

<u>Understanding the modulation of walking speed and</u> <u>exploring how this differs in people with Parkinson's</u> <u>disease.</u>

By

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Declaration

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Date: 8/9/2023

Signed:

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Abstract

Background: Parkinson's disease (PD) affects the ability of individuals to initiate movement and change muscle activity during gait initiation (GI) and during variations in walking speed. The present study aims to investigate the biomechanics parameters (kinetics and kinematics) and muscle activity characteristics during GI and variation in speed while walking on a treadmill and overground (OG) for PD-affected individuals and physically fit people. **Methods**: In this study, participants (n=17) included a physical fit (n= 11, aged 31.72 +/-17.91 years) and a Parkinson's (n= 6, aged 67.33 +/-11.57 years, disease duration 13.5 +/-8.69). Both groups were evaluated while walking on the treadmill and over the ground for two phases. The first phase was Gait initiation, where the participants were asked to start walking at their comfortable speed for two gait cycles on the treadmill and OG. The second phase was speed variation, where the participants also walked at their comfortable speed, and increased their speed in response to visual instruction on screen. However, on the ground, they were asked to change their speed after their fifth walking step. A self-pacing treadmill synchronised with a virtual reality screen (MotekMedical, the Netherlands) and A 12-camera motion capture system (Vicon Motion Systems, UK) integrated with two embedded force plates and a wireless EMG system (Trigno, Delsys, USA) collected the biomechanical and muscle excitation data. Three gait cycles; before, during and immediately after the speed change was used for the analysis of the speed variation. Data were limited to lower limb joints and three muscles (tibialis anterior, gastrocnemius and soleus. Differences in the percentage of contraction and magnitude of muscle activation (area under the curve, AUC) were compared before and during the speed change.

Results: PD-affected individuals spent less time on GI during treadmill walking (2.06 s \pm 0.39) than the healthy reference group (2.25 s \pm 0.42) but more time with OG walking (1.95s \pm 0.25) compared to the reference group (1.49s \pm 0.56). The reference group had a greater range of lower limb joint movement than the PD group during GI on both walking surfaces. The power produced at the hip and ankle joint by the reference group was higher than the overall PD group. The magnitude of muscle activation was lower in the PD group than the reference group, and the severity of the disease affected the magnitude of the muscle activation. At speed variation, both the reference and PD groups showed an increase in speed. Cadence declined in the reference group but elevated in the PD group. Soleus muscle activity increased with an increase in speed in PD-affected individuals, particularly in severely affected individuals compared to the reference group.

Discussion/Conclusion: The mechanism for increasing speed appears to differ between PDaffected individuals and physically fit individuals. Soleus excitation during stance may be a control parameter for walking speed that is disturbed in PD, although age is likely to be a confounding factor. Further research is needed to understand the mechanisms underpinning these positive responses to interactive treadmill training and its impact on community walking.

Keywords: Parkinson's disease, Gait initiation, Gait Cycles, treadmill walking, speed change.

List of publications and conference presentations

Abstracts

A1 E. Aldayil, A. Kerr (2020) Differences in the way Parkinson's and control participants increase walking speed Gait & Posture 81 (2020) 9–10

A2 E. Aldayil^{*}, A. Kerr (2021) **plantarflexor muscle activity during a change in walking speed on a treadmill: Comparison between Parkinson's and unimpaired controls.** Virtual Physiotherapy UK 2020 Conference Abstract Poster Presentations / Physiotherapy 113S1 (2021) e48–e202

Posters

P1 Aldayil, A. Kerr 2020 plantar flexor muscle activity during a change in walking speed on a treadmill: Comparison between Parkinson's and unimpaired controls. the Online Research Conference 2020 on 24-25 September 2020. the Royal Colleges of Physicians

P2 Aldayil, A. Kerr 2020 plantar flexor muscle activity during a change in walking speed on a treadmill: Comparison between people with Parkinson's and physically fit controls. Virtual conference SRR 2020 10 – 11 November 2020

P3 Aldayil, A. Kerr 2020 **plantar flexor muscle activity during a change in walking speed on a treadmill: Comparison between Parkinson's and unimpaired controls.** Physiotherapy UK 2020. Virtual conference from 13 and 14th November 2020

P4 Aldayil, A. Kerr 2022 Differences in the way speed is increased during self-paced treadmill and overground walking. ESMAC Dublin 2022, 19-24 September 2022

P5 Aldayil, 2023 **Differences in the way Parkinson's and control participants initiate walking.** WCPT23 Conference 2023 Dubai, 2-4 June 2023.

Communication

C1 E Esraa Aldayil. **How people with Parkinson's differ in the way they start walking and change speed.** online presentation for Parkinson's UK Glasgow Research interest group 14th April 2021

List of Abbreviation

ADL	Activities of daily living	
AUC	Area under the curve	
BG	Basal ganglia	
CAREN	Computer Assisted Rehabilitation Environment	
CNS	Central nervous system	
EMG	Electromyography	
FOG	Frozen of gait	
GAS	Gastrocnemius	
GI	Gait initiation	
GP	global peduncle	
MLR	Mesencephalic locomotor region	
OOP	object-oriented programming	
PD	Parkinson's disease	
PIG	Plug in gait	
PMRF	Pontomedullary reticular formation	
PNS	Peripheral nervous system	
PPN	Pedunculopontine nucleus	
PWP	People with Parkinson	
QSBB	Queen Square Brain Bank for Neurological Disorders	
REF	Reference group	
SENIAM	Surface Electromyography for the Non-Invasive Assessment of Muscles	
SD	Standard deviation	
SOL	Solus	
SN	Substantial Nigra	
STN	Subthalamic nucleus	
ТА	Tibialis anterior	
UPDRS	the Unified PD Rating Scale	
VR	Virtual reality environment	

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Chapter 1

1.1 Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder, affecting an estimated 9.4 million people globally (Maserejian et al., 2020). In the United Kingdom, the prevalence is one in 500 people (National Health Services (NHS, 2019). PD was first described by James Parkinson in 1817 as *paralysis agitans* (shaky palsy) in six men who presented with symptoms of what is now known as PD (Ben-Shlomo, 1996). Although PD can affect individuals as young as 18 years old (de Carvalho et al., 2018), it is more common in older people with approximately 4% of people aged 80 years and over are affected worldwide (Mutch et al., 1986). PD is a progressive, multisystemic illness that affects the neural and musculoskeletal systems. The clinical symptoms of PD include nonmotor (e.g., depression, psychosis, and sleep disturbances; Witjas et al., 2002) and motor disturbances (e.g., speech and gait impairments; Mutch et al., 1986) that worsen over time as seen in Figure 1-1.



Figure 1-1 Typical motor symptoms of Parkinson's disease (figure adapted from www.legacyneuro.com/parkinsons-disease/).

Gait impairments (e.g., slow shuffling gait with incidences of gait freezing and higher risk of falling; Shine et al., 2013) can restrict an individual's ability to live as full a life as possible. Walking is the most prominent activity that allows individuals to participate in occupational and social life (Mendes de Leon et al., 2009). Maintaining walking ability is likely to preserve a good quality of life despite disease progression (Shumway-Cook et al., 2002). While many individuals maintain walking ability in less challenging environments, such as their own home (Spencer, 1993), community walking is more demanding in terms of speed (magnitude and change), changes in direction and pattern to accommodate environmental challenges, including visual, auditory, and physical (e.g., slopes, kerbs, and pot holes) perturbations that affect the quality of walking (Khanmohammad et al., 2015; Lamont et al., 2012). The multitasking nature of community walking requires a high level of motor and cognitive function and the ability to smoothly and automatically switch between movement patterns. This ability is impaired in people with Parkinson's disease (PwP); Mohammadi et al., 2015; Shumway-Cook et al., 2000). Community mobility is required for many physical activities, which help with the restoration and maintenance of physical health, and psychological and mental wellbeing (Hwang et al., 2019). It is an important aspect in the rehabilitation of people living with neurological impairment, which affects ambulation (Lee et al., 2019; Hwang et al., 2019; Miller et al., 2022).

To improve the maintenance and rehabilitation of community walking ability in PwP, there is a need to understand the details of the kinematics and kinetics while changing walking speed, as well as the muscle activation characteristics during these changes.

This thesis provides background information regarding Parkinson's disease and the research around gait in particular, **in Chapter 1**. **Chapter 2** presents the literature review of the characteristic of gait variables during gait transition among PwP compared with healthy control, as well as the factors that affect community walking. **Chapter 3** describes the methods and materials used in this research. **Chapters 4 and 5** present the results and outcomes obtained using the methods outlined in **Chapter 3**. **Chapter 6** discusses the results and makes a critical evaluation and comparison of this research with the results of previous studies by other researchers; it also highlights the present study's limitations and makes recommendations for future work. **Chapter 7** includes the conclusion that this study reached. The thesis ends with appendices containing additional information/evidence, and a list of references.

1.2 Background: Parkinson's Disease Pathology

It was first suggested that PD occurred due to the loss of dopaminergic neurons in the substantia nigra (SN), Hassler, 1967;. Subsequent research showed that dopamine a neurotransmitter produced and secreted in the SN was deficient in PwP (Girault and Greengard., 2004; Luedtkea and Mach., 2003; Petzinger et al., 2010). The deficiency of dopamine neurotransmitters has been shown to disturb the function of the motor control system and to affect the rhythmical processes of movement (Grosset et al., 2009). This deficiency is associated with degeneration of the tracts which are responsible for the direct and indirect pathways in the SN (Johns, 2014).

1.2.1 Basal ganglia

The term "basal ganglia" (BG) refers to a group of subcortical nuclei responsible primarily for motor control and other roles, such as motor learning, executive functions and behaviours, and emotions (Lanciego et al., 2012). The BG are composed of three sets of motor nuclei located at the base of the cerebrum—the main part of the brain that helps to initiate and modify the speed of the motor movement from the cortex to the limbs (Graybiel, 2000; Lanciego et al., 2012). The motor pathways run from the motor cortex to the thalamus via the BG, striatum, and globus pallidus and return to the cortex (Figure 1-2; Grosset et al., 2009



1.2.2 The direct and indirect Pathway in PwP

Figure 1-2 (A) shows a sagittal plane of the brain composition of the cerebrum, cerebellum, and brain stem with the three nuclei of the basal ganglia positioned deep in the cerebrum. The green line shows the connection between the midbrain and the cortex via the nigrostriatal projections (Grosset et al., 2009). (B) the direct and indirect Pathways from cortex to BG back to the cortex by excitatory projection (green) line or inhibitory projection (red) line (First Aid 2014 page 596)

As shown in Figure 1-2 (B), in a healthy brain, the direct pathway increases dopamine production in the SN, which leads to activation of the striatum. Striatum activation inhibits the SN reticulate neurons (SNr) which lead to stimulate thalamus, resulting in exciting the cortex function to produce motor activity .The indirect (hypokinetic) pathway inhibits the global peduncle (GP) and the thalamus by neurotransmitter (GABA) which results in inhibitory cortex activity (Frohlich, 2016).

Dopamine 1 (D1) and 2 (D2) receptors are abundant in the striatal neurons of the SN. D1 activates the direct pathway, which promotes movement (hyperkinetic). The D2 dopamine receptor system initiates the inhibitory pathway. Dopamine 3 (D3) receptors play a similar role to D2 receptors, although they are not so distinct in function in healthy conditions. D3 receptors are known to become upregulated in disease states such as PD (Luedtkea & Mach, 2003). Dopamine 4 (D4) and 5 (D5) receptors activate and inhibit the direct and indirect pathways, respectively (Girault & Greengard, 2004).

In PwP, the activity of the striatum in BG in the midbrain depends on the balance between the direct and indirect pathways to produce D1 and D2, respectively (<u>Lindroos</u> et al., 2018). The D2 receptor plays the main role in PD; the deficiency of dopamine results in difficulties in initiating movement, inhibition of purposeful movement, and increased unwanted movement (e.g., tremors) at rest (Gantous et al., 2007; Surmeier et al., 2017). Firing more GABA neurons in global peduncle external nuclei (GPe) and subthalamic nucleus (STN) produces more inhibition in the thalamus and generates motor deficits (Mathew et al., 2019).

Cui et al. (2013) observed that both pathways were activated during both movement and rest. Wang et al. (2015) and Freeze et al. (2013) have, however, argued that the direct pathway promote and initiate movement whereas the indirect pathway inhibits unwanted movements. Freeze et al. (2013) stated that activities within both pathways could influence SNr neurons in more than one way. Cazorla et al. (2014) ported that the (GPe) externally regulated the activation of the indirect pathway when the direct pathway was at work.

The second suggested cause of PD is the presence of the protein α -synuclein—known as Lewy bodies—in the cytoplasm of neurons. These were discovered by Frederick Lewy in the early 20th century (Engelhardt., 2017; Holdorff., 2002; Lewis & Spillane., 2018). Lewy body proteins are known to be extensively present in people with cognitive problems, such as hallucinations, Alzheimer's disease, dementia, and some forms of PD (Michael-Titus & Shortland, 2018; Reisberg, 2001). It was suggested that Lewy body proteins poison the cell body and the synapses around the cell, leading to neurodegeneration (Lucking & Brice, 2000). In the diagnosis of PD, there continues to be a debate about whether an individual who has all the clinical features of PD without the presence of Lewy bodies in the brain should be diagnosed as having PD (International Parkinson and Movement Disorders Society [MDS]; Queen Square Brain Bank for Neurological Disorders [QSBB]; UK PD Society).

1.3 Clinical Features of PD

Irrespective of the underlying mechanism, the resulting signs and symptoms can be divided into four phases: pre-physiological, preclinical, premotor, and motor (Frohlich, 2016). Table 1-1 presents the motor and non-motor symptoms. Anxiety and change in mood appear to emerge first with Cognitive deficits such feeling distraction and difficulty to plane task, while motor control deficits appear after a 50% loss of dopamine synthesis (Grosset et al., 2009; Riederer et al., 2006). Researchers have observed that neurologists take a long time to diagnose people aged 20–40 years with PD due to their lack of symptoms (Schrag et al., 1998; Schrag and Schott, 2006; Tzallas et al., 2014). It is thought that motor symptoms start to appear when approximately half of the SN cells are lost (Fearnley et al., 1991). PD features may also occur secondary to other neurological conditions, such as cerebrovascular disease and Alzheimer's disease (Grosset et al., 2009).

Motor symptoms	Non-motor symptoms
Tremor	Fatigue
Rigidity	Cognitive change, Anxiety and change mood
Bradykinesia (slowness of	Sleep disturbance
movement)	
Postural instability	Bladder and gastrointestinal problems

 Table 1-1 Clinical signs and symptoms of Parkinson's disease. These have been broadly categorised into the motor and non-motor features (Frohlich, 2016; Grosset et al., 2009)

1.3.1 Motor signs and symptoms

The movements of PwP are characterised in general by slowness (Lewis & Spillane, 2018). The main motor deficits are rigidity, tremors, bradykinesia, and postural instability (Fahn, 2003; Jankovic, 2007; Parkinson, 2002), which will be discussed in greater detail below. According to the severity of these features, mobility and independence are affected, which impacts the psychological status of PwP (de Pablo-Fernández et al., 2018; Fereshtehnejad et al., 2017).

A) Rigidity

In PwP, rigidity manifests as muscle stiffness in the limbs' joints as well as observable resistance during joint movement upon clinical examination (Levin et al., 2009). It is noteworthy that clinicians observe rigidity in the later stage of PD (Jankovic, 2008) and that rigidity in PwP does not increase with high-speed movement, as is seen in upper motor neuron lesions such as stroke (Jankovic, 2007, 2008).

B) Tremors

A tremor is an involuntary movement which is mostly asymmetrical and appears at rest in the hand, chin, and jaw in approximately 70% of PwP. It is observed to increase when a PwP feels anxious or performs a task (Lewis & Spillane, 2018), and it disappears during sleep (Jankovic, 2008). The frequency of the tremors has been measured at 3–6 Hz (Bain, 2007), and worsening tremors in PwP point to the need to increase the dose of anti-Parkinsonism treatment (Grosset et al., 2009).

C) Bradykinesia

Bradykinesia is movement slowness and a reduction in the sustained speed of movement (Grosset et al., 2009). It appears when the BG begin to fail in their function of sending outputs to the motor cortex or when a delay occurs in sending messages to the motor cortex to prepare for and subsequently activate movement. Bradykinesia might affect walking (e.g., shuffling gait, reduced swinging of the upper limbs, and/or inability to initiate movement) and result in generally slow movement during the execution of common physical activities, such as the activities of daily living (ADL; Berardelli et al., 2001; Lewis & Spillane, 2018). The gait specific features of PwP will be discussed in detail in the chapter 2.

1.3.2 Non-Motor Symptoms

More than 40% of PwP complain about cognitive symptoms such as slow thinking, memory loss, and difficulty solving problems, which arise due to the disturbance in the brain's higher functions in the motor cortex and subcortex areas (Pandya et al., 2008). There are also disturbances in the autonomic system, which lead to impaired senses, weight change, excessive sweating, and urinary and gastrointestinal interruptions such as constipation and increased urinary frequency and urgency (Berganzo et al., 2016; Massano & Bhatia., 2012). As the disease progresses, PwP may exhibit changes in mood, such as apathy and low motivation (Aarsland et al., 2005, 2009). Furthermore, depression can occur at any stage of PD as a main psychosocial factor, due to the often poor quality of life (Pandya et al., 2008). Fatigue is suggested to result from a combination of sleep disturbance and depression in around 80% of PwP, and it can be reflected in further gait impairment and postural instability (Barbieri et al., 2013; Berganzo et al., 2014; Hagell & Brundin, 2009).

1.4 Clinical Management of PwP

The main pharmaceutical treatment for PwP is the prescription of the dopamine replacement drug levodopa—an amino acid precursor of dopamine—with the dose determined by the severity of the symptoms helps to increase the dopamine production in brain (Johns, 2014; Levine et al., 2012). Such treatment is effective in the short term, with the dose becoming less effective as the disease progresses (Frohich, 2016; Grosset et al., 2009). Studies on levodopa in animals, such as rats and monkeys, have shown that it improves and stabilises fluctuations in motor function over the long-term period after around 4–8 weeks of treatment (Lewis & Spillane., 2018; Rylander et al., 2010).

Impaired cognition, in PwP, can respond to levodopa because cognitive symptoms such as memory loss develop first due to dopamine depletion in the striatum of the BG (Cools, 2006). Several studies have investigated the effects of dopamine medication on the motor and cognitive functions of PwP, and the results have shown that motor and cognitive functions are both improved through medication (i.e., receiving prescribed levels of levodopa); furthermore, the overall quality of life is improved (Berganzo et al., 2016; Lloret et al., 2014; Lord et al., 2010).

The next part will discuss the process of rehabilitation that helps to reduce the effect of these impairments among PwP through the process of neuroplasticity.

1.5 Rehabilitation for PwP

Neuroplasticity is the process whereby the brain can continuously remodel its functions during an individual's life to adapt and enable new neural networks after brain injury or in the presence of pathology (Duffau, 2016; Sasmita et al., 2018).

This is achieved through the generation of new neural pathways, new fibre branches or by the growth of new cells (neurogenesis). Furthermore, the neuroplastic process can help recover functional and behavioural systems that have been impaired by neural diseases (Pascual-Leone et al., 2005; Hirsch and Farley., 2009).

Barnes (2003) stated that neurorehabilitation educates the disabled person on how to be independent and to participate with the community by achieving goals and plans that are related to their circumstances. According to WHO (2006), neurorehabilitation is an interdisciplinary clinical process that ensures those who need rehabilitation acquire the knowledge, skills and support for their optimal physical, physiological, social and economic functioning. The rehabilitation process includes a number of tasks that help to reach the recovery goals (WHO 2011).

The majority of physiotherapy/neurorehabilitation guidelines, worldwide, rely on an exercise program to improve functional impairment (Tomlinson et al 2012). Ceravolo (2009) introduced strategies and guidelines for the rehabilitation of PwP as an evidence-based practice. While there is evidence on the improvement of general functional impairment among PwP, there is insufficient evidence to support the specific or targeted modality for these improvements.

There is growing evidence that applying exercise for PwP as a rehabilitation process helps to recover motor function through neuroplastic recovery, which enhances dopamine production in the SN and slows down the loss of motor skills and cognitive impairment (Petzinger et al. 2013; Kolb & Gibb., 2010). Various types of exercise interventions have been used as part of rehabilitation programme across several studies , for example, treadmill walking (Uchida et al., 2005: Fisher et al., 2008), aerobic exercise (Schenkman et al., 2012) and dance (Madeleine et al., 2010).

In addition to improvement of motor skills, improvement of behavioural deficits (Fisher et al. 2004; Tillerson et al., 2001) psychological and cognitive impairments might also occur (Tanaka et al., 2008) through rehabilitation. To gain the maximum benefit from

rehabilitation, patients must find the type of exercise feasible and acceptable, as well as find suitable times and places to practise the exercise (Kolk et al., 2013).

One of the most recent rehabilitation treatment in PwP involves the application of virtual reality (VR) screens connected to motion cameras which record their body movements while moving on ground or on the treadmill (Lei et al., 2019). The participants were able to recognize their body parts on the screen and modulate the parts according to the responses on they observed on the screen that help to improve motor imparment (Lei et al., 2019).

Another rehabilitation intervention being developed is interactive treadmill training using synchronised virtual reality environment that provides the capacity to deliver intensive practice with cognitive engagement (Mirelman et al., 2011, 2013, 2016). The sensory perturbations that are created during interactive treadmill walking help to simulate variables and challenges that might occur during real community walk environment, thus creating a closer analogue to community walking than standard treadmill walking (Mehrholz et al., 2015). Training with these interactive treadmills has been shown to reduce the incidence of falls in PwP by a greater extent than training with standard treadmills alone (p< 0.0001) (Mirelman et al., 2013, 2016; Nudeau et al., 2013.

Research on interactive treadmill training for PwP is scarce; there is need for further research to understand the mechanisms underpinning these positive responses to interactive treadmill training and its impact on community walking. Elucidating the factors that may influence outcome, for example training intensity, walking parameters (frequency of start/stop, changing speed, and, considering disease severity, when should this training commence, is now important to optimising this promising intervention. The background of PD has been presented with an explanation of the pathology and clinical features and management that result from the disease, and the chapter has ended by touching on the neuroplasticity and rehabilitation that are needed to improve the functional and cognitive impairment among PwP

Chapter 2 Literature review

This chapter is organised into foursections. The first section presents the phases of gait and common measurements used in gait analysis, the second section discusses research on community walking and the factors that affect it, and the third section will present the current understanding of the transitions in gait including 1) gait initiation, for healthy and impaired populations, and 2) changes in walking speed (increase or decrease) due to different events (e.g., turning, obstacle avoidance,) and how it can impact the community walking, in healthy and impaired populations. The gait transition section describes the kinematic and kinetic changes during gait as well as the changes that occur in muscle activity. The final section will review the literature on motor control to gain a better understanding of including gait transitions and specifically how people with Parkinson's successfully, or unsuccessfully, execute them.

2.1 Gait analysis

Gait analysis is the study of human walking, that is used in the assessment of various disease conditions, and related interventions, that affect walking ability (Alharthi & Ozanyan, 2019; Barth *et al.*, 2011; Levine *et al.*, 2012).

2.1.1 Phases of gait

There are two phases of gait, a stance phase (foot on the ground) and a swing phase (foot off the ground), which overlap and alternate for each leg (Cicirelli *et al.*, 2021). There are seven major events during the gait cycle, as described by (Kharb *et al.*, 2011) and (Levine *et al.*, 2012);

- 1- Initial contact
- 2- Opposite toe-off
- 3- Heel-rise
- 4- Opposite initial contact
- 5- Toe-off
- 6- Feet adjacent
- 7- Tibia vertical

The first four events occur during the stance phase, while the last three occur in the swing phase. The stance phase, also known as the contact or support phase, makes up 60% of the gait cycle and starts from initial contact and ends at the toe-off event. On the other hand, the

swing phase, which constitutes 40% of the gait cycle, lasts from the toe-off event to the next initial contact, as mentioned by (Gouwanda & Gopalai, 2015). The stance phase is further divided into initial contact, loading response, mid-stance, terminal stance, and pre-swing. Similarly, the swing phase is subdivided into initial swing, mid-swing, and terminal swing, according to (Kharb et al., 2011; Levine et al., 2012; Whittle, 2001). During normal walking, there are two periods of double support, where both feet are in contact with the ground, and a period of single support, where only one limb is in contact with the ground, as explained by (Dicharry, 2010).

2.1.2 Motor tasks during the phases of gait

The gait cycle includes three primary tasks: weight acceptance, single limb stance, and limb advancement, as illustrated in Figure 2-1. In the weight acceptance task, involving two phases of the gait cycle (initial contact and loading response), the body's weight is shifted from one limb to the other. During the single limb support task (comprising mid stance and terminal stance), the stance limb bears the body's weight while the swing limb continues its forward movement (Kharb *et al.*, 2011). In the final task of limb advancement, which consists of four phases (pre-swing, initial swing, mid-swing, and terminal swing), the opposite limb enters the terminal double support phase. The swing limb is raised off the ground, propelled forward, and its foot contacts the floor. The limb advancement task concludes when the leg surpasses the thigh, propelling the rest of the body forward (Kharb *et al.*, 2011) as depicted in as depicted in figure 2-1.



Figure 2-1 The gait cycle; periods, tasks, and phases. Phases are initial/heel contact, loading response, mid stance, terminal stance, pre-swing, initial swing, mid swing, and terminal swing. A complete gait cycle on the right limb starts from the heel contact and ends at the terminal swing (adapted from Resan, 2012)

The typical gait pattern is established between the ages of 4 and 8, children typically develop a walking pattern characterized by rhythmic movements of the body and limbs, with the centre of mass (CoM) moving forward (Olver et al., 2010). In healthy adults up to 59 years old, the average walking speed is around 1.4 m/s, and the average distance covered with each step ranges from 150 to 170 cm (Cuccurullo, 2019; Pirker & Katzenschlager, 2017; Vazquez-Galliano *et al.*, 2014). According to (Herrero-Larrea et al., 2018), stride length is influenced by factors such as age, gender, physical activity, balance, and strength, while step width appears to be related only to balance. The study found that older adults typically have a stride length ranging from 36 to 141 cm and a step width ranging from 1.6 to 20 cm when walking at home. Compared to younger individuals, older adults tend to have a wider step in relation to their normalized stride length (Herrero-Larrea et al., 2018).

2.1.3 Measurement of Gait

Gait analysis, as described by (Chambers & Sutherland, 2002) can be conducted through simple observation or more advanced three-dimensional analysis. The latter involves measuring various factors such as joint angles (kinematics), muscular activity (electromyography, EMG), joint forces (kinetics), foot pressure, and energetics (measurement of energy utilisation). It enables clinicians to design approaches that are adapted to each patient's condition (Chambers & Sutherland, 2002). Spatiotemporal parameters of gait i.e. stride length, gait speed, stride time, swing and stance phase times, along with heel-strike (HS) success, foot clearance, and toe-off (TO) angles and gait variation measures are all measured as a first step and are the most common measurements taken during the clinical assessment of gait (Levine et al. 2012). These spatiotemporal parameters of gait can be used to assess a range of mobility problems, and the likelihood of future falls for an individual (Camicioli et al., 1998; Hausdorff et al., 2001; Montero-Odasso et al., 2005; Dodge et al., 2012). Gait analysis is widely utilised in monitoring human gait movement in (PwP) (Demonceau et al., 2015; Ellis et al., 2015). Multiple instrumented walkway systems are used to analyse gait information of patients with PwP, such and GaitRite system, are widely used to measure gait patterns for clinical experiments. Moreover, some optical capture systems, such as (Vicon motion capture system (Vicon Ltd, Oxford, UK) and Codamotion optical tracking system, are also frequently utilised to capture walking motion and calculate gait parameters (Chang et al., 2016).

In studies involving PwP, (Demonceau et al., 2015) placed a trunk accelerometer system on the lower back near the body's center of mass to extract spatiotemporal gait information. They observed that stride length, normalised to height, is reduced in PwP patients 1.36 ± 0.19 m compared healthy controls 1.43 ± 0.16 m p<0.01. Following the same methodology (Del Din et al., 2015) obtained the step time, swing time, stance time, step length, and step velocity in PwP individuals.

Gait Shoes developed by (Bamberg et al., 2008) and (Morris & Paradiso, 2002) were utilised to measure gait patterns in PwP and control groups. Based on the aforementioned literature, gait analysis and spatiotemporal gait parameters offer valuable techniques for evaluating medical care and treatment options for PwP.

2.2 Community walking

Walking is key to many community-based activities. A study by Chastin et al. (2014) examined the walking behaviour of older adults in a community setting and found that individuals were able to successfully adapt to changes in area, such as walking on slopes and uneven surfaces. The study also found that individuals were able to adjust their walking speed in response to changes in the environment, such as facing crowds or narrow sidewalks. Another study by Schwickert et al. (2014) examined the walking behaviour of older adults in a variety of community settings, including urban and rural environments. The study found that individuals were able to adapt their walking behaviour to the specific challenges of each environment, such as crossing busy streets or navigating uneven surface.

A study by Hwang et al. (2019) investigated the effect of different lighting conditions on walking behaviour in a community setting. The study found that individuals were able to adapt their walking behaviour in response to changes in lighting, such as walking more slowly in dimly lit areas and adjusting their gait to maintain stability. A study by Shigematsu et al. (2010) examined the walking behaviour of older adults in a community setting and found that individuals were able to successfully navigate complex environments, such as crossing busy streets and avoiding obstacles. It has been stated as locomotion in environments other than one's home or place of residence (Lamont et al., 2012). This involves the potential to navigate public and private spaces, both inside and outside, that combines a variety of environmental demands, which could be challenging for people with Parkinson's disease (PwP) (Lord et al., 2004). Community walking involves independent gait (walking without assistance or support from other individuals or objects), dynamic equilibrium, and cognitive control in response to obstacles or changes in direction (Courtine & Schieppati, 2003). It is a generally automated task in healthy adults with most adults able to perform other tasks, with minimal disruption, while walking in community, such as holding a conversation or making plans (Bond & Morris, 2000; Canning, 2005; Lajoie et al., 1996).

2.2.1 Measuring Community Walking

Community walking tests can be used to predict community participation and reintegration after an illness or injury. Qualitative tools for assessment, such as questionnaires, interview methods, and direct observation of walking have helped to investigate the facilitators and barriers to community walking as perceived by people living with Parkinson's (Blennerhassett et al., 2018, Alvelino et al., 2022; Lamont et al., 2012). These tests do not, however, provide objective measurement of the gait parameters described in section 2.2.3 during community walking. There is a need for quantitative tools that measure and allow greater understanding of the specific characteristics of community walking (i.e., changes in speed to avoid obstacles or change of direction in situations of uneven or slippery surfaces, ramps, and slopes). Understanding these challenging aspects of community walking will help inform the rehabilitation process for an individual with gait problems. Several tests have been developed to evaluate community walking and the underlying studies provide an

overview of the most commonly used tests of community walking, their psychometric properties, and their clinical relevance.

Understanding how these biomechanical variables differ between people with and without Parkinson's disease would also help to isolate targets for rehabilitation. In addition, to understand these differences in people's gait, it is important to test whether these differences are the same for treadmill walking as normal overground walking. This will elucidate factors (if any) that may influence patients' responses to treadmill-based rehabilitation. Furthermore, investigating these factors will support the way rehabilitation technology is used in PWP, which will help future rehabilitation processes address impairments and arrive at better intervention outcomes for people living with PwP (Asakawa et al., 2019).

In conclusion, tests of community walking are valuable tools for clinicians and researchers to assess the functional status of individuals with mobility impairments. Each test has its unique strengths and limitations, and the choice of test should be based on the specific goals of the assessment.

2.2.2Measurement Tools used in Gait Analysis

Gait analysis is often performed with quantitative methods which are sometimes integrated with the results of timed tests such as the 10-meter and 6- minute walking test, the Timed Up and Go (TUG) etc (Pau et al., 2018). Unfortunately, such methods do not allow a detailed and precise knowledge of all the spatiotemporal and kinematic variables associated with the gait cycle, so that more refined analyses cannot be performed without the instrumental support of devices specifically designed for human movement analysis(Cappozzo et al., 2005; Pau et al., 2018). However, instrumented gait assessment that provides measures with three-dimensional gait kinematics and kinetics and the electrical activity of muscles remains the gold standard for gait assessment (Toro et al., 2003).

Two systems are commonly used: non-wearable sensors (NWS) and wearable sensors (WS) (Muro-De-La-Herran et al., 2014). The gold standard for gait analysis is optoelectronic stereophotogrammetry, a NWS, but is costly and requires a controlled and specialised movement environment (Bouça-Machado et al., 2020; Cappozzo et al., 2005). This approach is conducted by (Corona et al., 2016; Maranesi et al., 2015; Peppe et al

2007; Sofuwa et al., 2005; Speciali D S et al., 2014), to assess gait abnormalities in individuals affected by Parkinson's Disease (PwP).

This technique is, however, expensive, requiring a dedicated laboratory (i.e. the whole system is not easily portable), and data acquisition and processing is time-consuming and can be performed only by specialised personnel. Moreover, the final report of a gait analysis is complex and not easy for the clinician to interpret (Pau et al., 2018). One of the most promising solutions for mobility assessment in everyday life is the use of wearable inertial measurement units (IMUs) (Bonci et al., 2020; Mobbs et al., 2022).

In the current review, nine different studies (Buckley et al., 2015; Caramia et al., 2018; Chang et al., 2016; Mariani., 2012; Muthukrishnan et al, 2020; Pacilli et al., 2016; Shirai et al., 2015; Suppa et al., 2017; Vítecková et al., 2020) used a wearable sensor approach in PwP patients for gait analysis. All of these studies used IMU sensors with a combination of two to eight IMU units. One study (Pacilli et al., 2016) proposed a combination of sensitised insoles and six IMUs to estimate the gait phases and step length while also providing rhythmic auditory feedback to the user. The PwP group has also been used as a disease control group to identify other neurological conditions such as spinocerebellar degeneration (Shirai et al., 2015). Other applications such as analysis of the upper body and postural control were discussed in (Buckley et al., 2015), whereas the comparison of several machine learning-based classifications of PwP patients was extensively discussed by (Caramia et al., 2018). EMG is another tool, that is used to measure the electrical activity of the muscles and has been widely used since 1920 for human movement studies to identify the activity of muscles during movement (Levine et al., 2012).

2.3 Gait Transitions

This section will discuss research on speed modulation which define as the ability to regulate walking speed; including initiating from standing, increasing and decreasing speed and even changing direction. The modulation in speed is a feature of everyday walking and problematic for PwP. Initially, the research will focus on studies of healthy adults before considering adults with Parkinson's.

2.3.1Gait initiation

Gait initiation (GI) refers to the task of transferring from standing to steady-state walking (Breniere and Do, 1991; Novak et al., 2014; Cau et al., 2014). The GI process requires a propulsive force to move the body across a distance (from a bipedal stance to repeating gait

cycles) (Breniere and Do, 1991; Lepers et al., 1995; Grosset et al., 2009; Martin et al., 2011; Cau et al., 2014) while maintaining postural stability (Mickleborough et al., 2004). During gait initiation, the complex interactions of muscles in the lower limbs generate a force that separates the center of pressure CoP (location of the vertical force vector on the ground (Chesnin et al., 2000)) from the center of mass, CoM (point about which the body's mass appears to be concentrated) to create the forward propulsion moment (Fiolkowski et al 2002).

The dorsiflexor muscles, including the tibialis anterior, extensor digitorum longus, extensor hallucis longus, and peroneus tertius, counteract the plantarflexion moment by engaging in a controlled eccentric contraction, as described by (Jacquelin Perry, 2010; Richards, 2018). This contraction extends the period of heel support, propelling the tibia forward and shifting the body weight onto the heel. The dominant force decelerating this movement is the activity of the soleus, owing to its larger size and direct attachment between the tibia and calcaneus. The gastrocnemius and soleus almost lock the ankle, causing the heel to rise as the tibia advances. The ankle further dorsiflexes, reaching a maximum movement of 10 degrees. As the ground reaction force (GRF) progresses anterior to the metatarsal head's axis, the foot smoothly rolls with the body, resulting in an increased heel rise and a rising dorsiflexion moment. The peak activities of the soleus and gastrocnemius only facilitate heel rise and accelerate the advancement of the unloaded limb. In response to the action of the gastrocnemius and soleus muscles, commonly referred to as push off (Burnfield, 2010; Jacquelin Perry, 2010), the ankle plantarflexes. This transfer of body weight prepares the other limb for forward movement. Simultaneously, the tibia moves forward, with the toe stabilized by ground contact, and the knee flexes in preparation for the swing phase (Burnfield, 2010). During toe-off, the ankle plantarflexes approximately 20-25 degrees. In the initial swing, the dorsiflexor muscles intensify to bring the foot to a neutral position during mid-swing, essential for foot ground clearance. Finally, the activity of the dorsiflexor muscles increases to ensure the ankle is in a neutral position for optimal heel contact and to meet the increased force requirements of the initial contact phase (Burnfield, 2010; Jacquelin Perry, 2010).

Gait initiation is divided into two different phases, the preparatory and the execution (or stepping) phases (Cau et al., 2014). The preparatory phase lasts from onset until the toe-off of the swing foot (SW TO) (Mickelborough *et al.*, 2004). The initiation movement requires control and balance to start the movement and maintain postural stability, which may be

challenging for people living with neurological conditions such as Parkinson's PwP (Roemmich et al. 2012; Rosin et al., 1997). Any modification to the GI program could affect postural stability and the velocity of the movement (Stone et al., 2014) and any impairment in muscle activation of the lower limb will interfere with the GI process, ultimately affecting the velocity of the generated CoM displacement and consequently the initial step lengths (Lelrad et al., 2017; Hiraoka. et al 2005; Warabi et al 2005).

The preparatory phase is further divided into two sub-phases, release and unloading (Halliday et al., 1998; Fiolkowski et al 2002; Mickleborough et al., 2004). As shown in Figure 2-2, the CoP is initially located between the feet (point 1) during steady standing. During the release phase the CoP is moved postero laterally through muscle action towards the swing foot (point 2), increasing the horizontal GRF components that accelerate the CoM in the opposite direction (Mickelborough *et al.*, 2004). This release phase lasts until the furthest point of posterolateral CoP movement (maxCoP), when the CoP abruptly changes direction, marking the start of the unloading phase. During the unloading phase, the CoP is moved rapidly across to the stance foot, unloading the swing foot for toe-off (Mickelborough *et al.*, 2004). In the second GI phase, stepping phase (execution), the CoP reaches the end at the lateral side of the stance side foot, and the heel-off phase is immediately followed by the toe-off as in points 3 to 5 (the final position of the CoP) (Lepers *et al.*, 1995; Cimolin *et al.*, 2017).


Figure 2-2 The displacement of CoP during GI. The left foot is the stance side and the right foot is the swing side. Point 1: Origin (initial CoP position), point 2: posterior position of the CoP on the swing side, point 3: maximum anterior position during the CoP transition from the swing to the stance side, point 4: posterior position of the CoP on the stance side, point 5: the final CoP position (Adapted from Cimolin et al., 2017).

Muscle is composed of both contractile and non-contractile elements, as outlined in the Hills model of muscle (Cadova et al., 2014; Jovanović et al., 2015). The contractile component, activated by a motor unit action potential, generates tension through the interaction of actin and myosin proteins. The non-contractile element consists of connective tissues, such as tendons, which are parallel and in series with the contractile components, linking muscle fibers to bones. While tendons are passive structures, their viscoelastic properties impact motor control, with tendon length influenced by applied force (Latash, 1998; Van Soest & van Ingen Schenau, 1998). Skeletal muscles comprise diverse tissues containing both slow and fast muscle fibers, classified based on the myosin heavy chain (MHC) isoform compartment. There is one slow type (MHC I) and several fast types (MHC IIa, MHC IIb, MHC IId, and MHC IIx) (Pette & Staron, 2000). Muscle fibers of the skeletal system are categorized based on their contractile and metabolic characteristics, with the contractile properties being contingent upon the presence of specific myosin heavy chain isoforms (MyHC) (Schiaffino & Reggiani, 2011). The tibialis anterior muscle (TA) and soleus muscle (SOL) have been widely utilized in physiological and pathological studies involving both animals and humans (Punkt et al., 1999). The TA primarily consists of fast muscle fibers, while the SOL predominantly consists of slow muscle fibers (Punkt et al., 1998). The distribution of fast and slow muscle fibers is influenced by various factors, such as neuromuscular activity, passive mechanical loading (Carroll et al., 1999; Yan et al., 2011), aging (Nilwik et al., 2013; Trappe, 2009), and hormonal balance (Peng et al., 2017).

In summary, the process of Gait Initiation (GI) involves transitioning from a stationary stance to steady-state walking. This intricate process relies on the coordination of various muscles, particularly the tibialis anterior, dorsiflexors, soleus, and gastrocnemius. The initiation is divided into preparatory and execution phases, demanding control, and balance. Individuals with neurological conditions may face challenges in maintaining postural stability. The preparatory phase, further divided into release and unloading, involves shifting the center of pressure (CoP) and accelerating the center of mass (CoM). Understanding these

phases is crucial for comprehending the complexities of human movement during gait initiation.

3.2.1.1 Gait Initiation in Healthy People

Gait initiation (GI) is a voluntary transition from a state of relatively stable to a state of continuously instability (Hass et al., 2004; Uemura et al., 2012), which is characterised by a preparatory phase that precedes the initiation of stepping and an execution phase that propels the body in the intended direction (Rogers et al., 2011; Rosin et al., 1997). In the preparatory phase of the GI, the central nervous system (CNS) elicits motor responses to prepare the body for movement, which is also known as an anticipatory postural adjustments (APAs) (Rogers et al., 2011). In healthy individuals, gait initiation is characterised by an anticipatory postural adjustment (APA) phase that precedes and accompanies the initiation of the stepping phase (Rogers et al., 2011). For forward stepping, APAs involve a sequence of muscle activations and changes in the ground reaction forces (GRFs) that move the net centre of pressure(CoP) beneath the feet backward and toward the initial swing limb (MacKinnon et al., 2007). This motor sequence produces the forces and moments necessary to propel the body centre of mass (CoM) forward in the intended direction of stepping and laterally toward the single stance limb prior to the onset of the first step..

Mickleborough et al., (2004) measured the EMG activity of the ankle muscles in each phase of GI in healthy elderly participants (n= 21, 11/10 F/M, aged 65 years) by analysing the tibialis anterior (TA), gastrocnemius (GAS) in the lower leg and gluteus medias (GM) at the hip. The CoP and CoM trajectories were also measured. The results showed that activation of GAS, on the swing side, occurred at the beginning of GI and later at the end of the release sub-phase. The TA activated early at 10% of gait initiation onset on both swing and stance sides while the GAS activated 21% on the swing and 16% on the stance side. This study evaluates the pattern of the ankle muscle (TA and GAS), in healthy elderly individuals, however, they didn't measure the activity of the soleus which is critical during GI assessment (Mickelborough et al., 2004). In general, the older adults produced smaller and less coordinated movement of the CoP during lateral and forward directed gait initiation than yeang adult (Hass et al., 2008).

Developing successful training programmes to avoid falls in older adults and their efficient rehabilitation when required, a thorough understanding of the normal age-related changes in

motor behaviour is essential. Gait initiation is a phase of walking during which falls often occur (Topper et al., 1993). (Henriksson & Hirschfeld, 2005) findings indicated that, the elderly displayed several striking differences compared to the young individuals such as (wight bearing during GI was 46% longer in elderly p<0.01. They reported that, ageing leads to alterations in weight bearing and ankle muscle activation in relation to gait initiation.. The findings of (Polcyn et al., 1998) manifests some minor differences in muscle activity patterns between young and elderly people at gait initiation onset(p<0.01), which is later on confirmed by (Mickelborough et al., 2004) study, that reported that muscle activity to be more variable in the preparatory phase of gait initiation. Furthermore, gait and cognitive impairments, caused by aging or disease, commonly occur in older people (Wolinsky et al., 2011) have been shown to predict falls (Anstey et al., 2006; Callisaya et al., 2011). The associations between cognitive function and gait variability has been reported by Martin et al (Martin et al., 2013). According to their results, poorer cognitive function seems to have the greatest impact on double support phase (DSP, the phase of the gait cycle when both feet are in contact with the ground) variability, an important factor in balance control during walking (Martin et al., 2013).

Gait variability is the fluctuation in a gait measure from one step to the next and thought to represent disruption in motor or postural control (Hausdorff, 2005). Gait variability is also thought to be a more sensitive predictor of falls and mobility decline than gait speed (Hausdorff et al., 2001) and is increased in disease of the central nervous system such as Parkinson's disease (Dubost et al., 2008). The decline in this neural function increases the rate of falls (Rubenstein & Josephson 2002) mainly during change speed i.e., gait initiation (Martin et al., 2011).

Reduced muscle reaction time which are associated with aging (Arnold et al., 2015; Jiménez-García et al., 2021; Winter, 1995), may lead to possible protective adaptations to maintain stability, which may explain some of these changes (Winter, 1995) that have the effect of reducing displacement of CoP to initiate the movement and produce forwarded progression (Hass et al .2008). Martin et al., (2011); Muir et al., (2014) observed the age-related changes in the first four steps of gait in three different age groups, from young's to adults. They found that the gait speed during the first four steps of gait were reduced 20% for 65–79 year's old compared with 20–25 year's old, and further reduced for 35% 80–91 year's old. Step width (SW) did not change as a function of age, but SW variability was higher for the two older groups p<0.01. Higher SL and SW variability may produce more errors in foot placement

and/or decreased centre of mass control in the older groups. When comparing the two older groups, healthy 80–91 walked slower with a shorter SL p<0.01, but did not demonstrate changes associated with falls (Muir et al., 2014). However, the older groups that were studied by (Muir et al., 2014) were healthy and fit, and they may have excluded those participants who have experienced greater compromises to balance. This is supported by the observation of higher SL variability during the first steps of gait in older fallers (Mbourou et al., 2003), and people with Parkinson's disease (Mbourou et al., 2003). The population of interest for current review is people living with Parkinson's (PwP) therefore it's important to review the studies which explain the impairment in GI among this population.

3.2.1.2 Gait Initiation in people with Parkinson

People with Parkinson's disease (PwP) experience freezing of gait and slow movement that both interfere with gait initiation (Nutt et al., 2011; Schlenstedt et al., 2018; Warabi et al., 2018).

Impairments in the typical anticipatory postural adjustments (APA) are considered a major pathophysiological mechanism underlying impaired GI performance in PwP (Hass et al., 2005). Observation and/or measurement of GI allows APA to be assessed, such as muscular synergies that generate the propulsion, aiming to destabilise the antigravity postural set by shifting the center of pressure (CoP) to generate a gravitational moment favouring the center of mass (CoM) forward acceleration.

According to Martin et al (Martin et al .,2002) persons with PwP displayed smaller 6.45 ± 032.5 cm CoP-CoM magnitudes compared with healthy older adults 21.16 ± 43.5 cm to reach the toe off of the swing side of GI and suggested that the CoP-CoM relation provided a means of identifying problems during gait initiation in patients during the early stages of PwP.. Onuma et al (Onuma et al., 2022) investigated the CoP separately for the stance and stepping legs. In the PwP patients, the posterior displacement of CoP was larger in the stance leg11.9 \pm 9.8mm than in the swing leg3.56 \pm 3.6mm p<0.01. Okada et t al (Okada et al., 2011) observed the deviation of the 3rd CoP peak and the first heel contact position toward the initial swing side, indicating excessive weight shifting toward the initial swing side during the first gait initiation step. Their findings showes abnormality in weight shifting between the legs. and that medial deviation of the CoP from the first heel contact position affected by the severity of FoG during the first three steps of gait initiation in PwP patients with FOG. Palmisano et al (Palmisano et al., 2022) studied the APA during GI in PwP, and observed an

impaired posture instability and also impairment in APAs' production at GI, which is in line with previous findings (Halliday et al., 1998; Palmisano et al., 2020).

In summary, research has shown that PwP display smaller magnitudes of the centre of pressure (CoP) and centre of mass (CoM) relationship, indicating problems during gait initiation. Studies have also observed abnormal weight shifting and impaired motor programming during gait initiation in PwP, highlighting the significance of APA in this process.

To understand the fundamental basis for gait disturbance in PwP, it is useful to consider motor and attentional constraints on spatiotemporal, kinematic and kinetic variables. Spatiotemporal (distance and time) variables concerning the foot step pattern include the step length, walking speed and stepping rate (cadence) as well as the proportion of gait cycle spent in double limb stance (Morris et al., 1999). According to (Roemmich et al., 2012), PwP produce shortened step lengths ($0.46\pm0.01m$) compared to control group ($0.54\pm0.01m$) and increased step time ($0.58\pm0.01m$ in compared to control group $0.57\pm0.01m$ in of their first steps during GI. In PwP, increased gait variability between swing and stance side with step time ($0.58\pm0.01m$, $0.73\pm0.01m$) and step length($0.46\pm0.01m$, $0.97\pm0.01m$) p<0.05 has been reported and has been associated with an increased incidence of future falls (Roemmich et al., 2012). Hass and colleagues observed that persons with more advanced PwP demonstrated greater impairment in dynamic stability during GI when compared to persons with less severe PwP p<0.04(Hass et al., 2005). In addition, Carpinella et al and Dibble et al (Carpinella et al., 2007; Dibble et al., 2004) reported the decreased step length and step velocity during the first step of gait initiation in PwP p<0.05=.

Understanding the details of the way GI, for PwP, deviates from the normal mechanism described in section 2.3.1 is important for future studies aimed at improving community walking, the next section considers more detailed studies of GI in PwP, including the use of instrumented gait analysis.

Rosin et al., (1997) compared the phases of GI between 31 PwP and 20 age (42-78years old) and sex matched, physically fit, control participants. The PwP spent more time ($0.375\pm0.1s$) than the control group (0.302 ± 0.08 s) in the preparation phase (p<0.01). A longer execution phase was also observed for PwP, 1.321 ± 0.2 s compared with $1.28\pm0.2s$ in the control group.

Okada et al. (2011) compared the displacement of the CoP during GI between 17 PwP aged 60-80 years old (10 with FoG, 7 without FoG) and 7 healthy aged-matched controls. The centre of pressure (CoP), heel contact positions, and spatiotemporal parameters were

estimated from the vertical pressures on the surface of the force platform. The PwP recorded a significantly longer step time, 1.14 ± 0.06 s compared to the control group 0.97 ± 0.03 s, p<0.05, and a shorter, initial step length among PwP, 38.0 ± 3.8 cm compared with the control group, 52.5 ± 1.1 cm and a lower velocity (22.0 ± 2.4 m/min versus control group 33.1 ± 1.1 , p<0.05). While no differences were observed in step width, the CoP movement in the anteroposterior direction in PwP was noticed to be statistically smaller than the control group (1.1 ± 0.2 versus 1.8 ± 0.1 , p<0.05). The results also showed that the spatiotemporal parameters were all different for the participants who had freezing of gait (7/10) compared with the non-freezers (p<0.05).

These differences in gait parameters may be indicative of an impaired motor function associated with dysfunction in the basal ganglia in PwP. The maintenance of balance during perturbations experienced when walking is one of the most important roles of the central nervous system (Ray et al., 2022). It has been noted that walking on a treadmill could impose challenges to stability control as compared to overground walking due to different proprioceptive inputs arising from lower limbs (the legs are stable on the ground during overground walking while being pulled posteriorly during treadmill walking) (Bayat et al., 2005), the lack of optical flow and the absence of forward progression during treadmill walking (Warren et al., 2001), and the constrained walking speed upon a narrower raised path on treadmill than over ground (Dingwell et al., 2001).

According to Lu et al (Lu et al., 2017) young adults are able to modulate time and space differently on each surface probably because the displacement of their centre of mass was smaller when they walked on the treadmill than when they did over the ground<0.001. Yang et al (Yang & King, 2016) observed slower comfortable gait speeds during treadmill walking 1.15 ± 0.1 m/s in comparison to the overground walking 1.41 ± 0.1 m/s p<0.001 that is also reported by (Rosenblatt & Grabiner, 2010) concerning older (p<0.001), and (Dal et al., 2010) concerning young participants (p<0.05). According to Nagano et al and Yang and King (Nagano et al., 2013; Yang & King, 2016) participants take a shorter step when walking on a treadmill than over ground(p=0.008).

Herman et al (2005) reported gait spatiotemporal parameters modifications as safety-related adaptations, that indicates "cautious gait" used by the participants during walking on the treadmill. Therefore, these adaptive changes may serve as responses to the destabilising nature of treadmill walking in order to preserve balance and stability during treadmill walking (Nagano et al., 2013). It was previously revealed that individuals exhibit comparable

inter-joint coordination variability between treadmill and overground walking (Chiu et al., 2015). It has also been reported that the metabolic energy cost is larger during treadmill walking than overground walking at the same speed (Berryman et al., 2012) suggesting that individuals try to ensure their stability when walking at the expense of efficiency.

In summary, spatiotemporal parameters in people with Parkinson's disease (PwP) show shortened step lengths, increased variability, and decreased muscle activity compared to healthy individuals. These parameters are associated with increased gait variability and higher risk of falls. PwP also exhibit differences in gait initiation, spending more time in the preparation phase and demonstrating longer execution phases. Treadmill walking poses additional challenges, leading to adaptations such as shorter steps, altered gait speed, and safety-related modifications. Understanding these parameters is crucial for developing interventions to improve gait abnormalities and freezing of gait in PwP.

According to Crenna et al (Crenna & Frigo, 1991), gait initiation includes a single motor sequence programme that starts with inhibition of the soleus (SOL) and activation of the tibialis anterior (TA) on the starting moving side. They observed that these was inhibition of the (SOL) tonic activity during standing while TA burst is responsible for the CoP backward shift. This pattern of muscle activity is consistent with reports that the CNS governs initiation of gait through use of pre-designed motor programs (Fiolkowski et al., 2002; Hass et al., 2004; Queralt et al., 2010). These motor programmes define the detailed characteristics of the movement, which allows the CNS to precisely control the muscle activity/inhibition sequences. This coordination between muscles is a vital component of well controlled movements (Wakeling et al., 2010). Several studies have confirmed this (Cau et al., 2014; Fiolkowski et al., 2002; Queralt et al., 2010) in observing a highly reproducible pattern of muscle activation/inhibition during GI in healthy adults, which involves inhibition of gastrocnemius/soleus (GS/SOL) muscle activity followed by activation of the tibialis anterior (TA) muscle bilaterally and then soleus activity to assist the forward propulsion. The delay in the switching between inhibition and activation of soleus muscle activity is believed to result in an increase in time taken to execute GI (Warabi et al., 2017) and lower resulting gait speed.

The altered control of voluntary movement, evident in a range of neurological conditions like stroke and PwP, can also include an impaired ability to switch, automatically, between muscle synergies, affecting a range of functional movements. Several authors, including Rosin et al. (1997), Halliday et al. (1998), and Cioni et al. (1997), have investigated the

effects of L-Dopa, a neurotransmitter replacement drug that is the mainstay of drug management for patients with Parkinson's disease (PwP). These studies have found qualitative disturbances in muscle activation patterns during walking in PwP when they are OFF L-Dopa, such as an absence or extreme reduction in TA activations in early stance or during the early and late swing phases.

During GI, it has been observed that each lower limb muscle, such as planter flexors (SOL and GAS) or dorsiflexors (TA), has distinct functions in gait, such as stability or propulsion (Dessery et al., 2011; Michel et al., 2004; Sadeghi et al., 2000). Leteneur et al (Leteneur et al., 2013) reported postural factors in GI with natural forward leaning (FW) participants presenting smaller hip flexion moments than backward leaning (BW) participants just prior to heel-off in GI. They explained these results by suggesting a more efficient use of gravity in FW leaners to initiate gait. But natural trunk inclination and its effect on the EMG sequence during GI have not been investigated. This is important knowing that impairment in muscular agonist-antagonist synergy in both lower limbs could lead to abnormal patterns of propulsive forces and postural instability (Fortin et al., 2015).

The above-mentioned studies suggest that PwP are less able to switch between muscle synergies, particularly when off their medication. Okada et al. (2011); and Rosin et al., 2004 agreed that PwP need more time (1.14 s) for GI than the control group, even when age-matched p<0.05 ;P<0.01. Also, although there were methodological differences (Okada et al., focused on weight shifting during the first three steps while Rosin et al., investigated the kinematic patterns during gait initiation), both studies observed that the plantar flexor muscles, mainly the soleus muscle, showed an altered ability to switch between inhibition and activation during GI phases (Hiroaki. et al 2005; Warabi et al 2005).

Table (2.1) summary of research investigating gait initiation in people with and without Parkinson's disease.

Authors	Method	Outcome measures	Findings	Comments and limitation
Falkofske., et al	• 10 healthy	To understand the effect of	• Fz loading forces decreased from pre-	• The study recruited 10 healthy participants
2002	Participants start to	forces during GI pre- and	test 111.23 \pm 8.0% (BW) to post-test	therefore unable to generalise results to
	walk following	post-desensitise leg and	106.41 ±6.2% BW (P=0:03).	neurological conditions.
	visual cues on the	whether that affects the TA	• Fx propulsion force decreased from	• lack of control group
	walkway underneath	and SOL muscle activity	87.10 ± 13.4 to $66.73 \pm 8.8\%$ BW (P =	• Gastrocnemius muscle as part of the plantar
	the force plate with	during GI.	0:01)	flexor was missing during the investigation
	and without tibial		• Increase the time of the propulsion	which may affect the propulsion phase and help
	nerve		phase from 30 ms to 34 ms P=0.03.	in postural stability as the study aimed.
	desensitisation.		• Decreased in percentage of TA	
			activation 8.5±.9% and SOL	
			2.3±3.3% of the total GI time from	
			pre-test to post-test.	
			• The loss of sensation effect GRF	
			which affects muscle activation	
			during GI, resulting in postural	
			instability.	

Table 2-1 summary of research investigating gait initiation in people with Parkinson's disease and healthy participants.

(Mickelborough	• 21 healthy	• The percentage of	• The TA activated early at 10% gait	• The study includes 21 older adults without a
et al., 2004)	Participants Mean aged 70.8 ± 3.48 stood on the force plate and initiated gait at their normal, self-selected speed, in response to a cue light	activation of GAS, TA, and Muscles during GI	 initiation on both swing and stance sides while the GAS activated 21% on the swing and 16% for the stance side CoP goes backward to the word swing side and inhibits the activity of GAS, and activate the TA 	 control group to show differences in CoP displacement. Results didn't measure the activity of the soleus muscle Walking on different surfaces may produce a change in biomechanics and muscle activity.
Cau et al 2014	 20 obese aged 49±13 years old, 15 control aged match The participants stood on a force plate and initiated walking after following the verbal cue. 	• CoP movement (velocity and length) to identify the postural adjustment during GI	 The velocity of the CoP reduced in the anteroposterior direction but increased in the mediolateral direction in obese compared with the control group. p<0.05 Obese participants walk longer for CoP displacement compared with the control which may be to maintain the postural adjustment during GI to produce more balance. 	• The study did not include kinematic and kinetic data for the lower limb which helps to understand the main differences between the two groups.
Muir et al., 2014	• 48 adults healthy Participants stood on a force plate and	• Speed of GI movement among elderly	• Walking speed decreased by 35% in elderly (80-91 years old) participants compared with young adults.	• Participants were asked to start three times with the right and then left side and that may disturb the way that the subject used to walk mainly

Rosin et al., 1997	 initiated gait at their normal, self-selected speed, in response to a cue (light) 31 PwP aged 60-80 Years old 20 control aged match Participants stood at 	• The change in GI time for PwP	 Elder people walk with slow and longer steps to maintain more stability PwP spent a long time in the preparation phase (0.37±0.12s) compared to the control group (0.30± 0.83 s) (p<0.01). longer execution phase time for PwP 	 with older adults, better to keep walking with the preferred side. Small sample size Examine the lower limb muscle activity help in understanding the main cause of delaying the time of the GI phases mainly with PwP due to the impairment in BG which effect the motor
	the start line and initiate gait with self- selected speed, in response to a cue signal		• longer execution phase time for PwP 1.32±0.21s compared to the 1.28±0.15s control group.	 The impairment in BG which effect the motor program and postural adjustment The change in the walking surface may produce greater differences in spatiotemporal parameters due to the need to maintain stability with the treadmill
(Okada et al., 2011)	 17 PwP aged 60-80 Years old 7 control aged match participants stood at the beginning of the walkway and initiated gait with self-selected speed, 	displacement of the CoP among PwP	 small displacement of CoP in AP direction with PwP compared to control P>0.05 shorter step length time for PwP compared to the control group p>0.05) PwP was slower in GI compared to the control group p>0.05 	 Small sample size The study includes PwP during ON medication status which may affect the Freezing episodes which increase during gait initiation that may affect the results possible to investigate the kinetics and kinematics data with GI

(Delval et al., 2014)	 in response to an auditory signal FoG = 30 aged 64.4±9.9 years old ,Non-FoG= 30 aged 61.8±15.3 years old ,Control = 30 aged 80-91 years old Participants walked on a walkway underneath force plate following verbal cues or by self-initiation 	• GI parameters during cued and non-cued GI	 FoG produced shorter APA compared to non FoG and healthy(47 ± 27mm FoG , non FoG 65±29mm, healthy 78±26mm P<0.0001 FoG was slower than non-FoG and healthy in the first step GI cued without cued P<0.0001 FoG reduced in step length and time with cued GI 0.45±0.16m and 0.52±0.09s than NOT cued 0.51±0.15m and 0.60±0.14s 	 The subjects were asked to start walking as fast as they can which disturbs their balance and generate a freezing phenomenon due to disturbance in motor control that needs more cation and stability which leads to having a short step to provide more stability which may affect results
(Hass et al., 2005)	 PwP 43 split according to H&Y score(23 PwP > 2.0 H&Y aged 61±10 Years old, 20 PwP <2.0 H&Y Aged 70±9Years old The participants stood on a force plate and initiate walking after following the verbal cue. 	• Max displacement of CoP and CoM	 Displacement of CoP-CoM was greater during the single-support phase with PwP mild disable group <0.2 (H&Y score) compared to moderate disable score> 2.5 (P=.004) PwP with impaired postural generates shorter CoM-CoP displacement which affects the balance during GI single support phase 	• The study used the H&Y scale to identify the level of disease progression and it could be better to use the Freezing scale to identify the freezing that effect GI as well as muscle activity to help to clear the results
Lin et al 2016	 15 PwP, Eight healthy aged match The participants stood on a force plate 	• Timing and magnitude of vertical GRF force during GI.	• PwP spend longer APA time at swing and stance step compared to healthy p<0.01	• The study recruited PwP with moderate to severe disease but not individuals with mild disease which may have different results.

	and initiate walking after following the verbal cue.		• Smaller GRF (Fz) on both swing and stance during transfer in PwP compared to control group p<0.01	Findings not applicable to whole population of PwP
(Cohen et al., 2017)	 25 PwP (FoG = 12 aged 67.7±8.9Years old, non-FoG= 13 aged 66.5±5.9Years old, Control = 12 aged 66.9±6.6Years old The participants stood on a force plate and initiate walking after following an auditory cue 	• APA time during GI	• APA time in FoG was longer in time compared to non-FOG and healthy 0.14 s and 0.10 s respectively (p<0.0001)	 The study didn't use a freezing scale to identify the level of freezing which will support the result. Possible to analysis the kinematic and kinetic may help to identify the differences It could be feasible for future study to investigate similar parameters on treadmill walking
(Palmisano et	• 26 PwP, 27 control aged matched	• CoP displacement time and velocity	• PwP showed a short time for CoP displacement 31.8±13.4 mm	• Possible to measure the anthropometric parameters that may produce differences on
al., 2020)	• The participants stood on a force plate and initiate walking after following the verbal cue.		 compared to the control group 36.9±15.1mm P<0.01 faster CoP movement with PwP 82.4±51.3 mm/s compared to control 103.6±50.5mm/s 	step length, time, and speed during GI for PwP, especially in advanced disease.
(Lu et al., 2017)	 PwP :FoG 11 aged 66.3±1.6y; NON-FoG 14 aged 64.3±9.1y Investigate GI from standing over a force plate walkway with self-initiated fixed cue timing protocols: delay (3s) 	• CoP AP displacement	 Reduced the time of the cued GI in all situations (0.31±0.07s,0.34±0.70s,0.30±0.07s) than non-cued 0.375±0.08s for FOG compared to another group of PwP p<0.004 In PwP, delayed (3)s cues had longer APA time than the fixed delay and countdown conditions p<0.04. FOG started GI slower than Non-FOG to maintain balance. 	 The study investigated a different type of cueing during the session that may produce fatigue to PwP mainly with the number of repetitions of trial The severe condition may have different results due to FoG which may be excited due to variation in the type of cue

•	• random delay (4-			
	12s)			
•	• countdown (3-2-1-			
	go, 1-s intervals)			
(McCandless et	• 20 FoG aged	• Investigate the effect of	• shorter step length 0.143±0.1m than	• possible to investigate joint movement
	68±11.5 Yo	three types of the cue on	Non-FoG 0.241±0.01m with a	(kinematic) with different cuing among PwP
al., 2016)	• The participants	the GI process among	reduced velocity of CoM and CoP	with FoG to analyse the differences
	stood on a force plate	FoG	among FOG p<0.05 than non-FoG	
	and initiate walking	 FoG episode 	• The study showed that the number of	
	with:	• CoP displacement AP	FoG episodes reduced with	
	• no cued	• First Step length	somatosensory curing than other	
	 vibration cue 	1 0	p<0.05	
	 Visual cue 		• PwP was easily affected by the	
	 Auditory cue 		surrounding environment during	
	5		walking	
(Hiraoka et al.,	• Nine PwP 66.1±11.8	• EMG activity of TA and	• Larger RMS activation of TA during	• Small sample size
````	Years old, Seven	SOL	the cued trial compared non cued in	• Absence of mild PwP subjects, not generalisable
2005)	healthy aged		both groups $p < 0.05$	to whole PwP population
	64.6±4.3 Years old		• The activity of Sol reduced in PwP	• The FoG phenomenon needs to be examined to
	• participants started		with cued compared to non-cued	identify the differences between cued and non-
	to walk following		p<0.05 but not with healthy	cued among PwP and that will affect the activity
	verbal cued or		• The external cued effect on the	of the soleus muscle
	without cued with		muscle activity of the ankle joint	
	self-selected speed		during the GI process among PwP due	
	-		to the delay in motor control	

**PWP:** parkonson people, **TA:** tibialis anterior, **GAS:** gastrocnemius, **SOL:** soleus, **FoG:** freezing of gait, **CoM:** center of mass, **CoP:** Centre of pressure, **GRF(Fz):** vertical ground reaction force, **GRF(Fx)** horizontal ground reaction force, **APA:** anticipatory postural adjustment.

Table 2.1 illustrates the key differences in gait initiation between healthy people and people with Parkinson's disease:

- The commonly used outcome measure in research is gait speed. However, it is important to note that an increase in gait speed does not always indicate an improvement in gait quality, especially for individuals with balance issues.
- Any modification in the motor program reduces gait velocity and postural stability.
- The separation of the centre of pressure (CoP) and centre of mass (CoM) pathways is generated by plantar flexor activity, primarily the soleus muscle, which shows continuous activation during gait initiation phases among PwP (Warabi et al., 2018).
- Abnormal control of voluntary movement from the brain impairs the ability to switch between muscle synergies, particularly in the lower limbs (Rosin et al., 1997) Holliday et al., 1998).
- The reduction in tibialis anterior (TA) activation during the stepping phase, along with increased activation of the soleus muscle during the preparation phase, leads to failure in the gait initiation process among individuals with Parkinson's disease (Hiraoka et al., 2005; Warabi et al., 2005)
- PwP are less able to maintain postural stability through the ankle strategy, as observed in unimpaired individuals (Chastan et al., 2008; Dimitrova et al., 2003).
- It should be noted that the studies by Okada et al. and Palmisano et al. (Okada et al., 2011; Palmisano et al., 2020) include individuals with Parkinson's disease during the "ON" medication status, which may affect freezing episodes that increase during gait initiation and subsequently impact the results.
- Methodological limitations of the reviewed studies include small sample sizes (range: PwP = 9-43, control = 7-48).
- The absence of mild Parkinson's disease participants in these studies limits the generalisability of the findings to the entire Parkinson's disease population.
- Understanding the differences in gait phases during clinical assessment can provide a better understanding of the walking difficulties experienced by patients in their daily lives and may contribute to the development of more personalised treatment plans in the future.

## 2.3.2 Change in walking speed (increase, decrease).

### **2.3.2.1** Change in walking speed Healthy people

Humans can reach a steady walking speed after taking four steps from standing (Strutzenberger et al., 2021). Maintaining a steady speed during everyday indoor or outdoor walking is, however, unlikely; individuals must change their speed, stop altogether or change direction to get around various obstacles or situations they may encounter while walking in everyday life (Strutzenberger et al., 2021). The next part will present the differences in the biomechanics parameters and muscle activation during speed transition with healthy participants.

Several studies have investigated the spatiotemporal changes during speed variation among healthy individuals. In a study by (Menz et al., 2004), the authors analysed the gait patterns of 60 healthy adults aged 20-87 years during slow, comfortable, and fast walking speeds. The results showed that step length, step time, and walking speed increased with faster walking speeds, whereas double support time decreased. Additionally, older adults had slower walking speeds, shorter step lengths, and longer double support times compared to younger adults p<0.05.

Chui &Lusardi., (Chui & Lusardi, 2010), analysed the gait patterns of 118 healthy older adults during slow, normal, and fast walking speeds. The results showed that walking speed was positively associated with stride length and step length, while negatively associated with step width and double support time p<0.001. Additionally, age-related changes in gait speed were associated with changes in stride length and cadence. According to Verghese et al. ,2009 community dwelling older adults in an urban setting were 28% more likely to fall if their gait speed was below 1 m/s and 54% more likely to fall if their gait speed was below 0.7 m/s.

Segers et al., (Segers et al., 2006) examined the change in spatiotemporal parameters when gait speed is altered, for instance, during the increase and decrease walking speed. Twenty healthy participants performed 25 trials (increase and decrease walking speed) on a treadmill with a rest period of 30 seconds after every five trials. The duty factor (DF, the ratio of contact time and total stride time), step frequency (SF, the number of steps per minute), speed (v), and step length (SL) were calculated. T-tests showed a difference (from  $1.09\pm0.2$  to  $2.41\pm0.3$ Hz p<0.01) in SF and a corresponding decrease ( $1.09\pm0.07$  to  $0.87\pm0.12$  m p<0.01) in SL. In the decrease walking speed, the T-test showed a statistical difference in DF from  $0.46\pm0.02$  to  $0.55\pm0.03$ m/s2 while a decrease in SF from  $1.98\pm0.10$  to  $1.96\pm0.2$ Hz

and a slight decrease in SL from  $1.12\pm0.07$  to  $1.08\pm0.09$ m. They concluded that the processes for increasing and decreasing speed are not similar, but in both tasks the transition from one speed to another takes place in the walking steps close to transition, emphasising the importance of studying the cycles before and after the speed transition. While this study is useful it represents a change in the type of gait (increase) as opposed to a change in the speed of one type of gait.

The previous study, Segers et al., (2006), investigated the change in speed among healthy young women which limits generalisability to whole population. The authors mentioned that the change in speed does not occur at the same point in time and is more likely to be a process.

In conclusion, the spatiotemporal differences between slow, comfortable, and fast walks among individuals depend on age and other factors, such as health condition.

Understanding these differences can help to improve the assessment and treatment of gait disorders and provide insights into the biomechanics of walking at different speeds. However, none of these studies have looked at the actual transition point in walking speed. Just compared different speeds. Future research in this area should focus on identifying the underlying mechanisms of these spatiotemporal differences and their implications for clinical practice.

There have been several studies investigating the kinetic and kinematic differences during speed variation among healthy people. The majority of the studies used various gait analysis methods, including motion capture systems, force plates, and electromyography. One of the key findings in the literature is that different walking speeds elicit different joint kinematics and kinetics.

Li and Hamill (Li & Hamill, 2002) analysed the vertical ground reaction forces (VGRF) for five steps during the transitional period of a speed change (normal walking to increased speed and back to normal) among 20 healthy young adults. The peak VGRF increased during the speed increase, from 12.5.5 to 13.5 N/kg (recorded during the cycles preceding the gait change) to 14.3 to 14.4 N/ kg (after the change), with greater changes observed during the last step before the speed increase was observed. During the decrease in speed (decreased speed from normal walking), the peak VGRF, unsurprisingly, decreased from a range of 20.8 to 19.7 N/kg and maintain the 19.7 N/kg after change speed. In a similar experiment, Sun et

al. (Sun et al., 2018) reported that vertical GRFs significantly (p<0.001) increased with increasing speed from  $1.42\pm0.04$  to  $1.71\pm0.5$  B/W and decreased from  $1.71\pm0.5$  to  $1.36\pm0.07$  BW p<0.001with decrease in walking speed. Stride length and cadence could also influence propulsive GRF and increase with a change in walking speed as stride length decrease by  $0.06\pm0.01$ m with slow speed and increases by  $0.06\pm0.02$  m with fast speed p<0.05. Cadence also decreases ( $17.9\pm0.1$  s/m) with slow speed and increases ( $27.2\pm2$  s/m) with fast speed (p<0.05).

The study by Sun et al., (2018) investigated the effects of walking speed on lower limb joint kinematics, ground reaction forces, and moments. Their findings supported the idea put forward by Li & Hamill, (2002) that there is a necessary increase in the ground reaction force component prior to gait transition. Furthermore, their results reinforced the idea proposed by Segers et al (Segers et al., 2006) that there are distinct spatiotemporal characteristics associated with the increase and decrease transition when gradually changing speed. Thus, the Sun et al., (2018) study provided evidence to support and strengthen the existing literature on biomechanics during walking speed changes.

In summary during speed increases, the VGRF exhibits an increase in magnitude, particularly during the early stance phase. This increase is due to the need to generate greater propulsive forces to accelerate the body forward. In contrast, during decrease walking speed, the VGRF exhibit a decrease in magnitude , particularly during mid stance. This decrease is due to the need to decelerate the body, to brake.

Riley et al., (Riley et al., 2001) analysed the normal, slow, and fast gait of 24 healthy young subjects to investigate their hypothesis, that adaptations for changing speed requirements occur primarily with increased speed from normal to fast the ROM increased at the hip (flexion and extension) 5 degrees, knee flexion 3 degrees and ankle planter flexion 2 degrees while ankle dorsiflexion showed decreased 2 degrees with speed increase from normal. With change speed to lower from normal speed the three joints showed decreased around 3 degrees in movement except the ankle dorsiflexion increased in ROM. At late stance early swing , with increase speed the analyses of the hip linear power decrease to  $-0.2\pm0.7$ w/kg and increase to  $0.6\pm0.3$ W/kg with decrease speed. also, the knee showed a decrease to  $-0.7\pm0.4$  W/Kg with increase speed and increase to  $-0.14\pm0.4$  W/Kg with decrease speed. While the ankle maintained the positive value of increased linear power with increased speed of  $3.2\pm0.8$  W/Kg and  $1.4\pm0.4$ W/Kg with decreased speed.

the study revealed that the propulsive adaptations to speed changes occur primarily and secondarily at the hip and ankle, respectively. Their findings also showed that the hip extensors contributed more to horizontal than vertical force generation. This suggests that the hip extensors play a key role in propelling the body forward during walking as this is the joint mainly responsible for creating a speed change.

Den Otter et al., (2004) aimed to investigate the neuromuscular activity during very slow walking speeds (<0.28 m/s) in order to better understand the mechanisms underlying speed regulation during walking and aid the interpretation of gait data in patients who walk slowly. Nine healthy young adults were recruited and walked at seven different walking speeds on a treadmill, while electromyographic (EMG) activity was recorded from eight lower extremity muscles. The results showed that the phasing of muscle activity remained relatively constant over walking speeds, with high changes in amplitude.

At very slow speeds, the Peroneus longus during midstance and Rectus femoris in late swing increased in activation to produce new bursts of activity with decreasing speed (44.0%,38.2%). During the gait cycle, the GAS and SOL muscles showed one large burst of muscle activation time with slow speed, mainly during the stance phase (39.9%,24.4%). On the other hand, the TA showed two bursts of activation during the gait cycle, late swing, and early stance , while the second was more strongly affected by speed than the first burst

The authors propose that these activities from muscles may be leads to increased ability stabilised the postural and the altered dynamics of the swinging limb at very slow speeds. Overall, this study provides important insights into the neuromuscular mechanisms underlying speed regulation during walking, which may be useful for developing interventions to improve gait in individuals who walk slowly.

A study conducted by Kibushi et al., (2018) on muscle activity during changes in speed variation among healthy people involved surface electromyography (sEMG) to measure the muscle activity of 10 healthy individuals during treadmill walking at various speeds. The participants were instructed to walk at slow, medium, and fast speeds, with each speed maintained for five minutes. The EMG data were collected from six lower limb muscles: tibialis anterior, gastrocnemius lateralis, biceps femoris, vastus lateralis, rectus femoris, and gluteus medius. The data were then analysed to determine the muscle activity patterns during speed variation. Their findings were in line with the previous studies (Den Otter et al., 2004) indicating that there are true differences in muscle activity patterns in comparison to speed. This study contributes to the growing body of knowledge on the biomechanics of walking

and provides valuable insights for the development of rehabilitation programs for recovery of community walking that requires frequent speed changes.

The studies by Seger et al., (2006), Li et al., (2008), Riley et al., (2001), Sun et al., (2018), Kibushi et al., (2018), and Den Otter et al., (2004) investigated muscle activity during speed variation in healthy individuals. So the findings may not be applicable to individuals with gait abnormalities. Additionally, the studies only examined forward velocity and did not investigate other aspects of gait, such as stride length or cadence.

Overall, these studies suggest that changing in walking pattern, speed or direction is challenging movement that is influenced by age, and cognitive function. Therefore, further research is needed to better understand the underlying mechanisms of Change walking pattern and to develop effective interventions to improve turning performance in individuals with mobility impairments.

## 2.3.2.2Change in walking speed for People with Parkinson's disease

One of the characteristic motor symptoms of PwP is bradykinesia, or slowness of movement (Fahn, 2003). Speed modulation, or the ability to grade movement speed to match the task demands, is often impaired in PwP patients, leading to difficulties with activities of daily living and reduced quality of life (Mazzoni *et al.*, 2012).

Freezing of gait (FoG) is a common and disabling symptom among people with Parkinson's disease (PwP) characterised by a sudden, usually transient, cessation of walking that can result in falls and has an impact on quality of life (Fasano et al, 2017, Okuma, 2006).

As explained in Chapter 1 (1.2.1), the interaction between the motor cortex area and the basal ganglia slows down among PwP, inducing changes in gait parameters, such as reduced step length, cadence, and speed (Shine et al., 2010).

Peterson et al (2020) identified the changes in spatiotemporal parameters during the change from a comfortable speed to faster walking among PwP. The test was conducted for PwP when OFF medication, and an age matched control group were recruited from other neurological conditions individuals (n=40). The study asked participants to walk for two min at their preferred speed and two min with a faster walk. They observed that during the faster walk both groups exhibited larger stride lengths, higher cadence, and longer swing time, compared to a comfortable speed. The PWP, however, showed less change in stride length (0.11m), cadence 12.02 steps/min, and swing time 1.71%) compared to control group 0.12m,16.92steps/min, and 2.22%. These differences were statistically significant (p<0.001).

In conclusion, typical walking speed is reduced in people with Parkinson's disease, which impacts on independence and quality of gait. PwP also exhibit spatiotemporal parameter differences during speed variations, particularly during slow walking speeds. Interventions such as exercise programs may help to improve walking speed and reduce falls risk in people with PwP (Tomlinson et al., 2012; Rochester et al., 2005). Further research is needed to investigate the effectiveness of these interventions and their long-term effects on gait in people with PwP.

Svehlik et al. (2009) compared spatiotemporal, kinematic, and kinetic gait parameters between 20 PD patients off dopaminergic therapy and 20 healthy controls.. They found that the PwP group had decreased walking velocity ( $101.9\pm20.8$  cm/s) and stride length ( $102.18\pm18.5$ cm) compared to control ( $121.7\pm16.5$ cm/s) and ( $127.1\pm13.2$ cm), and the double-limb support PwP ( $28.73\pm4.8\%$ ) and the stance phase ( $64.13\pm2.6\%$ ) of gait were prolonged, in comparison to control ( $24.77\pm2.2\%$ , and  $61.71\pm1.4\%$ , respectively) (P<0.001).

The range of joint motion (RoM) during the gait cycle among PwP was reduced at all lowerextremity joints ( $21.84\pm5.1$ ,  $49.07\pm6.2$ ,  $37.31\pm6.6$  degrees , in the ankle angle, knee angle, and hip angle respectively) compared to control group ( $25.13\pm5.2$ ,  $55.6\pm5.0$ , and  $45.5\pm8.6$ degrees (P<0.001), and they walked with an increased pelvic tilt ( $12.87\pm4.1$ ) compared to control  $8.7\pm6.2$ . The maximum hip flexion was comparable between the groups (mean  $33.59\pm5.1$  in PwP, and  $32.89\pm6.9$  control group), but the maximum hip extension showed higher values in the control group ( $-12.70\pm8.3$ ) as compared to PwP ( $-3.71\pm7.3$ ). The PwP group walked with an increased knee flexion during the single-support phase ( $7.68\pm4.6$ ) degrees compared to control  $3.42\pm4.4$  degrees. Differences were most pronounced at the ankle joint, where the mean plantar flexion during the start movement was reduced in the PwP group, resulting in decreased ankle ROM during push-off ( $19.63\pm5.1$ ) as compared to control ( $23.70\pm5.7$ ).

This study also looked at kinetic gait parameters and found abnormal patterns of motion in the PwP group. The maximum hip flexor moment was reduced ( $-0.83\pm0.32$ Nm/kg, and power generation was reduced ( $1.13\pm0.45$ W/kg) in the PwP group for the first double support and for the pre-swing phase compared to control group ( $-1.22\pm0.3$ Nm/kg and  $1.44\pm0.46$ W/kg). Also, maximum hip power absorption during the stance phase was reduced

in the PwP group (- $0.73\pm0.5$ W/kg compared to control (- $1.2\pm0.47$ W/kg). This differences could be due to the slowness in movement among PwP compared to control group.

At the knee, the maximum extensor moment during stance was higher in the control group  $(0.29\pm0.22$ Nm/kg, and the PwP group generated less power during a single stance $(0.26\pm0.18$ W/kg). At the ankle, the moment at loading response and the maximal extensor moment during stance was reduced in the PwP group, and the power generation in the PwP group deteriorated in the late stance(p<0.001).

The study concluded that altered kinetic parameters play an important role in the characterisation of gait in PwP patients off therapy, in addition to previously described dysfunctional kinematics. The study suggests that these parameters could be used to document the treatment effects of Parkinsonian gait disorders.

Svehlik et al. (2009) added that joint movement is reduced with severe PwP, which affects the spatiotemporal and muscle action. The reduction in hip extension in the late stance and knee flexion during the mid-swing creates a forward trunk posture while walking.

Albani et al. (2003) and Warabi et al. (2017) investigated the activation of lower limb muscles during changes in walking speed with group of PwP and healthy control. Albani et al. (2003) recruited 10 participants diagnosed with PwP (five with freezing of gait and five without) and seven healthy controls age matched. The methods included measurement of gastrocnemius and tibialis anterior (GAS and TA) activity (present as AUC) while treadmill walking at slow (0.30m/s) and fast (1.5 m/s) speeds. At the slow speed, GAS showed reduced activation in both PwP groups compared with the control group (p<0.0001), during the stance phase. By contrast, during the swing phase, TA showed greater activation in of muscle activation as measured by the AUC (area under the curve) of the electromyography (EMG) signal in PwP compared to the control (p<0.0001). When the speed was increased to 1.5 m/s, the PwP showed reduction in GAS muscle than the controls (p<0.0001), with overactivation from TA in the PwP compared with the control group (p<0.0001). This finding may represent a basic distinction between control subjects and PwP, irrespective of the presence of a gait disorder. This reduction on activation at planter flexors muscles with the increased activation of dorsiflexors may explain the typical flexed posture of the parkinsonian patient. Warabi and his colleagues (2018) measured activity of TA and SOL muscles during the change speed for PwP. Their findings suggest that the decreased gait speed is linked to prolonged activity of soleus caused, they speculate, by an inability to switch this muscle off at the correct time, which slows down the forward rotation of the tibia during stance, this was particularly so for people with more advanced disease. The authors suggested that difficulty terminating the competing motor programs linked to postural control (soleus being a major contributor), particularly during transitions, is one of the major reasons for the gait disorders noted in Parkinson's disease i.e. bradykinesia and freezing. Community walking involves adapting speed when encountering obstacles or changing direction. Research emphasizes the central nervous system's role in smooth obstacle avoidance and the complexity of turning, influenced by age and cognitive function. Turning challenges are heightened in individuals with neurological conditions like Parkinson's disease, especially those experiencing Freezing of Gait (FoG). Adaptive interventions are essential for addressing specific mobility issues in this population.

Table 2.2 provides a summary of research that investigating change in walking speed in people with Parkinson's disease and healthy participants while walking on the treadmill and overground.

		Outcome		
Authors	Method	Measures	Findings	Comments and Limitation
Segers et al., 2006	<ul> <li>20 women healthy 24.5±2.76 years old</li> <li>participants walked on a treadmill with different speeds for 30 seconds after every 5 trials</li> </ul>	• spatiotemporal parameters when speed change (increase speed) and (decrease speed) during the transition	<ul> <li>Increase speed</li> <li>Duty factor (df): decreases 0.58±0.01 to 0.47±0.01(M/s2) with more decrease at end of movement to 0.43±0.02 m/s2 P&lt;0.01</li> <li>Step frequency: increase 1.90±0.2 to 2.41±0.3Hz p&lt;0.01</li> <li>Step length: decrease (1.09±0.07 to 0.87±0.12 m p&lt;0.01)</li> <li>Decrease speed</li> <li>Duty factor(df): increased from 0.46±0.02 to 0.55±0.03m/s2 p&lt;0.01</li> <li>Step length decreased from 1.98±0.10 to 1.96±0.2 Hz p&lt;0.01</li> <li>Step length decreased from 1.12±0.07 to 1.08±0.09m p&lt;0.01</li> <li>in both situations, adapting to tasks (transition from one mode to another) takes place in the walking steps</li> </ul>	<ul> <li>The study recruited young healthy women which could not generalise results to another gender.</li> <li>The presence of a transition step with specific spatiotemporal characteristics during increase speed was the most striking difference, whereas this was not observed with decrease speed.</li> </ul>
Orendurff et	• 12 healthy adults 26.67±7.34	• Position of Centre of mass	• CoM velocity increased to 1.475	• Small sample size
al., 2008	years old	(CoM) • Velocities	m/s with fast speed and decrease with slow speed to 1.065 m/s (P<0.001).	• Recruited only young healthy and could be different with older with a neurological condition

Table 2-2 summaries of research investigating change in speed in people with Parkinson's disease and healthy participants while walking on a treadmill or ground

Li & Hamill	<ul> <li>Participants walked on a walkway with two force plates at different speeds.</li> <li>20 healthy aged 24+ 5 years</li> </ul>	the kinetic data were collected They analysed the vertical	<ul> <li>Ankle moment at 30% of gait cycle decreased with fast speed to 0.47±0.19 Nm/KG compared to slow speed 0.50±0.23 Nm/KG P&lt;0.001</li> <li>These plantarflexes muscle activations affect shifting the CoP forward relative to the CoM</li> </ul>	<ul> <li>Walking with different surfaces may produce a change in results mainly with CoM and CoP may change to produce more stability mainly with the treadmill</li> <li>The study recruited young participants which</li> </ul>
Li & Hamill, 2002	<ul> <li>20 healthy aged 24± 5 years old</li> <li>Participants were asked to walk on the treadmill with a force plate at 0.89m/s for 30 s then gradually increase speed.</li> <li>Then they need to run for 30 s at a speed of 2.7 m/s, followed by decreasing the speed.</li> </ul>	They analysed the vertical ground reaction forces during the speed transition	<ul> <li>Increase speed</li> <li>increase in GRF from 12.5.5 to 13.5 N/kg and more increase until the last step of the transition to 14.3 to 14.4 N/ kg</li> <li>Decrease speed</li> <li>decreased in GRF on the stance phase from 20.8 to 19.7 % especially in the last step before transition, with the most dramatic difference observed in the last two steps of the transition.</li> <li>The speed transition speed produced different reactions in</li> </ul>	<ul> <li>The study recruited young participants which may have a different result than the elderly with or without the neurological condition who may be afraid of walking on the treadmill</li> <li>The study observed the two types of gait transition produced different reactions to the acceleration magnitude. First, parameters related increase speed were more sensitive to the magnitude of acceleration, whereas parameters related to decrease speed were not as sensitive to the magnitude of deceleration.</li> </ul>

			GRF which was more sensitive
			with increased speed compared to
			decrease speed
	- 10 hardtha and 04 (* 0.2	- Oraciatana and anamati	
Sun et al.,	• 10 healthy aged 24.6± 2.3	• Spatiotemporal parameters	• Stride time increases by $0.20 \pm 0.02s$ • A small healthy young sample size may ha
2018	years old	• GRF	with slow speed and decreases by a different result with an older adults
	• Participants were asked to	• During speed change	0.20±0.02s with the fast opposite to neurological condition
	walk on a walkway above a		stride length which decreases • The study asks the participants to wa
	force plate		0.06±0.01m with slow speed and barefoot which is not normal in real life. At
	• They were asked to walk at		increases 0.06±0.02 m with fast may produce change with parameters during
	25% slower and 25% faster		speed. P<0.05 change speed.
	than their self-selected speed		• Cadence decrease 17.9±0.1 s/m with • The slow speed was 1.0 m/s which is fast
			slow and increase 27.2±2 s/m with for older participants or with a neurologic
			fast P<0.05 condition
			• Vertical GRF peak increase with
			increased speed from 1.42±0.04 BW
			to 1.71±0.5 BW p<0.001.
			• Vertical GRF peak decrease with
			decrease speed from 1.71±0.5 BW to
			1.36±0.07 BW p<0.001
Riley et al.,	• 24 healthy aged 23.9±4.4	• Kinematic and kinetic data of	• Decreased at the hip, knee, and ankle • The study showed the kinetic and kinemat
2001	years old	joint movement at the hip,	plantar flexion joints by 3 degrees results for healthy young which could
		knee, and ankle	with slow speed but increased by

	• Participants were asked to	• Data were analysed from		more than four degrees with fast		different for the elderly or people with a
	walk on the walkway at	three trials at each speed for		speed.		neurological condition
	different speeds after self-	each subject's left and right	•	The ankle dorsiflexion joint showed	•	The contribution of the ankle is significant,
	selected speed	lower limbs.		a decrease by two degrees with slow		but relatively constant, across the range of
	1			speed and increased by two degrees		walking speeds, especially at slow speeds.
				with fast speed		
			•	Positive ankle power peaks at the		
				late swing and early stance increased		
				from from1.93±0.54 W/kg m to		
				2.93±0.67 W/kg m with speed		
				increase while decreasing slightly to		
				1.26±0.42 W/kg m with decrease		
				speed p<0.00		
			•	Ankle plantar flexor power provides		
				potential energy to the leg to help in		
				the propulsive effect in a late swing		
				because it is limited in a late stance.		
Den Ottar et	• 9 Healthy age = 22.4 ± 2,35	EMG of lower limb muscles	•	the percentage of muscle activation	•	The study recruited healthy young which
al 2004	• The participants walked on	(GAS, SOL, ans TA) with speed		decreased with decreased speed to		could show different results with the elderly
	the treadmill after the	change		(39.9%,24.4% for GAS and		or participants with foot conditions mainly
	familiarised period at			SOL.		the dorsi. and planers flexors muscles.
	different walking speeds.					

Peterson et al. 2020	<ul> <li>67 PwP aged (69.06±7.5 years old)</li> <li>40 control aged (69.7±5.03 years old)</li> <li>With other neurological condition</li> <li>participants walk for two min at their preferred speed and two min with a faster walk</li> </ul>	• spatiotemporal parameters during changing speed	<ul> <li>TA muscle was sensitive to change speed, especially at early stance and late swing with 31.8%</li> <li>Both group showed significant differences (p&lt;0.001) between two speeds during over ground 0.23m/s foe PwP and 0.31 m/s for control group</li> <li>Both group were generated larger stride length, cadence, and swing time, compared to a comfortable speed p&lt;0.001.</li> <li>PwP were exhibited small stride length 0.11m, cadence 12.02steps/min, and swing time1.71%) compared to control group 0.12m,16.92steps/min,and 2.22% p&lt;0.001.</li> <li>Control group showed double swing time 2.22% compared to PwP 1.71%</li> </ul>	<ul> <li>The study showed TA activation during slow movement while the fast movement needs to be recognised.</li> <li>The study tested PwP during off medication which may produce fatigue, and feezing gait that effect on results</li> <li>The study conducted won over grond which may generate difrent result when conducted on treadmill</li> </ul>
Švehlík et al.,	• 20 PwP aged 50-80years	Spatiotemporal parameters	Spatiotemporal parameters	• The study tested PwP during off medication
2009	old, 20 healthy matched	Kinetics	• PwP walk with slow, short stride	which may produce fatigue,
	aged	• kinematics	length, and cadence, long double	• It could be useful if tested during OFF and
			limb support time with longer Stance	ON to observe differences
				•

	• Participants walked on		time compared to control group	
	Walkway at a self-selected		P<0.001	
	speed		Kinematic	
			• PwP walk with reduced all joint	
			movement during walking compared	
			to control P<0.001	
			Kinetics	
			• PwP walk with reduced push-off	
			ankle power and lift-off hip	
			extension compared to control,0.001	
			• Reduced joint power at the hip, knee,	
			and ankle during double support in	
			PWP compared to control P<0.001	
Albani et al.,	• 10 PWP (5 FOG 72.8	EMG for TA and GAS during	At speed 0.3m/s	Small sample size
2003	±5.9years old, 5 PWw Non-	change speed	• At stance: Reduce the activation of	• The study did not mention any
	FOG 54.8±11.02 years old,		GAS PwP compared to control	familiarisation period for the treadmill
	7 seven control aged match		group P<0.0001	before starting the test to train participants
	63		• At swing: greater activation in TA	and to have real activation muscles as
	• participants walk on a		for PwP compared to control	walking on the treadmill, not walking
	treadmill with different		P<0.0001	
	speeds of 0.3 m/sec and 1.5		At a speed of 1.5 m/s	
	m/sec.			

PWP :Parkinson people, TA: tibialis anterior, GAS: gastrocnemius, SOL: soleus, FoG: freezing of gait, CoM: center of mass, CoP: Centre of pressure, GRF(Fz): vertical ground reaction force, GRF(Fx) horizontal ground.

In Table 2.2, it can be seen that the studies generally found that individuals with PwP have slower walking speeds and shorter stride lengths compared to healthy controls. However, the extent of these findings varies depending on the severity of the disease and the task demands. Some studies also found that PwP participants had increased variability in stride length and step length, which is independent of gait speed. These findings suggest that gait bradykinesia in PwP is caused by disease-related pathology, and that controlling for gait speed is important when investigating gait variability.

However, the studies have several limitations. Most studies investigated only gait speed and stride length, while other important gait parameters such as foot clearance, joint angles and kinetics, muscle activity and power were not investigated but could add insight on the underlying mechanism. Additionally, the studies used small sample sizes and lacked control over confounding factors, such as disease severity and comorbidities. Moreover, some studies only investigated either treadmill or overground walking, which limits the generalizability of the findings.

In conclusion, the review suggests that individuals with PwP generally have slower walking speeds and shorter stride lengths compared to healthy controls. However, more studies with larger sample sizes and better control over confounding factors are needed to provide a more comprehensive understanding of gait changes in PwP patients during speed changes. Moreover, future research should investigate other important gait parameters and consider using a combination of overground walking and treadmill walking to increase the generalizability of the findings.

The following section of the thesis will address motor control theories, this was considered important to include in the thesis to put the research findings in the context of the current theories of how the motor output is modified in health and Parkinson's, therefore providing the theoretical underpinning for potential rehabilitation interventions.

# 2.4 Motor control theory

The Medical Dictionary for the Health Professions and Nursing (2012) defines motor control as the process of initiating, directing, and grading purposeful voluntary movement. It is also defined as "the nervous system's ability to regulate the mechanism of movement by directing the joints and muscles according to the surrounding environment and needs" (Shumway-Cook and Woollacott, 2007).

Movement results from three interacting factors.

1) The environments,

2) The task,

#### 3) The individual

#### Latash et al., 2010

Motor control theory is a field of study aimed at understanding how the brain system coordinate and control movement. It encompasses various approaches, such as neurophysiology, biomechanics, and psychology, to improve the quality and quantity of posture and movement, with the ultimate goal of optimising movement and enhancing therapeutic interventions (Shumway-Cook et al., 2007). For example, motor control theory has been used in rehabilitation settings to help individuals recovering from stroke regain their ability to walk. Therapists may use techniques such as task-specific training, where patients practice functional tasks, such as stepping over obstacles or reaching for objects, to improve their motor control and functional movement (Winstein et al., 2016). In addition, a systematic review of randomised controlled trials found that motor control exercises were effective in reducing pain and improving function in patients with chronic low back pain (Saragiotto et al., 1996).

Motor control theories include the reflex theory (Sherrington, 1906), hierarchical theory (Adams, 1971), motor program theory (Schmidt, 1975), systems control theory (Shumway-Cook, 2007) dynamic action theory (Turvey and Fonseca, 2009), and ecological theories (Gibson and Pick, 2000). Although the different theories reflect the evolution of ideas explaining how the CNS controls movement, with each theory emphasising specific neural components of movement, this review will focus on the equilibrium-point theory (Cano-dela-Cuerda et al., 2015). One reason why the equilibrium-point theory is considered a more comprehensive model of motor control compared to other theories is that it can explain the rich variability of human movements (Sainburg et al., 2015). Unlike other theories that assume the nervous system uses predetermined motor programs or commands to execute movements, the equilibrium-point theory proposes that movements arise from the interaction between the neural control system and the mechanical properties of the musculoskeletal system. This interaction allows for flexible and adaptable movements that can be adjusted in real-time to account for changes in the environment or task demands (Feldman et al., 2009;(Latash et al., 2010). For example, experiments that manipulate the mechanical properties of the musculoskeletal system have shown that the nervous system adjusts the equilibrium point to maintain stability and optimise task performance (Feldman et al., 2009;Latash et al., 2010).

In contrast, other motor control theories, such as the motor program theory or the hierarchical control theory, have limitations in explaining the complexity and variability of human movements. The motor program theory assumes that movements are preprogrammed sequences of muscle activations that are retrieved from memory and executed without modification (Mussa-Ivaldi, 1992). This theory cannot account for the adaptability of movements to changing task demands. The hierarchical control theory proposes that movements are generated by a hierarchy of neural structures that send commands to lowerlevel structures for execution (Profeta et al., 2018). This theory is unable to explain how the nervous system coordinates the many degrees of freedom of the musculoskeletal system to produce smooth and efficient movements. Therefore, the equilibrium-point theory is a more comprehensive model of motor control that can account for the complexity and variability of human movements and is supported by empirical evidence (Latash et al., 2010; Latash et al., 2007; Profeta et al., 2018). The equilibrium-point theory is a model that explores the complexity of motor control and its variability- it specifies the physiological variables that are used by the CNS to achieve control and can be used to explain how the impairment in the ability (for example in PwP) to manipulate or shift reflexes within normal range leads to movement disorders (Cano-de-la-Cuerda et al., 2011).

In summary, motor control involves initiating purposeful movements, regulated by the nervous system based on environmental, task, and individual factors. The equilibrium-point theory stands out among motor control theories, explaining human movement variability by emphasizing the interaction between the neural control system and musculoskeletal mechanical properties. Its adaptability surpasses other theories, making it a comprehensive model for understanding and improving movement coordination.

## 2.4.1 The Equilibrium-Point Theory

The equilibrium-point hypothesis, first proposed by Feldman (1986), states that the CNS controls the equilibrium position through the balance of forces in the muscle. Latash and his colleagues (2010) further elaborated on the theory, by describing the activation of voluntary and involuntary movement alongside the work of synergies in controlling motor movement. According to the equilibrium-point hypothesis, muscle activation increases through stretch reflex pathways. Posture-stabilising mechanisms ensure that the equilibrium point (a combination of muscle length and forces) is stable as external forces are changing (Latash et al., 2010). Furthermore, aside from the central signals, signals from

the sensory receptors of other muscles and the activation history all contribute to the stretch reflex (Feldman & Latash et al., 2005). According to Latash et al., (2010), the fundamental to the EP theory is the notion that threshold position control underlies intentional motor actions. To carry out these actions, motor neurons receive electrochemical signals from the brain in response to sensory (proprioceptive/visual/audio/vestibular) feedback, which are then converted into changes in the threshold muscle lengths or joint angles at which these motor neurons start to be recruited. This describes the spatial activation range concerning the body's geometry, allowing the CNS's control levels to specify where, in spatial coordinates, muscles are activated without being concerned about the precise aspects of when and how they are triggered.

In summary, the equilibrium-point theory examine how the nervous system interacts with other body parts and the environment to produce purposeful, coordinated movements by the present perception and controlling from synergies (Ricotta & latish, 2021). However, people with neurological conditions such as Parkinson's find it challenging to modify movement in response to environmental changes. The next section explains how PWP can compensate for this challenge in the environment.

# **2.4.2Principle of Motor Abundance:**

The approach to the control of movement can be used to suggest how the CNS can take advantage of its muscle and kinematic redundancy (Bernstein, 1967) and find multiple motor-equivalent solutions to movement problems (Lashley, 1951). The concept of kinematic redundancy was originally described by Bernstein (Bernstein, 1967) who observed that movement does not repeat itself. It was later reformulated by Latash (Latash, 2012) as "abundance", to remove the negative connotation of the original term. The principle of abundance states that all the elements (i.e., degrees of freedom, DoFs) may participate in all tasks, assuring both the stability and flexibility of the performance. Indeed, kinematic abundance refers to the many ways in which different kinematic degrees of freedom can be combined to accomplish a particular task (Bernstein, 1967; Latash, 2012). The CNS can use the somatosensory signals depending on the reliability and availability of those signals (Mauer et al., 2006). They concluded that motor abundance allows an individual to perform a task effectively while varying movement parameters.

Thus, motor control consists of the CNS finding a set of potential solutions using available degrees of freedom, rather than instructing the system on one specific movement pattern to produce a given movement task. An understanding of this basic principle of the control of movement should be used to shape therapeutic interventions to improve or recover normal movement in patients with motor deficits.

### 2.4.3 Motor control theory in the context of Parkinson's disease

According to Ricotta & Latish (2021), the impaired neural control of stability in PwP suggests direct effects on the perception across modalities or on planning to produce quick action. Moreover, the basic assumption that the basal ganglia are essential for ensuring correct synergic regulation during a variety of tasks, including motor, perceptual, and possibly cognitive, is also supported by clinical observations in other groups with basal ganglia damage (Ricotta et al., 2021). Thus, people with basal ganglia disorders are unable to produce motor function efficiently and they face difficulties maintaining stability and change in movement (Andres and Darbin, 2018). Along with the difficulty in initiating movement, PwP usually find it difficult to transfer from one movement pattern to another, adapt to changing conditions or monitor multiple tasks, all of which are required for stability during gait. All the relevant elements of the synergy control are compromised as a result of the loss of dynamic stability. Thus, this could explain the equilibrium point theory of the importance of muscle springs in the regulation of movement and maintaining postural stability.

A safe and successful transition from sitting to walking and from walking to sitting requires muscle strength, balance, and motor control (Goetz et al., 2008). According to Mazzoni et al (Mazzoni et al., 2012), the slowness of movement in Parkinson's disease explained the disruption in the control processes during the normal speed of movement peed. Two long-term benefits of understanding the motor control basis of motor symptoms (movement variables, such as a limb's position and speed, are controlled and coordinated) include the future design of neural prostheses to replace the function of damaged basal ganglia circuits and the rational design of rehabilitation strategies. This type of understanding, however, remains limited, partly because of limited knowledge available regarding the normal motor control. In the current study, the concept of motor control abnormalities were reviewed, to identify how the disease disrupts normal control processes in Parkinson disease.

#### 2.5 Summary

This comprehensive literature review has provided a detailed examination of the spatiotemporal, kinematic, and kinetic characteristics of gait, along with the associated motor control aspects, in both Parkinson's disease (PwP) patients and healthy controls. The exploration has shed light on the nuanced differences in gait performance between these two groups, contributing to a deeper understanding of the neuro-biomechanics and motor control involved in the initiation of gait. Gait initiation (GI) involves the complex process of transitioning from a stationary stance to walking, requiring coordinated muscle interactions in the lower limbs for forward propulsion while maintaining stability. In healthy individuals, GI includes anticipatory postural adjustments, while age-related changes and impairments can impact gait variability. In people with Parkinson's disease (PwP), GI is affected by freezing of gait and altered muscle activation patterns, leading to impaired motor programming. Studies show differences in spatiotemporal parameters, such as step lengths, and adaptations during treadmill walking. Understanding these biomechanical aspects is crucial for developing interventions to improve gait and prevent falls in both healthy individuals and those with neurological conditions like PwP. In the context of PwP, a notable finding is the decrease in ankle power around pre-swing, as reported by Švehlík et al. (2009). Additionally, consistent alterations in spatiotemporal parameters—such as decreased walking speed, step length, stride length, cadence, increased double support time, and variability in gait parameters-highlight these as reliable markers of gait impairment in PwP. Kinematic analysis has further revealed decreased joint range of motion, particularly at the ankle and knee joints, and altered joint timing and sequencing during gait. Moreover, kinetic gait characteristics indicate decreased ground reaction forces and moments, indicative of lower limb muscle weakness and reduced power in PwP patients. Motor control emerges as a critical factor in understanding gait impairment in PwP, involving impaired sensory and motor integration. This impairment affects their adaptability to environmental changes and task demands during gait. PwP patients also exhibit challenges in automaticity of gait, leading to increased falls and freezing episodes. The integration of vestibular, proprioceptive, and visual inputs for equilibrium control during curved walking becomes a complex task for individuals with Parkinson's disease. Despite the wealth of information presented, a notable gap exists in research focusing on muscle activity during the transition as GI from standing to walking or changes in speed during walking. This gap hinders a comprehensive understanding of the biomechanical parameters involved in these transitions, an essential
aspect in formulating effective rehabilitation strategies for PwP. Highlighting the neurodegenerative nature of Parkinson's disease, this literature review emphasizes the importance of addressing impairments in gait initiation and forward propulsion. The identified gaps in the literature, especially the need for direct comparisons between overground walking and treadmill walking in PwP and older adults, underscore the necessity for future research initiatives. A deeper understanding of these differences could significantly impact the design of tailored interventions to improve gait function in these populations. In conclusion, this review consolidates evidence of various gait impairments in PwP, encompassing spatiotemporal, kinematic, and kinetic characteristics, as well as motor control deficits. The identified gaps underscore the urgency for further investigations, particularly during gait transitions, to unravel the underlying mechanisms of these impairments and facilitate the development of targeted interventions for enhancing gait function in PwP

# **Chapter 3 Methods of study**

## 3.1 Design of study

This study used a two-cohort comparison study. It aimed to compare changes in biomechanical (kinematic and kinetic) and physiological (EMG) variables in response to a requested change (increase) in gait speed (from both standing at rest and from a comfortable speed) while walking on both a treadmill (study 1) and on level ground (study 2).

This was designed to understand the differences in the mechanism of change speed between the two groups whether walking on this differed surfaces treadmill and normal overground walking. There were two participant groups included: 1) a group of people with Parkinson's disease (PwP) and 2) a reference group (Ref) of physically fit adults. Each group-initiated walking and changed their walking speed on both a self-paced treadmill and on the ground. These two very different groups were selected to allow comparisons to be made and thereby gain more insight on the specific gait problems that exist in PwP.

#### **3.1.1** Justification of study design

A two-cohort comparison study is sometimes referred to as a comparative study because it compares two groups of people based on their exposure to a particular intervention (Mann ., 2003). A two cohort comparison study could be the best way to determine if there is an association between the exposure and an outcome of interest (Boyko., 2013).

A two-cohort comparison study includes several advantages to use for example , randomisation might be a big issue, challenging some kinds of experimental designs, such as randomised controlled trails (RCT). Unlike other experimental methods, a A two-cohort comparison study does not rely on random group allocation, with participants assigned using a nonrandomised procedure (Mann., 2003). The reason for not randomising participants is that in healthcare it is difficult to have a true control group due to ethical reasons. Thus, a A two-cohort comparison study is a useful research method when strictly applied research is inapplicable due to practical or ethical issues.

In rehabilitation research, it is typical to apply a two-cohort comparison study, as it

Help to compares between groups of according to a particular intervention to identify the differences between the treatment modalities used in the rehabilitation process and the outcomes observed in the participants (Nielsen et al 2020). Participants prefer to join studies that yield results that are directly applicable to daily activities in the real world (Bastiaens et al 2013; Duncan et al.,2020). This justifies the choice in this instance, as two-cohort comparison study design could be the best way to facilitate the research process, in the real world, and still answer the research question.

The current chapter will present the study's methods in detail and will introduce and explain the equipment and data collection protocol utilised.

# 3.2Aim and objectives.

The current study aims to obtain a clear understanding of community walking problems in PwP while changing their walking speed by analysing the changes in the biomechanics and muscle activity characteristics and comparing them with a physically fit reference group. There is a lack of research focused on evaluating the biomechanical characteristics of the gait pattern (kinetics and kinematics) among PwP and determining the lower limb muscle activity, especially the plantar flexors, which are largely responsible for controlling movement about the ankle during the initiation process or when there is a need to change walking speed, which is considered one of the main problems involved in community walking. Accordingly, the study focused on the following objectives:

# **3.2.1** Objectives

- 1. Recruit representative samples of people with Parkinson's disease (PwP group) and a reference group of physically fit adults (Ref)
- Collect biomechanical (three-dimensional joint rotation angles), power and simultaneous percentage of muscle excitation data (EMG) during the key stages of changes in gait speed on a treadmill and overground.
- 3. To extract and process the data, including removing noise and separating the data into 1) gait initiation (GI) period and 2) three distinct gait cycles (Before, During and After) for the change in gait speed.
- 4. Compare the change in key variables across the three cycles in people with and without Parkinson's during overground and treadmill walking.

- 5. Discuss the findings of study and how they compare with published research.
- 6. Make recommendations for future work, including design, recruitment, protocol and analysis changes.
- 7. Understand the clinical implication for the rehabilitation of people with Parkinson's' disease.

# 3.3Ethics and participant recruitment

This study received ethical approval to recruit the reference group from the Department of Biomedical Engineering ethics committee, University of Strathclyde (DEC18/248) and (UEC18/78) See Appendix (1) for the ethics application and information sheet.

# 3.3.1 The reference group (Ref)

Recruitment targeted independently ambulant participants who were adults aged 18 and over. The remaining criteria for recruiting participants are given below.

# Inclusion criteria:

- $\Rightarrow$  Currently healthy
- $\Rightarrow$  Able to walk for more than 60 minutes unaided.
- ⇒ Weigh less than 136 kg and have a height of 195 cm (limits of the falls arrest harness system)
- $\Rightarrow$  Able to follow simple instructions and communicate, orally, in English.
- $\Rightarrow$  Have good vision (with or without corrective aids)
- $\Rightarrow$  Able to provide informed consent.
- ⇒ Able to come to the University of Strathclyde during working hours (9–5) Monday to Friday for a single two-hour appointment between the  $25^{\text{th}}$  of September and the  $15^{\text{th}}$  of March (2018)

# **Exclusion criteria:**

- $\Rightarrow$  Known to be pregnant.
- ⇒ Known musculoskeletal, neurological, or sensory deficits impairing their ability to walk.
- $\Rightarrow$  Currently on medication that could affect balance.
- $\Rightarrow$  Known motion sickness.
- $\Rightarrow$  History of vestibular or balance problems
- $\Rightarrow$  Unable to give written consent.
- $\Rightarrow$  An active skin condition that could be irritated by contact with sticky tape.

Subsequently, the department administrative staff emailed invitations on behalf of the

researchers to the students and staff in the Department of Biomedical Engineering.

Volunteers indicating an interest in participating were sent an information sheet (see

appendix B) before arrangements were made to sign a consent form and attend the data collection session.

# **3.3.2** The Parkinson's group (PwP)

The participants in this group were adults diagnosed by their neurologist with Parkinson's disease who were stable on anti-Parkinson's drugs and able to walk independently without a frame or walking stick.

#### **Inclusion criteria:**

- $\Rightarrow$  Independent in activities of daily living
- $\Rightarrow$  Able to follow simple instructions and communicate in English.
- $\Rightarrow$  Able to provide informed consent.
- ⇒ Able to come to the University of Strathclyde during working hours (9–5) Monday to Friday for a single two-hour appointment.

## **Exclusion criteria:**

- $\Rightarrow$  Known pregnancy.
- $\Rightarrow$  Known cardiac problems exacerbated by exercise.
- $\Rightarrow$  Currently complaining of joint or muscle problems that affect walking ability.
- $\Rightarrow$  Known neurological conditions that affect walking ability.
- $\Rightarrow$  Uncorrected hearing or vision problems
- $\Rightarrow$  History of severe motion sickness
- $\Rightarrow$  History of vestibular or balance problems
- $\Rightarrow$  An active skin condition that could be irritated by contact with sticky tape.

This group was recruited through the West of Scotland Parkinson's Disease Research Group. The recruitment process for the PwP included joining members of the research group at one of their meetings and explaining the study. When individuals expressed interest in joining the study, a participant information sheet (PIS) and a consent form were sent out to them by email. This was done for potential participants from both groups (PwP and Ref).

The information sheet provided further details on the research process. The potential participants were given at least 48 hours to read it and ask questions before an arrangement was made to attend the movement laboratory for testing. Once both groups had consented to participate in the study, an appointment was arranged at a mutually convenient time. The

testing process was conducted at the Motek Laboratory in the National Centre of Prosthetics and Orthotics (Curran Building) at the University of Strathclyde.

# 3.4 Measurement equipment

# 3.4.1 Motion capture system set up

The data were collected in the Motek gait laboratory at the University of Strathclyde, using the extended Computer Assisted Rehabilitation Environment (CAREN, Motek Medical, Amsterdam). Due to renovation work to the Wolfson Centre (Biomedical Engineering) during the data collection period, a temporary re-location of the CAREN system was used which meant some of the functions were not available at the time of data collection, including a 180 degree immersive environment (this was replaced with a single flat screen in front of a treadmill), as shown in Figure 3-1. The CAREN system is utilised by clinicians and researchers as a rehabilitation requirement for physically fit people (Plotnik et al., 2015) or people with pathological gait problems (Banas et al., 2013; Kilic et al., 2018). The motion capture hardware and software systems used in this project are manufactured by Vicon (Vicon Motion Systems, Oxford, UK) and will be discussed later in this chapter.



Figure 3-1 The modified CAREN Motek laboratory at the University of Strathclyde. A self-paced treadmill system. Arrows indicated cameras, screen, treadmill, and safety harness). The picture shows a Vicon Bonita infrared camera hold by frames. The green arrow shows the direction of the treadmill belt. The blue arrow shows the direction of participants' walk.

Three-dimensional motion analysis systems provide accurate and objective measurements within three planes (Schurr et al., 2017). The Vicon system is widely recognised as the "gold standard" for evaluating human gait and kinematic movement for clinical and research purposes (Schurr et al., 2017). Motion analysis systems include different types of hardware and software, such as optical systems and inertial-based systems, and they provide good reliability (r > 0.8) in the sagittal plane except for pelvic tilt for kinetic and kinematic measurements during movement with good to excellent agreement (ICC > 0.7) and consistency (r > 0.7) (McGinley et al., 2009; Wilken et al., 2011). System setup procedures vary from being simple to being set up to having a more complicated configuration (Springer et al., 2016).

# **3.4.1.1** Treadmill configuration set up.

The CAREN system includes a treadmill (N-Mill, Netherlands) with a dual  $1 \times 2$ -metre split belt and two oversized force plates (Motekforce Link, Amsterdam, Netherlands) located underneath the treadmill's right and left belts. The force plates' pressure sensitivity centre is stated by the manufacturer to be less than 2 mm for loads under 1,000 N (Sinitski & Lemaire, 2015). The treadmill can be used in self-pacing mode, which means that the treadmill alters the belt speed according to the participant's position and speed to produce variations in belt speed while walking (Plotnik et al., 2015). The gait laboratory coordinate system used in the current study is shown in Figure 3-2,



Figure 3-2 The calibration wand on the treadmill showing the global reference frame axes X, Y and Z.

Utilising the treadmill helps both researchers and clinicians to control walking speed, measuring several gait cycles within a short time and a limited area, especially compared to over-ground walking, which takes place over longer distances (Papegaaij and Steenbrink, 2017). Walking on the treadmill or on the ground at different speeds shows similar results in gait parameters after a brief 2–6-minute familiarisation period (Parvataneni et al., 2009; Holman et al., 2016). The CAREN system incorporates a virtual reality (VR) environment created through D-flow software (Motek Medical), which will be discussed in more detail later in this chapter. The treadmill and VR are synchronised to provide a realistic optical flow, as when one would walk outdoors. In this regard it is considered a reasonable analogue of normal overground walking.

## **3.4.1.2** Camera configuration

The current study involved 12 Bonita (B-10) cameras (Vicon Motion Systems, Oxford, UK). The cameras' resolution was approximately one megapixel, with a frame capture rate of 250 frames per second (fps) and an accuracy reported to be <10 mm (Summan et al, 2015).

The cameras were attached to poles surrounding the treadmill in fixed positions, see Figure 3.1, to track the motion of retroreflective markers attached to participants walking on the treadmill. A calibration process was performed using an active wand that consisted of a metal T-shaped instrument with five LED markers embedded at fixed locations. By moving this active wand within the camera capture volume where the individual intends to move, the cameras capture the position of each LED. The difference between the locations captured by the cameras and the known distance between the markers was then calculated by the manufacturer's software (Nexus, Vicon Motion Systems, Oxford, UK) to provide a calibration matrix.

To correctly orient the camera system, the wand was then placed at a specific position in the middle of the lab space to identify the origin and ground plane of the treadmill and to determine the axes of the global reference frame, as shown in figure 3-2.

Each B-10 camera captures the 2D location of a marker's position in the capture volume. The Vicon system can convert the active markers' 2D images into 3D position information from each marker during movement. Each camera emits infrared radiation that is reflected off the retroreflective markers placed on the body. Consequently, the markers should be positioned so that the infrared radiation intersects from two or three cameras to localise the markers in 3D. Interestingly, it is not necessary that all of the cameras' radiation intersect to find the 3D marker position if the system includes more than three cameras. So, the markers should be seen through all the capture volume, and if they are missed, that means fewer than three cameras see the markers (Tormanen, 2019).

The Vicon system capture software VICON Nexus (Oxford, UK) applies the "least-squares" method to calculate the 3D location of the markers in space Figure 3-3. The least-squares technique should be used to calculate the location of a point in space such that the sum of the squares of the shortest distances from that point to each ray is a minimum. This calculated point then represents the best estimate of the observed point's centre. The individual residual components are the shortest distances (perpendiculars) from the calculated point to each ray. The smaller the distance the system calculates, the more accurate the detected marker position. The motion capture system's manufacturer has advised that the system can detect accurate positions if the mean of the residual value is less than 0.5 mm.



Figure 3-3 An example of applying the "least squares" method to measure the marker's centre residual with three cameras' radiation, where C1, C2 and C3 are the cameras' positions and D1, D2 and D3 are the markers on individual bodies (Motion Lab Systems, 2016).

## **3.4.1.3** Marker locations

The biomechanical model used in this study was the Plug-In Gait (PIG) system (discussed in more detail in (section 3.4.3.1) which requires retro-reflective markers to be attached to specific anatomical points on the body to determine the 3D orientation of the tracked segments. The system requires that each participant's anthropometric measurements, including height, weight, leg length, knee width, ankle width and pelvis width allow the system to create a computer model tailored to each participant, including the location of the joint centres and joint angles during movement. The current study used 16 reflective markers attached to body segments see Figure 3-4 (A). The accuracy of the limb measurements recorded by clinicians and researchers depends on the variability of the marker placement (Nair et al., 2010). Vicon® (2002) explained the process of calculating a joint's movement by estimating the nearest joints above and below the one that needs to be measured and by applying markers around the three joints to detect the centre of the middle joint's movement. Therefore, the static calibration trial utilises the global coordinates (X, Y and Z) of anatomical landmarks to identify the anatomical references of segments that help to calculate the position of the joints and the axes.



# Figure 3-4 (A) The placement of the retro-reflective markers adapted from Vicon® 2010. (B) The reflective marker

sphere (14mm in diameter), as illustrated in Figure 3-4 (B). The markers are attached to the surface of the tight-fitting of the participants clothing, typically lycra or the participants' skin according to the anatomical landmarks, as shown in Figure 3-4 and Table 1. Cappozzo et al. (1991) advised that each segment during dynamic trials should include two to three

markers with an adequate distance between them to decrease the number of errors that the system might produce and to provide full information about the segment's 3D movement

Location	Anatomical position
Left ASIS	Placed directly over the left anterior superior
	iliac spine.
Right ASIS	Placed directly over the right anterior superior
	iliac spine.
Left PSIS	Placed directly over the left posterior superior
	iliac spine
Right PSIS	Placed directly over the right posterior superior
	iliac spine.
Left Knee	Placed on the lateral epicondyle of the left knee.
Right Knee	Placed on the lateral epicondyle of the right
	knee.
Left Thigh	The greater trochanter of the left femur is
	located here, and the marker is placed 1/3 of the
	way on the superior part of an imaginary line
	between this location and the LKNE marker
Right Thigh	The greater trochanter of the right femur is
	located here, and the marker is placed 1/3 of the
	way on the inferior part of an imaginary line
	between this location and the RKNE marker
Left Ankle	Placed on the lateral malleolus of the left ankle
Right Ankle	Placed on the lateral malleolus of the right ankle
Left Tibia	Placed on the inferior 1/3 of an imaginary line
	between the LKNE and the LANK markers
Right Tibia	Placed on the superior 1/3 of an imaginary line
	between the RKNE and the RANK markers
	<ul> <li>Left ASIS</li> <li>Right ASIS</li> <li>Left PSIS</li> <li>Right PSIS</li> <li>Left Knee</li> <li>Right Knee</li> <li>Left Thigh</li> <li>Right Thigh</li> <li>Left Ankle</li> <li>Right Ankle</li> <li>Left Tibia</li> </ul>

 Table 3-3 Markers used in the lower limb version of the PIG model that show their label, location and anatomical position.

LTOE	Left Toe	Placed over the left second metatarsal head, on the mid-foot side of the equinus break between the forefoot and mid-foot
RTOE	Right Toe	Placed over the right second metatarsal head, on the mid-foot side of the equinus break between the forefoot and mid-foot.
LHEE	Left Heel	Placed on the calcaneus at the same height as the LTOE marker
RHEE	Right Heel	Placed on the calcaneus at the same height as the RTOE marker



Figure 3-5 (A) A static trail of the markers (B) The markers after labelling

Finally, an algorithm included in the Vicon Nexus software then filled in any gaps in the marker trajectory which was digitised and labelled as shown in the figure 3-5 (typically using a cubic spline function with gaps of less than ten frames, if needed ) to improve the quality of the resulting data.

The Vicon Nexus system stores the raw data from the EMG and IMU as analogue data and then transfers the dynamic trial information as C3D files or to a Microsoft Excel worksheet, this will be discussed later as EMG processing data in section 3.4.2, depending on the program that is required for analysis. In this thesis, both C3D files and Microsoft Excel worksheet programmes were used to transfer the data for analysis. The data were then processed offline using MATLAB software (Matlab Version R2018b, MathWorks, Inc. USA).

## **3.4.2 Electromyography (EMG)**

EMG is a measurement tool that has been used widely since 1920 in human movement studies to identify patterns of electrical activity in muscles (Amrutha & Arul, 2017; Kleissen et al., 1998; Roeder et al., 2020; Tikkanen et al., 2013). In this study, EMG was used to quantify specific parameters of the electrical activity (numbers of active periods during the gait cycle, total percentage of muscle activation and total magnitude of activation using area under the curve) of target lower limb muscles while walking at a comfortable speed and when the walking speed change while walking on a treadmill and over ground.

During motor tasks, EMG recording systems measure the number of motor units firing, which change with the increase or decrease in the intensity of the movement task (Asmussen and Tscharner, 2018). EMG is mostly utilised during gait analysis studies to determine the onset and offset of muscles (Hiraoka et al., 2006; Warabiet et al., 2018).

The Delsys Trigno EMG system (Delsys Trigno, Boston, USA) was used in this study. It is composed of a base station that wirelessly receives (via WiFi) the data from the EMG electrodes (removing a potential source of noise from movement of the wires) and includes the potential for 8-channels of data EMG. Each sensor can send the pre-amplified data by WiFi to the PC-connected base station across a maximum distance of 20 metres see



Figure 3-6 (A)The EMG base station (B) EMG sensors with the arrow showing the direction (C) The position of the electrodes on the muscle fibers (copied from Trigno Wireless, 2013 User Guid)

The electrode sensors include a concave feature that helps to reduce the noise produced by skin movement and allows for closer skin contact for better quality in detecting signals from the muscles (Young et al., 2011). EMG surface electrodes have shown moderate to very high-reliability ICC=0.832-0.937 with good to excellent validity compared with BTS-FREEEMG1000 R =0.943 (Jang et al.,2018). Each electrode includes two strips of silver/silver chloride placed 10mm apart to record maximum EMG signals with fewer artefacts (Amrutha & Arul, 2017).

# **3.4.2.1 EMG processing data**

EMG signals are collected using surface or indwelling needle electrodes; the signals are amplified and transmitted by wires or a wireless system for further processing. The raw data from the EMG signal are mainly produced with low voltage (microvolts, typically ranging between 1 and 10 mV) and can be affected by background electrical noise from electrical equipment and magnetic radiation as well as movement artefacts (e.g., the movement of cables or skin) (Amrutha & Arul, 2017). Locating a muscle's EMG signal can be challenging due to the potential for interference from adjacent muscles (cross-talk interference) (Levine & Richards, 2012). Consequently, EMG signals require amplification before being filtered to remove the noise. EMG signals include positive and negative values to represent the action potential process during muscle contraction, the rectification process is therefore a simple step that enables the analysis of EMG by calculating the root

mean square (RMS), which powers the signal to identify the accurate measurement of muscle activation; this is necessary because the raw data are inadequate to show the muscles' activity (Reaz et al., 2006; De Luca et al., 2010).

Additionally, due to the low voltage of the EMG signal, which might be affected by biases from other signal resources, the raw data needs to be normalised to assist in comparing the muscles' performance during the motor task (Levine & Richards, 2012; Kamen & David, 2010). In the current study, the gait cycle time will be time normalised to 100% using sequential foot contact events so the EMG data of muscle activation during each cycle will be identical to the percentage gait cycle and be placed in context of the kinematics and gait phases/events.

Band-pass filters were used to minimise the noise included in the analysis and remove artefacts that emerge from muscle movements to prevent improper interpretation (De Luca et al., 2010). The cut-off frequencies were 20 and 400 Hz, and a 6th order Butterworth filter was used to control the high- and low-frequency EMG signals that might produce noise while recording the signal (Staudemann et al., 2007; Khanmohammadi et al., 2016) as in Figure 3-7. The EMG data depends on the time and frequency domains, which are used in muscle studies to determine muscle activities (Xi et al., 2018).

In the current study, EMG data were reduced to a percentage of gait cycle time, the number of discrete contractions per muscle per cycle, and the total magnitude of muscle activation, by integrating the signal to obtain the area under the curve (AUC) of the six muscles —the tibialis anterior, gastrocnemius and soleus on both sides—during speed modulation (gait initiation and full gait cycle during speed change) while walking on the treadmill and on the ground.

The AUC was used to represent the magnitude of the muscle's overall activation. Arabadzhiev et al. (2010) advised that the AUC is the best mathematical measurement to describe the neural effect's intensity and magnitude during maintained activity because the muscle's magnitude increases with the EMG signal's activation.

Rissanen et al. (2007) recognised that the histogram and cross vector values of PwP's EMGs were characterised by a bursting and spiky pattern that was different than other neurological conditions. Accordingly, the height of the histogram, sharpness of the peak and side differences was visualised by applying the high pass filtered to smooth and remove the low frequency signal to recognise the Parkinson's disease signal from other condition (Ruonala et al., 2013; Oung et al., 2014). Also, freezing of gait among

Parkinson's people during change speed was able to be determined using EMG signals (Oung et al., 2014; Cole et al., 2011).

Baryan et al (2011) informed that FoG among PwP can only analysed during gait initiation or with change speed to continue walking so they placed the sensors at lower leg however EMG is so sensitive to dynamic movement and may influence by any medication that effect the nervous system (Network, B.N ,2009). Figure 3-7 showed the process of EMG to have clear data.



Figure 3-7 The processing of EMG: (A) The raw EMG data (B) The rectified signal

# 3.4.3 Biomechanical model

# **3.4.3.1** Plug-In Gait Biomechanical Model (PIG)

Different biomechanical models are used to represent the movement of body parts in relation to each other. Kains et al. (2016) asserted that only one model should be used within a study to ensure the consistency of measurements of musculoskeletal joint

movement. The current study applied the Plug-In Gait (PIG) kinematic model for the lower limbs only to collect kinematic measurements during movement.

The lower limb (PIG) tracks seven segments (the pelvis, two thighs, two lower legs and two feet), which are connected by simplified joints. Kainz et al. (2017) tested the reliability of the PIG model by assessing the intra- and inter-tester standard deviations (SD) and standard error of measurement (SEM) to evaluate the kinematic PIG and the six degrees of freedom model using Vicon system software. The study showed that the PIG model had an SD lower than five degrees in all joint movements in the sagittal and frontal planes, with high reliability, r>0.9 (Nair et al., 2010) in the sagittal plane. The model showed a high SD with a mean of 7.2-degree intra-tester knee internal-external rotation angles, a high SD a mean of 3.2 regarding all other joints. Lohrer et al. (2009) asserted that by adding a few more markers can improve the reliability of knee angles in the frontal plane. Stief et al. (2013) reported that the PIG model produces less accurate and reliable measurements in the frontal plane for knee angle movements, with 4.7 degrees more flexion or extension and 6.5 degrees less varus and valgus than the custom-made lower body protocol. Ferrari et al. (2008) accepted that improper marker placement leads to incorrect alignment of the knee axis of rotation, which produces measurement errors in the PIG model in some studies.

Khamis et al. (2017) tested the validity of the PIG model by comparing the outputs of the model with values taken by X-ray of leg length discrepancy (LLD) in the femur and tibia segments of 15 participants (10 children and 5 adults) with neurological conditions, such as cerebral palsy and stroke. The PIG model was found to be a valid model for finding LLD during gait to calculate the differences in joint angle . There were no differences between the tibias (p = 0.45) and femurs (p = 0.3) of the two models, while a high correlation appeared between the models, with R = 0.808–0.962 and P < 0.0001.

During a static calibration process, the Vicon system requires specific algorithms to be processed from the cameras and the reflective markers via specialised software (Nexus, Vicon, Oxford, etc.) to measure the relationship between the data from each camera and the calibrated volume. Using the static capture positional data of reflective markers located on the body, the PIG model is constructed for each individual using anthropometric data—body mass (Kg), height (mm), leg lengths (mm), knee widths (mm) and ankle widths (mm).

Following this calibration process and the construction of the biomechanical model, the movements of the individuals will be tracked and processed after data capture. This post-processing includes filling any gaps in the marker trajectories (cubic spline function) and filtering (6th order Butterworth) to remove soft tissue artefacts (Leardini et al., 2005).

#### **3.4.3.2** The synchronised virtual reality system

When people are walking on the treadmill, Motek's D-Flow software (Motekforce Link, Amsterdam, the Netherlands) is able to create a virtual reality (VR) environment that is displayed on a flat screen, see figure 3-1. The Motek CAREN (Computer assisted Rehabilitation Environment) can generate an immersive setting that gives the impression of walking through a community environment, such as a forest, a path or an urban street. The data from the Vicon system, treadmill and force plates (as well as other digital or analogue signals) are streamed into the D-flow software to create a synchronised virtual environment and visualisation of specific movement parameters, as shown in figure 3-8. The system optimises the control of visualisation and the treadmill, including self-pacing (Collins et al., 2015). In the system, the participants are considered to be the main parts of the input devices of a real-time feedback loop that conveys motor-sensory, visual and auditory feedback to the subject via the output devices (Geijtenbeek et al., 2011). The picture appears on a flat screen in a problem-solving way as they walk; this includes avoiding virtual obstacles, moving through virtual doorways, reaching for targets and changing speed. It also completes cognitive tasks, such as recalling the properties (e.g. the shape, colour or words) of passing objects. Notably, the system is controlled by the researcher to manipulate the speed and stopping and starting points Figure 3-8.

In this study, the participants observed a walking path in the forest on a screen. The word 'FAST' appeared on the screen after approximately 10 seconds of walking at a self-selected comfortable speed, requiring the participants to increase their walking speed. This word disappeared after 10 seconds, and participants returned to their normal speed. It should be noted that the examiner controlled the appearance of the word 'FAST', as well as the start and stop points. See 3.5.3.1 for more details.

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Figure 3-8 The D-flow proceeding system: (A) The application system and (B) The runtime console of the participant (copied from Geijtenbeek et al., 2011).

# **3.4.4 Determination of gait cycle events**

## 3.4.4.1 The Gait events.

It is important to identify gait events to allow individual cycles to be defined; this is particularly important when studying a change in walking behaviour, for example, a change in speed. Researchers have long sought accurate devices and methods to detect gait events for both physically fit people (Chambers et al., 2002; Chang et al., 2016) and those characterised by abnormal gait cycle patterns—for example, with neurological patients or older adults (Demonceau *et al.*, 2015; Sofuwa *et al.*, 2005; Danielli Souza Speciali *et al.*, 2014). Determining the time of each event as a percentage allows researchers to detect differences across the entire cycle (Ewins & David, 2014).

In the current study, all gait events were identified using the gyroscope signal from a small  $(2 \times 1 \times 1 \text{ cm})$  inertial measurement unit (IMU) (TrignoTM Wireless System, Delsys Inc., Boston, MA, USA), as in the study by Li et al., (2016). The gyroscope measures the angular velocity of a rigid body to which it is attached. In this way, it can help characterise movement patterns during indoor and outdoor activities with low energy expenditure by attaching them directly to the user's body without the requirement of cameras or markers (Lau et al., 2009; Levine et al., 2012). However, the detection of foot contact time (initial contact and foot off) extracted from the gyroscope seems to be 0.01 seconds later than real-time gait analysis (Aminian et al., 2001).

# **3.4.4.2** Detection algorithm from the single-axis gyroscope

A gyroscope (component of the Delsys Trigno sensor) was positioned, laterally, at the distal end of the lower leg (shank) on the skin overlying the distal fibula. It was hoped this boney location would produce a clearer signal by reducing movement artefact due to soft tissue "wobble" (Catalfamo et al., 2010). McGrath et al. (2012) attached gyroscopes to the lower legs of healthy participants to record gait events during walking and running by detecting each foot contact. This will be discussed in more details later in this chapter, demonstrating that the gyroscope has high accuracy and presents fewer errors (by 1.6%) than other devices, such as foot switches that foot contact events outside of laboratories.



Figure 3-9 (A)The position of gyroscope on participant. (B)The three direction axes on the gyroscope

The direction of the axis is represented in Figure 3-9, showing that the X-axis is positive, and the Z-axis indicates the movement on the sagittal plane.

McGrath et al. (2012) demonstrated the IMU gyroscope signals as positive and negative peaks to help identify the gait events (i.e., initial contact, mid-swing, and toe-off) of the lower limbs. The positive peaks in Figure 3-10 indicate the mid-swing, while the negative peaks on the left and right of the positive peaks represent the foot's initial contact and the events when the toes have begun to lift from the ground, respectively (Aminian et al., 2002).



Figure 3-10 Number of gait cycles during walking. (B) Calculation of the stance, swing and stride time (adapted from McGrath et al. (2012).

The stride time is calculated from the time interval between the two red points (initial contacts), which determines the time between the two sequential foot contacts. The stance time is calculated from the time interval between the red and green points Figure 3-10. The amplitude of the peaks varies among subjects due to velocity or body weight (Aminian et al., 2002).

# **3.5 Data collection**

#### **3.5.1** Preparation of the gait laboratory

The capture system was calibrated as explained in section 3.4. The motion capture (Vicon Nexus) and treadmill operating (D-flow system) software were checked to ensure that the measurement systems (EMG sensors, the 3D-markers' trajectories and the treadmill) were synchronised as in section 3.4.

## **3.5.2** Participant preparation

Prior to data capture the protocol was again explained to the participants and they were given a further opportunity to ask questions. The PwP group were also asked to complete the Parkinson's Disease Questionnaire (PDQ-39), which will be explained later in this chapter. The participants were then asked to change into a T-shirt and shorts to allow attachment of the reflective markers to positions on the skin (and tight-fitting clothes) using double-sided adhesive tape according to the PIG model guidelines (VICON, Oxford,

UK), see Figure 3-4. Each participant's anthropometric measurements (height, weight, leg length and width of the pelvis, knees and ankles) were taken to allow the model (PIG) to be adjusted to each individual.

# **3.5.2.1 EMG and IMU preparation**

The skin was prepared for the placement of the six EMG electrodes, as in Figure 3-11, and two IMU were placed on the distal lateral shank of each side of the lower limb. The process includes light rubbing to remove dead skin cells, wiping with alcohol and shaving an area of approximately 2cm2 if required to reduce noise, reduce impedance and receive an accurate EMG signal from the muscle (Amrutha & Arul, 2017). The six EMG electrodes were then placed over the bellies of the tibialis anterior, gastrocnemius and soleus muscles with double-sided adhesive tape according to the Surface EMG for Non-Invasive Assessment of Muscles (SENIAM) system (Hermens et al., 1999). The IMU were also attached with double-sided adhesive tape to the lateral shank of the lower third of the leg on both lower limbs. The IMU were wirelessly paired with the Trigno base station, which was linked to the Vicon nexus software to ensure synchronisation with the force plate, treadmill and motion capture systems. The IMU and EMG data were combined in a similar Delsys Trigno system base station.



Figure 3-11 Delsys EMG. (A) Position of electrodes on lower limbs for Gastrocnemius, soleus, and tibialis anterior. IMU are positioned on the lateral shank of both lower limbs. B) Position of the electrode on the muscle fibres (adapted from Hermens et al., 1999).

#### **3.5.2.2** The Parkinson's Disease Questionnaire (PDQ-39)

PDQ-39 is widely used to assess the functional status of PwP since it reflects the severity of the disease (Horrison et al., 2000). It is also used to monitor the effects of interventions on PwP (Hagell and Nilsson, 2009). The scale includes eight items that assess the impact of disease severity on mobility, emotional health, wellbeing, cognitive ability, stigma and social support, and how much it affects the quality of life on a score range of 0–4, where "0" represents no effect and "4" represents that it always has high impact. The higher the score the lower the participant's functional ability and quality of life (Grosset et al., 2009). Numerous versions of the PDQ-39 have been translated and abbreviated to reduce the duration of the instructions, which takes approximately 10–20 minutes (Keus et al., 2007; Schenkman et al., 2012). The English version of PDQ-39 has a reported internal consistency alpha of 0.59–0.94 and test-retest reliability (ICC) of 0.67 - 0.87 in a study with PwP, n=68 (Tan et al., 2004), demonstrating its high sensitivity to functional and psychological changes in PwP group (Horrison et al., 2000) (see Appendix C) for the English version).

After completing the PDQ-39 questionnaire, the PwP group was divided into severity categories according to their sum of score: participants with higher scores > 40 have a more severe impact on the PD disease, those with lower scores < 20 had low impact on PD and the middle score between 20 to 40 correlated with moderate impact on PD. The PwP group was consequently divided into the following two subgroups: 'mild/moderate' and 'severe'. One participant had a lower score than the rest of the group but was included in the 'mild/moderate' group since a group cannot be formed by a single participant.

## **3.5.3** Movement task

The current study includes two testing protocols:

- 1) Walking on a treadmill-study 1
- 2) Over ground walking -study 2

#### **3.5.3.1** Study (1) walking on a treadmill

The treadmill study included two parts: (1) GI from a standing position to walking and (2) an increase in walking speed from a comfortable baseline.

Once all the reflective markers, EMG sensors and IMUs were in place, each participant stood on the treadmill. As participants may need a little time to get used to a treadmill, a

familiarisation period (approximately 10 minutes) of treadmill walking was performed at the participant's comfortable speed.

# A Gait initiation

GI, participants were asked to walk forward on the treadmill from a standing position and then return to the starting position. The forward movement of the participant triggers the treadmill to commence; this is achieved through a control mechanism that uses the mean horizontal position (and velocity) of the four pelvic markers (tracked by the Vicon system and streamed to D-Flow). The full movement was recorded from three seconds before the signal to walk was given, until the movement had been fully completed (i.e. after three steps). The GI period was calculated from standing to the second heel contact to having clear sequences of gait events in both situations.

# B change in waking speed (increase speed)

the second part (speed increase), participants walked on the same treadmill at a comfortable speed (determined during the familiarisation period). They responded to the word 'FAST', which appeared on the screen in front of the treadmill while walking after 10 seconds; the word disappeared after 10 seconds.



Figure 3-12 the word FAST appeared on screen during increasing speed.

As in Figure 3-12. The collected data included three distinct gait cycles: 1) immediately before changing the speed (Bef), during the change in speed (Dur) and immediately after

changing the speed (Aft). These cycles were detected through the change in the signals from the IMU attached to the lateral shank (IMU^{shank}).

## 3.5.3.2 Study (2) walking over ground

Participants for this study were the same as in the first study. The size of the movement lab (housing just the Motek treadmill system) meant that an overground trial could not be carried out in the same laboratory space. The ground walking data were therefore collected using a temporary path (10 metres in length) marked on the ground in the corridor outside the laboratory. This setup meant that the motion could not be tracked by the motion capture system. Instead, signals from the wearable IMU sensors were used to identify the time of gait events, i.e. foot contact and loss of contact with the ground. These IMU signals were used to separate the EMG signals into two parts of the study as in treadmill GI and for an increase in walking speed.

## A Gait initiation



Figure 3-13 A diagram of GI walking during on-ground movement. The participants started the movement from standing and walked on the 10-meter path. SWO1= the first foot off on the swing side, SWC1 = the first foot contact of the swing side, STO= the toe-off of the stance side, STC = the first foot contact of the stance side, SWO2= the second foot off of the swing side, SWC2 = the second foot contact of the swing side. The diagram was adapted from Jhapate & Singh (2011).

During overground walking the gait initiation data was collected from standing until the second foot contact as in Figure 3-13. The gait initiation events were similar in both studies, see table 3-3 for more explanation.

# **B** Change in walking speed during over-ground.

In speed change, the participants walk on ground for four steps with a comfortable walking speed and change speed with the fifth step. See Figure 3-14.



Figure 3-14 Diagram of walking on-ground. The participants started the movement from standing and walked for four steps from [1] to [4]. At the fifth step [5], the participant was instructed to increase their walking speed. The blue arrows indicate (A) gait cycle 'before' a change of speed, (B) gait cycle 'during' a change of speed, (C) gait cycle 'after' a change in speed. The diagram is adapted from Jhapate and Singh (2011).

As shown in Figure 3-14, the participants performed the first four steps at a comfortable speed and on the fifth step, they were asked to increase their walking speed. The variables were calculated as the time spent between two sequential foot contacts for the three distinct cycles as in the treadmill test see section 3.5.2.1 into: 1) Bef was calculated from step (3 to step 5), 2) Dur was calculated from step 5 to step 7 and 3) Aft was calculated from step 7 to step 9.

The next section will present the data processing and of analyses for both studies during two types of walking.

#### **3.6 Data processing and analysis**

The raw data (both treadmill and overground studies) were trimmed to either a period of two gait cycles to calculate the biomechanical data and muscle activation during the GI section or to three gait cycles to calculate similar parameters when increasing walking speed from a comfortable pace.

# 3.6.1 Separation into gait cycles during study (1) treadmill walking

The gait events were detected from the gyroscope signal attached to the lateral lower leg to identify the time of toe-off and foot contact events using a bespoke MATLAB code.

# 3.6.1.1 Gait initiation

The full movement was recorded from three seconds before the signal to walk until after the movement had been fully completed. The GI period was calculated from a change in the standing position that was detected by the gyroscope when the shank (lower leg) is rotating clockwise direction to measure the start of GI until the end of the GI period which is defined as the point when the second-foot contact occurred, see Figure 3-15. The starting side is called the swing side while the opposite side is called the stance side.





The key event of that represented in Figure 3-15 is related to:

- GI Start = The first time a negative change (lasting more than 0.5 s) occurred about the Z axis (sagittal plane) of the gyroscope located on the lower leg.
- A = the first negative peak related to the foot-off event (SWO).
- B =The second negative peak of the swing side related to the first swing contact (SWC1)

- C = the first positive peak of the stance side; indicated the first foot off on the stance side (STO).
- D = the second positive peak of the stance side; indicating the first foot contact of the stance side (STC).
- E= the third negative peak second foot off the swing side(SWO2).
- F= the second foot contact of the swing side; indicated the endpoint of the GI (SWC2).

As explained in section 3.4.4.2, and in Figure 3-15, The blue line of the first negative movement of the gyroscope was related to the swing side (the side that started first). Thus, the stance side (opposite side) represents the opposite direction as the red line.

Events	Definition		
SW01	The first foot off on the swing side. Which calculated from the start GI movement of the lower limb tell foot off		
SWC1	The first foot contact on the swing side.		
STO	The foot off of the stance side.		
STC	The first foot contact of the stance side.		
SWO2	The second foot off the swing side.		
SWC2	The second foot contact of the swing side, which indicates the end of the GI period.		
Phases			
Swing (1)	The time from the starting time to the first foot contact of the swing side point [C].		
Swing (2)	The time from the starting point to the first foot contact of the stance side point [F].		
Swing (3)	The time when the swing side leaves the ground a second time[G] to contact again for the second foot contact point [I]		
Stance (1)	The time from the starting point until the stance side leaves the ground point [D].		

 Table 3-2 The events and phases of the GI events according to IMU recording time (events and phases are adapted from Lee and Park (2011)).

Stance (2)	The time from the first contact of the swing side point [C] until
	the time that the same foot leave the ground point [G].

#### A. Spatiotemporal parameters.

The start time (start GI) was calculated from the change (lasting more than 0.5 s) that occurred at (the sagittal plane) of the lower leg. All the timings then began from the baseline start event (GI start).

Gait speed (m/s) was calculated as follows from the change in forward position of the averaged location of the four pelvic markers divided by time using the following equation:

Equation 
$$1 = Gait speed = \frac{Distance of the change position of the pelvic markers}{Total GI period time} = m/s$$

#### **B.** Joint rotation

The mean maximum (flexion) and minimum (extension) movement of the hips, knees and ankles in the sagittal plane during GI movement events were recorded using the PIG model at a frequency of 100 Hz for both the Ref and PwP groups to identify the flexion and extension range of motion (ROM) of the three joint movements of interest.

#### C. Joint power

During the first half of the stance phase, the hip extensor generates positive power to produce more stability for the trunk and maintain the flexion posture with the help of the knee extensor that prevents the knee from collapsing, generating forward propulsion (Winter, 2009). The second half of the stance phase, which is controlled by the hip flexors, prevents the trunk posture from backward flexion and prepares the transference of the thigh from the pre-swing phase to the swing phase. This process requires power to transfer the segment of the hip, knee or ankle with a smooth movement and without restriction (Winter, 2009). The concentric muscle contraction generates power (positive), while the eccentric muscle contraction absorbs power (negative) (Butler et al., 2016).

Accordingly, the maximum peak of the power, which is calculated as the angular velocity multiplied by the joint moment normalised to the body weight to yield W/kg, was

calculated for the hip and ankle at each GI event for the Ref and PwP groups, the knee was not considered to be a major contributor to forward propulsion (Riley et al 2001).

Equation  $2 = Power = angular velocity (W) \times Moment (M) = W/Kg$ 

#### **D.** Muscle activity parameters extracted from the EMG signal.

The EMG data were sampled at 2000 Hz using the Trigno[™] Wireless System (Delsys Inc., Boston, MA, USA) to record the electrical activity of three muscles of the lower leg (tibialis anterior, gastrocnemius and soleus) of both limbs.

The GI period data were calculated for the interval between standing until the second foot contact of the swing side using the following process: (1) rectifying and smoothing the data with a notch filter at 50 Hz (2) filtering with a 6th-order Butterworth filter using a bandpass of 20–400 Hz to produce an EMG envelope that was interpreted and analysed.

To characterise the muscle behaviours, the following metrics were extracted from each envelope:

The percentage of the six muscles activation of both limbs activity during the GI
period was calculated from the time of functioning of the muscles during the
walking period (the GI period) divided by the total time of the walking period and
multiplied by 100.

Equation  $3 = \frac{\text{ON period}}{\text{total time of GI period}} \times 100 = \%$ 

- Calculated how many times that the muscle was on ON period (ie active) during GI period
- 3. The magnitude of the muscle activation was calculated as the AUC of the muscles for the GI period for both walking events, i.e., on the treadmill or the ground.

AUC= calculate the integral area of the rectified EMG signal.

#### **3.6.1.2** Change in walking speed.

Three cycles were calculated for both the right and left limbs Before, During, and After the change speed. See Figure 3-16.



Figure 3-16 The three cycles calculated from the gyroscope.  $\bigcirc$  indicated the foot-off events,  $\bigstar$  indicating the foot contact. The dash lined indicated the three cycles (before , during ,and after ) change speed.

# A Spatiotemporal parameters

The stride time was calculated as the period between the two black stars as in Figure 3-16. The change in speed from Bef to Dur (B-D) and from Dur to Aft were identified and analysed for differences between the Ref and PwP groups.

The variables used for the analysis were as follows:

- ⇒ Step length (mm) = the distance between the foot contact on one side and the foot contact on the other side. For both the right and left sides, extracted by the from marker that position on heel. The three cycles were Before (Buf), During (Dur) and after(Aft).
- ⇒ Stride time (s) = the time spent between two sequential foot contacts. This is similar to gait cycle time. Both the right and left sides had the same three cycles Buf , Dur, and Aft.

⇒ The cadence (s/m) = always related to walking speed; it helps to calculate the number of steps taken in minutes for the three cycles (Buf, Dur, and Aft). The cadence in the current study was calculated from the stance time divided by 60 because the participants didn't not complete one complete minute.

This leads us to

Equation 4= Cadence = 
$$\frac{stance\ time}{60}$$
 Step /M

 $\Rightarrow$  The percentage of the swing and stance time (%) = the percentage of stance and swing as a percentage of the total gait cycle for both the right and left sides and the three gait cycles.

Equation 5 =Swing time in percentage =  $\frac{Swing \ time \ in \ Seconds}{total \ time \ of \ cycle} \times 100 \%$ Equation 6= Stance time in percentage =  $\frac{Stance \ time \ in \ Seconds}{total \ time \ of \ cycle} \times 100 \%$ 

# **B** Joint rotation parameters

Joint rotation parameters calculate as in section C in GI however measurement will be for the three gait cycle Buf, Dur and Aft cycles to explore the differences in the ways the two groups increased the treadmill speed.

# C Joint power

Joint power as explained in the GI section while during increasing speed the power was calculated as the peak of the power during the early stance phase (H1) and the hip and ankle during the pre-swing phase (H2 and A1) for the REF and PwP groups during the change in speed while walking on the treadmill.

# **D** Muscle activity extracted from EMG data

The EMG data for speed change was calculated during the gait cycle time for the Buf, Dur and Aft cycles of both the Ref and PwP groups, with a further stratified analysis for the two PwP subgroups (i.e., mild/moderate and severe groups).

The EMG data (sampling rate, filtered, smoothed and rectified data) were analysed similar to the process during the GI movement. The muscles' behaviours were

characterised according to the metrics extracted from each envelope as described for the GI movement, documenting differences in the time of the three gait cycles among the Ref group and the two PwP subgroups during the two walking events, i.e., on the treadmill and the ground. The EMG data were calculated for differences of each gait cycle Buf, Dur and Aft cycles of both the Ref and PwP groups

# 3.6.2 Separation into gait cycles during study (2) overground walking

The test protocol and analysis of the EMG and STP variables were similar to those of the GI and speed change tests conducted on the treadmill. However, it was not possible to include joint motion and the force with the motion capture system since the task was carried out in a corridor outside the laboratory. Thus, the kinematics and kinetics data were not available. Instead, wearable IMU sensors were used to identify the gait events (foot contact and loss of contact with the ground) to allow the calculation of STP (step time, and phases duration) and the separation of the EMG signals according to the three gait cycles of increase speed as used for the GI movements.

# 3.6.2.1 Gait initiation

# A Spatiotemporal parameter

As previously explained, the overground walking events are similar to the GI events of treadmill walking Table 3-3. Timing began at the baseline start events in Figure 3-15. Gait speed was calculated as the total distance (m) using a measuring tape covered during the GI period for IMU (s).

# **B** Muscle activation

The EMG data analysis was also calculated as in the treadmill study for

1) the activity of muscle (normalised as a percentage of the whole GI movement) for the three sets of muscles (tibialis anterior, gastrocnemius and soleus on both sides)

2) the number of discrete activity periods for each muscle

3) magnitude of muscle activation, calculated from area under the curve (AUC) during the GI period, for the previous muscles.

# 3.6.2.2 Change in walking speed during over-ground walking.

In this section, the overground walking related to the increase in walking speed is presented. The variables to be compared between groups include spatiotemporal (stride time and percentage of the swing and stance phases' time) and EMG signals separated according to the three gait cycles of increased speed as used in treadmill study.

As explained in section 3.5.3.2, the participants were asked to change their walking speed on the fifth steps after four comfortable walking speeds. The differences between gait cycles were measured for the B-D (i.e. difference between the during and before cycles) and the D-A (i.e. difference between the during and after cycles) to identify the variations between the Ref and PwP groups, as well as the PwP subgroups, during overground walking.

Due to the lack of measurements of each gait cycle's distance, the change in speed was expressed as the change in the stride time. As in the previous section 3.6.2

## **3.7** Statistical analysis

During walking on treadmill (study 1), the spatiotemporal data was calculating the timings of the key events were recorded with reference to the whole GI period, and gait speed was calculated over the distance covered using the change in the position of the pelvic markers.

The kinematic data was analysing the sagittal plane motion of the hip, knee and ankle joints during GI and the kinetic data was analysing the power for the hip and ankle at each key of GI event on the treadmill for the Ref and PwP groups. Finally, A wireless EMG system (Trigno, Delsys, USA) recorded the electrical activity of three sets of muscles in the lower leg (tibialis anterior, gastrocnemius and soleus) on both sides.

During change in the walking speed from normal to faster walk, As in gait initiation (GI), the comparison between both groups the biomechanical data (kinematics, kinetics and the physiological (EMG) variables categorised into three distinct gait cycles: 1) immediately before the change in speed (Bef), 2) during the change in speed (Dur) and 3) immediately after the change in speed (Aft).

While walking on over ground, the data of the spatiotemporal and the EMG with IMU were just analysed for both group due to the absence of the cameras in corridor for both GI and change in walking speed.

The Shapiro-Wilk test of normality was employed to assess whether the data were normally distributed to determine which statistical test was appropriate.

Unfortunately, although the data were normally distributed, because of the very small sample size (n=17) the use of statistical tests was not advisable due to risk of type 1 and 2 errors. Instead, the patterns in the data will be examined exclusively by using descriptive statistics as the mean and SD and graphs and tables. By adopting this approach, it was felt

that conclusions could be expressed more confidently and clear recommendations for larger, statistically powered, studies could be provided.
# Chapter 4 Study 1: speed modulation during walking on self pace treadmill

This chapter presents the results of the first study, which looks at modulation of speed during treadmill walking. This study aims to understand the differences between a group (n=6) of people with Parkinson's (PwP) and a reference group (Ref) (n=11) during a requested change in gait speed. It included both the initiation of gait (GI) from a standing position and an increase in speed while walking on a self-paced treadmill. The comparison includes biomechanical (kinematic and kinetic) and physiological (EMG) variables to uncover differences between the two groups.

### 4.1Gait initiation

In this study, the GI period was extended to include the second heel contact so that the swing and stance phases of both sides are included. It is worth noting that three members of the PwP group stepped with their right side first, while the other three started with their left first. In the (Ref) group, seven participants stepped with their right and four with their left.

### 4.1.1 Participants

### **4.1.1.1 People with Parkinson's group (PwP)**

The PwP group (n=6) was successfully recruited from the West of Scotland Parkinson's Disease Research Group following an informed consent process. The PwP participants Using the PDQ_39, the PwP group was divided into two categories: mild/moderate (participants 2, 3, 5 and 6) i.e. those below 70 on the PDQ_39 score and severe (participants 1 and 4) i.e. those that scored above 70 and up to 104 see Table 4-1for more detail.

### 4.1.1.2 The Reference group (Ref)

The reference group (n=11) was recruited from the staff and student community of the University of Strathclyde's Biomedical Engineering (BME) Department. No adverse events (from the study) were reported. It is worth noting from Table 4-1, that the groups were not matched for age; the implications of this will be discussed later in the thesis.

Table 4-1 presents the characteristics of the participants from both groups and

subcategories of the PwP group.

	All PWP	PwP g	roups	Reference (Ref)
	Mean (SD)	Mild/Moderate	Severe	Mean (±SD)
	(± <b>n=6</b> )	Mean (±SD)	Mean (±SD)	( <b>n=11</b> )
		(n=4)	(n=2)	
Age (years)	70.30	70.33	73.0	29.90
	±13.80	±8.07	±11.32	±16.50
Gender	M/F	М	M/F	M/F
	5/1	4	1/1	3/8
Height (cm)	168.00	168.0	167.0	168.0
	±6.15	±0.08	±1.41	±6.90
Weight (Kg)	74.20	71.12	80.25	71.10
	±7.20	±6.66	±3.18	±13.60
Years since	13.5	12.5	20.5	NA
diagnosis	±18.38	±6.45	±13.43	
PDQ-39	73	62	94.5	NA
	±18.5	±6.22	±13.4	

 Table 4-1 Demographic characteristics of the Ref and PwP groups, including the subgroups; values are shown as mean and SD as appropriate

## 4.1.2 Results

## 4.1.2.1 Spatiotemporal parameters (STP)

The timings of the key events were recorded with reference to the whole GI period, all the timings began from the baseline start event (GI start), and gait speed was calculated over the distance covered using the change in the position of the pelvic markers.

Parameter	All PwP	PwP gr	oups	Reference group
		Mild/Moderate	Severe	- ( <b>Ref</b> )
	Mean	Mean	Mean	Mean
	(SD) (n=6)	( <b>SD</b> )	( <b>SD</b> )	(SD)
	(11-0)	( <b>n</b> =4)	(n=2)	( <b>n=11</b> )
SWO1 (s)	0.35	0.33	0.39	0.37
	±0.06	±0.06	±0.06	±0.17
SWC1 (s)	0.70	0.67	0.76	0.84
	±0.16	±0.19	±0.15	±0.22
STO (s)	0.95	0.87	1.11	1.03
	±0.32	±0.28	±0.47	±0.22
STC (s)	1.37	1.31	1.5	1.62
	±0.31	±0.25	±0.50	±0.33
SWO2 (s)	1.67	1.60	1.83	1.67
	±0.45	±0.32	±0.80	±0.44
SWC2 (s)	2.06	2.03	2.12	2.25
	±0.39	±0.24	±0.76	±0.42
Swing 1 (s)	0.35	0.34	0.37	0.48
	±0.12	±0.15	±0.09	±0.08
Swing2 (s)	0.42	0.44	0.39	0.58
	±0.06	±0.08	±0.03	±0.14
Swing3 (s)	0.39	0.35	0.46	0.57
	±0.14	±0.04	±0.26	±0.26
Stance1 (s)	1.37	0.86	1.14	1.03
	±0.31	±0.29	±0.43	±0.22
Stance 2 (s)	0.97	0.93	1.05	0.83
	±0.36	±0.25	±0.65	±0.35
Speed m/s	0.29	0.30	0.17	0.35
	±0.04	±0.04	±0.11	±0.11

Table 4-2 Timing in seconds of events during gait initiation for the Reference group (Ref) and PwP groups. the time measured by second and speed m/s.

This table definitions: SWO1= the first foot off on the swing side, SWC1 = the first foot contact of the swing side, STO= the toe-off of the stance side, STC = the first foot contact of the stance side, SWO2= the second foot off of the swing side, SWC2 = the second foot contact of the swing side, Swing 1= the time from the starting time to the first foot contact of the swing side, Swing 2= The time from the starting point to the first foot contact of the stance side, Swing 3= the time when the swing side leaves the ground a second time to contact again for the second foot contact, Stance 1= the time from the starting point until the stance side leaves the ground, Stance 2= the time from the first contact of the swing side point until the time that the same foot leaves the ground

Table 4-2 shows the mean and standard deviation of the GI event times for all participants. The Ref spent a mean of 2.25 s ( $\pm$  0.42) in the GI period, while the PwP took a shorter time, 2.06 s ( $\pm$  0.39s). The Ref had longer swing phases on average; Swing1 (0.48s  $\pm$  0.08s), Swing2 (0.58s  $\pm$  0.14s) and Swing3 (0.57  $\pm$  0.26s), compared with the PwP group (0.35  $\pm$  0.12 s, 0.42  $\pm$  0.06 s and 0.39  $\pm$  0.14 s). On the other hand, the PwP spent more time in the stance phases (Stance1 and Stance2) (1.37  $\pm$  0.31 s and 0.97  $\pm$  0.36 s) than the Ref (1.03  $\pm$  0.22 s and 0.83  $\pm$  0.35 s. Finally, the Ref reached a faster walking speed during

the GI period (0.35 m/s  $\pm$  0.11) compared with the PWP group (0.29 m/s  $\pm$  0.04). It is notable that the severe group took more time than mild/moderate group to complete each GI event, with the exception of the swing2.

In summary, differences were observed in the GI phase times and events between both groups when starting to walk on a self-paced treadmill. The Ref took a longer time to complete the whole GI period than the PwP group. The longest times from the PwP were recorded by the more severely affected PwP individuals. Finally, the duration of the swing phase was longer in the Ref than PWP group. In the PwP group, the time taken to complete the swing and stance phases were longer in the severe category. The next section will present the differences in joint rotations (hip, knee and ankle) between the groups.

#### **4.1.2.2** Lower limb joint rotations

Figure 4.1 shows the sagittal plane motion of the hip, knee and ankle joints during GI on the treadmill for the Ref and PwP groups. The Ref group reached maximum hip flexion at SWC1 (24.10 degrees  $\pm$  09.6) and maximum extension at STC (-5.38 degrees  $\pm$  05.6). This represented a total range of hip movement of around 30 degrees in the Ref group compared with the PwP group, who achieved, less hip motion, on average (17.8 $\pm$ 6.2 degrees) with maximum hip flexion (21.03 degrees  $\pm$  11.6) occurring at SWC2 and without achieving any hip extension, at any point, minimum hip flexion of 03.17 degrees  $\pm$  05.4 recorded at STC. This means there was around sex degrees more hip flexion in the Ref group than the PwP, and, importantly, the PwP failed to extend their hips at any point during GI, while the Ref group achieved around five degrees of extension at STC. Knee motion generally differed between the swing and stance sides. Both groups started and ended the GI period with a similar range of knee motion on the swing side, however, the PwP group increased knee flexion by around five degrees more than the Ref group between the SWC and the STC. On the stance side, the PwP generated more knee flexion (between 6 and 10 degrees) than the Ref group, except for the SWO2 event, which was similar in both groups.

The Ref group reached a maximum dorsiflexion angle, on the swing side, of 16.51 degrees,  $(\pm 04.8)$  at STC and maximum plantarflexion at STO of 2.02 degrees,  $(\pm 08.1)$  while, on the stance side the maximum dorsiflexion (14.40 degrees,  $\pm 04.8$ ) at SWC and maximum plantarflexion (- 4.20 degrees  $\pm 08.1$ ) at STC. The PwP group, generated maximum dorsiflexion (13.29 degrees,  $\pm 04.1$ ) at STC and maximum plantarflexion (04.84 degrees  $\pm 06.1$ ) at SWC on the swing side while on stance side generated maximum dorsiflexion (13.80 degrees,  $\pm 07.3$ ) at SWC and maximum plantarflexion (4.84 degrees  $\pm 06.1$ ) at STC.

This meant the ankle moved, on average, 14.9 degrees on the swing side, while there were 18.9 degrees of movement on the stance side among Ref and PwP group respectively.

As noted in the previous section, the Reference group (Ref) performed GI on the treadmill with more ROM at their hip, and ankle joints than the PwP (with 15% more at the hip, 10% more for ankle difference. The PwP completed the GI movement with more flexion at the knees (10%) than the Ref group. The Reference group had 16 degrees of ankle dorsiflexion during GI, while overall, the PwP group showed less movement the dorsiflexion (13 degrees), however, both groups showed only a small amount of ankle plantarflexion (around 10 degrees) during the movement.

Lastly, as disease severity increased among the PwP, there was generally less ROM in the hip, knees and ankle joints.



Figure 4-1 The mean of the sagittal plane rotations of the hip, knee, and ankle joints at key events during GI initiation separated into movement phases for Ref and PwP group. Positive values represent flexion (dorsiflexion for ankle), and negative values represent extension (plantarflexion for ankle)

#### 4.1.2.3 Joint power

Power (normalised to body weight, W/kg) was calculated for the hip and ankle at key GI events using equation in section 3.6.1.1. The knee was omitted as it is known to minimally contribute to forward propulsion (Riley et al 2001).

As presented in Table 4-3, the Ref group produced considerably more power from the hip during foot contact event on the swing side (23.24 W/kg,  $\pm$  10.6) than the PwP group (14.27 W/kg,  $\pm$  8.9).

The PwP group produced less power from the ankle than the Ref group at all events, especially on the swing side, as in SWO (5.03 W/kg  $\pm$  3.40), SWO2 (5.8 W/kg  $\pm$  4.7). The lower ankle value appeared in the stance foot STC during the swing side, with 4.3 W/kg  $\pm$  6.5. This is further explained in figure 4-2.

The ankle power during the foot-off for the swing side was higher in the more severe group  $(8.80 \pm 3.7 \text{ W/kg})$ , than the Mild/Moderate group  $(4.69 \pm 5.9 \text{ W/kg})$ , see table 4-4

Parameter		Reference	Group (Ref)	PwP group					
		Μ	ean	Mean					
		(S	5 <b>D</b> )		(SD)				
		( <b>n</b> =	=11)			(	n=6)		
	Sw	ving	S	tance	S	wing	St	56) Stance	
	HIP	ANKLE	HIP	ANKLE	HIP	ANKLE	HIP	ANKLE	
SW01	18.44	7.5	1.06	8.7	13.85	5.03	4.0	12.7	
(W/kg)	±07.5	±3.8	±07.5	±4.3	±5.4	±3.40	±8.99	±10.12	
SWC1	23.24	1.23	4.12	16.03	8.59	9.19	14.7	9.20	
(W/kg)	±10.6	±7.7	±10.19	±6.73	±6.3	±7.09	±15.6	±9.2	
STO	19.12	0.99	0.42	13.11	14.27	5.6	4.79	13.93	
(W/kg)	±08.4	±5.7	±7.40	±7.02	±8.9	±3.89	±7.5	±4.61	
STC	0.70	22.7	23.5	0.78	13.3	4.3	12.5	12.9	
(W/kg)	±09.7	±5.7	±7.30	±6.40	±12.0	±6.5	±7.50	±8.5	
SWO2	5.80	7.87	11.8	5.25	11.3	5.8	8.9	10.04	
(W/kg)	±14.3	±7.08	±10.23	±4.70	±11.7	±4.7	±7.7)	±6.73	
SWC2	21.8	1.29	1.01	10.7	11.5	6.07	15.9	8.40	
(W/kg)	±10.89	±4.11	±8.55	±08.4	±7.6	±8.5	±11.6	±5.4	

Table 4-3 The mean and standard deviation of the power calculated at the hip and ankle joints during GI events for the Reference (Ref) and PWP groups (W/kg).

Parameter		Mild/Mode	rate PwP group		Severe PwP group				
		Ι	Mean		Mean				
	(SD)					(SD)			
		(n=4)				(n=2)	)		
	Sw	ring	S	Stance	Sv	ving	Sta	nce	
	HIP	ANKLE	HIP	ANKLE	HIP	ANKLE	HIP	ANKLE	
SW01	15.07	4.55	5.01	10.72	11.4	5.97	2.23	16.7	
(W/kg)	±6.2	±2.8	±10.9	±12.4	±4.2	±5.5	±12.16	±0.8	
SWC1	7.78	8.89	16.62	8.2	10.22	9.78	11.01	11.6	
( <i>W/kg</i> )	±6.3	±9.2	±24.1	±9.5	±8.3	±0.20	±4.4	±12.8	
STO	17.20	6.37	4.25	13.7	8.43	4.11	5.85	14.4	
(W/kg)	±7.1	±3.9	±10.3	±5.2	±12.33	±4.78	±3.01	±4.9	
STC	12.90	4.9	13.9	12.61	14.22	2.9	9.6	13.6	
(W/kg)	±15.5	±5.9	±8.7	±10.9	±1.48	±10.13	±17.5	±1.16	
SWO2	12.62	4.41	10.53	8.5	8.57	8.80	5,82	12.9	
(W/kg)	±14.7	±4.9	±2.1	±8.7	±4.62	±3.7	±14.16	±1.9	
SWC2	11.9	4.75	18.16	7.62	10.86	8.70	11.6	9.93	
( <i>W/kg</i> )	±8.4	±10.7	±16.9	±3.2	±9.17	±1.44	±3.5	±10.5	

Table 4-4 The mean and standard deviation of the power calculated at the hip and ankle joints during GI events for the PwP subgroups (W/kg)



A





Figure 4-2 The GI event during treadmill walking. (A) The GI events with colored the swing (green) and stance side(red). The arrows indicated (B) the maximum joint power at hip and ankle for the Ref (C) the maximum joint power at hip and ankle for the PwP group.

The power produced at the hip and ankle joint by the Ref was higher than the PwP group, power generation also appeared to decrease with disease severity.

The next section will present the differences in muscle activity percentages and magnitude of muscle activation 'during' GI events while walking on the treadmill.

# 4.1.2.4 Muscle activity during the GI period while walking on the treadmill

Electromyographic (EMG) signals recorded and processed during GI period allowed for the calculation of three variables:

- The percentage of muscle activity (normalised as a percentage of the whole GI movement) for the three sets of recorded muscles (tibialis anterior, gastrocnemius and soleus on both sides)
- The number of discrete activity periods for each muscle
- The magnitude of muscle activation, calculated from area under the curve (AUC) during GI period, for the previous muscles.

## A) Percentage of muscle activity of total GI period.

Table 4-5 presents the percentage of activation for each of the six muscles active period during GI on the treadmill. It shows that all three pairs of muscles were active for longer periods in the PwP compared with the Ref, however, there was no clear pattern of difference between the two PwP groups. A longer percentage of muscle activation time of the gastrocnemius (on the swing side) in the mild/moderate group and tibialis anterior (swing and stance) in the severe group are notable.

Parameter	All PWP	PwP gro	oups	Ref Group
	Mean	Mild/Moderate	Severe	Mean
	( <b>SD</b> )	Mean	Mean	(SD)
	( <b>n=6</b> )	(SD)	( <b>SD</b> )	( <b>n=11</b> )
		( <b>n</b> =4)	(n=2)	
SWTA	49.97%	44.0%	61.8%	40.22%
	±17.8	±9.0	±30.4	±22.6
STTA	53.05%	50.8%	57.8%	38.51%
	±16.8	±20.7	±8.1	±25.2
SWGAS	41.12%	56.2%	10.1%	25.53%
	±30.1	±23.5	±1.8	±14.9
STGAS	34.94%	35.2%	34.2%	24.10%
	±20.1	±8.2	±42.5	±17.2
SWSOL	33.43%	35.2%	29.8%	27.10%
	±13.9	<b>§17.6</b>	±1.0	±11.1
STSOL	37.80%	43.4%	26.5%	20.41%
	±12.7	±11.9	±1.0	±14.5

Table 4-5 The percentage of muscle activity of a total GI period for the Reference group (Ref) and PwP groups.

SWTA: swing-side tibialis anterior. STTA: stance-side tibialis anterior. SWGAS: swing-side gastrocnemius. STGAS: stance-side gastrocnemius. SWSOL: swing-side soleus. STSOL: stance-side

The percentage of tibialis anterior activity (on the swing and stance sides) for the PwP group (49.97% and 53.05% respectively) was longer than the Ref's activity period (40.22% and 38.51% respectively). The swing side gastrocnemius (SWGAS) was activated for the third-longest period during the GI within the PwP group (41.12%), compared with the Ref (25.52%.) However, the less active SWGAS for the Severe PwP participants (10.1%) is notable. The soleus muscles on both sides (SWSOL, STSOL) were active for longer (33.43% and 37.80%, respectively) in the PwP compared with the Ref group (27.10% and 20.41% respectively). The possible reasons for these observed differences will be discussed in Chapter 6.

#### **B)** Mean number of activity periods

Table 4-6, it can be seen that there were two to three periods of activity for all muscles in the Ref during gait initiation on the treadmill. The PwP appears to generate an additional period of activity for most muscles: for example, four periods of TA activity on the swing side compared to three in the Ref during GI movement. Regarding the PwP subgroups, the number of activations was different among the three sets of muscles. The SWTA had fewer active period in the Severe PwP participants unlike the gastrocnemius (swing and stance sides) which was activated on more occasions in the Severe PwP participants. The soleus muscles were largely similar across the PwP participants, except for one more period of activity on the swing side among the mild/moderate PwP subgroup.

Parameter	All PwP	PwP g	groups	Ref group
	Mean	Moderate	Severe	Mean
	( <b>n=6</b> )	Mean	Mean	(n=11)
		( <b>n=3</b> )	(n=2)	
SWTA	3	3	2	3
STTA	4	3	3	3
SWGAS	3	3	4	2
STGAS	3	3	4	3
SWSOL	3	4	3	2
STSOL	3	3	3	2

 Table 4-6 The average number of muscle activity periods during the GI for the Ref and PwP groups while walking on the treadmill.

SWTA: Swing tibialis anterior. STTA: stance tibialis anterior. SWGAS: Swing gastrocnemius. STGAS: stance gastrocnemius. SWSOL: Swing soleus. STSOL: stance soleus.

Figure 4-3 shows an example number of the activation periods for one participant (P1) from the Ref and another participant (PwP3) from the Mild/Moderate PwP subgroup during GI events. The PwP participants' muscles (in general) activated more frequently and for longer, proportionally, than the Reference participants, especially the SWSOL, which was active much earlier in the GI sequence (after 10% of the movement). The stance side soleus (STSOL) was also active for longer periods in the PwP participants compared to the two brief periods of activity from the Reference participants.



SWO1 SWC1 STC STC SWO2 SWC2



Figure 4-3 Example of the activity periods of the lower limb muscle for(A) a participant from the Ref group (P1) and (B) the Moderate group (PwP3) during GI movement while walking on the treadmill. the orange line indicated the GI events during treadmill walking.

#### C) Magnitude of Muscle activation (AUC)

This section presents the calculations for the magnitude of the muscle activation during the treadmill gait initiation movement. The area under the curve (AUC), as detailed in Section 3.6.1.1, provides a unit less measure of the magnitude of muscle activation. This was calculated for the whole GI period for the six muscles of the lower limb for both the Ref and PwP groups.

Parameter	All PwP	PwP	group	Reference group		
	Mean	Moderate	Severe	Mean		
	(SD)	Mean	Mean	(SD)		
	( <b>n=6</b> )	(SD)	(SD)	( <b>n=11</b> )		
		( <b>n</b> =4)	( <b>n</b> =2)			
SWTA	0.06	0.08	0.05	0.04		
	±0.03	±0.05	±0.08	±0.04		
STTA	0.06	0.07	0.05	0.19		
	±0.03	±0.04	±0.06	±0.42		
SWGAS	0.04	0.05	0.03	0.02		
	±0.01	±0.02	±0.02	±0.01		
STGAS	0.03	0.04	0.03	0.04		
	±0.01	±0.02	±0.02	±0.04		
SWSOL	0.33	0.06	0.69	0.04		
	±0.47	±0.03	±0.90	±0.01		
STSOL	0.06	0.06	0.07	0.11		
	±0.04	±0.04	±0.08	±0.11		

Table 4-7 The AUC for the six muscles during the GI period for the Ref and PwP groups.

SWTA: Swing tibialis anterior. STTA: stance tibialis anterior. SWGAS: Swing gastrocnemius. STGAS: stance gastrocnemius. SWSOL: Swing soleus. STSOL: stance soleus. Values have been uniformly multiplied by 1000 for ease of interpretation.

Table 4.7 shows the magnitude of muscle activation for the Ref and overall PwP group while walking on the treadmill. From the results, some differences were observed between the two main groups; both STTA and STSOL were higher in the (Ref) (0.19 +/- 0.42 and 0.11 +/- 0.11, respectively) than in the PwP group (0.06 +/- 0.03 and 0.06 +/- 0.04, respectively). In the other two muscle sets SWTA, SWGAS, STGAS and SWSOL magnitudes were lower for the (Ref) when compared with the PwP group. The PwP group showed an increase in the magnitude of the muscle activation for the SWSOL (approximately 0.33 ± 0.47), which was significantly higher than that of the (Ref) (0.04 ± 0.01). Among the PwP, muscle activation was higher (0.69 ± 0.90) in the severe PwP subgroup than (0.04 ± 0.01) in the Mild/Moderate group. On other hand, the Mild/Moderate group showed a higher magnitude of muscle activity in the STTA and STSOL (0.07 ± 0.05 and 0.07 ± 0.05, respectively) than in the other muscles.

Arguably the most interesting difference in muscle activity between the groups was observed in the Soleus muscle on the swing side as illustrated in Figure 4-4. It can be seen that the GI period started with a relatively high amplitude of SWSOL activity (~0.8mV), possibly to help control the upright posture, before decreasing rapidly around SWO1.

In the PwP, however, a different pattern was observed. Starting with a lower amplitude of activity  $<(\sim0.2\text{mV})$  there was no drop-in Soleus activity in the first 20% (as the Ref did) rather there was a clear increase in activity which appeared to be more pronounced in the severe participant (PwP4) compared with the Mild/Moderate (PwP5).

The Mild/Moderate PwP participants showed an increase in magnitude of the SWTA before the STC event, but the SWGAS was lower inactivation than the tibialis and the soleus.



Figure 4-4 An example of the processed EMG signals of the three muscles on the swing side for one participant from each PwP group and the Ref group during the GI period of treadmill walking. The red line represents the tibialis anterior (TA) muscle, the green line represents the gastrocnemius (GAS) and the black line represents the soleus muscle (SOL). The vertical lines show GI events.

# 4.1.3 Summary of the findings for the GI period while walking on the treadmill

This study was conducted to investigate the differences in the way walking is initiated on a treadmill between a group of unimpaired individuals (Ref) and a group of independently mobile individuals with Parkinson's disease (PwP).

It was evident that the PwP group spent short time carrying out GI on a treadmill walk than the (Ref) (2.06 s  $\pm$  0.39 compared with 2.25 s  $\pm$  0.42). The severity of Parkinson's was reflected in a directly proportional increase in the time taken to complete the GI sequence: the moderate PwP subgroup spent 2.02 s ( $\pm$  0.24) while the severe PwP group spent 2.12 s  $(\pm 0.76)$ . Consistent with this, was the finding that the Ref had a greater range of lower limb joint movement than the PwP group during GI. In particular the Ref showed greater ROM in the hip joint by almost 5 degrees compared with the PwP group. The ankle movements was however largely similar in both the Ref and the overall PwP group with the exception of the more severe PwP subgroup which showed a general reduction in movement at all three joints. and finally, the knee movements was more flex in overall PWP than Ref with more increase with severe group. The power produced at the hip and ankle joint by the Ref was (23.24±10.6W/Kg,22.7±5.7W/Kg)much higher than the PwP group(14.27±8.9W/kg,9.19±7.09W/kg), with even lower values in the severe group. The PwP had generally longer muscle activation periods; in particular, the tibialis anterior (stance and swing) was active for 53.05% and 49.97% respectively as opposed to 38.51% and 40.22% in the Ref. Overall, the period of muscle activity was affected by the severity of the disease, for example, the plantar flexors were activated for shorter periods as the disease increased in severity.

In general, the magnitude of muscle activation during GI period (calculated as AUC) showed less activation with the PwP group than the Ref. Also, the severity of the disease affected the magnitude of the muscle activation; among the PwP, the SWSOL in the severe PwP subgroup had the highest intensities of excitation ( $0.69 \pm 0.09$ ) followed by the moderate PwP subgroups ( $0.04 \pm 0.01$ ).

In conclusion, there are clear differences between people with Parkinson's and unimpaired individuals Ref group during the gait initiation process on a treadmill. PwP being slower, with reduced joint movement and longer periods of muscle activity, including activity in

the dorsiflexion and plantar flexors. These differences were more evident in the more severe cases of Parkinson's disease.

# 4.2 Changes in walking speed (increasing walking speed) during walking on self pace treadmill

The second part of the treadmill walking study includes increase speed after walking has been initiated. This section will present the methods and results for those walking on a treadmill at self-selected speeds in response to an instruction to walk faster, which was projected onto a screen.

As in gait initiation (GI), the comparison between both groups includes the biomechanical data (kinematics) and the physiological (EMG) variables categorised into three distinct gait cycles: 1) immediately before the change in speed (B), 2) during the change in speed (D) and 3) immediately after the change in speed (A).

### 4.2.1 Results

#### **4.2.1.1 Spatiotemporal parameters (STP)**

Table 4-7 shows the differences in STP parameters of the Ref and PwP group from Bef to Dur (**B-D** cycle) and from the Dur to Aft (cycle **D-A**).

Table 4-8, it can be seen that the Ref group was able to increase walking speed by  $0.12 \pm 0.06$  m/s. The difference in standard deviation is notable for the Ref group, as it more than doubled, from 0.06 and 0.15. This 0.12 m/s increase in speed was achieved by a moderate increase in step length during the change speed cycle (B-D) of 15% (R side increase = 6.30cm, L side increase = 8.80cm) while cadence actually decreased. The step length decreased by around 10% (R side decrease = 5.1 cm, and L side decrease = 6.3 cm) in the following cycle (i.e. D-A). Most of the Ref group (70%) were on their R side stance phase when the change occurred, which may explain the greater increase on the left (8.80 compared with 6.30).

Parameter		group	PV	WP		
	Μ	lean	M	ean		
	±	SD	SI	D±		
	Ν	=11	N=6			
	Change	Change	Change	Change		
	B-D	D-A	B-D	D-A		
Speed (m/s)	0.12	0.00	0.06	-0.03		
	±0.06	±0.15	±0.08	±0.08		
L Step Length (cm)	8.80	-6.29	1.00	1.80		
	±1.92	±0.58	±2.20	±0.60		
R Step Length (cm)	6.30	-05.1	1.70	2.30		
	±0.30	±0.07	±3.50	±1.50		
L Stride Time (s)	-0.06	-0.06	-0.03	-0.01		
	±0.03	±0.07	±0.06	±0.06)		
R Stride Time (s)	-0.06	-0.04	-0.02	-0.01		
	±0.07	±0.10	±0.09	±0.03)		
Cadence (steps per	-4.42	12.31	2.40	-3.21		
minute)	±1.15	±1.68	±7.65	±1.03		
L Stance	-4.50	-5.60	-3.17	-1.83		
Time (%) (s)	±2.84	±8.02	±5.27	±5.56)		
R Stance	-5.90	-2.00	-3.17	-1.00		
Time (%) (s)	±6.21	±9.21	±8.86	±3.58)		
L Swing	4.50	5.60	3.17	1.83		
Time (%)(s)	±2.84	±8.02	±5.27	±5.56		
R Swing	5.90	2.00	3.17	1.00		
Time (%)(s)	±6.21	±9.21	8.86	±3.58)		

 Table 4-8 The change in STP parameters of the right and left sides during walking on the treadmill for Reference (Ref) and PwP groups.

(B-D) the change from Before to during cycle. (D-A) the change from During to After cycle.

In contrast, the PwP group showed a more modest increase in gait speed of  $0.06 \pm 0.08$  m/s during the change in speed (B -D), followed by a mild decrease of  $0.03 \pm 0.08$  m/s change in the after cycle (D-A). Like the Ref group the increase in speed was associated with an increase in step length, however, this was much smaller than the Ref (R side increase = 1.7 cm, L side increase = 1.0 cm). Yet, in contrast with the Ref, the (D-A) cycle showed a further increase in step length from the initial speed change (R side increase = 2.3 cm, L side increase = 1.80 cm), suggesting a greater number of cycles was required to create the desired change in step length. Cadence also changed in the PwP, but in a different manner from the Ref, rather than a decrease there was instead an increase of around 2.40  $\pm$  10.19 s/m, suggesting a different mechanism was being used to increase speed. Most of the PwP group (90%) were on their L stance phase when the change occurred, which may explain the slightly greater change in the R step length. Figure 4-5 shows the differences in the speed m/s, the step length cm and, cadence in step/min between the two groups.









Figure 4-5 (A). gait speed m/s,(B) The L and R step lengths in cm (C) Cadence in between the RG and PWP groups between the Ref and PwP groups during the three cycle(B,D,A) while walking on the treadmill

Table 4-9The change in STP parameters of the right and left sides during walking on the treadmill for PwP subgroups (Moderate and Severe).(B-D) the change from Before to during cycle. (D-A) the change from During to After cycle

Parameter	Л	oderate Mean (SD (n=4)	M (S	vere (ean SD) n=2)
	Change	n=4) Change	Change	Change
	B-D	D-A	B-D	D-A
Speed (m/s)	0.07	0.04	0.04	-0.01
	±0.09	±0.09	±0.04	±0.08
L Step Length (cm)	1.0	-2.45	0.48	-1.2
	±5.41	±6.34	±7.61	±8.01
R Step Length (cm)	6.81	-20.42	2.32	-2.37
	±7.40	±3.80	±0.84	±1.00
L Stride Time (s)	-0.02	0.02	-0.07	-0.07
	±0.06	±0.05	±0.04	±0.04
R Stride Time (s)	0.02	-0.01	-0.09	0.00
	±0.08	±0.04	±0.06	±0.01
Cadence (steps per minute)	0.05	2.12	1.90	1.03
	±0.24	±2.18	±2.85	±0.50
L Stance	-1.5	1.25	-6.5	-8.00
Time (%)	±5.19	±3.60	±4.9	±1.40
R Stance	-0.25	-1.25	-9.00	-0.05
Time (%)	±8.53	±4.57	±8.50	±0.71
L Swing	1.5	-1.25	6.50	8.00
Time (%)	±5.19	±3.60	±4.90	<b>±1.41</b>
R Swing	0.25	1.25	9.00	0.50
Time (%)	±8.50	±4.57	±8.50	±0.70

Table 4-9, shows the change from Before to During cycle and from the During to After cycle for the Mild/Moderate and the Severe groups. The PwP subgroups showed different degrees of change in speed from B to D and from D to A. The Mild/Moderate subgroup showed a modest increase with 0.07 and 0.04 m/s in the 'B-D' and the 'D-A' cycle respectively, however, as disease severity increased, the speed in the 'B-D' cycle decreased with 0.04 and -0.01 for the 'B-D' and the 'D-A' changes respectively.

Both the Mild/Moderate and Severe PwP subgroups increased their step length with the change in speed but then subsequently reduced their step length in the After cycle. The swing time increased more in the Severe (9.0%) than Moderate (0.25%) group.

In summary, both the Ref and PwP groups were able to increase their gait speed, in response to an instruction, while walking on the treadmill. The Ref generating a greater change in speed than the PwP group. The speed change was more strongly associated with an immediate and relatively large increase in step length (and concurrent decrease in cadence) in the Ref group whereas there was only a small increase in step length, produced over two cycles, (and concurrent increase in cadence) in the PwP group. The next section will present the differences in joint kinematics for both groups before, during and after the increase in treadmill walking speed.

#### **4.2.1.2** Kinematic parameters

In this part, the sagittal plane movements (flexion and extension) at the hip, knee and ankle joints, on both sides, are presented for the three cycles; 'B, D, and A, to explore further differences between the way these two groups increased their treadmill speed.

Table 4-10 shows the kinematic change during the change in gait speed across the main lower limb joints between Ref and PWP group. There was no clear change in movement at any of the joints, the greatest change, for both groups, was a small increase in hip and knee flexion of around 3 degrees in both groups. The ankle joint only showed a small (one to two degrees) change, for both groups. Both groups showed a negative change (one to two degrees) between them during and after cycles indicating a decrease in joint range of motion in the Aft cycle.

Table 4-11 presents the kinematic change during the change in gait speed across the three cycles for the two PwP subgroups. This showed an increase in joint movement of around 3 degrees at the hip and the knee in both groups between the B and D cycles. Although the Mild/Moderate subgroup generally maintained this increase in movement, the Severe

subgroup had a mild decrease in ROM. At the ankle joint, no more than one-degree changes were observed in both subgroups.

Evidently, the Ref group has more ROM at the hips, knees, and ankles when walking on the treadmill compared with the PwP group, see Figure 4-8. During the increase in speed, both groups showed small to modest increases in hip and knee flexion with the more severe sub-group showing slightly greater hip flexion, this may relate to the more flexed posture observed in this group compared with the Ref group. These observations will be discussed in chapter 6.

To illustrate potential differences Figure 4-6 shows the sagittal plane kinematics (hip, knee and ankle) for one participant from Ref group (P9) and one from the PwP group (PwP1). A general observation is the much greater ROM at the three joints in the Ref group compared with the PwP. The three cycles (B, D and A) are also very similar for the individual participants, both in amplitude and pattern, with the exception of a small increase in left knee flexing in the D cycle for PwP1. It is worth noting the lack of change at the ankle in PwP1, which is held in a dorsiflexed posture throughout, compared with Ref 9 who demonstrates a typical ankle pattern including periods of dorsiflexion and plantarflexion (Pistacchi et al. (2017); Svehlik et al., 2009).

The next section will explore changes and group differences in joint power during the increase in speed on the treadmill.



Figure 4-6 The ROM in degree for the Hip, Knee, and Ankle on both sides for the Ref P9 and wP1 during the three gait cycles B, D and A of changing speed while walking on a treadmill.

Parameter Ref group **PwP group** Mean Mean (SD) (SD) N=11 N=6 Change Change Change Change D-B A-D D-B A-D L Hip Flexion (degrees) 2.68 -2.89 3.08 -1.06  $\pm 2.00$  $\pm 2..27$ ±1.37  $\pm 2.22$ L Hip Extension (degrees) 1.75 -1.08 1.97 -1.05 ±1.77 ±2.65 ±1.29 ±1.56 **R Hip Flexion (degrees)** 2.82 -1.51 3.00 -1.87  $\pm 2.14$  $\pm 2.21$ ±0.95 ±1.13 **R** Hip Extension (degrees) 0.88 1.91 -2.08 -1.65 ±2.16 ±2.15 ±0.97 ±1.06 L Knee Flexion (degrees) 2.77 -0.65 1.45 -0.57 ±1.13 ±1.08  $\pm 2.32$ ±1.88 L Knee Extension (degrees) 0.76 0.31 1.97 -1.09 ±0.94  $\pm 2.08$ ±0.51 ±1.24 **R Knee Flexion (degrees)** 2.63 1.34 3.45 1.46 ±1.17 ±3.18 ±1.35 ±2.07 **R Knee Extension (degrees)** 1.49 -2.14 0.68 0.14 ±1.25  $\pm 2.15$  $\pm 2.67$ ±1.87 L Ankle dorsi flexion (degrees) 0.50 1.91 -2.30 1.03 ±1.68  $\pm 2.80$ ±0.87 ±1.48 L Ankle planter flexion (degrees) 1.98 -1.23 1.58 -1.38 ±1.57 ±1.98 ±2.49  $\pm 2.63$ **R** Ankle dorsi Flexion (degrees) 1.97 -1.23 1.27 0.43 ±1.94 ±1.98 ±0.97 ±1.66 **R** Ankle planter flexion (degrees) 1.03 -2.33 1.14 -0.73 ±1.89 ±2.79 ±2.16 ±0.94

Table 4-10 The change in the peak of the sagittal plane movement in degree for the hip, knee and ankle joints on both sides during the change in speed for the Ref and PwP groups. Change is shown between 'Before' to 'During' cycle (B-D), and from 'During' to 'After' cycle (D-A) while walking on the treadmill.

Mild/Moderate Parameter Severe Mean Mean (SD (SD) (n=4) (n=2)Change Change Change Change B-D D-A B-D D-A L Hip Flexion (degrees) 3.07 -1.79 3.10 0.39 ±1.19 ±1.97 ±1.95 ±1.61 0.37 L Hip Extension (degrees) 0.24 -0.66 -0.15  $\pm 1.22$ ±1.30 ±0.80 ±1.05 **R Hip Flexion (degrees)** -2.08 3.15 3.19 -1.44 ±0.88 **§1.06** ±1.17 ±0.63 **R** Hip Extension (degrees) 0.91 -1.60 0.81 -1.75 ±0.98 ±0.91 ±1.21 ±1.21 L Knee Flexion (degrees) 2.98 -2.15 -0.21 2.24  $\pm 2.95$ ±0.19 ±1.97 ±1.59 0.72 -0.07 0.86 1.09 L Knee Extension (degrees) ±0.17  $\pm 1.20$ ±1.07 ±0.13 **R Knee Flexion (degrees)** 2.18 1.59 3.05 1.21  $\pm 2.45$ ±1.34 ±2.07 ±1.31 **R** Knee Extension (degrees) 0.38 0.55 0.78 -0.67 ±1.39  $\pm 3.17$  $\pm 2.80$ ±1.77 L Ankle dorsi flexion (degrees) -0.67 0.69 1.12 1.21 ±0.83 ±0.65 ±0.80  $\pm 2.23$ L Ankle planter flexion (degrees) -0.57 1.94 -1.58 0.86 ±0.57 ±0.99 ±2.67 ±3.04 **R** Ankle dorsi Flexion (degrees) 0.98 0.01 1.36 0.26 ±1.09 ±0.41 ±1.08 ±1.26 **R** Ankle planter flexion (degrees) 1.52 0.15 -1.17 0.41  $\pm 2.24$ ±0.59 ±0.79  $\pm 2.24$ 

Table 4-11 The change in the peak of the sagittal plane movement in degree for the hip, knee and ankle joints on both sides during the change in speed of the PwP subgroups (Mild/ Moderate and Severe) group from the 'Before' cycle to 'During' cycle (B-D), and from 'During' to 'After' cycle (D-A) while walking on the treadmill.

#### 4.2.1.3 Joint power

As explained in Chapter 3 (section 3.6.1.2.), power, calculated as the product of joint angular velocity and joint moment, was normalised to body weight (W/kg) and calculated for the hip and ankle, the knee was not considered to be a major contributor to forward propulsion (Riley et al 2001). The key points of interest were the hip during early stance (H1) and the hip and ankle during the pre-swing phase (H2 and A1), this was based on previous work indicating these were the joints and gait phases most involved in generating forward propulsion (Svehlik et al, 2009; Sloot et al 2021)

Table 4-12presents the peak power at the hip and ankle for the Ref and PwP groups during the change in treadmill walking speed. It can be seen that the Ref group produce a greater change in hip power at early stance (H1) (0.26 W/kg) during the change in speed (B-D cycle), compared with the PwP group who only generated a change of 0.06 W/kg. On the other hand, the sum of hip power during pre-swing (H2) was greater in the PwP (0.24 W/kg) compared with the Ref (0.17 W/kg). The sum of ankle power during pre-swing (A1) showed a small increase in power among the Ref group (0.04 W/kg) while no power change was shown in the sum of ankle movement among the PwP (0.01 W/kg). These observations point to differences in the way gait speed is increased in these groups with a much greater change in power at the hip during early stance in the Ref compared with pre-swing in the PwP. The ankle showed a modest increase at pre-swing in the Ref which was even smaller in the PwP.

As observed in table 4-13, hip joint power appears to be affected by disease severity, the severe PwP subgroup had a greater increase at H2 compared with the Mild/ Moderate group (0.29 W/kg and 0.19 W/kg) who seemed to favour an increase in power at H1 (0.00 W/kg compared with 0.09 W/kg ). Similar to hip power, ankle power was generally lower in the more severe participants.

Overall, there were greater increases observed in joint power in the Ref group compared with the PwP group which is consistent with the longer steps achieved by the Ref group. The pattern of power generation in the PwP group, particularly the two more severely affected participants, suggests these individuals increased their walking speed through greater input from the hip during pre-swing (H2) rather than the hip during early stance (H1). Power generation at the ankle (i.e. in a plantarflexing direction), is known to be a major contributor to gait propulsion (Sloot et al, 2021) but did not really alter in the PwP to change speed and only modestly changed in the Ref group. The preference for a hip strategy to change gait speed, in the PwP, may relate to the underlying pathology but may also be a manifestation of ageing (Sloot et al 2021).

Parameter	]	Ref	PV	VP		
	Μ	lean	Me	ean		
	()	SD)	(SD) N=6			
	Ν	=11				
	Change	Change	Change	Change		
	B-D	D-A	B-D	D-A		
L Hip power (H1)	0.14	0.03	0.04	0.01		
W/kg	±0.27	±0.05	±0.06	±0.02		
R Hip power (H1)	0.12	-0.05	0.02	0.01		
W/kg	±0.19	±0.09	±0.01	±0.04		
L Hip power (H2)	0.07	-0.04	0.13	-0.07		
W/kg	±0.16	±0.17	±0.11	±0.02		
R Hip power (H2)	0.10	0.12	0.11	-0.12		
W/kg	±0.04	±0.01	±0.18	±0.21		
L ankle power (A1)	-0.01	-0.02	0.00	-0.02		
W/kg	±0.05	±0.01	±0.10	±0.08		
R ankle power (A1)	0.05	-0.04	0.01	-0.01		
W/kg	±0.05	±0.06	±0.02	±0.01		
Sum of Hip power (H1)	0.26	0.18	0.06	0.02		
W/kg						
Sum of Hip power (H2)	0.17	0.05	0.24	-0.19		
W/kg						
Sum of ankle power	0.04	-0.06	0.01	0.01		
(A1) W/kg						

Table 4-12 The change in the power at the hip (H1), (H2) and ankle (A1) joints (W/kg) during the three-walking cycle (B, D, and A) for the Ref and PwP groups during walking on a treadmill.

(B-D) the change from Before to During cycle. (D-A) the change from During to After cycle. Ankle and hip power were summed between the two sides to simplify the metric, as no difference was measured between the sides.

Parameter Mild/Moderate Severe Mean Mean (SD (SD) (n=4)(n=2) Change Change Change Change B-D D-A B-D D-A L Hip power (H1) 0.06 0.02 -0.01 -0.01 W/kg ±0.06 ±0.06 ±0.01 ±0.01 R Hip power (H1) 0.03 0.01 0.01 0.01 ±0.04 ±0.09 W/kg ±0.03 ±0.03 L Hip power (H2) 0.13 -0.13 0.10 0.03 W/kg ±0.15 ±0.33 ±0.04 ±0.02 R Hip power (H2) -0.15 0.19 0.06 -0.06 W/kg ±0.22 ±0.27 ±0.02 ±0.04 L ankle power (A1) 0.00 -0.01 -0.02 -0.01 W/kg ±0.09 ±0.10 ±0.04 ±0.01 R ankle power (A1) 0.01 -0.01 -0.02 0.01 W/kg ±0.02 ±0.01 ±0.01 ±0.01 Sum of Hip power 0.09 0.03 0.00 0.00 (H1) W/kg Sum of Hip power 0.19 -0.28 0.29 -0.03 (H2) W/kg Sum of ankle power -0.02 0.01 -0.3 0.01 (A1) W/kg

Table 4-13 The change in the power at the hip (H1), (H2) and ankle (A1) joints (W/kg) during the three walking cycles (B, D, and A) for the PwP subgroups (Mild/ Moderate, Severe) during walking on a treadmill.

(B-D) the change from Before to during cycle. (D-A) the change from During to After cycle. Ankle and hip power were summed between the two sides to simplify the metric, as no difference was measured between the sides.

Muscle activity during the speed variation while walking on the treadmill

The electromyography (EMG) signals of three muscles (tibialis anterior, gastrocnemius and soleus on both sides) on both sides were processed and expressed as a percentage of the gait cycles: (B, D, and A). The percentage of activation of muscle contraction, a number of discrete contractions and area under the curve were calculated to characterise the muscle activity during each of the three cycles around the time of a change in speed.

# 4.2.1.4 Muscle activity during the speed variation while walking over ground.

#### A) The percentage of muscle activity for each gait cycle

Table 4-14shows the activity periods for each of the three cycles during the speed increase and the differences in the muscle activity from the B-D cycle phase and from the D-A for each of the three muscles on both sides. The Ref group showed generally longer activity periods in the B cycle compared with the PwP, which give a negative result (that mean the D cycle is smaller than B in activation time during changing speed than the PwP which showed a positive result which mean the D cycle in longer than B cycle in activation time, except for the left soleus (LSOL), which showed less activity in Ref (33.89% compared with 51.16%) in PwP. On the other hand, the PwP activated the muscles for longer with greater differences compared with the Ref in the D cycle than B which showed positive result from (B-D) more than the D-A cycle. The only exception was the LSOL, which showed a decrease in the B-D cycle and maintained that decrease in the D-A in the PwP.

Table 4-15 shows the differences in muscle activation among the PwP group. Generally, in PwP subgroup participants there was longer activity in the B cycle than D which showed negative result as in table; this was seen in most of the muscles, except RTA in the Mild/Moderate subgroup and LTA and LGAS in the Severe subgroup. A notable change was seen in the RSOL and LGAS (26% and 36% respectively), which had longer activation periods in B cycle than D in the Severe subgroup. The muscle activation in the D-A cycle showed opposite activation, either by reducing activity after the increase or increasing activity after reduction across all groups.

		Ref					PWP		
	Mean								
		±SD					±SD		
		N=11					N=6		
Bef	Dur	Aft	Change	Change	Bef	Dur	Aft	Change	Change
			B-D	D-A				B-D	D-A
51.87%	48.75%	43.5%	-3.12%	-5.25%	44.1%	59.17%	56.33%	15.07%	-2.84%
±20.70	±16.50	±21.71	±4.20	±5.21	±19.18	±25.71	±18.45	±6.53	±7.26
49.62%	43.25%	47.37%	-6.37%	4.12%	45.5%	46.5%	48.67%	1.00%	2.17%
±21.32	±24.67	±19.76	±3.35	±4.91	±25.75	±20.56	±13.58	±5.19	±6.98
52.12%	50.37%	36.87%	-1.75%	-13.5%	45.2%	49.2%	16.8%	4.00%	-32.4%
±21.81	±27.06	±27.14	±5.25	±7.22	±25.60	±32.37	±9.54	±6.77	±22.83
46.0%	43.25%	50.75%	-2.75%	7.5%	44.33%	50.83%	43.83%	6.50%	-7.00%
±17.92	±19.83	±12.61	±1.91	±7.22	±22.44	±29.90	±20.08	±7.46	±9.82
51.83%	47.16%	41.0%	-4.67%	-6.16%	30.0%	55.67%	32.33%	25.67%	-23.34%
±25.17	±11.63	±21.89	±13.54	±10.26	±13.70	±36.25	±28.39	±22.55	±7.86
33.89%	50.0%	43.25%	16.11%	-6.75%	51.16%	50.33%	50.17%	-0.83%	-0.16%
±17.95	±10.75	±14.79	±7.20	±4.04	±24.70	±23.95	±26.32	±0.75	±2.37
	51.87% ±20.70 49.62% ±21.32 52.12% ±21.81 46.0% ±17.92 51.83% ±25.17 33.89%	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{tabular}{ c c c c c c } \hline Mean & \pm SD & \\ \hline N=11 & \\ \hline Bef & Dur & Aft & \\ \hline 51.87\% & 48.75\% & 43.5\% & \\ \pm 20.70 & \pm 16.50 & \pm 21.71 & \\ \hline 49.62\% & 43.25\% & 47.37\% & \\ \pm 21.32 & \pm 24.67 & \pm 19.76 & \\ \hline 52.12\% & 50.37\% & 36.87\% & \\ \pm 21.81 & \pm 27.06 & \pm 27.14 & \\ \hline 46.0\% & 43.25\% & 50.75\% & \\ \pm 17.92 & \pm 19.83 & \pm 12.61 & \\ \hline 51.83\% & 47.16\% & 41.0\% & \\ \pm 25.17 & \pm 11.63 & \pm 21.89 & \\ \hline 33.89\% & 50.0\% & 43.25\% & \\ \hline \end{tabular}$	Mean $\pm$ SD N=11BefDurAftChange B-D51.87%48.75%43.5%-3.12% $\pm 20.70$ $\pm 16.50$ $\pm 21.71$ $\pm 4.20$ 49.62%43.25%47.37%-6.37% $\pm 21.32$ $\pm 24.67$ $\pm 19.76$ $\pm 3.35$ $52.12\%$ $50.37\%$ $36.87\%$ $\pm 27.14$ -1.75% $\pm 52.5$ $46.0\%$ $43.25\%$ $50.75\%$ $\pm 17.92$ -2.75% $\pm 19.83$ $\pm 12.81$ $\pm 27.06$ $\pm 12.61$ $\pm 1.91$ $51.83\%$ $47.16\%$ $\pm 11.63$ $\pm 12.89$ $\pm 13.54$ $33.89\%$ $50.0\%$ $43.25\%$ $16.11\%$	Mean $\pm$ SD N=11BefDurAftChange B-DChange D-A $51.87\%$ 48.75%43.5%-3.12%-5.25% $\pm 20.70$ $\pm 16.50$ $\pm 21.71$ $\pm 4.20$ $\pm 5.21$ 49.62%43.25%47.37%-6.37%4.12% $\pm 21.32$ $\pm 24.67$ $\pm 19.76$ $\pm 3.35$ $\pm 4.91$ 52.12%50.37%36.87%-1.75%-13.5% $\pm 21.81$ $\pm 27.06$ $\pm 27.14$ $\pm 5.25$ $\pm 7.22$ 46.0%43.25%50.75%-2.75%7.5% $\pm 17.92$ $\pm 19.83$ $\pm 12.61$ $\pm 1.91$ $\pm 7.22$ 51.83%47.16%41.0%-4.67%-6.16% $\pm 25.17$ $\pm 11.63$ $\pm 21.89$ $\pm 13.54$ $\pm 10.26$ 33.89%50.0%43.25%16.11%-6.75%	Mean $\pm$ SD N=11BefDurAftChange B-DChange D-A51.87%48.75%43.5%-3.12%-5.25%44.1% $\pm 20.70$ $\pm 16.50$ $\pm 21.71$ $\pm 4.20$ $\pm 5.21$ 49.62%43.25%47.37%-6.37%4.12%49.62%43.25%47.37%-6.37%4.12%45.5% $\pm 21.71$ $\pm 4.20$ $\pm 5.21$ $\pm 19.18$ 49.62%43.25%47.37%-6.37%4.12%45.2% $\pm 21.32$ $\pm 24.67$ $\pm 19.76$ $\pm 3.35$ $\pm 4.91$ $\pm 21.32$ $\pm 27.06$ $\pm 27.14$ $\pm 5.25$ $\pm 7.22$ $\pm 25.60$ 46.0%43.25%50.75% $-2.75\%$ 7.5%44.33% $\pm 17.92$ $\pm 19.83$ $\pm 12.61$ $\pm 1.91$ $\pm 7.22$ $\pm 22.44$ 51.83%47.16%41.0% $-4.67\%$ -6.16%30.0% $\pm 25.17$ $\pm 11.63$ $\pm 21.89$ $\pm 13.54$ $\pm 10.26$ $\pm 13.70$ 33.89%50.0%43.25%16.11%-6.75%51.16%	Mean $\pm SD$ N=11BefDurAftChange B-DChange D-ABefDur $51.87\%$ $48.75\%$ $43.5\%$ $-3.12\%$ $-5.25\%$ $44.1\%$ $59.17\%$ $\pm 20.70$ $\pm 16.50$ $\pm 21.71$ $\pm 4.20$ $\pm 5.21$ $\pm 19.18$ $\pm 25.71$ $49.62\%$ $43.25\%$ $47.37\%$ $-6.37\%$ $4.12\%$ $45.5\%$ $46.5\%$ $\pm 21.32$ $\pm 24.67$ $\pm 19.76$ $\pm 3.35$ $\pm 4.91$ $\pm 25.75$ $\pm 20.56$ $52.12\%$ $50.37\%$ $36.87\%$ $-1.75\%$ $-13.5\%$ $45.2\%$ $49.2\%$ $\pm 21.81$ $\pm 27.06$ $\pm 27.14$ $\pm 5.25$ $\pm 7.22$ $\pm 25.60$ $\pm 32.37$ $46.0\%$ $43.25\%$ $50.75\%$ $-2.75\%$ $7.5\%$ $44.33\%$ $50.83\%$ $\pm 17.92$ $\pm 19.83$ $\pm 12.61$ $\pm 1.91$ $\pm 7.22$ $\pm 22.44$ $\pm 29.90$ $51.83\%$ $47.16\%$ $41.0\%$ $-4.67\%$ $-6.16\%$ $30.0\%$ $55.67\%$ $\pm 25.17$ $\pm 11.63$ $\pm 21.89$ $\pm 13.54$ $\pm 10.26$ $\pm 13.70$ $\pm 36.25$ $33.89\%$ $50.0\%$ $43.25\%$ $16.11\%$ $-6.75\%$ $51.16\%$ $50.33\%$	$\begin{tabular}{ c c c c c c c c c c c c c c c c c c c$	$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$

Table 4-14 The percentage of muscle activation during the change in speed between the Ref and PwP groups for the Bef, Dur, and Aft cycles. (B-D) the change from Before to During cycle and (D-A) the change from During to After cycle.

RTA: Right tibialis anterior. LTA: Left tibialis anterior. RGAS: Right gastrocnemius. LGAS: Left gastrocnemius. RSOL: Right soleus. LSOL: Left soleus.

Parameters		Ν	fild/Moderat	e		severe					
		Mean					Mean				
			( <b>SD</b> )			(SD)					
			N=11					N=6			
	Bef	Dur	Aft	Change	Change	Bef	Dur	Aft	Change	Change	
				B-D	D-A				B-D	D-A	
RTA	35.0%	58.55	45.5%	23.5%	-13.0%	62.0%	60.5%	78.0%	-1.5%	17.5%	
	±13.9	±25.82	±5.56	±11.9	±20.2	±16.97	±36.06	±14.14	±19.0	±21.9	
LTA	39.7%	35.3%	47.0%	-4.5%	11.7%	57.0%	69.0%	52.0%	12.0%	-17.0%	
	±17.05	±10.04	±10.19	±7.0	±0.1	±45.25	±16.97	±24.04	±28.2	±7.07	
RGAS	42.0%	54.75%	14.25%	-12.7%	-40.5%	62.0%	46.5%	49.5%	-15.5%	3.0%	
	±28.39	±34.52	±8.8	±6.1	±25.6	±5.65	±27.57	±31.81	±21.9	±4.24	
LGAS	52.25%	44.0%	38.25%	-8.2%	-5.7%	28.5%	64.5%	55.0%	36.0%	-9.5%	
	±24.24	±26.15	±22.69	±1.9	±3.46	±2.12	±43.13	±9.89	±41.0	±33.2	
RSOL	25.25%	50.75%	35.75%	-25.5%	-15.0%	39.5%	65.5%	25.5%	26.0%	-40.0%	
	±12.73	±39.8	±35.95	±27.1	±3.91	±13.43	±38.89	±3.53	±25.5	±35.5	
LSOL	46.75%	44.5%	43.25%	-2.25%	-87.7%	60.0%	62.0%	64.0%	2.0%	2.0%	
	±25.40	±13.40	±20.07	±12.0	±6.6	±29.69	±43.84	±41.01	±14.1	±2.8	

Table 4-15 The percentage of muscle activation during the change in speed between the PwP subgroups (Mild/Moderate and severe) group for the Bef, Dur, and Aft cycles. (B-D) the change from Before to During cycle and (D-A) the change from During to After cycle.

RTA: Right tibialis anterior. LTA: Left tibialis anterior. RGAS: Right gastrocnemius. LGAS: Left gastrocnemius. RSOL: Right soleus. LSOL: Left soleus.

#### B) Mean number of separate activity periods for each muscle



Number of activation periods

Figure 4-7 The average number of activity periods of the six muscles during change speed for the Ref and PwP groups during the three cycles of walking on a treadmill: (B) 'Before', (D) 'During' and (A) 'After'. RTA: Right tibialis anterior. LTA: Left tibialis anterior. RGAS: Right gastrocnemius. LGAS: Left gastrocnemius. RSOL: Right soleus. LSOL: Left soleus

Figure 4-7 presents the mean number of activity periods for the three muscles for the Ref and the PwP groups on both sides. All muscles were active between one and three times in each cycle for the Ref, while the PwP showed generally a greater number of muscle activations, at around three to 10 times in the Dur cycle and more than 10 in the A cycle. The increase in the number of activity periods in the LSOL and RSOL amongst the PwP was greater than in the Ref, as well as the activity in the LTA and RGAS, which both show more activation periods in the PwP than in the Ref group. The two PwP subgroups showed different activation patterns during the three cycles; the increase in a number of activity periods seemed to be associated with an increase in disease severity, especially in the activation for the RSOL.

#### C) Magnitude of Muscle activation, (AUC)

The magnitude of muscle activation will be presented to illustrate the differences amongst the Ref and PwP groups. The AUC, as mentioned in Section 3.6.1.2 is a unitless parameter indicating the magnitude of muscle activation of each gait cycle B, D, and A the change in speed—for the three muscles of the lower limbs on both sides for both the Ref and PwP groups.

Parameters	Ref Mean (SD) N=11					PwP Mean (SD) N=6														
												Bef	Dur	Aft	Change	Change	Bef	Dur	Aft	Change
														B-D	D-A				B-D	D-A
RTA	1.28	1.42	1.57	0.13	0.15	1.66	1.66	1.73	0.00	0.07										
	±0.75	±0.63	±1.04	±0.28	±0.71	±0.28	±0.76	±0.55	±0.61	±0.59										
LTA	1.74	1.98	2.26	0.22	0.24	1.62	1.69	1.72	0.07	0.03										
	±0.92	±1.02	±1.89	±0.34	±0.85	±0.32	±0.40	±0.25	±0.19	±0.20										
RGAS	5.29	5.62	5.77	0.33	0.15	1.69	1.79	1.93	0.10	0.14										
	±2.67	±13.52	±13.51	±0.87	±0.33	±1.02	±1.10	±1.21	±0.35	±0.12										
LGAS	8.02	9.20	9.01	1.18	-1.19	1.19	1.25	1.31	0.05	0.07										
	±11.62	±12.69	±12.08	±1.92	±3.27	±0.64	±0.49	±0.67	±0.32	±0.25										
RSOL	16.63	15.83	15.74	-0.80	-0.10	12.22	15.13	16.79	2.90	1.66										
	±34.40	±1.70	±29.89	±2.79	±2.39	±23.40	±29.28	±33.33	±6.05	±4.33										
LSOL	14.18	17.35	18.02	2.48	0.55	2.48	2.57	3.09	0.09	0.52										
	±21.74	±26.51	±26.75	±2.45	±2.42	±2.45	±2.42	±3.12	±0.38	±0.90										

Table 4-16 AUC for the six muscles during the three cycles (Bef, Dur, and Aft) of changing speed for the Ref and PwP groups while walking on the treadmill. (B-D) the change from Before to During cycle and (D-A) the change from During to After cycle.

RTA: Right tibialis anterior. LTA: Left tibialis anterior. RGAS: Right gastrocnemius. LGAS: Left gastrocnemius. RSOL: Right soleus. LSOL: Left soleus.
Most of the participants in the Ref (7/10) changed speed during the L side, which may explain the larger increases in the soleus and gastrocnemius activity on the L side (2.48  $\pm$  2.45 and 1.18  $\pm$  1.92), while the R side showed a decrease (soleus 0.80  $\pm$  2.79) or modest increase (Gastrocnemius 0.33  $\pm$  0.87). During the change (B-D) the PwP showed very little change in magnitude of muscle activation in the RTA, LTA, RGAS, LGAS and LSOL (ranging between 0.01 and 0.1). RSOL, however, showed a clear change in the AUC, with an increase of 2.90  $\pm$  6.05 with change speed from B-D. Five of six PwP were on the right-sided when the change occurred which may explain the observed increase on the R more than L among the PwP. The EMG pattern in Figure 4-8 shows that there were clear differences in the change in the magnitude muscle activation among two subgroups



Figure 4-8 The differences in muscle work (AUC) of the six muscles for the PwP subgroups (Moderate, and Severe) during the change in speed from the Bef cycle to Dur cycle (B-D), and from 'Dur to 'Aft cycle (D-A). SWTA: Right tibialis anterior. STTA: Left tibialis anterior. SWGAS: Right gastrocnemius. STGAS: Left gastrocnemius. SWSOL: Right soleus.



Figure 4-9 The activation of the soleus muscle during the three cycles of walking on the treadmill for one participant each from the Ref, Mild/Moderate and Severe PwP subgroups. The red line indicates the cycle Bef, the green line in indicates the cycle Dur and the blue line indicates the cycle immediately Aft the change in speed.

Figure 4-9 gives a graphical overview of the soleus activation for one participant from each group. The soleus muscle of the Ref participant (Ref1) increased incrementally with the change in speed from before to after the speed change, particularly at the start and end of the gait cycles. This biphasic pattern was less apparent in the PwP participants. The Mild/Moderate participant (PwP3) showed a clear change in activity from before to during the speed change but this was focussed on the later stages of the cycle (~75%) during the swing phases. While the severe participant (PwP5) shows a bi-phasic pattern there was no obvious change in amplitude during the change the speed.

#### **4.2.2** Summary of overall findings (increase in gait speed)

From these results, it can be seen that both groups were able to increase their gait speed on a self-paced treadmill when requested. Expectedly, the Ref was able to produce a greater, and more immediate, speed change than the PwP groups. Consistent with these findings was the increase in step length, which was greater in the Ref than in the PwP group. Cadence, however, decreased in the Ref, but increased for the PwP group. The sagittal plane hip, knee and ankle joint movements increased in both groups, combined with an increase in hip (H1) power in the Ref and PwP groups except the Severe PwP subgroup, which showed a greater increase in (H2) than (H1) during the change in speed. A little unexpectedly ankle power showed only modest increases in power for the Ref group and barely changed in the PwP.

Finally, it was observed that the muscle activation characteristics varied between the groups. The Ref showed a decrease in the percentage of all muscle activation, except in the LSOL, which increased with 16% in the Dur cycle. The PwP showed more increase in the percentage of muscle activation, which increase with disease severity. The Ref showed an increase in the magnitude of muscle activation (AUC) in the L soleus and the LGAS of during the cycle from before cycle , while PwP showed an increase in the RSOL during the change in speed.

The previous section presented the methods and results for the first study (speed modulation, including gait initiation and an increase in gait speed, during treadmill walking), which aimed to explore the differences in motor control between the PwP and the Ref. The comparison was made across biomechanical (kinematic and kinetic) and physiological (EMG) variables during variations in speed while walking on the treadmill. The study included (1) GI from a standing position and an increase in speed while walking on a self-paced treadmill and (2) changing speed after walking at a regular speed.

The second part of the study will be presented in the next chapter, this seeks to understand whether these differences observed during treadmill walking are apparent during overground walking.

# **Chapter 5 Study 2: speed modulation during overground** walking

This chapter will present the findings of the second study as well as briefly describe the methods in order to provide context. This section aimed to build on the findings of the treadmill study by comparing speed modulation (gait initiation from quiet standing to increase speed and when the speed change) during overground walking between people with Parkinson's (PwP) and an unimpaired Reference group (Ref). This is an important step because in real-life situations, most gait, and perhaps most gait training, will take place overground rather than on a treadmill.

To gain some insights into the potential use of treadmills in rehabilitation, comparisons were drawn between speed modulation on a treadmill and overground. The variables used for comparison included both spatiotemporal (stride time, swing and stance time, and speed) and physiological (EMG) parameters. These were selected to explore the motor control differences between the two groups during the variations in walking speed. Kinematics and kinetics data were not available for recording since testing had to occur away from the movement analysis laboratory. The chapter is organised into two main sections: one considering gait initiation from quiet standing and the other focusing on an increase in gait speed from a comfortable self-selected speed.



Figure 5-1 The walking path in the corridor outside the laboratory. The participants were asked to begin the test at the start line (horizontal arrow) and continue walking in the direction indicated by the vertical arrow – when were they instructed to stop

#### 5.1Gait initiation during overground walking

The testing protocol and analysis of the EMG and STP variables were similar to the GI tests conducted on the treadmill, which defined the time of GI as the period from the standing position until the second ground contact of the foot on the swing side (see chapter 4, section 4.2). This definition ensured a swing and stance phase were available for analysis from both sides.

## 5.1.1 Participants

The participants were the same as in the first study (see section 4.1.1). There were 11 individuals in the Ref, (aged 29.90 SD 16.50 years). There were six individuals in the PwP group, (aged 70.30 SD 13.80 years), see chapter 3, section 3.3, Table 3.2 for further information on group characteristics.

Briefly, the side with which participants started their movement was identified as the swing side, the other side being the stance side. It is worth noting that all participants started to walk with the same side as in the treadmill tests (three members of the PwP group stepped with their right side first, while the other three started with their left first). In the reference group, seven participants stepped with their right and four with their left.

## 5.1.2 Results

## 5.1.2.1 Spatiotemporal parameters (STP)

Table 5-1 present the timings of the key events. All times have been normalised to the start event (GI start, see section 3.6.1.1 for definition). These included the foot contact times on the swing side, the stance side and the swing phase time. The gait speed was calculated by the distance covered using a measuring tape over the total time of GI measured by IMU.

	All PwP	PwP g	roups	Ref group	
	Mean	Moderate	Severe	Mean	
	(SD) (n=6)	Mean	Mean	(SD) (n=11)	
		(SD)	( <b>SD</b> )	~ /	
		( <b>n=4</b> )	( <b>n</b> =2)		
SWO1 (s)	0.26	0.25	0.28	0.20	
	±0.13	±0.11	±0.20	±0.12	
SWC1 (s)	0.76	0.77	0.76	0.55	
	±0.15	±0.12	±0.26	±0.25	
STO (s)	0.91	0.87	0.97	0.71	
	±0.21	±0.16	±0.331	±0.26	
STC (s)	1.35	1.30	1.45	1.09	
	±0.24	±0.18	±0.39	±0.42	
SWO2 (s)	1.49	1.44	1.61	1.25	
	±0.24	±0.14	±0.43	±0.47	
SWC2 (s)	1.95	1.89	2.06	1.49	
	±0.25	±0.14	±0.47	±0.56	
Swing 1 (s)	0.51	0.52	0.49	0.56	
	±0.04	±0.03	±0.05	±0.25	
Swing2 (s)	0.44	0.43	0.46	1.09	
	±0.04	±0.02	±0.05	±0.42	
Swing3 (s)	0.45	0.45	0.46	0.94	
	±0.05	±0.06	±0.04	±0.35	
Stance1 (s)	0.91	0.87	0.84	0.71	
	±0.21	±0.16	±0.17	±0.26	
Stance 2 (s)	0.72	0.67	0.84	0.69	
	±0.12	±0.02	±0.17	±0.26	
Speed m/s	0.52	0.53	0.49	0.97	
	±0.06	±0.03	±0.11	±0.29	

Table 5-2 Timing of events in seconds during gait initiation for the Reference group (Ref) and PwP group (including subgroups), the speed of the GI period was measured in m/s

This table definitions: SWO1= the first foot off on the swing side, SWC1 = the first foot contact of the swing side, STO= the toe-off of the stance side, STC = the first foot contact of the stance side, SWO2= the second foot off of the swing side, SWC2 = the second foot contact of the swing side, Swing 1= the time from the starting time to the first foot contact of the swing side, Swing 2= The time from the starting point to the first foot contact of the stance side, Swing 3= the time when the swing side leaves the ground a second time to contact again for the second foot contact, Stance 1= the time from the starting point until the stance side leaves the ground, Stance 2= the time from the first contact of the swing side point until the time that the same foot leaves the ground

To get a clear representation of the gait event times Table 5-1 shows the mean and standard deviation of the GI event times for all participants. The Ref group spent a mean of  $1.49s \pm 0.56$  in the GI period, while the PwP took longer, at  $1.95s \pm 0.25$ ). The Ref spent longer in the swing phases; Swing1( $0.56s \pm 0.25$ ), Swing2 ( $1.09s \pm 0.42$ ) and Swing3 ( $0.94 \pm 0.35s$ ), compared with all the PwP groups Swing 1 ( $0.51 \pm 0.04$  s, swing 2  $0.44 \pm 0.04$  s and swing  $3 \ 0.45 \pm 0.05$  s). On the other hand, the PwP spent more time in the stance phases (Stance1 and Stance2) ( $0.91 \pm 0.21$  s and  $0.72 \pm 0.12$  s) than the Ref group ( $0.71 \pm 0.26$  s and  $0.69 \pm 0.26$  s). Finally, the PwP group was substantially slower in walking speed during the GI period ( $0.52 \pm 0.04$  m/s) than the Ref group ( $0.97 \pm 0.11$  m/s).

Longer times were recorded for total GI time  $(2.06 \pm 0.47s)$  in the Severe PwP subgroup than in the Mild/Moderate group  $(1.89 \pm 0.14s)$ . From these data, it can be suggested that the severity of the disease had an effect on the time needed to complete the task.

Overall, it was observed that the Ref group was able to complete the GI movement within a shorter time than the PwP (this was reflected by the speed of movement during overground walking). On the other hand, the swing phases times were longer with Ref group than PWP while the stance phases were shorter with in Ref group than PwP. Finally, longer time was observed as disease severity increased.

The next section will describe the broad differences in muscle activation during the GI period across the groups while walking over ground.

## 5.1.2.2 Muscle activity during the GI period while walking over ground

Using electromyographic (EMG) signals, this section will describe the muscle activity during GI movement while walking on the ground. The EMG signals recorded and processed during GI period allowed for the calculation of the same three variables used in the treadmill study:

- The percentage of muscle activity (normalised as a percentage of the whole GI movement) for the three targeted muscles (tibialis anterior, gastrocnemius and soleus on both sides).
- The number of discrete activity periods for each muscle.
- The magnitude of muscle activation, calculated from area under the curve (AUC), during GI period, for the previous muscles.

	All PwP	PwP gr	oups	Ref group
	Mean (SD)	Mild/Moderate	Severe	Mean
	( <b>n=6</b> )	Mean	Mean	( <b>SD</b> )
		(SD)	(SD)	(n=11)
		( <b>n=4</b> )	( <b>n=2</b> )	(11–11)
SWTA	47.61%	52.31%	36.84%	43.17%
	±18.85	±22.01	±2.48	±25.88
STTA	74.61%	93.90%	35.83%	33.57%
	±30.46	±6.50	±1.36	±27.90
SWGAS	58.74%	64.77%	46.67%	21.21%
	±15.41	±14.60	±10.54	±10.46
STGAS	36.80%	41.22%	27.97%	25.70%
	±11.82	±11.85	±6.59	±10.13
SWSOL	56.19%	57.40%	53.77%	24.64%
	±17.01	±17.21	±23.24	±13.28
STSOL	43.67%	46.10%	38.80%	35.34%
	±15.67	±17.82	±14.34	±22.46

A) The percentage of muscle activity of the total GI period.

 Table 5-3 The percentage of muscle activity of total GI period for the Reference group (Ref) and PwP groups.

SWTA: swing-side tibialis anterior. STTA: stance-side tibialis anterior. SWGAS: swing-side gastrocnemius. STGAS: stance-side gastrocnemius. SWSOL: swing-side soleus. STSOL: stance-side

Table 5-2 shows the percentage of muscle activation for each of the six muscles during the GI period overground. In general, all muscles were active for longer in the PwP group (particularly in the Mild/Moderate subgroup) compared to the Ref group; in some cases, this was more than double: SWSOL (56.19% compared with 24.64%), SWGAS (58.74% compared with 21.21%) and STTA (74.61% compared with 33.57%).

The PwP sub-groups again showed variations in the activation periods with consistently shorter activation period in the Severe PwP subgroup compared with the Mild/Moderate PwP subgroup. Notably the STTA activation period in the Mild/Moderate group lasted virtually the whole GI period (93.90%), compared with the Severe group (35.85%) which was closer to the Ref values. The SWGAS was the second-longest activated muscle within the Mild/Moderate PwP subgroup (59.51%), but, interestingly, this activation of the SWGAS decreased in the Severe PwP subgroup. The possible reasons for these observations will be discussed in chapter 6.

#### B) Number of muscle activation periods

Table 5-3 shows the number of times each muscle was activated during the GI period for all groups. All the muscles in the Ref group activated two or three times, while the PwP's muscles activated more frequently, three or four times. The number of activity periods was generally the same between the PwP subgroups.

	All PwP	PwP grou	Ref group	
	( <b>n=6</b> )	Mild/Moderate	Severe	(n=11)
		(n=3)	(n=2)	
SWTA	3	3	3	3
STTA	3	4	3	2
SWGAS	4	4	4	3
STGAS	3	4	3	2
SWSOL	4	3	3	2
STSOL	3	3	3	2

 Table 5-4 The average number of muscle activation periods during the GI period while walking on the ground for the Ref and PwP groups.

Figure 5-3 an example of the activation periods for one participant (P1) from the Ref group and a participant (PwP 4) from the Severe PwP subgroup. The PwP participants' muscles were generally observed to activate more frequently and proportionally longer, than the Ref group. The SWGAS in the PwP became active later in the GI sequence (after 50% of the movement), contrary to the Ref group, in which activation was early in the GI sequence (before 50% of the movement). Likewise, the stance side soleus (STSOL) was also active early in Ref (P1) compared to the PwP participants, which activated later.



Figure 5-2 Example of the activity periods of the lower limb muscle for(A) a participant from the Ref (P1) and (B) the Severe group (PwP4) during GI movement while over ground walking. the orange line indicated the GI events during walking over ground.

#### C) Magnitude of muscle activation (AUC)

This section presents the results for the magnitude of the muscle activation during GI movement. The AUC, as mentioned previously, provides a unitless measure of muscle activity.



AUC during GI movemnt in the Ref and PwP groups

Figure 5-3 AUC for the six muscles during the GI period for the Ref and PwP groups while walking on the ground. SWTA: right tibialis anterior. STTA: left tibialis anterior. SWGAS: right gastrocnemius STGAS: left gastrocnemius. SWSOL: right soleus. STSOL: left soleus. Values have been uniformly multiplied by 1000 for ease of interpretation

Figure 5-3 presents the magnitude of muscle activation (AUC) during the GI period for the PwP groups and Ref group. The results show that the magnitude of muscle activation for the Ref group was generally higher than for the PwP group, except for the soleus on the swing side (SWSOL). There were differences in muscle activation across the PwP sub-groups; the severity of the disease had effect on muscle activation, for example the SWSOL had the longest activation ( $0.48 \pm 0.07$ ) during the GI period in the Severe PwP subgroup.

The magnitude of muscle activation of the three muscles (TA, GAS and SOL) on the swing side which was the start side was analysed, the most interesting difference in the muscle activity between the groups was observed in the Soleus muscle on the swing side (SWSOL) as illustrated in figure 5-4.

In the Ref it can be seen that the GI period started with a relatively high amplitude of SWSOL activity (~03.0 mV), possibly to help control the upright posture, before decreasing rapidly before SWC1 and return to increase to reach above (~03.5mV) after STC to lower again when end of movement. In the PwP, on the other hand, showed a different pattern of muscle activity. The soleus activity started with low amplitude of activity <(~0.2mV) then a clear increase in activity which appeared to be more pronounced in the severe participant (PwP1) compared with the MIL/moderate. Noteworthily, The Mild/Moderate PwP participants showed an increase in magnitude of the SWTA before the STC event and lowered before the SWC2 event, but the SWGAS was lower inactivation than the tibialis and the soleus.



SWTA SWGAS SWSOL

100

100

SWTA SWGAS SWSOL

SWC2

1 0.5 0 L 0 20 40 60 80 100 % GI Period Figure 5-4 An example of the processed EMG signals of the three muscles on the swing side for one

Severe PWP 1

STC

SWC1

participant from each PwP group and the Ref during the GI period of overground walking. The red line represents the tibialis anterior (TA) muscle, the green line represents the gastrocnemius (GAS) and the black line represents the soleus muscle (SOL). The vertical lines show the SWC and STC GI events.

 $\times 10^{-4}$ 3

2.5

2

MVolts 1.5

#### 5.1.3 Summary findings for the GI period Overground

This study was designed to gather information about the differences in Gait initiation overground, (defined as occurring during the change in speed from zero movement to walking) between a group of unimpaired individuals (Ref) and a group of independently mobile individuals with Parkinson's disease (PwP).

It was evident that the Reference group (Ref) took considerably less time to complete the GI period than the PwP groups, with faster speed  $(0.97 \pm 0.11 \text{ m/s})$  m/s for the Reference group and  $0.52 \pm 0.04$  m/s for the PwP. The disease severity was reflected in the increased GI time  $(2.06 \pm 0.47\text{s})$  for the Severe PwP subgroup compared with the other groups at  $1.89 \pm 0.14\text{s}$  and  $1.49 \pm 0.56$  for the Mild/Moderate PwP subgroup and Ref group respectively. The swing phases were longer in Ref than PWP group who increases the time with severity of disease. This observation may confirm the difficulty in initiating movement in severe disease.

The percentage of muscle activation of all the muscles in the PwP was essentially double of those of the Ref group. On the other hand, the magnitude of muscle activation (AUC) during GI period was the opposite, showing a higher value for the muscle activation in the Ref group than in the PwP group in all muscles except for the SWSOL, which showed a high value of activation. This suggests weaker but longer muscle activity in the PwP group compared with the Ref group.

The next section will consider what happened when the speed was increased from a regular walking speed to a fast pace.

#### 5.2Change in walking speed speed during over ground walking

This section will present the results for increasing speed during overground walking. Variables are compared between groups, including spatiotemporal (stride time, and swing and stance phases time) and the EMG parameters, which, as before, were selected to explore the motor control differences between the two groups. The variables were separated into three distinct cycles: 1) before changing speed (B), during the change in speed (D) and immediately after changing speed (A).

## 5.2.1 Results

## **5.2.1.1 Temporal parameters (TP)**

This section will present the temporal differences between the Ref and PwP groups during an increase in overground walking speed. Due to the limitations of the instrumentation, the change in speed across the cycles was identified by the differences in the gait cycle time. This is considered to be a limitation of this study.

Table 5-4 shows the differences in the temporal parameters (TP) between the Ref and PwP group from Buf cycle to Dur (**D-B**) cycle and from the Dur to Aft (**A-D**) cycle.

Parameter		lef	Pw			
	M	ean	Mean			
	±	SD	SE	)±		
	N=	=11	N=	=6		
	Change	Change	Change	Change		
	B-D	D-A	B-D	D-A		
Left Stride	-0.15	0.00	-0.09	-0.03		
Time (s)	±0.09	±0.07	±0.16	±0.34		
Right Stride	-0.12	-0.03	-0.11	0.05		
Time (s)	±0.14	±0.08	±0.12	±0.14		
Cadence (steps per	15.97	-9.34	13.16	-2.5.22		
minute)	±5.61	±17.5	±6.66	±4.10		
Left Stance	-2.64	1.75	-3.93	3.02		
Time (%)	±5.88	±4.35	±6.85	±7.94		
Right Stance	-3.09	-1.98	-0.90	0.90		
Time (%)	±5.83	±3.34	±8.33	±3.50		
Left Swing	2.64	-1.75	3.93	-3.02		
Time (%)	±5.88	±4.35	±6.85	±7.94		
Right Swing	3.09	1.98	0.90	-0.90		
Time (%)	±5.83	±3.34	±8.33	±3.50		

Table 5-5 the change in the (TP) of the Ref and PwP groups on the right and left sides. B-D is the change from 'Before' to 'During' cycle, D-A is the change from 'During' to 'After' cycle

As seen in Table 5-4, the Ref participants were able to change their walk (reducing stride time) from B to D, the cycle, R (-0.12s,  $\pm 0.14$ ) and L (-0.15s,  $\pm 0.09$ ). In the PwP group, a reduction in stride time was also observed on both the right and left sides but this was much less than the Ref by (L: -0.09s,  $\pm 0.16$  and R: -0.11s,  $\pm 0.12$ ). Both groups showed mild or no change from D to A cycle. The stance time was reduced in both groups with a

relative increase in swing time during change speed. while the opposite results were shown in the following cycle for both groups

In summary, all participants decreased their stride time around the point of the requested change in speed, this reduction averaged 0.09 s from the B cycle to the D cycle but was substantially greater in the Ref group. Both groups showed increase in cadence with change speed in Ref group  $15.97\pm5.61$  s/m compared  $13.16\pm6.6$  s/m PwP while decrease in following cycle. Generally, there were few differences observed among the PwP subgroups see Table 5-5.

Table 5-6 the change in temporal parameters of the PwP subgroups (Mild/moderate and Severe) of the right and left sides. B-D is the change from 'Before' to 'During' cycle, D-A is the change from 'During' to 'After' cycle.

Parameter	Mild/m	oderate	Severe Mean			
	Μ	ean				
	±;	SD	±	SD		
	Ν	=3	Ν	=2		
	Change	Change	Change	Change		
	B-D	D-A	B-D	D-A		
Left Stride	-0.09	0.03	-0.09	0.03		
Time (s)	±0.08	±0.01	$\pm 0.01$	±0.01		
Right Stride	-0.08 0.01		-0.06	0.00		
Time (s)	±0.2	±0.08	$\pm 0.04$	±0.03		
Cadence (steps per	14.72	-2.6	9.51	3.90		
minute)	±7.44	9±4.9	±1.89	±12.97		
Left Stance	-1.84	-4.10	-4.08	0.22		
Time (%)	±0.96	±3.91	$\pm 2.90$	±1.24		
Right Stance	-0.59	1.10	-2.72	1.40		
Time (%)	±0.40	±0.24	±0.49	±1.21		
Left Swing	1.85	4.09	4.03	-0.21		
Time (%)	±0.98	±3.91	±2.9	±1.24		
Right Swing	0.59	-1.10	2.72	-1.41		
Time (%)	±0.41	±0.26	±0.48	±1.21		

The next section will present the change in muscle activation during the overground change in speed.

# 5.2.1.2 Muscle activity during the speed variation while walking over ground.

## A) The percentage of muscle activity for each gait cycle .

As explained previously, the electromyography (EMG) signals were processed to present the percentage of muscle activity of the eacg gait cycle, number of discrete contractions 160

per cycle, and magnitude of muscle activation of each cycle (by integrating the signal to obtain the area under the curve (AUC)) of the six muscles—the tibialis anterior, the gastrocnemius and the soleus on both sides—of the three gait cycles— B, D, and A, of changing speed while walking over the ground. All recorded muscles were activated during the increase in speed.

Table 5-6 shows the differences in the percentage of muscle activity from the B to D cycles and from the D to A cycles for each of the three muscles on both sides. The Ref group showed generally longer activation period in all muscles with a change in speed from B to Dcycle except in LTA and LSOL (-14.13  $\pm$  3.62 and -4.13  $\pm$  -3.45 respectively. In contrast, the PwP had generally shorter activation time as percentage for RTA, RGAS, and RSOL (-7.83 $\pm$ 2.17, -13.17 $\pm$ 16.9, 19.16 $\pm$ 1.51) and longer activation time on the left side (2.5 $\pm$ 6.62, 8.84 $\pm$ 1.00, 8.84 $\pm$ 0.58). It is worth noting the RSOL which showed a much larger decrease in the activity period (-19.16 %  $\pm$  -1.51).

In the following (A) cycle both groups decreased the activation time for all muscles (except the soleus muscle on both sides for both groups) which continued to increase (R  $3.52\pm2.00$  and  $L29.5\pm11.9$ ) for the Ref and (R7.16 $\pm0.97$  and 7.66 $\pm3.07$ ) for the PwP group.

Table 5-7, the activity period was compared between the B cycle and D cycle for the two PwP subgroups. The activity period for the plantar flexors in B cycle showed longer activation periods than D cycle on the right side compared with the left, which increases with disease severity. While in A cycle the percentage of muscle activation are reduced with all muscles in both groups except the soleus muscle which showed the opposite activation.

The activation of the soleus muscle on both sides showed increased activation with more disease severity.

It is noteworthy that the two sub-groups were different in percentage of muscle activation, with the more severe showing decreased activity periods.

Parameters		PWP									
			Mean			Mean					
			±SD		±SD						
			N=11					N=6			
	В	D	Α	Change	Change	B	D	A	Change	Change	
				B-D	D-A				B-D	D-A	
RTA	55.50%	57.63%	52.63%	2.13%	-5.0%	55.50%	47.67%	38.17%	-7.83%	-9.50%	
	±20.48	±15.64	±19.70	±4.84	±4.06	±20.48	±18.31	±14.23	±2.17	±4.08	
LTA	65.13%	51.00%	50.25%	-14.13%	-0.75%	54.83%	57.33%	44.33%	2.5%	-13.0%	
	±9.44	±13.06	±16.99	±3.62	±3.93	±24.45	±17.83	±11.31	±6.62	±6.52	
RGAS	38.37%	41.25%	38.25%	2.88%	-3.00%	52.17%	39.00%	33.17%	-13.17%	-5.83%	
	±17.22	±7.13	±15.07	±10.09	±7.94	±6.85	±23.75	±23.36	±16.90	±0.39	
LGAS	37.87%	48.50%	38.75%	10.63%	-9.75%	37.33%	46.17%	39.33%	8.84%	-6.84%	
	±14.45	±25.01	±19.51	±10.56	±5.50	±24.28	±25.28	±19.34	±1.00	±5.94	
RSOL	32.35%	44.71%	48.23%	12.36%	3.52%	66.16%	47.00%	54.17%	-19.16%	7.16%	
	±18.21	±18.75	±20.75	±0.54	±2.00	±14.17	±12.66	±11.69	±1.51	±0.97	
LSOL	29.00%	24.87%	54.37%	-4.13%	29.5%	36.33%	45.17%	52.83%	8.84%	7.66%	
	±13.34	±9.89	±21.79	±3.45	±11.9	±12.04	±12.62	±9.55	±0.58	±3.07	

5-6 The percentage of muscle activation during the change in speed between the Ref and PwP groups for the 'B', 'D', and 'A' cycles. B-D is the change from before to during cycle and D-A is the change from during to after cycle.

RTA: Right tibialis anterior. LTA: Left tibial anterior. RGAS: Right gastrocnemius. LGAS: Left gastrocnemius. RSOL: Right soleus. LSOL: Left soleus

Parameters	Mild/moderate					Severe						
	Mean						Mean					
	±SD N=3							±SD				
								N=2				
	В	D	Α	Change	Change	В	D	Α	Change	Change		
				B-D	D-A				B-D	D-A		
RTA	43.00%	41.5%	34.7%	-1.50	-6.75	80.50%	60.00%	45.00%	-20.5	-15.0		
	±7.70	±16.03	±15.4	±8.24	±0.64	±6.40	±21.12	±12.72	±14.84	±8.48		
LTA	55.00%	58.00%	46.75%	3.00	-11.25	54.50%	56.00%	39.50%	1.5	-16.5		
	±22.19	±9.50	±13.72	±15.72	±7.23	±38.89	±38.18	±2.12	±0.71	±3.6		
RGAS	51.50%	44.75%	31.25%	-6.75	-13.5	53.50%	27.50%	37.00%	-26.00	9.5		
	±8.66	±25.80	±22.60	±17.19	±3.24	±2.12	±20.51	±33.94	±18.38	±13.43		
LGAS	40.00%	53.50%	48.5%	13.5	-5.00	32.00%	31.50%	21.00%	-6.00	-10.5		
	±16.06	±26.8	±16.00	±10.75	±10.03	±4.24	±12.03	±4.24	±0.50	±7.77		
RSOL	64.25%	49.25%	64.25%	-15.00	15.00	70.00%	42.50%	34.00%	-27.50	-8.50		
	±14.24	±15.71	±20.46	±1.42	±4.75	±19.80	±0.71	±9.89	±19.09	±9.19		
LSOL	38.00%	49.75%	56.73%	11.7	7.00	32.50% 3	36.00%	45.00%	3.5	9.00		
	±14.38	±13.05	±6.94	±1.31	±6.13	±7.78	±5.65	±11.32	±2.12	±5.65		

Table 5-7 The percentage of muscle activation during the change in speed for PwP subgroups (Mild/Moderate and severe )group in the 'B', 'D', and 'A' cycles. B-D is the change from before to during cycle and D-A is the change from during to after cycle.

RTA: Right tibialis anterior. LTA: Left tibial anterior. RGAS: Right gastrocnemius. LGAS: Left gastrocnemius. RSOL: Right soleus. LSOL: Left soleus



B) The number of separate activity periods for each muscle

Figure 5-5 Mean number of activity periods of the six muscles during change in speed for the Ref and PwP groups during the three cycles of overground walking (B) Bef, (D) Dur and (A) Aft. RTA: Right tibialis anterior. LTA: Left tibialis anterior. RGAS: Right gastrocnemius. LGAS: Left gastrocnemius. RSOL: Right soleus. LSOL: Left soleus

Figure 5-5 illustrates the mean number of discrete periods of activity for each muscle during the three cycles of overground walking around the speed change. It can be seen that the frequency of muscle activity in PwP was greater than the Ref. While the Ref group consistently produced 4 to 7 activity periods across the three cycles the PwP were much more variable with a generally higher number of activations with 3 to 15 active periods especially in soleus muscles. It seems that the two subgroups were different with a greater number of activations in the severe group with change speed.

## C) Magnitude of muscle activation (AUC)

The AUC is a unitless parameter indicating the intensity of magnitude of muscle activation amongst the Ref and PwP groups during the each cycles B, D and A of the change in speed for the six muscles of the lower limbs

Parameters			Ref			PwP					
		Mean									
			±SD					±SD			
			N=11					N=6			
	В	D	A	Change	Change	В	D	Α	Change	Change	
				B-D	D-A				B-D	D-A	
RTA	0.05	0.06	0.05	0.01	-0.01	0.05	0.06	0.05	0.01	-0.01	
	±0.04	±0.03	±0.03	±0.01	±0.02	±0.01	±0.02	±0.01	±0.02	±0.01	
LTA	0.05	0.07	0.08	0.02	0.01	0.05	0.09	0.09	0.04	0.00	
	±0.03	±0.06	±0.07	±0.03	±0.01	±0.02	±0.04	±0.05	±0.04	±0.01	
RGAS	0.12	0.18	0.18	0.06	0.00	0.05	0.10	0.09	0.04	-0.01	
	±0.29	±0.43	±0.42	±0.14	±0.02	±0.04	±0.08	±0.07	±0.04	±0.02	
LGAS	0.17	0.23	0.29	0.09	0.06	0.05	0.06	0.06	0.01	0.00	
	±0.24	±0.33	±0.40	±0.13	±0.10	±0.03	±0.02	±0.03	±0.01	±0.01	
RSOL	0.35	0.19	0.19	-0.16	0.00	0.34	0.45	0.50	0.11	0.05	
	±0.61	±0.28	±0.31	±0.57	±0.06	±0.62	±0.68	±0.85	±0.08	±0.17	
LSOL	0.24	0.21	0.23	-0.03	0.02	0.10	0.12	0.11	0.02	-0.01	
	±0.55	±0.36	±0.34	±0.19	±0.12	±0.14	±0.15	±0.14	±0.01	±0.01	

Table 5-8 AUC for the six muscles during the three cycles ('Before', 'During' and 'After') of changing speed for the Ref and PwP groups while walking over ground. (B-D) the change from Bef to Dur cycle and (D-A) the change from During to After cycle.

RTA: Right tibialis anterior. LTA: Left tibialis anterior. RGAS: Right gastrocnemius. LGAS: Left gastrocnemius. RSOL: Right soleus. LSOL: Left soleus. (NOTE: Values have been uniformly scaled up by 1000 to improve readability)

As can be seen in Table 5-8, both groups, in general, showed an increased magnitude of muscle activity with the change in speed (B-D), as might be expected. There was, however, a notable difference between the groups for the activity of soleus. In the Ref group the soleus activity, on both sides, decreased (R-0.16  $\pm$  0.57 and L-0.03 $\pm$ 0.19 ) during the change in speed while the PwP increased (R (0.11 $\pm$ 0.08 and L (0.02 $\pm$ 0.01)



Figure 5-6 The differences in magnitude of muscle activation (AUC) of the six muscles for the PWP subgroups (Moderate, and Severe) during the change in speed from the 'Before' cycle to 'During' cycle (B-D), and from 'During' to 'After' cycle (D-A). SWTA: Right tibialis anterior. STTA: Left tibialis anterior. SWGAS: Right gastrocnemius. STGAS: Left gastrocnemius. SWSOL: Right soleus. STSOL: Left soleus. (Values uniformly scaled up by 1000 to facilitate reading*)

There was a clear difference in muscle activation among the PwP subgroups, as shown in figure 5-6. The AUC shows that there was a greater increase in activation in RSOL by 0.16 from B to D cycle and decrease to 0.05 from D to A cycle.

Figure 5-7 illustrates the RSOL muscle activity within the three cycles for one participant from each group to show the relationship in muscle activation and disease severity. In the Ref group the soleus muscle is clearly activated twice, during early (20-30%) and mid/late (40-60%), stance, to control the forward rotation of the tibia, this is well described in the (Neptune et al, 2001). As the speed changes this pattern persists but the amplitude of activity decreases. In the two examples from the PwP group (mild/moderate and severe) it can be seen that while the early stance period of soleus can still be observed the second period is more delayed (around 60%) and appears to increase in magnitude across the three cycles spanning the change in speed, in contrast with the ref group.





Figure 5-7 The activation of the soleus muscle during the three cycles of walking on the treadmill for one participant from the Ref group (P6) and one each from the two PwP sub groups. The red line indicates the cycle 'Before', the green line indicates the cycle 'During', and the blue line indicates the cycle immediately 'After' the change in speed

# 5.2.2 Summary: Findings from the study on the increase in overground speed

From these results, it can be observed that there were some differences in the way the participants increased their overground walking speed, especially during the stance phase. The mechanism for increasing speed seemed to be based on a change in cadence; step length was not measured due to the lack of a measurement system, however, so this may have varied as well. It is interesting, nonetheless, that these findings differed from treadmill walking, where an increase in speed was linked with a decrease in cadence for the Ref group. The PwP had similar increases in cadence for both treadmill and overground walking. The Ref group showed an increase in cadence during overground walking, which was opposite to treadmill walking. There were also differences in the overall pattern of muscle activity during the increase in speed. Most notably the soleus muscle clearly decreased in the Ref group while the speed increase was being executed but it increased in the PwP, particularly in the severe participants.

# **Chapter 6 Discussion**

#### **6.1 Introduction**

This chapter is divided into four sections. The first section focuses on summarising and discussing the primary findings of the research. The purpose is to offer a clear and concise representation of the key discoveries the study has uncovered. In the second section, the findings are placed in the context of published literature. The third section will explain the findings through the lens of motor control theory, addressing whether the results support the theory's principles and augment the existing body of knowledge. These discussions will inspire the development of new research hypotheses. The fourth section outlines the limitations of the current study and provides recommendations for further research. The section serves to acknowledge the potential constraints of the methodology or data collection and to suggest improvements in areas that could enhance future studies. Before presenting these distinct sections, it is beneficial to revisit the overarching objective of this study.

The central aim was to investigate the biomechanical and muscle timing challenges faced by people with Parkinson's (PwP) when they initiate movement or change their walking speed, as might be experienced during community walking. This was achieved by measuring the changes in biomechanical attributes and muscle activity characteristics and comparing these changes with a reference group of physically fit individuals. Both treadmill and overground walking conditions were evaluated to provide a comprehensive understanding of the problem and valuable insight on the potential role of treadmill walking in future rehabilitation research.

#### 6.2 Summary of primary findings

#### 6.2.1 Gait Initiation: Treadmill and Overground

When initiating gait on a self-pacing treadmill the PwP group took less time (~8%) to complete than the Ref group ( $2.06 \pm 0.39$  s compared with  $2.25 \pm 0.42$  s) and spent less time, relatively, performing the swing (~2%) with more stance phase (~3%) compared to the Ref group. Similarly, the PwP group had approximately 5 degrees less movement at all the joints and less power at the hips (~16%) (PwP 12.11\pm0.8W/kg, Ref 14.45\pm0.5w/kg) and ankles (~1%) (PwP 5.99\pm0.7w/kg, Ref 6.80\pm0.5w/kg) compared to the Ref group.

Unsurprisingly the resulting speed was lower (17%) in the PwP group during the subsequent gait cycle ( $0.29\pm0.04$  m/s compared with  $0.35\pm0.11$  m/s).

In terms of muscle activity, a key finding was the longer period of soleus muscle activity in the PwP group (33.43% and 37.80%) compared with the Ref group (27.10% and 20.41%).

These findings differed somewhat when participants were asked to initiate gait in a more natural situation, overground. Both groups took less time to complete the movement overground, however, the Ref group took much less time ( $\downarrow$ 33%,1.49±0.56s) compared with the PwP who took more or less the same time as during the treadmill gait initiation ( $\downarrow$ 5%, 1.95±0.25s). A large part of this difference was observed during the initial phase (movement initiation to foot off) with the PwP taking almost 25% more time (0.26±0.13s versus 0.20±0.12s) to complete this initial movement.

While kinematic and kinetic variables were not available during the overground trials there was a similar finding of prolonged activity in the soleus and gastrocnemius muscles of the PwP which were active for more than twice as long as the Ref group (Soleus 56.19% and Gastrocnemius 58.74% compared with Soleus 24.64% and Gastrocnemius 21.21%).

In short, gait took around 2s to initiate and was quicker when attempted overground than on a treadmill, particularly for the Ref group. The PwP were generally slower, with less joint movement and joint power than the Ref group, when this could be recorded on the instrumented treadmill. Longer activity of the plantar flexor muscles was a hallmark of gait initiation for the PwP in both treadmill and overground conditions. These findings will be addressed in detail later in this chapter.

#### 6.2.2 Speed increases during walking on a treadmill and over ground

During the self-pacing treadmill exercise, the Ref group and the PwP increased their speed by approximately 12% and 6% respectively. The Ref group increased their step length by around 15%, (0.08+/-0.04 m) which was much greater than the PwP group, which only had a 6% (0.02+/-0.05 m) increase. The Ref group's step length did, however, decrease during the following cycle  $(0.06\pm0.58\text{m})$  while the PwP 's increased  $(0.02\pm1.5\text{m})$ . There was a small increase in hip and knee flexion of around 3 degrees in both groups, corresponding with the slightly longer step length. The ankle joint only showed a small (one to two degrees) change, for both groups. Cadence altered, but in different ways, with the Ref group briefly decreasing cadence (-4.42 +/-3.23; -4%) while the Parkinson's group increased (4.40+/- 10.19, +3%).

When it came to the power metrics, the Ref group had higher combined hip power during early stance, at around 0.26 W/kg, and around 0.04 W/kg at the ankle during pre-swing compared to PwP (0.06,0.01 W/kg). They also had a moderate increase in hip power during pre-swing at around 17% (0.17 W/kg). On the other hand, the PwP group showed increased hip power during pre-swing around 0.24 W/kg during moderate speed changes, but there were no real change in ankle power. The percentage of muscle activation during this increase in speed was largely observed in PwP with 15%, 2%, and 25% for Tibialis anterior, Gastrocnemius, and Soleus muscles while slightly decreased 3%, 2%, and 4% on Ref group.

When participants were asked to change their walking speed overground, both groups reduced their stride time, with the Ref group decreasing by about  $\downarrow 10\%$  and the PwP reducing by about  $\downarrow 9\%$ . Interestingly, when comparing muscle excitation during overground walking versus treadmill walking, PwP showed a decrease in percentage of muscle activation in the soleus and gastrocnemius muscles by about  $\downarrow 19\%$  and  $\downarrow 13\%$ , respectively, compared to the Ref group. So PwP reduced the excitation periods when trying to increase overground speed compared to Ref group who showed increased by 12% and 10%.

In summary, an increase in speed was executed over a shorter time when attempted overground than on a treadmill, particularly for the Ref group. Less joint movement and power were observed in the PwP in treadmill walking compared with overground. Finally, the plantar flexor muscles had longer activation periods during the treadmill speed increases compared with overground walking. These will be discussed in detail later in this chapter.

# 6.3 Comparison with Literature

## 6.3.1 Gait Initiation

The gait initiation (GI) process during overground walking has been extensively studied, as mentioned in Chapter 2, including works by Breniere and Do (1991), Novak et al. (2014), and Cau et al. (2014). However, the comparison of GI parameters in this study focuses exclusively on overground data, as there is a lack of available data for GI on a treadmill.

This aspect of the research contributes to the novelty of this thesis. It is important to mention that while kinematic and power data were not available, the study focused on electromyography (EMG) and spatiotemporal measures.

The results of the present study reveal that the group of individuals with Parkinson's disease (PwP) required a longer time  $(1.95 \pm 0.25s)$  to execute the gait initiation (GI) sequence during over ground walking, compared to the reference (Ref) group  $(1.49 \pm 0.56s)$ . These findings align with previous studies conducted by Roemmich et al. (2012), Rosin et al. (1997), and Deval et al. (2014), which also reported longer GI times for PwP compared to control groups. Specifically, Roemmich et al. (2012), Rosin et al. (1997), and Deval et al. (2014), Roemmich et al. (2012), Rosin et al. (1997), and Deval et al. (2014), Roemmich et al. (2012), Rosin et al. (1997), and Deval et al. (2014) reported GI times of  $0.58 \pm 0.1s$ ,  $0.57 \pm 0.1s$ ,  $1.32 \pm 2.0s$ ,  $1.9 \pm 0.3s$ , and  $0.53 \pm 0.14s$ ,  $0.51 \pm 0.01s$  for PwP compared to control groups, respectively. Despite variations in the definition of GI among these studies, they consistently demonstrated longer GI times for individuals with Parkinson's disease.

It should be noted that in the present study, GI was measured from the onset of movement until the second heel contact, as described in Chapter 3. In contrast, the previous studies calculated GI only until the first heel contact of the swing side. This accounts for the longer time (approximately 0.5 to 1s) reported in this study. The rationale behind including a longer period in this study was to ensure that both sides had completed a full step sequence, allowing for a comprehensive comparison between the leg that swings first and the one that follows.

The current study's findings, however, contradict those of Okada et al. (2011), who reported longer GI times in healthy individuals  $(0.53 \pm 0.01s)$  compared to PwP  $(0.52 \pm 0.02s)$  using a similar methodology of calculating GI until the second heel contact. The discrepancy in results could be attributed to differences in the method of calculation, as the current study utilised inertial measurement units (IMUs) while Okada et al. used force plates embedded in an instrumented walkway.

In the current study, there were slight differences in the time of the gait initiation (GI) sequence between treadmill and over ground walking. Both groups exhibited a GI period that was 0.50s shorter during over ground walking compared to treadmill walking. The disparity in time for treadmill walking may be attributed to the restricted walking space and the use of a safety harness. However, further investigation is needed to confirm this possible explanation.

The longer GI sequence times observed in individuals with Parkinson's disease (PwP) are likely related to a reduced joint movement at the hips, knees, and ankles within this group. Advanced stages of the disease have been associated with less joint movement compared to milder and moderate stages (Schrag et al., 2000).

Regarding muscle activation during overground walking, the PwP group demonstrated longer periods of activation in all six measured muscles during GI compared to the Ref group, with the exception of plantarflexors (Gas and Sol) on the initiating side, which showed approximately over 58% and 56% activation time in PwP compared to 21% and 24% in the Ref group, respectively. Hiraoka et al. (2005) also reported that the soleus muscle was active for approximately 75% of GI in PwP, inhibiting the forward rotation of the body and delaying the dorsiflexion of the ankle during GI. The prolonged activation of the soleus muscle promotes anterior and medial deviation of the centre of pressure (COP), leading to a freezing pattern that prolongs movement initiation. This delayed deviation of COP is caused by abnormal pauses in the soleus and tibialis anterior (TA) muscles, disrupting the sequence and increasing the overall time required to execute GI, potentially leading to a gait freezing event (Warabi et al., 2017). Furthermore, TA activation on the swing side in the current study lasted for 47% of the period in PwP compared to 43% in the Ref group. Additionally, a study by Mickelborough et al. (2004) observed that TA activation during GI among healthy participants reached 56% of the activation time of muscle activation, which is the relative time observed in the current study among healthy participants.

Moreover, our study found notable differences in gait initiation between treadmill walking and overground walking. PwP demonstrated twice the muscle activation time compared to the Ref group during treadmill walking, consistent with previous studies by Neptune et al. (2001) and Hiraoka et al. (2005). The significance of this finding lies in understanding the motor control adaptations and challenges that individuals with Parkinson's disease experience during treadmill walking. The specific reasons for this discrepancy will be discussed in more detail in Section 6.4 of the motor control part of this study. This finding aligns with the observations made by Kibushi et al. (2008), Brouwer et al. (2009), and Khademi-Kalantari et al. (2017), who suggested that healthy individuals may require additional muscle effort and engage different muscles during walking on a treadmill compared to those typically used for speed control, ensuring postural control and safety.

#### 6.3.2 Change speed (increase speed)

While the number of studies assessing speed change in both treadmill and over ground walking for both groups is limited, several papers have explored gait speed variation on both surfaces (Chee et al., 2009; Segers et al., 2006; Li & Hamill, 2002; Sun et al., 2018; Riley et al., 2001). In our current study, we analysed three consecutive gait cycles around the time of a speed change, namely before, during, and after. During treadmill walking, the PwP group demonstrated a speed increase of  $0.06 \pm 0.08$  m/s when asked to walk "faster," while the Ref group produced double this increase:  $0.12 \pm 0.06$  m/s. This finding aligns with Li & Hamill's 2002 study, where they observed five steps during the transition of speed change in 20 young healthy participants on a fixed-paced treadmill, reporting a mean speed increase of 0.20 m/s in healthy individuals, despite variations in sample size and calculation methods.

On the other hand, Segers et al. (2006) reported that healthy individuals were capable of transitioning from a normal speed to a faster pace during fixed-paced treadmill walking, showing an approximate increase of  $2.16 \pm 0.12$  m/s, which is notably higher than the speed increase observed in our current study ( $0.12\pm0.06$  m/s). The considerable difference in findings could be attributed to variations in methodology, as Segers et al. (2006) calculated the speed transition by having participants perform five blocks of speed changes (0.05, 0.07, 0.1 m/s) and observing the speed transition by giving -1, 0, or +1 for each cycle. Additionally, Segers et al. (2006) used a larger sample size of twenty healthy female participants, and their treadmill was fixed, while our current study utilised a self-paced system that might have affected participant speed (Ibala et al., 2019).

There is indeed a lack of specific evidence concerning speed changes during treadmill walking in individuals with Parkinson's disease (PwP). If available, the limited studies have focused on the calculation of variability of speed patterns. For instance, Peterson et al. (2020) investigated spatiotemporal parameters during speed changes from a comfortable pace to a faster pace among PwP. In their study, they examined 67-year-old PwP during OFF medication, and the control group consisted of individuals with other neurological conditions (n=40) matched for age. Participants were asked to walk at their preferred speed for two minutes and then at a faster pace for another two minutes on walkway.

The findings of Peterson et al. (2020) revealed that both groups exhibited larger stride length, cadence, and swing time during faster walking compared to their comfortable

speed. However, PwP demonstrated less improvement in these parameters compared to the control group. Specifically, PwP exhibited stride length 0.11m, cadence 12.02 steps /min, respectively, compared to the control group with increases of 0.12 m, 16.92 step /min , respectively. These differences were statistically significant (p<0.001). The current study could not reach the same level of differences during over-ground walking, it showed mean differences in swing time during change speed for PwP of 3.93% and 2.64% compared to the control group, while Peterson et al. (2020) showing mean differences for swing time around 2.22% in the control group which were double to 1.71% in PwP.

The discrepancy in the observed differences between the current study and Peterson et al. (2020) could be influenced by the medication status of PwP. In the current study, PwP were on ON medication, while Peterson et al. (2020) assessed PwP during OFF medication. Medication status may affect motor performance and variability. Moreover, variations in methodology could contribute to differences in the results. The current study calculated speed based on walking in a 10-meter corridor with only four steps and asking for a change on the fifth step. This methodological difference could impact the observed differences in spatiotemporal parameters during change speed overground. Furthermore, the current study conducted assessments in a corridor using IMU without camera tracking, while Peterson et al. (2020) utilised an open lab environment, which might have provided more open space to minimize environmental stimuli that could provoke freezing (Fahn, 1995).

Additionally, it should be noted that the control group in Peterson et al. (2020) was agematched with PwP and had other neurological conditions, while the current study had healthy and young individuals as the control group. These differences in participant characteristics may have contributed to variations in the measured parameters during speed change between the two studies.

Regarding the Ref group in the current study, they exhibited an immediate change in step length, increasing it by  $8.80 \pm 1.9$  cm, to achieve a new faster walking speed on the treadmill. In contrast, the PwP group only generated a smaller step length change of  $1.0 \pm 2.2$  cm during treadmill walking. A similar study by Segers et al. (2006) observed that healthy participants were able to increase their step length with speed changes during treadmill walking, but with a twofold greater distance of  $20 \pm 0.05$  cm. These differences in step length adjustments between the studies could be attributed to variations in methodology and the larger sample size of healthy individuals in the study by Segers et al. (2006). As for the modulation of cadence during treadmill walking in the current study, as walking speed increased, the Ref group exhibited a decrease in cadence  $(-4.42 \pm 3.23)$ , while the Parkinson's disease (PwP) group demonstrated an increase in cadence  $(2.40 \pm 10.19)$ . It is important to note that there is limited existing literature specifically analysing cadence during treadmill walking. Cadence is influenced by both step length and stride time when adjusting speed. In our study, PwP reduced their step length and cycle time to modulate walking speed in response to visual cues on the treadmill screen, which potentially led to an increased cadence. On the other hand, the Ref group increased their speed immediately through a change in step length rather than cadence adjustment. These findings highlight the different strategies employed by the two groups in response to changes in walking speed on the treadmill.

Our study's findings are consistent with those of Riley et al. (2001), who observed increased cadence in healthy participants ( $0.2 \pm 0.05$  steps/meter). However, a study by Bayle et al. (2016) reported opposite results during over ground walking, noting a correlation between increased step length (R=0.05, P<0.0001) and reduced cadence with speed changes (R=0.11, P<0.0001) among healthy individuals. In contrast, in individuals with Parkinson's disease (PwP), cadence increased (R=0.44, P<0.0001), which aligns with our study's findings. The differences in cadence responses between healthy individuals and PwP emphasize the importance of considering the specific population when studying speed change during walking. Moreover, it should be noted that cadence differed between the two walking surfaces (treadmill and over ground) for both the Ref group and the PwP group. These differences in cadence could be attributed to spatial constraints imposed by the treadmill, as suggested by Nagano et al. (2013). The treadmill's confined space may influence the step size and, consequently, the cadence during speed changes. The presence of spatial limitations on the treadmill may explain the variations in cadence observed between treadmills and over ground walking. Lastly, in our study, cadence was calculated as the stance time divided by 60, as the measurement period only included three sequential gait cycles and not a complete minute. Therefore, the calculated cadence represented a surrogate measure due to the limited time frame of measurement. Despite this limitation, our study was able to provide valuable insights into the cadence patterns during speed changes in both the Ref group and the PwP group.

There is a notable gap in research investigating the kinetics and kinematics of speed change during walking on a self paced treadmill. Most studies have primarily focused on analysing these variations during over ground walking (Segers et al., 2002; Riley et al., 2001; Bayle et al., 2016; Svehlik et al., 2009). For instance, Riley et al. (2007) specifically explored kinetic and kinematic parameters in healthy individuals at their preferred walking speed but did not investigate speed changes. Therefore, there is a clear need for further investigation to understand the effects of speed modulation on a treadmill, particularly in both individuals with Parkinson's disease (PwP) and healthy individuals.

In the current study, both groups exhibited comparable results regarding the percentage of muscle activation during speed increase on the treadmill. Specifically, individuals with Parkinson's disease (PwP) increased the percentage activation of all lower limb muscles activation by more than 15%, transitioning from 40% during their self-selected speed to over 55% with the speed increase. The percentage of the muscle activation for all six muscles in both limbs during speed modulation was calculated by dividing the time each muscle was active during the walking cycle by the total time of the walking period and multiplying it by 100.

In contrast, the reference (Ref) group in our study demonstrated a decrease in muscle activation from over 52% to 48% during speed changes, except for the LSOL muscle, which showed an increase from 33% to 51%. These findings diverge from the results reported by Hagio et al. (2015), Kibushi et al. (2018), and Den Ottar et al. (2004), all of which pointed to increased muscle activation with speed changes.

Hagio et al. (2015) conducted a study on fixed-pace treadmill walking with five healthy young participants. They asked the participants to start walking at 3.0 km/h, with the treadmill speed continuously increasing by 0.1 km/h every 1 second. The data were analyzed for 8 steps before and 8 steps after the speed transition, totalling 17 cycles. Hagio et al. (2015) observed an increase of 30-40% in SOL muscle activation during speed increases on both sides in healthy individuals, whereas our study demonstrated a reduction of 4% in RSOL muscle activation and an increase of 16% in LSOL muscle activation during speed changes.

Similarly, Kibushi et al. (2018) reported contrasting results to our study, showing an increase of 75% in plantar flexors (SOL and GAS) and 80% in dorsiflexors (TA) muscle activation during fixed pace treadmill walking in healthy participants. Den Ottar et al. (2004) also found that muscle activation in the lower limb (GAS, SOL, and TA) decreased as treadmill speed reduced, with percentages reaching 39.9%, 24.4%, and 31.8% among healthy individuals. It is important to note that while our study examined muscle activation during speed increases, Den Ottar et al. (2004) focused on muscle activation during speed

reductions. Nonetheless, the underlying principle of the ability to modulate speed remains consistent.

Furthermore, our study's findings contradict those of Albani et al., (2003) regarding muscle activation of the lower limb during speed changes on the fixed pace treadmill among individuals with Parkinson's disease (PwP). Albani et al. (2003) conducted a study with a group of 10 participants diagnosed with Parkinson's disease (PwP), averaging 63 years of age, along with seven healthy controls. They reported a reduction of approximately 30% in GAS muscle activation with an over activation of the TA muscle by 70% at increased treadmill speeds in PwP. These discrepancies between studies highlight the complex nature of muscle activation during speed modulation and underscore the need for further research to fully understand these variations in different populations and contexts. Additionally, their research focused on measuring the activity of the gastrocnemius and tibialis anterior (GAS and TA) muscles during fixed pace treadmill walking at slow (0.30 m/s) and fast (1.5 m/s) speeds. At the slow speed, the GAS muscle demonstrated reduced activation in both PwP groups, approximately 30%, compared to the control group, which showed 50% activation during the stance phase (p<0.0001). Conversely, during the swing phase, the TA muscle showed greater increase in the percentage of muscle activation in both PwP groups, reaching 60%-70%, while the control group exhibited 30-40% activation (p<0.0001). When the speed was increased to 1.5 m/s, the PwP group exhibited a more significant reduction in GAS muscle activation than the control group (p<0.0001), coupled with an over activation of the TA muscle in PwP compared to the control group (p<0.0001). This observation suggests that the impairment in planter flexor muscles and the increased activation of dorsiflexors may represent a fundamental distinction between normal subjects and PwP patients, regardless of the presence of a gait disorder. The weakness in planter flexor muscles and the resultant activation pattern of the dorsiflexors may help explain the characteristic flexed posture often observed in individuals with Parkinson's disease.

The disparities in muscle activity observed between the studies conducted by Albani et al. (2003), Hagio et al. (2015), and our current study may be attributed to variations in methodology. For instance, Albani et al. (2003) specifically examined muscle activation during slow and fast speeds on a fixed pace treadmill, focusing on PwP and healthy controls. On the other hand, Hagio et al. (2015) explored muscle activation during continuous speed changes on a fixed pace treadmill in healthy individuals. Similarly, our study aimed to understand muscle activation during speed increases on a self-pace treadmill for both PwP and the reference group. These differing methodologies, along with

the distinct populations studied as well as the type of treadmill pace(fixed or self pace, could account for the observed differences in muscle activation patterns. To further understand these variations and their implications, additional research is warranted, exploring muscle kinetics and kinematics during speed modulation in diverse populations and contexts.

Hagio et al. (2015) utilised a different approach in their study, calculating muscle activation over a total of 17 cycles, encompassing 8 steps before and after the speed change. In contrast, our current study focused on three sequential gait cycles during speed changes, as described in Chapter 3. Additionally, the mode of treadmill control differed between the studies. While our study employed a self-paced system controlled by participants themselves, Albani et al. (2003) and Hagio et al. (2015) utilized a fixed-speed treadmill, which could potentially influence the time of muscle activation (Ibila et al., 2019). These variations in methodologies, the process of calculating speed changes, and the sample sizes used can all contribute to the nuanced interpretation of results.

During over ground walking, the Reference (Ref) group demonstrated an increase in the percentage of muscle activation by 2% and 10% for the muscles involved in dorsiflexion and plantar flexion on the right side, while the left side muscles exhibited a decrease in activation by 14% and 4%. In contrast, the Parkinson's disease (PwP) group showed an opposite pattern, with an 8% increase in activation on the left side muscles and a decrease of 7%, with a more pronounced reduction of 19% in the right soleus (Sol) muscle.

An essential consideration is that the two groups did not follow a unified approach in terms of the specific side from which they initiated speed changes. The Ref group initiated speed changes from the left (LT) side, whereas the PwP group did so from the right (RT) side. Therefore, the observed differences in muscle activation between the groups are specific to the side from which each group initiated their speed changes.

The implications of the differences in speed change findings are significant for gait control and motor function in PwP. The ability to change speed is crucial for adapting to various walking conditions, avoiding obstacles, and maintaining stability during locomotion, all of which are fundamental to community mobility. The observed disparities in speed change between PwP and the reference group offer valuable insights into the motor impairments associated with Parkinson's disease. The reduced ability of PwP to change their walking speed on the self-pace treadmill suggests potential difficulties in adjusting their gait patterns to accommodate changes in task demands. These difficulties may be attributed to underlying motor impairments, such as bradykinesia and reduced proprioception, commonly observed in Parkinson's disease. The findings underscore the impact of the disease on the capacity to adapt and respond to speed variations, which can have profound implications for functional mobility and overall quality of life. Further research in this area is warranted to better understand the intricate motor control challenges faced by individuals with Parkinson's disease and to explore potential interventions for enhancing the change gait speed and community mobility in this population.

# 6.3.3 A possible reason for the differences between PwP and Ref group during change speed

In general, the PwP demonstrated smaller speed changes with smaller changes in joint rotation and reduced power compared to the Ref group during gait initiation (GI) on different walking surfaces. Hiraoka et al. (2005) suggested that this may be due to the PwP's concerted efforts to maintain postural stability or due to impairment in motor function.

These findings confirm the results of Capady & Stain (1986), Neptune et al. (2000), Mickleborough et al. (2004), and Delafontaine et al. (2021) and emphasize the need for heightened postural control in PwP to ensure stability during destabilizing movements such as GI.

PwP produced less power from the swing side hip during push-off, which could possibly be due to reduced temporal separation of the Center of Pressure (COP) and Center of Gravity (COG), thereby limiting postural adjustment flexibility (Roemmich et al., 2012). This suggests that enhancing hip power during the stance phase may contribute to improving stability in PwP (Lu et al., 2017).

The current study also observed differences between the two walking surfaces for both groups, which could support Nagano et al. (2013), who suggested that safety-related gait adaptations on a treadmill require greater balance control from participants, potentially affecting GI timing compared to over-ground walking.

Overall, during speed change, the time available to generate the new speed reduced with the severe group more than moderate of Parkinson's disease. This is due to the increasingly shorter step length and the challenges of maintaining posture during a change in speed on the treadmill. Morris et al. (2005) reported that PwP has an impaired ability to alter step length and consequently speed during an environmental change.

The current study showed differences in cadence between both groups, which may be influenced by step length and stride time during speed changes. Bello et al. (2014) supported the notion that changing cadence is preferred by PwP during treadmill walking to enable the maintenance of continuous walking, without falls, during speed changes.

During increased speed while walking on a treadmill, the percentage of muscle activation among PwP increases and that may raise the risk of falls (Khademi-Kalantari et al., 2017). It can be suggested that PwP compensates for this by producing shorter steps during speed changes, thus adopting a safer strategy (Klamroth et al., 2016).

## 6.4 Exploring the Implications of our findings within the Context of Motor Control Theory



Figure 6.1 The direct and indirect pathways (A) healthy BG, (B) the Parkinson's disease pathway. The "no entry" sign represent the inhibition or reduction of specific process

This schematic illustration depicts the normal as healthy and the disruption of the direct and indirect pathways in Parkinson's disease, leading to unwanted stimulation of limb muscles during movement. In the normal basal ganglia circuitry, the direct pathway facilitates movement initiation and speed regulation. However, reduced dopamine production in the substantia nigra pars compacta inhibits the production of gamma-aminobutyric acid (GABA) neurons in the striatum, resulting in decreased GABAergic output from the substantia nigra reticulata (SNr)/internal segment of the globus pallidus (GPi) to the thalamus. This increased inhibition of the thalamus diminishes excitatory output to the motor cortex, causing characteristic motor deficits such as bradykinesia, rigidity, and tremors. Conversely, reduced dopamine levels lead to hyperactivity in the indirect pathway, characterized by diminished GPe (globus pallidus external) inhibition by the striatum, subsequently increasing inhibitory signals from GPe to the subthalamic nucleus (STN). Consequently, the STN overactivity intensifies inhibitory output from basal ganglia output nuclei (SNr, GPi) to the thalamus, further reducing excitatory output from the thalamus to the motor cortex. This exacerbates motor impairments, contributing to increase the unwanted movement at limbs. The red arrows depict inhibitory processes mediated by GABA neurons, while the green arrows indicate excitatory processes by glutamate neurons. The "no entry" signs represent inhibition or reduction of specific processes.
As shown in figure 6.1, In a healthy brain, the direct pathway enhances dopamine production in the substantia nigra (SN), leading to the activation of the striatum. Striatum activation inhibits the substantia nigra reticulate neurons (SNr), stimulating the thalamus, ultimately exciting cortical function to produce motor activity (Frohlich, 2016). Conversely, the indirect (hypokinetic) pathway inhibits the globus pallidus (GP) and the thalamus through the neurotransmitter GABA, resulting in inhibitory cortical activity. Dopamine receptors, specifically D1 and D2, play crucial roles in the striatal neurons of the substantia nigra. D1 activates the direct pathway, promoting hyperkinetic movement, while the D2 dopamine receptor system initiates the inhibitory pathway. D3 receptors, though less distinct in function in healthy conditions, share a similar role with D2 receptors. Furthermore, in healthy individuals, gait initiation involves an anticipatory postural adjustment (APA) phase preceding and accompanying the stepping phase. APAs for forward stepping entail a sequence of muscle activations and changes in ground reaction forces (GRFs) that move the net center of pressure (CoP) beneath the feet backward and toward the initial swing limb. This motor sequence produces forces and moments necessary to propel the body center of mass (CoM) forward in the intended stepping direction.

During gait initiation, complex interactions among lower limb muscles generate forces separating the center of pressure (CoP) from the center of mass (CoM), creating the forward propulsion moment (Fiolkowski *et al.*, 2002). Plantarflexion is resisted by dorsiflexion moments of dorsiflexor muscles, particularly the tibialis anterior, providing controlling eccentric contractions (Perry and Burnfield, 2010; Richards, 2018). Gastrocnemius and soleus muscles lock the ankle, causing the heel to rise during tibial advancement. The ankle dorsiflexes to a maximum of 10 degrees, followed by plantarflexion in response to the gastrocnemius and soleus muscles, known as push-off (Perry and Burnfield, 2010). The body weight is then transferred to the other limb in preparation for movement. According to the equilibrium-point hypothesis, muscle activation increases through stretch reflex pathways, stabilizing the equilibrium point as external forces change (Latash et al., 2010). Motor neurons receive signals from the brain in response to sensory feedback, converting them into changes in threshold muscle lengths or joint angles. This spatial activation range allows the central nervous system (CNS) to specify muscle activation without precise details of when and how they are triggered.

In summary, the equilibrium-point theory examines how the nervous system interacts with the body and the environment, producing purposeful, coordinated movements. Motor control involves the CNS finding potential solutions using available degrees of freedom rather than prescribing specific movement patterns. This principle should guide therapeutic interventions for patients with motor deficits, shaping approaches to improve or restore normal movement. However, individuals with neurological conditions like Parkinson's struggle to adapt movement to environmental changes. The next section elucidates how individuals with Parkinson's (PWP) can compensate for this challenge. This study's key finding reveals that individuals with Parkinson's disease (PwP) exhibit prolonged muscle activation times, especially in the soleus muscle, during gait initiation and when instructed to increase speed on a self-paced treadmill. Nevertheless, the percentage of muscle activation increases in PwP compared to the reference group during overground gait initiation and speed changes. The inhibition of the soleus during standing facilitates tibial anterior rotation and the elevation of the heel from the ground (Chapter 2). However, persistent soleus activation hinders the forward progression of the tibia, contributing to freezing of gait (FOG), as depicted in Figure 6.2.



Figure 6.2 demonstrates the crucial role of timely inhibition of the soleus muscle in facilitating the forward rotation of the tibia (and consequently, the entire body) during gait. This rotation enables the foot to elevate in preparation for the toe-off and swing phase (copyright, 2011 Wolters Kluwer Health, Lippincott Williams & Wilkins).

The soleus muscle plays a pivotal role in maintaining stability during static postures such as standing and dynamic activities like walking (Sherbondy et al., 2003). Moreover, PwP tend to keep the plantar flexor muscles mainly (solus) contracted for longer time compared to Ref group. This prolonged muscle activity interferes with the gravity-assisted forward rotation of the body, which is facilitated by the separation of the Center of Pressure (CoP) and Center of Mass (CoM). Consequently, it adversely affects the timing of subsequent events during both gait initiation and speed increase. The coordination of muscle excitation states is regulated by various brain centres, with the basal ganglia playing a crucial role in this process (Monchi et al., 2006).

Our findings indicate that PwP displays longer muscle activation periods specifically during gait initiation and speed increase when compared to the Ref group on both surfaces of walking. This underscores the significance of the altered muscle excitation pattern observed in PwP and its potential impact on motor control. While the current study highlights the association between prolonged muscle activation and alterations in basal ganglia circuitry, it is important to acknowledge that direct evidence linking the basal ganglia to the observed muscle activity during speed change requires further investigation. Considering these results, it is crucial to discuss and explore the comprehensive relationship between the altered muscle excitation pattern observed in PwP and the regulatory role of the basal ganglia in motor control (Monchi et al., 2006).

The disrupted balance and postural control observed in individuals with Parkinson's disease (PwP), as described in the previous paragraph, can be attributed to the degeneration of dopaminergic neurons in the substantia nigra pars compacta, which leads to an alteration in the fine-tuning of motor control by the basal ganglia see figure 6.1 (B) for PWP. Dopaminergic neurons in the substantia nigra pars compacta, establish synaptic connections and transmit their neural outputs to the striatum to regulate the motor function were degenerated in PwP, resulting in the disruption of the balance between the direct (D1 receptor-mediated, excitatory) and indirect (D2 receptor-mediated, inhibitory) pathways of the basal ganglia (Obeso et al., 2008). This disruption is commonly considered to be the underlying cause of the classic motor symptoms of PwP, including rigidity, bradykinesia, postural instability, and gait freezing. These symptoms were also investigated in the study conducted by Smith et al. (2021) (4). The findings of their study align with the notion that the impaired balance and postural control observed in people with Parkinson's disease (PwP) may be attributed to the disruption in the fine-tuning of motor control by the basal ganglia. It is worth noting that the role of the soleus muscle in postural control and stability during standing and walking has been well-documented (5). Furthermore, the extended activation time for the tibialis anterior during the gait initiation phase, and the reduced activity periods in severe PwP could be associated with the impairment of the direct and indirect pathways. Impairment of the direct pathway can have different effects on the soleus muscle during walking.

Disruption in dopamine production from the substantia nigra (SN) impairs the inhibition of the thalamus, resulting in excessive activation. This excessive activation affects specific areas of the cortex, such as the motor cortex, which ultimately causes excessive movement. On the other hand, in the case of indirect pathway dopamine depletion, the production of neurons in the subthalamic nuclei (STN) is inhibited. This disruption affects the normal process of neuron transmission. It's important to know that in healthy individuals, the direct and indirect pathways do not work in isolation and interact with each other to regulate movement initiation (direct pathway) and the ability to inhibit unwanted movement (indirect pathway). Therefore, impairment of either or both pathways can have complex effects on motor control that can vary depending on the specific circumstances and individual differences. The decreased activity period in severe Parkinson's disease patients could reflect exhaustion or failure of compensatory mechanisms, such as the dopaminergic system, that is typically responsible for maintaining normal movement functions as summarised in Figure ( 6-2). This imbalance can contribute to the prolonged muscle activation times and differential speed changes observed in muscle activation patterns (Ting & McKay, 2007; Ivanenko et al., 2004). Therefore, therapies aimed at restoring the balance between these pathways may help improve motor control and balance in individuals with Parkinson's disease (PwP).

# 6.4.1 Possible Intervention may improve the imbalance between both pathways.

One potential approach to address this imbalance is by focusing on interventions aimed at improving central nervous system (CNS) function (Behrman et al., 2000; Bhalsing et al., 2018). Cognitive training, for example, involves exercises and tasks that challenge cognitive abilities such as attention, memory, and problem-solving. By engaging the brain in these activities, cognitive training has shown promise in enhancing overall CNS function, which could lead to improvements in lower limb function and movement quality in PwP (Fisher et al., 2008; Jackson et al., 2016; Pompeu et al., 2012). Another avenue to explore is the use of specific medications targeted at addressing the underlying imbalances in the CNS. These medications work by influencing the levels of neurotransmitters in the brain that are involved in movement regulation, such as dopamine. By restoring the balance of these neurotransmitters, these medications can help improve muscle function and coordination, thereby enhancing overall motor control and balance in PwP (Barone, 2010; Devos et al., 2010).

In addition to interventions aimed at improving CNS function, targeted muscle training can also play a crucial role in addressing muscle imbalances and enhancing overall motor control, complementing the comprehensive approach to improving motor function in people with Parkinson's disease. By focusing on specific muscle groups and engaging in targeted exercises, PwP can improve muscle strength, flexibility, and coordination. It is worth noting that targeted muscle training not only directly improves muscle function but also has the potential to indirectly enhance CNS function and overall coordination (Schenkman *et al.*, 1998; van der Kolk & King, 2013). Furthermore, rehabilitation approaches in PwP focus on modulating muscle activation during walking by using cues or external stimuli to enhance motor planning and coordination (Hiraoka et al., 2005), and specific exercise programs targeting the muscles involved in gait initiation. Considering these observations, strategies targeting the soleus muscle for purposeful deactivation, such as motor control therapy, have been implemented. Motor control therapy involves specific interventions aimed at training and optimising the function of the lower limb muscles.

The therapeutic landscape for functional rehabilitation encompasses various interventions, among which cueing therapy stands out as a noteworthy example (Wegan et al., 2015; McCandless et al., 2016; Clark et al., 2018). In a systematic exploration of cueing therapy's impact on gait and balance in individuals with Parkinson's disease, Clark et al. (2018) revealed its efficacy. This approach, involving external cues such as auditory or visual prompts to enhance movement, exhibited substantial improvements in gait and balance, especially during dual-task activities. The findings from this study highlight cueing therapy as a promising intervention for addressing gait and balance challenges in Parkinson's disease. Another significant approach for functional rehabilitation is the utilization of balance boards, as underscored by Mhatre et al. (2013). Investigating the effectiveness of a Wii FitTM-based balance board exercise program in the elderly population, Mhatre et al. demonstrated compelling results. The exercise regimen, which provided visual feedback on balance performance, led to substantial enhancements in balance and a reduction in the risk of falls. The intervention group, compared to the control group, exhibited noteworthy progress in balance performance and a decrease in fall risk. Consequently, Mhatre et al. concluded that the Wii FitTM balance board exercise program represents a valuable tool for augmenting balance and mitigating fall risk among older adults.

In the context of functional rehabilitation, these interventions, particularly cueing therapy and balance board exercises, signify promising avenues for improving motor function and addressing challenges associated with gait and balance. Consideration of these therapeutic approaches is crucial for devising comprehensive and effective rehabilitation strategies tailored to the unique needs of individuals undergoing functional rehabilitation. In summary, the study findings indicate that alterations in kinaesthetic perceptions may arise due to impaired basal ganglia and neural functions, as these components are recognised for their significant involvement in motor functions. However, it is important to note that this study does not provide direct evidence regarding the functioning of the basal ganglia in these participants.

## 6.4.2 The Modified Equilibrium Point Hypothesis for Parkinson's Disease: Exploring Impaired Motor Control and Muscle Activation Patterns

The increased activation period observed in the soleus muscle in PwP can be understood by considering the concept of the equilibrium point hypothesis (EPH), a novel hypothesis proposed in this study. The EPH proposes that the nervous system uses sensory feedback to establish and adjust the resting position of muscles during movement in real-time. In simpler terms, the central nervous system (CNS) regulates limb movements by making small adjustments to the position where the muscles are at rest. This concept, previously discussed by Latash and Yamagata (2022), highlights the important role of the CNS in controlling limb movements. The EPH provides a framework for explaining the impaired dynamic stability, and the difficulties in which PwP experience maintaining a steady and controlled movement pattern, leading to variations in the lower limb muscles activation. This instability can make it challenging for PwP to control the trajectory of their body segments, especially when faced with external force perturbations (Ricotta & Latash, 2021). In addition to the EPH, Latash (2012) introduced the concept of "abundance" to describe the inherent variability in movement patterns. The principle of abundance suggests that the brain's capacity to learn and perform new tasks is enhanced by motor abundance, which provides greater stability and flexibility during movement (Bernstein, 1967; Latash, 2012). In other words, having a certain degree of variability in movement patterns allows the brain to adapt and respond effectively to different task demands.

Based on the current investigations and supporting evidence from different studies, the present study proposes a Modified Equilibrium Point Hypothesis for Parkinson's Disease (mEPH-PD). This hypothesis expands on the equilibrium point hypothesis (EPH) and incorporates additional elements observed in Parkinson's Disease, such as prolonged muscle activation, specific changes in gait, and the role of dopamine production in the Basal Ganglia (BG). The mEPH-PD theory suggests that Parkinson disease affects the brain's ability to control muscles properly. This happens because there are problems with certain pathways in the brain called dopaminergic pathways, specifically within a region called the basal ganglia (BG) as mentioned previously. This impairment leads to inefficient motor command and

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control from the central nervous system (CNS) and contributes to observed phenomena in PD.

Figure 6.3 The concept of equilibrium using a seesaw analogy.

The seesaw represents the neural control system, while the equilibrium point indicates the balanced state of muscle activity(A). In the presence of PD, the impaired dopaminergic pathways in the BG disrupt the precise positioning of the equilibrium point, leading to an imbalance in muscle control (B), (C) demonstrating the prolonged activity associated with PwP. By shifting the equilibrium point to the left or right, we depict the persistently heightened or reduced muscle activity observed in PD, respectively. This illustration serves to highlight the consequences of impaired dopaminergic pathways on the equilibrium points and subsequent motor control in PwP.

In summary, this study introduces the novel mEPH-PD hypothesis, which offers a scientific framework to understand the increased activation period observed in the soleus muscle of individuals with Parkinson's disease (PwP). By investigating the variations in the percentage of muscle activation and motor control strategies between treadmill and overground walking in PwP, the study reveals that both walking methods engage similar muscle groups but differ in their utilisation and coordination. The increased percentage of muscle activation on the treadmill indicates that PwP exerts greater effort and engage muscles for extended periods to maintain stability and control their gait. This can be attributed to the constant belt speed of the treadmill, leading to alterations in muscle activation and coordination, as reported by (Ibala et al., 2019). By using this novel hypothesis, researchers can explore targeted therapeutic interventions to alleviate symptoms and enhance movement and balance control in PwP, potentially leading to new therapeutic strategies for symptom alleviation. Moreover, understanding the differences between treadmill and overground walking is crucial for developing tailored rehabilitation strategies and interventions that optimize gait patterns and improve motor control in PwP. This knowledge can also contribute to the development of assistive devices or technology designed to inhibit muscle activity and better accommodate

the challenges faced by PwP during treadmill walking. Ultimately, by focusing on improving speed change capabilities, clinicians and researchers have the potential to enhance gait control, functional mobility, and overall motor performance in individuals with Parkinson's disease, thereby improving their quality of life and independence.

In summary, the biomechanical and muscle timing challenges investigation during gait initiation and speed changes in individuals with Parkinson's disease (PwP) has been successfully accomplished by this study, fulfilling its primary objectives. The research employed representative samples and collected extensive data on biomechanical attributes and muscle activity, comparing key variables across various gait cycles in both treadmill and overground conditions. The findings shows distinct differences between PwP and the reference group, providing valuable insights into the unique characteristics of gait initiation and speed changes in Parkinson's disease. However, it is crucial to acknowledge certain limitations in the study. Notably, the absence of kinematic and kinetic variables during overground trials restricts a comprehensive examination of these aspects, which might have further enhanced the scope of the study objectives. Despite these limitations, the study lays a solid foundation for future research endeavour's by offering essential insights and recommendations for refining experimental protocols and analysis methods. In conclusion, this study significantly contributes to our understanding of the biomechanical complexities involved in gait alterations in Parkinson's disease. The identified differences between PwP and the reference group provide a basis for further exploration in rehabilitation strategies tailored to address these specific challenges, thereby advancing the field of Parkinson's disease research.

#### 6.5 The limitations and recommendations of the study

In the presented study, caution was taken to ensure the elimination of any extraneous variables at the start of the study. However, some limitations were still identified and the recommendations for mitigations are outlined below.

## 6.5.1 Limitation of study

### 6.5.1.1 Sample size

The study under consideration features a limited sample size, encompassing 11 participants in the Reference group and a six (6) in the Parkinson's (PwP) group. Given that over 140,000 individuals live with Parkinson's in the UK, with 12,500 residing in Scotland, this

modest cohort will not give more statistical differences to the results. Consequently, this constrains the generalisability of the research outcomes. Furthermore, the study's participants were volunteers from the West of Scotland Parkinson's Disease Research Group displaying an uncommon degree of enthusiasm towards research participation, which may be indicative of a higher than typical level of activity and motivation.

## 6.5.1.2 The statistical analysis

The statistical analysis approach was restricted due to the exploratory nature of the study and the small sample size. The data patterns were evaluated using descriptive statistics, such as means and standard deviations, as well as graphical and tabular presentations. However, the unequal distribution of participants between groups and subgroups limited the use of statistical tests like ANOVA for hypothesis testing.

## 6.5.1.3 PDQ-39 questionnaire

The PDQ-39 questionnaire was not utilised as a metric for disease severity but rather to measure functional impairment in people with Parkinson's (PwP). This choice was made due to the questionnaire's ability to capture various aspects of daily functioning and its established validity in assessing functional impairment in PwP, as explained in section 3.5.2.2. However, it is important to acknowledge that not using a disease severity metric could be considered a limitation of this study. The absence of a disease severity measure may restrict our ability to fully comprehend the relationship between functional impairment and the overall disease progression in PwP.

## 6.5.1.4 Age match

A limitation of the study was the age disparity between the Ref and PwP groups. The Ref group were predominantly composed of younger and physically fit participants, had only one member (a 77-year-old female) within the age range of the PwP group (64-81 years). The absence of age matching suggests that we should exercise caution when interpreting the comparisons made between the groups.

To examine the differences between the elderly participants, we re-evaluated the walking patterns and muscle activity of a 77-year-old individual from the reference group, comparing them to a similar-aged group of people with Parkinson's disease (PwP). The analysis showed that the PwP group took 0.1 seconds longer to transition between walking speeds, and they had a 5-degree decrease in the range of motion (ROM) at the hip, knee, and ankle joints throughout the walking cycle. These findings support previous research by Svehilik et al.

(2009), which also observed reduced ROM mobility in the lower limb joints around (5 degrees hip, 5 degrees knee, 2 degrees ankle) with PwP compared to their age-matched counterparts (p < 0.001). Additionally, the results revealed differences in the timing of muscle activation between the reference and PwP groups.

#### **6.5.1.5 Environmental factors**

The study's environmental conditions also presented a limitation. While walking tests on treadmills were conducted in a controlled lab setting, overground tests were performed outside the lab (on the corridor), without the necessary equipment to capture kinematic and kinetic parameters. This limitation arises because the absence of such equipment prevents comprehensive analysis and measurement of the participants' movements and forces during overground walking. Consequently, the study's findings may be limited in terms of providing a complete understanding of the biomechanical aspects associated with real-world walking scenarios.

## 6.5.1.6 Step length and speed

Lastly, step length and speed could not be measured during the three gait cycles (before, during, and after) in overground walking tests. This limitation was due to the lack of equipment outside the lab setting, although changes in speed were identified by time changes detected by the Inertial Measurement Unit (IMU).

#### 6.5.2 **Recommendation for future studies**

The observed age discrepancy between study groups instigates speculation that age-induced walking speed decline may have contributed to the differences noted between PwP and the Ref group. Future investigations should strive to segregate age and disease effects on PwP's gait patterns, thereby facilitating a deeper understanding of the intrinsic mechanisms. The noted variations in muscle activation and joint movement between PwP and healthy individuals during overground and treadmill walking indicate the potential for devising targeted interventions and therapies to rectify these specific gait anomalies. Interventions that enhance postural control and balance may be particularly advantageous for PwP. Additionally, the influence of Parkinson's disease medication on gait initiation and other parameters should be further investigated to refine pharmacological approaches.

The study emphasises the need for additional research on the impact of the walking surface, such as treadmill versus overground walking, on PwP's gait patterns and muscle activation. This could contribute to more effective rehabilitation program designs for Parkinson's

patients. For instance, treadmill walking, which appeared to necessitate increased muscle effort for safety, might be integrated into therapy plans to augment muscle strength and control. Recommendations for future research encompass augmenting the sample size, agematching between groups, and the use of motion analysis in a gait laboratory for detailed overground walking parameters. Randomised study designs could be adopted to mitigate biases and improve result precision. An eight-week rehabilitation study might clarify interactive treadmill training's impacts on lower limb muscle activity, thus providing valuable insights into the utilisation of this emerging technology in patient-centric tools with theoretical foundations.

## **Chapter 7 Conclusion**

In conclusion, this study provides further evidence regarding the nature of impairment in PwP and aims to enhance our understanding of community walking problems in individuals with PwP while adjusting their walking speed. Despite some limitations in data collection, the study clearly demonstrates variations in biomechanics and muscle activity between the PwP group and the reference group, particularly during speed changes.

The findings of this study can be summarised as follows:

- 1. Biomechanical and muscle activity characteristics, including spatiotemporal parameters, joint angles movement, power, and the physiological change in muscle activity, differed between the PwP group and the Ref group during speed changes, whether it was gait initiation from standing or during regular walking. These differences were evident in terms of both timing and magnitude.
- The PwP group exhibited slower initiation and propulsion moving from standing to walking compared to the physically fit reference group, with prolonged soleus muscle activitya possible cause, which influenced lower limb power and joint movement.
- Clear differences were observed between the PwP and reference groups in joint movement during speed changes while walking on a treadmill. The PwP group exhibited slower and smaller changes in joint movement compared to the physically fit reference group.
- 4. The results support the notion that increasing walking speed affects lower limb muscle activity in individuals with PwP, leading to reduced joint movement and power, particularly at the hip and ankle joints. This suggests a shift in speed change

strategy from ankle to hip joint in individuals with PwP due to increase activation of the soleus muscle with disease progression and age.

- 5. The study also found differences in biomechanics and muscle characteristics between the PwP and reference groups while walking on different surfaces (treadmill and over ground). These differences may be attributed, at least in part, to the use of harnesses for safety purposes during treadmill walking. Furthermore, it is important to note that over ground walking is a skill that individuals acquire, whereas treadmill walking requires prior training.
- 6. The research highlights the influence of the basal ganglia on regulating and smoothing lower limb movements during speed changes. The impairment of the basal ganglia in individuals with PwP contributes to their difficulty in modulating walking speed compared to the control group.

In conclusion, this study provides valuable insights into the biomechanics and muscle activity characteristics of individuals with PwP during speed changes, shedding light on the impact of the disease on their walking abilities. These findings contribute to our understanding of the challenges faced by individuals with PwP in modulating their walking speed and may inform the development of targeted interventions to improve their mobility and quality of life.

## Appendices

## Appendix (A) University Ethics UEC18/78

## **Ethics Application Form**

Please answer all questions

## 1. Title of the investigation

Characterising muscle activity during gait initiation and speed variation on a treadmill and over the ground for People with Parkinson's Disease

Please state the title on the PIS and Consent Form, if different:

A study to understand the way the muscles in the leg work to start walking and change walking speed in people with Parkinson's Disease

# 2. Chief Investigator (must be at least a Grade 7 member of staff or equivalent)

Name: Dr Andy Kerr

Professor

Reader

Senior Lecturer

⊠ Lecturer

Senior Teaching Fellow

Teaching Fellow

Department: Biomedical Engineering

Telephone: 0141 548 2855

E-mail: <u>a.kerr@strath.ac.uk</u>

## 3. Other Strathclyde investigator(s)

Name: Esraa Aldayil

Status (e.g. lecturer, post-/undergraduate): postgraduate researcher

Department: Biomedical Enginnering

Telephone:

E-mail: Esraa.aldayil@strath.ac.uk

## 4. Non-Strathclyde collaborating investigator(s) (where applicable)

Name:

Status (e.g. lecturer, post-/undergraduate):

Department/Institution:

If student(s), name of supervisor:

Telephone:

E-mail:

Please provide details for all investigators involved in the study:

## 5. Overseas Supervisor(s) (where applicable)

Name(s):

Status:

Department/Institution:

Telephone:

Email:

I can confirm that the local supervisor has obtained a copy of the Code of

Practice: Yes 🗌 No 🗌

Please provide details for all supervisors involved in the study:

## 6. Location of the investigation

At what place(s) will the investigation be conducted

The National Centre of Prosthetic and Orthotics (Curran building), Department of Biomedical Engineering. This location has full wheelchair access including toilet and shower facilities

The first part of project will take place in CU 242 (clinic room 3)

The second part will take place in the Motek laboratory (Curran Building).

If this is not on University of Strathclyde premises, how have you satisfied yourself that adequate Health and Safety arrangements are in place to prevent injury or harm?

N/A

## 7. Duration of the investigation

Duration(years/months): 12

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Start date (expe	ected):	01 / 03 / 2019	Completion date
(expected):	01 / 03 / 202	20	

## 8. Sponsor

Please note that this is not the funder; refer to Section C and Annexes 1 and 3 of the Code of Practice for a definition and the key responsibilities of the sponsor.

Will the sponsor be the University of Strathclyde: Yes 🖂	No 🗌
If not, please specify who is the sponsor:	

9. Funding body or proposed funding body (if applicable)				
Name of funding body: self-funded				
Status of proposal – if seeking funding	g (plea	se click approp	oriate box):	
In preparation				
Submitted				
⊠ Accepted				
Date of submission of proposal:	/	/	Date of start of	
funding: / /				

## 10. Ethical issues

Describe the main ethical issues and how you propose to address them: We have conducted a number of research projects in the past five years using the department's (Biomedical Engineering) virtual reality treadmill system without injury or incident. Nevertheless, we fully appreciate the need to remain vigilant when it comes to ethical issues. With this in mind we have identified the following potential ethical issues along with solutions for their mitigation:

- Risk of skin being irritated from wearing sensors. This risk will be reduced by excluding individuals with an active skin condition, limiting the time the sensors will be on the skin to a maximum of 60 minutes, using hypoallergenic tape and asking participants to inform us if their skin becomes irritable during the session so that they can be removed immediately.
- 2) For EMG preparation, the investigators will use single-use disposable razors for each participant in a specific area in the legs and will dispose of the razor in a sharps box according to infection control regulation.

## F. G.

- The risk of a slip or trip falls during the testing. We will use a safety harness during all the treadmill walking tests and ensure the ground is free of obstacles and any slip risks (e.g. water spillage) during the overground walking.
   H.
- As the data capture requires participants to wear close-fitting clothing, there is a risk of embarrassment. The investigator will need to palpate the skin to ensure the correct position of markers. Participants will be aware of this from the information sheet. The operator and researcher will be present during the data capture and the room will be locked for privacy.

   I.
- 5) As we are asking participants to walk repetitively, there is a small risk of muscle/joint discomfort and fatigue during participation and in the following 48 hours. Nevertheless, we will inform participants that some muscle and joint discomfort may occur in the hours and the days after the experiment. We always ask participants to have rest time if they need.
  - J.
- 6) Although we are excluding individual's with known motion sickness there is the possibility that walking on the treadmill with the virtual reality screen may induce feelings of nausea, should this occur we will stop the treadmill and ask the participant to sit down until they feel well again. We will then help these individuals to change back into their normal clothing and thank them for their participation. K.
- 7) To mitigate against issues around insecure data, we will comply with departmental data management policy to ensure data safety. L.
- 8) Regarding the possibility of an unusual event occurring when walking (i.e. freezing of gait), the safety procedures that we will employ for people with Parkinson's Disease are using a safety harness to prevent a fall while on the treadmill and the use of a treadmill designed to automatically stop when the participant stops. The system also includes a number of safety features such as automatically stopping if they move close to the edges of the treadmill and an emergency stop button which can be pressed at any moment. Additionally, to minimise the risk of fatigue, participants will be given regular 5-minute breaks throughout the testing procedure where they will be seated and offered a drink.

the sessions will be supervised by an experienced UK registered (Health and Care Professions Council) physiotherapist. Also, there is a telephone in the laboratory to contact security should an incident arise.

# 11. Objectives of investigation (including the academic rationale and justification for the investigation) Please use plain English.

Gait disorders are considered to be the main feature of People with Parkinson's disease and are characterised by slow steps, a shuffling gait, difficulties in initiating movement, which is known as the freezing of gait (FOG), and a decrease in gait velocity (Shine et al. 2011). Walking in the community requires frequent changes in speed, including stopping and starting. Treadmill training has been suggested to help individuals with these conditions to recover their walking ability, but it does not typically include variations in speed, so it might not be specific enough to improve walking in everyday environments, indoors and outdoors. The interactive treadmill seems to have a positive effect in improving gait and in decreased the risk of falls in PD patients (Mirelman et al. 2011). Mehrholz et al. (2015) reported that gait training on a treadmill improves gait impairment and educates patients to cope with the variation in gait speed in community walking as overground walking. Plotnik et al. (2015) introduced self -pacing treadmills which are controlled by the individual through their body position and speed, allowing speed variation to occur.

We are currently engaged in a programme of research using treadmills linked with virtual environments (MotekMedical, Amsterdam, the Netherlands) which have the capacity to simulate everyday walking situations, including speed variations. According to previous studies, the work of tibialis anterior, gastrocnemius and soleus muscles during gait initiation over ground is to control the movement of the lower limb and able to propel the body forward to a new position (Mickelborough et al.,2003; Neptune et al.,2000).

This research has so far been conducted without speed variation and has not considered gait initiation on a treadmill. To understand real life walking and the therapeutic use of treadmills we would like to replicate these studies in the context of gait initiation and speed variation overground and on a treadmill. This study aims to record the muscle activity of people with Parkinson's Disease as they start to walk and change their walking speed both on a treadmill and over the ground. This data will be compared with data currently being collected from unimpaired adults (ethical approval granted from the BME department ethics committee). This comparison will allow us to identify the key differences and help in the planning of a future intervention study.

### References:

MEHRHOLZ, J., et al., 2015. Treadmill training for patients with Parkinson's disease. *The Cochrane Database of Systematic Reviews*. (8):CD007830. doi(8), pp. CD007830.

MICKELBOROUGH, J., VAN DER LINDEN, M., TALLIS, R. and ENNOS, A., 2004. Muscle activity during gait initiation in normal elderly people. *Gait & Posture.* **19**(1), pp. 50-57.

MIRELMAN, A., et al., 2011. Virtual reality for gait training: can it induce motor learning to enhance complex walking and reduce fall risk in patients with Parkinson's disease?. *The Journals of Gerontology: Series A.* **66**(2), pp. 234-240.

NEPTUNE, R., KAUTZ, S. and ZAJAC, F., 2001. Contributions of the individual ankle plantar flexors to support, forward progression and swing initiation during walking. *Journal of Biomechanics*. **34**(11), pp. 1387-1398.

SHINE, J., NAISMITH, S. and LEWIS, S., 2011. The pathophysiological mechanisms underlying freezing of gait in Parkinson's disease. *Journal of Clinical Neuroscience*. **18**(9), pp. 1154-1157.

PLONTIC, M., Azrad, T., Bondi, M., Bahat, Y., Gimmon, Y., Zeilig, G., Inzelberg, R. and Siev-Ner, I., 2015. Self-selected gait speed-over ground versus self-paced treadmill walking, a solution for a paradox. *Journal of neuroengineering and rehabilitation*, *12*(1), p.20.

## 12. Participants

Please detail the nature of the participants:

the participants will be recruited from West of Scotland Parkinson's Disease Research Group

Summarise the number and age (range) of each group of participants:

We have been recruited a participant to our study as an adult with Parkinson's disease, stable on anti-Parkinson's drugs and who is able to walk

independently without a frame or walking stick. The following additional criteria Inclusion criteria:

- Are independent in activities of daily living. Able to follow simple instructions and communicate in English.
- Are able to provide informed consent.
- Are able to come to the University of Strathclyde during working hours (9-5) Monday to Friday, for a single two-hour appointment. M.

- Pregnant
- Known cardiac problems exacerbated by exercise.
- Currently complaining of joint or muscle problems that affect walking ability.
- Known neurological conditions affect walking ability.
- Parkinson's disease participants with a severe ambulatory
- Uncorrected hearing or vision problems.
  - N. History of severe motion sickness.
- History of vestibular or balance problems,
- An active skin condition which could be irritated with sticky tape.

## **13. Nature of the participants**

Please note that investigations governed by the Code of Practice that involve any of the types of participants listed in B1(b) must be submitted to the University Ethics Committee (UEC) rather than DEC/SEC for approval. Do any of the participants fall into a category listed in Section B1(b) (participant considerations) applicable in this investigation?: Yes  $\Box$  No  $\boxtimes$ If yes, please detail which category (and submit this application to the UEC):

## 14. Method of recruitment

Describe the method of recruitment (see section B4 of the Code of Practice), providing information on any payments, expenses or other incentives.

The recruitment will be through the West Scotland Parkinson's Disease Research Group. They required ethical approval, a participant information sheet (PIS) and the consent form to start the recruitment process. Then, we should complete the form Which includes the summary of the project such as inclusion and exclusion criteria, the requirement of participants and any risks involved, as well as the investigator contact details. After that, if she/he is willing to participate in the project, they will be contacted to arrange an appointment time. Potential participants will receive the participant information sheet via email or can request a hard copy.

## 15. Participant consent

Please state the groups from whom consent/assent will be sought (please refer to the Guidance Document). The PIS and Consent Form(s) to be used should be attached to this application form.

Individuals who contact the research team will be sent an information sheet giving further details of the research process and given at least 48 hours to read and ask questions before an arrangement is made to attend the movement laboratory for testing. During this appointment, the protocol will be explained again to the individual, and they will be given a further opportunity to ask questions. If, after this, they are still willing to proceed, they will be invited to sign the consent form. The researcher will remind the participant that they are free to withdraw from the procedure any time if they wish.

## 16. Methodology

Investigations governed by the Code of Practice which involve any of the types of projects listed in B1(a) must be submitted to the University Ethics Committee rather than DEC/SEC for approval.

Are any of the categories mentioned in the Code of Practice Section B1(a) (project considerations) applicable in this investigation?  $\Box$  Yes  $\boxtimes$  No If 'yes', please detail:

Interested participants who contact the researchers will be provided with a participant information sheet. If, after 48 hours, they contact the researchers expressing their interest in participating they will be offered a two hours appointment at a mutually convenient time in the Motek laboratory in the National Centre of Prosthetic and Orthotics (Curran building). They will be asked to wear close-fitting attire of a T-shirt and shorts during the study or, if they prefer, this can be provided for them on the day. Transport can be provided if requested.

After arriving, the investigators will be happy to answer any further questions about the project and will familiarise the participants with the layout of the building including toilets and the changing room. If they are happy with the procedure will ask them to sign a consent form. Measurement of the participant's height, weight, leg lengths and width of pelvis, knees, and ankles will be taken. The skin will be prepared for the placement of the EMG electrodes; this will include light rubbing to remove dead skins cells, wiping with an alcohol wipe and shaving an area of approximately 2cm² if required. Six wireless EMG electrodes will then be placed over the bellies of the following muscles and secured with double sided sticky tape.

-Tibialis Anterior (left and right).

-Medial head of Gastrocnemius (left and right).

-Soleus (left and right).

See (1) figure for more detail.

-Sixteen retroreflective markers will then be placed over the skin of the following landmarks and secured with double sided sticky tape.

-Anterior Superior Iliac Spine (left and right).

-Posterior Superior Iliac Spine (left and right).

-Lateral border of thigh (left and right).

-Lateral femoral epicondyle (left and right).

-Lateral border of lower leg (left and right).

-Lateral Malleolus (left and right).

-Heel (left and right).

-Base of 1st metatarsal (left and right).

See in fig (2).

The procedure will take approximately 15 minutes.

The session consists of two parts

Part (one):

In a coridore, there will be a temporary path marked out on the ground ten meters in length. Three meters along the path there will either be a green or a red signboard on the right side of the gait path which will indicate an increase or decrease in walking speed. The participants will walk along the path nine times: The first four steps will be at their regular speed; then they need to increase on fifth steps indicating either an increase (e.g. if they were hurrying to a class) or decrease (e.g. walking alongside an older adult or young child) in speed. The participants will be encouraged to take rests between walks. The participants will walk the short distance (approximately 20 meters) to another room for the second part of the study

## Part two

In this part, the participants will walk on a treadmill for approximately 15 minutes. We will ask them to walk at different speeds, slow, usual and fast. The treadmill is self-pacing, which means it will begin to move when they are moving and will adjust automatically according to their speed, this may need a little time to get used to, so we will include a familiarisation period of up to 15 minutes. During the treadmill walking, we will ask them to wear a parachute style harness to prevent any harm from a slip or trip as you walk. If they are any stumble or freeze while they walk the treadmill will automatically stop. We will wait them commence when you they are happy to proceed. If they are feeling uncomfortable walking on the treadmill or find it frustrating to use, we will record their views and end the session.

The investigators will conduct the session. Esraa Aldayil student investigator will conduct the test and the second investigator (Kerr) will help to guide and supervise the process. Both researchers are trained physiotherapists with experience working in this area. Data analysis will be carried out by the student Describe the research methodology and procedure, providing a timeline of activities where possible. Please use plain English.

What specific techniques will be employed and what exactly is asked of the participants? Please identify any non-validated scale or measure and include any scale and measures charts as an Appendix to this application. Please include questionnaires, interview schedules or any other non-standardised method of data collection as appendices to this application.

 Three-dimensional motion analysis using the Vicon system. Motion capture units will track the movement of reflective markers placed on the skin/clothing of participants. This will require participants to wear relatively tight-fitting clothes (lycra shorts and top). This is a well used measurement technology, which the BME Dept, has used frequently and recently for different experiments with healthy and impaired people.  Electric activity of the muscles using the wireless EMG measurement system (DELSYS Inc, Boston, USA). The system will track the activity of lower leg muscle groups.

Where an independent reviewer is not used, then the UEC, DEC or SEC reserves the right to scrutinise the methodology. Has this methodology been

subject to independent scrutiny? Yes  $\Box$  No  $\boxtimes$ 

If yes, please provide the name and contact details of the independent reviewer:

## 17. Previous experience of the investigator(s) with the procedures

**involved.** Experience should demonstrate an ability to carry out the proposed research in accordance with the written methodology.

Name: Andy Kerr

Experience: 25 years have experience working with motion capture analysis system and carry out movement analysis students with volunteers within and without the University of Strathclyde. Dr Kerr has been trained to use the CAREN system and the EMG and inertial sensors and is a registered Physiotherapist (HCPC).

## Name: Esraa Aldayil

Experience: PH.D student completed training sessions and online course for (clinical gait analysis, Vicon and D-flow training program) prior to the commencement study and is a qualified physiotherapist (BSc & MSc Physiotherapy) with more than ten years' experience.

## 18. Data collection, storage and security

How and where are data handled? Please specify whether it will be fully anonymous (i.e. the identity unknown even to the researchers) or pseudoanonymised (i.e. the raw data is anonymised and given a code name, with the key for code names being stored in a separate location from the raw data) - if neither please justify.

The data and the consent form will be treated confidentially, in a locked cabinet in a locked room in the Department of Biomedical Engineering. This information will be available for those named in this application and will be kept indefinitely. The Pseudo-anonymous data will transfer from laboratory computers using an encrypted memory stick and to strathcloud with access only to the investigators only. All pseudo-anonymised experimental data will be coded with an IDnumber. Upon completion of the study, the ID key will be destroyed, making data anonymous. Anonymous data will be kept indefinitely. The information will be needed for production of related documents (publication and conferences) on the University responsibility.

Explain how and where it will be stored, who has access to it, how long it will be stored and whether it will be securely destroyed after use:

All data will be kept on Strathcloud with secure code which is available for the named researchers. Its access and destructed according to the University of Strathclyde Data Protection Policy and GDPR. As well as, the consent form and anonymous data will be kept indefinitely

Will anyone other than the named investigators have access to the data? Yes  $\hfill \hfill \$ 

If 'yes', please explain:

The data will be used in case of related researches (publication and conferences) on the University responsibility

## **19. Potential risks or hazards**

Briefly describe the potential Occupational Health and Safety (OHS) hazards and risks associated with the investigation:

No more risks or hazards are concerned in this project unless minimal risk such as tripping, falling or slipping. Careful setup of experimental space will treat these. Furthermore, the use of a parachute style harness to prevent any harm from a slip or trip during walking. If the participants stumble or freeze while walking the treadmill will automatically stop. Also, we will provide breaks upon required to decrease the fatigue. We will exclude any skin irritation condition from markers or EMG electrodes. Finally, all the equipment will be cleaned with alcohol-based wipes (the harness, treadmill, and the electrodes) to prevent any infection

Please attach a completed OHS Risk Assessment (S20) for the research. Further Guidance on Risk Assessment and Form can be obtained on Occupational Health, Safety and Wellbeing's webpages

# 20. What method will you use to communicate the outcomes and any additional relevant details of the study to the participants?

The result of this project will not be available for participants unless they ask. If a request is received, we will provide a summary report of the collated anonymised findings

21. How will the outcomes of the study be disseminated (e.g. will you seek to publish the results and, if relevant, how will you protect the identities of your participants in said dissemination)?

This project will be published as part of a PhD thesis and the data could be used in a scientific publication in journals, clinical peer review, a poster, or conferences.

Checklist	Enclosed	N/A
Participant Information Sheet(s)	$\square$	
Consent Form(s)	$\boxtimes$	
Sample questionnaire(s)		
Sample interview format(s)		
Sample advertisement(s)		
OHS Risk Assessment (S20)	$\boxtimes$	

Any other documents (please specify	
below)	

#### 22. Chief Investigator and Head of Department Declaration

Please note that unsigned applications will not be accepted and both signatures are required

I have read the University's Code of Practice on Investigations involving Human Beings and have completed this application accordingly. By signing below, I acknowledge that I am aware of and accept my responsibilities as Chief Investigator under Clauses 3.11 – 3.13 of the <u>Research</u> <u>Governance Framework</u> and that this investigation cannot proceed before all approvals required have been obtained.

Signature of Chief Investigator

Andrew Kerr.

Please also type name here:

Dr. Andy Kerr

I confirm I have read this application, I am happy that the study is consistent with departmental strategy, that the staff and/or students involved have the appropriate expertise to undertake the study and that adequate arrangements are in place to supervise any students that might be acting as investigators, that the study has access to the resources needed to conduct the proposed research successfully, and that there are no other departmental-specific issues relating to the study of which I am aware.

Signature of Head of Department		
Please also type name here		
Date:	/	/

23. Only for University sponsored projects under the remit of the DEC/SEC, with no external funding and no NHS involvement

#### Head of Department statement on Sponsorship

This application requires the University to sponsor the investigation. This is done by the Head of Department for all DEC applications with exception of those that are externally funded and those which are connected to the NHS (those exceptions should be submitted to R&KES). I am aware of the implications of University sponsorship of the investigation and have assessed this investigation with respect to sponsorship and management risk. As this particular investigation is within the remit of the DEC and has no external funding and no NHS involvement, I agree on behalf of the University that the University is the appropriate sponsor of the investigation and there are no management risks posed by the investigation.

2	N	8
4	v	o

If not applicable, tick here 🗌				
Signature of Head of Department				
Please also type name here				
Date:	/		/	
For applications to the University Ethics Committee, the	completed	form	should be sent to	
ethics@strath.ac.uk with the relevant electronic signatur	es.			

## 24. Insurance

The questionnaire below must be completed and included in your submission to the UEC/DEC/SEC:

Is the proposed research an investigation or series of investigations conducted on any person for a Medicinal Purpose? Medicinal Purpose means:	Yes <b>/ No</b>
<ul> <li>treating or preventing disease or diagnosing disease or</li> <li>ascertaining the existence degree of or extent of a physiological condition or</li> <li>assisting with or altering in any way the process of conception or</li> <li>investigating or participating in methods of contraception or</li> <li>inducing anaesthesia or</li> <li>otherwise preventing or interfering with the normal operation of a physiological function or</li> <li>altering the administration of prescribed medication. O.</li> </ul>	

If "Yes" please go to Section A (Clinical Trials) – all questions must be completed

If "No" please go to Section B (Public Liability) – all questions must be completed

Section A (Clinical Trials)

Does the proposed research involve subjects who are either:	Yes / No
<ul> <li>i. under the age of 5 years at the time of the trial;</li> <li>ii. known to be pregnant at the time of the trial</li> <li>P.</li> </ul>	

If "Yes" the UEC should refer to Finance

Is the	proposed research limited to:	Yes / No
iii.	Questionnaires, interviews, psychological activity including CBT;	
iv.	Venepuncture (withdrawal of blood);	
<b>v</b> .	Muscle biopsy;	
vi.	Measurements or monitoring of physiological processes including scanning;	
vii.	Collections of body secretions by non-invasive methods;	
viii.	Intake of foods or nutrients or variation of diet (excluding administration of drugs).	
	Q.	

If "No" the UEC should refer to Finance

Will the proposed research take place within the UK?	Yes / No
------------------------------------------------------	----------

Title of Research		
Chief Investigator		
Sponsoring Organisation		
Does the proposed research i	nvolve:	
a) investigating or pa contraception?	articipating in methods of	Yes / No
b) assisting with or a	Itering the process of conception?	Yes / No
c) the use of drugs?		Yes / No
d) the use of surgery (other than biopsy)?		Yes / No
e) genetic engineerir	ıg?	Yes / No
<li>f) participants under i-vi above)?</li>	5 years of age(other than activities	Yes / No
g) participants know activities i-vi abov	n to be pregnant (other than e)?	Yes / No
<ul> <li>h) pharmaceutical pr manufactured by t</li> </ul>	oduct/appliance designed or he institution?	Yes / No
i) work outside the l		Yes / No

If "YES" to any of the questions a-i please also complete the Employee Activity Form (attached).

If "**YES**" to **any** of the questions a-i, <u>and this is a follow-on phase</u>, please provide details of SUSARs on a separate sheet.

If "Yes" to any of the questions a-i then the UEC/DEC/SEC should refer to Finance (insurance-

services@strath.ac.uk).

Section B (Public Liability)		
Does the proposed research involve :		
a) aircraft or any aerial device	Yes / No	
b) hovercraft or any water borne craft	Yes / No	
c) ionising radiation	Yes / No	
d) asbestos	Yes / No	
e) participants under 5 years of age	Yes / No	
f) participants known to be pregnant	Yes / No	
g) pharmaceutical product/appliance designed or manufactured by the institution?	Yes / No	
h) work outside the United Kingdom?	Yes / No	

If "YES" to any of the questions the UEC/DEC/SEC should refer to Finance (insurance-

services@strath.ac.uk)

## For NHS applications only - Employee Activity Form

Has NHS Indemnity been provided?	Yes / No
Are Medical Practitioners involved in the project?	Yes / No
If YES, will Medical Practitioners be covered by the MDU or	Yes / No
other body?	

This section aims to identify the staff involved, their employment contract and the extent of their involvement in the research (in some cases it may be more appropriate to refer to a group of persons rather than individuals).

Chief Investigator				
Name	Employer	NHS Honorary		
		Contract?		
		Yes / No		
Others				
Name	Employer	NHS Honorary		
		Contract?		
		Yes / No		
		Yes / No		
		Yes / No		
		Yes / No		

Please provide any further relevant information here:

# Appendix (B) Participants and consent sheet

## **Participant Information Sheet for**

## [People with Parkinson's Disease]

## [FOR USE WITH STANDARD PRIVACY NOTICE FOR RESEARCH PARTICIPANTS]

Name of department: Department of Biomedical Engineering

Title of the study: A study to understand the way the muscles in the leg work to start

walking and change walking speed in people with Parkinson's Disease

#### Introduction

Walking in the community requires frequent changes to speed, including stopping and starting. This can be challenging for people with neurological conditions such as Parkinson's Disease. People with Parkinson's often complain of slowness in movement and difficulty with starting movements. Training on a treadmill has been suggested to help people with Parkinson's disease recover their walking ability but this does not typically include variations in speed so may not be specific enough to improve walking in everyday environments, indoor and outdoor. We are currently engaged in a programme of research using treadmills linked to virtual environments which can simulate everyday walking conditions, including changing speed.

The main researchers in this study will be a PhD student: Esraa Aldayil from the biomedical engineering department of Strathclyde university and experienced physiotherapist. The Chief Investigator of the study: Andrew Kerr is a lecturer in the same department and also a physiotherapist in (HCPC).

#### What is the purpose of this research?

In this project, we would like to understand how muscles of the lower limbs of people with Parkinson's Disease are working when starting walking and while changing speed, also we would like to observe how they are able to control their walking during changes in speed on a treadmill as well as over ground. This information will help us plan a trial using these treadmills with people with Parkinson's disease.

#### Do you have to take part?

It is up to you whether you take apart in the investigation or not. You can refuse to be a participant in the study, and you can withdraw at any time you feel, without having a reason. If you wish to withdraw from the study after you have already taken part, all non-anonymous and pseudoanonymised data relating to you will be deleted at your request before the data are anonymised. Once the data have been anonymised and analysed your data can no longer be removed



#### What will you do in the project?

Interested individuals will be invited to attend a 2-hour appointment at the Biomechanics Laboratory in the National Centre for Prosthetics and Orthotics at the University of Strathclyde which will be arranged via email correspondence or by telephone. We can provide transportation if required. you will need to wear close-fitting attire of T-shirt and shorts. (we can provide that for you, or you can bring your own). Also, you will need to wear the shoes that you usually wear to walk in. If you need help, we can assist you. If you prefer to attend the study with someone else, such as a friend or family member, we absolutely accept that.

In the first appointment, the protocol will be explained again to the individual, and they will be given a further opportunity to ask questions, and we will familiarise you with the place and changing room if required as well as the protocol. If you are happy, we will ask you to sign a consent form. We will take measurements of your weight, height, leg lengths and width of your pelvis, knees, and ankles. This is needed for the computer to make the calculations as you walk. We will also ask you to complete a short questionnaire about your experience with freezing gait.

The study will be recruited in the gait laboraory (Wolfson centre) that includes 12 infra-red cameras which are not a video camera, so you will not be identifiable from recording. The researcher will then place 16 small markers over the skin of specific parts of your body (e.g. knee, ankle and heel) as in figure (1) below. Six special sensors will then be attached to the skin overlying your calf and shin muscles using hypoallergenic tape. As in figure (2), these will record the activity of your muscles. This may require a small area (10 pence piece) to be shaved. After these preparations, which will take approximately 15 minutes, we will proceed with the experiment which has two parts:

#### Part one

The researcher will show you a path on the ground ten meters in length. Two meters along the path there will either be a green or a red signboard on the right side of the gait path which will indicate an increase or decrease in walking speed. You will walk along this path nine times: the four steps with your regular speed then you nees to change peed on the fifth step either an increase (as if you were hurrying to reach a bus or rushing to the toilet) or decrease (as if you were in a crowded street) in speed. In between these walks, you will be invited to rest as often as you need. You will then be asked to walk a short distance (approximately 20 meters) to another room for the second part of the study

#### Part two

In this part, you will walk on a treadmill for approximately 15 minutes. We will ask you to walk at different speeds, slow, usual and fast. The treadmill is self-pacing, which means it will begin to move when you move and will adjust automatically to your speed, this may need a little time to get used to, so we will include a familiarisation period of up to 15 minutes. During the treadmill walking, we will ask you to wear a parachute style harness to prevent any harm from a slip or trip as you walk. If you stumble or freeze while you walk the treadmill will automatically stop, and only commence when you are happy to proceed. If you feel uncomfortable walking on the treadmill or find it frustrating to use, we will record your views and end the session.

When all the walks have been completed, all the markers will be removed, and you will be free to change back into your normal clothes.

Note that: the harness and any other equipment will be cleaned with alcohol-based wipes before being used for participants

#### Why have you been invited to take part?

You have been invited to take part in our study as an adult with Parkinson's disease, stable on anti-Parkinson's drugs and who is able to walk independently without a frame or walking stick. The

following additional criteria

inclusion criteria:

- Are independent in activities of daily living. Able to follow simple instructions and communicate in English.
- Are able to provide informed consent.
- Are able to come to the University of Strathclyde during working hours (9-5) Monday to Friday, for a single two-hour appointment.

Exclusion criteria:

- Pregnant
- Known cardiac problems exacerbated by exercise.
- Currently complaining of joint or muscle problems that affect walking ability.
- Known neurological conditions affect walking ability.
- Parkinson's disease participants with a severe ambulatory
- Uncorrected hearing or vision problems.
  - S. History of severe motion sickness.
- History of vestibular or balance problems,
- An active skin condition which could be irritated with sticky tape.

#### What are the potential risks to you in taking part?

There should be a minimal risk from participating in our study. Slipping and tripping on the treadmill will be minimised by wearing a safety harness when walking. There is a possibility that you will experience motion sickness from walking on the treadmill. The treadmill will be in self-paced mode and will, therefore, stop automatically. In the unlikely circumstances of this mechanism not functioning correctly the emergency stop button will be depressed to stop the treadmill immediately. You may also feel some joint or muscle discomfort from all the walking we will ask you to do, although this is a small risk it is worth bearing in mind. We will keep checking on how you feel so that if you feel tired, sore or unwell, we will stop the experiment immediately.

#### What information is being collected in the project?

At the beginning of the study, we will ask you some questions regarding your age and gender as well as we will take your height and weight from our scale. Also, there are some assessments you will go through it to measure your ability to walk and your level of balance, and daily activity. This information will help the system to collect the measurement of your joints during the walking in both situations on the treadmill and over the ground. The cameras system on both trails (treadmill and overground) will record your movement during regular speed especially at the beginning of walking

from standing position and during changing speed either by an increase or decrease. Also, the EMG electrodes will measure the activity of your lower limb muscles during movement. **Who will have access to the information?** 

The anonymised results of this study may be submitted for the purpose of presentation at scientific and clinical conferences and may be submitted for scientific and clinical peer-reviewed publication. Furthermore, the results will be included in the research students' PhD theses. Any research publications or presentations resulting from this work will only discuss group results and will not report on the individual. At no time will any personal or identifiable information be released

#### Where will the information be stored and how long will it be kept for?

The information will be stored securely in the university and will only be accessible to the researchers named in the information sheet. We will a copy of your consent form for five years

Thank you for reading this information – please ask any questions if you are unsure about what is written here.

#### What happens next?

Please send an e-mail to **Esraa.aldayil@strath.ac.uk** if you would like to participate to this study. If you do not wish to participate then please accept our thanks for taking the time to read this information.

Also, if you are interested in receiving feedback after the research is completed, we will happy to inform you when the results are to be published

#### **Researcher contact details:**

Researcher: Esraa Aldayil Status: PHD student Department: Biomedical Engineering Contact: Esraa.aldayil@strath.ac.uk

#### Chief Investigator details:

Researcher: Andrew Kerr Status: Lecturer Department: Biomedical Engineering Contact: a.kerr@strath.ac.uk

This research was granted ethical approval by the University of Strathclyde Ethics Committee. If you have any questions/concerns, during or after the research, or wish to contact an independent person to whom any questions may be directed or further information may be sought from, please contact:

Secretary to the University Ethics Committee Research & Knowledge Exchange Services University of Strathclyde Graham Hills Building 50 George Street Glasgow G1 1QE Telephone: 0141 548 3707 Email: <u>ethics@strath.ac.uk</u>

#### Figure 1: placement of the reflective markers



#### Figure 2: Placement of the EMG sensors



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## **Consent Form [People with Parkinson's Disease]**

Name of department: Department of Biomedical Engineering

Title of the study: A study to understand the way the muscles in the leg work to start

walking and change walking speed in people with Parkinson's Disease

- I confirm that I have read and understood the Participant Information Sheet for the above project and the researcher has answered any queries to my satisfaction.
- I understand that my participation is voluntary and that I am free to withdraw from the project at any time, up to the point of completion, without having to give a reason and without any consequences.
- I understand that I can request the withdrawal from the study of some personal information and that whenever possible researchers will comply with my request. This includes the following personal data:
  - my personal information from transcripts.
- I understand that anonymised data (i.e. data that do not identify me personally) cannot be withdrawn once they have been included in the study.
- I understand that any information recorded in the research will remain confidential and no information that identifies me will be made publicly available.
- I consent to being a participant in the project.

For research where it has been decided that "no fault compensation" cover will be provided, the following wording needs to be included: In agreeing to participate in this research, I am aware that I may be entitled to compensation for accidental bodily injury, including death or disease, arising out of the research without the need to prove fault. However, such compensation is subject to acceptance of the Conditions of Compensation, a copy of which is available on request.

(PRINT NAME)	
Signature of Participant:	Date:

## Appendix (C) PDQ 39 questionnaires



# **PDQ-39 QUESTIONNAIRE**

Please complete the following

Please tick one box for each question Due to having Parkinson's disease, how often during the last month Sometimes Often Occasionally have you.... Never Always or cannot do 1 Had difficulty doing at all the leisure activities which you would like to do? 2 Had difficulty looking after your home, e.g. DIY, housework, cooking? 3 Had difficulty carrying bags of shopping? 4 Had problems walking half a mile? 5 Had problems walking 100 yards? 6 Had problems getting around the house as easily as you would like? Had difficulty getting 7 around in public? 8 Needed someone else to accompany you when you went out? 9 Felt frightened or worried about falling over in public? 10 Been confined to the house more than you would like? Had difficulty washing 11 yourself? Had difficulty dressing 12 yourself? Had problems doing up 13 your shoe laces?

Please check that you have ticked one box for each question before going on to the next page

Due to having Parkinson's disease, how often <u>during the last month</u> have you		Please tick <u>one</u> box for each question					
		Never	Occasionally	Sometimes	Often	Always	
30	Unexpectedly fallen asleep during the day?						
31	Had problems with your concentration, e.g. when reading or watching TV?						
32	Felt your memory was bad?						
33	Had distressing dreams or hallucinations?						
34	Had difficulty with your speech?						
35	Felt unable to communicate with people properly?						
36 37	Felt ignored by people? Had painful muscle cramps or spasms?						
38	Had aches and pains in your joints or body?						
39	Felt unpleasantly hot or cold?						

#### Please check that you have ticked one box for each question before going on to the next page

Thank you for completing the PDQ 39 questionnaire

### List of Reference

- Aarsland, D., Marsh, L., & Schrag, A. (2009). Neuropsychiatric symptoms in Parkinson's disease. *Movement disorders: official journal of the Movement Disorder Society*, 24(15), 2175-2186.
- Aarsland, D., Perry, R., Brown, A., Larsen, J. P., & Ballard, C. (2005). Neuropathology of dementia in Parkinson's disease: a prospective, community-based study. *Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society*, 58(5), 773-776.
- Aarsland, D., Tandberg, E., Larsen, J. P., & Cummings, J. L. (1996). Frequency of dementia in Parkinson disease. *Archives of Neurology*, 53(6), 538-542.
- Abel, R., Schablowski, M., Rupp, R., & Gerner, H. (2002). Gait analysis on the treadmill–monitoring exercise in the treatment of paraplegia. *Spinal Cord*, 40(1), 17-22.
- Abellan Van Kan, G., Rolland, Y., Andrieu, S., Bauer, J., Beauchet, O., Bonnefoy, M.,
  ... Inzitari, M. (2009). Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people an International Academy on Nutrition and Aging (IANA) Task Force. *The journal of nutrition, health & aging, 13*(10), 881-889.
- Acharya, S. and Kim, K.-M. (2021) 'Roles of the functional interaction between brain cholinergic and dopaminergic systems in the pathogenesis and treatment of schizophrenia and Parkinson's disease'. *International Journal of Molecular Sciences*, 22 (9), pp. 4299.
- Adams, J. A. (1971). A closed-loop theory of motor learning. *Journal of motor behavior*, 3(2), 111-150.
- Adler, C.H. (2002) 'Relevance of motor complications in Parkinson's disease'. *Neurology*, 58 (suppl 1), pp. S51-S56.
- Albani, G., Sandrini, G., Kunig, G., Martin-Soelch, C., Mauro, A., Pignatti, R., . . .
  Leenders, K. L. (2003). Differences in the EMG pattern of leg muscle activation during locomotion in Parkinson's disease. *Functional neurology*, *18*(3), 165-178.
- Alharthi, A. S., Yunas, S. U., & Ozanyan, K. B. (2019). Deep learning for monitoring of human gait: A review. *IEEE sensors journal*, 19(21), 9575-9591.

gyroscopes. Journal of biomechanics, 35(5), 689-699.

- Aminian, K., Najafi, B., Büla, C., Leyvraz, P. F., & Robert, P. (2001). Ambulatory gait analysis using gyroscopes. 25th Annual Meeting of the American Society of Biomechanics,
- Amrutha, N. and Arul, V. (2017a) 'A review on noises in EMG signal and its removal'. *Int. J. Sci. Res. Publ*, 7 (5), pp. 23-27.
- Andres, D. S., & Darbin, O. (2018). Complex dynamics in the basal ganglia: health and disease beyond the motor system. *The Journal of neuropsychiatry and clinical neurosciences*, 30(2), 101-114.
- Arabadzhiev, T. I., Dimitrov, V. G., Dimitrova, N. A., & Dimitrov, G. V. (2010). Interpretation of EMG integral or RMS and estimates of "neuromuscular efficiency" can be misleading in fatiguing contraction. *Journal of electromyography and kinesiology*, 20(2), 223-232.
- Archer, S. E., Winter, D. A., & Prince, F. (1994). Initiation of gait: A comparison between young, elderly, and Parkinson's disease subjects. *Gait & Posture*, 2(1), 56.
- Arias, P., Espinosa, N., Robles-García, V., Cao, R., & Cudeiro, J. (2012). Antagonist muscle co-activation during straight walking and its relation to kinematics: insight from young, elderly and Parkinson's disease. *Brain research*, 1455, 124-131.
- Asmussen, M.J., Von Tscharner, V. and Nigg, B.M. (2018a) 'Motor unit action potential clustering—theoretical consideration for muscle activation during a motor task'. *Frontiers in human neuroscience*, 12 15.
- Avelino, P. R., Nascimento, L. R., Menezes, K. K., Alvarenga, M. T. M., Faria Fortini, I., & Teixeira-Salmela, L. F. (2022). Test–retest reliability and measurement error of the modified gait efficacy scale in individuals with stroke. *Physiotherapy Theory and Practice*, 38(13), 2956-2961.
- Bain, P.G. (2007) 'Parkinsonism & related disorders. Tremor'. *Parkinsonism & related disorders*, 13 S369-374.

- Balice-Gordon, R., Honey, G. D., Chatham, C., Arce, E., Duvvuri, S., Naylor, M. G., . .
  Harel, B. T. (2020). A neurofunctional domains approach to evaluate D1/D5 dopamine receptor partial agonism on cognition and motivation in healthy volunteers with low working memory capacity. *International Journal of Neuropsychopharmacology*, 23(5), 287-299.
- Banaś, A., Majchrzycki, M., Stryła, W., Kruszyński, M., & Piotrowska, S. (2013). Technologie wirtualnej rzeczywistości w procesie usprawniania funkcji chodu oraz równowagi u osób po przebytym udarze mózgu [Virtual reality technologies in the process of improving gait and balance function in patients after stroke]. *Dysfunkcje narządów ruchu. Diagnostyka i usprawnianie pacjentów z dysfunkcjami narządów ruchu. Wydawnictwo Naukowe Uniwersytetu Medycznego im. Karola Marcinkowskiego w Poznaniu, Poznań, 4*, 112-119.
- Barbieri, F. A., Dos Santos, P. C. R., Lirani-Silva, E., Vitório, R., Gobbi, L. T. B., & Van Diëen, J. H. (2013). Systematic review of the effects of fatigue on spatiotemporal gait parameters. *Journal of back and musculoskeletal rehabilitation*, 26(2), 125-131.
- Barbieri, F. A., dos Santos, P. C. R., Simieli, L., Orcioli-Silva, D., van Dieën, J. H., & Gobbi, L. T. B. (2014). Interactions of age and leg muscle fatigue on unobstructed walking and obstacle crossing. *Gait & posture*, *39*(3), 985-990.
- Barbieri, F. A., dos Santos, P. C. R., Vitório, R., van Dieën, J. H., & Gobbi, L. T. B. (2013). Effect of muscle fatigue and physical activity level in motor control of the gait of young adults. *Gait & posture*, *38*(4), 702-707.
- Barker, S., Craik, R., Freedman, W., Herrmann, N., & Hillstrom, H. (2006). Accuracy, reliability, and validity of a spatiotemporal gait analysis system. *Medical engineering & physics*, 28(5), 460-467.
- Barnes, M. (2003) 'Principles of neurological rehabilitation'. *Journal of Neurology, Neurosurgery & Psychiatry*, 74 (suppl 4), pp. iv3-iv7.
- Barth, J., Klucken, J., Kugler, P., Kammerer, T., Steidl, R., Winkler, J., Hornegger, J., & Eskofier, B. (2011). Biometric and mobile gait analysis for early diagnosis and therapy monitoring in Parkinson's disease. 2011 annual international conference of the IEEE engineering in medicine and biology society,
- Basso, C.P. (2012) 'Designing control loops for linear and switching power supplies: a tutorial guide'.

- Battin, J. (2004) 'When good animals love bad habitats: ecological traps and the conservation of animal populations'. *Conservation Biology*, 18 (6), pp. 1482-1491.
- Ben-Shlomo, Y., White, I.R. and Marmot, M. (1996) 'Does the variation in the socioeconomic characteristics of an area affect mortality?'. *Bmj*, 312 (7037), pp. 1013-1014.
- Bender, L.F. (1967) 'Muscles alive: their functions revealed by electromyography'. *JAMA*, 201 (4), pp. 277-277.
- Benedetti, M. G., Agostini, V., Knaflitz, M., & Bonato, P. (2012). Muscle activation patterns during level walking and stair ambulation. *Applications of EMG in clinical and sports medicine*, 8(2), 117-130.
- Berardelli, A., Rothwell, J. C., Thompson, P. D., & Hallett, M. (2001).
  Pathophysiology of bradykinesia in Parkinson's disease. *Brain*, *124*(11), 2131-2146.
- Bengevoord, A., Vervoort, G., Spildooren, J., Heremans, E., Vandenberghe, W., Bloem,
  B., & Nieuwboer, A. (2016). Center of mass trajectories during turning in patients with
  Parkinson's disease with and without freezing of gait. *Gait & posture*, 43, 54-59.
- Berg, D., Postuma, R. B., Bloem, B., Chan, P., Dubois, B., Gasser, T., . . . Lang, A. E. (2014). Time to redefine PD? Introductory statement of the MDS Task Force on the definition of Parkinson's disease. *Movement Disorders*, 29(4), 454-462.
- Berganzo, K., Tijero, B., González-Eizaguirre, A., Somme, J., Lezcano, E., Gabilondo, I., . . . Gómez-Esteban, J. (2016). Motor and non-motor symptoms of Parkinson's disease and their impact on quality of life and on different clinical subgroups. *Neurología (English Edition)*, *31*(9), 585-591.
- Bezard, E., Dovero, S., Belin, D., Duconger, S., Jackson-Lewis, V., Przedborski, S., . .
  Jaber, M. (2003). Enriched environment confers resistance to 1-methyl-4-phenyl-1, 2,
  3, 6-tetrahydropyridine and cocaine: involvement of dopamine transporter and trophic factors. *Journal of Neuroscience*, 23(35), 10999-11007.
- Bigelow, J., Korth, M., Jacobs, J., Anger, N., Riddle, M., & Gifford, J. (2004). A picture of amputees and the prosthetic situation in Haiti. *Disability and Rehabilitation*, 26(4), 246-252.
- Bojanic, D. M., Petrovacki-Balj, B. D., Jorgovanovic, N. D., & Ilic, V. R. (2011).
  Quantification of dynamic EMG patterns during gait in children with cerebral palsy. *Journal of neuroscience methods*, *198*(2), 325-331.

- Brassai, A., Suvanjeiev, R.-G., Bán, E.-G., & Lakatos, M. (2015). Role of synaptic and nonsynaptic glutamate receptors in ischaemia induced neurotoxicity. *Brain research bulletin*, *112*, 1-6.
- Braun, S., Beurskens, A., Kleynen, M., Schols, J., & Wade, D. (2011). Rehabilitation with mental practice has similar effects on mobility as rehabilitation with relaxation in people with Parkinson's disease: a multicentre randomised trial. *Journal of Physiotherapy*, 57(1), 27-34.
- Breniere, Y. and Do, M.C. (1991) 'Control of gait initiation'. *Journal of motor behavior*, 23 (4), pp. 235-240.
- Brockett, C.L. and Chapman, G.J. (2016) 'Biomechanics of the ankle'. *Orthopaedics* and trauma, 30 (3), pp. 232-238.
- Brouwer, B., Parvataneni, K. and Olney, S.J. (2009) 'A comparison of gait biomechanics and metabolic requirements of overground and treadmill walking in people with stroke'. *Clinical biomechanics*, 24 (9), pp. 729-734.
- Browne, M.G. and Franz, J.R. (2018) 'More push from your push-off: Joint-level modifications to modulate propulsive forces in old age'. *PLoS One*, 13 (8), pp. e0201407.
- Bond, J. M., & Morris, M. (2000). Goal-directed secondary motor tasks: their effects on gait in subjects with Parkinson disease. *Archives of physical medicine and rehabilitation*, 81(1), 110-116.
- Buchanan, P.A. and Ulrich, B.D. (2001) 'The Feldenkrais Method®: A dynamic approach to changing motor behavior'. *Research Quarterly for Exercise and Sport*, 72 (4), pp. 315-323.
- Burke, R.E. (2007) 'Sir Charles Sherrington's the integrative action of the nervous system: a centenary appreciation'. *Brain*, 130 (4), pp. 887-894.
- Burnfield, J. and Norkin, C.C. (2013) 'Examination of gait'. Physical Rehabilitation, 6.
- Busch, T. d. A., Duarte, Y. A., Pires Nunes, D., Lebrão, M. L., Satya Naslavsky, M., dos Santos Rodrigues, A., & Amaro, E. (2015). Factors associated with lower gait speed among the elderly living in a developing country: a cross-sectional population-based study. *BMC geriatrics*, 15(1), 1-9.

- Butler, E. E., Steele, K. M., Torburn, L., Gamble, J. G., & Rose, J. (2016). Clinical motion analyses over eight consecutive years in a child with crouch gait: a case report. *Journal of medical case reports*, *10*(1), 1-10.
- C Clark, B. and L Taylor, J. (2011) 'Age-related changes in motor cortical properties and voluntary activation of skeletal muscle'. *Current aging science*, 4 (3), pp. 192-199.
- Caliandro, P., Ferrarin, M., Cioni, M., Bentivoglio, A. R., Minciotti, I., D'urso, P., ...
  Padua, L. (2011). Levodopa effect on electromyographic activation patterns of tibialis anterior muscle during walking in Parkinson's disease. *Gait & posture*, *33*(3), 436-441.
- Campanini, I., Merlo, A., Degola, P., Merletti, R., Vezzosi, G., & Farina, D. (2007).
  Effect of electrode location on EMG signal envelope in leg muscles during gait. *Journal* of Electromyography and Kinesiology, 17(4), 515-526.
- Cano-De-La-Cuerda, R., Molero-Sánchez, A., Carratalá-Tejada, M., Alguacil-Diego, I., Molina-Rueda, F., Miangolarra-Page, J., & Torricelli, D. (2015). Theories and control models and motor learning: Clinical applications in neurorehabilitation. *Neurología* (*English Edition*), 30(1), 32-41.
- Capaday, C., Ethier, C., Brizzi, L., Sik, A., van Vreeswijk, C., & Gingras, D. (2009). On the nature of the intrinsic connectivity of the cat motor cortex: evidence for a recurrent neural network topology. *Journal of neurophysiology*, *102*(4), 2131-2141.
- Cappozzo, A. (1991) 'Three-dimensional analysis of human walking: Experimental methods and associated artifacts'. *Human Movement Science*, 10 (5), pp. 589-602.
- Carlsson, A. (1959) 'The occurrence, distribution and physiological role of catecholamines in the nervous system'. *Pharmacological reviews*, 11 (2), pp. 490-493.
- Carswell, C. and Rea, P.M. (2021) 'What the tech? The management of neurological dysfunction through the use of digital technology'. *Biomedical Visualisation: Volume* 9. Springer, pp. 131-145.
- Castagna, A., Frittoli, S., Ferrarin, M., Del Sorbo, F., Romito, L. M., Elia, A. E., & Albanese, A. (2016). Quantitative gait analysis in parkin disease: possible role of dystonia. *Movement Disorders*, *31*(11), 1720-1728.
- Catalfamo, P., Ghoussayni, S. and Ewins, D. (2010) 'Gait event detection on level ground and incline walking using a rate gyroscope'. *Sensors*, 10 (6), pp. 5683-5702.

- Cau, N., Cimolin, V., Galli, M., Precilios, H., Tacchini, E., Santovito, C., & Capodaglio, P. (2014). Center of pressure displacements during gait initiation in individuals with obesity. *Journal of neuroengineering and rehabilitation*, 11(1), 1-8.
- Cazorla, M., de Carvalho, F. D., Chohan, M. O., Shegda, M., Chuhma, N., Rayport, S., .
  . Kellendonk, C. (2014). Dopamine D2 receptors regulate the anatomical and functional balance of basal ganglia circuitry. *Neuron*, *81*(1), 153-164.
- Ceravolo, R., Frosini, D., Rossi, C., & Bonuccelli, U. (2009). Impulse control disorders in Parkinson's disease: definition, epidemiology, risk factors, neurobiology and management. *Parkinsonism & Related Disorders*, 15, S111-S115.
- Chastin, S. F., Fitzpatrick, N., Andrews, M., & DiCroce, N. (2014). Determinants of sedentary behavior, motivation, barriers and strategies to reduce sitting time in older women: a qualitative investigation. *International journal of environmental research and public health*, 11(1), 773-791.
- Chesnin, K. J., Selby-Silverstein, L., & Besser, M. P. (2000). Comparison of an in-shoe pressure measurement device to a force plate: concurrent validity of center of pressure measurements. *Gait & posture*, *12*(2), 128-133.
- Cimolin, V., Cau, N., Galli, M., Santovito, C., Grugni, G., & Capodaglio, P. (2017). Gait initiation and termination strategies in patients with Prader-Willi syndrome. *Journal of neuroengineering and rehabilitation*, 14(1), 1-8.
- 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(4), 195-208.
- Clark, R. A., Mentiplay, B. F., Pua, Y.-H., & Bower, K. J. (2018). Reliability and validity of the Wii Balance Board for assessment of standing balance: A systematic review. *Gait & posture*, *61*, 40-54.
- Cole, B.T., Roy, S.H. and Nawab, S.H. (2011a) 'Detecting freezing-of-gait during unscripted and unconstrained activity'. 2011 Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 2011a. IEEE, pp.5649-5652.
- Collins, J.-D. *et al.* (2015) 'A systematic literature review of the use and effectiveness of the Computer Assisted Rehabilitation Environment for research and rehabilitation as it relates to the wounded warrior'. *Work*, 50 (1), pp. 121-129.

- Comeau, W.L., McDonald, R.J. and Kolb, B.E. (2010) 'Learning-induced alterations in prefrontal cortical dendritic morphology'. *Behavioural brain research*, 214 (1), pp. 91-101.
- Contin, M., Provini, F., Martinelli, P., Riva, R., Albani, F., Vetrugno, R., . . . Baruzzi, A. (2003). Excessive daytime sleepiness and levodopa in Parkinson's disease: polygraphic, placebo-controlled monitoring. *Clinical neuropharmacology*, 26(3), 115-118.
- Contreras, A. and Grandas, F. (2012) 'Risk of falls in Parkinson's disease: a crosssectional study of 160 patients'. *Parkinson's Disease*, 2012.
- Cools, R. (2006) 'Dopaminergic modulation of cognitive function-implications for L-DOPA treatment in Parkinson's disease'. *Neuroscience & Biobehavioral Reviews*, 30 (1), pp. 1-23.
- Costandi, M. (2016) Neuroplasticity. MIt Press.
- Courtine, G., & Schieppati, M. (2003). Human walking along a curved path. I. Body trajectory, segment orientation and the effect of vision. *European Journal of Neuroscience*, 18(1), 177-190.
- Cui, G., Jun, S. B., Jin, X., Pham, M. D., Vogel, S. S., Lovinger, D. M., & Costa, R. M. (2013). Concurrent activation of striatal direct and indirect pathways during action initiation. *Nature*, 494(7436), 238-242.
- Danion, F. and Latash, M.L. (2011) Motor control: theories, experiments, and applications. Oxford University Press.
- De Carvalho, A. O., Sá Filho, A. S., Murillo-Rodriguez, E., Rocha, N. B., Carta, M. G., & Machado, S. (2018). Physical exercise for parkinson's disease: Clinical and experimental evidence. *Clinical practice and epidemiology in mental health: CP & EMH*, 14, 89.
- De Goede, C. J., Keus, S. H., Kwakkel, G., & Wagenaar, R. C. (2001). The effects of physical therapy in Parkinson's disease: a research synthesis. *Archives of physical medicine and rehabilitation*, 82(4), 509-515.
- De Haan, S.H.S.-W. (2017a) Work stress in two health systems: an international survey. Stellenbosch: Stellenbosch University.
- De Luca, C. J., Gilmore, L. D., Kuznetsov, M., & Roy, S. H. (2010). Filtering the surface EMG signal: Movement artifact and baseline noise contamination. *Journal of biomechanics*, 43(8), 1573-1579.

- de Melo, G. E. L., Kleiner, A. F. R., Lopes, J. B. P., Dumont, A. J. L., Lazzari, R. D.,
  Galli, M., & Oliveira, C. S. (2018). Effect of virtual reality training on walking distance and physical fitness in individuals with Parkinson's disease. *NeuroRehabilitation*, 42(4), 473-480.
- De Pablo-Fernandez, E., Goldacre, R., Pakpoor, J., Noyce, A. J., & Warner, T. T. (2018). Association between diabetes and subsequent Parkinson disease: a record-linkage cohort study. *Neurology*, *91*(2), e139-e142.
- de Souza Fortaleza, A. C., Mancini, M., Carlson-Kuhta, P., King, L. A., Nutt, J. G., Chagas, E. F., . . . Horak, F. B. (2017). Dual task interference on postural sway, postural transitions and gait in people with Parkinson's disease and freezing of gait. *Gait & posture*, 56, 76-81.
- Decker, L. M., Cignetti, F., Potter, J. F., Studenski, S. A., & Stergiou, N. (2012). Use of motor abundance in young and older adults during dual-task treadmill walking. *PloS one*, 7(7), e41306.
- Dehaene, S. (2009) 'Reading in the brain'. New York.
- Delafontaine, A., Fourcade, P., Zemouri, A., Guisse Diakhaté, D., Saiydoun, G., & Yiou, E. (2021). In patients with Parkinson disease in an OFF-medication state, does bilateral electrostimulation of Tibialis Anterior improve anticipatory postural adjustments during gait initiation? *Frontiers in Human Neuroscience*, 15, 415.
- Delval, A., Dujardin, K., Tard, C., Devanne, H., Willart, S., Bourriez, J.-L., . . .
  Defebvre, L. (2012). Anticipatory postural adjustments during step initiation: elicitation by auditory stimulation of differing intensities. *Neuroscience*, *219*, 166-174.
- Delval, A., Tard, C. and Defebvre, L. (2014) 'Why we should study gait initiation in Parkinson's disease'. *Neurophysiologie Clinique/Clinical Neurophysiology*, 44 (1), pp. 69-76.
- Den Otter, A., Geurts, A., Mulder, T., & Duysens, J. (2004). Speed related changes in muscle activity from normal to very slow walking speeds. *Gait & posture*, 19(3), 270-278.
- Dickson, L. and Greenwood, G. (1904a) '221'. *The American Mathematical Monthly*, 11 (5), pp. 116-116.
- Doidge, N. (2007) The brain that changes itself: Stories of personal triumph from the frontiers of brain science. Penguin.

- Dicharry, J. (2010). Kinematics and kinetics of gait: from lab to clinic. *Clinics in sports medicine*, 29(3), 347-364.
- Dresbach, T., Neeb, A., Meyer, G., Gundelfinger, E. D., & Brose, N. (2004). Synaptic targeting of neuroligin is independent of neurexin and SAP90/PSD95 binding. *Molecular and Cellular Neuroscience*, 27(3), 227-235.
- Dresbach, T., Qualmann, B., Kessels, M., Garner, C., & Gundelfinger, E. (2001). The presynaptic cytomatrix of brain synapses. *Cellular and Molecular Life Sciences CMLS*, 58(1), 94-116.
- Duffau, H. (2016) 'Brain plasticity and reorganization before, during, and after glioma resection'. *Glioblastoma*, 225-236.
- Duvernoy, H.M. (1995) 'Structure and functions of the brain stem'. *The Human Brain* Stem and Cerebellum. Springer, pp. 41-89.
- Duvernoy, H.M. (2012) The human brain stem and cerebellum: surface, structure, vascularization, and three-dimensional sectional anatomy, with MRI. Springer Science & Business Media.
- Engelhardt, E. (2017a) 'Lafora and Tretiakoff: the naming of the inclusion bodies discovered by Lewy'. *Arquivos de neuro-psiquiatria*, 75 751-753.
- Erni, T., & Dietz, V. (2001). Obstacle avoidance during human walking: learning rate and cross-modal transfer. *The Journal of physiology*, *534*(1), 303-312.
- Espy, D. D., Yang, F., Bhatt, T., & Pai, Y.-C. (2010). Independent influence of gait speed and step length on stability and fall risk. *Gait & posture*, 32(3), 378-382.
- Ewins, D. and Collins, T. (2014) 'Clinical gait analysis'. *Clinical Engineering*. Elsevier, pp. 389-406.
- Faherty, C. J., Shepherd, K. R., Herasimtschuk, A., & Smeyne, R. J. (2005).
  Environmental enrichment in adulthood eliminates neuronal death in experimental Parkinsonism. *Molecular brain research*, *134*(1), 170-179.
- Fahn, S. (2003) 'Description of Parkinson's disease as a clinical syndrome'. Annals of the New York Academy of Sciences, 991 (1), pp. 1-14.
- Fasano, A., Canning, C. G., Hausdorff, J. M., Lord, S., & Rochester, L. (2017). Falls in Parkinson's disease: a complex and evolving picture. *Movement disorders*, 32(11), 1524-1536.

- Fazekas, F., Kleinert, R., Offenbacher, H., Schmidt, R., Kleinert, G., Payer, F., ...
  Lechner, H. (1993). Pathologic correlates of incidental MRI white matter signal hyperintensities. *Neurology*, *43*(9), 1683-1683.
- Fearnley, J.M. and Lees, A.J. (1991) 'Ageing and Parkinson's disease: substantia nigra regional selectivity'. *Brain*, 114 (5), pp. 2283-2301.
- Feldman, A.G. (1986) 'Once more on the equilibrium-point hypothesis (λ model) for motor control'. *Journal of motor behavior*, 18 (1), pp. 17-54.
- Feldman, A.G. (2009) 'Origin and advances of the equilibrium-point hypothesis'. *Progress in motor control*. Springer, pp. 637-643.
- Fereshtehnejad, S.-M., Zeighami, Y., Dagher, A., & Postuma, R. B. (2017). Clinical criteria for subtyping Parkinson's disease: biomarkers and longitudinal progression. *Brain*, 140(7), 1959-1976.
- Ferrari, A., Benedetti, M. G., Pavan, E., Frigo, C., Bettinelli, D., Rabuffetti, M., . . .
  Leardini, A. (2008). Quantitative comparison of five current protocols in gait analysis. *Gait & posture*, 28(2), 207-216.
- Ferrarin, M., Carpinella, I., Rabuffetti, M., Calabrese, E., Mazzoleni, P., & Nemni, R. (2006). Locomotor disorders in patients at early stages of Parkinson's disease: a quantitative analysis. 2006 International Conference of the IEEE Engineering in Medicine and Biology Society,
- Field, A. (2009) Discovering statistics using SPSS. Sage publications.
- Fiolkowski, P., Brunt, D., Bishop, M., & Woo, R. (2002). Does postural instability affect the initiation of human gait? *Neuroscience Letters*, *323*(3), 167-170.
- Fisher, B. E., Petzinger, G. M., Nixon, K., Hogg, E., Bremmer, S., Meshul, C. K., & Jakowec, M. W. (2004). Exercise-induced behavioral recovery and neuroplasticity in the 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine-lesioned mouse basal ganglia. *Journal of neuroscience research*, 77(3), 378-390.
- Fisher, B. E., Wu, A. D., Salem, G. J., Song, J., Lin, C.-H. J., Yip, J., . . . 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(7), 1221-1229.
- Flannigan, B. D., Bradley, W. G., Mazziotta, J. C., Rauschning, W., Bentson, J. R.,
  Lufkin, R. B., & Hieshima, G. B. (1985). Magnetic resonance imaging of the brainstem:

normal structure and basic functional anatomy. *Radiology*, *154*(2), 375-383. <u>https://doi.org/10.1148/radiology.154.2.3966125</u>

- Flavio Fröhlich (2016) Network Neuroscience, 2016, Pages 2291-2296.
- Forsyth, A. L., Paul, S. S., Allen, N. E., Sherrington, C., Fung, V. S., & Canning, C. G. (2017). Flexed truncal posture in Parkinson disease: measurement reliability and relationship with physical and cognitive impairments, mobility, and balance. *Journal of Neurologic Physical Therapy*, *41*(2), 107-113.
- Freeze, B. S., Kravitz, A. V., Hammack, N., Berke, J. D., & Kreitzer, A. C. (2013).
  Control of basal ganglia output by direct and indirect pathway projection neurons. *Journal of Neuroscience*, *33*(47), 18531-18539.
- Fuchs, E. and Flügge, G. (2014) 'Adult neuroplasticity: more than 40 years of research'. *Neural plasticity*, 2014.
- Fukuchi, C.A., Fukuchi, R.K. and Duarte, M. (2019) 'Effects of walking speed on gait biomechanics in healthy participants: a systematic review and metaanalysis'. *Systematic reviews*, 8 (1), pp. 1-11.
- Fuller, J. R., Adkin, A. L., & Vallis, L. A. (2007). Strategies used by older adults to change travel direction. *Gait & posture*, 25(3), 393-400.
- Galna, B., Murphy, A.T. and Morris, M.E. (2010a) 'Obstacle crossing in people with Parkinson's disease: foot clearance and spatiotemporal deficits'. *Human movement science*, 29 (5), pp. 843-852.
- Gantois, I., Fang, K., Jiang, L., Babovic, D., Lawrence, A. J., Ferreri, V., . . . Morganti-Kossmann, C. M. (2007). Ablation of D1 dopamine receptor-expressing cells generates mice with seizures, dystonia, hyperactivity, and impaired oral behavior. *Proceedings of the National Academy of Sciences*, 104(10), 4182-4187.
- Gaßner, H., Steib, S., Klamroth, S., Pasluosta, C. F., Adler, W., Eskofier, B. M., . . .
  Klucken, J. (2019). Perturbation treadmill training improves clinical characteristics of gait and balance in Parkinson's Disease. *Journal of Parkinson's disease*, 9(2), 413-426.
- Geijtenbeek, T., Steenbrink, F., Otten, B., & Even-Zohar, O. (2011). D-flow: immersive virtual reality and real-time feedback for rehabilitation. Proceedings of the 10th International Conference on Virtual Reality Continuum and Its Applications in Industry,

- Gelat, T. and Brenière, Y. (2000) 'Adaptation of the gait initiation process for stepping on to a new level using a single step'. *Experimental brain research*, 133 (4), pp. 538-546.
- Georgiades, M. J., Gilat, M., Martens, K. A. E., Walton, C. C., Bissett, P. G., Shine, J. M., & Lewis, S. J. (2016). Investigating motor initiation and inhibition deficits in patients with Parkinson's disease and freezing of gait using a virtual reality paradigm. *Neuroscience*, *337*, 153-162.
- Ghielen, I., van den Heuvel, O. A., de Goede, C. J., Houniet-de Gier, M., Collette, E. H., Burgers-Bots, I. A., Rutten, S., Kwakkel, G., Vermunt, K., & van Vliet, B. (2015). BEWARE: Body awareness training in the treatment of wearing-off related anxiety in patients with Parkinson's disease: study protocol for a randomized controlled trial. *Trials*, *16*(1), 1-7.
- Gibb, R. L., Gonzalez, C. L., Wegenast, W., & Kolb, B. E. (2010). Tactile stimulation promotes motor recovery following cortical injury in adult rats. *Behavioural brain research*, 214(1), 102-107.
- Gibson, E. J., & Pick, A. D. (2000). An ecological approach to perceptual learning and development. Oxford University Press, USA.
- Gilat, M., Shine, J. M., Bolitho, S. J., Matar, E., Kamsma, Y. P., Naismith, S. L., & Lewis, S. J. (2013). Variability of stepping during a virtual reality paradigm in Parkinson's disease patients with and without freezing of gait. *PloS one*, *8*(6), e66718.
- Girault, J.-A. and Greengard, P. (2004a) 'The neurobiology of dopamine signaling'. *Archives of neurology*, 61 (5), pp. 641-644.
- Glaister, B. C., Bernatz, G. C., Klute, G. K., & Orendurff, M. S. (2007). Video task analysis of turning during activities of daily living. *Gait & posture*, 25(2), 289-294.
- Goetz, C. G., Poewe, W., Rascol, O., Sampaio, C., Stebbins, G. T., Counsell, C., . . .
  Wenning, G. K. (2004). Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: status and recommendations the Movement Disorder Society Task Force on rating scales for Parkinson's disease. Movement disorders, 19(9), 1020-1028.
- Gouwanda, D. and Gopalai, A.A. (2015) 'A robust real-time gait event detection using wireless gyroscope and its application on normal and altered gaits'. *Medical engineering & physics*, 37 (2), pp. 219-225.

- Grafton, S.T. and Hamilton, A.F.d.C. (2007) 'Evidence for a distributed hierarchy of action representation in the brain'. *Human movement science*, 26 (4), pp. 590-616.
- Gray, P. and Hildebrand, K. (2000) 'Fall risk factors in Parkinson's disease'. *Journal of Neuroscience Nursing*, 32 (4), pp. 222.
- Graybiel, A.M. (2000) 'The basal ganglia'. Current biology, 10 (14), pp. R509-R511.
- Greengard, P. (2001a) 'The neurobiology of slow synaptic transmission'. *Science*, 294 (5544), pp. 1024-1030.
- Griffin, H., Greenlaw, R., Limousin, P., Bhatia, K., Quinn, N., & Jahanshahi, M. (2011). The effect of real and virtual visual cues on walking in Parkinson's disease. *Journal of neurology*, 258(6), 991-1000.
- Grosset, D., Fernandez, H., Grosset, K., & Okun, M. (2009). Parkinson's Disease: Clinican's Desk Reference. CRC Press.
- Guan, X., Zeng, Q., Guo, T., Wang, J., Xuan, M., Gu, Q., . . . Zhang, M. (2017).
  Disrupted functional connectivity of basal ganglia across tremor-dominant and akinetic/rigid-dominant Parkinson's disease. *Frontiers in Aging Neuroscience*, *9*, 360.
- Gulley, E., Ayers, E., & Verghese, J. (2020). A comparison of turn and straight walking phases as predictors of incident falls. *Gait & posture*, 79, 239-243.
- Hackney, M.E. and Earhart, G.M. (2009a) 'Effects of dance on movement control in Parkinson's disease: a comparison of Argentine tango and American ballroom'. *Journal of rehabilitation medicine*, 41 (6), pp. 475-481.
- Hagell, P. and Brundin, L. (2009a) 'Towards an understanding of fatigue in Parkinson disease'. *Journal of Neurology, Neurosurgery & Psychiatry*, 80 (5), pp. 489-492.
- Hagell, P. and Nilsson, M.H. (2009) 'The 39-item Parkinson's Disease Questionnaire (PDQ-39): is it a unidimensional construct?'. *Therapeutic Advances in Neurological Disorders*, 2 (4), pp. 205-214.
- Halaki, M. and Ginn, K. (2012) 'Normalization of EMG signals: to normalize or not to normalize and what to normalize to'. *Computational intelligence in electromyography analysis-a perspective on current applications and future challenges*, 175-194.
- Halliday, S. E., Winter, D. A., Frank, J. S., Patla, A. E., & Prince, F. (1998). The initiation of gait in young, elderly, and Parkinson's disease subjects. *Gait & posture*, 8(1), 8-14.
- Harischandra, N., Knuesel, J., Kozlov, A., Bicanski, A., Cabelguen, J.-M., Ijspeert, A.
  J., & Ekeberg, Ö. (2011). Sensory feedback plays a significant role in generating

walking gait and in gait transition in salamanders: a simulation study. *Frontiers in neurorobotics*, *5*, 3.

- Harrison, J.E., Preston, S. and Blunt, S.B. (2000) 'Measuring symptom change in patients with Parkinson's disease'. *Age and ageing*, 29 (1), pp. 41-45.
- Hase, K., & Stein, R. (1999). Turning strategies during human walking. *Journal of neurophysiology*, 81(6), 2914-2922.
- Hassler, R. (1967) 'Private communication to O'. *Hornykiewicz. Letter dated February*, 9 1967.
- Hassler, R., Mundinger, F. and Riechert, T. (1979) 'Basis of the Parkinson syndrome: morphology, physiology, biochemistry, and pathology'. *Stereotaxis in Parkinson Syndrome*. Springer, pp. 2-45.
- Herbet, G., Maheu, M., Costi, E., Lafargue, G., & Duffau, H. (2016). Mapping neuroplastic potential in brain-damaged patients. *Brain*, *139*(3), 829-844.
- Hermens, H. J., Freriks, B., Merletti, R., Stegeman, D., Blok, J., Rau, G., ... Hägg, G. (1999). European recommendations for surface electromyography. *Roessingh research and development*, 8(2), 13-54.
- Herrero-Larrea, A., Miñarro, A., Narvaiza, L., Gálvez-Barrón, C., León, N. G., Valldosera, E., . . . Sabater, J. B. (2018). Normal limits of home measured spatial gait parameters of the elderly population and their association with health variables. *Scientific reports*, 8(1), 1-8.
- Hiraoka, K. and Abe, K. (2007a) 'Cortical and spinal control of ankle joint muscles before and during gait initiation'. *Somatosensory & Motor Research*, 24 (3), pp. 127-133.
- Hiraoka, K. and Iwata, A. (2006) 'Cyclic modulation of H-reflex depression in ipsilateral and contralateral soleus muscles during rhythmic arm swing'. *Somatosensory* & *motor research*, 23 (3-4), pp. 127-133.
- Hiraoka, K., Matuo, Y., Iwata, A., Onishi, T., & Abe, K. (2006). The effects of external cues on ankle control during gait initiation in Parkinson's disease. *Parkinsonism & related disorders*, *12*(2), 97-102.
- Hirsch, M., & Farley, B. (2009). Exercise and neuroplasticity in persons living with Parkinson's disease. *Eur J Phys Rehabil Med*, 45(2), 215-229.

- Hirsch, M.A., Iyer, S.S. and Sanjak, M. (2016a) 'Exercise-induced neuroplasticity in human Parkinson's disease: What is the evidence telling us?'. *Parkinsonism & related disorders*, 22 S78-S81.
- Holdorff, B. (2002a) 'Friedrich Heinrich Lewy (1885–1950) and his work'. *Journal of the History of the Neurosciences*, 11 (1), pp. 19-28.
- Hollman, J. H., Watkins, M. K., Imhoff, A. C., Braun, C. E., Akervik, K. A., & Ness, D.
  K. (2016). A comparison of variability in spatiotemporal gait parameters between treadmill and overground walking conditions. *Gait & posture*, 43, 204-209.
- Horak, F.B. (1991) 'Assumptions underlying motor control for neurologic rehabilitation'. *Contemporary management of motor control problems: Proceedings of the II STEP conference*, 1991. Foundation for Physical Therapy Alexandria, Va, pp.11-28.
- Hornykiewicz, O. (2001a) 'Dopamine and Parkinson's disease: A personal view of the past, the present, and the future'. *Advances in neurology*, 86 1-11.
- Hornykiewicz, O. (2001b) 'How L-DOPA was discovered as a drug for Parkinson's disease 40 years ago'. *Wiener klinische Wochenschrift*, 113 (22), pp. 855-862.
- Hornykiewicz, O. (2002) 'Brain dopamine: A historical perspective'. *Dopamine in the CNS I*. Springer, pp. 1-22.
- Hornykiewicz, O. (2006) 'The discovery of dopamine deficiency in the parkinsonian brain'. *Parkinson's Disease and Related Disorders*, 9-15.
- Hwang, C.-L., Lim, J., Yoo, J.-K., Kim, H.-K., Hwang, M.-H., Handberg, E. M., ...
  Cusi, K. (2019). Effect of all-extremity high-intensity interval training vs. moderateintensity continuous training on aerobic fitness in middle-aged and older adults with type 2 diabetes: A randomized controlled trial. *Experimental gerontology*, *116*, 46-53.
- Ibala, E., Coupaud, S., & Kerr, A. (2019). Comparison of the muscle pattern variability during treadmill walking (fixed and self-pace) and overground walking of able-bodied adults. *Journal of Annals of Bioengineering*, 1, 1-11.
- Ishikawa, M. and Komi, P.V. (2007) 'The role of the stretch reflex in the gastrocnemius muscle during human locomotion at various speeds'. *Journal of Applied Physiology*, 103 (3), pp. 1030-1036.
- Ivancevic, T., Greenberg, H. and Greenberg, R. (2015) Enhancing Performance and Reducing Stress in Sports: Technological Advances. Springer.

- Iwamoto, Y., Takahashi, M. and Shinkoda, K. (2017) 'Differences of muscle cocontraction of the ankle joint between young and elderly adults during dynamic postural control at different speeds'. *Journal of physiological anthropology*, 36 (1), pp. 1-9.
- Jackson-Lewis, V., Jakowec, M., Burke, R. E., & Przedborski, S. (1995). Time course and morphology of dopaminergic neuronal death caused by the neurotoxin 1-methyl-4phenyl-1, 2, 3, 6-tetrahydropyridine. *Neurodegeneration*, 4(3), 257-269.
- Jang, M.H. *et al.* (2018) 'Validity and reliability of the newly developed surface electromyography device for measuring muscle activity during voluntary isometric contraction'. *Computational and mathematical methods in medicine*, 2018.
- Jankovic, J. (2007) 'Pathophysiology and assessment of parkinsonian symptoms and signs'. *Handbook of Parkinson's disease. New York: Taylor and Francis Group LLC*, 79-104.
- Jankovic, J. (2008) 'Parkinson's disease: clinical features and diagnosis'. *Journal of neurology, neurosurgery & psychiatry*, 79 (4), pp. 368-376.
- Jankovic, J. and Tolosa, E. (2007) Parkinson's disease and movement disorders. Lippincott Williams & Wilkins.
- Johns, P. (2014a) Clinical Neuroscience E-Book. Elsevier Health Sciences.
- Johnston, M.V., Ottenbacher, K.J. and Reichardt, C.S. (1995) 'Strong quasiexperimental designs for research on the effectiveness of rehabilitation'. *American journal of physical medicine & rehabilitation*, 74 (5), pp. 383-392.
- Kainz, H., Graham, D., Edwards, J., Walsh, H. P., Maine, S., Boyd, R. N., . . . Carty, C.
  P. (2017). Reliability of four models for clinical gait analysis. *Gait & posture*, 54, 325-331.
- Kainz, H., Modenese, L., Lloyd, D., Maine, S., Walsh, H., & Carty, C. (2016). Joint kinematic calculation based on clinical direct kinematic versus inverse kinematic gait models. *Journal of biomechanics*, 49(9), 1658-1669.
- Kamen, G. and Kinesiology, E. (2004a) 'Research methods in biomechanics'. *Champaign, IL, Human Kinetics Publ.*
- Kebabian, J.W. and Greengard, P. (1971) 'Dopamine-sensitive adenyl cyclase: possible role in synaptic transmission'. *Science*, 174 (4016), pp. 1346-1349.
- Kemoun, G. and Defebvre, L. (2001a) 'Gait disorders in Parkinson disease. Gait freezing and falls: therapeutic management'. *Presse Medicale (Paris, France: 1983)*, 30 (9), pp. 460-468.

- Keus, S. *et al.* (2007a) 'Effectiveness of physiotherapy in Parkinson's disease: the feasibility of a randomised controlled trial'. *Parkinsonism & related disorders*, 13 (2), pp. 115-121.
- Khademi-Kalantari, K. *et al.* (2017a) 'Lower limb muscular activity during walking at different speeds: Over-ground versus treadmill walking: A voluntary response evaluation'. *Journal of bodywork and movement therapies*, 21 (3), pp. 605-611.
- Khamis, S., Danino, B., Springer, S., Ovadia, D., & Carmeli, E. (2017). Detecting anatomical leg length discrepancy using the plug-in-gait model. *Applied Sciences*, 7(9), 926.
- Khanmohammadi, R., Talebian, S., Hadian, M. R., Olyaei, G., & Bagheri, H. (2016).
  Characteristic muscle activity patterns during gait initiation in the healthy younger and older adults. *Gait & posture*, 43, 148-153.
- Kharb, A., Saini, V., Jain, Y., & Dhiman, S. (2011). A review of gait cycle and its parameters. *IJCEM International Journal of Computational Engineering & Management*, 13, 78-83.
- Kibushi, B., Hagio, S., Moritani, T., & Kouzaki, M. (2018). Speed-dependent modulation of muscle activity based on muscle synergies during treadmill walking. *Frontiers in human neuroscience*, *12*, 4.
- Kilic, M., Aydin, M. D., Demirci, E., Kilic, B., Yilmaz, I., Tanriverdi, O., & Kanat, A. (2018). Unpublished neuropathologic mechanism behind the muscle weakness/paralysis and gait disturbances induced by sciatic nerve degeneration after spinal subarachnoid hemorrhage: an experimental study. *World Neurosurgery*, *119*, e1029-e1034.
- Kılıc, M.M., Muratlı, O.C. and Catal, C. (2017) 'Virtual reality based rehabilitation system for Parkinson and multiple sclerosis patients'. 2017 International Conference on Computer Science and Engineering (UBMK), 2017. IEEE, pp.328-331.
- King, L.A. and Horak, F.B. (2009) 'Delaying mobility disability in people with Parkinson disease using a sensorimotor agility exercise program'. *Physical therapy*, 89 (4), pp. 384-393.
- Klamroth, S., Steib, S., Gaßner, H., Goßler, J., Winkler, J., Eskofier, B., . . . Pfeifer, K. (2016). Immediate effects of perturbation treadmill training on gait and postural control in patients with Parkinson's disease. *Gait & posture*, 50, 102-108.

- Klassen, K. (2014) 'Stanislas Dehaene (2009). Reading in the Brain: The New Science of How We Read. New York: Penguin+ 388 pp. ISBN: 978-0-14-311805-3'. Wiley Online Library.
- Kleissen, R., Buurke, J., Harlaar, J., & Zilvold, G. (1998). Electromyography in the biomechanical analysis of human movement and its clinical application. *Gait & posture*, 8(2), 143-158.
- Kolb, B. and Gibb, R. (2010) 'Tactile stimulation after frontal or parietal cortical injury in infant rats facilitates functional recovery and produces synaptic changes in adjacent cortex'. *Behavioural brain research*, 214 (1), pp. 115-120.
- Kopell, B.H. and Greenberg, B.D. (2008a) 'Anatomy and physiology of the basal ganglia: implications for DBS in psychiatry'. *Neuroscience & Biobehavioral Reviews*, 32 (3), pp. 408-422.
- Kyröläinen, H., Avela, J. and Komi, P.V. (2005) 'Changes in muscle activity with increasing running speed'. *Journal of sports sciences*, 23 (10), pp. 1101-1109.
- Lajoie, Y., Teasdale, N., Bard, C., & Fleury, M. (1996). Upright standing and gait: are there changes in attentional requirements related to normal aging? *Experimental aging research*, 22(2), 185-198.
- Lamont, R.M. *et al.* (2012) 'Community walking in people with Parkinson's disease'. *Parkinson's Disease*, 2012.
- Lanciego, J.L., Luquin, N. and Obeso, J.A. (2012) 'Functional neuroanatomy of the basal ganglia'. *Cold Spring Harbor perspectives in medicine*, 2 (12), pp. a009621.
- Latash, M.L. (2012) 'The bliss (not the problem) of motor abundance (not redundancy)'. *Experimental brain research*, 217 (1), pp. 1-5.
- Latash, M.L. *et al.* (2010) 'Motor control theories and their applications'. *Medicina*, 46 (6), pp. 382.
- Lau, H.-y., Tong, K.-y. and Zhu, H. (2009) 'Support vector machine for classification of walking conditions of persons after stroke with dropped foot'. *Human movement science*, 28 (4), pp. 504-514.
- Lauhoff, P., Murphy, N., Doherty, C., & Horgan, N. F. (2013). A controlled clinical trial investigating the effects of cycle ergometry training on exercise tolerance, balance and quality of life in patients with Parkinson's disease. *Disability and rehabilitation*, 35(5), 382-387.

- Le, P., Best, T. M., Khan, S. N., Mendel, E., & Marras, W. S. (2017). A review of methods to assess coactivation in the spine. *Journal of electromyography and kinesiology*, *32*, 51-60.
- Le Ray, D. and Guayasamin, M. (2022) 'How Does the Central Nervous System for Posture and Locomotion Cope With Damage-Induced Neural Asymmetry?'. *Frontiers in Systems Neuroscience*, 16.
- Leardini, A., Chiari, L., Della Croce, U., & Cappozzo, A. (2005). Human movement analysis using stereophotogrammetry: Part 3. Soft tissue artifact assessment and compensation. *Gait & posture*, 21(2), 212-225.
- Lee, J.-A., Cho, S.-H., Lee, Y.-J., Yang, H.-K., & Lee, J.-W. (2010). Portable activity monitoring system for temporal parameters of gait cycles. *Journal of medical systems*, 34(5), 959-966.
- Lee, J.K. and Park, E.J. (2011) 'Quasi real-time gait event detection using shankattached gyroscopes'. *Medical & biological engineering & computing*, 49 (6), pp. 707-712.
- Lee, M.H. (2019) 'Intelligent Agent for Assessing and Guiding Rehabilitation Exercises'. *IJCAI*, 2019. pp.6444-6445.
- Lee, S.J. and Hidler, J. (2008a) 'Biomechanics of overground vs. treadmill walking in healthy individuals'. *Journal of applied physiology*, 104 (3), pp. 747-755.
- Lees, A.J., Blackburn, N.A. and Campbell, V.L. (1988a) 'The nighttime problems of Parkinson's disease'. *Clinical neuropharmacology*, 11 (6), pp. 512-519.
- Lei, C., Sunzi, K., Dai, F., Liu, X., Wang, Y., Zhang, B., . . . Ju, M. (2019). Effects of virtual reality rehabilitation training on gait and balance in patients with Parkinson's disease: a systematic review. *PLoS One*, *14*(11), e0224819.
- Leisman, G., Moustafa, A.A. and Shafir, T. (2016) 'Thinking, walking, talking: integratory motor and cognitive brain function'. *Frontiers in public health*, 4 94.
- Lelard, T., Doutrellot, P.-L., Temfemo, A., & Ahmaidi, S. (2017). Electromyographic pattern during gait initiation differentiates yoga practitioners among physically active older subjects. *Frontiers in human neuroscience*, *11*, 300.
- Lepers, R. and Breniere, Y. (1995) 'The role of anticipatory postural adjustments and gravity in gait initiation'. *Experimental brain research*, 107 (1), pp. 118-124.

- Levin, J., Krafczyk, S., Valkovič, P., Eggert, T., Claassen, J., & Bötzel, K. (2009).
  Objective measurement of muscle rigidity in Parkinsonian patients treated with subthalamic stimulation. *Movement disorders*, 24(1), 57-63.
- Levine, D., Richards, J. and Whittle, M.W. (2012a) Whittle's Gait Analysis-E-Book. Elsevier health sciences.
- Levitan, I.B., & Kaczmarek, L. K. (2015). The neuron: Cell and molecular biology Oxford University Press, USA. (2015).
- Levitan, I.B., Levitan, I.B. and Kaczmarek, L.K. (2002) *The neuron: cell and molecular biology*. Oxford University Press, USA.
- Lewis, P.A. and Spillane, J.E. (2018a) *The molecular and clinical pathology of neurodegenerative disease*. Academic Press.
- Li, X., Xu, H. and Cheung, J.T. (2016) 'Gait-force model and inertial measurement unitbased measurements: A new approach for gait analysis and balance monitoring'. *Journal of Exercise Science & Fitness*, 14 (2), pp. 60-66.
- Liang, J., Lang, S., Zheng, Y., Wang, Y., Chen, H., Yang, J., ... Ou, H. (2019). The effect of anti-gravity treadmill training for knee osteoarthritis rehabilitation on joint pain, gait, and EMG: Case report. *Medicine*, 98(18).
- Liao, Y.-Y., Yang, Y.-R., Wu, Y.-R., & Wang, R.-Y. (2014). Factors influencing obstacle crossing performance in patients with Parkinson's disease. *PLoS One*, 9(1), e84245.
- Lieberman, A.N. (1993) Parkinson's disease: The complete guide for patients and caregivers. Simon and Schuster.
- Lim, Y.P., Lin, Y.-C. and Pandy, M.G. (2017) 'Effects of step length and step frequency on lower-limb muscle function in human gait'. *Journal of biomechanics*, 57 1-7.
- Lin, C.-C., Creath, R.A. and Rogers, M.W. (2016) 'Variability of anticipatory postural adjustments during gait initiation in individuals with Parkinson's disease'. *Journal of neurologic physical therapy: JNPT*, 40 (1), pp. 40.
- Lindroos, R., Dorst, M. C., Du, K., Filipović, M., Keller, D., Ketzef, M., . . . Nair, A. G. (2018). Basal ganglia neuromodulation over multiple temporal and structural scales—simulations of direct pathway MSNs investigate the fast onset of dopaminergic effects and predict the role of Kv4. 2. *Frontiers in Neural Circuits*, *12*, 3.

- Lo, J., Lo, O.-Y., Olson, E. A., Habtemariam, D., Iloputaife, I., Gagnon, M. M., ...
  Lipsitz, L. A. (2017). Functional implications of muscle co-contraction during gait in advanced age. *Gait & posture*, 53, 110-114.
- Lord, S., Rochester, L., Hetherington, V., Allcock, L. M., & Burn, D. (2010). Executive dysfunction and attention contribute to gait interference in 'off' state Parkinson's Disease. *Gait & posture*, *31*(2), 169-174.
- Lotfian, M., Dadashi, F., Rafieenazari, Z., Shahroki, A., Rasteh, M., Molavi, M., . . . Mirbagheri, M. M. (2019). The Effects of Anti-gravity Treadmill Training on Gait Characteristics in Children with Cerebral Palsy. 2019 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC),
- Luchies, C. W., Schiffman, J., Richards, L. G., Thompson, M. R., Bazuin, D., & DeYoung, A. J. (2002). Effects of age, step direction, and reaction condition on the ability to step quickly. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 57(4), M246-M249.
- Luedtke, R.R. and Mach, R.H. (2003a) 'Progress in developing D3 dopamine receptor ligands as potential therapeutic agents for neurological and neuropsychiatric disorders'. *Current pharmaceutical design*, 9 (8), pp. 643-671.
- Löhrer, H.B. *et al.* (2009) 'Comparison of two protocols for clinical gait analysis regarding frontal plane knee angles and moments'. *Abstracts/Gait & Posture 30S*, 1 S153.
- Lücking, C. and Brice, A. (2000a) 'Alpha-synuclein and Parkinson's disease'. *Cellular* and Molecular Life Sciences CMLS, 57 (13), pp. 1894-1908.
- Mabtrila, R. and Rinne, U. (1976a) 'Epidemiology of Parkinson's disease in Finland'. *Acta Neurologica Scandinavica*, 53 (2), pp. 81-102.
- Madeleine, P. (2010) 'On functional motor adaptations: from the quantification of motor strategies to the prevention of musculoskeletal disorders in the neck–shoulder region'. *Acta Physiologica*, 199 1-46.
- Maidan, I., Nieuwhof, F., Bernad-Elazari, H., Reelick, M. F., Bloem, B. R., Giladi, N., Deutsch, J. E., Hausdorff, J. M., Claassen, J. A., & Mirelman, A. (2016). The role of the frontal lobe in complex walking among patients with Parkinson's disease and healthy older adults: an fNIRS study. *Neurorehabilitation and neural repair*, *30*(10), 963-971.
- Mancini, M., Schlueter, H., El-Gohary, M., Mattek, N., Duncan, C., Kaye, J., & Horak,
  F. B. (2016). Continuous monitoring of turning mobility and its association to falls and

cognitive function: a pilot study. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, 71(8), 1102-1108.

- Martin, K., Blizzard, L., Garry, M., Thomson, R., McGinley, J., & Srikanth, V. (2011).
  Gait initiation in older people—Time to first lateral movement may be the measure of choice. *Gait & posture*, *34*(3), 374-378.
- Maserejian, N., Vinikoor-Imler, L. and Dilley, A. (2020) 'Estimation of the 2020 global population of Parkinson's disease (PD)'. *Movement Disorders*, 2020. WILEY 111
  RIVER ST, HOBOKEN 07030-5774, NJ USA, pp.S79-S80.
- Massano, J. and Bhatia, K.P. (2012a) 'Clinical approach to Parkinson's disease: features, diagnosis, and principles of management'. *Cold Spring Harbor perspectives in medicine*, 2 (6), pp. a008870.
- Massion, J. (1992a) 'Movement, posture and equilibrium: interaction and coordination'. *Progress in neurobiology*, 38 (1), pp. 35-56.
- Mathew, B. *et al.* (2019) 'Emerging therapeutic potentials of dual-acting MAO and AChE inhibitors in Alzheimer's and Parkinson's diseases'. *Archiv der Pharmazie*, 352 (11), pp. 1900177.
- Mathiowetz, V. and Haugen, J.B. (1994) 'Motor behavior research: implications for therapeutic approaches to central nervous system dysfunction'. *American Journal of Occupational Therapy*, 48 (8), pp. 733-745.
- Mbourou, G.A., Lajoie, Y. and Teasdale, N. (2003) 'Step length variability at gait initiation in elderly fallers and non-fallers, and young adults'. *Gerontology*, 49 (1), pp. 21-26.
- McDonald, J.H. (2009a) *Handbook of biological statistics*. sparky house publishing Baltimore, MD.
- McGinley, J. L., Baker, R., Wolfe, R., & Morris, M. E. (2009). The reliability of threedimensional kinematic gait measurements: a systematic review. *Gait & posture*, 29(3), 360-369.
- McGrath, D., Greene, B. R., O'Donovan, K. J., & Caulfield, B. (2012). Gyroscopebased assessment of temporal gait parameters during treadmill walking and running. *Sports Engineering*, 15(4), 207-213.
- 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*(8).

- Menary, R. (2014) 'Neural plasticity, neuronal recycling and niche construction'. *Mind & Language*, 29 (3), pp. 286-303.
- Mendes de Leon, C.F. *et al.* (2009) 'Neighborhood social cohesion and disorder in relation to walking in community-dwelling older adults: a multilevel analysis'. *Journal of aging and health*, 21 (1), pp. 155-171.
- Mengarelli, A., Maranesi, E., Burattini, L., Fioretti, S., & Di Nardo, F. (2017). Cocontraction activity of ankle muscles during walking: A gender comparison. *Biomedical signal processing and control*, 33, 1-9.
- Mhatre, P. V., Vilares, I., Stibb, S. M., Albert, M. V., Pickering, L., Marciniak, C. M., .
  . Toledo, S. (2013). Wii Fit balance board playing improves balance and gait in Parkinson disease. *Pm&r*, 5(9), 769-777.
- Michael-Titus, A.T., Revest, P. and Shortland, P. (2018) Organsysteme verstehen: Nervensystem: Integrative Grundlagen und Fälle. Elsevier Health Sciences.
- Mickelborough, J., Van Der Linden, M., Tallis, R., & Ennos, A. (2004). Muscle activity during gait initiation in normal elderly people. *Gait & posture*, 19(1), 50-57.
- Mikami, Y., Fukuhara, K., Kawae, T., Kimura, H., & Ochi, M. (2015). The effect of anti-gravity treadmill training for prosthetic rehabilitation of a case with below-knee amputation. *Prosthetics and orthotics international*, 39(6), 502-506.
- Mirelman, A., Maidan, I. and Deutsch, J.E. (2013) 'Virtual reality and motor imagery: promising tools for assessment and therapy in Parkinson's disease'. *Movement Disorders*, 28 (11), pp. 1597-1608.
- Mirelman, A., Maidan, I., & Deutsch, J. E. (2013). Virtual reality and motor imagery: promising tools for assessment and therapy in Parkinson's disease. *Movement Disorders*, 28(11), 1597-1608.
- Mirelman, A., Maidan, I., Herman, T., Deutsch, J. E., Giladi, N., & Hausdorff, J. M. (2011). Virtual reality for gait training: can it induce motor learning to enhance complex walking and reduce fall risk in patients with Parkinson's disease? *The Journals of Gerontology: Series A*, 66(2), 234-240.
- Mirelman, A., Rochester, L., Maidan, I., Del Din, S., Alcock, L., Nieuwhof, F., . . . Avanzino, L. (2016). Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): a randomised controlled trial. *The Lancet*, 388(10050), 1170-1182.

- Mirelman, A., Rochester, L., Reelick, M., Nieuwhof, F., Pelosin, E., Abbruzzese, G., . .
  Hausdorff, J. M. (2013). V-TIME: a treadmill training program augmented by virtual reality to decrease fall risk in older adults: study design of a randomized controlled trial. *BMC neurology*, *13*(1), 1-12.
- Mohammadi, F., Bruijn, S. M., Vervoort, G., van Wegen, E. E., Kwakkel, G., Verschueren, S., & Nieuwboer, A. (2015). Motor switching and motor adaptation deficits contribute to freezing of gait in Parkinson's disease. *Neurorehabilitation and neural repair*, 29(2), 132-142.
- Monchi, O., Petrides, M., Strafella, A. P., Worsley, K. J., & Doyon, J. (2006).
  Functional role of the basal ganglia in the planning and execution of actions. *Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society*, 59(2), 257-264.
- Montero-Odasso, M., Schapira, M., Soriano, E. R., Varela, M., Kaplan, R., Camera, L. A., & Mayorga, L. M. (2005). Gait velocity as a single predictor of adverse events in healthy seniors aged 75 years and older. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 60(10), 1304-1309.
- Morris, M., Iansek, R. and Churchyard, A. (1998) 'The role of the physiotherapist in quantifying movement fluctuations in Parkinson's disease'. *Australian Journal of Physiotherapy*, 44 (2), pp. 105-114.
- Morris, M., Iansek, R., McGinley, J., Matyas, T., & Huxham, F. (2005). Threedimensional gait biomechanics in Parkinson's disease: evidence for a centrally mediated amplitude regulation disorder. *Movement disorders: official journal of the Movement Disorder Society*, 20(1), 40-50.
- Morris, M. E., Huxham, F., McGinley, J., Dodd, K., & Iansek, R. (2001). The biomechanics and motor control of gait in Parkinson disease. *Clinical biomechanics*, *16*(6), 459-470.
- Morris, M. E., Huxham, F. E., Mcginley, J., & Iansek, R. (2001). Gait disorders and gait rehabilitation in Parkinson's disease. *Advances in neurology*, 87, 347-361.
- Mowery, B.D. (2011) 'The paired t-test'. Pediatric nursing, 37 (6), pp. 320-322.
- Muir, B., Rietdyk, S. and Haddad, J.M. (2014) 'Gait initiation: the first four steps in adults aged 20–25 years, 65–79 years, and 80–91 years'. *Gait & posture*, 39 (1), pp. 490-494.

- Mutch, W. J., Dingwall-Fordyce, I., Downie, A. W., Paterson, J. G., & Roy, S. K. (1986). Parkinson's disease in a Scottish city. *Br Med J (Clin Res Ed)*, 292(6519), 534-536.
- Münchau, A. and Bhatia, K.P. (2000) 'Pharmacological treatment of Parkinson's disease'. *Postgraduate medical journal*, 76 (900), pp. 602-610.
- Mussa-Ivaldi, F. A., & Giszter, S. F. (1992). Vector field approximation: a computational paradigm for motor control and learning. *Biological cybernetics*, 67(6), 491-500.
- Nadeau, A., Pourcher, E. and Corbeil, P. (2014a) 'Effects of 24 weeks of treadmill training on gait performance in Parkinson disease'. *Med Sci Sports Exerc*, 46 (4), pp. 645-655.
- Nagano, H., Begg, R. K., Sparrow, W. A., & Taylor, S. (2013). A comparison of treadmill and overground walking effects on step cycle asymmetry in young and older individuals. *Journal of applied biomechanics*, 29(2), 188-193.
- Nair, S. P., Gibbs, S., Arnold, G., Abboud, R., & Wang, W. (2010). A method to calculate the centre of the ankle joint: A comparison with the Vicon® Plug-in-Gait model. *Clinical Biomechanics*, 25(6), 582-587.
- Neptune, R.R., Kautz, S.A. and Zajac, F.E. (2001a) 'Contributions of the individual ankle plantar flexors to support, forward progression and swing initiation during walking'. *Journal of biomechanics*, 34 (11), pp. 1387-1398.
- Network, B.N. 'Electromyography(EMG): Monitors Peripheral, Lumbar, and Cranial Nerves'.
- Novak, D., Reberšek, P., De Rossi, S. M. M., Donati, M., Podobnik, J., Beravs, T., . . .
  Munih, M. (2013). Automated detection of gait initiation and termination using wearable sensors. *Medical engineering & physics*, *35*(12), 1713-1720.
- Nutt, J. G., Bloem, B. R., Giladi, N., Hallett, M., Horak, F. B., & Nieuwboer, A. (2011).
  Freezing of gait: moving forward on a mysterious clinical phenomenon. *The Lancet Neurology*, *10*(8), 734-744.
- Okada, Y., Fukumoto, T., Takatori, K., Nagino, K., & Hiraoka, K. (2011).
  Abnormalities of the first three steps of gait initiation in patients with Parkinson's disease with freezing of gait. *Parkinson's disease*, 2011.
- Okuma, Y. (2006a) 'Freezing of gait in Parkinson's disease'. *Journal of neurology*, 253 (7), pp. vii27-vii32.

- Oliveira de Carvalho, A., Murillo-Rodriguez, E., Rocha, N. B., Carta, M. G., & Machado, S. (2018). Physical exercise for parkinson's disease: clinical and experimental evidence. *Clinical Practice and Epidemiology in Mental Health*, 14(1).
- Olver, J., Esquenazi, A., Fung, V., Singer, B., & Ward, A. (2010). Botulinum toxin assessment, intervention and aftercare for lower limb disorders of movement and muscle tone in adults: international consensus statement. *European journal of neurology*, 17, 57-73.
- Opdenakker, R. (2006) 'Advantages and disadvantages of four interview techniques in qualitative research'. *Forum qualitative sozialforschung/forum: Qualitative social research*, 2006.
- Organization, W.H. (2006) *The world health report 2006: working together for health*. World Health Organization.
- Oude Nijhuis, L. B., Allum, J. H., Borm, G. F., Honegger, F., Overeem, S., & Bloem,
  B. R. (2009). Directional sensitivity of "first trial" reactions in human balance
  control. *Journal of neurophysiology*, *101*(6), 2802-2814.
- Oung, Q. W., Hariharan, M., Basah, S. N., Yaacob, S., Sarillee, M., & Lee, H. L.
  (2014). Use of technological tools for Parkinson's disease early detection: A review.
  2014 IEEE International Conference on Control System, Computing and Engineering (ICCSCE 2014),
- Pacini Panebianco, G., Ferrazzoli, D., Frazzitta, G., Fonsato, M., Bisi, M. C., Fantozzi, S., & Stagni, R. (2020). A Statistical Approach for the Assessment of Muscle Activation Patterns during Gait in Parkinson's Disease. *Electronics*, 9(10), 1641.
- Page, P. (2012). Research designs in sports physical therapy. *International journal of* sports physical therapy, 7(5), 482.
- Pandya, M., Kubu, C.S. and Giroux, M.L. (2008a) 'Parkinson disease: not just a movement disorder'. *Cleveland Clinic Journal of Medicine*, 75 (12), pp. 856-864.
- Papegaaij, S. and Steenbrink, F. (2017) 'Clinical gait analysis: Treadmill-based vs overground'. *Motek Inc.: Amsterdam, The Netherlands*.
- Pappas, I. P., Keller, T., Mangold, S., Popovic, M. R., Dietz, V., & Morari, M. (2004).
  A reliable gyroscope-based gait-phase detection sensor embedded in a shoe insole. *IEEE sensors journal*, 4(2), 268-274.

- Park, H.-S., Yoon, J. W., Kim, J., Iseki, K., & Hallett, M. (2011). Development of a VR-based treadmill control interface for gait assessment of patients with Parkinson's disease. 2011 IEEE International Conference on Rehabilitation Robotics,
- Parkinson, J. (2002) 'An essay on the shaking palsy'. *The Journal of neuropsychiatry and clinical neurosciences*, 14 (2), pp. 223-236.
- Parvataneni, K., Ploeg, L., Olney, S. J., & Brouwer, B. (2009). Kinematic, kinetic and metabolic parameters of treadmill versus overground walking in healthy older adults. *Clinical biomechanics*, 24(1), 95-100.
- Pascual-Leone, A., Amedi, A., Fregni, F., & Merabet, L. B. (2005). The plastic human brain cortex. *Annu. Rev. Neurosci.*, 28, 377-401.
- Patla, A. E., Prentice, S. D., Robinson, C., & Neufeld, J. (1991). Visual control of locomotion: strategies for changing direction and for going over obstacles. *Journal of Experimental Psychology: Human Perception and Performance*, 17(3), 603.
- Patla, A.E. and Shumway-Cook, A. (1999) 'Dimensions of mobility: defining the complexity and difficulty associated with community mobility'. *Journal of Aging and Physical Activity*, 7 (1), pp. 7-19.
- Patrick, H.T. and LEVY, D.M. (1922) 'Parkinson's disease: a clinical study of one hundred and forty-six cases'. *Archives of Neurology & Psychiatry*, 7 (6), pp. 711-720.
- Pau, M. *et al.* (2018) 'Quantitative assessment of gait parameters in people with Parkinson's disease in laboratory and clinical setting: Are the measures interchangeable?'. *Neurology international*, 10 (2), pp. 7729.
- Pavčič, J., Matjačić, Z. and Olenšek, A. (2014) 'Kinematics of turning during walking over ground and on a rotating treadmill'. *Journal of neuroengineering and rehabilitation*, 11 (1), pp. 1-12.
- Pazzaglia, C., Imbimbo, I., Tranchita, E., Minganti, C., Ricciardi, D., Monaco, R. L., . .
  Padua, L. (2020). Comparison of virtual reality rehabilitation and conventional rehabilitation in Parkinson's disease: A randomised controlled trial. *Physiotherapy*, *106*, 36-42.
- Perez-Lloret, S., Negre-Pages, L., Damier, P., Delval, A., Derkinderen, P., Destée, A., Meissner, W. G., Schelosky, L., Tison, F., & Rascol, O. (2014). Prevalence, determinants, and effect on quality of life of freezing of gait in Parkinson disease. *JAMA neurology*, *71*(7), 884-890.

- Perez-Lloret, S. and Rascol, O. (2018) 'Efficacy and safety of amantadine for the treatment of L-DOPA-induced dyskinesia'. *Journal of Neural Transmission*, 125 (8), pp. 1237-1250.
- Peruzzi, A., Cereatti, A., Della Croce, U., & Mirelman, A. (2016). Effects of a virtual reality and treadmill training on gait of subjects with multiple sclerosis: a pilot study. *Multiple sclerosis and related disorders*, 5, 91-96.
- Peterson, D. S., Mancini, M., Fino, P. C., Horak, F., & Smulders, K. (2020). Speeding up gait in Parkinson's disease. *Journal of Parkinson's disease*, 10(1), 245-253.
- Petzinger, G. M., Fisher, B. E., McEwen, S., Beeler, J. A., Walsh, J. P., & Jakowec, M. W. (2013). Exercise-enhanced neuroplasticity targeting motor and cognitive circuitry in Parkinson's disease. *The Lancet Neurology*, *12*(7), 716-726.
- Petzinger, G. M., Fisher, B. E., Van Leeuwen, J. E., Vukovic, M., Akopian, G., Meshul, C. K., . . . Jakowec, M. W. (2010). Enhancing neuroplasticity in the basal ganglia: the role of exercise in Parkinson's disease. *Movement disorders*, 25(S1), S141-S145.
- Piepoli, M. F., Corra, U., Benzer, W., Bjarnason-Wehrens, B., Dendale, P., Gaita, D., . .
  Zwisler, A.-D. O. (2010). Secondary prevention through cardiac rehabilitation: from knowledge to implementation. A position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. *European Journal of Cardiovascular Prevention & Rehabilitation*, 17(1), 1-17.
- Ricotta, J., & Latash, M. L. (2021). Stability of Action and Kinesthetic Perception in Parkinson's Disease. *Journal of Human Kinetics*, 76(1), 145-159.
- Pirker, W. and Katzenschlager, R. (2017) 'Gait disorders in adults and the elderly'. *Wiener Klinische Wochenschrift*, 129 (3), pp. 81-95.
- Pistacchi, M., Gioulis, M., Sanson, F., De Giovannini, E., Filippi, G., Rossetto, F., & Marsala, S. Z. (2017). Gait analysis and clinical correlations in early Parkinson's disease. *Functional neurology*, 32(1), 28.
- Plotnik, M., Azrad, T., Bondi, M., Bahat, Y., Gimmon, Y., Zeilig, G., ... Siev-Ner, I. (2015). Self-selected gait speed-over ground versus self-paced treadmill walking, a solution for a paradox. *Journal of neuroengineering and rehabilitation*, *12*(1), 1-11.
- Rochester, L., Hetherington, V., Jones, D., Nieuwboer, A., Willems, A.-M., Kwakkel, G., & Van Wegen, E. (2005). The effect of external rhythmic cues (auditory and visual) on walking during a functional task in homes of people with Parkinson's disease. *Archives of physical medicine and rehabilitation*, 86(5), 999-1006.

- Poitras, I., Bielmann, M., Campeau-Lecours, A., Mercier, C., Bouyer, L. J., & Roy, J.-S. (2019). Validity of wearable sensors at the shoulder joint: Combining wireless electromyography sensors and inertial measurement units to perform physical workplace assessments. *Sensors*, *19*(8), 1885.
- Polcyn, A. F., Lipsitz, L. A., Kerrigan, D. C., & Collins, J. J. (1998). Age-related changes in the initiation of gait: degradation of central mechanisms for momentum generation. *Archives of physical medicine and rehabilitation*, 79(12), 1582-1589.
- Ponti, G., Peretto, P. and Bonfanti, L. (2008) 'Genesis of neuronal and glial progenitors in the cerebellar cortex of peripuberal and adult rabbits'. *PLoS One*, 3 (6), pp. e2366.
- Poskanzer, D.C. and Schwab, R.S. (1963) 'Cohort analysis of Parkinson's syndrome: evidence for a single etiology related to subclinical infection about 1920'. *Journal of chronic diseases*, 16 (9), pp. 961-973.
- Postuma, R.B. and Berg, D. (2017) 'The new diagnostic criteria for Parkinson's disease'. *International review of neurobiology*, 132 55-78.
- Pradhan, G. N., Engineer, N., Nadin, M., & Prabhakaran, B. (2007). Integration of motion capture and EMG data for classifying the human motions. 2007 IEEE 23rd International Conference on Data Engineering Workshop,
- Rampon, C., Jiang, C. H., Dong, H., Tang, Y.-P., Lockhart, D. J., Schultz, P. G., . . . Hu, Y. (2000). Effects of environmental enrichment on gene expression in the brain. *Proceedings of the National Academy of Sciences*, 97(23), 12880-12884.
- Real, C. C., Ferreira, A. F., Hernandes, M. S., Britto, L. R., & Pires, R. S. (2010).
  Exercise-induced plasticity of AMPA-type glutamate receptor subunits in the rat brain. *Brain research*, *1363*, 63-71.
- Reaz, M.B.I., Hussain, M.S. and Mohd-Yasin, F. (2006) 'Techniques of EMG signal analysis: detection, processing, classification and applications'. *Biological procedures online*, 8 (1), pp. 11-35.
- Reisberg, B., Finkel, S., Overall, J., Schmidt-Gollas, N., Kanowski, S., Lehfeld, H., . . .
  Heininger, K. (2001). The Alzheimer's disease activities of daily living international scale (ADL-IS). *International Psychogeriatrics*, *13*(2), 163-181.
- Riederer, P., Reichmann, H., Youdim, M. B., & Gerlach, M. (2006). *Parkinson's Disease and Related Disorders*. Springer Science & Business Media.

- Riley, P.O., Della Croce, U. and Kerrigan, D.C. (2001) 'Propulsive adaptation to changing gait speed'. *Journal of Biomechanics*, 34 (2), pp. 197-202.
- Rissanen, S., Kankaanpää, M., Tarvainen, M. P., Nuutinen, J., Tarkka, I. M., Airaksinen, O., & Karjalainen, P. A. (2007). Analysis of surface EMG signal morphology in Parkinson's disease. *Physiological measurement*, 28(12), 1507.
- Rodriguez, E. B., Chagas, P. S., Silva, P. L., Kirkwood, R. N., & Mancini, M. C. (2013). Impact of leg length and body mass on the stride length and gait speed of infants with normal motor development: A longitudinal study. *Brazilian Journal of Physical Therapy*, *17*, 163-169.
- Roeder, L., Boonstra, T.W. and Kerr, G.K. (2020a) 'Corticomuscular control of walking in older people and people with Parkinson's disease'. *Scientific reports*, 10 (1), pp. 1-18.
- Roemmich, R. T., Nocera, J. R., Vallabhajosula, S., Amano, S., Naugle, K. M., Stegemöller, E. L., & Hass, C. J. (2012). Spatiotemporal variability during gait initiation in Parkinson's disease. *Gait & posture*, *36*(3), 340-343.
- Roller, M. L., Duff, S. V., Umphred, D. A., & Byl, N. N. (2019). Contemporary issues and theories of motor control, motor learning, and neuroplasticity. *Umphred's Neurological Rehabilitation-E-Book*, 51.
- Rosin, R., Topka, H. and Dichgans, J. (1997) 'Gait initiation in Parkinson's disease'. *Movement disorders: official journal of the Movement Disorder Society*, 12 (5), pp. 682-690.
- Rossi, P.H., Lipsey, M. and Freeman, H. (2004) 'Evaluation: A systematic approach (7e éd.)'. Thousand Oaks, CA: Sage.
- Rubenstein, L. Z., & Josephson, K. R. (2002). Risk factors for falls: A central role in prevention. *Generations: Journal of the American Society on Aging*, 26(4), 15-21.
- Rylander, D., Iderberg, H., Li, Q., Dekundy, A., Zhang, J., Li, H., ... Cenci, M. A.
  (2010). A mGluR5 antagonist under clinical development improves L-DOPA-induced dyskinesia in parkinsonian rats and monkeys. *Neurobiology of disease*, *39*(3), 352-361.
- Sainburg, R. L. (2015). Should the equilibrium point hypothesis (eph) be considered a scientific theory? *Motor Control*, *19*(2), 142-148.
- Sasmita, A.O., Kuruvilla, J. and Ling, A.P.K. (2018) 'Harnessing neuroplasticity: modern approaches and clinical future'. *International Journal of Neuroscience*, 128 (11), pp. 1061-1077.

- Schenkman, M., Hall, D. A., Barón, A. E., Schwartz, R. S., Mettler, P., & Kohrt, W. M. (2012). Exercise for people in early-or mid-stage Parkinson disease: a 16-month randomized controlled trial. *Physical therapy*, 92(11), 1395-1410.
- Schlenstedt, C., Mancini, M., Nutt, J., Hiller, A. P., Maetzler, W., Deuschl, G., & Horak, F. (2018). Are hypometric anticipatory postural adjustments contributing to freezing of gait in Parkinson's disease? *Frontiers in aging neuroscience*, *10*, 36.
- Schlossmacher, M. G., Frosch, M. P., Gai, W. P., Medina, M., Sharma, N., Forno, L., . .
  Hattori, N. (2002). Parkin localizes to the Lewy bodies of Parkinson disease and dementia with Lewy bodies. *The American journal of pathology*, *160*(5), 1655-1667.
- Schmidt, R. A. (1975). A schema theory of discrete motor skill learning. *Psychological review*, 82(4), 225.
- Schmidt, R. A., Lee, T. D., Winstein, C., Wulf, G., & Zelaznik, H. N. (2018). *Motor* control and learning: A behavioral emphasis. Human kinetics.
- Schrag, A., Ben-Shlomo, Y., Brown, R., David Marsden, C., & Quinn, N. (1998).
  Young-onset Parkinson's disease revisited—clinical features, natural history, and mortality. *Movement disorders: official journal of the Movement Disorder Society*, *13*(6), 885-894.
- Schrag, A. and Schott, J.M. (2006) 'Epidemiological, clinical, and genetic characteristics of early-onset parkinsonism'. *The Lancet Neurology*, 5 (4), pp. 355-363.
- Schuna Jr, J. M., Brouillette, R. M., Foil, H. C., Fontenot, S. L., Keller, J. N., & Tudor-Locke, C. (2013). Steps per day, peak cadence, body mass index, and age in community-dwelling older adults. *Med Sci Sports Exerc*, 45(5), 914-919.
- Schurr, S. A., Marshall, A. N., Resch, J. E., & Saliba, S. A. (2017). Two-dimensional video analysis is comparable to 3D motion capture in lower extremity movement assessment. *International journal of sports physical therapy*, *12*(2), 163.
- Semaan, M. B., Wallard, L., Ruiz, V., Gillet, C., Leteneur, S., & Simoneau-Buessinger,
  E. (2022). Is treadmill walking biomechanically comparable to overground walking? A systematic review. *Gait & Posture*, *92*, 249-257.
- Seo, J. S., Yang, H. S., Jung, S., Kang, C. S., Jang, S., & Kim, D. H. (2018). Effect of reducing assistance during robot-assisted gait training on step length asymmetry in patients with hemiplegic stroke: a randomized controlled pilot trial. *Medicine*, 97(33).

- Shah, V. V., McNames, J., Harker, G., Mancini, M., Carlson-Kuhta, P., Nutt, J. G., ...
  Horak, F. B. (2020). Effect of bout length on gait measures in people with and without parkinson's disease during daily life. *Sensors*, 20(20), 5769.
- Sherbondy, P. S., Queale, W. S., McFarland, E. G., Mizuno, Y., & Cosgarea, A. J. (2003). Soleus and gastrocnemius muscle loading decreases anterior tibial translation in anterior cruciate ligament intact and deficient knees. *The journal of knee surgery*, *16*(3), 152-158.
- Shigematsu, R., Sallis, J. F., Conway, T. L., Saelens, B. E., Frank, L. D., Cain, K. L., Chapman, J. E., & King, A. C. (2009). Age differences in the relation of perceived neighborhood environment to walking. *Medicine and science in sports and exercise*, 41(2), 314.
- Shin, M.-S., Jeong, H.-Y., An, D.-I., Lee, H.-Y., & Sung, Y.-H. (2016). Treadmill exercise facilitates synaptic plasticity on dopaminergic neurons and fibers in the mouse model with Parkinson's disease. *Neuroscience letters*, 621, 28-33.
- Shine, J., Moustafa, A. A., Matar, E., Frank, M. J., & Lewis, S. J. (2013). The role of frontostriatal impairment in freezing of gait in Parkinson's disease. *Frontiers in systems neuroscience*, 7, 61.
- Shine, J. M., Matar, E., Ward, P. B., Bolitho, S. J., Pearson, M., Naismith, S. L., & Lewis, S. J. (2013). Differential neural activation patterns in patients with Parkinson's disease and freezing of gait in response to concurrent cognitive and motor load. *PloS one*, 8(1), e52602.
- Shine, J. M., Matar, E., Ward, P. B., Frank, M. J., Moustafa, A. A., Pearson, M., . . .
  Lewis, S. J. (2013). Freezing of gait in Parkinson's disease is associated with functional decoupling between the cognitive control network and the basal ganglia. *Brain*, *136*(12), 3671-3681.
- Shine, J., Naismith, S. and Lewis, S. (2011a) 'The pathophysiological mechanisms underlying freezing of gait in Parkinson's disease'. *Journal of Clinical Neuroscience*, 18 (9), pp. 1154-1157.
- Shulman, L. M., Gruber-Baldini, A. L., Anderson, K. E., Fishman, P. S., Reich, S. G., & Weiner, W. J. (2010). The clinically important difference on the unified Parkinson's disease rating scale. *Archives of neurology*, 67(1), 64-70.

- Shumway-Cook, A., Brauer, S. and Woollacott, M. (2000) 'Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go Test'. *Physical therapy*, 80 (9), pp. 896-903.
- Shumway-Cook, A., Brauer, S., & Woollacott, M. (2000). Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go Test. *Physical therapy*, 80(9), 896-903.
- Shumway-Cook, A. and Woollacott, M.H. (2007) *Motor control: translating research into clinical practice*. Lippincott Williams & Wilkins.
- Simonsen, E.B. (2014) Contributions to the understanding of gait control. University of Copenhagen Copenhagen.
- Sinitski, E. H., Lemaire, E. D., Baddour, N., Besemann, M., Dudek, N. L., & Hebert, J. S. (2015). Fixed and self-paced treadmill walking for able-bodied and transtibial amputees in a multi-terrain virtual environment. *Gait & posture*, *41*(2), 568-573.
- Sloot, L., Van der Krogt, M. and Harlaar, J. (2014) 'Self-paced versus fixed speed treadmill walking'. *Gait & posture*, 39 (1), pp. 478-484.
- Smith, A.J. and Lemaire, E.D. (2018) 'Temporal-spatial gait parameter models of very slow walking'. *Gait & posture*, 61 125-129.
- Smulders, K., Dale, M. L., Carlson-Kuhta, P., Nutt, J. G., & Horak, F. B. (2016).
  Pharmacological treatment in Parkinson's disease: Effects on gait. *Parkinsonism & related disorders*, *31*, 3-13.
- Sofuwa, O., Nieuwboer, A., Desloovere, K., Willems, A.-M., Chavret, F., & Jonkers, I. (2005). Quantitative gait analysis in Parkinson's disease: comparison with a healthy control group. *Archives of physical medicine and rehabilitation*, 86(5), 1007-1013.
- Sohur, U. S., Gray, D. L., Duvvuri, S., Zhang, Y., Thayer, K., & Feng, G. (2018). Phase
  1 Parkinson's disease studies show the dopamine D1/D5 agonist PF-06649751 is safe
  and well tolerated. *Neurology and therapy*, 7(2), 307-319.
- Soria, G., De Notaris, M., Tudela, R., Blasco, G., Puig, J., Planas, A. M., ... Prats-Galino, A. (2011). Improved Assessment of Ex Vivo Brainstem Neuroanatomy With High-Resolution MRI and DTI at 7 Tesla. *The Anatomical Record: Advances in Integrative Anatomy and Evolutionary Biology*, 294(6), 1035-1044.
- Spencer, G.F. (1993a) 'Automatic generation of programs for crawling and walking'. *Proceedings of the 5th International Conference on Genetic Algorithms*, 1993a. pp.654.

- Spildooren, J., Vercruysse, S., Meyns, P., Vandenbossche, J., Heremans, E.,
  Desloovere, K., Vandenberghe, W., & Nieuwboer, A. (2012). Turning and unilateral cueing in Parkinson's disease patients with and without freezing of gait. *Neuroscience*, 207, 298-306.
- Springer, S. and Yogev Seligmann, G. (2016) 'Validity of the kinect for gait assessment: A focused review'. *Sensors*, 16 (2), pp. 194.
- Staudenmann, D., Potvin, J. R., Kingma, I., Stegeman, D. F., & van Dieën, J. H. (2007).
  Effects of EMG processing on biomechanical models of muscle joint systems: sensitivity of trunk muscle moments, spinal forces, and stability. *Journal of biomechanics*, 40(4), 900-909.
- Stenroth, L., Sipilä, S., Finni Juutinen, T., & Cronin, N. (2017a). Slower walking speed in older men improves triceps surae force generation ability. *Medicine and Science Sports and Exercise*, 49.
- Stief, P. (2013) 'Stimulation of microbial nitrogen cycling in aquatic ecosystems by benthic macrofauna: mechanisms and environmental implications'. *Biogeosciences*, 10 (12), pp. 7829-7846.
- Stone, E. E., Skubic, M., & Back, J. (2014). Automated health alerts from kinect-based in-home gait measurements. 2014 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society,
- Strutzenberger, G., Claußen, L. and Schwameder, H. (2021) 'Analysis of sloped gait: How many steps are needed to reach steady-state walking speed after gait initiation?'. *Gait & Posture*, 83 167-173.
- Summan, R., Pierce, S., Macleod, C., Dobie, G., Gears, T., Lester, W., . . . Smyth, P. (2015). Spatial calibration of large volume photogrammetry based metrology systems. *Measurement*, 68, 189-200.
- Surmeier, D. J., Ding, J., Day, M., Wang, Z., & Shen, W. (2007). D1 and D2 dopaminereceptor modulation of striatal glutamatergic signaling in striatal medium spiny neurons. *Trends in neurosciences*, 30(5), 228-235.
- Surmeier, D. J., Obeso, J. A., & Halliday, G. M. (2017). Selective neuronal vulnerability in Parkinson disease. *Nature Reviews Neuroscience*, 18(2), 101-113.
- Tan, L. C., Luo, N., Nazri, M., Li, S. C., & Thumboo, J. (2004). Validity and reliability of the PDQ-39 and the PDQ-8 in English-speaking Parkinson's disease patients in Singapore. *Parkinsonism & related disorders*, *10*(8), 493-499.

- Tanaka, K., de Quadros Jr, A. C., Santos, R. F., Stella, F., Gobbi, L. T. B., & Gobbi, S. (2009). Benefits of physical exercise on executive functions in older people with Parkinson's disease. *Brain and cognition*, 69(2), 435-441.
- Tesio, L. (2003) 'Outcome research in rehabilitation: variable construction, trial design and statistical inference'. *Advances in physical and rehabilitation medicine*. *Monduzzi Editore, Bologna*, 449-505.
- Thigpen, M. T., Light, K. E., Creel, G. L., & Flynn, S. M. (2000). Turning difficulty characteristics of adults aged 65 years or older. *Physical therapy*, 80(12), 1174-1187.
- Tikkanen, O., Haakana, P., Pesola, A. J., Häkkinen, K., Rantalainen, T., Havu, M., . . .
  Finni, T. (2013). Muscle activity and inactivity periods during normal daily life. *PloS* one, 8(1), e52228.
- Tillerson, J. L., Cohen, A. D., Philhower, J., Miller, G. W., Zigmond, M. J., & Schallert, T. (2001). Forced limb-use effects on the behavioral and neurochemical effects of 6-hydroxydopamine. *Journal of Neuroscience*, *21*(12), 4427-4435.
- Tinsley, R. B., Bye, C. R., Parish, C. L., Tziotis-Vais, A., George, S., Culvenor, J. G., . .
  Horne, M. K. (2009). Dopamine D2 receptor knockout mice develop features of Parkinson disease. *Annals of neurology*, 66(4), 472-484.
- Tomlinson, C. L., Patel, S., Meek, C., Herd, C. P., Clarke, C. E., Stowe, R., . . .
  Wheatley, K. (2012). Physiotherapy intervention in Parkinson's disease: systematic review and meta-analysis. *Bmj*, 345.
- Turvey, M.T. and Fonseca, S. (2009) 'Nature of motor control: perspectives and issues'. *Progress in motor control*, 93-123.
- Tzallas, A. T., Tsipouras, M. G., Rigas, G., Tsalikakis, D. G., Karvounis, E. C., Chondrogiorgi, M., . . . Waldmeyer, M. T. A. (2014). PERFORM: a system for monitoring, assessment and management of patients with Parkinson's disease. *Sensors*, *14*(11), 21329-21357.
- Törmänen, J. (2019a) 'Comparison of entry level motion capture suits aimed at indie game production'.
- Uchida, S., Suzuki, A., Kagitani, F., & Hotta, H. (2006). Responses of acetylcholine release and regional blood flow in the hippocampus during walking in aged rats. *The Journal of Physiological Sciences*, 56(3), 253-257.

- Uno, H., Tarara, R., Else, J. G., Suleman, M. A., & Sapolsky, R. M. (1989).
  Hippocampal damage associated with prolonged and fatal stress in primates. *Journal of Neuroscience*, 9(5), 1705-1711.
- Vallabhajosula, S., Buckley, T. A., Tillman, M. D., & Hass, C. J. (2013). Age and Parkinson's disease related kinematic alterations during multi-directional gait initiation. *Gait & posture*, *37*(2), 280-286.
- van der Kolk, N.M. and King, L.A. (2013) 'Effects of exercise on mobility in people with Parkinson's disease'. *Movement Disorders*, 28 (11), pp. 1587-1596.
- van der Krogt, M.M., Delp, S.L. and Schwartz, M.H. (2012a) 'How robust is human gait to muscle weakness?'. *Gait & posture*, 36 (1), pp. 113-119.
- Van Kan, G.A. *et al.* (2009) 'Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people an International Academy on Nutrition and Aging (IANA) Task Force'. *The journal of nutrition, health & aging,* 13 (10), pp. 881-889.
- Van Praag, H., Shubert, T., Zhao, C., & Gage, F. H. (2005). Exercise enhances learning and hippocampal neurogenesis in aged mice. *Journal of Neuroscience*, 25(38), 8680-8685.
- VanLeeuwen, J. E., Petzinger, G. M., Walsh, J. P., Akopian, G. K., Vuckovic, M., & Jakowec, M. W. (2010). Altered AMPA receptor expression with treadmill exercise in the 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine-lesioned mouse model of basal ganglia injury. *Journal of neuroscience research*, 88(3), 650-668.
- Vazquez-Galliano, J., Kimawi, I., & Chang, L. (2014). Biomechanics of gait and treatment of abnormal gait patterns. *Physical Medicine and Rehabilitation*.
- Verghese, J., Holtzer, R., Lipton, R. B., & Wang, C. (2009). Quantitative gait markers and incident fall risk in older adults. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, 64(8), 896-901.
- Yogev-Seligmann, G., Giladi, N., Gruendlinger, L., & Hausdorff, J. M. (2013). The contribution of postural control and bilateral coordination to the impact of dual tasking on gait. *Experimental brain research*, 226, 81-93.
- Voytek, B. (2006) 'Emergent basal ganglia pathology within computational models'. *Journal of Neuroscience*, 26 (28), pp. 7317-7318.
- Wang, K. S., McClure Jr, J. P., Alselehdar, S. K., & Kanta, V. (2015). Direct and indirect pathways of the basal ganglia: opponents or collaborators? *Frontiers in neuroanatomy*, 9, 20.

- Warabi, T., Furuyama, H., Sugai, E., Kato, M., & Yanagisawa, N. (2018). Gait bradykinesia in Parkinson's disease: a change in the motor program which controls the synergy of gait. *Experimental brain research*, 236(1), 43-57.
- Washabaugh, E. P., Kalyanaraman, T., Adamczyk, P. G., Claflin, E. S., & Krishnan, C. (2017). Validity and repeatability of inertial measurement units for measuring gait parameters. *Gait & posture*, 55, 87-93.
- Wenger, N., Moraud, E. M., Raspopovic, S., Bonizzato, M., DiGiovanna, J., Musienko, P., . . . Courtine, G. (2014). Closed-loop neuromodulation of spinal sensorimotor circuits controls refined locomotion after complete spinal cord injury. *Science translational medicine*, 6(255), 255ra133-255ra133.
- Whittle, M. W. (2014). Gait analysis: an introduction. Butterworth-Heinemann.
- Wielinski, C. L., Erickson-Davis, C., Wichmann, R., Walde-Douglas, M., & Parashos,
  S. A. (2005). Falls and injuries resulting from falls among patients with Parkinson's disease and other parkinsonian syndromes. *Movement Disorders*, 20(4), 410-415.
- Wilken, J., Rao, S., Saltzman, C., & Yack, H. J. (2011). The effect of arch height on kinematic coupling during walking. *Clinical Biomechanics*, 26(3), 318-323.
- Winter, D.A. (1995) 'Human balance and posture control during standing and walking'. *Gait & posture*, 3 (4), pp. 193-214.
- Winter, D. A., Patla, A. E., Ishac, M., & amp; Gage, W. H. (2003). Motor mechanisms of balance during quiet standing. Journal of Electromyography and Kinesiology, 13(1), 49-56.
- Winter, D.A. (2009) *Biomechanics and motor control of human movement*. John Wiley & Sons.
- Witjas, T. *et al.* (2002) 'Nonmotor fluctuations in Parkinson's disease: frequent and disabling'. *Neurology*, 59 (3), pp. 408-413.
- Wright, D.B. (1996) Understanding statistics: An introduction for the social sciences. Sage.
- Wrightson, J. and Smeeton, N. (2017) 'Walking modality, but not task difficulty, influences the control of dual-task walking'. *Gait & posture*, 58 136-138.
- Xi, X., Tang, M. and Luo, Z. (2018) 'Feature-level fusion of surface electromyography for activity monitoring'. *Sensors*, 18 (2), pp. 614.

- Young, A.J., Hargrove, L.J. and Kuiken, T.A. (2011a) 'The effects of electrode size and orientation on the sensitivity of myoelectric pattern recognition systems to electrode shift'. *IEEE Transactions on Biomedical Engineering*, 58 (9), pp. 2537-2544.
- Zhao, Y. J., Wee, H. L., Chan, Y. H., Seah, S. H., Au, W. L., Lau, P. N., . . . Tan, L. C. (2010). Progression of Parkinson's disease as evaluated by Hoehn and Yahr stage transition times. *Movement Disorders*, 25(6), 710-716.
- Švehlík, M., Zwick, E. B., Steinwender, G., Linhart, W. E., Schwingenschuh, P., Katschnig, P., . . . Enzinger, C. (2009). Gait analysis in patients with Parkinson's disease off dopaminergic therapy. *Archives of physical medicine and rehabilitation*, 90(11), 1880-1886.