001; Hely et al., 2008). Further, more than 45% of these falls occur during ambulation or tasks of daily living (Ashburn et al., 2008). Because falls often lead to a fear of falling in the future, PwPD may restrict activities to avoid a potential fall leading to further deconditioning and limiting their quality of life (Adkin et al., 2003; Bloem et al., 2001).

Because postural stability does not respond well to anti-Parkinsonian medication, exercise interventions are necessary to improve postural instability and reduce falls in PwPD (Bronte-Stewart et al., 2002). A meta-analysis reported that exercise, including balance training, Tai Chi, and strength training, could reduce short-term and long-term fall rates in PwPD (Shen et

al., 2016; Simpkins and Yang, 2023). Most treadmill training research focuses on gait speed and step length, while limited studies have examined the effects of treadmill training on balance and falls in PwPD. For example, PwPD who participated in a treadmill training intervention in which they walked in 4 directions (forwards, backwards, and sideways) on a treadmill while supported by a safety harness showed improvements in balance and a significant reduction in falls two weeks after the end of the 8-week intervention period (Protas et al., 2005). In a separate study utilizing speed-dependent treadmill training during an 8-week intervention, PwPD exhibited improvements in the Berg Balance Test, Dynamic Gait Index, and Falls Efficacy Scale, though falls were not reported (Cakit et al., 2007).

Similarly, few studies have evaluated the effect of gait training with RAS on postural stability. When comparing speed-dependent treadmill training and overground RAS on balance function, both groups improved the Rapid Step-up Test and the Sensory Organization Test (evaluates postural sway) scores, suggesting a carryover effect of gait training on balance scores (Harro et al., 2014). In a different study that combined rhythmic auditory and visual stimulation during gait training, PwPD significantly increased gait velocity, step length, and Berg Balance Scores (Song et al., 2015). Although limited, these studies indicate that gait training can improve balance function and has the potential to reduce fall risk.

Feasible Stability Region

Stability requires continuous control of the body's center of mass (COM) relative to its base of support (BOS). Balance is preserved during a static task, like standing, when the COM's projection is confined within the BOS (Figure 2.2a) (Shumway-Cook and Horak, 1986). However, static stability limits do not apply to dynamic tasks (Yang, 2018). For example, during the early single stance phase of a gait cycle, the COM's projection on the ground is always behind or

outside the BOS, defined as the leading foot-ground contact area. According to the static stability limit concept, a person should encounter a backward balance loss in this scenario, which does not occur in reality. Therefore, a different metric must be utilized when considering dynamic conditions.

The Feasible Stability Region (FSR) theory simultaneously considers the COM position and velocity relative to the BOS (Pai and Patton, 1997; Yang et al., 2007). When the COM motion state (i.e., the combination of its position and velocity relative to the BOS) is within the FSR (Figure 2.2-b, point A), a person can maintain body balance without changing the BOS. When the COM motion state is below the FSR (Figure 2.2-b, point B), forward momentum is insufficient to move the COM over the BOS, leading to backward balance loss. When the COM motion state is above the FSR (Figure 2.2-b, point C), the COM has excessive forward momentum, which would carry the COM beyond the toe of the BOS. A forward recovery step is necessary to avoid falling forward.

Determined as the shortest distance from the COM's motion state to the lower limb of the FSR, dynamic gait stability (Figure 2.2-b, solid lines) has been used to quantify fall risk in both healthy and pathological populations during walking and sit-to-stand tasks under unperturbed or perturbed conditions (Ahn et al., 2024a; Ahn et al., 2024b; Ahn et al., 2022a; Ahn et al., 2022b; Ban et al., 2024; Bhatt et al., 2011; Bhatt et al., 2013; Kajrolkar et al., 2014; Lin et al., 2020; Liu and Yang, 2017; Mak et al., 2011; Shin et al., 2024; Simpkins et al., 2022; Simpkins and Yang, 2024; Wang et al., 2011; Yang et al., 2022; Yang et al., 2009; Yang and Liu, 2021; Yang and Pai, 2013; Yang and Pai, 2014; Yang et al., 2008; Yang et al., 2018; Yang et al., 2019). Dynamic gait stability has been closely related to the fall risk during walking in young and older adults compared with other stability measures (Yang et al., 2009; Yang and Pai, 2014).

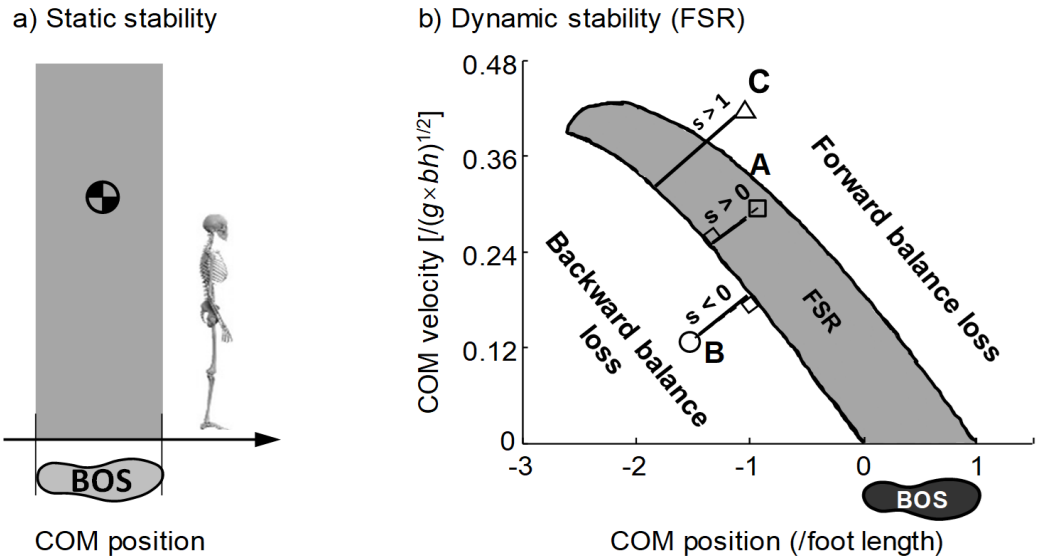


Figure 2.2 A depiction of a) static stability and b) dynamic stability based on the Feasible Stability Region (FSR) theory. Static stability limits are determined by the center of mass (COM) position relative to the base of support (BOS). Whenever the COM projection is within the BOS, a person is stable. The FSR simultaneously considers the COM position and velocity relative to BOS. The system's COM motion state's two components (i.e., its anteroposterior position and forward velocity) are calculated relative to the rear of the BOS (i.e., the leading heel) and normalized by foot length and $\sqrt{g \times bh}$, respectively, where g represents the acceleration due to gravity and bh the body height. For point A, the COM's motion state is within the boundaries of the FSR, and balance is maintained without changing the BOS. When the COM's motion state is below the FSR's bottom limit (point B), dynamic stability is negative, indicating an unstable state against experiencing a backward fall. When the COM's motion state is above the FSR's upper limit (point C), dynamic stability is greater than 1, indicating an unstable state against experiencing a forward fall (a trip). The dynamic gait stability value (s) is calculated as the shortest distance from the COM motion state to the bottom limit of the FSR.

2.7 Treadmill Intervention

It has been demonstrated that PwPD tend to present with a shuffling gait which looks like walking slower, with shorter steps and a higher cadence (Canning et al., 2006; Morris et al., 1996). Because pharmacological therapy can be less effective at improving gait deficits, cause side effects, and experience a low response rate, gait training is encouraged as a supplemental therapy to medication for PwPD (Lewitt, 2008; Rascol et al., 2000). RAS can help PwPD synchronize their ground contact to an external auditory cue, improving joint movements and

variability (Koshimori and Thaut, 2018). Previous RAS-based studies utilized a tempo at or above the baseline cadence to increase gait speed (Arias and Cudeiro, 2008; Ashoori et al., 2015; McIntosh et al., 1997). This method can increase cadence, without increasing step length to increase gait speed in a population that already undergoes an increased cadence.

In a recent case study involving three PwPD, Sherron, et al. proposed a gait training sequence that consisted of using RAS at a tempo slower than baseline cadence on the treadmill to promote longer step lengths, followed by RAS at a faster tempo than baseline during overground walking to promote faster walking speed (Sherron et al., 2020). This sequence resulted in all participants increasing gait speed and step length without significantly increasing cadence after the 6-week intervention. Consequently, using a metronome to modulate step length and treadmill speed to control gait velocity may be an effective method to maintain cadence while increasing step length and velocity during walking in PwPD (Figure 2.1). This project was dedicated to answering this question.

3 METHODOLOGY

3.1 Study Design

This pilot study was a randomized controlled trial investigating the acute effects of a treadmill intervention that controlled speed and cadence compared to speed alone on gait outcomes in PwPD. Participants were sex-matched and randomized into two groups: advanced and regular treadmill intervention groups. Participants in the advanced group walked on a treadmill for 30 minutes. Both treadmill speed and walking cadence were gradually adjusted to increase step length and gait speed. Cadence was controlled using a metronome, and the gait speed was controlled by the treadmill belt. The regular treadmill group followed the same procedures as the advanced treadmill group, except they did not listen to a metronome, and only the treadmill belt speed progressively increased. Immediately before, during, and after the treadmill intervention, overground walking was assessed.

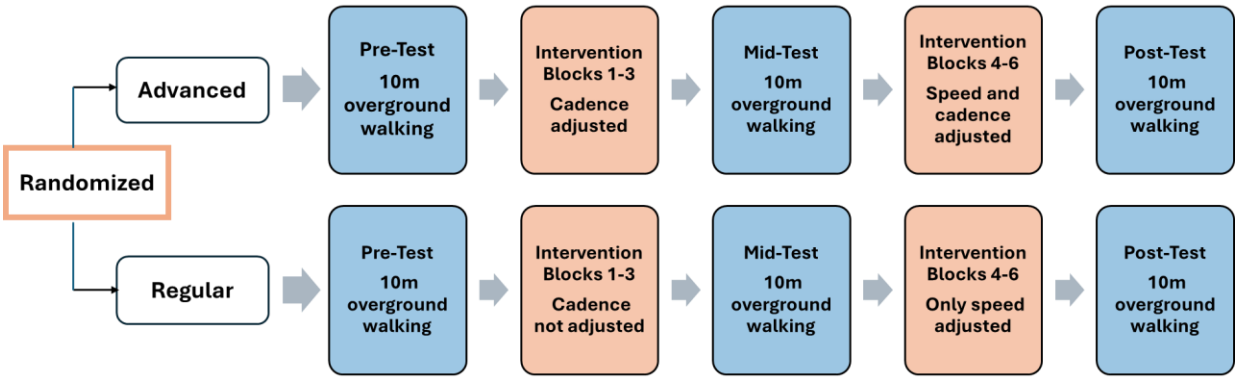


Figure 3.1 The schematic of the study design to test spatiotemporal, kinetic, and dynamic gait stability variables during overground walking at a self-selected speed before, during, and after a 30-minute treadmill walking intervention. For the advanced intervention, participants walked at the self-selected treadmill speed during blocks 1-3 while cadence was progressively decreased. During blocks 4-6, the cadence from block 3 was maintained and treadmill speed progressively increased. For the regular intervention, cadence was not controlled at all. During blocks 1-3, participants walked at their self-selected treadmill speed. During blocks 4-6, treadmill speed progressively increased. See Figures 3.4 and 3.5 for details on the schedule for adjusting the cadence and speed for both groups.

3.2 Participants

No restrictions were applied to the participants in terms of their sex, race, or ethnicity. However, the following inclusion criteria were implemented to ensure that this study examines characteristics of the targeted subset of PwPD and to control the excessive heterogeneity among the participants.

1) a PD diagnosis by a neurologist with a reported H&Y Stage between 1 and 3,
2) Aged 50 years and over,
3) a Parkinson's Disease Quality of Life Questionnaire - 8 score < 40 to ensure that participants had the physical and cognitive capabilities to complete the study (Jenkinson et al., 1997),
4) a Montreal Cognitive Assessment score > 23 to make sure that all participants could follow instructions throughout the study (Hoops et al., 2009),
5) the ability to walk at least 10 m overground and on a treadmill for at least 30 minutes without the use of a walking aid,
6) no known uncontrolled cardiorespiratory or metabolic disease,
7) no other neurologic disorders that can affect walking ability,
8) no visual or communication impairments, and
9) no history of lower extremity injury within the last six months.

By using the preliminary data from six PwPD (Appendix D), a power analysis (Appendix E) was conducted, which indicated that at least 15 PwPD per group were required to detect the difference in the stride length between groups with a statistical power of 0.80 at an alpha level of 0.05.

Participants were recruited from Atlanta, GA, and the surrounding area. Recruitment flyers were distributed to hospitals, gyms, PD support groups, rehabilitation centers, and senior

centers in the greater Atlanta area and via email to the community. The Georgia chapter of the Parkinson's Foundation was contacted for recruitment. The investigator also visited several of the above-mentioned facilities and participated in events organized for PwPD in the metro Atlanta area.

Seventy-five people expressed interest in participating in this study and were contacted to set up a phone screen. Among them, 19 were not reachable, and 56 PwPD were screened for eligibility to participate (Figure 3.2). Nine declined to participate after completing the phone screen, 10 were disqualified for not meeting inclusion criteria, and five did not follow up to schedule participation. Therefore, 32 PwPD were initially included in this study. After reading and signing an informed consent approved by the Institutional Review Board at Georgia State University (Approval protocol number: H22192), they were randomly assigned to either the advanced or control group based on pre-generated random numbers.

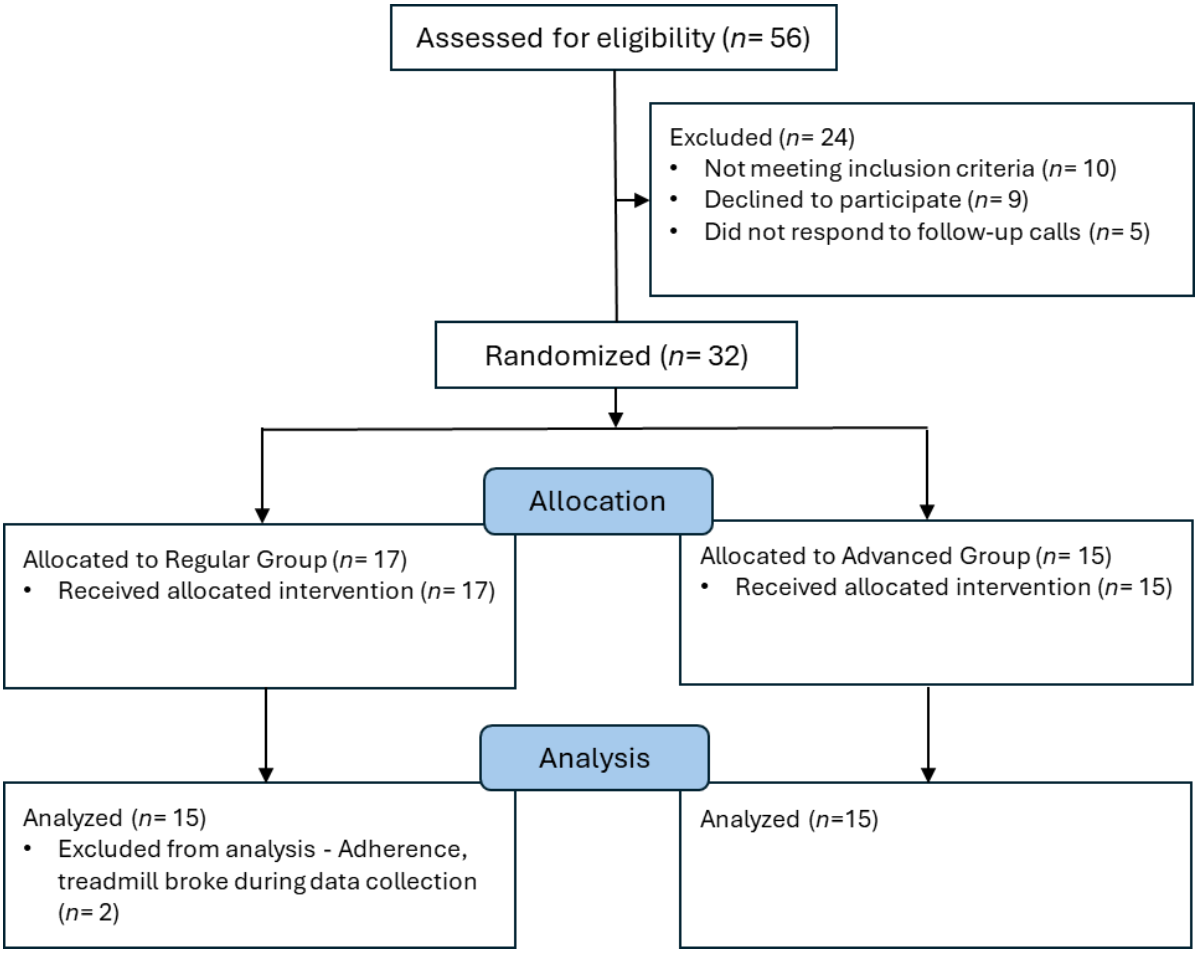


Figure 3.2 Flow chart of participant screening and recruitment. Seventy-five individuals showed interest in this study. However, 56 of them were able to be reached and assessed for eligibility.

Table 3.1 Comparisons of demographic information (mean ± standard deviation) between the advanced and regular intervention groups for 32 participants who were initially enrolled in this study. Independent *t*-test compared age, height, mass, Parkinson's Disease Quality of Life Questionnaire-8 (PDQ-8) scores, self-selected treadmill speed, and physical activity scores. The maximum score for physical activity level is 10. (A 0 indicates an inactive person and a 10 signifies a highly active person.) Mann-Whitney *U* test analyzed the Montreal Cognitive Assessment (MoCA) scores, Hoehn and Yahr (H&Y) stage, and disease duration. Fisher's exact test compared sex, medication status, and medication phase.

Parameter	**Group**		***p*-value**
	Advanced (n = 15)	Regular (n = 17)	
Age (years)	67.60 ± 4.66	67.53 ± 7.84	0.98
Height (m)	1.73 ± 0.09	1.72 ± 0.09	0.79
Mass (kg)	77.05 ± 11.60	80.47 ± 15.72	0.49
Sex (female/male)	3/12	3/14	1.00
MoCA (/30)	28.13 ± 1.55	27.29 ± 1.69	0.17
PDQ-8 (/100)	11.46 ± 7.11	13.17 ± 10.07	0.59
H&Y	1.53 ± 0.40	1.59 ± 0.40	0.82
Disease duration (years)	3.10 ± 2.78	3.41 ± 2.71	0.39
Medication (yes/no)	14/1	16/1	1.00
Phase (on/off)	14/1	15/2	1.00
Comfortable treadmill speed (*bh*/s)	0.57 ± 0.17	0.51± 0.17	0.33
Physical activity score* (/10)	8.75 ± 2.09	7.99 ± 2.06	0.21

*: Physical activity value was missing for 3 participants in the advanced group and 4 in the regular group.

3.3 Instruments

Motion Capture System

Kinematic data were collected using a 9-camera VICON motion capture system (VICON, Denver, CO, USA) sampling at a frequency of 100 Hz. The model used 26 reflective markers that were applied to the following body landmarks: vertex, ears, rear neck (C7), shoulders, right scapular, elbows, wrists, sacrum, greater trochanters, mid-thighs, knees, tibias, ankles, heels, and toes. The marker set was based on the Helen-Hayes marker set, which has been broadly used in the relevant research area (Tabakin, 2000). Markers were attached to the skin with double-sided tape. Vicon Nexus 2.11 software (Oxford Metrics, Oxford, UK) was used during the data

collection trials. All cameras were calibrated before each testing session to ensure accurate data collection.

Force Plates

Two in-serial AMTI force plates (Advanced Mechanical Technology Inc., Watertown, MA, USA) were used to collect GRFs during overground walking. Data were collected at a frequency of 1000 Hz. The GRF data was synchronized with the motion data through Vicon Nexus. The force plates are embedded in the middle section of a 10-m linear walkway, which is in the center of the capture volume of the motion capture system.

ActiveStep Treadmill

The ActiveStep treadmill (ActiveStep, Simbex, NH) was used for the treadmill intervention for both groups. Participants were fitted with a safety harness that was attached to an overhead arc from the shoulders via ropes. The length of the ropes was adjusted such that the harness did not provide body weight support or restrict movement. However, it provided necessary protection in case a loss of balance or fall occurred.

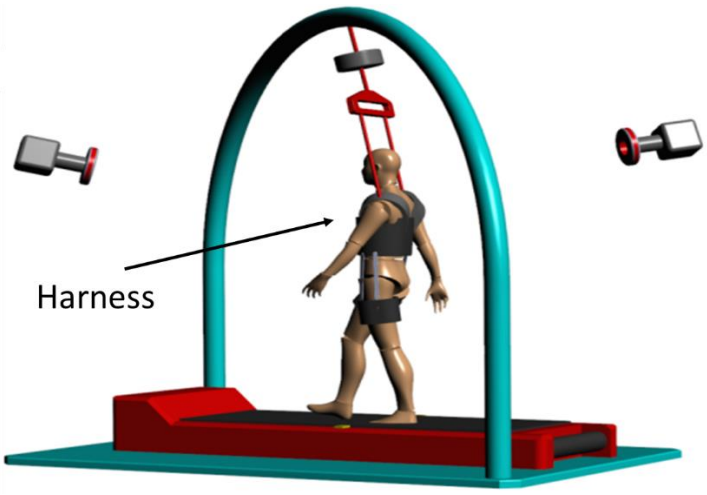


Figure 3.3 The ActiveStep treadmill used to deliver both the advanced and regular treadmill interventions. A full-body safety harness connected to an overhead arch via dynamic ropes

protected participants from loss of balance or falls without interfering with their movement on the treadmill.

3.4 Physical/Cognitive Functions Assessment Tools

Parkinson's Disease Quality of Life-8 Questionnaire (PDQ-8)

The PDQ-8 is a shortened version of the patient-reported 39-item Parkinson's Disease Questionnaire (PDQ-39) used to quantify the quality of life among PwPD (Peto et al., 1998). The PDQ-8 consists of one question from each of the domains of the PDQ-39 and has been reported as a reliable and valid alternative (Chen et al., 2017; Huang et al., 2011). The maximum score is 100. A higher score represents a poorer quality of life.

Montreal Cognitive Assessment

The Montreal Cognitive Assessment (MoCA) is a reliable, and well-validated screening tool to detect mild cognitive decline (Hoops et al., 2009). MoCA assesses short-term memory, visuospatial abilities, executive function, attention, concentration, working memory, language, and orientation to time and place (Nasreddine et al., 2005). The maximum score is 30, which indicates normal cognition. The MoCA has been widely used among PwPD (Hoops et al., 2009; Vásquez et al., 2019).

3.5 Procedures

All data collection took place in the Biomechanics Laboratory at Georgia State University. Prior to participant arrival, all the instruments and equipment, such as the motion capture system and AMTI force plates, were calibrated in order to ensure accurate data.

Screening Session

Phone-based screenings were first conducted with potential participants to determine eligibility for inclusion in the study. At the beginning of the phone screening, the investigator explained the purpose of this study, study procedures, and requirements for participation. The investigator also informed participants that participation is voluntary. If they were still interested in participating, each participant completed the PDQ-8 (Appendix B) and answered questions to ensure they met the inclusion criteria. Based on normative data for PwPD with an H&Y stage 1-3, those who scored above 40 were disqualified from participating to ensure that participants had the physical and cognitive capabilities to complete the study (Jenkinson et al., 1997). If the potential participant who passed the screening was still willing to participate in the study, they scheduled a time to come to the Biomechanics Laboratory for data collection.

Participation Preparation

When the participants came to the lab, the investigator explained the purpose and requirements of this study to them, followed by obtaining written consent from the participant. Then, they completed the MoCA (Appendix C). Those who scored below 23 on the MoCA were excluded to ensure that all participants could follow instructions throughout the study (Hoops et al., 2009).

Once the cognitive assessment was completed, anthropometric measurements were taken, including body height, body mass, ankle width, knee width, and inter-ASIS distance. Twenty-six reflective markers used for motion capture data collection were placed on bony landmarks using double-sided tape. All participants then completed a five-minute warm-up session on the treadmill.

Pre-Intervention Test

Participants walked on a 10-m linear walkway at their comfortable gait speed three times.

Intervention

Participants were then fitted with a safety harness and stepped on the ActiveStep treadmill (Simbex, NH, Figure 3.3). They began with a familiarization period that was also used to determine their self-selected treadmill walking speed. The self-selected treadmill speed and cadence were used to determine the parameters for the training protocol. All participants then completed an assigned 30-minute treadmill walking intervention.

Advanced Treadmill Group

Participants completed 30 minutes of treadmill walking broken down into six blocks of 5 minutes (Figure 3.4). During the first three blocks (blocks 1-3), an online metronome through a speaker was used as a rhythmic auditory cue for cadence. The participant was instructed to walk to the beat of the metronome. The cadence of the metronome was determined by the participant's self-selected treadmill walking cadence and progressively decreased by 5% each block or as tolerated. Gait speed was determined by the participant's self-selected speed on the treadmill and remained constant for the first three blocks. A 2-minute rest break occurred between each block pair.

During blocks 4-6, the metronome remained constant as determined by the 3rd block, and gait speed was progressively increased by 5% each block or as tolerated. Participants were given a 2-minute rest break between each block pair.

As mentioned above, participants were instructed to walk to the beat of the metronome. For each new cadence in blocks 1-3, participants were given about 30-60 seconds to familiarize themselves with the step frequency. If the participant visibly could not walk to the beat, or they

indicated walking at the cadence was too uncomfortable, the cadence was adjusted. Similarly, for blocks 4-6, participants were given 30-60 seconds to familiarize themselves with the new treadmill speed. If the participant could not continue walking at the cadence with the new treadmill speed, the treadmill speed was adjusted so the participant could maintain the desired step frequency.

If not all participants were able to comply with intervention parameters, a sub-analysis was conducted to examine any differences in the primary gait parameters (cadence, gait speed, and stride length) between participants who were able to complete the intervention as intended versus those who could not. Such comparisons may provide insight into how the intensity of the intervention parameters influence post-assessment overground walking.

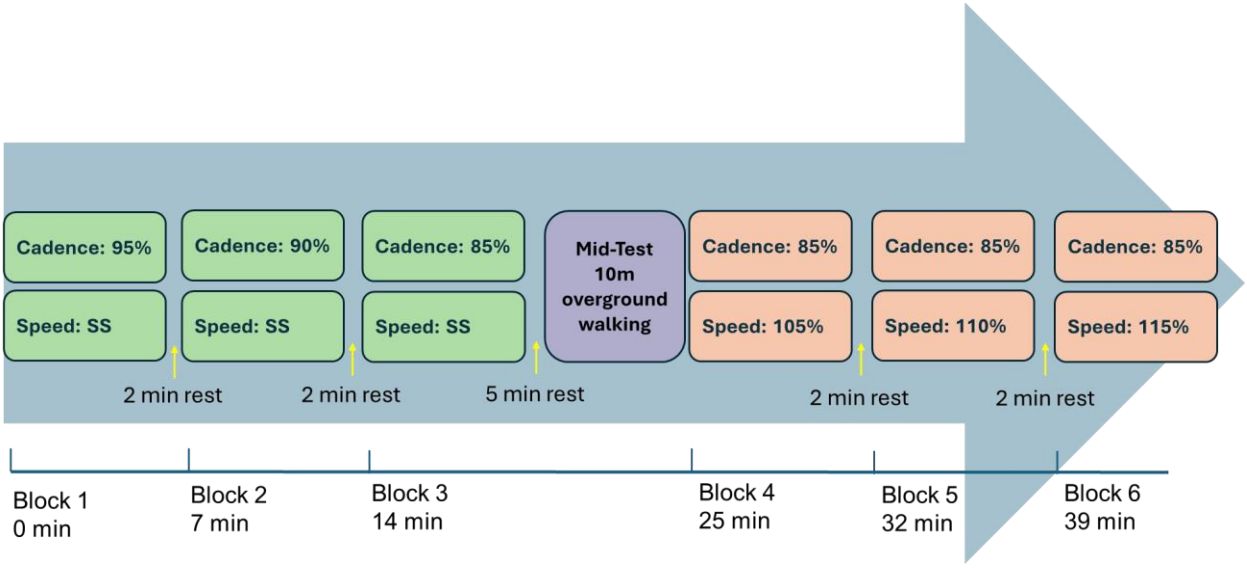


Figure 3.4 A flow chart of the advanced group. After determining their self-selected speed and cadence on the treadmill, each participant completed 30 minutes of treadmill walking broken down into six 5-minute blocks. Blocks 1-3: participants walked at their self-selected (SS) speed while cadence, controlled by a metronome, decreased by 5%, or as tolerated, each block. Blocks 4-6: Participants maintained the cadence from block 3, while gait speed progressively increased by 5%, or as tolerated, in each block. A 2-minute rest break was given between each pair of blocks except for blocks 3 and 4 which were about 6 minutes apart due to the 5-minute rest time following block 3 and the about 1-minute mid-point gait assessment.

Regular Treadmill Group

Participants in the regular treadmill group also completed 30 minutes of treadmill walking broken down into six 5-minute blocks (Figure 3.5). During blocks 1-3, participants walked at their self-selected speed (the cadence was not controlled). Throughout blocks 4-6, treadmill speed was incrementally increased by 5% each block, or as tolerated, and participants continued to walk at their self-selected cadence. A 2-minute rest break separated each block.

During blocks 3-6, participants were given 30-60 seconds to familiarize themselves with the new treadmill speed. If participants said it was too fast to maintain for the 5-minute block, the speed was adjusted.

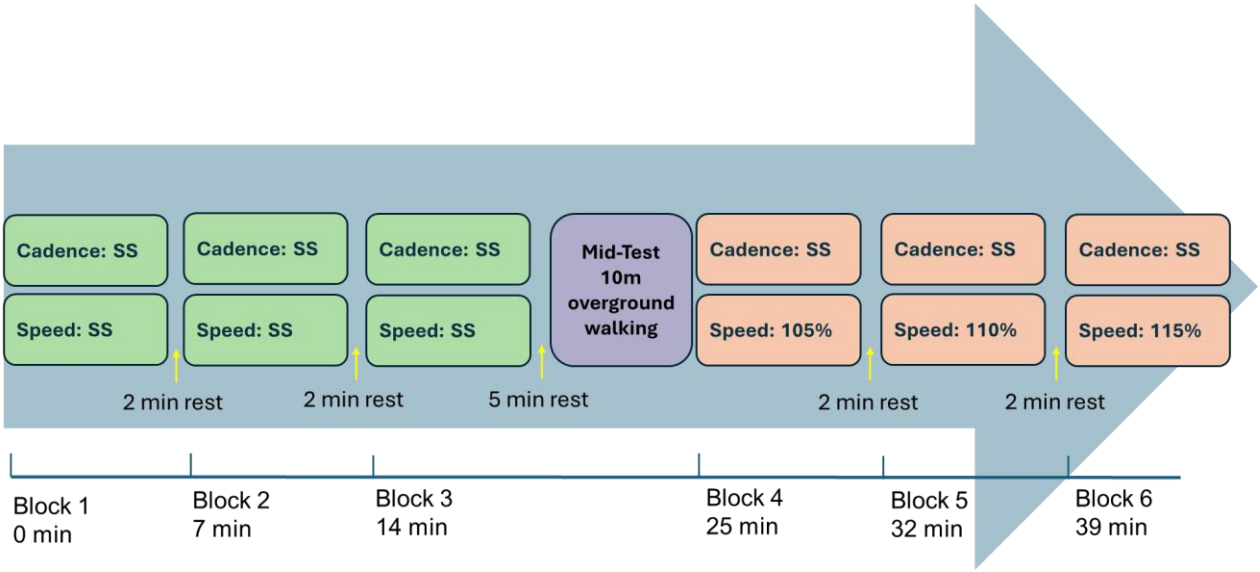


Figure 3.5 A flow chart of the regular group. Each participant in the regular treadmill group completed six 5-minute treadmill walking blocks for a total of 30 minutes. Blocks 1-3: participants walked at their self-selected (SS) speed. Blocks 4-6: Participants continued to walk while treadmill speed progressively increased by 5%, or as tolerated, in each block. Participants walked at their self-selected cadence. A 2-minute rest break was given between each pair of blocks except for blocks 3 and 4 which were about 6 minutes apart due to the 5-minute rest time following block 3 and the about 1-minute mid-point gait assessment.

Mid-Intervention Test

Immediately after block 3, the safety harness was removed, and participants rested for five minutes to reduce any inertial effects of the treadmill. Participants then walked on the 10-m linear walkway at their comfortable gait speed three times. The safety harness was re-fitted, and the participants completed the remainder of the treadmill intervention.

Post-Intervention Test

Upon completing the intervention, subjects rested for five minutes to reduce the inertial effects of the treadmill. All participants completed three more overground walking trials, following the same procedure as the pre- and mid-intervention tests.

3.6 Data Processing and Reduction

Vicon Nexus (Oxford Metrics, Oxford, UK) was used to collect the full-body kinematics and kinetics during overground walking before and after the intervention session. Marker paths and ground reaction force were low-pass filtered using fourth-order, zero lag, Butterworth filters with a frequency ranging from 4.5 to 9 Hz (determined by the residual analysis) and 30 Hz, respectively (Winter, 2009). Locations of joint centers, heels, and toes were computed from the filtered marker positions (Pai et al., 2006; Vaughan et al., 1992). The body's center of mass (COM) position was computed using gender-dependent segmental inertial parameters (Yang et al., 2019). COM's instantaneous velocity was determined as the first-order derivative of COM position with respect to time. The two transitional gait events, touchdown (TD) and liftoff (LO), were determined based on the foot kinematic data for as many steps as possible on each trial (Ahn et al., 2022a; Yang et al., 2012). The following three categories of outcome measures were determined based on the body kinematics and GRF data for all walking trials during the three (pre-intervention, midpoint, and post-intervention) assessment sessions.

Outcome Variables

Stride length was the *primary* outcome measure as it not only reflects the quality of gait but is related to the risk of falls (Espy et al., 2010a; Espy et al., 2010b) (Figure 3.6-a). It was measured as the anteroposterior distance between ipsilateral heel markers at two consecutive touchdowns and was normalized to body height (*bh*).

The *secondary* outcome variables included the following spatiotemporal and kinetic gait parameters: gait speed, cadence, single leg stance time, double leg stance time, peak vertical and anteroposterior GRF, braking and propulsive impulses, and rate of loading. Gait speed was determined as the average value of the instantaneous COM velocity over the middle 5-meter region of the walkway to eliminate the accelerating and decelerating effects. It was also normalized by *bh.* Stride time (s) was calculated as the time elapsed between consecutive touchdowns on the same side. Cadence (steps/min) was calculated by the following equation:

$$\text{Cadence} = 1/\text{stride time} \times 120 \qquad \text{(Eq. 1)}$$

Single leg stance time (s) was determined as the time between touchdown and toe-off for each respective limb. Double leg stance time (s) was defined as the time over which both limbs are in contact with the ground. As many as possible single stance and double stance phases were identified for each trial. The average value for all identified single and double stance phases over the three trials was computed.

Peak vertical and anteroposterior GRF were respectively determined as the maximum value of the vertical, anterior, and posterior components of GRF (Figure 3.6-a, b). Braking and

propulsive impulses were calculated by integrating GRF over the braking and propulsive phases, respectively (Figure 3.6-a). The rate of loading was calculated as the slope of the vertical GRF from TD to the first peak vertical GRF during the loading phase (Ahn et al., 2022a) (Figure 3.6-b). The GRF-related measurements were normalized to the body weight (*bw*).

Two components of the COM motion state (position and velocity) were calculated relative to the rear of the BOS and normalized by the foot length and $\sqrt{g \times bh}$, respectively, where g is the gravitational acceleration (Yang, 2018; Yang et al., 2008). Dynamic gait stability, serving as the *tertiary* outcome measure, was calculated as the shortest distance from the COM motion state to the lower boundary of the FSR (Figure 2.1). Given that both the COM position and velocity are normalized, dynamic gait stability is a unitless metric. Dynamic gait stability was first calculated for all valid TDs and LOs within each walking trial (Figure 3.6-b). This procedure was repeated for all trials, and the average value over all TDs or LOs across the three trials was calculated for analysis.

To further quantify the effects of each intervention program and compare the intervention-induced alterations in outcome measures between groups, the changes from pre-intervention to post-intervention assessment for the outcome measures were also calculated.

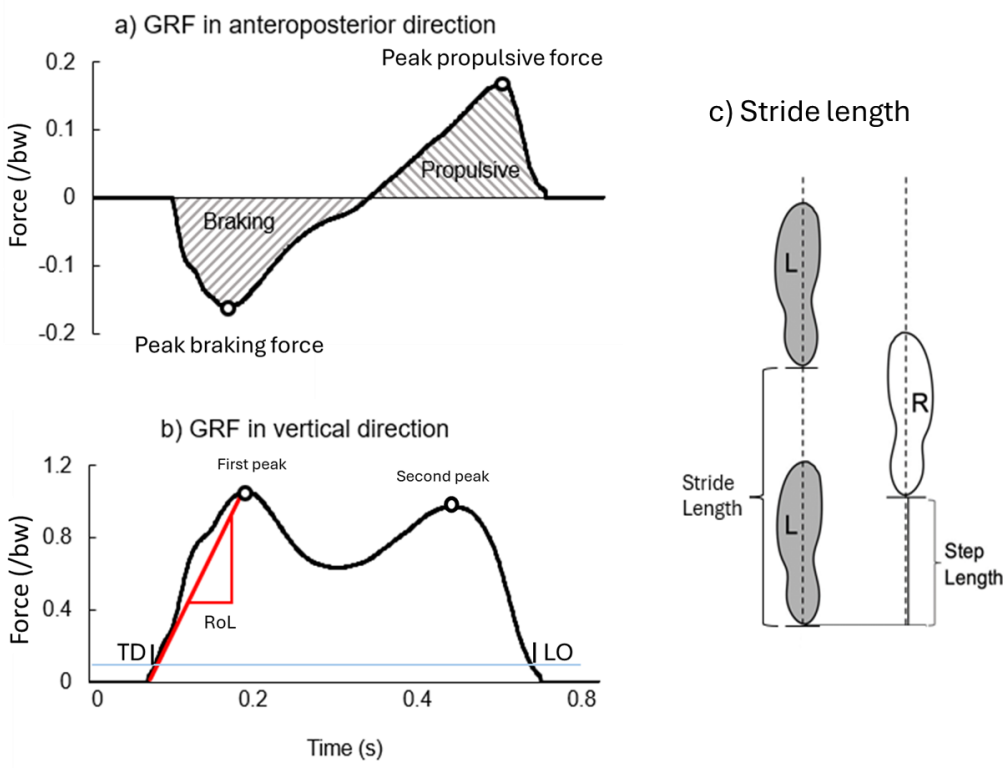


Figure 3.6 Representation of the a) ground reaction force (GRF) in the anteroposterior, b) GRF in the vertical direction, and c) stride length measured as the anteroposterior distance between ipsilateral heel markers at two consecutive touchdowns. Peak braking force, peak propulsive force, and peak vertical GRF were determined as the maximum values in the anterior, posterior, and vertical components of GRF (open circles). The braking impulse is the area enclosed above the GRF curve and below the time axis. The propulsive impulse is the area enclosed above the time axis and below the GRF curve. The rate of loading (RoL, red line) was calculated as the slope of the vertical GRF from touchdown (TD) to the first peak of vertical GRF during the loading phase. TD is the impact between the heel and the ground and liftoff (LO) is identified as terminal contact between the foot and the ground. Both events are determined by a threshold of greater or less than 10 N at TD and LO events (Yang et al., 2012) as shown as a horizontal line in b).

3.7 Statistical Analyses

Normality and homogeneity of variance were checked before analyses for all continuous variables (demographic parameters, disease information, outcome measures, change in outcome measures) with Shapiro-Wilk and Levene's tests, respectively. Variables that were not normally distributed were transformed as needed depending on the skew direction and the normality was rechecked. For variables that continued to violate the normality and variance assumptions

following transformation, non-parametrical approaches were used.

For demographic parameters, disease information, and change in outcome measures, two-tailed independent *t*-tests and Fisher's exact tests were used to compare the two groups. The Mann-Whitney *U* test was used for variables that could not be corrected by transformation.

A mixed model analysis of variance (ANOVA) was used to test all hypotheses, particularly for the normally distributed variables. Specifically, the ANOVA model analyzed all three categories of outcome measures (*primary*: stride length; *secondary*: gait speed, cadence, step times, peak vertical GRF, peak anteroposterior GRF, braking impulse, propulsive impulse, rate of loading; and *tertiary*: dynamic gait stability) to identify the influence of advanced and regular treadmill interventions on overground gait measures. The within-subject factor was the session (pre-intervention vs. post-intervention gait assessment), and the between-subject factor was the group (advanced vs. regular treadmill intervention). The appropriate planned post-hoc tests (either independent *t*-test or paired *t*-test) followed significant interaction or main effects. For variables that violated the normality or variance assumptions, a Generalized Estimating Equation (GEE) model was used for statistical analysis. The corresponding non-parametric independent *t*-test (Mann-Whitney *U*) and dependent *t*-test (Wilcoxon Signed Rank test) were used for analysis.

To show the magnitude of the difference between groups, the effect size was calculated for each variable. Cohen's *d* was used for the *t*-tests' effect size. The original effect sizes from the repeated-measures ANOVA (partial η^2), GEE (φ), Mann-Whitney test ($r = \frac{Z-statistic}{\sqrt{sample\ size}}$), and Wilcoxon Signed Rank test ($r = \frac{Z-statistic}{\sqrt{sample\ size}}$) were converted to Cohen's *d*. For tests involving repeated measures, the conversion used a pooled standard deviation, controlling for the intercorrelation of both groups (Lakens, 2013). Effect sizes were interpreted as small ($0.2 \leq d < 0.5$), medium ($0.5 \leq d < 0.8$), or large ($d \geq 0.8$) (Sullivan and Feinn, 2012). The 95% confidence

intervals (95% CI) for Cohen's *d* were also calculated. A priori alpha level of ≤ 0.05 was set to determine statistical significance for all statistical analyses. All statistical analyses were performed using the IBM SPSS 29.0 (IBM Corp., Armonk, NY) software package.

4 RESULTS

4.1 Participant Demographics

Thirty-two qualified participants with PD were enrolled in this study. Participants were randomly assigned to either the advanced or regular treadmill intervention group (Figure 3.2). Two participants were excluded from the analysis. For one participant, the treadmill stopped working and the participant did not complete the intervention. The other participant mistakenly and accidentally walked at their fastest speed even though this participant was told to walk at normal speed. For these two participants, their data was not used in the analysis. Therefore, thirty participants (15 in the advanced group and 15 in the regular group) completed all pre-intervention and post-intervention overground walking trials, and their data were analyzed.

Among them, twenty-one participants (advanced group: $n = 10$; regular group: $n = 11$) completed the mid-intervention overground walking trials. This portion of the procedures was added after some participants had completed data collection. Due to the uneven number of participants who underwent the mid-point assessment, the mid-intervention test was not included in the statistical analysis of the main text. However, their values and statistical analyses are provided in the appendix.

There were no significant group-related differences for sex ($p = 1.00$), age ($p = 0.69$), body height ($p = 0.95$), and body mass ($p = 0.47$), Table 4.2). Similarly, there were no group-related differences in MoCA ($p = 0.22$) and PDQ-8 ($p = 0.64$) scores. Disease duration ($p = 0.40$) and H&Y stage ($p = 0.78$) were also comparable between groups. It has been reported that the effects of rhythmic auditory cueing do not depend on dopaminergic medication (Ghai et al., 2018). Therefore, the “on” and “off” state of the medication was not controlled.

All participants were able to complete the treadmill intervention without adverse effects, discomfort, or injury. Although a majority of the participants were able to tolerate the changes in

the cadence and speed, some of them could not reach the expected 15% decrease in the cadence and/or 15% increase in the speed (Table 4.1). In the advanced group, 8 participants decreased their cadence by 15%, while the other 7 participants decreased their cadence by 10-14% during the intervention (Table 4.1). Seven participants increased the treadmill speed by 15%, 6 increased the treadmill speed by 10-14%, and 2 participants increased the treadmill speed by 8%. All participants in this group also successfully stepped to the beat of the metronome and controlled their cadence as expected during the training. In the regular group, 11 participants increased their speed by 15%, while the other 4 participants increased their treadmill speed by 12%.

Table 4.1 Actual total adjustments of the cadence and speed for participants in the advanced (n = 15) and regular (n = 15) groups for the treadmill intervention during the experiment. Speed values for both groups are the total percentage increase from block 3 to block 6 for both groups. Cadence values are the total percentage decrease from block 1 to block 3 for the advanced group.

Participant	Advanced		Regular
	Cadence (reduction)	Speed (increase)	Speed (increase)
1	15%	15%	15%
2	15%	10%	15%
3	12%	8%	15%
4	15%	13%	15%
5	15%	15%	15%
6	15%	15%	15%
7	15%	12%	15%
8	12%	15%	12%
9	15%	13%	15%
10	12%	8%	12%
11	15%	15%	12%
12	14%	15%	15%
13	12%	15%	12%
14	10%	10%	15%
15	14%	12%	15%

Table 4.2 Comparisons of demographic information (mean ± standard deviation) between the advanced and regular intervention groups for 30 participants whose data were included in the final analyses. Independent *t*-test compared age, height, mass, Parkinson's disease Quality of Life Questionnaire-8 (PDQ-8) scores, and physical activity scores. The maximum score for physical activity level is 10. (A 0 indicates an inactive person and a 10 indicates a highly active person.) Mann-Whitney *U* test analyzed the Montreal Cognitive Assessment (MoCA) scores, Hoehn and Yahr (H&Y) stage, and disease duration. Fisher's exact test compared sex, medication status, and medication phase.

Parameter	**Group**		***p*-value**
	Advanced (n = 15)	Regular (n = 15)	
Age (years)	67.60 ± 4.66	66.67 ± 7.63	0.69
Height (m)	1.73 ± 0.09	1.73 ± 0.09	0.95
Mass (kg)	77.05 ± 11.60	80.94 ± 16.74	0.47
Sex (female/male)	3/12	2/13	1.00
MoCA (/30)	28.13 ± 1.55	27.33 ± 1.76	0.22
PDQ-8 (/100)	11.46 ± 7.11	13.05 ± 10.75	0.64
H&Y stage	1.53 ± 0.40	1.60 ± 0.43	0.78
Disease duration (years)	3.10 ± 2.78	3.40 ± 2.89	0.40
Medication (yes/no)	14/1	15/0	1.00
Phase (on/off)	14/1	14/1	1.00
Physical activity score* (/10)	8.75 ± 2.09	7.99 ± 2.06	0.21

*: Data is missing for 3 participants in the advanced group and 2 in the regular group.

4.2 Primary Outcome (Stride Length)

Results of a mixed ANOVA displayed a significant group by time interaction effect on the stride length (p = 0.02, d = 0.7, 95% CI: [-0.01, 1.48], Figure 4.1). Both groups took a longer step after the intervention compared to before the intervention (advanced group: p <0.001, d = 3.7, 95% CI: [2.86, 4.53]; regular group: p = 0.002, d = 0.92, 95% CI: [0.16, 1.67], Figure 4.1). However, the increase in the stride length from the pre-intervention to post-intervention assessment among the advanced group (0.064 ± 0.036 *bh*) was significantly longer than in the regular group (0.032 ± 0.033 *bh*, p = 0.04, d = 0.78).

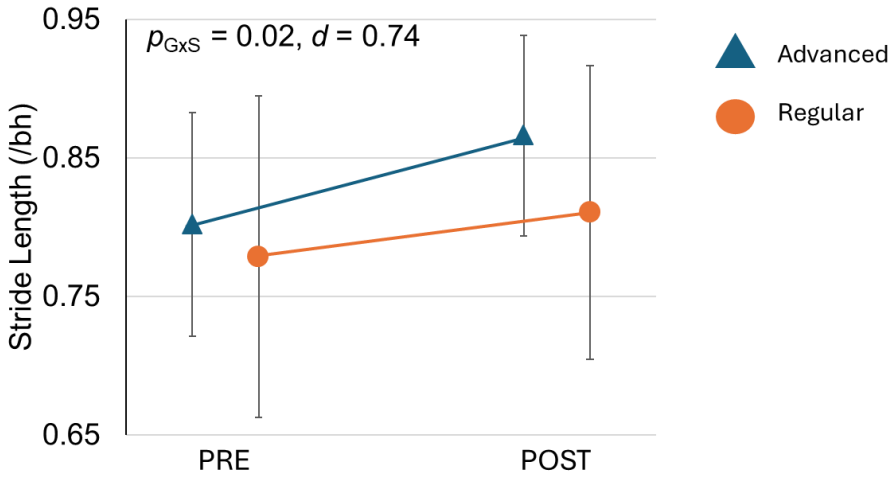


Figure 4.1 Comparison (group mean ± standard deviation) of stride length (normalized to body height, *bh*) during overground walking at a self-selected speed before (Pre) and after (Post) completing a 30-minute treadmill intervention between the advanced (n = 15) and regular (n = 15) groups. The p-value of the group by session interaction effect is reported ($p_{G\times S}$). The effect size is provided as Cohen's d.

4.3 Secondary Outcomes (Spatiotemporal and Kinetic Gait Parameters)

4.3.1 Spatiotemporal Gait Parameters

Double leg stance time violated the assumption of normality and could not be corrected by transformation. Therefore, a GEE was used to analyze the presence of an interaction and main effects. Mann-Whitney U test and Wilcoxon Signed Rank test were used as post-hoc tests.

During overground walking at participants' preferred walking speed, cadence showed a significant main effect for the session (p = 0.008, d = 1.03, 95% CI: [0.52, 1.55], Figure 4.2-a), but not a significant group main effect (p = 0.68, d = 0.15, 95% CI: [-0.57, 0.86], Figure 4.2-a) or interaction effect (p = 0.14, d = 0.51, 95% CI: [-0.17, 1.29], Figure 4.2-a). The advanced group took more steps after the intervention compared to before the intervention (p = 0.004, d = 2.47, 95% CI: [1.74, 3.24], Figure 4.2-a), while there was no significant difference from pre- to post-intervention in the regular group (p = 0.42, d = 0.33, 95% CI: [-0.39, 1.04], Figure 4.2-a).

Gait speed displayed a significant group by session interaction ($p = 0.05$, $d = 0.74$, 95% CI: [-0.01, 1.48], Figure. 4.2-b). Both groups increased their walking speed from pre- to post-intervention (advanced group: $p < 0.001$, $d = 2.89$, 95% CI: [2.09, 3.69], Figure 4.2-b; regular group: $p = 0.01$, $d = 1.56$, 95% CI: [0.83, 2.3], Figure 4.2-b). However, the increase in the gait speed from the pre-intervention to post-intervention assessment among the advanced group (0.09 ± 0.06 *bh/s*) was not statistically larger than the regular group (0.04 ± 0.06 *bh/s*, $p = 0.09$, $d = 0.63$).

For single leg stance time, there was no significant group by session interaction effect ($p = 0.9$, $d = 0.04$, 95% CI: [-0.67, 0.76], Figure 4.2-c). Both groups spent the same amount of time in single leg stance after the intervention compared to before the intervention (advanced group: $p = 0.87$, $d = 0.00$, 95% CI: [-0.72, 0.72], Figure 4.2-c; regular group: $p = 0.70$, $d = 0.23$, 95% CI: [-0.49, 0.94], Figure 4.2-c). Change scores for the single leg stance phase were similar between groups (advanced group: 0.001 ± 0.02s; regular group: 0.002 ± 0.02s; $p = 0.90$, $d = 0.05$).

Double leg stance time displayed a significant group by session interaction ($p = 0.04$, $d = 0.32$, 95% CI: [-0.40, 1.05], Figure 4.2-d). From pre- to post-intervention, the advanced group significantly reduced the amount of time spent in double leg stance ($p = 0.003$, $d = 0.99$, 95% CI: [-0.74, 2.26], Figure 4.2-d) while there was no difference for the regular group ($p = 0.23$, $d = 0.66$, 95% CI: [-0.06, 1.39], Figure 4.2-d). Although the double leg stance time was comparable between the two groups before the intervention ($p = 0.94$), the advanced group exhibited a significant reduction in double stance time after the intervention than those in the regular group ($p = 0.03$). As such, the advanced group significantly reduced the amount of time spent in double leg stance (-0.018 ± 0.017s) compared to the regular group (-0.006 ± 0.015s, $p = 0.049$, $d = 0.75$).

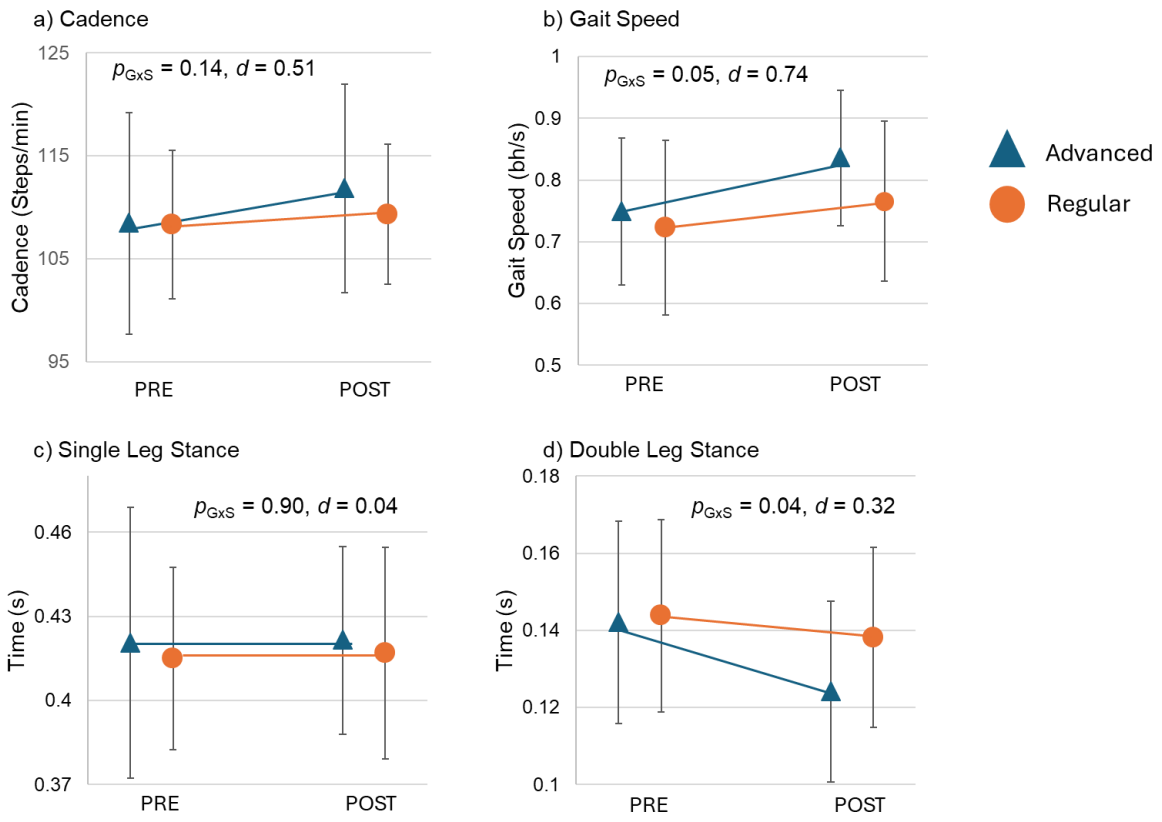


Figure 4.2 Comparison (group mean ± standard deviation) of the a) cadence, b) gait speed (normalized to body height, *bh*), c) single leg stance time, and d) double leg stance time during overground walking at a self-selected speed before (Pre) and after (Post) completing a 30-minute treadmill intervention between the advanced (n = 15) and regular (n = 15) groups. The p-value of the group by session interaction effect is reported ($p_{G\times S}$). The effect size is also provided as Cohen's d.

4.3.2 Kinetic Gait Parameters

Thiry participants (15 per group) completed all overground walking trials during the pre- and post-intervention assessments. Of these participants, two did not produce a clean landing on the force plate (1 per group) during any post-intervention overground walking trials. Thus, the kinetics results represent data from 14 participants from either group. Because there were no statistical differences between the left and right sides for any of the variables ($p \geq 0.44$ for all variables), the results reported here reflect the average of the left leg and right leg across the trials. The first and second peak vertical GRFs and peak propulsive force did not meet the normality

and/or variance assumptions and could not be corrected by transformation. Therefore, they were analyzed by using a GEE model to detect the group or session main effect and the interaction effect. The Mann-Whitney *U* test and Wilcoxon Signed Rank tests followed as post-hoc tests.

The first peak vertical GRF displayed a significant group by session interaction effect ($p = 0.04$, $d = 0.71$, 95% CI: [-0.16, 1.38], Table 4.3). The advanced group significantly increased first peak vertical GRF ($p = 0.01$, $d = 0.83$, 95% CI: [0.72, 2.21], Table 4.3) from the pre-intervention to the post-intervention test while no difference in the regular group ($p = 0.36$, $d = 0.36$, 95% CI: [0.08, 1.53], Table 4.3) was spotted from pre- to post-walking intervention. Additionally, the advanced group displayed a significantly larger increase in the first peak vertical GRF resulting from the intervention (0.06 ± 0.07 *bw*) compared to the regular group (0.02 ± 0.05 *bw*, $p = 0.04$, $d = 0.82$).

A significant group main effect was seen for the second peak vertical GRF ($p = 0.04$, $d = 0.39$, 95% CI: [-0.42, 1.08], Table 4.3) without a significant interaction effect ($p = 0.21$, $d = 0.24$, 95% CI: [-0.3, 1.22], Table 4.3) or session main effect ($p = 0.26$, $d = 0.48$, 95% CI: [-0.28, 1.25], Table 4.3). The second peak vertical GRF was similar between the two groups before the intervention ($p = 0.30$) and the advanced group exhibited a significantly larger second peak vertical GRF than their peers in the regular group ($p = 0.01$, $d = 0.17$, 95% CI: [-0.84, 1.19]). The change score in the second peak vertical GRF was comparable between groups (advanced group: 0.02 ± 0.05 *bw*; regular group: 0.001 ± 0.05 *bw*, $p = 0.26$, $d = 0.43$).

Results did not show a significant interaction effect for the rate of loading during overground walking ($p = 0.53$, $d = 0.24$, 95% CI: [-0.51, 0.98], Table 4.3). Neither group ($p = 0.14$, $d = 0.45$, 95% CI: [-0.25, 1.2], Table 4.3) nor session main effect ($p = 0.052$, $d = 0.71$, 95% CI: [0.19, 1.22], Table 4.3) was significant. Additionally, the rate of loading change scores did not

differ between groups (advanced group: 0.79 ± 1.91 *bw*/s; regular group: 0.34 ± 1.14 *bw*/s, p = 0.31, d = 0.40).

While the peak braking force did not display a significant group by session interaction effect (p = 0.08, d = 0.7, 95% CI: [-0.07, 1.46], Table 4.3) or group main effect (p = 0.16, d = 0.49, 95% CI: [-0.23, 1.22], Table 4.3), the session main effect was significant ($p < 0.001$, d = 1.17, 95% CI: [0.65, 1.7], Table 4.3). Planned post-hoc *t*-tests were conducted to determine the time course for each group. The advanced group significantly increased the peak braking force (p = 0.002, d = 1.53, 95% CI: [0.76, 2.29], Table 4.3) from the pre-intervention to the post-intervention test yet the regular group did not (p = 0.15, d = 0.89, 95% CI: [0.17, 1.62], Table 4.3). The alteration in the peak braking force from pre- to post-intervention assessment among the advanced group (0.03 ± 0.03 *bw*) was not significantly different from in the regular group (0.01 ± 0.03 *bw*, p = 0.12, d = 0.62).

The peak propulsive force displayed a significant session main effect ($p < 0.001$, d = 1.37, 95% CI: [0.85, 1.89], Table 4.3), but not a significant group by session interaction effect (p = 0.17, d = 0.44, 95% CI: [-0.32, 1.2], Table 4.3) or group main effect (p = 0.07, d = 0.35, 95% CI: [-0.4, 1.11], Table 4.3). Post-hoc *t*-tests revealed propulsive force significantly increased in the advanced group (p = 0.003, d = 1.17, 95% CI: [1.29, 2.84], Table 4.3) resulting from the intervention. However, the change in the peak propulsive force from the pre-assessment to the post-assessment test was not significant for the regular group (p = 0.14, d = 0.48, 95% CI: [0.24, 1.69], Table 4.3). The increase in the propulsive force from before to after the intervention for the advanced group (0.02 ± 0.02 *bw*) was not significantly larger than in the regular group (0.01 ± 0.03 *bw*, p = 0.18, d = 0.53).

Braking impulse did not display a significant interaction effect (p = 0.19, d = 0.5, 95% CI: [-0.25, 1.22], Table 4.3), session main effect (p = 0.14, d = 0.32, 95% CI: [-0.19, 0.83], Table 2), or group main effect (p = 0.46, d = 0.33, 95% CI: [-0.39, 1.05], Table 4.3). From pre- to post-intervention, neither group displayed a significant increase in the braking impulse (advanced group: 0.002, 0.01 *bw·s*; regular group: 0.00 ± 0.004 *bw·s*, p = 0.11, d = 0.63).

For propulsive impulse, a significant session effect was reported (p = 0.001, d = 1.25, 95% CI: [0.73, 1.78], Table 4.3) but not a significant group by session interaction (p = 0.63, d = 0.19, 95% CI: [-0.56, 0.93], Table 4.3) or a significant group main effect (p = 0.3, d = 0.49, 95% CI: [-0.23, 1.22], Table 4.2). Post-hoc *t*-tests showed the advanced group increased their propulsive impulse (p = 0.003, d = 1.54, 95% CI: [0.75, 2.33], Table 4.3) significantly from the pre- to post-intervention test. On the other hand, the regular group did not show a significant change in the propulsive impulse between the test sessions (p = 0.08, d = 0.8, 95% CI: [-0.08, 1.52], Table 4.3). In addition, the change score was comparable between the two groups (advanced group: 0.003 ± 0.003 *bw·s*; regular group: 0.002 ± 0.01 *bw·s*, p = 0.69, d = 0.15).

Table 4.3 Comparison of kinetic variables during overground walking at a self-selected speed presented as group mean ± standard deviation before (Pre) and after (Post) a 30-minute treadmill walking intervention for the advanced (ADV, n = 14) and regular (REG, n = 14) groups. The Generalized Estimating Equation (GEE) or the Analysis of Variance (ANOVA) with repeated measures were used. Effect sizes (Cohen's d) and 95% Confidence Intervals (95% CI) of the effect size are provided.

Variable	Group	Session		Group × session interaction		Group main effect		Session main effect	
		Pre	Post	F/χ^2, p-value	d [95% CI]	F/χ^2, p-value	d [95% CI]	F/χ^2, p-value	d [95% CI]
First Peak vGRF	ADV	1.20 ± 0.13	1.27 ± 0.12	**4.25, p = 0.04**	0.66[-0.16, 1.38]	2.39, p = 0.12	0.41[-0.35, 1.16]	**12.38, p < 0.001**	0.16[-0.58, 0.91]
(*bw*)†	REG	1.16 ± 0.11	1.17 ± 0.11						
Second Peak	ADV	1.07 ± 0.08	1.10 ± 0.08	1.59, p = 0.21	0.46[-0.30, 1.22]	**4.16, p = 0.04**	0.33[-0.42, 1.08]	1.26, p = 0.26	0.48[-0.28, 1.23]
vGRF (*bw*)†	REG	1.04 ± 0.07	1.04 ± 0.03						
Rate of Loading	ADV	8.83 ± 2.45	9.92 ± 1.75	0.40, p = 0.53	0.24[-0.51, 0.98]	2.36, p = 0.14	0.48[-0.23, 1.20]	**4.16, p = 0.052**	0.71[0.19, 1.22]
(*bw*/s)	REG	7.78 ± 1.61	8.17 ± 2.07						
Braking Force	ADV	-0.20 ± 0.05	-0.24 ± 0.04	3.43, p = 0.08	0.70[-0.07, 1.46]	2.05, p = 0.16	0.49[-0.23, 1.22]	**14.24, p < 0.001**	1.17[0.65, 1.70]
(*bw*)	REG	-0.18 ± 0.05	-0.20 ± 0.06						
Propulsive Force	ADV	0.21 ± 0.03	0.23 ± 0.03	1.88, p = 0.17	0..44[-0.32, 1.20]	3.39, p = 0.07	0.36[-0.39, 1.11]	**17.18, p < 0.001**	1.37[0.85, 1.89]
(*bw*)†	REG	0.19 ± 0.05	0..20 ± 0.03						
Braking Impulse	ADV	-0.03 ± 0.01	-0.04 ± 0.004	1.77, p = 0.20	0.50[-0.25, 1.22]	0.55. p = 0.46	0.33[-0.40, 1.05]	2.38, p = 0.14	0.32[-0.19, 0.83]
(*bw*·s)	REG	-0.03 ± 0.001	-0.03 ± 0.001						
Propulsive	ADV	0.03 ± 0.004	0.04 ± 0.001	0.24, p = 0.63	0.19[-0.56, 0.93]	1.11, p = 0.30	0.49[-0.23, 1.22]	**13.08, p < 0.001**	1.25[0.73, 1.78]
Impulse (*bw*·s)	REG	0.03 ± 0.01	0.03 ± 0.001						

†: GEE model was used. F/χ^2 represents the statistic for the ANOVA/GEE model.
bw: body weight.
p-values ≤ 0.05 are bolded.

4.4 Tertiary Outcome (Dynamic Gait Stability)

Thiry participants (15 participants in either group) completed all overground walking trials. The results reflect dynamic gait stability on the participants' dominant leg due to the between-side symmetry ($p \geq 0.08$). The position of COM at liftoff (LO) and dynamic gait stability at LO violated the assumption of normality and could not be corrected by transformation. For these variables, a GEE was used to analyze the presence of an interaction effect and main effects followed by appropriate non-parametric post-hoc tests.

During overground walking at a self-selected speed, a significant session main effect was found for the COM position at touchdown (TD) ($p = 0.002$, $d = 1.0$, 95% CI: [0.5, 1.53], Table 4.4), however, no significant interaction effect ($p = 0.45$, $d = 0.29$, 95% CI: [-0.73, 1.3], Table 4.4) or group main effect ($p = 0.71$, $d = 0.14$, 95% CI: [-0.58, 0.86], Table 4.4) were displayed. After conducting follow-up *t*-tests, it was determined from pre- to post-intervention, both groups shifted the COM position posteriorly ($p = 0.04$, $d = 0.8$, 95% CI: [0.07, 1.53] for the advanced group, $p = 0.006$, $d = 2.12$, 95% CI: [1.38, 2.87] for the regular group, Table 4.4). The change scores were similar between groups (advanced group: -0.08 ± 0.14; regular group: -0.05 ± 0.06, $p = 0.39$, $d = 0.32$).

COM velocity at TD did not demonstrate a significant interaction effect ($p = 0.22$, $d = 0.48$, 95% CI: [-0.55, 1.5], Table 4.4) or significant group effect ($p = 0.15$, $d = 0.48$, -0.24, 1.21], Table 4.4). However, COM velocity at TD showed a significant session effect ($p < 0.001$, $d = 1.4$, 95% CI: [0.83, 1.9], Table 4.4). Post-hoc *t*-tests showed the advanced group increased their COM velocity ($p < 0.001$, $d = 3.21$, 95% CI: [2.39, 1.03], Table 4.4) from the pre- to the post-intervention sessions. The regular group showed a marginal increase in their COM velocity between the test sessions ($p = 0.05$, $d = 0.71$, 95% CI: [-0.21, 1.44], Table 4.4). The change scores in the COM velocity were comparable (advanced group: 0.05 ± 0.03; regular group: 0.03 ± 0.05,

$p = 0.43$, $d = 0.29$) between groups.

Dynamic gait stability at TD did not display a significant interaction effect ($p = 0.31$, $d = 0.36$, 95% CI: [-0.66, 1.38], Table 4.4) or significant group effect ($p = 0.16$, $d = 0.49$, 95% CI: [-0.24, 1.21], Table 4.4). However, there was a significant session effect ($p < 0.001$, $d = 1$, 95% CI: [0.48, 1.52], Table 4.4). Specifically, post-hoc *t*-tests demonstrated the advanced group increased significantly dynamic stability at this event after the intervention (advanced: $p = 0.003$, $d = 1.66$, 95% CI: [0.9, 2.41], Table 4.4) but not for the regular group ($p = 0.10$, $d = 0.54$, 95% CI: [-0.19, 1.26], Table 4.4). The between-session change in dynamic gait stability was similar between groups (advanced group: 0.03 ± 0.03; regular group: 0.02 ± 0.04, $p = 0.47$, $d = 0.27$).

The position of COM at LO displayed a significant session main effect ($p < 0.001$, $d = 0.08$, 95% CI: [00.64, 0.79], Table 4.4) without a significant interaction effect ($p = 0.19$, $d = 0.44$, 95% CI: [-0.29, 1.18], Table 4.4) or group main effect ($p = 0.08$, $d = 0.37$, 95% CI: [-0.30, 1.09], Table 4.4). Separate *t*-tests conducted for each group showed that both groups significantly shifted the COM position more posteriorly ($p = 0.003$, $d = 0.88$, 95% CI: [0.60, 2.09] for the advanced group, $p = 0.02$, $d = 1.46$, 95% CI: [0.72, 2.20] for regular group, Table 4.4) from pre-to post-intervention. However, the change scores from the pre- to the post-assessment were comparable between groups (advanced group: -0.09 ± 0.10; regular group: -0.05 ± 0.07, $p = 0.81$, $d = 0.74$).

The COM velocity at LO demonstrated a significant session main effect ($p < 0.001$, $d = 1.25$, 95% CI: 0.73, 1.78], Table 4.4) but not a group by session interaction effect ($p = 0.57$, $d = 0.21$, 95% CI: [-0.8, 1.23], Table 4.4) or group main effect ($p = 0.26$, $d = 0.39$, 95% CI: [-0.33, 1.11], Table 4.4). Post-hoc *t*-tests revealed both groups significantly increased their COM velocity from pre- to post-assessment (advanced group: $p < 0.001$, $d = 2.95$, 95% CI: [2.15, 3.75];

regular group: $p = 0.04$, $d = 0.72$, 95% CI: [-0.02, 1.45], Table 4.4). However, the increases in velocity between groups did not differ (advanced group: 0.04 ± 0.03; regular group: 0.03 ± 0.05, $p = 0.81$, $d = 0.09$).

Dynamic gait stability at LO displayed a significant session main effect ($p = 0.01$, $d = 0.28$, 95% CI: [-0.44, 1.00], but not a group main effect ($p = 0.6$, $d = 0.006$, 95% CI: [-0.11, 1.39], Table 4.4) or significant interaction ($p = 0.88$, $d = 0.87$, 95% CI: [0.09, 1.66], Table 4.4). Though a significant session main effect was reported, post-hoc tests revealed no difference from pre- to post-intervention in dynamic gait stability at LO for the advanced group ($p = 0.07$, $d = 1.33$, 95% CI: [0.60, 2.06], Table 4.4) or the regular group ($p = 0.13$, $d = 0.41$, 95% CI: [-0.24, 1.21], Table 4.4). Similarly, the between-session change in dynamic gait stability at this moment was comparable between groups (advanced group: 0.01 ± 0.02; regular group: 0.01 ± 0.03, $p = 0.31$, $d = 0.37$).

Table 4.4 Comparison of dynamic gait stability variables during overground walking at a self-selected speed presented as group mean ± standard deviation before (Pre) and after (Post) a 30-minute treadmill walking intervention for the advanced (ADV, n = 15) and regular (REG, n = 15) groups. The Generalized Estimating Equation (GEE) or the Analysis of Variance (ANOVA) with repeated measures were used. Effect sizes (Cohen's d) and 95% Confidence Intervals (95% CI) of the effect size are provided. The COM position, velocity, and dynamic gait stability are dimensionless variables.

Variable	Group	Session		Group × session interaction		Group main effect		Session main effect	
		Pre	Post	F/χ^2, p-value	d [95% CI]	F/χ^2, p-value	d [95% CI]	F/χ^2, p-value	d [95% CI]
COM Position TD	ADV	-0.80 ± 0.19	-0.87 ± 0.20	0.60, p = 0.45	0.29[-0.73, 1.30]	0.14, p = 0.71	0.14[-0.58, 0.86]	**11.07, p = 0.002**	1.01[0.50, 1.53]
	REG	-0.79 ± 0.16	-0.84 ± 0.17						
COM Velocity TD	ADV	0.34 ± 0.06	0.38 ± 0.05	1.61, p = 0.22	0.48[-0.55, 1.50]	2.17, p = 0.15	0.48[-0.24, 1.21]	**25.15, p < 0.001**	1.36[0.83, 1.90]
	REG	0.32 ± 0.06	0.34 ± 0.06						
Stability at TD	ADV	0.11 ± 0.06	0.15 ± 0.05	1.06, p = 0.31	0.36[-0.66, 1.38]	2.09, p = 0.16	0.48[-0.24, 1.21]	**13.56, p < 0.001**	1.00[0.48, 1.52]
	REG	0.10 ± 0.05	0.11 ± 0.04						
COM Position LO†	ADV	-0.27 ± 0.24	-0.36 ± 0.22	1.69, p = 0.19	0.44[-0.29, 1.18]	3.12, p = 0.08	0.37[-0.3, 1.1]	**20.96, p < 0.001**	0.08[-0.64, 0.79]
	REG	-0.17 ± 0.14	-0.22 ± 0.14						
COM Velocity LO	ADV	0.32 ± 0.05	0.36 ± 0.05	0.33, p = 0.57	0.21[-0.80, 1.23]	0.26, p = 0.26	0.39[-0.33, 1.11]	**21.19, p < 0.001**	1.25[0.74, 1.78]
	REG	0.31 ± 0.06	0.33 ± 0.06						
Stability at LO†	ADV	0.23 ± 0.06	0.24 ± 0.05	0.02, p = 0.88	0.87[0.09, 1.66]	0.27, p = 0.60	0.06[-0.11, 1.39]	**6.10, p = 0.01**	0.28[-0.44, 1.00]
	REG	0.24 ± 0.04	0.25 ± 0.04						

†: GEE model was used. F/χ^2 represents the statistic for the ANOVA/GEE model.
p-values ≤ 0.05 are bolded.

4.5 Subgroup Analyses

4.5.1 Subgroup Analyses Based on Protocol Tolerance in Advanced Group

Participants in the advanced group had both cadence and speed adjusted during the treadmill intervention. Given that 7 and 8 participants in the advanced group could not respectively meet the 15% decrease in cadence and 15% increase in treadmill speed during the intervention (Table 4.5), two subgroup analyses were conducted.

The first subgroup analysis was to determine if there were any differences in the intervention-induced improvements in the three main gait characteristics (stride length, cadence, and gait speed) between participants who were able to reduce their cadence by 15% (n = 8) and those who decreased cadence by less than 15% (n = 7). Results of the independent t-tests comparing change scores between groups indicated no significant differences for stride length (p = 0.68, d = 0.22, 95% CI: [-0.80, 1.23]), cadence (p = 0.63, d = 0.25, 95% CI: [-0.77, 1.27]), or gait speed (p = 0.56, d = 0.24, 95% CI: [-0.78, 1.26]) (Table 4.5).

A separate subgroup analysis was performed to compare participants in the advanced group who were able to achieve the desired treadmill speed increase of 15% (n = 7) during the intervention and those who increased the treadmill speed less than 15% (n = 8). Similar to the above results, independent t-tests comparing change scores demonstrated no statistical differences between groups in stride length (p = 0.21, d = 0.87, 95% CI: -0.19, 1.93]), cadence (p = 0.22, d = 0.66, 95% CI: [-0.38, 1.71]), or gait speed (p = 0.18, d = 0.75, 95% CI: [-0.30, 1.80]) (Table 4.5).

Table 4.5 Comparison of the change scores for cadence, gait speed, and stride length during overground walking at a self-selected speed presented as group mean ± standard deviation before and after a 30-minute treadmill walking intervention for participants in the advanced group who were able to increase speed by 15% (n = 7) and those who were not (n = 8), and participants who were able to decrease cadence by 15% (n = 8) and those who were not (n = 7). Two-sided independent t-tests are used. Effect sizes (Cohen's d) and 95% confidence intervals (95% CI) of the effect size are provided.

Variable	Speed				Cadence			
	15% (n = 7)	<15% (n = 8)	p-value	d [95% CI]	15% (n = 8)	<15% (n = 7)	p-value	d [95% CI]
Cadence (steps/min)	4.69 ± 4.08	2.21 ± 3.33	0.22	0.66[-0.38, 1.71]	3.83 ± 3.13	2.84 ± 4.62	0.63	0.25[-0.77, 1.27]
Speed (*bh/s*)	0.11 ± 0.05	0.07 ± 0.06	0.18	0.75[-0.30, 1.80]	0.09 ± 0.06	0.08 ± 0.06	0.56	0.24[-0.78, 1.26]
Stride length (/*bh*)	0.08 ± 0.03	0.05 ± 0.04	0.21	0.87[-0.19, 1.93]	0.07 ± 0.04	0.06 ± 0.04	0.68	0.22[-0.80, 1.23]

bh: body height.
p-values ≤ 0.05 are bolded.

4.5.2 Subgroup Analyses Based on Disease Severity

This study recruited PwPD with a reported H&Y stage 1-3. To check if the disease severity played a role in modulating the effects of the advanced gait training program, two additional subgroup analyses were conducted. For each analysis, participants with H&Y stage 1 and H&Y stage 2 were compared to investigate how disease severity influenced the effects of two interventions on the stride length, gait speed, and cadence during overground walking.

For participants with H&Y stage 1 (advanced group: n = 10; regular group: n = 10), there were no significant differences in the change scores between groups for stride length (p = 0.22, d = 0.57, 95% CI: [-0.33, 1.46]), cadence (p = 0.77, d = 0.13, 95% CI: [-0.75, 1.01]), or gait speed (p = 0.40, d = 0.39, 95% CI: [-0.50, 1.27]) (Table 4.6).

A secondary subgroup analysis was conducted to compare the advanced (n = 5) and regular (n = 5) treadmill interventions on overground stride length, cadence, and gait speed, for participants with H&Y stage 2. Results indicated there was a statistical difference in change score for stride length (p = 0.02, d = 2.50, 95% CI: [-0.34, 3.28], Table 4.6). The participants in the advanced group with H&Y stage 2 increased stride length from pre- to post-intervention more than participants in the regular group with H&Y stage 2 (Table 4.6). There were no group differences for cadence (p = 0.08, d = 1.25, 95% CI: [-0.11, 2.60], Table 4.6). The gait speed showed a borderline significance (p = 0.051, d = 1.46, 95% CI: [-0.07, 2.85], Table 4.6), with participants with H&Y stage 2 in the advanced group increasing their gait speed more relative to those in the regular group.

Table 4.6 Comparison of the change scores for cadence, gait speed, and stride length during overground walking at a self-selected speed presented as group mean ± standard deviation before and after a 30-minute treadmill walking intervention for participants in the advanced (ADV) and regular (REG) groups analyzed by disease severity (Hoehn and Yahr stage 1 and 2). Effect sizes (Cohen's *d*) and 95% Confidence Intervals (95% CI) of the effect size are provided.

Variable	Hoehn and Yahr Stage 1				Hoehn and Yahr Stage 2			
	ADV (n = 10)	REG (n = 10)	p-value	d [95% CI]	ADV (n = 5)	REG (n = 5)	p-value	d [95% CI]
Cadence (steps/min)	3.21 ± 3.21	2.76 ± 3.59	0.77	0.13[-0.75, 1.01]	3.69 ± 5.18	-2.52 ± 4.79	0.08	1.25[-0.11, 2.60]
Speed (*bh/s*)	0.09 ± 0.06	0.07 ± 0.05	0.40	0.39[-0.50, 1.27]	0.09 ± 0.04	0.005 ± 0.06	0.051	1.46[-0.07, 2.85]
Stride length (/*bh*)	0.06 ± 0.04	0.04 ± 0.03	0.22	0.57[-0.33, 1.46]	0.06 ± 0.04	0.008 ± 0.02	**0.02**	2.50[-0.34, 3.28]

bh: body height.
p-values ≤ 0.05 are bolded.

5 DISCUSSION

The overall purpose of this pilot, single-session, randomized controlled trial was to examine how the advanced treadmill intervention, by controlling both gait speed and cadence simultaneously, improves gait functions relative to the regular treadmill intervention via manipulating the speed only in PwPD. The following objectives were investigated:

1. Does modulating speed and cadence concurrently (advanced treadmill intervention) elicit a greater improvement in stride length compared to controlling speed alone (regular treadmill intervention) in a single treadmill session in PwPD?
2. How does the advanced treadmill intervention affect spatiotemporal and kinetic gait parameters relative to regular treadmill intervention?
3. Does the advanced treadmill intervention improve dynamic gait stability more than the regular treadmill intervention in a single session of treadmill walking in PwPD?

Correspondingly, the following hypotheses were tested:

1. The advanced treadmill intervention group would display a significantly larger increase in stride length compared to the regular treadmill intervention group following the training.
2. The advanced intervention group exhibits more improvements in the spatiotemporal and kinetic gait parameters compared to the regular intervention group.
3. The advanced treadmill intervention group would show a higher increase in dynamic gait stability than the regular treadmill intervention group from the pre-intervention to the post-intervention assessment.

5.1 Stride Length (primary)

The first hypothesis was supported as the results of this study indicated that completing a 30-minute treadmill training intervention that controls speed and cadence concurrently increases stride length more than an intervention that only controls speed. Specifically, participants in the advanced group significantly increased their stride length (Figure. 4.1), more than participants in the regular group. After the intervention, all participants demonstrated longer stride lengths at their comfortable overground walking speed, unlike some participants in the regular who displayed a reduction in stride length. The combination of progressively reducing cadence using rhythmic auditory cueing and progressively increasing gait speed on the treadmill resulted in larger improvements in stride length compared to only increasing speed on the treadmill.

Since gait hypokinesia is a common symptom of PD and is directly related to an inability to generate large steps (Ebersbach et al., 1999; Morris et al., 1994; Rubinstein et al., 2002), improving stride length as a strategy to increase gait speed is critical. Treadmill walking has been established as an effective intervention to improve step length (Herman et al., 2009; Mehrholz et al., 2015). However, most treadmill-based gait training programs for PwPD solely focus on increasing the gait speed during the training without controlling or reporting the cadence (Bello et al., 2008; Canning et al., 2008; Herman et al., 2007; Pohl et al., 2003; Skidmore et al., 2008; Verghese et al., 2009). Because PwPD display difficulty in regulating stride length and therefore increase cadence as a compensatory strategy to maintain and increase walking speed (Bayle et al., 2016; Morris et al., 1994), they could be relying on increasing cadence as a primary strategy, more than stride length, to increase the gait speed (Protas et al., 2005).

Treadmill-based interventions are commonly utilized because the continuous movement of the belt encourages more automatic gait (Bello et al., 2008; Frenkel-Toledo et al., 2005) resulting in less gait variability compared to overground walking (Bello and Fernandez-Del-Olmo,

2012). Additionally, rhythmic auditory stimulation (RAS) has been successful at improving gait parameters in PwPD (Thaut et al., 1996), as it can serve as a stimulus to bypass the impaired internal timing present in PwPD (Ashoori et al., 2015). Therefore, the combination of using RAS to control cadence, which influences stride length, in addition to the controlled speed of the treadmill, was used in the advanced intervention group to explore if gait outcomes were improved more than controlling treadmill speed alone.

The advanced treadmill intervention, explored in this dissertation project, showed more benefits in improving the stride length and gait speed but similar effects on the cadence in comparison to the regular treadmill intervention (Figures 4.1 & 4.2). Such observations could be accounted for by the concurrently controlled gait speed and cadence in the advanced intervention group. As indicated above, the three fundamental gait characteristics (cadence, gait speed, and stride length) are closely interrelated. The simultaneous control of the gait speed and cadence means that the stride length would be regulated by the training protocol as well. Therefore, the advanced intervention forced the trainees to walk in a certain manner, in which all three basic gait parameters were manipulated. However, the regular training group had more options for responding to the increased gait speed by altering the cadence and/or stride length.

In this study, a slower cadence was used as a strategy to increase stride length on the treadmill in the advanced group. Previous literature has focused on using RAS at faster tempos to increase walking speed (McIntosh et al., 1997) because increasing cadence is a tactic to increase gait speed (Arias and Cudeiro, 2008; Ashoori et al., 2015). Increasing cadence while on a treadmill at a constant speed, especially when cadence is already within or above a normal range, may promote even shorter steps without encouraging PwPD to increase stride length while walking, possibly exaggerating a shuffling gait. Moreover, fast gait speed, coupled with a reduced step

length and a forward-leaning trunk could increase the risk of forward balance loss or falls for PwPD who display freezing of gait (Urakami et al., 2021). These characteristics result in a reduced distance between the COM position and the anterior boundary of the BOS, which can lead to an increased risk of losing forward balance.

Given the loss of automaticity and rhythmicity of movements, PwPD are still able to synchronize their movements with external rhythmic cues through an innate internal timing process (Thaut et al., 2015). The cyclic nature of RAS can help PwPD synchronize ground contact when walking and control variability in musculoskeletal activation patterns (Ford et al., 2010; Koshimori and Thaut, 2018). Matching their steps to a slower cadence increased the stride length while simultaneously increasing gait speed on the treadmill, preventing participants from relying on shorter, faster steps to increase the walking speed. Subgroup analyses were conducted to compare participants in the advanced group who could comply with the 15% decrease in cadence and 15% increase in gait speed and those who could not. There were no statistical differences in stride length, cadence, and gait speed between participants who could decrease cadence by 15% and those who could not. The results were similar for participants who could increase treadmill speed by 15% and those who could not. Given the advanced group displayed more improvements in stride length, cadence, and gait speed compared to the regular group, these results highlight the importance of utilizing parameters that are individualized to the participants and consistently matching step frequency is more important than the parameter intensity. This could be considered a candidate explanation of why the advanced intervention is more beneficial in lengthening the stride than the regular treadmill intervention.

5.2 Spatiotemporal and Kinetic Gait Parameters (secondary)

5.2.1 Spatiotemporal Gait Parameters

The second hypothesis was partially supported, and the results indicated that the advanced group displayed larger improvements in gait speed (Figure 4.2) and double leg stance time (Figure 4.2) compared to the regular group. No differences were reported from pre- to post-intervention in single leg stance time for both groups (Figure 4.2), and the advanced group took more steps after the intervention than before the intervention while there was no difference in cadence for those in the regular group (Figure 4.2).

The procedures of this study were based on a small case series involving 3 participants who completed a 6-week intervention that combined treadmill walking at 85% of their self-selected cadence, followed by overground walking at 115% of their self-selected cadence (Sherron et al., 2020). It has been demonstrated that walking to a slower auditory cue on the treadmill increases stride length (Chawla et al., 2020). Due to the connections of auditory and motor areas of the brain, walking to a beat (music or metronome) seems to help PwPD organize and initiate movement (Thaut and Abiru, 2010). It was proposed the coupling of a slower cadence on the treadmill to increase stride length, followed by a faster overground walking cadence to increase gait speed, would have a positive effect on the spatiotemporal characteristics of gait (Sherron et al., 2020). The combination and use of RAS proposed by these researchers was a novel intervention, in that previous study increased speed or cadence, without considering stride length, to improve gait speed (Arias and Cudeiro, 2008; Ashoori et al., 2015; McIntosh et al., 1997).

The current study completed the entire intervention on the treadmill, and speed was increased on the treadmill in lieu of increasing walking cadence overground. Although difficult to compare given the previous intervention lasted six weeks and the intervention in the current pilot study consisted of a single session, the results for the advanced group from this study align with those from Sherron et al. displaying an increase in stride length and gait speed, with a small (but

nonsignificant) increase in cadence (Sherron et al., 2020). From pre- to post-intervention, both groups displayed significant increases in stride length (advanced group: $p < 0.001$; regular group: $p = 0.002$) and gait speed (advanced group: $p < 0.001$; advanced group: $p = 0.01$), with larger increases in the advanced group. The advanced group also increased their cadence from 108 steps/min to 111 steps/min ($p = 0.004$, $d = 2.49$) while the regular group increased the number of steps from 108 steps/min to 109 steps/min ($p = 0.42$, $d = 0.33$). However, the statistically significant increase in the stride length within the advanced group from the pre- to the post-intervention session could be considered less clinically meaningful. Firstly, the effect size of the stride length is small ($d = 0.33$) and the increase in the cadence was smaller than the minimum detectable change for cadence is 15 steps/min (Lang et al., 2016), suggesting participants in both groups took bigger steps as a primary strategy to walk faster. Additionally, the cadence at pre-test was 108 steps/min in this study is within the range of cadence for healthy adults (Hollman et al., 2011; Senden et al., 2024). Because PwPD in this study did not demonstrate a walking cadence significantly higher compared to those of healthy adults, the increase in cadence after the intervention is not likely to be clinically meaningful, as it is still within the range of healthy adults. Lastly, the increase of 3 steps/min in the cadence would potentially cause little changes in the gait speed (2.8%). Therefore, the lengthened stride was the dominant factor leading to the increased gait speed in the advanced group.

In the present study, only speed was increased on the treadmill for the regular group, as previous studies have used increasing the treadmill speed to increase overground gait speed (Bello et al., 2013; Protas et al., 2005). This study aimed to examine if the advanced group showed more improvements in gait characteristics relative to the regular group. Compared to other acute treadmill interventions that only manipulated gait speed, our results are inconsistent

(Bello et al., 2008; Pohl et al., 2003). During a 30-minute single-session treadmill intervention in which the treadmill speed was increased by 10% each time the participant completed 10 seconds of walking safely and without stumbling, participants increased their stride length by 8.3% (Pohl et al., 2003). This is significantly more than the 4% increase in stride length of the regular group, but the same as the 8% increase in stride length demonstrated by the advanced group.

Further, Pohl et al. reported a 13.8% increase in gait speed among participants (Pohl et al., 2003). The present study reported the regular group increased gait speed by 6% and the advanced group walked 11.6% faster after the intervention. These differences are likely attributed to the study design. In the current study, gait speed was increased by 5% for three 5-minute blocks. Therefore, the total gait speed never increased more than 15%. In the previous study, the treadmill speed was increased 10% for every 10 seconds of safe walking, for up to 5 training periods. Gait speed is determined by stride length and cadence. With such a large increase in gait speed, it is reasonable that both stride length and cadence would also increase, however, the previous study did not report cadence. It is possible participants walked at a faster cadence compared to healthy adults before the intervention, which was then further increased to produce a faster gait after the intervention. Therefore, this past study does not provide a complete picture of the impact and relationship of cadence and stride length on gait speed (Pohl et al., 2003).

In terms of double leg stance time, the results agree with those of Pohl et al., in which participants in the advanced group displayed a significant decrease in the amount of time spent in double leg stance, while there was no change for the regular group (Pohl et al., 2003). The duration of double leg stance time is a function of gait speed and a decrease in the double stance phase is associated with an increase in walking speed (Morris et al., 1998; Perry and Burnfield, 2024). This can further explain the increases in gait speed demonstrated by the two groups, as the

advanced group increased gait speed significantly more than the regular group ($p = 0.05$).

In a different study that utilized a single-session intervention consisting of five 4-minute blocks of treadmill walking at their self-selected overground speed, participants immediately increased their gait speed and stride length during overground walking (Bello et al., 2008). Unlike the current study that increased gait speed by 15%, Bello et al. demonstrated improvements in spatiotemporal characteristics by walking on the treadmill at the same speed as participants' self-selected overground speed. These improvements could be attributed to the disease severity of the participants and the difference in the training protocol.

First, it has been shown that the disease severity may play a role in the effects of treadmill-based gait training for PwPD (Frenkel-Toledo et al., 2005). In the previous study, after walking at their self-selected overground speed on a treadmill, people with moderate PD (stage 2) increased their cadence and step length as a strategy to increase their gait speed, while people with advanced PD (stage 3) increased their step length as a means to increase their gait speed, without increasing their cadence (Bello et al., 2008). The prior study involved PwPD with H&Y stage spanning between 2 and 3 (moderate to advanced) with an average of 2.67 ± 0.41. On the other hand, the current dissertation study recruited PwPD with the H&Y stage of 1-3. More specifically, most participants ($n = 20$) reported H&Y stage 1-1.5 (1.6 ± 0.43), with the most advanced participant stage 2.5.

Two separate sub-analyses were conducted to compare the advanced and regular interventions for participants with H&Y stage 1 and H&Y stage 2. No statistical differences were detected in the change score for stride length, cadence, or gait speed during overground walking when comparing the participants with H&Y stage 1 in the regular and advanced groups. However, when comparing the participants with H&Y stage 2, those in the advanced group

statistically increased their stride length from pre- to post-intervention compared to the regular group (p = 0.02, Table 4.6), and gait speed displayed a trend for significance (p = 0.051). There was no significant difference in change score between groups for cadence (p = 0.08). These results suggest participants with H&Y stage 2 in the advanced group displayed the greatest improvements during the intervention. On the other hand, participants with H&Y stage 2 in the regular group showed decreases in cadence (-2.52 ± 4.79 steps/min) and gait speed (-0.005 ± 0.06 *bh*/*s*) from pre- to post-intervention. This implies that PwPD with a higher H&Y stage would benefit from the advanced training modality more than those with a lower stage. However, further studies are warranted to investigate how treadmill interventions affect disease severity given the relatively small sample sizes (10 per group for stage 1 and 5 per group for stage 2).

Second, the discrepancies in the training protocol could have also accounted for the difference in the findings between this dissertation and the previous study. In the present dissertation study, all participants started the walking intervention with their comfortable treadmill walking speed, while the initial treadmill speed was the participants' self-selected overground speed in the prior study (Bello et al., 2008). It is well known that the self-selected overground speed is higher than the self-selected treadmill gait speed (Malatesta et al., 2017; Yang and King, 2016). For 25 out of the 30 participants in this dissertation project, their speed during the last treadmill intervention block did not reach their pre-test self-selected overground speed. Therefore, the intervention protocol could have been more intense in the previous study than in the current dissertation project, possibly contributing to the difference in the findings between studies.

5.2.2 Kinetic Gait Parameters

Vertical Ground Reaction Force

The peak vertical GRF was determined at two points during overground walking: the first peak at heel strike (the first or passive peak vertical GRF during the weight acceptance phase) and the second peak at toe-off (the second or active peak vertical GRF at push off). The results indicate a significant interaction effect for the first peak vertical GRF in which the advanced group significantly increased their vertical GRF more than those in the regular group from pre- to post-test (Table 4.3). Additionally, the advanced group exhibited a significantly larger second vertical GRF at the post-intervention test than the regular group (Table 4.3). A strong association between gait speed and peak vertical GRF has been established during linear walking (Andriacchi et al., 1977). A faster gait speed results in more acceleration and deceleration of the body's COM in the vertical direction. PwPD predominantly walk slower than the healthy population (Morris et al., 1994) and demonstrate a concurrent reduction in peak vertical GRF (Alam et al., 2017; Farashi, 2020). However, the time-domain pattern of vertical GRF during the stance phase is shown to be similar between PwPD and healthy individuals (Farashi, 2021; Giardini et al., 2023). This notion is further confirmed by the findings of the two vertical GRFs in this dissertation study.

The results of this study partially align with those of Pohl et al. (Pohl et al., 2003). For example, after completing a single-session treadmill intervention in which speed was increased by 10% after 10 seconds of safe walking, participants displayed increases in both peak vertical GRFs, though these increases were not statistically significant (Pohl et al., 2003). Results from these studies further emphasize the association between gait speed and vertical GRF among PwPD, suggesting that it is necessary to consider gait speed when interpreting vertical GRF.

Rate of Loading

The rate of loading represents the rate at which the acceleration of the body's COM changes immediately following touchdown (Schmida et al., 2022), and is thought to describe the intensity at which force develops at touchdown (Stacoff et al., 2005). The results from this study suggest neither intervention influenced the rate of loading during overground walking at a self-determined speed (Table 4.3). These results are similar to those previously reported in PwPD that demonstrated no significant increase in the rate of loading after completing a single-session treadmill intervention in which speed was progressively increased (Pohl et al., 2003).

Given the significantly increased first peak vertical GRF in the advanced group during the post-intervention assessment versus pre-intervention, it is reasonable to expect to see an increase in the rate of loading in this group after the intervention. However, non-significant findings in the advanced group related to the rate of loading in this dissertation study could be because participants in this group altered their joint positions and limb movement before and during touchdown which affected the rate of loading. A function of skeletal muscle is to act as a shock absorber during movement, which can also reduce the rate of loading. Because this study did not analyze joint angles or EMG activity, it is difficult to determine the underlying characteristics of the rate of loading. The EMG activity should be taken as additional metrics for future studies to further investigate the rate of loading related to the advanced treadmill gait training for PwPD.

Braking and Propulsive Force

It was anticipated the advanced group would portray a larger increase in both peak braking and peak propulsive forces. This was hypothesized because the advanced group was expected to walk faster after the intervention, and in healthy populations, increased gait speed requires larger braking and propulsive forces (Nilsson and Thorstensson, 1989). The results do not

support this hypothesis. From pre- to post-intervention, the advanced group increased both peak braking and propulsive forces, compared to no significant increase in the regular group, while no significant interaction effect was seen for either variable (Table 4.3). Along with increased walking speed (Peterson et al., 2011), the step length (Balasubramanian et al., 2007; Martin and Marsh, 1992) has been recognized as a key component related to peak braking force. A longer step length places the foot more anterior and may cause a greater posterior GRF. Both groups displayed increases in gait speed and stride length, but the improvements were larger in the advanced group. As such, the advanced group also displayed an increase in peak braking force.

The results for the peak braking force are similar to those of peak propulsive force with the advanced group displaying an increase in peak propulsive force from pre- to post-intervention, while the regular group reported no improvement (Table 4.3). Again, the improvements seen in the advanced group are likely related to the increases in gait speed and stride length. It's been estimated that producing horizontal propulsion forces during walking makes up half of its metabolic cost in a healthy population (Gottschall and Kram, 2003). In pathological gait, the metabolic energy needed is over twice that of a healthy gait (Gonzalez and Corcoran, 1994; Kuo and Donelan, 2010). In PwPD, disturbances in gait are one of the first signs of motor dysfunction, and propulsion is frequently compromised. Increased co-activation of antagonistic muscles and reduced amplitude of distal lower extremity musculature has been shown to affect gait in PwPD (Cioni et al., 1997; Dietz et al., 1995; Rodriguez et al., 2013). This can result in an under-scaling of power generation at push-off during walking (Dietz et al., 1995; Morris et al., 1999). Like vertical GRF, propulsive force is reduced in PwPD compared to age and sex-matched healthy controls (Sharifmoradi and Farahpour, 2016).

Given that PwPD have demonstrated a diminished ability to propel themselves forward (Albani et al., 2014), the improvements in peak propulsive force seen in the advanced group warrant further investigation. It is reasonable to infer this improvement is the result of increased gait speed and stride length. Similar to how step length is a component of peak braking force, propulsive force is affected by the distance between the body's COM and its center of pressure (Hsiao et al., 2015). However, it is not clear how these kinematic strategies altered muscle activity, specifically at the ankle joint.

Braking and Propulsive Impulse

It was hypothesized that the advanced group would display larger increases in braking and propulsive impulse after the intervention relative to the regular group. Despite the lack of the group by session interaction effects, the advanced group produced a statistically larger propulsive impulse from pre- to post-testing (Table 4.3). This was expected, as increases in step length are associated with increased braking and propulsive impulses when walking at a steady-state speed in healthy populations (Martin and Marsh, 1992). However, neither group increased braking impulse after the intervention. Given the small sample size whose ground reaction force is available in this study, it is premature to make any definitive conclusion on this. One candidate explanation could be related to the change in the gait speed for the two groups. Currently, interpretations of impulse involve analyzing how healthy subjects accelerate and decelerate across steady-state speeds. When healthy participants increased their steady state speed from 1.0 to 2.0 m/s, both braking and propulsive impulses increased (Nilsson and Thorstensson, 1989). While both groups increased their walking speed significantly from pre- to post-intervention, the advanced group increased their speed more than the regular (though not a significant amount), which could explain the increase they demonstrated in propulsive impulse. More studies are

needed to further explore how the advanced intervention could affect braking and propulsive impulses.

5.3 Dynamic Gait Stability (tertiary)

This study also sought to determine if a treadmill intervention that controlled speed and cadence improved dynamic gait stability more than a treadmill intervention that only controlled speed. The findings revealed that both groups displayed similar dynamic gait stability after the intervention, rejecting the hypothesis (Table 4.4).

The COM motion state used to determine dynamic gait stability simultaneously considers the COM position and COM velocity relative to the BOS. At the beginning (TD) and end (LO) of the stance phase (two transitional instants during human gait), both groups similarly positioned their COM less anteriorly compared to pre-test overground walking, with a larger posterior shift occurring in the advanced group (Table 4.4). According to the FSR theory, a value of zero of the COM position indicates the COM is located directly over the heel, a value of one indicates the COM position is located directly over the toes, and a value of negative one is the position of one-foot-length behind the heel (Figure 2.2). Both groups displayed slightly more negative values after the intervention. This can be explained by the increase in stride length displayed by both groups. A larger stride length creates more distance between the body's COM and the BOS at TD and LO, which can lead to greater instability. Numerous studies have reported a positive correlation between the step length and COM position at TD among various populations (Liu and Yang, 2017; Yang et al., 2016; Yang and King, 2016; Yang and Pai, 2013). An increase in COM velocity can compensate and provide forward momentum to avoid instability against balance loss. As such, both groups increased the COM velocity from before to after the

intervention, with the advanced group displaying a relatively larger, but not significant, improvement in velocity.

The combination of a more negative COM position and an increase in COM velocity resulted in similar dynamic gait stability in both groups. These outcomes align with a previous study that found PwPD displayed similar dynamic gait stability compared to healthy individuals during overground walking at a self-selected speed (Ban et al., 2024). In the previous study, PwPD walked slower and took shorter steps compared to healthy individuals, which is consistent with earlier findings (Canning et al., 2006; Hobert et al., 2019). Relative to healthy adults, PwPD display a decreased step length, decreased gait speed, and increased gait variability (Knutsson, 1972). These alterations may indicate a "cautious gait" strategy, which has been previously reported as a safety adaptation (Browning and Kram, 2007). A slower gait speed may allow PwPD a more controlled gait, aiding in their ability to maintain dynamic balance. According to the FSR theory, a slower walking speed reduces the velocity of the body's COM relative to the BOS, jeopardizing dynamic gait stability in PwPD (Yang et al., 2008). To offset the instability created by a slower walking speed, PwPD adjusted by taking shorter steps. Shortening the step length shifts the COM forward, bringing it closer to the BOS, thereby improving dynamic gait stability (Yang and King, 2016).

In summary, both groups displayed a posterior shift in COM position, coupled with an increase in COM velocity, resulting in comparable dynamic gait stability.

5.4 Conclusions

Overall, the advanced group exhibited more improvements in gait characteristics during overground walking than the regular group, which was predicted due to the intervention aimed at increasing stride length and gait speed. Contrary to what was expected, the improvements seen in

the advanced group are similar to previous research that only increased gait speed during treadmill interventions. Specifically, the advanced group significantly increased gait speed, stride length, first and second peak vertical GRF, and reduced double leg stance time. Given this was a single-session intervention for PwPD, and the kinematic and kinetic characteristics of gait analyzed in this study are interrelated, it is reasonable that a 30-minute treadmill intervention will not have a significant effect on all gait parameters. However, the trends displayed in the results are promising.

In terms of stride length and gait speed, the advanced group displayed a significantly larger increase during overground walking than the regular group. This was anticipated as the protocol was designed to increase stride length by walking at a lower frequency on the treadmill, forcing the participant to take larger steps, followed by increasing the speed on the treadmill to increase walking speed. Given gait speed is determined by stride length and cadence, it was expected that cadence would remain the same, if not decrease. However, the advanced group increased cadence, though not by a clinically meaningful amount.

The increases in gait speed and stride length demonstrated by the advanced group influenced improvements in peak vertical GRFs, peak braking and propulsive force, and propulsive impulse from pre- to post-intervention compared to the regular group. Because PwPD display a reduced ability to propel themselves forward, investigating the relationship between joint moments and GRFs may be meaningful for future rehabilitation program design. In terms of dynamic gait stability, the results indicate the advanced and regular groups have similar dynamic gait stability during overground walking at their self-selected speed. Though originally unexpected, this result is reasonable given it has recently been demonstrated that PwPD exhibit dynamic gait stability comparable to healthy controls. These results are the combination of a

posteriorly shifted COM position and increased gait speed. The findings suggest that an intervention that concurrently controls cadence and gait speed shows more improvements in gait characteristics than only controlling speed in this intervention protocol. Overall, increasing stride length and gait speed have a positive effect on spatiotemporal variables, though the underlying mechanisms deserve further investigation.

5.5 Implications

Walking has been identified as the first activity in which PwPD report difficulty. This is the first study to concurrently control speed and cadence during a treadmill intervention for PwPD. The results of this study show walking speed, stride length, and vertical GRF significantly increased, and double leg stance time significantly decreased, with a combination of progressive decreases in step frequency and progressive increases in treadmill speed in PwPD. These findings suggest that the utilization of an external auditory cue while simultaneously manipulating gait speed can improve walking speed and stride length. These findings provide meaningful evidence that larger increases in stride length and gait speed influence improvements in other gait characteristics that diminish in PwPD.

5.6 Limitations and Further Research

This study has limitations. First, the participants' disability level was at the mild to moderate stage, with most participants (10/15 in each group) showing a stage between 1 and 1.5 on the H&Y scale. It is unknown if the results of the intervention are generalizable to other PD stages. Given that more advanced stages exhibit worsening symptoms, it is meaningful to investigate how the interventions compare in this population. Second, this study did not analyze joint angles, joint moments, or muscle activity, impeding our ability to analyze the underlying

mechanisms. Given the lack of kinetics included in PD research, future work should examine the relationships between joint moments, joint positions, and kinetics to determine how PwPD alter their limb movements to improve gait characteristics. Third, this was a single-session 30-minute intervention, and the results were an analysis of the immediate effects. It is unknown how long the results persisted. Long-term interventions and follow-up tests to determine the length of the adaptation should be included in future work.

Fourth, all participants in their respective groups followed the same training schedule. Additional research should include utilizing different parameters in persons with different disease severity, including different frequency and progression rates. Fifth, most of the participants in this study were male (advanced group: 80%; regular group: 86%), so the findings may not be generalizable to both sexes. However, men are about 1.5 times more likely to be diagnosed with PD than women, and this study sample could be a reasonable reflection of this population. Sixth, fatigue, quality of sleep, hydration, nutrition, and the time of day of testing were not controlled. Further, participants wore the shoes they deemed best for treadmill walking, so footwear was not standardized. Sensory function was also not measured. Unassessed sensations in the feet may have affected the ability to detect sensory feedback. However, given this was a randomized controlled trial, differences between groups, if any, could have been alleviated by the study design. Lastly, the intervention took place in a laboratory setting and participants completed overground walking on a flat, safe surface. It is unknown if the results extend to real-world scenarios. Therefore, more studies with larger sample sizes and more rigorous study designs are needed to further investigate the clinical implications of the advanced treadmill intervention. With the compelling results from the current study, the following future research directions could be tackled before clinically deploying the advanced treadmill paradigm:

1. The long-term training and retention effects. In this study, participants completed a single-session treadmill walking intervention, and gait characteristics were analyzed immediately following completion of the intervention. Though previous studies have reported improvements in gait outcomes after a single session (Bello et al., 2008; Pohl et al., 2003), a long-term intervention in line with typical rehabilitation timelines (8-12 weeks) may yield greater improvements. Based on a mini-review of treadmill training interventions for PwPD, only 5 out of the 14 training programs included a follow-up test (Herman et al., 2009). These ranged from 1 to 6 months after the final intervention session. Including follow-up visits can help determine the length of the biomechanical adaptations of the intervention, along with ensuring participant progress and identifying any reduction in compliance.
2. Including PwPD showing a more severe disability level. Depending on the severity level, PwPD may utilize different strategies to execute faster walking (Bello et al., 2008). Investigating how people with more severe PD respond to gait interventions can improve training effectiveness. Given that gait disturbances are one of the most incapacitating symptoms of PD, improving gait in more advanced PD stages may improve quality of life and prolong independence.
3. Identifying the optimal training dosage in terms of the frequency of the training, the length of the training bouts, and the protocol for manipulating the gait speed and cadence. During long-term interventions, frequent testing may help determine progression guidelines to optimize progress and identify plateaus. Guidelines for PwPD suggest performing aerobic exercise 3x/week, for 30-40 minutes of the main exercise set,

at 70-85% of heart rate max (Alberts and Rosenfeldt, 2020). Incorporating these parameters may provide additional benefits beyond gait improvements.

4. To further examine how the physiological, kinematic, and kinetic gait parameters are correlated to determine the neuro-biomechanical mechanisms of advanced treadmill intervention. Analyzing muscle activity, joint kinetics, and kinematics can help explain the mechanisms underlying the changes in gait characteristics and dynamic stability induced by the intervention.
5. To investigate if and how the footwear, fatigue, quality of sleep, hydration, nutrition, the time of day of testing were not controlled, and sensorimotor function impairment could play a role in determining the effects of the advanced treadmill intervention.
6. To explore how the foot landing pattern interacts with the advanced intervention to improve gait quality among PwPD. For example, walking with a heel strike instead of a forefoot strike may reduce gait variability, increase toe clearance during walking (Ginis et al., 2017), and reduce fall risk. It would be clinically meaningful to examine if such benefits with heel strike landing technique could be enhanced, maintained, or diminished.

REFERENCES

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

Ahn, J., Ban, R., Simpkins, C., Yang, F., 2024a. Android obesity could be associated with a higher fall risk than gynoid obesity following a standing-slip: a simulation-based biomechanical analysis. Journal of Biomechanics 164, 111962.

Ahn, J., Simpkins, C., Shin, S., Yang, F., 2024b. Shoe sole impedes leg muscle activation and impairs dynamic balance responding to a standing-slip. Journal of Biomechanics. 169, 112138.

Ahn, J., Simpkins, C., Yang, F., 2022a. Effects of anterior load carriage on dynamic gait stability during level overground walking. Human Movement Science 85, 102981.

Ahn, J., Simpkins, C., Yang, F., 2022b. Ground reaction forces and muscle activities during anteriorly-loaded overground walking: preliminary results. International Journal of Industrial Ergonomics 90, 103328.

Alam, M.N., Garg, A., Munia, T.T.K., Fazel-Rezai, R., Tavakolian, K., 2017. Vertical ground reaction force marker for Parkinson's disease. PLoS One 12, e0175951.

Albani, G., Cimolin, V., Fasano, A., Trotti, C., Galli, M., Mauro, A., 2014. “Masters and servants” in parkinsonian gait: a three-dimensional analysis of biomechanical changes sensitive to disease progression. Functional Neurology 29, 99.

Albani, G., Veneziano, G., Lunardon, C., Vinci, C., Daniele, A., Cossa, F., Mauro, A., 2019. Feasibility of home exercises to enhance the benefits of tango dancing in people with Parkinson’s disease. Complementary Therapies in Medicine 42, 233-239.

Alberts, J.L., Rosenfeldt, A.B., 2020. The universal prescription for Parkinson's disease: exercise. Journal of Parkinson's Disease 10, S21-s27.

Andriacchi, T.P., Ogle, J.A., Galante, J.O., 1977. Walking speed as a basis for normal and abnormal gait measurements. Journal of Biomechanics 10, 261-268.

Arias, P., Cudeiro, J., 2008. Effects of rhythmic sensory stimulation (auditory, visual) on gait in Parkinson's disease patients. Experimental Brain Research 186, 589-601.

Ashburn, A., Stack, E., Ballinger, C., Fazakarley, L., Fitton, C., 2008. The circumstances of falls among people with Parkinson's disease and the use of falls diaries to facilitate reporting. Disability and Rehabilitation 30, 1205-1212.

Ashoori, A., Eagleman, D.M., Jankovic, J., 2015. Effects of auditory rhythm and music on gait disturbances in Parkinson's disease. Frontiers Neurology 6, 234.

Balasubramanian, C.K., Bowden, M.G., Neptune, R.R., Kautz, S.A., 2007. Relationship between step length asymmetry and walking performance in subjects with chronic hemiparesis. Archives of Physical Medicine and Rehabilitation 88, 43-49.

Ban, R., Ahn, J., Simpkins, C., Lazarus, J., Yang, F., 2024. Dynamic gait stability in people with mild to moderate Parkinson's disease. Clinical Biomechanics 118, 106316.

Bayle, N., Patel, A.S., Crisan, D., Guo, L.J., Hutin, E., Weisz, D.J., Moore, S.T., Gracies, J.-M., 2016. Contribution of step length to increase walking and turning speed as a marker of Parkinson’s disease progression. PLoS One 11, e0152469.

Bello, O., Fernandez-Del-Olmo, M., 2012. How does the treadmill affect gait in Parkinson's disease? Current Aging Science 5, 28-34.

Bello, O., Marquez, G., Camblor, M., Fernandez-Del-Olmo, M., 2010. Mechanisms involved in treadmill walking improvements in Parkinson's disease. Gait and Posture 32, 118-123.

Bello, O., Sanchez, J.A., Fernandez-del-Olmo, M., 2008. Treadmill walking in Parkinson's disease patients: adaptation and generalization effect. Movement Disorders 23, 1243-1249.

Bello, O., Sánchez, J.A., Lopez-Alonso, V., Márquez, G., Morenilla, L., Castro, X., Giraldez, M., Santos-García, D., Fernández-del-Olmo, M., 2013. The effects of treadmill or overground walking training program on gait in Parkinson's disease. Gait and Posture 38, 590-595.

Berardelli, A., Rothwell, J.C., Thompson, P.D., Hallett, M., 2001. Pathophysiology of bradykinesia in Parkinson's disease. Brain 124, 2131-2146.

Betarbet, R., Sherer, T.B., MacKenzie, G., Garcia-Osuna, M., Panov, A.V., Greenamyre, J.T., 2000. Chronic systemic pesticide exposure reproduces features of Parkinson's disease. Nature Neuroscience 3, 1301-1306.

Bhatt, T., Espy, D., Yang, F., Pai, Y.C., 2011. Dynamic gait stability, clinical correlates, and prognosis of falls among community-dwelling older adults. Archives of Physical Medicine and Rehabilitation 92, 799-805.

Bhatt, T., Yang, F., Mak, M.K., Hui-Chan, C.W., Pai, Y.C., 2013. Effect of externally cued training on dynamic stability control during the sit-to-stand task in people with Parkinson disease. Physical Therapy 93, 492-503.

Blauwendraat, C., Heilbron, K., Vallerga, C.L., Bandres-Ciga, S., von Coelln, R., Pihlstrøm, L., Simón-Sánchez, J., Schulte, C., Sharma, M., Krohn, L., Siitonen, A., Iwaki, H., Leonard, H., Noyce, A.J., Tan, M., Gibbs, J.R., Hernandez, D.G., Scholz, S.W., Jankovic, J., Shulman, L.M., Lesage, S., Corvol, J.C., Brice, A., van Hilten, J.J., Marinus, J., Eerola-Rautio, J., Tienari, P., Majamaa, K., Toft, M., Grosset, D.G., Gasser, T., Heutink, P., Shulman, J.M.,

Wood, N., Hardy, J., Morris, H.R., Hinds, D.A., Gratten, J., Visscher, P.M., Gan-Or, Z., Nalls, M.A., Singleton, A.B., 2019. Parkinson's disease age at onset genome-wide association study: Defining heritability, genetic loci, and α-synuclein mechanisms. Movement Disorders 34, 866-875.

Bloem, B.R., Grimbergen, Y.A., Cramer, M., Willemsen, M., Zwinderman, A.H., 2001. Prospective assessment of falls in Parkinson's disease. Journal of Neurology 248, 950-958.

Boonstra, T.A., van der Kooij, H., Munneke, M., Bloem, B.R., 2008. Gait disorders and balance disturbances in Parkinson's disease: clinical update and pathophysiology. Current Opinion in Neurology 21, 461-471.

Brienesse, L.A., Emerson, M.N., 2013. Effects of resistance training for people with Parkinson’s disease: a systematic review. Journal of the American Medical Directors Association 14, 236-241.

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

Browning, R.C., Kram, R., 2007. Effects of obesity on the biomechanics of walking at different speeds. Medicine and Science in Sports and Exercise 39, 1632-1641.

Cakit, B.D., Saracoglu, M., Genc, H., Erdem, H.R., Inan, L., 2007. The effects of incremental speed-dependent treadmill training on postural instability and fear of falling in Parkinson's disease. Clinical Rehabilitation 21, 698-705.

Calabresi, P., Picconi, B., Tozzi, A., Ghiglieri, V., Di Filippo, M., 2014. Direct and indirect pathways of basal ganglia: a critical reappraisal. Nature Neuroscience 17, 1022-1030.

Canning, C., Allen, N., Fung, V., Morris, J., Dean, C., Year Home-based treadmill walking for individuals with Parkinson's disease: A pilot randomized controlled trial. In Movement Disorders.

Canning, C.G., Ada, L., Johnson, J.J., McWhirter, S., 2006. Walking capacity in mild to moderate Parkinson's disease. Archives of Physical Medicine and Rehabilitation 87, 371-375.

Chaudhuri, K.R., Schapira, A.H., 2009. Non-motor symptoms of Parkinson's disease: dopaminergic pathophysiology and treatment. Lancet Neurology 8, 464-474.

Chawla, G., Hoppe, M., Browner, N., Lewek, M.D., 2020. Individuals with Parkinson's disease retain spatiotemporal gait control with music and metronome cues. Motor Control 25, 33-43.

Chen, K., Yang, Y.J., Liu, F.T., Li, D.K., Bu, L.L., Yang, K., Wang, Y., Shen, B., Guan, R.Y., Song, J., Wang, J., Wu, J.J., 2017. Evaluation of PDQ-8 and its relationship with PDQ-39 in China: a three-year longitudinal study. Health and Quality of Life Outcomes 15, 170.

Chen, S., Zhang, Y., Wang, Y.T., Liu, X.L., 2016. Traditional Chinese mind and body exercises for promoting balance ability of old adults: a systematic review and meta-analysis. Evidence-Based Complementary and Alternative Medicine 2016, 7137362.

Cheung, C., Bhimani, R., Wyman, J.F., Konczak, J., Zhang, L., Mishra, U., Terluk, M., Kartha, R.V., Tuite, P., 2018. Effects of yoga on oxidative stress, motor function, and non-motor symptoms in Parkinson’s disease: a pilot randomized controlled trial. Pilot and Feasibility Studies 4, 1-11.

Cioni, M., Richards, C., Malouin, F., Bedard, P., Lemieux, R., 1997. Characteristics of the electromyographic patterns of lower limb muscles during gait in patients with Parkinson's

disease when OFF and ON L-Dopa treatment. The Italian Journal of Neurological Sciences 18, 195-208.

Crispino, P., Gino, M., Barbagelata, E., Ciarambino, T., Politi, C., Ambrosino, I., Ragusa, R., Marranzano, M., Biondi, A., Vacante, M., 2020. Gender differences and quality of life in Parkinson's disease. International Journal of Environmental Research and Public Health 18.

Cunnington, R., Iansek, R., Bradshaw, J.L., Phillips, J.G., 1995. Movement-related potentials in Parkinson's disease. Presence and predictability of temporal and spatial cues. Brain 118 (Pt 4), 935-950.

Curtze, C., Nutt, J.G., Carlson-Kuhta, P., Mancini, M., Horak, F.B., 2015. Levodopa is a double-edged sword for balance and gait in people with Parkinson's disease. Movement Disorders 30, 1361-1370.

Debaere, F., Wenderoth, N., Sunaert, S., Van Hecke, P., Swinnen, S.P., 2003. Internal vs external generation of movements: differential neural pathways involved in bimanual coordination performed in the presence or absence of augmented visual feedback. NeuroImage 19, 764-776.

Dibble, L.E., Hale, T.F., Marcus, R.L., Gerber, J.P., LaStayo, P.C., 2009. High intensity eccentric resistance training decreases bradykinesia and improves quality of life in persons with Parkinson's disease: A preliminary study. Parkinsonism & Related Disorders 15, 752-757.

Dietz, V., Zijlstra, W., Prokop, T., Berger, W., 1995. Leg muscle activation during gait in Parkinson's disease: adaptation and interlimb coordination. Electroencephalography and Clinical Neurophysiology 97, 408-415.

Dorsey, E.R., Bloem, B.R., 2018. The Parkinson pandemic-A call to action. JAMA Neurology 75, 9-10.

Dorsey, E.R., Sherer, T., Okun, M.S., Bloem, B.R., 2018. The emerging evidence of the Parkinson pandemic. Journal of Parkinson's Disease 8, S3-s8.

Duchesne, C., Gheysen, F., Bore, A., Albouy, G., Nadeau, A., Robillard, M.E., Bobeuf, F., Lafontaine, A.L., Lungu, O., Bherer, L., Doyon, J., 2016. Influence of aerobic exercise training on the neural correlates of motor learning in Parkinson's disease individuals. NeuroImage: Clinical 12, 559-569.

Duchesne, C., Lungu, O., Nadeau, A., Robillard, M.E., Boré, A., Bobeuf, F., Lafontaine, A.L., Gheysen, F., Bherer, L., Doyon, J., 2015. Enhancing both motor and cognitive functioning in Parkinson’s disease: Aerobic exercise as a rehabilitative intervention. Brain and Cognition 99, 68-77.

Ebersbach, G., Heijmenberg, M., Kindermann, L., Trottenberg, T., Wissel, J., Poewe, W., 1999. Interference of rhythmic constraint on gait in healthy subjects and patients with early Parkinson's disease: evidence for impaired locomotor pattern generation in early Parkinson's disease. Movement Disorders 14, 619-625.

Espy, D.D., Yang, F., Bhatt, T., Pai, Y.C., 2010a. Independent influence of gait speed and step length on stability and fall risk. Gait and Posture 32, 378-382.

Espy, D.D., Yang, F., Pai, Y.C., 2010b. Control of center of mass motion state through cuing and decoupling of spontaneous gait parameters in level walking. Journal of Biomechanics 43, 2548-2553.

Farashi, S., 2020. Distinguishing between Parkinson’s disease patients and healthy individuals using a comprehensive set of time, frequency and time-frequency features extracted from vertical ground reaction force data. Biomedical Signal Processing and Control 62, 102132.

Farashi, S., 2021. Analysis of the stance phase of the gait cycle in Parkinson’s disease and its potency for Parkinson’s disease discrimination. Journal of Biomechanics 129, 110818.

Faul, F., Erdfelder, E., Buchner, A., Lang, A.-G., 2009. Statistical power analyses using G* Power 3.1: Tests for correlation and regression analyses. Behavior Research Methods 41, 1149-1160.

Feng, Y.-S., Yang, S.-D., Tan, Z.-X., Wang, M.-M., Xing, Y., Dong, F., Zhang, F., 2020. The benefits and mechanisms of exercise training for Parkinson's disease. Life Sciences 245, 117345.

Fisher, B.E., Wu, A.D., Salem, G.J., Song, J., Lin, C.-H.J., Yip, J., Cen, S., Gordon, J., Jakowec, M., Petzinger, G., 2008. The effect of exercise training in improving motor performance and corticomotor excitability in people with early Parkinson's disease. Archives of Physical Medicine and Rehabilitation 89, 1221-1229.

Ford, M.P., Malone, L.A., Nyikos, I., Yelisetty, R., Bickel, C.S., 2010. Gait training with progressive external auditory cueing in persons with Parkinson's disease. Archives of Physical Medicine and Rehabilitation 91, 1255-1261.

Forte, R., Tocci, N., De Vito, G., 2021. The impact of exercise intervention with rhythmic auditory stimulation to improve gait and mobility in Parkinson disease: An umbrella review. Brain Science 11.

Frazzitta, G., Maestri, R., Uccellini, D., Bertotti, G., Abelli, P., 2009. Rehabilitation treatment of gait in patients with Parkinson's disease with freezing: a comparison between two physical therapy protocols using visual and auditory cues with or without treadmill training. Movement Disorders 24, 1139-1143.

Frenkel-Toledo, S., Giladi, N., Peretz, C., Herman, T., Gruendlinger, L., Hausdorff, J.M., 2005. Treadmill walking as an external pacemaker to improve gait rhythm and stability in Parkinson's disease. Movement Disorders 20, 1109-1114.

Gallagher, D.A., Lees, A.J., Schrag, A., 2010. What are the most important nonmotor symptoms in patients with Parkinson's disease and are we missing them? Movement Disorders 25, 2493-2500.

Galna, B., Lord, S., Burn, D.J., Rochester, L., 2015. Progression of gait dysfunction in incident Parkinson's disease: impact of medication and phenotype. Movement Disorders 30, 359-367.

Georgiou, N., Iansek, R., Bradshaw, J.L., Phillips, J.G., Mattingley, J.B., Bradshaw, J.A., 1993. An evaluation of the role of internal cues in the pathogenesis of parkinsonian hypokinesia. Brain 116 (Pt 6), 1575-1587.

Ghai, S., Ghai, I., Schmitz, G., Effenberg, A.O., 2018. Effect of rhythmic auditory cueing on parkinsonian gait: A systematic review and meta-analysis. Scientific Reports 8, 506.

Giardini, M., Turcato, A.M., Arcolin, I., Corna, S., Godi, M., 2023. Vertical ground reaction forces in Parkinson's disease: a speed-matched comparative analysis with healthy subjects. Sensors (Basel) 24.

Ginis, P., Nackaerts, E., Nieuwboer, A., Heremans, E., 2018. Cueing for people with Parkinson's disease with freezing of gait: A narrative review of the state-of-the-art and novel perspectives. Annals of Physical Rehabilitation and Medicine 61, 407-413.

Ginis, P., Pirani, R., Basaia, S., Ferrari, A., Chiari, L., Heremans, E., Canning, C.G., Nieuwboer, A., 2017. Focusing on heel strike improves toe clearance in people with Parkinson’s disease: an observational pilot study. Physiotherapy 103, 485-490.

Goldman, S.M., 2014. Environmental toxins and Parkinson's disease. Annual Review of Pharmacology and Toxicology 54, 141-164.

Gonzalez, E.G., Corcoran, P.J., 1994. Energy expenditure during ambulation, The Physiological Basis of Rehabilitation Medicine. Elsevier, pp. 413-446.

Goodwin, V.A., Richards, S.H., Taylor, R.S., Taylor, A.H., Campbell, J.L., 2008. The effectiveness of exercise interventions for people with Parkinson's disease: a systematic review and meta-analysis. Movement Disorders 23, 631-640.

Gottschall, J.S., Kram, R., 2003. Energy cost and muscular activity required for propulsion during walking. Journal of Applied Physiology 94, 1766-1772.

Habets, J.G.V., Heijmans, M., Kuijf, M.L., Janssen, M.L.F., Temel, Y., Kubben, P.L., 2018. An update on adaptive deep brain stimulation in Parkinson's disease. Movement Disorders 33, 1834-1843.

Hackney, M.E., Earhart, G.M., 2010. Effects of dance on balance and gait in severe Parkinson disease: a case study. Disabililty and Rehabilitation 32, 679-684.

Harro, C., Shoemaker, M., Frey, O., Gamble, A., Harring, K., Karl, K., McDonald, J., Murray, C., VanDyke, J., Tomassi, E., 2014. The effects of speed-dependent treadmill training and rhythmic auditory-cued overground walking on balance function, fall incidence, and quality of life in individuals with idiopathic Parkinson's disease: a randomized controlled trial. NeuroRehabilitation 34, 541-556.

Hausdorff, J.M., Cudkowicz, M.E., Firtion, R., Wei, J.Y., Goldberger, A.L., 1998. Gait variability and basal ganglia disorders: stride-to-stride variations of gait cycle timing in Parkinson's disease and Huntington's disease. Movement Disorders 13, 428-437.

Hely, M.A., Reid, W.G., Adena, M.A., Halliday, G.M., Morris, J.G., 2008. The Sydney multicenter study of Parkinson's disease: the inevitability of dementia at 20 years. Movement disorders 23, 837-844.

Herman, T., Giladi, N., Gruendlinger, L., Hausdorff, J.M., 2007. Six weeks of intensive treadmill training improves gait and quality of life in patients with Parkinson's disease: a pilot study. Archives of Physical Medicine and Rehabilitation 88, 1154-1158.

Herman, T., Giladi, N., Hausdorff, J., 2009. Treadmill training for the treatment of gait disturbances in people with Parkinson's disease: a mini-review. Journal of Neural Transmission 116, 307-318.

Hirsch, M.A., Farley, B.G., 2009. Exercise and neuroplasticity in persons living with Parkinson's disease. European Journal of Physical Rehabilitation and Medicine 45, 215-229.

Hobert, M.A., Nussbaum, S., Heger, T., Berg, D., Maetzler, W., Heinzel, S., 2019. Progressive gait deficits in Parkinson's disease: A wearable-based biannual 5-year prospective study. Frontiers in Aging Neuroscience 11, 22.

Hollman, J.H., McDade, E.M., Petersen, R.C., 2011. Normative spatiotemporal gait parameters in older adults. Gait and Posture 34, 111-118.

Holmes, W.M., Hackney, M.E., 2017. Adapted tango for adults with Parkinson's disease: a qualitative study. Adapted Physical Activity Quarterly 34, 256-275.

Hoops, S., Nazem, S., Siderowf, A., Duda, J., Xie, S., Stern, M., Weintraub, D., 2009. Validity of the MoCA and MMSE in the detection of MCI and dementia in Parkinson's disease. Neurology 73, 1738-1745.

Hoppe, M., Chawla, G., Browner, N., Lewek, M.D., 2020. The effects of metronome frequency differentially affects gait on a treadmill and overground in people with Parkinson's disease. Gait and Posture 79, 41-45.

Howe, T.E., Lövgreen, B., Cody, F.W., Ashton, V.J., Oldham, J.A., 2003. Auditory cues can modify the gait of persons with early-stage Parkinson's disease: a method for enhancing parkinsonian walking performance? Clinical Rehabilitation 17, 363-367.

Hsiao, H., Knarr, B.A., Higginson, J.S., Binder-Macleod, S.A., 2015. Mechanisms to increase propulsive force for individuals poststroke. Journal of Neuroengineering and Rehabilitation 12, 1-8.

Huang, T.T., Hsu, H.Y., Wang, B.H., Chen, K.H., 2011. Quality of life in Parkinson's disease patients: validation of the short-form eight-item Parkinson's Disease Questionnaire (PDQ-8) in Taiwan. Quality of Life Research 20, 499-505.

Jankovic, J., 2008. Parkinson's disease: clinical features and diagnosis. Journal of Neurology, Neurosurgery and Psychiatry 79, 368-376.

Jankovic, J., Rajput, A.H., McDermott, M.P., Perl, D.P., 2000. The evolution of diagnosis in early Parkinson's disease. Parkinson's study group. Archieves of Neurology 57, 369-372.

Jenkinson, C., Fitzpatrick, R., Peto, V., Greenhall, R., Hyman, N., 1997. The PDQ-8: development and validation of a short-form Parkinson's disease questionnaire. Psychology and Health 12, 805-814.

Jenner, P., Olanow, C.W., 1998. Understanding cell death in Parkinson's disease. Annals of Neurology 44, S72-84.

Kajrolkar, T., Yang, F., Pai, Y.C., Bhatt, T., 2014. Dynamic stability and compensatory stepping responses during anterior gait-slip perturbations in people with chronic hemiparetic stroke. Journal of Biomechanics 47, 2751-2758.

Kalia, L.V., Lang, A.E., 2016. Parkinson disease in 2015: Evolving basic, pathological and clinical concepts in PD. Nature Reviews Neurology 12, 65-66.

Kang, M.G., Yun, S.J., Shin, H.I., Kim, E., Lee, H.H., Oh, B.M., Seo, H.G., 2019. Effects of robot-assisted gait training in patients with Parkinson's disease: study protocol for a randomized controlled trial. Trials Journal 20, 15.

Kim, H.-D., Jae, H.D., Jeong, J.H., 2014. Tai Chi exercise can improve the obstacle negotiating ability of people with Parkinson’s disease: a preliminary study. Journal of Physical Therapy Science 26, 1025-1030.

Knutsson, E., 1972. An analysis of Parkinsonian gait. Brain 95, 475-486.

Koch, S.C., Mergheim, K., Raeke, J., Machado, C.B., Riegner, E., Nolden, J., Diermayr, G., Von Moreau, D., Hillecke, T.K., 2016. The embodied self in Parkinson's disease: feasibility of a single tango intervention for assessing changes in psychological health outcomes and aesthetic experience. Frontiers in Neuroscience 10, 287.

Koshimori, Y., Thaut, M.H., 2018. Future perspectives on neural mechanisms underlying rhythm and music based neurorehabilitation in Parkinson's disease. Ageing Research Reviews 47, 133-139.

Kuo, A.D., Donelan, J.M., 2010. Dynamic principles of gait and their clinical implications. Physical Therapy 90, 157-174.

Kyrdalen, I.L., Thingstad, P., Sandvik, L., Ormstad, H., 2019. Associations between gait speed and well-known fall risk factors among community-dwelling older adults. Physiotherapy Research International 24, e1743.

Lakens, D., 2013. Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t-tests and ANOVAs. Frontiers in Psychology 4, 863.

Lang, J.T., Kassan, T.O., Devaney, L.L., Colon-Semenza, C., Joseph, M.F., 2016. Test-retest reliability and minimal detectable change for the 10-meter walk test in older adults with Parkinson's disease. Journal of Geriatric Physical Therapy 39, 165-170.

Langston, J.W., Ballard, P., Tetrud, J.W., Irwin, I., 1983. Chronic Parkinsonism in humans due to a product of meperidine-analog synthesis. Science 219, 979-980.

Lewitt, P.A., 2008. Levodopa for the treatment of Parkinson's disease. New England Journal of Medicine 359, 2468-2476.

Li, T., Le, W., 2020. Biomarkers for Parkinson's disease: how good are they? Neuroscience Bulletin 36, 183-194.

Lima, L.O., Scianni, A., Rodrigues-de-Paula, F., 2013. Progressive resistance exercise improves strength and physical performance in people with mild to moderate Parkinson's disease: a systematic review. Journal of Physiotherapy 59, 7-13.

Lin, M.W., Liu, W., Yang, F., 2020. Influence of multiple sclerosis on dynamic gait stability. Journal of Biomechanics 106, 109827.

Liu, X.L., Chen, S., Wang, Y., 2016. Effects of health qigong exercises on relieving symptoms of Parkinson’s disease. Evidence-Based Complementary and Alternative Medicine 2016, 5935782.

Liu, Z.-Q., Yang, F., 2017. Obesity may not induce dynamic stability disadvantage during overground walking among young adults. PLoS One 12, e0169766.

Mak, M.K., Yang, F., Pai, Y.C., 2011. Limb collapse, rather than instability, causes failure in sit-to-stand performance among patients with parkinson disease. Physical Therapy 91, 381-391.

Malatesta, D., Canepa, M., Menendez Fernandez, A., 2017. The effect of treadmill and overground walking on preferred walking speed and gait kinematics in healthy, physically active older adults. European Journal of Applied Physiology 117, 1833-1843.

Martin, P.E., Marsh, A.P., 1992. Step length and frequency effects on ground reaction forces during walking. Journal of Biomechanics 25, 1237-1239.

McIntosh, G.C., Brown, S.H., Rice, R.R., Thaut, M.H., 1997. Rhythmic auditory-motor facilitation of gait patterns in patients with Parkinson's disease. Journal of Neurology, Neurosurgery, and Psychiatry 62, 22-26.

Mehrholz, J., Kugler, J., Storch, A., Pohl, M., Elsner, B., Hirsch, K., 2015. Treadmill training for patients with Parkinson's disease. Cochrane Database of Systematic Reviews.

Michel, P.P., Hirsch, E.C., Hunot, S., 2016. Understanding dopaminergic cell death pathways in Parkinson disease. Neuron 90, 675-691.

Miller-Patterson, C., Buesa, R., McLaughlin, N., Jones, R., Akbar, U., Friedman, J.H., 2018. Motor asymmetry over time in Parkinson's disease. Journal of Neurological Sciences 393, 14-17.

Moisan, F., Kab, S., Mohamed, F., Canonico, M., Le Guern, M., Quintin, C., Carcaillon, L., Nicolau, J., Duport, N., Singh-Manoux, A., Boussac-Zarebska, M., Elbaz, A., 2016.

Parkinson disease male-to-female ratios increase with age: French nationwide study and meta-analysis. Journal of Neurology, Neurosurgery, and Psychiatry 87, 952-957.

Morens, D.M., Folkers, G.K., Fauci, A.S., 2009. What is a pandemic? Journal of Infectious Diseases 200, 1018-1021.

Morris, Iansek, R., Matyas, T.A., Summers, J.J., 1994. The pathogenesis of gait hypokinesia in Parkinson's disease. Brain: A Journal of Neurology 117 (Pt 5), 1169-1181.

Morris, M., 2000. Movement disorders in people With Parkinson disease: a model for physical therapy. Physical therapy 80, 578-597.

Morris, M., Iansek, R., Matyas, T., Summers, J., 1998. Abnormalities in the stride length-cadence relation in parkinsonian gait. Movement Disorders 13, 61-69.

Morris, M.E., Iansek, R., Matyas, T.A., Summers, J.J., 1996. Stride length regulation in Parkinson's disease. Normalization strategies and underlying mechanisms. Brain: A Journal of Neurology 119 (Pt 2), 551-568.

Morris, M.E., McGinley, J., Huxham, F., Collier, J., Iansek, R., 1999. Constraints on the kinetic, kinematic and spatiotemporal parameters of gait in Parkinson's disease. Human Movement Science 18, 461-483.

Murgia, M., Pili, R., Corona, F., Sors, F., Agostini, T.A., Bernardis, P., Casula, C., Cossu, G., Guicciardi, M., Pau, M., 2018. The use of footstep sounds as rhythmic auditory stimulation for gait rehabilitation in Parkinson's disease: a randomized controlled trial. Frontiers in Neurology 9, 348.

Murray, M.P., Sepic, S.B., Gardner, G.M., Downs, W.J., 1978. Walking patterns of men with parkinsonism. American Journal of Physical Medicine and Rehabilitation 57, 278-294.

Muslimovic, D., Post, B., Speelman, J.D., Schmand, B., de Haan, R.J., 2008. Determinants of disability and quality of life in mild to moderate Parkinson disease. Neurology 70, 2241-2247.

Muthukrishnan, N., Abbas, J.J., Shill, H.A., Krishnamurthi, N., 2019. Cueing paradigms to improve gait and posture in Parkinson's disease: a narrative review. Sensors (Basel) 19.

Nadeau, A., Lungu, O., Duchesne, C., Robillard, M., Bore, A., Bobeuf, F., Plamondon, R., Lafontaine, A.L., Gheysen, F., Bherer, L., Doyon, J., 2016. A 12-week cycling training regimen improves gait and executive functions concomitantly in people with Parkinson's disease. Frontiers in Human Neuroscience 10, 690.

Nasreddine, Z.S., Phillips, N.A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J.L., Chertkow, H., 2005. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. Journal of the American Geriatrics Society 53, 695-699.

Nieuwboer, A., Kwakkel, G., Rochester, L., Jones, D., van Wegen, E., Willems, A.M., Chavret, F., Hetherington, V., Baker, K., Lim, I., 2007. Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. Journal of Neurology, Neurosurgery, and Psychiatry 78, 134-140.

Nilsson, J., Thorstensson, A., 1989. Ground reaction forces at different speeds of human walking and running. Acta Physiologica Scandinavia 136, 217-227.

Owais, S., Siddique, Y.H., 2023. A comprehensive study of miRNAs in Parkinson's disease: diagnostics and therapeutic approaches. CNS & Neurological Disorders - Drug Targets 22, 353-380.

Pai, Y.-C., Yang, F., Wening, J.D., Pavol, M.J., 2006. Mechanisms of limb collapse following a slip among young and older adults. Journal of Biomechanics 39, 2194-2204.

Pai, Y.C., Patton, J., 1997. Center of mass velocity-position predictions for balance control. Journal of Biomechanics 30, 347-354.

Parkinson, J., 2002. An essay on the shaking palsy. 1817. Journal of Neuropsychiatry and Clinical Neuroscience 14, 223-236; discussion 222.

Pelosin, E., Faelli, E., Lofrano, F., Marinelli, L., Bove, M., Ruggeri, P., Abbruzzese, G., Year Treadmill training improves functional ability and cardiopulmonary capacity in stable Parkinson's disease. In Movement Disorders.

Perry, J., Burnfield, J., 2024. Gait analysis: normal and pathological function. CRC Press.

Peterson, C.L., Kautz, S.A., Neptune, R.R., 2011. Braking and propulsive impulses increase with speed during accelerated and decelerated walking. Gait and Posture 33, 562-567.

Peto, V., Jenkinson, C., Fitzpatrick, R., 1998. PDQ-39: A review of the development, validation and application of a Parkinson's disease Quality of Life Questionnaire and its associated measures. Journal of Neurology 245 Suppl 1, S10-14.

Plotnik, M., Hausdorff, J.M., 2008. The role of gait rhythmicity and bilateral coordination of stepping in the pathophysiology of freezing of gait in Parkinson's disease. Movement Disorders 23 Suppl 2, S444-450.

Pohl, M., Rockstroh, G., Rückriem, S., Mrass, G., Mehrholz, J., 2003. Immediate effects of speed-dependent treadmill training on gait parameters in early Parkinson's disease. Archives of Physical Medicine and Rehabilitation 84, 1760-1766.

Polymeropoulos, M.H., Lavedan, C., Leroy, E., Ide, S.E., Dehejia, A., Dutra, A., Pike, B., Root, H., Rubenstein, J., Boyer, R., Stenroos, E.S., Chandrasekharappa, S., Athanassiadou, A.,

Papapetropoulos, T., Johnson, W.G., Lazzarini, A.M., Duvoisin, R.C., Di Iorio, G., Golbe, L.I., Nussbaum, R.L., 1997. Mutation in the alpha-synuclein gene identified in families with Parkinson's disease. Science 276, 2045-2047.

Postuma, R.B., Gagnon, J.F., Montplaisir, J., 2010. Clinical prediction of Parkinson's disease: planning for the age of neuroprotection. Journal of Neurology, Neurosurgery, and Psychiatry 81, 1008-1013.

Pötter-Nerger, M., Volkmann, J., 2013. Deep brain stimulation for gait and postural symptoms in Parkinson's disease. Movement Disorders 28, 1609-1615.

Protas, E.J., Mitchell, K., Williams, A., Qureshy, H., Caroline, K., Lai, E.C., 2005. Gait and step training to reduce falls in Parkinson's disease. NeuroRehabilitation 20, 183-190.

Rajput, A.H., Rozdilsky, B., Rajput, A., 1991. Accuracy of clinical diagnosis in parkinsonism--a prospective study. Canadian Journal of Neurological Sciences 18, 275-278.

Rascol, O., Brooks, D.J., Korczyn, A.D., De Deyn, P.P., Clarke, C.E., Lang, A.E., 2000. A five-year study of the incidence of dyskinesia in patients with early Parkinson's disease who were treated with ropinirole or levodopa. New England Journal of Medicine 342, 1484-1491.

Redgrave, P., Rodriguez, M., Smith, Y., Rodriguez-Oroz, M.C., Lehericy, S., Bergman, H., Agid, Y., DeLong, M.R., Obeso, J.A., 2010. Goal-directed and habitual control in the basal ganglia: implications for Parkinson's disease. Nature Reviews Neuroscience 11, 760-772.

Rocca, W.A., 2018. The burden of Parkinson's disease: a worldwide perspective. Lancet Neurology 17, 928-929.

Rochester, L., Baker, K., Nieuwboer, A., Burn, D., 2011. Targeting dopa-sensitive and dopa-resistant gait dysfunction in Parkinson's disease: selective responses to internal and external cues. Movement Disorders 26, 430-435.

Rodriguez, K.L., Roemmich, R.T., Cam, B., Fregly, B.J., Hass, C.J., 2013. Persons with Parkinson’s disease exhibit decreased neuromuscular complexity during gait. Clinical Neurophysiology 124, 1390-1397.

Rubinstein, T.C., Giladi, N., Hausdorff, J.M., 2002. The power of cueing to circumvent dopamine deficits: a review of physical therapy treatment of gait disturbances in Parkinson's disease. Movement Disorders 17, 1148-1160.

Saltychev, M., Bärlund, E., Paltamaa, J., Katajapuu, N., Laimi, K., 2016. Progressive resistance training in Parkinson's disease: a systematic review and meta-analysis. BMJ Open 6, e008756.

Sasco, A.J., Paffenbarger, R.S., Jr., Gendre, I., Wing, A.L., 1992. The role of physical exercise in the occurrence of Parkinson's disease. Archives of Neurology 49, 360-365.

Scheperjans, F., Pekkonen, E., Kaakkola, S., Auvinen, P., 2015. Linking smoking, coffee, urate, and Parkinson's disease - a role for gut microbiota? Journal of Parkinson's Disease 5, 255-262.

Schmida, E.A., Wille, C.M., Stiffler-Joachim, M.R., Kliethermes, S.A., Heiderscheit, B.C., 2022. Vertical loading rate is not associated with running injury, regardless of calculation method. Medicine and Science in Sports and Exercise 54, 1382-1388.

Senden, R., Marcellis, R., Willems, P., Witlox, M., Meijer, K., 2024. Normative 3D gait data of healthy adults walking at three different speeds on an instrumented treadmill in virtual reality. Data Brief 53, 110230.

Sethi, K., 2008. Levodopa unresponsive symptoms in Parkinson disease. Movement Disorders 23 Suppl 3, S521-533.

Sharifmoradi, K., Farahpour, N., 2016. An assessment of gait spatiotemporal and GRF of Parkinson patients. Health Rehabilitation 1, 1-6.

Shen, X., Wong-Yu, I.S., Mak, M.K., 2016. Effects of exercise on falls, balance, and gait ability in Parkinson's disease: a meta-analysis. Neurorehabilitatioin and Neural Repair 30, 512-527.

Sherron, M.A., Stevenson, S.A., Browner, N.M., Lewek, M.D., 2020. Targeted rhythmic auditory cueing during treadmill and overground gait for individuals with Parkinson disease: a case series. Journal of Neurologic Physical Therapy 44, 268-274.

Shin, S., Simpkins, C., Ahn, J., Yang, F., 2024. Impact of standing perturbation intensities on fall and stability outcomes in healthy young adults. Journal of Biomechanics 168, 112123.

Shumway-Cook, A., Horak, F.B., 1986. Assessing the influence of sensory interaction on balance: suggestion from the field. Physical Therapy 66, 1548-1550.

Silva-Batista, C., de Brito, L.C., Corcos, D.M., Roschel, H., de Mello, M.T., Piemonte, M.E.P., Tricoli, V., Ugrinowitsch, C., 2017. Resistance training improves sleep quality in subjects with moderate Parkinson's disease. The Journal of Strength & Conditioning Research 31.

Simpkins, C., Ahn, J., Shin, S., Yang, F., 2022. Recovery from an unexpected standing-slip in professional ballet dancers. Journal of Biomechanics 145, 111366.

Simpkins, C., Yang, F., 2023. Do dance style and intervention duration matter in improving balance among people with Parkinson's disease? A systematic review with meta-analysis. Parkinsonism and Related Disorders 106, 105231.

Simpkins, C., Yang, F., 2024. Dynamic gait stability and spatiotemporal gait parameters during overground walking in professional ballet dancers. Journal of Dance Medicine and Science 28, 28-36.

Skidmore, F.M., Patterson, S.L., Shulman, L.M., Sorkin, J.D., Macko, R.F., 2008. Pilot safety and feasibility study of treadmill aerobic exercise in Parkinson disease with gait impairment. Journal of Rehabilitation Research & Development 45.

Song, J.H., Zhou, P.Y., Cao, Z.H., Ding, Z.G., Chen, H.X., Zhang, G.B., 2015. Rhythmic auditory stimulation with visual stimuli on motor and balance function of patients with Parkinson's disease. European Review for Medical Pharmacological Sciences 19, 2001-2007.

Stacoff, A., Diezi, C., Luder, G., Stüssi, E., Kramers-de Quervain, I.A., 2005. Ground reaction forces on stairs: effects of stair inclination and age. Gait & Posture 21, 24-38.

Steib, S., Wanner, P., Adler, W., Winkler, J., Klucken, J., Pfeifer, K., 2018. A single bout of aerobic exercise improves motor skill consolidation in Parkinson's disease. Frontiers in Aging Neuroscience 10, 328.

Sullivan, G.M., Feinn, R., 2012. Using effect size—or why the P value is not enough. Journal of Graduate Medical Education 4, 279-282.

Tabakin, D., 2000. A comparison of 3D gait models based on the Helen Hayes Hospital marker set. University of Cape Town.

Takakusaki, K., Tomita, N., Yano, M., 2008. Substrates for normal gait and pathophysiology of gait disturbances with respect to the basal ganglia dysfunction. Journal of Neurology 255 Suppl 4, 19-29.

Tang, L., Fang, Y., Yin, J., 2019. The effects of exercise interventions on Parkinson’s disease: a Bayesian network meta-analysis. Journal of Clinical Neuroscience 70, 47-54.

Thanvi, B., Lo, N., Robinson, T., 2007. Levodopa-induced dyskinesia in Parkinson's disease: clinical features, pathogenesis, prevention and treatment. Postgraduate Medical Journal 83, 384-388.

Thaut, McIntosh, G.C., Rice, R.R., Miller, R.A., Rathbun, J., Brault, J., 1996. Rhythmic auditory stimulation in gait training for Parkinson's disease patients. Movement Disorders 11, 193-200.

Thaut, M.H., Abiru, M., 2010. Rhythmic auditory stimulation in rehabilitation of movement disorders: a review of current research. Music Perception 27, 263-269.

Thaut, M.H., Kenyon, G.P., Schauer, M.L., McIntosh, G.C., 1999. The connection between rhythmicity and brain function. IEEE Engineering in Medicine and Biology 18, 101-108.

Thaut, M.H., McIntosh, G.C., Hoemberg, V., 2015. Neurobiological foundations of neurologic music therapy: rhythmic entrainment and the motor system. Frontiers in Psychology 5, 1185.

Thaut, M.H., Rice, R.R., Braun Janzen, T., Hurt-Thaut, C.P., McIntosh, G.C., 2019. Rhythmic auditory stimulation for reduction of falls in Parkinson's disease: a randomized controlled study. Clinical Rehabilitation 33, 34-43.

Tran, M.D., Holly, R.G., Lashbrook, J., Amsterdam, E.A., 2001. Effects of Hatha yoga practice on the health-related aspects of physical fitness. Preventive Cardiology 4, 165-170.

Tsang, H.W., Cheung, L., Lak, D.C., 2002. Qigong as a psychosocial intervention for depressed elderly with chronic physical illnesses. International Journal of Geriatric Psychiatry 17, 1146-1154.

Urakami, H., Nikaido, Y., Kuroda, K., Ohno, H., Saura, R., Okada, Y., 2021. Forward gait instability in patients with Parkinson's disease with freezing of gait. Neuroscience Research 173, 80-89.

Uygur, M., Bellumori, M., Knight, C.A., 2017. Effects of a low-resistance, interval bicycling intervention in Parkinson's Disease. Physiotherapy Theory Practice 33, 897-904.

Van Den Eeden, S.K., Tanner, C.M., Bernstein, A.L., Fross, R.D., Leimpeter, A., Bloch, D.A., Nelson, L.M., 2003. Incidence of Parkinson's disease: variation by age, gender, and race/ethnicity. American Journal of Epidemiology 157, 1015-1022.

Vásquez, K.A., Valverde, E.M., Aguilar, D.V., Gabarain, H.-J.H., 2019. Montreal Cognitive Assessment scale in patients with Parkinson Disease with normal scores in the Mini-Mental State Examination. Dementia and Neuropsychologia 13, 78-81.

Vaughan, C.L., Davis, B.L., O'Connor, J.C., 1992. Dynamics of human gait. Human Kinetics Publishers.

Verghese, J., Holtzer, R., Lipton, R.B., Wang, C., 2009. Quantitative gait markers and incident fall risk in older adults. The Journals of Gerontology 64, 896-901.

Voss, M.W., Nagamatsu, L.S., Liu-Ambrose, T., Kramer, A.F., 2011. Exercise, brain, and cognition across the life span. Journal of Applied Physiology 111, 1505-1513.

Wang, T.Y., Bhatt, T., Yang, F., Pai, Y.C., 2011. Generalization of motor adaptation to repeated-slip perturbation across tasks. Neuroscience 180, 85-95.

Weiss, D., Schoellmann, A., Fox, M.D., Bohnen, N.I., Factor, S.A., Nieuwboer, A., Hallett, M., Lewis, S.J.G., 2020. Freezing of gait: understanding the complexity of an enigmatic phenomenon. Brain 143, 14-30.

Wells, M., Yang, F., 2021. Ballroom dance as a form of rehabilitation: a systematic review. Biomechanics 1, 307-320.

Whetten-Goldstein, K., Sloan, F., Kulas, E., Cutson, T., Schenkman, M., 1997. The burden of Parkinson's disease on society, family, and the individual. Journal of the American Geriatric Society 45, 844-849.

Winter, D.A., 2009. Biomechanics and motor control of human movement. John Wiley & Sons.

Wirdefeldt, K., Adami, H.O., Cole, P., Trichopoulos, D., Mandel, J., 2011. Epidemiology and etiology of Parkinson's disease: a review of the evidence. European Journal of Epidemiology 26 Suppl 1, S1-58.

Wu, P.L., Lee, M., Huang, T.T., 2017. Effectiveness of physical activity on patients with depression and Parkinson's disease: a systematic review. PLoS One 12, e0181515.

Wu, T., Hallett, M., 2008. Neural correlates of dual task performance in patients with Parkinson's disease. Journal of Neurology, Neurosurgery, and Psychiatry 79, 760-766.

Xiao, C.M., Zhuang, Y.C., 2016. Effect of health Baduanjin Qigong for mild to moderate Parkinson's disease. Geriatrics and Gerontology International 16, 911-919.

Yang, F., 2018. Slip and fall risk assessment, in: Müller, B., Wolf, S.I., Brueggemann, G.-P., Deng, Z., McIntosh, A., Miller, F., Selbie, W.S. (Eds.), Handbook of Human Motion. Springer International Publishing, Cham, pp. 1-22.

Yang, F., 2020. Application of vibration training in people with common neurological disorders. Manual of Vibration Exercise and Vibration Therapy, 343-353.

Yang, F., Anderson, F.C., Pai, Y.C., 2007. Predicted threshold against backward balance loss in gait. Journal of Biomechanics 40, 804-811.

Yang, F., Ban, R., Yang, F., 2022. Anterior load carriage increases the risk of falls in young adults following a slip in gait. Safety Science 145, 105489.

Yang, F., Bhatt, T., Pai, Y.C., 2009. Role of stability and limb support in recovery against a fall following a novel slip induced in different daily activities. Journal of Biomechanics 42, 1903-1908.

Yang, F., Espy, D., Bhatt, T., Pai, Y.-C., 2012. Two types of slip-induced falls among community dwelling older adults. Journal of Biomechanics 45, 1259-1264.

Yang, F., Kim, J., Munoz, J., 2016. Adaptive gait responses to awareness of an impending slip during treadmill walking. Gait and Posture 50, 175-179.

Yang, F., King, G.A., 2016. Dynamic gait stability of treadmill versus overground walking in young adults. Journal of Electromyography and Kinesiology 31, 81-87.

Yang, F., Liu, W., 2021. Individual analysis of dynamic stability for twenty-four Tai Chi forms among persons with knee osteoarthritis: A pilot study. Gait and Posture 86, 22-26.

Yang, F., Pai, C.Y., 2013. Alteration in community-dwelling older adults' level walking following perturbation training. Journal of Biomechanics 46, 2463-2468.

Yang, F., Pai, Y.C., 2014. Can stability really predict an impending slip-related fall among older adults? Journal of Biomechanics 47, 3876-3881.

Yang, F., Passariello, F., Pai, Y.C., 2008. Determination of instantaneous stability against backward balance loss: two computational approaches. Journal of Biomechanics 41, 1818-1822.

Yang, F., Saucedo, F., Qiao, M., 2018. Effects of a single-session stance-slip perturbation training program on reducing risk of slip-related falls. Journal of Biomechanics 72, 1-6.

Yang, F., Su, X., Wen, P.-S., Lazarus, J., 2019. Adaptation to repeated gait-slip perturbations among individuals with multiple sclerosis. Multiple Sclerosis and Related Disorders 35, 135-141.

Yang, W., Hamilton, J.L., Kopil, C., Beck, J.C., Tanner, C.M., Albin, R.L., Ray Dorsey, E., Dahodwala, N., Cintina, I., Hogan, P., Thompson, T., 2020. Current and projected future economic burden of Parkinson's disease in the U.S. NPJ Parkinson's Disease 6, 15.

APPENDICES

Appendix A: PD Questionnaire

1. When were you diagnosed with Parkinson's disease? (MM/YYYY) _____

2. Based on Hoehn and Yahr (H&Y), what stage are you diagnosed with? _____

3. Are you able to walk overground more than 30 feet without the need of walking aid or assistance? [Disqualified if answers NO] YES NO

4. Are you able to walk on a treadmill for at least 15 minutes without the need of walking aid or rest? [Disqualified if answers NO] YES NO

   About how long can you walk without needing to rest? _____

5. Have you been diagnosed with any uncontrolled cardiorespiratory or metabolic diseases? [Disqualified if answers YES.] YES NO

6. Do you experience any other known neurologic disorders that affect your ability to walk? [Disqualified if answers YES.] YES NO

7. Have you been diagnosed with any visual, auditory or communication disorders that might impede your understanding of the purpose of this study? [Disqualified if answers YES.] YES NO

8. Have you suffered a lower extremity injury within the last 6 months? [Disqualified if answers YES.] YES NO

Appendix B: Parkinsons Disease Quality of Life Questionnaire - 8

Due to having Parkinson's disease

how often during the last month have you…

*Please **check one box** for each question*

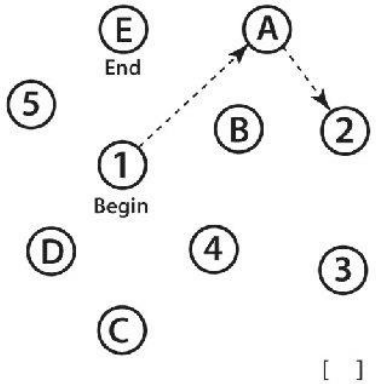
		Never	Occasionally	Sometimes	Often	Always or cannot do at all
1.	Had difficulty getting around in public places?	☐	☐	☐	☐	☐
2.	Had difficulty dressing?	☐	☐	☐	☐	☐
3.	Felt depressed?	☐	☐	☐	☐	☐
4.	Had problems with your close personal relationships?	☐	☐	☐	☐	☐
5.	Had problems with your concentration, for example, when reading or watching TV?	☐	☐	☐	☐	☐
6.	Felt unable to communicate effectively?	☐	☐	☐	☐	☐
7.	Had painful muscle cramps or spasms?	☐	☐	☐	☐	☐
8.	Felt embarrassed in public due to having Parkinson's disease?	☐	☐	☐	☐	☐

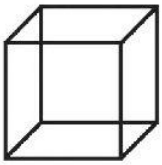
Appendix C: Montreal Cognitive Assessment

MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

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

VISUOSPATIAL / EXECUTIVE





Copy cube

[ ] [ ]

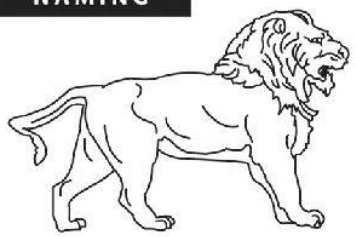
Draw CLOCK (Ten past eleven)
(3 points)

[ ] Contour [ ] Numbers [ ] Hands

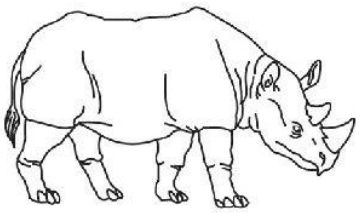
POINTS

__/5

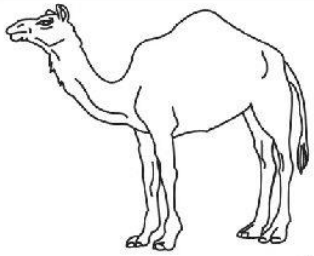
NAMING



[ ]



[ ]



[ ]

__/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. 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

www.mocatest.org

Normal ≥ 26 / 30

TOTAL __/30

Add 1 point if ≤ 12 yr edu

Administered by: _____

Appendix D: Preliminary Results

Six PwPD (2 females and 4 males, mean ± standard deviation age: 67 ± 2.97 years; body height: 1.65 ± 0.09 m; body mass: 72.8 ± 17.2 kg) participated in the pilot study. The protocol of the pilot study followed the one listed above in Section 3.5, with the exception that the mid-intervention overground walking assessment was excluded.

All outcomes were comparable between groups before the intervention (Table D1). No significant group-by-session interaction was observed for stride length ($F_{1,4}$ = 0.48, p = 0.5, partial η^2 = 0.11, Figure D1). However, the advanced group appeared to show a larger but non-significant increase in the stride length from pre- to post-intervention compared to the regular group (Figure D1, effect size of Cohen's d = 0.4). The non-significant finding could be due to the small sample size. No significant interaction effects were detected for cadence ($F_{1,4}$ = 0.04, p = 0.8, partial η^2 = 0.01), gait speed ($F_{1,4}$ = 0.14, p = 0.7, partial η^2 = 0.03), dynamic gait stability at touchdown ($F_{1,4}$ = 1.41, p = 0.3, partial η^2 = 0.26), and dynamic gait stability at liftoff ($F_{1,4}$ = 2.47, p = 0.2, partial η^2 = 0.38) (Table D1).

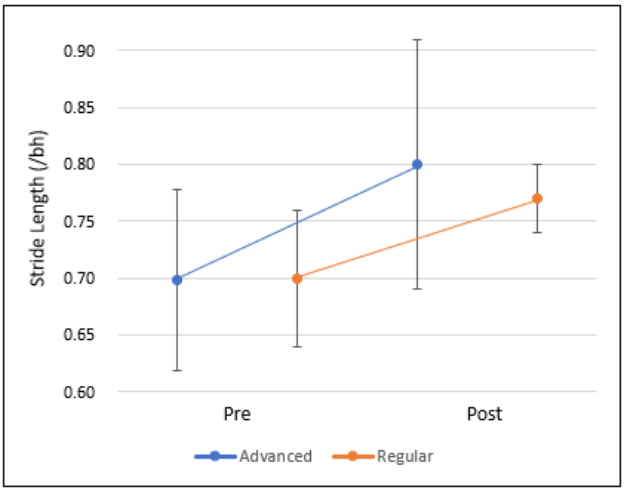


Figure D1 Comparisons of the stride length between the advanced training and regular training groups over the pre- and post-intervention assessments. The stride length is normalized by the body height.

Table D1 Gait parameters and dynamic gait stability presented as (mean ± standard deviation) before (Pre) after (Post) a 30-minute treadmill walking intervention for the advanced (n = 3) and regular (n = 3) groups.

Variable	Test session	Group	
		Advanced	Regular
Gait Characteristics			
Stride Length (/bh)	Pre	0.70 ± 0.08	0.70 ± 0.06
	Post	0.80 ± 0.11	0.77 ± 0.03
Cadence (steps/min)	Pre	113.55 ± 1.03	110.10 ± 18.30
	Post	119.69 ± 3.12	115.2 ± 25.80
Gait Speed (m/s)	Pre	1.19 ± 0.07	1.15 ± 0.14
	Post	1.40 ± 0.07	1.31 ± 0.28
Dynamic Gait Stability			
Touchdown	Pre	0.07 ± 0.01	0.05 ± 0.01
	Post	0.09 ± 0.02	0.05 ± 0.05
Liftoff	Pre	0.23 ± 0.03	0.22 ± 0.01
	Post	0.22 ± 0.02	0.17 ± 0.05

Appendix E: Power Analysis

The sample size for this study was determined based on the preliminary results from the pilot study (see Appendix D). Stride length was considered the primary outcome measure to calculate the sample size, as the reduced stride length is one of the most common gait deficits in PwPD. In addition, the main target of this dissertation project was to increase the stride length as a strategy to improve gait speed, which was not the focus in previous studies (Bello et al., 2013; Fisher et al., 2008; Herman et al., 2007; Morris et al., 1994; Protas et al., 2005). The estimated effect size (*d*) of stride length between groups calculated from a mixed ANOVA in the pilot study was 0.7. The software G*Power indicated that 15 participants in each group would allow us to detect a group-related difference in stride length with an alpha level of 0.05 and a statistical power of 0.80 (Faul et al., 2009).

Appendix F: Supplementary Results

Table F1 Kinematic gait variables during overground walking at a self-selected speed presented as (mean ± standard deviation) before (Pre), during (Mid), and after (Post) a 30-minute treadmill walking intervention for the advanced (ADV, n = 12) and regular (REG, n = 13) groups.

Variable	Group	Session		
		Pre	Mid	Post
Stride Length (/*bh*)	ADV	0.82 ± 0.07	0.87 ± 0.07	0.88 ± 0.03
	REG	0.79 ± 0.12	0.81 ± 0.12	0.82 ± 0.11
Cadence (steps/min)	ADV	106.72 ± 11.48	108.93 ± 12.31	110.00 ± 10.53
	REG	109.53 ± 6.20	110.27 ± 5.24	110.60 ± 5.50
Gait Speed (*bh*/s)	ADV	0.75 ± 0.13	0.82 ± 0.14	0.83 ± 0.12
	REG	0.74 ± 0.14	0.77 ± 0.13	0.78 ± 0.13
Single leg stance (s)	ADV	0.43 ± 0.05	0.43 ± 0.04	0.43 ± 0.03
	REG	0.41 ± 0.02	0.41 ± 0.02	0.41 ± 0.02
Double leg stance (s)	ADV	0.14 ± 0.03	0.14 ± 0.03	0.13 ± 0.03
	REG	0.14 ± 0.03	0.14 ± 0.02	0.14 ± 0.02

bh: body height

Table F2 Comparison of kinematic spatiotemporal variables during overground walking at a self-selected speed presented as group mean ± standard deviation before (Pre), during (Mid), and after (Post) a 30-minute treadmill walking intervention for the advanced (ADV, n = 12) and regular (REG, n = 13) groups. The Analysis of Variance (ANOVA) with repeated measures was used. The within-subject factor was the session (pre vs. mid vs. post) and the between-subject factor was the group (ADV vs. REG). Effect sizes (Cohen's d) are provided.

Variable	Group	Group × session interaction		Group main effect		Post-hoc p-value			Session main effect		Post-hoc p-value		
		F, p-value	d	F, p-value	d	Pre	Mid	Post	F, p-value	d	Pre - mid	Mid - post	Pre - post
Stride		**3.39, p = 0.04**	0.91	1.93, p = 0.18	0.55	0.40	0.15	0.09	**28.26, p <0.001**	1.2			
Length (/*bh*)	ADV										**<0.001**	0.07	**<0.001**
	REG										**0.03**	0.25	**0.005**
Cadence		1.02, p = 0.36	0.39	0.21, p = 0.65	0.18	0.45	0.73	0.86	**3.92, p = 0.04**	0.45			
(steps/min)	ADV										0.09	0.17	**0.02**
	REG										0.56	0.66	0.41
Gait		1.75, p = 0.19	0.62	0.62, p = 0.44	0.31	0.74	0.38	0.28	**17.82, p < 0.001**	0.94			
Speed (*bh*/s)	ADV										**0.001**	0.10	**< 0.001**
	REG										0.07	0.28	**0.02**
Single leg		0.61, p = 0.51	0.02	2.52, p = 0.13	0.66	0.11	0.19	0.13	0.56, p = 0.46	0.19			
stance (s)	ADV										0.14	0.48	0.44
	REG										0.98	0.92	0.94
Double leg		1.04, p = 0.36	0.63	0.32, p = 0.58	0.24	0.79	0.70	0.33	**5.78, p = 0.01**	1.0			
stance (s)	ADV										0.26	**0.02**	**0.01**
	REG										0.42	0.46	0.21

bh: body height.
p-values ≤ 0.05 are bolded.

Table F3 Kinetic variables during overground walking at a self-selected speed presented as (mean ± standard deviation) before (Pre), during (Mid), and after (Post) a 30-minute treadmill walking intervention for the advanced (ADV, *n* = 10) and regular (REG, *n* = 11) groups.

Variable	Group	Session		
		Pre	Mid	Post
1st peak vGRF (*bw*)	ADV	1.22 ± 0.15	1.3 ± 0.16	1.28 ± 0.14
	REG	1.17 ± 0.13	1.18 ± 0.12	1.19 ± 0.13
2nd peak vGRF (*bw*)	ADV	1.09 ± 0.09	1.1 ± 0.08	1.11 ± 0.09
	REG	1.04 ± 0.08	1.03 ± 0.05	1.04 ± 0.04
Rate of Loading (*bw/s*)	ADV	9.67 ± 2.46	10.33 ± 2.72	10.24 ± 1.92
	REG	1.96 ± 1.79	7.77 ± 1.95	8.29 ± 2.29
Peak Brake Force (*bw*)	ADV	-0.21 ± 0.05	-0.25 ± 0.05	-0.24 ± 0.04
	REG	-0.19 ± 0.06	-0.19 ± 0.05	-0.20 ± 0.06
Peak Propel Force (*bw*)	ADV	0.22 ± 0.03	0.24 ± 0.03	0.24 ± 0.003
	REG	0.20 ± 0.06	0.20 ± 0.04	0.21 ± 0.03
Braking Impulse (*bw·s*)	ADV	-0.03 ± 0.01	-0.04 ± 0.01	-0.04 ± 0.004
	REG	-0.03 ± 0.01	-0.03 ± 0.01	-0.03 ± 0.01
Propel Impulse (*bw·s*)	ADV	0.03 ± 0.003	0.04 ± 0.004	0.04 ± 0.005
	REG	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01

vGRF: vertical ground reaction force.
bw: Body weight.

Table F4 Comparison of kinetic variables during overground walking at a self-selected speed before (Pre), during (Mid), and after (Post) a 30-minute treadmill walking intervention for the advanced (ADV, $n = 10$) and regular (REG, $n = 11$) groups. The Analysis of Variance (ANOVA) with repeated measures was used. Effect sizes (Cohen's d) are provided.

Variable	Group	Group × session interaction		Group main effect		Post-hoc p-value			Session main effect		Post-hoc p-value		
		F, p-value	d	F, p-value	d	Pre	Mid	Post	F, p-value	d	Pre - Mid	Mid - Post	Pre - Post
1st Peak vGRF (*bw*)		**3.45, $p = 0.04$**	0.65	1.81, $p = 0.20$	0.57	0.52	0.78	0.19	**5.71, $p = 0.01$**	0.97			
	ADV										**0.001**	0.12	**0.02**
	REG										0.69	0.66	0.48
2nd Peak vGRF (*bw*)		0.75, $p = 0.48$	0.36	**4.61, $p = 0.05$**	0.88	0.25	0.34	0.03	0.31, $p = 0.73$	0.12			
	ADV										0.50	0.65	0.22
	REG										0.46	0.61	0.78
Rate of Loading (*bw*/s)		**0**.78, $p = 0.43$	0.14	3.01, $p = 0.10$	0.71	0.21	0.06	0.18	0.86, $p = 0.41$	0.34			
	ADV										0.35	0.81	0.31
	REG										0.74	0.08	0.42
Peak Brake Force (*bw*)		**3.36, $p = 0.05$**	0.63	2.06, $p = 0.17$	0.60	0.58	0.04	0.19	**5.40, $p = 0.01$**	1.10			
	ADV										**0.002**	0.36	**0.01**
	REG										0.88	0.29	0.25
Peak Propel Force (*bw*)		1.54, $p = 0.23$	0.61	2.46, $p = 0.13$	0.68	0.41	0.05	0.07	**7.68, $p = 0.003$**	1.16			
	ADV										**0.01**	0.43	**0.01**
	REG										0.63	0.04	0.11
Brake Impulse (*bw*·s)		1.98, $p = 0.15$	0.43	1.32, $p = 0.27$	0.49	0.73	0.07	0.34	1.45, $p = 0.25$	0.81			
	ADV										**0.01**	0.27	0.20
	REG										0.82	0.86	0.99
Propel Impulse (*bw*·s)		0.81, $p = 0.43$	0.29	1.44, $p = 0.24$	0.58	0.50	0.19	0.16	**10.14, $p < 0.001$**	0.97			
	ADV										**0.002**	0.32	**0.01**
	REG										0.14	0.18	0.06

vGRF: vertical ground reaction force; *bw*: body weight.
p-values ≤ 0.05 are bolded.

Table F5 Dynamic gait stability variable overground walking at a self-selected speed presented as (mean ± standard deviation) before (Pre), during (Mid), and after (Post) a 30-minute treadmill walking intervention for the advanced (ADV, *n* = 12) and regular (REG, *n* = 13) groups.

Variable	Group	Session		
		Pre	Mid	Post
COM Position at TD	ADV	-0.78 ± 0.20	-0.89 ± 0.17	-0.87 ± 0.18
	REG	-0.78 ± 0.15	-0.83 ± 0.15	-0.83 ± 0.16
COM Velocity TD	ADV	0.34 ± 0.06	0.37 ± 0.07	0.38 ± 0.06
	REG	0.32 ± 0.07	0.34 ± 0.06	0.35 ± 0.06
Stability at TD	ADV	0.13 ± 0.06	0.13 ± 0.06	0.15 ± 0.06
	REG	0.10 ± 0.05	0.11 ± 0.04	0.12 ± 0.04
COM Position at LO	ADV	-0.29 ± 0.26	-0.36 ± 0.25	-0.36 ± 0.23
	REG	-0.18 ± 0.14	-0.22 ± 0.14	-0.22 ± 0.15
COM Velocity at LO	ADV	0.33 ± 0.06	0.36 ± 0.06	0.36 ± 0.05
	REG	0.31 ± 0.06	0.33 ±0.06	0.33 ± 0.06
Stability at LO	ADV	0.23 ± 0.07	0.24 ± 0.06	0.25 ± 0.06
	REG	0.25 ± 0.04	0.25 ± 0.03	0.26 ± 0.04

COM: Center of mass; TD: Touchdown; LO: Liftoff.

Table F6 Comparison of dynamic gait stability variables during overground walking at a self-selected speed before (Pre) and after (Post) a 30-minute treadmill walking intervention for the advanced (ADV, $n = 12$) and regular (REG, $n = 13$) groups. The Analysis of Variance (ANOVA) with repeated measures was used. Effect sizes (Cohen's d) are provided.

Variable	Group	Group × session interaction		Group main effect		Post-hoc p-value			Session main effect		Post-hoc p-value		
		F, p-value	d	F, p-value	d	Pre	Mid	Post	F, p-value	d	Pre - Mid	Mid - Post	Pre - Post
COM		1.30, $p = 0.27$	0.41	0.31, $p = 0.59$	0.22	0.95	0.40	0.50	**12.36, $p<0.001$**	1.11			
Position TD	ADV										**0.002**	0.29	**0.01**
	REG										0.08	0.85	0.10
COM		0.36, $p = 0.63$	0.58	1.45, $p = 0.24$	0.47	0.37	0.32	0.14	**12.03, $p<0.001$**	1.21			
Velocity TD	ADV										0.06	**0.01**	**0.003**
	REG										0.07	0.18	**0.02**
Stability TD		0.38, $p = 0.62$	0.53	1.21, $p = 0.28$	0.42	0.31	0.47	0.19	**5.25, $p = 0.02$**	0.86			
	ADV										0.72	**0.002**	**0.04**
	REG										0.30	0.16	0.07
COM		0.48, $p = 0.56$	0.59	2.9, $p = 0.10$	0.69	0.17	0.09	0.08	**9.56, $p <0.001$**	1.66			
Position LO	ADV										0.13	0.72	**0.01**
	REG										0.84	0.91	0.07
COM		0.09, $p = 0.82$	0.54	1.02, $p = 0.32$	0.37	0.43	0.32	0.31	**10.7, $p <0.001$**	1.06			
Velocity LO	ADV										0.03	0.22	**0.01**
	REG										0.06	0.22	0.03
Stability LO		0.003, $p =0.98$	0.51	0.42, $p = 0.53$	0.21	0.57	0.54	0.51	2.93, $p = 0.08$	0.73			
	ADV										0.36	0.34	0.18
	REG										0.35	0.24	0.15

COM: Center of mass; TD: Touchdown; LO: Liftoff.
p-values ≤ 0.05 are bolded.