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Influence of different environmental contexts on gait parameters in patients with Parkinson's disease

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Abstract

Context Parkinson’s disease (PD) is the second most common neurodegenerative disease with an estimated 9.4 million people diagnosed with it in 2020 [1], [2]. It has an influence on people’s daily lives, notably by modifying their gait. One of the most severe gait impairment is freezing of gait which further reduces the patients’ mobility and independence [3].

Objective The goal of this thesis was to identify how the gait parameters of people with PD are influenced by specific environmental conditions. This thesis is part of the long-term objective to use an active pelvis orthosis for assistive and rehabilitative natures and to develop a real-time assistance for the patient.

Experiments Six patients, including three with freezing of gait (FOG), walked in four different environmental conditions: (1) 10 meters straight on flat ground, (2) 10 meters straight on gym mattresses, (3) 10 meters straight on flat ground with a doorway at mid-way and (4) 2x5 meters with a tight U-turn between the two. The control condition corresponds to the 10 meters straight on flat ground.

Results The statistical analysis showed that both (1) and (2) had an effect on the stride time and cadence for patients’ most and least affected side by PD. It also showed that both environmental conditions had an effect on their velocity and their least affected side’s step length. While no significant effects were found for freezers (patients with PD who experience FOG), they had longer stride, stance and swing time as well as slower cadence and smaller step length for both sides and both environmental conditions compared to non-freezers (patients with PD without FOG). Freezers’ velocity was also slower for both environmental conditions. The visual analysis showed that freezers increased their stride and stance time during the crossing of a doorway and decreased their swing time. Freezers kept their stride and stance time constant before the turn while they decreased their swing time. For both (3) and (4), freezers’ phasing was out of sync before and during the doorway crossing. Non-freezers increased their stride and stance time before and during the doorway crossing while decreasing their stride time. For (4), non-freezers increased their stride time before the turn and increased their stance time during the turn. They also increased their swing time before the turn and decreased it during the turn.

Discussion The stride time, cadence and velocity were significantly influenced by irregular surfaces. When passing through a doorway, the stride, stance and swing time were influenced and the swing time could be used as an indicator that a turn will occur soon. More specifically, for freezers, the phasing showed great variability before either the doorway was crossed or the turn was performed. These metrics thus show some promises for providing real-time assistance to people with PD.

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List of Abbreviations

APO Active Pelvis Orthosis

FOG Freezing Of Gait

H&Y Hoehn & Yahr

HS Heel Strike

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

MMSE Mini-Mental State Examination

MS Mid-Swing

NFOG-Q New Freezing Of Gait Questionnaire

PD Parkinson's disease

PT Physiotherapist

PWS Person With Stroke

RAGT Robot-Assisted Gait Training

SD Standard Deviation

SNpc Substantia Nigra pars compacta

TO Toe-Off

The study is divided into five main sections.

Chapter 1 shows why analyzing the gait of patients with Parkinson's disease in different environmental contexts is of interest. In addition, the necessary theoretical background about Parkinson's disease is given.

Chapter 2 examines the literature about environmental contexts that can influence the gait of people with PD. It also contains a review of compensation strategies used by them and of existing assist-as-needed protocols for parkinsonians.

Chapter 3 describes the materials and methods and explains the environmental condition chosen for the experimental protocol based on the literature review of section 2.1. The data processing, the studied metrics' choices and the data analysis steps are described afterwards.

Chapter 4 displays the results obtained after applying the statistical and visual analyses described in section 3.6.

Chapter 5 discusses the results obtained in Chapter 4 and addresses some limits of the study as well as perspectives for the future.

Chapter 1

Introduction

This chapter presents statistics about Parkinson's disease to show how it will become a growing concern for society over time. Parkinson's disease is then explained in more details to understand what are the causes, how it affects patients, how it is diagnosed and what are the current solutions to alleviate the symptoms.

1.1 Context

Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's disease with approximately 6.1 million individuals diagnosed with it around the world in 2016. This number, which was approximately 2.5 million in 1990, has thus increased in recent decades and continues to grow with an estimated 9.4 million people diagnosed with PD in 2020 [1], [2]. It is due to various factors such as an increasing number of older people but also a longer longevity for everyone, which will lead to a 12% increase in the age-standardized prevalence rate over 20 years. Even though the number of people diagnosed with PD increases with age, younger people are also concerned since an estimated 4% of people with PD are diagnosed before age 50 [5]. According to *Scheife et al.* [6], people with PD have a lower health-related quality of life due to their inability to move freely and perform everyday tasks. This lead to a greater reliance from the patients on their caregivers and assistive devices. PD thus also reduces the quality of life of the patient's carers, which may have a 'knock-on' effect for the patient. Moreover, patients' emotional and psychological well-being can also be negatively affected. The more the disease progresses, the more the quality of life of both the patient and its carers will decrease [7].

While the percentage of people with PD who experience episodes of gait freezing vary greatly through the literature (from 14.0 to 55.1%), Hong-Liang Ge *et al.* [8] state that the prevalence of freezing of gait (FOG) in patients with PD is 35.8%. Patients describe episodes of freezing as moments where they feel like their feet are 'glued' to the ground and they cannot move forward for several seconds or minutes. FOG will increase with PD's progression and will be another factor that reduces the patient's quality of life even more since the patient will feel the loss of an important part of their mobility and independence (i.e., loss of control, restriction in mobility and exposure to the risk of falling) [3].

As shown above, the prevalence of Parkinson's disease has increased over the years and its incidence in the future is going to continue growing, which will pose a significant health care burden. It will be a real challenge to find how to take care for the aging population over the coming decades. One way to answer this question would be to find a way to provide gait assistance in real-time to people with PD. It would give them more independence, which will increase both their and their carers' health-related quality of life.

1.2 Parkinson's disease

PD is a neurological disorder and the most common type of parkinsonism, a term that encompasses neurological disorders with movement problems similar to PD, such as rigidity, slowness and tremors [9].

1.2.1 Pathophysiology

PD is characterized by the death of dopaminergic neurons in the substantia nigra pars compacta (SNpc) and thus the death of dopamine-producing cells. Dopamine is a key element of the brain because it is a neurotransmitter which plays an important role in multiple brain activities such as memory and motor coordination. Dopamine also plays a role in the body's motivation and reward mechanism. It is transported through the brain along four specific pathways: nigrostriatal, mesolimbic, mesocortical and tuberoinfundibular pathways (Figure 1.1). For PD, the nigrostriatal and the mesolimbic systems are the pathways that come into play. The former links the substantia nigra to the basal ganglia and plays an important role in the motor function and motor planning. The latter connects the ventral tegmental area to the basal ganglia and is highly involved in the brain's pleasure and reward system [10], [11]. Dopamine-based treatments are the main way to treat PD but not the only one since other neurotransmitter systems (i.e. serotonin, acetylcholine, and norepinephrine systems) can also be dysfunctional. Dickson *et al.* [12] demonstrated in 2009 that the cause for motor features (e.g., bradykinesia and rigidity) in advanced PD is probably the moderate to severe loss of dopaminergic neurons within the SNpc. However, neuronal loss does not only happen in the SNpc as it also occurs in other brain regions such as locus ceruleus and the hypothalamus [9], [13].

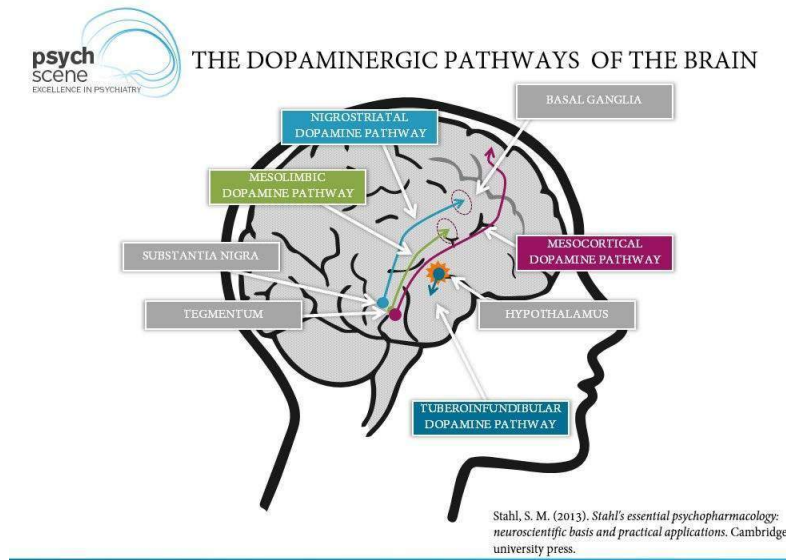


Figure 1.1: Four pathways to transport dopamine in the brain [14].

Lewy pathology, which is the aggregation of abnormally folded proteins, is another characteristic of PD. The most abundant protein in the associated protein inclusions for PD is the α -synuclein. It will become insoluble and aggregate to form intracellular inclusions within the cell body (Lewy bodies) and processes (Lewy neurites) of neurons when in a misfolded state. This pathology has been hypothesized to stereotype PD's neuropathological progression and explain it by the Braak hypothesis [15]. According to this model, PD can be described by three phases: early pathology (stages 1 and 2), stages 3 and 4 and finally advanced pathology. During stages 1 and 2, PD starts in the medulla and the olfactory bulb and generates nonmotor symptoms, such as rapid eye movement sleep behavior disorder and decreased smell. Stages 3 and 4 is when the classic PD motor symptoms appears and is thus generally when PD is diagnosed. At this stages, the pathology has progressed to the substantia nigra pars compacta and other midbrain and basal forebrain structures. Advanced pathology describes the stage of PD in which the pathology has progressed to the cerebral cortices with the onset of cognitive impairment and hallucinations [9], [13].

Lewy pathology has also been associated with non-motor symptoms by, for example, showing a strong correlation between dementia and severity of cortical Lewy pathology. While this pathology is hypothesised as a biological marker for neurodegeneration in PD, it is not the only reason for it. First, α -synuclein aggregates can have other forms, which might play an important role in PD's neurodegeneration. Second, other pathologies such as inclusions composed of other types of proteins can often be seen in the brain of patients with PD. They can synergise with Lewy pathology and thus contribute to PD's clinical expression. Third, monogenic forms of PD which occur without Lewy pathology have been identified. Most patients with PD who have parkin-related diseases are, for example, often characterized by the absence of Lewy pathology [13].

Another feature of PD is neuroinflammation which either triggers neurodegeneration or is activated as a response to neuronal damage. There is an active inflammatory response within areas of neurodegeneration in the brain due to the presence of resident astrocytes and microglia which results in microglial activation. Activated astrocytes and microglia will increase the production and release of the pro-inflammatory cytokines, which will accelerate the nigral dopaminergic neuron degeneration [13].

1.2.2 Etiology

PD is a multifactorial disease where both environmental and genetic factors play a role. The biggest risk factor is age with median age onset at 60 years. There are also cross-cultural variations with a lower prevalence reported in African, Asian and Arabic countries compared to Europe as well as North and South America. While not always fully understood, peoples' lifestyles can also have an impact on the disease. Caffeine consumption and cigarette smoking, for example, have been associated with a reduced risk of PD. On the contrary, exposure to pesticides and herbicides can increase the PD risk. Another factor is genetic because, although PD is often considered as an idiopathic disorder, 10 to 15% of PD cases report a family history. The genes for which a potential link was found between them and PD have been assigned a "PARK" name in the order they were identified such as PARK3 and PARK10 which are considered as risk factors [16], [17].

1.2.3 Symptoms

While PD is called a movement disorder, it affects many systems in the body and leads to different symptoms from person to person. The most common symptoms can be grouped in two groups: motor and nonmotor symptoms. The symptoms' severity increases over time along with PD's stage. Most patients are diagnosed with PD when motor symptoms appear even though nonmotor symptoms often appears several years earlier than motor ones [9].

"Motor symptoms" describes symptoms related to movement or physical tasks such as bradykinesia, rest tremor, rigidity and loss of postural reflexes which are the most commonly identified ones. Most of these motor symptoms are responsive to dopaminergic therapy. Bradykinesia is defined by slow movement, decrementing amplitude and problematic fine motor control due to the decreased neuronal density in the substantia nigra. Fast movements will be really complicated for parkinsonians with bradykinesia because they cannot provide sufficient energy to the executive muscles. It can be influenced by the emotional state of PD patients and will first appear with slow reaction times and difficulties with performing simultaneous tasks. Other impairment due to bradykinesia are impaired swallowing, loss of gesturing and decreased blinking. Rest tremor, which is one of the most easily recognised features of PD, is a rhythmic muscle contraction and relaxation. While it mainly happens on the extremities of the body, it can expand to lips, chin and jaw. Other types of tremors have been identified: postural and essential tremor. Postural tremor, which occurs when people maintain a position against gravity, is more prominent than rest tremor and is considered as one of the first sign of PD. Essential tremor, which is not as responsive

to dopaminergic therapy as rest and postural tremor, causes involuntary shaking in the hands and arms and can even affect the head and the voice. Having essential tremor from an early age is a potential risk factor in developing PD. Another motor symptom is rigidity. It is described as the inflexibility of the limbs and neck or trunk and limits the motion to a reduced range because of muscle stiffness and the lack of relaxation capability. A fourth motor symptom is postural instability which usually manifests at advanced stages and is responsible for most of the falls of PD patients. While it is not responsive to dopaminergic therapy, deep-brain stimulation has shown some promises [18].

Non-motor symptoms are not related to movement and can affect organ systems, such as gastrointestinal and genitourinary systems. There is a wide range of non-motor symptoms which is why they were grouped in four main categories: autonomic dysfunction, sleep disturbances, cognitive and psychiatric disturbances and sensory symptoms. Autonomic dysfunction may appear at any stages of PD and all aspects of it (e.g., gastrointestinal, cardiovascular or urinary dysfunction) may be affected. Sleep disturbances is a very common symptom and may occur in about 90% of patients. It manifests as sleep fragmentation with frequent nocturnal awakenings and rapid eye movement (REM) sleep behavior disorder. Another category consists of cognitive and psychiatric disturbances such as depression, anxiety, apathy and dementia. The last category is sensory symptoms and is about a variety of abnormalities of sensation by PD patients. These sensations can be olfactory impairment, vision problems and pain. Five types of pain have been defined: musculoskeletal pain, radicular or neuropathic pain, dystonia-related pain, primary or central parkinsonian pain, and akathitic discomfort [18], [19].

Freezing of gait

FOG is a common symptom in people with PD and is defined as brief, episodic absence or marked reduction of forward progression of the feet despite the intention to walk [20]. Patients feel like their feet are 'glued' to the ground and they cannot move forward for several seconds or minute. It mostly occurs in late stages of PD but can also occur in early stages. According to Bloem *et al.* [21], there are three subtypes of FOG: patients are unable to start walking for no apparent reason, patients' legs tremble because they try to overcome the block, and patients shuffle forward with small steps. Its duration can vary from 1 second to more than 30 seconds, and this increase is related to the disease progression. It happens more often in the OFF state and in certain environmental conditions and is a major risk factor for falls in parkinsonism. The OFF time is when the dose of levodopa starts to wear off and the motor symptoms (sometimes also the non-motor ones) return before the next dose of drugs is taken. The ON time is when the new dose of drugs starts to take effect and the patient thus feels better. FOG restricts the patient's mobility, autonomy and independence but also causes falls, which can have severe consequences and even decrease the patient's quality of life.

1.2.4 Assessment and Diagnosis

Diagnosing Parkinson's disease is based both on patient's medical and family history as well as on physical examination. Firstly, having a first-degree family member with PD increases the likelihood of being diagnosed with PD [22]. Secondly, the patient's medical history helps assess whether there are symptoms such as slowness, soft voice, tremor or gait changes. Thirdly, the physical examination must show both bradykinesia and rigidity (and/or tremor) and can include decreased arm swing or short step length. Once these check-ups are done, some additional features need to be assessed (e.g., rapid progression or recurrent falls) to differentiate between PD and atypical parkinsonism [9].

1.2.5 Therapies

PD can currently not be cured but, depending on the targeted symptoms, different therapies exist. These will have to change over time along with PD's progression. There are a lot of different approaches to treat motor symptoms such as pharmacologic treatments primarily based on dopamine [23] (i.e., levodopa preparations or dopamine agonists) or non-pharmacological approaches such as invasive or non-invasive stimulation, treadmill exercise, aerobic exercise and tai chi [24]. Physiotherapy, occupational therapy, and speech therapy (for speech and swallowing) are also useful. Interdisciplinary therapy is important and can help maintain or even improve motor symptoms, balance and gait. More advanced therapies such as deep brain stimulation, MRI-guided focused ultrasound, and therapy with levodopa-carbidopa enteral suspension can also be used even though they involve more constraints because they require specialty center assessments to determine patient eligibility, perform the procedures, and manage ongoing medication and device optimization. Nonmotor symptoms can also be treated through pharmacologic treatments by using neurotransmitters other than dopamine as it is done for people without PD [9].

Physiotherapy

Physiotherapy is an intervention commonly prescribed for people by PD because it shows great results as a complementary therapy to, for example, pharmacological treatments. Its goal is to improve multiple PD-related impairments such as gait, posture, balance and falls. Physiotherapy contains a lot of different therapy modalities that can vary from treadmill training to exergaming and each one leads to variable improvements. Some of the most well-known therapies are resistance training, treadmill training, conventional physiotherapy, strategy training, dance, martial arts, aerobic exercises, hydrotherapy, balance and gait training, dual tasking, exergaming, and Nordic walking. All of them, except dual tasking and exergaming, showed gait improvements in people with PD. On the other hand, only conventional physiotherapy, dance, martial arts, Nordic walking, and balance and gait training were shown to improve PD motor symptoms ((MDS)-UPDRS III). Physiotherapy can therefore take many different forms depending on the symptoms most present in the patient [25].

Recently, robot-assisted gait training (RAGT) devices have been used more frequently for people with PD. They improve endurance, gait capacity, performance, global independence in activities of daily living and perception of well-being for people with PD. Their advantage over simple treadmill training is that they lessen the burden on the therapists and, especially for people with greater walking disability, more effectively decrease FOG-Q score compared to treadmill training. Examples of RAGT which have improved the FOG-Q score are Lokomat (Lokomat®-Hocoma, Switzerland) and Gait Trainer GT (Reha-Stim Medtec, Switzerland) [26].

Chapter 2

State of the art

This chapter presents the environmental contexts that can influence the walking of people with PD. Afterwards, it shows what is currently used by patients to overcome gait impairment. Finally, this chapter explains assist-as-needed robots that already exist in PD and gives an example of an exoskeleton combined with assist-as-needed technology for post-stroke patients.

2.1 Environmental contexts influencing Parkinsonian walking

As mentioned in the previous chapter, people with PD often have gait impairments. These impairments, which occur spontaneously in their daily life, can also have more chances of occurring under certain more challenging conditions such as turning or dual-tasking. Once it occurs, patients will, for example, walk slower, make shorter steps or have an increase in postural instability. In the worst cases, they will experience FOG, which can lead to falls. Several factors, whether they are external or internal, can have a negative impact on patients' gait and even lead to freezing episodes. Rahman *et al.* [4] investigated these factors by interviewing people with PD. The specific triggers are summarized in Table 2.1 with the amount of people for whom the factor is a trigger and the number of people that answered the survey. More than half of the patients' freezings were triggered by the four first factors, i.e., turning around, fatigue, being in a confined space and being in a stressful situation. Other factors also provoked freezing for many patients such as narrow spaces, being in a crowd or going through doorways. There also seems to be an interplay between emotion and freezing since stress is one of the most common trigger. The relative importance of these factors also depends on the disease's stage of the patients. Walking in narrow spaces is for example only at the 6th place for mild and moderate pathology but is the first factor (on par with fatigue) that triggers FOG for people with advanced PD. The factors' distribution according to the disease's stage is summarized in Table 2.2.

Turning around

Turning is the most common factor that triggers FOG according to Rahman *et al.* and is also really common in daily life since Glaister *et al.* [27] analyzed videos of turning during activities of daily living and identified straight and turn steps. They reported that 35 to 45% of all steps made during daily life activities happen during turning. People with PD need more time and steps to perform the same turn as healthy age-matched people. Spildooren *et al.* [28] reviewed previous studies that compared freezers (people with PD and FOG) and non-freezers (people with PD but without FOG) to summarize the main tendencies about freezing occurring while turning. These studies either used infrared 3D camera systems with retroreflective markers or other measuring methods (i.e., foot switches on the sole of each foot, inertial sensors, video recordings or accelerometers). FOG occurred for 38.2% of the freezers during a turn and more often in freezers in the OFF-phase [38.5-100%] than in the ON-phase [11.1-40%]. Freezing also occurred more often in turns with larger turn angles such as a 180° turn angle compared to 90° turns. Freezing occurred more frequently at the end of the turn but are often shorter than freezing happening at the beginning of the turn (0.63 vs 3.71 seconds). Spildooren *et al.* also compared freezers and non-freezers' gait parameters during turns. The turn duration was longer for freezers compared to non-freezers, espe-

Table 2.1: Factors inducing freezing of gait according to the study of Rahman *et al.* [4]

Factor	% yes of sample	Number of responders (valid N)
Turning around	58.5%	107
Fatigue	58.5%	107
Being in a confined space	53.1%	103
Being in a stressful situation (<i>e.g., approaching or entering a crowd</i>)	53.1%	105
Walking in a narrow space (<i>e.g., a narrow corridor or between objects</i>)	49.2%	105
Being in a crowd	49.2%	105
Going through doorways	43.8%	103
Getting out of a chair	40.0%	104
Being surrounded by people who are talking	35.4%	102
Panic attacks	32.3%	104
Crossing roads	30.8%	97
Entering a lift as the door opens	30.0%	99
Hearing a doorbell or telephone ring	29.2%	103
Stepping onto an escalator	25.4%	97
Reaching for doorhandles	24.6%	100
Approaching a target or a destination	24.6%	100
Meeting somebody unexpectedly	23.8%	105
Getting off a bus	23.1%	86
Getting on a bus	22.3%	87
Using cutlery (<i>e.g., putting a fork or spoon into your mouth</i>)	18.5%	103
Loud noise	17.7%	102
Using a computer mouse	16.2%	93
Bright lights	11.5%	99

cially during 360° turns and the peak turn velocity was slower for freezers. Non-freezers needed a smaller number of steps (i.e., 3.3 steps for 90° turns, 3.19 steps for 180° turns and 4.98 steps for 360° turns) to perform the same turn as freezers. The cadence during the turn is higher for freezers compared to non-freezers for 180° turns. No differences have been measured for the step length during turning but the step width is significantly larger for non-freezers during 180° turns and especially at the end of the turn. A smaller step width was also associated with a pre-freezing phase. The phase coordination index showed that freezers had a worse coordination during turning compared to non-freezers.

Mancini *et al.* [29] studied the impact of FOG on everyday mobility by attaching a light-weight sensor including a triaxial accelerometer and a triaxial gyroscope on the lower back of the patients for three days. It allowed them to study whether turning in the daily living home environment is more impaired for freezers compared to non-freezers. They showed that the number of turns/30 min is equal for both groups. However, certain aspects of the quality of turn were worse for freezers (e.g., smaller turning angle,

Table 2.2: Factors inducing freezing of gait depending on PD’s stage according to the study of Rahman *et al.* [4]

	Mild (H&Y stage 0-1.5)	Moderate (H&Y stage 2-3)	Severe (H&Y stage 4-5)
Most common	Turning (48.3%)	Stressful situations (54.2%)	Fatigue & Walking in a narrow space (76.3%)
2nd	Fatigue (44.8%)	Fatigue & Turning (52.5%)	
3rd	Confined spaces (41.1%)		Turning (73.7%)
4th	Doorways (34.5%)	Confined spaces & Being in a crowd (47.5%)	Stressful situations & Confined spaces (68.4%)
5th	Getting out of a chair (31.0%)		
6th	Stressful situations & Walking in a narrow space & Being in a crowd (27.6%)	Walking in a narrow space & Getting out of a chair (40.7%)	Being in a crowd (65.8%)

higher mean jerk (2D and medio-lateral) and higher ML jerk variability). Moreover, freezers showed a higher gait variability in situations known to provoke FOG.

Going through doorways

Doorways are also one of the key factors in triggering FOG. Cowie *et al.* [30] studied the use of a variable-width doorway to provoke freezing behavior. They used a CODA motion-capture system with markers placed bilaterally on the following body areas: lateral malleolus, 2nd metatarsal head, posterior aspect of calcaneus at height of toe marker, anterior superior iliac spine, and sacrum. Several gait variables were analyzed: stride time variability, stride length and velocity. They confirmed that doorways increase the frequency at which freezing happen and that the freezing episodes occur near doorways. They also showed that gait parameters such as velocity and stride length decreased while the stride time variability rose as the body approached. Compared to healthy people, freezers will also have larger drops for the same reduction in door width. Medication can decrease the freezing frequency while stimulation cannot. Cowie *et al.* hypothesised that the larger slowdowns that come with narrower doorway are due to a visuomotor process that gives visual information to decide how much the patient will slowdown. The visuomotor process would thus work differently for freezers and generate exaggerated responses to visual information. Another explanation would be that the door attracts the attention of the patient, which is thus not anymore on its walking.

A study conducted in 2013 by Ehgoetz Martens *et al.* [31] supports the notion that sensory deficits may have a profound impact on FOG. They wanted to evaluate how sensory feedback’s availability from different sources can contribute to locomotion and FOG in patients with PD. Previous researchers hypothesized that proprioception is linked to FOG’s occurrence, which is why they decided to make individuals walk with different visual information to get through a doorway. The less visual information, the more patients will have to rely on proprioception, the more FOG should occur according to the hypothesis. They used Optotrak cameras with IRED markers placed in clusters on various areas of the body to analyze gait velocity, mean step length, step length variability, mean step width, step width variability, step time and step time variability. FOG episodes were also defined as any period where the gait velocity dropped

between a zero velocity and one standard deviation of their regular velocity above zero. The experiments' trials varied between walking towards the doorframe in complete darkness, with a lighted doorframe or with limbs and doorframe illuminated and walking away from the doorframe in complete darkness or with the limbs illuminated. During the experiments, a total of 151 episodes of freezing were experienced by 53% of all participants. The greatest amount of FOG episodes occurred when approaching the frame in complete darkness. The FOG occurrences were reduced by 38% when walking toward a lighted doorframe and by another 25% when the body is also illuminated. Instead of exaggerating the responses to visual information, this thus shows that visual information could help reduce the episodes of freezing. Velocity and step length were also reduced when walking in complete darkness compared to when a visual reference (either the body, the doorframe or both) existed.

Several studies have shown that being in natural environments can positively influence FOG. Ottosson *et al.* [32] wanted to confirm this and see if natural environment would not trigger reactions to the same extent as built environment with regard to FOG. Patients had to walk through a hedge with an opening especially created for the experience. They could add a doorframe to the opening when needed to replicate the built environment. Both the hedge and the doorframe had more or less the same width while the doorframe had a horizontal bar on top of it but not the hedge. Data were recorded by an accelerometer to identify cadence, stride and step-speed and each trial was videotaped. Every patient reacted with an episode of freezing when they passed through the doorframe (acceleration amplitude decreased) while none of them had any freezing while going through the hedge opening (no change in acceleration or stride). When they had limited vision, FOG reactions were triggered even when passing through the hedge opening because a feeling of insecurity was created. Each patient also had their own strategy to overcome FOG such as shutting their eyes before and during the passage of the hedge opening or increasing their walking pace to affect or delay the trigger of FOG reactions.

Gómez-Jordana *et al.* [33] went a step further and developed a virtual reality (VR) environment to reproduce doorways. They reproduced the experiments conducted by Cowie *et al.* presented above. They obtained similar results, namely smaller steps for freezers and reduced speed and step length when passing through narrower doorway. The majority of the freezers also experienced freezing-like episodes, where the narrower the doorway, the more episodes occurred. This shows that interactive VR is really immersive, ensures a high level of ecological validity and opens doors for new ways to test solutions for FOG or factors inducing it.

Obstacle avoidance

Snijders *et al.* [34] studied if freezing would be provoked when obstacles suddenly appear for patients with PD walking on a motorized treadmill. They also gathered data on how long the patients have to prepare for the obstacles will influence the appearance of freezing episodes. Patients first had to do an overground walking containing elements to provoke FOG such as walking through a narrow passage or turning. 12 out of 15 patients showed at least one FOG episode during the overground walk. Afterwards, patients had to walk on a treadmill and avoid obstacles. Eight patients had a total of 13 freezing episodes due to obstacle avoidance and only one had FOG during normal walking on the treadmill. Overground walking caused thus more patients to have freezing episodes, which can be explained by the fact that most of these freezing episodes did not happen during overground straight walking but for example when turning. Considering only episodes occurring during straight-line walking, obstacle avoidance caused more episodes than overground straight-line walking. On the treadmill, FOG occurred mostly during long distance condition (patient positioned at 1m from the appearing obstacle) and before crossing the obstacle. However, these episodes of freezing were much shorter compared with episodes during overground walking, which can be caused by the obstacles and treadmill that work as cues to overcome FOG quicker.

In 2013, Magdalini *et al.* [35] studied the differences in obstacle avoidance between people with PD and healthy people. Data were captured using a six-camera 3D motion analysis system with reflective markers placed on the lower limbs and pelvis. Patients were instructed to walk along an 8-meter walkway with an obstacle in the middle. The computed parameters were: maximal hip, knee and ankle joint flexion, trailing and leading limb placement in front and just after the obstacle and step length. Experiments showed that both groups had increased angles for the hip, knee and ankle joints. People with PD had a shorter and slower obstacle clearance and a slower velocity of clearance compared to healthy people. Their height of clearance, propulsive forces and agonist activity during contact time were also lower. Moreover, they put their foot closer to the obstacle before and after the clearance. They also discovered that, contrary to a moving obstacle which can be used as cue, a stable optical obstacle will complicate movement and could increase the probability of falling.

Sharon *et al.* [36] compared the effects of obstacle height and anticipation time on prefrontal activation for PD patients and older adults. Patients walked along a path and had different types of obstacles : tall vs short and expected vs unexpected. Four parameters were quantified with a Kinect camera: the distance of the trailing foot before the obstacle; the clearance of the leading foot; the distance of the leading foot after the obstacle; and the clearance of the trailing foot. Results showed that, while both PD and healthy patients had an increased prefrontal activation during and after the crossing of the obstacles compared to before, the increase for patients with PD was significantly greater. The avoidance of anticipated obstacles did not create any significant differences between both groups but the avoidance of unanticipated obstacles did since the prefrontal activation for PD patients was higher. On the contrary, no significant differences were seen for short or tall obstacles between groups. No differences were seen for the obstacle negotiation success rate except for tall-unanticipated obstacles where PD patients had a lower success rate compared to healthy patients. Sharon *et al.* thus showed that the activation's increase would vary depending on the obstacle type and that this increase was greater in PD patients.

Irregular terrain

Xu *et al.* [37] studied the gait parameters for person with PD on irregular surfaces because they may increase fall risks. Force plates and a 24-camera motion capture system were used to compute spatiotemporal parameters (i.e., speed, cadence, step length, step width, single, double limb supports), joint kinematics (i.e., range of motion and maximum joint angles for the hip, knee and ankle joints) and trunk kinematics (i.e., trunk RoM and root mean square of trunk acceleration in three axial directions). Healthy and PD patients walked on regular and irregular surfaces at self-selected speeds and had their performances compared. On the irregular surfaces, both groups walked at a slower speed with a reduced cadence and a shorter step length compared to the regular surfaces, which is in accordance with previous study with healthy old adults that showed that they adopted more conservative step patterns to cope with irregular surfaces which is more challenging than regular ones. The PD group chose the same adaptation strategy as the healthy group, which means that patients with PD retained the ability to adjust the gait pattern based on feedback from surface characteristics. However, the gait parameters such as speed, cadence and step length varied more for the PD group. They thus paid more attention to the irregular surfaces and were more careful by using a more conservative stepping pattern. Step width, whose variability is linked to the mediolateral stability, was not significantly affected by the uneven terrains. This means that irregular surfaces are not considered to significantly increase the risk of lateral falls either for PD and healthy patients. About the kinematics parameters, for both groups only the ankle RoM in the transverse plane was affected by the irregular surfaces. Moreover, PD patients showed a smaller knee sagittal plane RoM compared to healthy patients.

Mental aspects influencing FOG

FOG can also be provoked by mental aspects (e.g., anxiety and stress) as summarized by Giladi *et al.* [38]. First, stress can play a role in the occurrence of FOG. Stressful situations related to time pressures such as crossing the street while the light is green or getting the phone to answer it, often provoke freezing episodes. It has been shown by Plotnik *et al.* [39] that freezers have disturbed left/right leg synchronisation. The added stress of time constraints on the desynchronized system may provoke FOG. Plotnik *et al.* used force-sensitive insoles that contained embedded sensors to obtain the swing time, the swing time variability and the asymmetry (gait, CAPIT and UPDRS). Secondly, anxiety may also be a cause for FOG, hypothesis further supported by the increased frequency of FOG in stressful situations. Lieberman [40] studied this by making patients complete several forms such as the Activities of Daily Living of the Unified Parkinson Rating Scale, the Hamilton Anxiety Scale and the Hamilton Depression Scale. Patients were also assessed for panic attacks. According to the results, anxiety seems to be more common in freezers compared to non-freezers. This also explains why PD patient with panic attacks would have more freezing episodes compared to PD patients without panic attacks. Thirdly, depression may also be a trigger for FOG. Earlier development of FOG has been found in people with a higher degree of depression at baseline. Moreover, the presence of FOG at the end of the study has also been significantly associated with the presence of more severe depression at the end of the Deprenyl And Tocopherol Antioxidative Therapy of Parkinsonism (DATATOP) study [41]. Another study, a sub-study of the LARGO (Lasting effect in Adjunct therapy with Rasagiline Given Once daily) study [42], revealed that people with more severe depression would be less sensitive to the effect of rasagiline on FOG-Q scores.

In 2014, Ehgoetz Martens *et al.* [43] examined anxiety as a cause of FOG. Patients with PD were instructed to walk in two virtual environments: across a plank located on the ground (LOW) or across one located above a deep pit (HIGH). The use of virtual reality allowed to compare an anxious and a non-anxious situation. Patients walked on a GAITRite carpet and their percentage of time spent frozen for each trial were measured. Moreover, patients' velocity, mean step length, step length variability, mean step width, step width variability, step time and step time variability were analyzed. All patients showed more cautious gait (e.g., lower velocity and step length) when walking in the HIGH environment which shows that they found the virtual environment immersive enough to induce greater anxiety. During the experiments, 87.5% of the freezers have had freezing episodes, which confirms the hypothesis that anxiety is a trigger for freezing. Compared to walking in the LOW situation, freezers spent a lot more time of each trial frozen in the HIGH environment and experienced more freezing episodes. Their step length and time variability were also higher during the HIGH environment. Freezers had their anxiety level increased compared to non-freezers during the walking paradigm, which suggests that goal-oriented movement can induce greater anxiety, which can lead to freezing. This would explain why patients had more freezing episodes when walking in complete darkness or approaching narrow doorways.

Dual task

In 2006, Giladi *et al.* [38] reported the relationship between cognitive functions and FOG. The first time it has been noticed is when certain freezers had to "stop walking while talking" (SWWT). It may be explained by the fact that the available cognitive resources were not sufficient to handle walking and doing a second task at the same time. There will thus be a prioritization of one task on the other, hence SWWT [44]. In contrast with SWWT, FOG is unintentional which means that the prioritization is inadequate. In addition to causing FOG, dual-tasking might also exacerbate the predisposition to FOG among patients already prone to freezing.

Raffegau *et al.* [45] summarized the effects of dual-tasking on gait performance in people with PD by reviewing articles. It has often been reported in the literature that people with PD have difficulties to walk while performing another task at the same time. The gait velocity will for example decrease when

patients dual-task while walking. The velocity will drop from 1.07 m/s when single-tasking to 0.92 m/s when dual-tasking. Raffegeau *et al.* also reported that, depending on the velocity, the impact of dual-task may be different. People walking with single-task speed slower than 1.1 m/s will be less impacted by dual-task compared to patients walking at a quicker velocity. PD patients are also unable to prioritize gait while performing dual-task, which will increase their risk of falls. The type of dual-task performed may also influence the effect it has on gait. Tasks involving executive function skills such as arithmetic, language and motor tasks, would have a greater influence on gait velocity compared to other tasks such as memory ones. However, all tasks will have an impact on the velocity when dual-tasking.

Since both dual-tasking and turning influence FOG, Spildooren *et al.* [46] tried to understand how dual-tasking and turning at the same time would influence freezing. Controls as well as freezers and non-freezers in the OFF phase were asked to turn 180° and 360° with and without a cognitive dual-task. Data were recorded by an eight camera VICON data capturing system and retroreflective markers positioned on several body areas. They computed four parameters: total number of steps of the trial, total duration of the trial, cadence and freezing trials (trials where FOG occurred). During single-task, freezers had freezing episodes during 37.5% of the turning-trials for both the 180° and 360° turns compared to zero trials when walking straight ahead. During dual-task, a larger turning-degree came with more freezing episodes: 37.5% for 180° turns and 61.1% for 360° turns but no correlation could be found between NFOG-Q scores, dual-task interference, and the occurrence of actual freezing during the protocol. Dual-task did not provoke any change when walking straight ahead or turning by 180° but a significant effect was measured when turning by 360°. This thus shows that FOG is not only influenced by the turning degree but also by the cognitive load. Turning 360° while dual-tasking is the combination that provoked the most freezing episodes. Turning also seems to trigger FOG more importantly than dual-task since the effect of dual-task was only significantly seen on 360° turns. Another important finding is that both controls and non-freezers decreased their cadence during turning while freezers increased it, which is probably related to FOG.

Pieruccini-Faria *et al.* [47] tested the effect of dual-task on obstacle avoidance. They have varied the cognitive load during the approach and the crossing of obstacles for freezers and non-freezers to assess their performances. Three Optotrak cameras combined with active IREDs fixed to several body areas were used to record patients' movements. Patients' step length, step time and gait velocity as well as their foot clearance, crossing velocity and step width were computed. Moreover, clinical and cognitive assessments were made by using the MDS-UPDRS III and the Mini-Mental 3MS exam. Pieruccini-Faria *et al.* observed that controls and non-freezers were not influenced by dual-task whereas a difference of performance could be noted by freezers. Also, the closer freezers were to the obstacle, the more dual-task influenced them. The following hypotheses can be made: freezers' gait adjustments planning is not as automatic as for controls and non-freezers. Moreover, the closer they were to the obstacles, the more cognitive resources were dedicated to gait. Unfortunately, these resources are finite, which means that with the additional dual-task, not enough attention is put on gait and it leads to greater gait variability. They also noted that, after crossing the obstacles, freezers would land their lead foot closer to the obstacle and that it may demand greater resources from them to cross the same obstacle compared to controls and non-freezers.

As written above, both irregular terrain and dual-task can trigger freezing episodes. To go further, Xu *et al.* [48] decided to study how people with PD will react when walking on irregular surfaces and performing dual-task. They evaluated nine patients with PD on two different surfaces (regular and irregular) and for two different tasks (single- and dual-task). Data were collected via a 24-camera motion capture system and force plates. Spatiotemporal parameters (i.e., speed, cadence, step length, step width and single limb support), kinematics parameters (i.e., range of motion and maximum joint angles for the hip, knee and ankle joints) and trunk-related variables (i.e., trunk range of motion and trunk center of mass

acceleration root mean square in all three directions) were obtained. They found that for both control and PD participants, walking on irregular terrain decreased walking speed, cadence and step length while increased step width compared to walking on regular terrain. These results were significant for PD but were not for control participants. These changes show how irregular terrain is challenging for both groups but even more for PD patients. It also magnifies gait deficits during dual-task walking and accentuates body instability for PD, which was already identified in other studies and simply confirmed in this one. When only looking at the PD group, they had greater gait deficits when walking on irregular terrain and performing dual-task than when performing single-task.

Most of the studies about dual-task have been performed with tasks that are uncommon to perform while walking. Therefore, Yamada *et al.* [49] decided to study dual-task in older adults with PD by performing tasks that represent the daily activities. Their goal was to detect real fall risk situations of PD patients during their gait. Patients were divided between a control group and a PD group and had to walk under three different conditions: walking without dual task, walking carrying bags with weight, and walking talking on the cell phone. They used a GAITRite system for kinematic data collection and analyzed the gait speed, cadence, support time, swing time, double support time, step length, and step width. Yamada *et al.*'s experiments confirmed previous researches by having slower speed, lower cadence, and shorter step length for patients with PD compared to the control group during single-task gait. Moreover, while they found that both groups' gait parameters were significantly influenced by walking while dual-tasking, parkinsonians were the most influenced group. The third condition, walking and talking on the cell phone, also had the biggest influence on gait parameters. During condition two (walking while carrying bags), parkinsonians had shorter step length, smaller step width, and shorter swing time compared to single-task gait. Their time of double support and support time were significantly longer. This condition can be considered as a motor dual-task where PD patients tried to compensate the instability generated by the condition. As said above, condition three has been proven to be the most complicated one, both for the control and parkinson group. Walking while talking requires executive function, which has been shown to be altered in PD patients. Moreover, the questions asked on the phone needed episodic memory, which is also difficult for parkinsonians. This thus may have made the condition even more complicated as "simply" talking on the phone while walking.

2.2 Compensation strategies developed by patients

Nonnekes *et al.* [50] reviewed in 2019 the compensation strategies found/used by patients themselves and classified them by categories. Seven main categories came out. The first one, called external cueing, groups together external cues, widely used to compensate for gait impairments in individuals with PD. It is composed of an external stimulus such as an auditory, proprioceptive, or visual stimuli that provides a goal-directed behavior, which facilitates motor sequences. It provides a movement reference or target that is most likely predictive in nature and improves executive attention. There are a lot of examples such as walking at the rhythm of a metronome, stepping over a laser beam that can be projected by different objects (i.e., shoes, belt, or cane) or stepping over 2-dimensional or 3-dimensional visual cues placed in a regular pattern on the floor. The second category is composed of internal cues where patients will have their focus oriented toward gait. This is done by using specific self-prompting instructions or by concentrating themselves on performing a specific gait event in a rhythmic way (e.g., performing a heel strike at each count). The third category is about motor imagery and action observation which compensates for reduced automaticity by mental simulation or visualization of the action of gait without its actual execution. Motor imagery is when the patient rehearses walking in its head while not really walking. Observing someone else walking and concentrating on it is called action observation. Altering the mental state, which can for example happen under imminent threat, is the identified fourth category. In this case, the patient will suddenly be able to perform an action he was previously unable to do by

increasing its attention. While this cannot be used everyday, other altered mental states such as increased motivation could have a similar working mechanism. The fifth compensation strategies' category adapts walking to reduce the postural demands and is thus about changing the balance requirements. The patient would, for example, make wider rather than narrow turns. Adopting a new walking pattern is the sixth category. Patients adapt their gait by changing small details such as lifting their knees higher to become less dependent on automatic generation. The key element is to use less overlearned motor programs compared to normal walking. The last category is formed by other ways to move forward such as using a bicycle or riding a scooter, which do not use the legs to move forward. How these alternatives work is not completely clear since it could come from the fact that these model are less overlearned or come from other compensation strategies such as the external cueing linked to bicycling. There are also some compensation strategies that uses a combination of the above categories.

2.3 Assist-as-needed protocols for Parkinson's disease

Several studies such as the ones done by Hess *et al.* [51] and Ada *et al.* [52]) have shown that gait training provides better improvements compared to focused training on, for example, strength, balance or coordination. However, while resulting in greater improvements compared to focused training, it requires manual assistance from one or more therapists and it is labor intensive. Robot-assisted gait training (RAGT) has therefore been developed. It includes exoskeletons and end-effector robots and provides automatic training and is an alternative to gait training. Assisted-as-needed technologies provide assistance in real time because it adjusts the level of assistance according to the patient's real-time needs. Their main advantages are that it preserves movement variability while walking and at the same time encourages the patient's active participation in rehabilitation since it only provides assistance to the patient when he is in need of it [53].

In 2012, Fu *et al.* [54] made experiments with CAIROW (Context-aware Assisted Interactive RObotic Walker) which is an active robotic walker composed of many sensors such as laser range finder, camera and force sensor and that guide patients by a mild dragging force from the handle (Figure 2.1). These sensors allow it to localize itself in indoor environment, detect the gait of the user, and perform human-interactive functions. It drags stably with mild acceleration while the user steps and stops and waits for further instructions when the distance between it and the user is above a certain threshold. If the patient pushes but does not step forward, then CAIROW will step because the motorized wheels are locked. This functionality is important for patients with PD since they have a tendency to fall forward when using traditional walkers. An online music player has also been added because Pacchetti *et al.* [55] have shown that music therapy has a motor improvement with PD patients. The user can control the robotic walker to move forward, backward or to turn left and right through the interface. Tests showed that CAIROW enabled users to perform a stable gait, which may reduce FOG. In another study, Fu *et al.* [56] included a context analysis module in CAIROW. This module is divided in two parts: a road condition context analysis module and a user context analysis module. The former evaluates the condition of the road ahead of the robot to act within safety limits and refrain the robot's actions if needed. The latter evaluates the user's context via force sensors on the robot's handle and a mini laser near the user's legs. This laser monitors gait parameters such as the step length, velocity, and acceleration of each leg in each step. The robot will differentiate three contexts: festinating gait (patients continue to walk but by making small steps), FOG (patients grip the handle tightly and their leg's muscles get stiff) and normal gait (none of the two previous situations). The robot's speed will be increased or decreased if the distance between the robot and the user increases/decreases. If the user has a festinating gait, he cannot keep a normal length. Auditory cues will then be used to stimulate the patient and help him escape from it. During FOG, the same strategy will be used but the auditory cues will have another frequency. When the robot starts to turn, it will prompt the patient with synthesized speech.

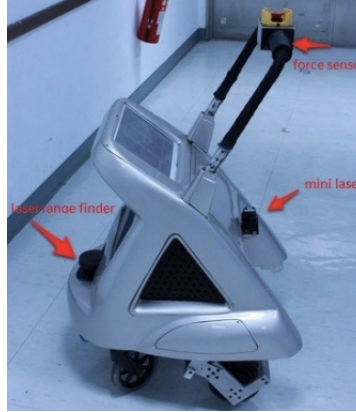


Figure 2.1: Side view of a Context-aware Assisted Interactive RObotic Walker (CAIROW) used by Fu *et al.* [54].

The AGoRA Smart Walker was presented by Sierra *et al.* [57] in 2019 and has been adapted to mimic the structural framework of a conventional walker by attaching two forearm support handles to the main deck of the platform (Figure 2.2). In 2021, Sierra *et al.* [58] tested the performances of this Smart Walker on the daily activities of patients with PD. It is composed of a Human–Robot–Environment Interaction (HREI) Interface which is further divided in a Human–Robot Interaction (HRI) and a Robot–Environment Interaction (REI) interfaces. A HREI provides natural user interactions, effective environment sensing and adaption while maintaining safety requirements. The HRI has multiple functions such as measuring the interaction forces between the user and the platform to analyze the interaction between them, only allowing the walker to move when the user properly interacts with it and adapt the walker’s behavior to each user gait pattern by computing several gait parameters. It also implements control strategies depending on the physical HRI between the user and the walker. The REI also has several functions, such as implementing navigation capabilities, executing the desired movements for the walker and detect the obstacles in the surroundings while differentiating them (e.g., fixed or moving obstacles, people). Due to all these functions, there is thus noticeable communications between the user and the walker, which allows the walker to adapt its assistance to the user. Different control strategies can also be used (i.e., user, navigation system or shared control) depending on the situation.

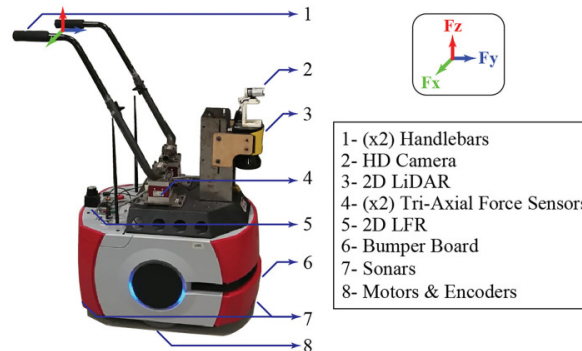


Figure 2.2: Description of the AGoRA Smart Walker used by Sierra *et al.* [57].

There exists a lot of other smart walkers which were however, to our knowledge, not yet tested on patients with PD. These smart walkers can either have different designs or can measure different metrics in various ways. Some studies focused themselves on extracting specific gait parameters from dedicated sensors [59]. Other studies measured, for example, gait cadence by placing ultrasound sensors faced to

each of the patients' legs [60]. Palermo *et al.* [61] used a full-body pose estimation framework obtained from two RGB+D camera streams with non-overlapping views placed on a smart walker. Another study, conducted by Scheidegger *et al.* [62], explored the use of user's gait and face orientation to command the displacement of the smart walker. Smart walkers can also be used to help patients get up. Werner *et al.* [63] used a smart walker with a sit-to-stand assistance that helped patients go from a seated position to a standing position.

Among RAGT, there are also exoskeletons that can adapt the assistance they provide to the user in real-time, depending on their need. But to our knowledge, such therapies have not been developed for PD patients yet.

Vaughan-Graham *et al.* [64] studied the use of an exoskeleton in post-stroke gait rehabilitation and the perspectives of people who have had a single-use experience with the exoskeleton. They used the Exo-H2 which has six actuated joints (i.e., hip, knee and ankle bilaterally) and provides lower limb assistance when the gait pattern deviates from a prescribed pattern by using an assistive gait control algorithm. Participants were divided in two groups: persons with stroke (PWS) and their physiotherapists (PT). The PWS walked approximately 45 to 60 minutes with the exoskeleton and the speed as well as the assistance were adjusted depending upon the PWS ability. Both the PT and primary researcher provided manual support via the upper limbs during the whole experiment. Interviews of both the PWS and the PT were conducted to obtain their insight about the exoskeleton. Vaughan-Graham *et al.* found that including PWS and PT is important to provide exoskeletons that meet their needs because they provided insightful knowledge with respect to exoskeleton use and design. They also showed that, while PWS are excited about exoskeleton technology, they also felt that the current exoskeletons were autonomous robots that imposed a walk on them instead of a device that augmented their function. The study also showed the need for a robust evidence base to support exoskeleton use. It is important to define clearly the people for whom the exoskeleton will be the most beneficial and the intent of the device (e.g., facilitate the walking pattern in a person who is not yet walking or improve the walking pattern in a person who is already walking).

Nolan *et al.* [65] tried to understand the changes in temporal and spatial characteristics and symmetry due to robotic exoskeleton overground walking for acute and chronic post stroke patients. They used the Indego which is a powered lower-limb robotic exoskeleton for individuals diagnosed with stroke for overground walking. It is composed of a hip segment as well as right and left upper/lower leg segments. Patients performed over the course of two weeks four sessions of overground walking with the exoskeleton. Their gait speed, gait deviations and Functional Ambulation Category (FAC) data were collected before and after the four walking sessions. Patients were divided between people with acute or chronic stroke. For both groups, after the four sessions, gait speed increased compared to baseline data. These sessions also improved patients' Functional Ambulation Category and, by observing the gait deviations, showed that overground walking with a robotic exoskeleton might have had a therapeutic benefit on patients.

Chapter 3

Materials and methods

This chapter starts by presenting the objectives of this work. It then presents the experiments' participants, the materials used during the experiments and the experimental protocol. The data processing steps and the studied metrics are described afterwards. Finally, it describes the analyses (statistical and visual) used on the metrics to assess whether they are conclusive or not.

3.1 Research question

As seen in sections 1.2 and 2.1, people with PD can have different kind of motor symptoms that affect their daily life. These motor symptoms can influence their gait during their daily life and especially in some environmental or mental conditions (e.g., lower speed, balancing issues, etc.). FOG is one of the more severe gait impairment possible for people with PD and has severe consequences on patients such as reducing their quality of life and get them to leave their homes less due to fear or anxiety. Having an exoskeleton that can provide help to the patients in real time could reduce the impact of freezing on their daily life.

This work is part of the long-term objective to use an active pelvis orthosis (APO) for assistive and rehabilitative natures and to develop a real-time assistance for the patient. An APO is a wearable exoskeleton aimed at improving the gait energy efficiency of users affected by mild impairments through the assistance of hip flexion-extension (Figure 3.1). It was build by the BioRobotics Institute (Pisa, Italy) to help people with mild gait disturbances (e.g., gait post-stroke hemiparesis, unilateral lower-limb amputation, senile gait, PD, etc.) to recover more stable, efficient, and independent locomotion [66].

To contribute to research in this field, the question it will try to answer is:

How will environmental conditions influence the gait parameters of people with Parkinson's disease?

The environmental conditions have been chosen according to the previous results mentioned above in section 2. The goal is to identify metrics that vary depending on the environmental conditions and if freezing is provoked or not. Afterwards, when the chosen metrics go over or under identified thresholds, a predefined amount of help could be provided to the user.

3.2 Participants

The study population was composed of two groups: healthy people (HP) and people diagnosed with PD. A total of two healthy people (1 male/1 female) and six patients with PD (4 males/2 females) took part in the study. Out of the six patients with PD, half of them had freezing episodes and where thus considered as freezers while the other half had not and were considered non-freezers. This decision was made in order to compare their gait parameters during the experiments.

A certain amount of information needed to be gathered from the patients before carrying out the experiments (Table 3.1). This information was obtained by performing the following tests on patients: the Mini-Mental State Examination (MMSE), the Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and the New Freezing Of Gait Questionnaire (NFOG-Q). The tests were

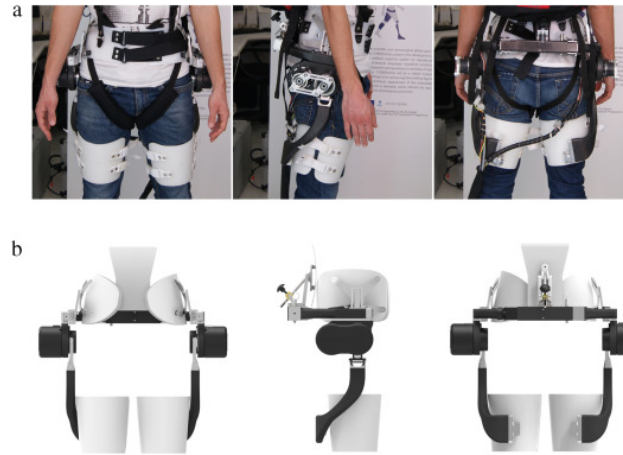


Figure 3.1: First version of the APO [66]. (a) Frontal, lateral and back view of APO worn by a healthy subject. (b) Frontal, lateral and back view of the APO CAD model.

assessed by the neurologist Dr Warlop (Cliniques universitaires Saint-Luc, Brussels, Belgium). Patients' most affected side of the body (left or right) by PD were identified through the MDS-UPDRS. They participated in the experiments 60-120 min after their last medication intake, when it was still active (ON phase), with the exception of one patient who forgot to take his medication.

All patients needed to be able to walk independently without walking aids and have stable medication for the four weeks preceding the study. The following conditions were inclusion criteria for the study: a minimum of 24/30 on the MMSE [67], stage of the disease (assessed through H&Y) below 3 and patients had to be free from any muscular, neurological (other than PD) or orthopaedic pathologies that could alter gait performances. Ethical clearance was obtained from the Hospital-Faculty Ethics Committee of Cliniques universitaires Saint-Luc (EudraCT n. 2019-002048-26) and informed consent was obtained from each of the patients prior to data collection.

3.3 Materials

This chapter presents the materials used to record data during the experiments. Three different type of equipment were used: Inertial Measurements Units (IMUs), a motion capture system and a heart rate sensor. All measurement sessions were recorded using a portable video camera in order to review some trials if needed.

Firstly, two IMUs (NGIMU GUI, x-io Technologies Limited, Bristol, UK [68]) were attached approximately 20 mm above the external malleoli with a Velcro strap, according to the alignment shown in Figure 3.2a. One IMU is composed of multiple types of sensors including a 3D gyroscope and a 3D accelerometer. It communicated with a computer via a Wi-Fi connection. The sampling frequency was set to 200 Hz [69].

Secondly, a motion capture system (MTw Awinda, Xsens, Enschede, the Netherlands [70]), which is a wireless human motion tracker for real-time applications, was used. It is composed of various IMUs placed on different parts of the lower and upper body. Eight IMUS were used in total for these experiments, and were placed as shown on Figure 3.2b.

Thirdly, a heart rate sensor (Polar H10, Polar Electro, Kempele, Finland [71]) was placed on the torso right under the sternum and connected via Bluetooth to a phone.

3.4 Experimental protocol

The experiments took place in a sports room in the *Mounier Sports Center* in Brussels. There were four different environmental conditions chosen according to the evidences shown by the papers in section 2.1.

Table 3.1: Characteristics of the study populations

	Parkinson (n=6)	Healthy (n=2)
Age (years)	68.2 $\pm$ 13.7	21.5 $\pm$ 0.7
Gender (male/female)	4/2	1/1
Leg length (cm)	89.5 $\pm$ 4.8	87.8 $\pm$ 0.35
Left (cm)	89.7 $\pm$ 5.1	88 $\pm$ 3.5
Right (cm)	89.3 $\pm$ 4.6	87.5 $\pm$ 2.1
Weight (kg)	66 $\pm$ 14.9	66 $\pm$ 2.83
MMSE score (/30)	27.0 [24-30]	-
H&Y scale	2.25 [2-3]	-
2 (n)	3	-
2.5 (n)	1	-
3 (n)	2	-
MDS-UPDRS III (/132)	23.5 [18-43]	-
Affected side (L/R)	2/4	-
Freezers (n/tot)	3/6	-
NFOG-Q (/28)	20 [15-26]	-

Mean ($\pm$ SD) are expressed for quantitative variables normally distributed while median [range] are expressed for both ordinal and non-normally distributed variables.

1. *Control* condition: patients had to walk straight ahead for a distance of 10 meters on the ground (Figure 3.3a).
2. *Mats* condition: patients had to walk straight ahead for a distance of 10 meters on gym mattresses. The mattresses' dimensions were 200 x 100 x 4 cm, weighed 5 kg and were composed of high density, dynamic polyethylene foam (30 kg/m³) [72]. Seven mattresses were lined up from end to end, which means that the total distance covered by the mattresses was 14 meters and they were stacked two by two. Before starting to walk, patients thus already stood on the mattresses, and when crossing the finish line, they still had two meters to go before the end. This decision was made so that patients did not have to climb on or off the mattresses during the acquisition (Figure 3.3b).
3. *Doorway* condition: composed of a 10 meters flat ground with a doorway at mid-way (5 meters) between the starting and finishing line. The doorway had the dimensions of a standard door (83 x 204 cm) to represent most everyday doors (Figure 3.3c).
4. *U-turn* condition: consisted of the patient walking for 5 meters, making the tightest possible U-turn without any constraint (e.g., number of steps, turning side, etc.) and then walking back through the starting line (Figure 3.3d).

Each condition was repeated three times in a randomized way to avoid fatigue or habituation effects. The patients thus performed a total of 12 trials, i.e. three trials for each of the four conditions. If necessary, patients could request a break between trials or between conditions. Patients were told to walk at their comfortable walking speed.

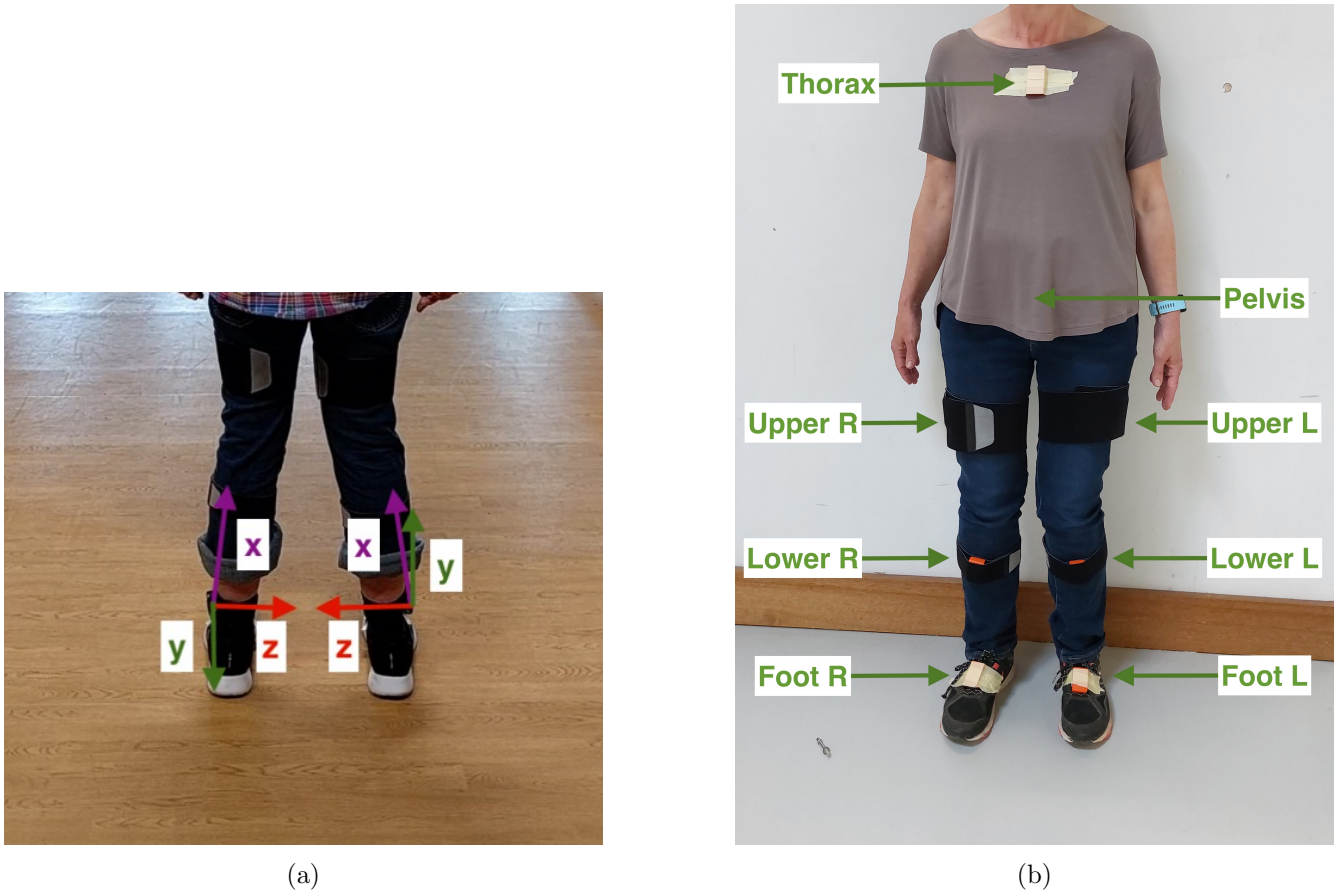


Figure 3.2: Participants were equipped with (a) two inertial measurement units (NGIMUs) attached to the lateral sides of the shanks and (b) a motion capture system (MTw Awinda) mainly on their lower limbs.

3.5 Data processing

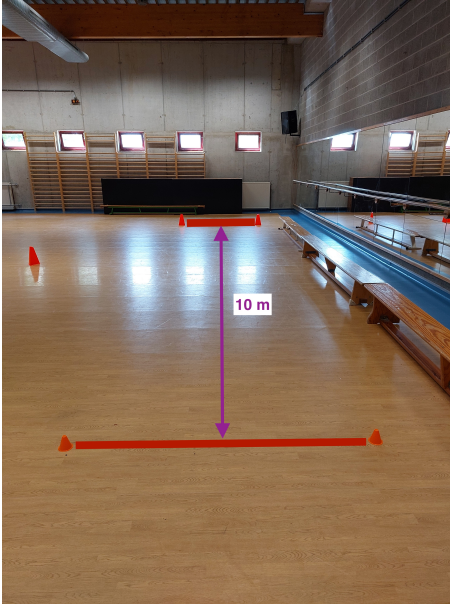
This chapter presents a description of the gait cycle shared by healthy (non-disabled) people, how the recorded signals were used, how the gait events were found, which metrics have been studied to identify parameters that vary according to the environmental conditions and finally how the statistical analysis were done.

This work focuses on IMUs data analysis due to time constraints, leaving the analysis of motion capture system data to future work.

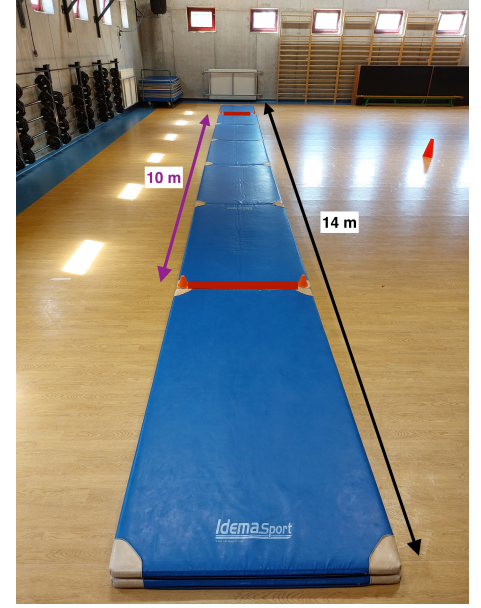
3.5.1 Gait cycle

The human's walking process can be studied by making the assumption that all walking cycles are the same and thus focus on one walking cycle. The gait cycle is considered as the time between two identical locomotion events of the same leg. It can be split in two phases: the stance phase, which is the period of time when the foot is in contact with the ground, and the swing phase, which is the period of time when the foot is off the ground [73], [74] (Figure 3.4). Hereunder, the ipsilateral leg is the leg of which the gait cycle is studied (here the right leg) and the contralateral leg is the opposite one.

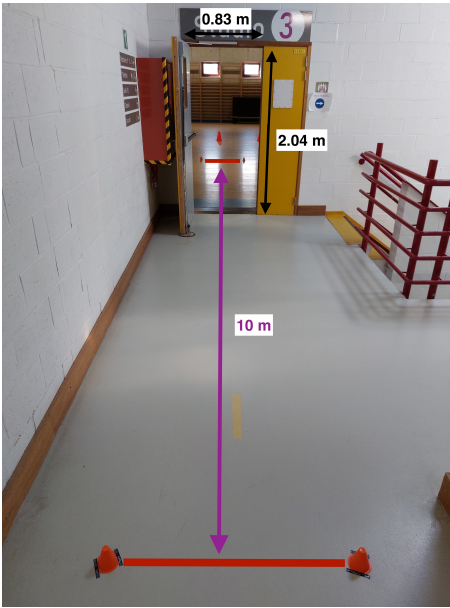
The stance phase constitutes approximately 60% of the gait cycle and starts when the foot makes its first contact with the ground (heel strike, also called initial contact). It ends when the foot of the ipsilateral leg leaves the ground (toe off, also called final contact). The stance phase is composed of four



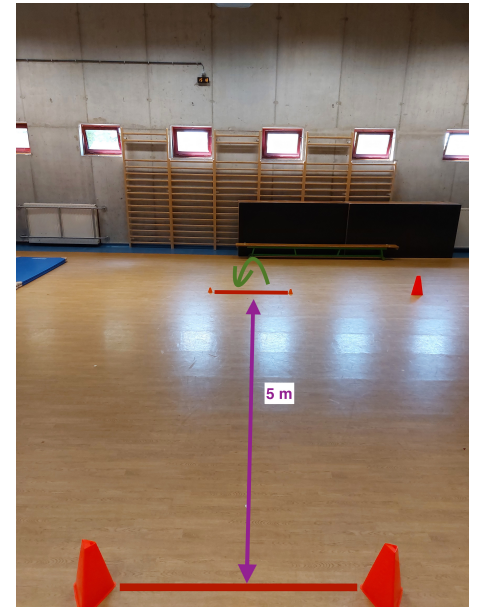
(a)



(b)



(c)



(d)

Figure 3.3: Environmental conditions walked by the patients during the experiments : (a) control, (b) mats, (c) doorway and (d) U-turn condition.

consecutive intervals [73], [74]:

- **Loading response:** begins as the heel strikes the ground and the ipsilateral leg bears most of the weight since the other leg starts its swing phase.
- **Midstance:** begins as the contralateral leg's toes take off the ground and lasts until the body weight is aligned over the forefoot.
- **Terminal stance:** begins when the ipsilateral heel lifts off the ground.
- **Preswing:** begins with the heel strike of the contralateral foot and ends with the ipsilateral toe-off.

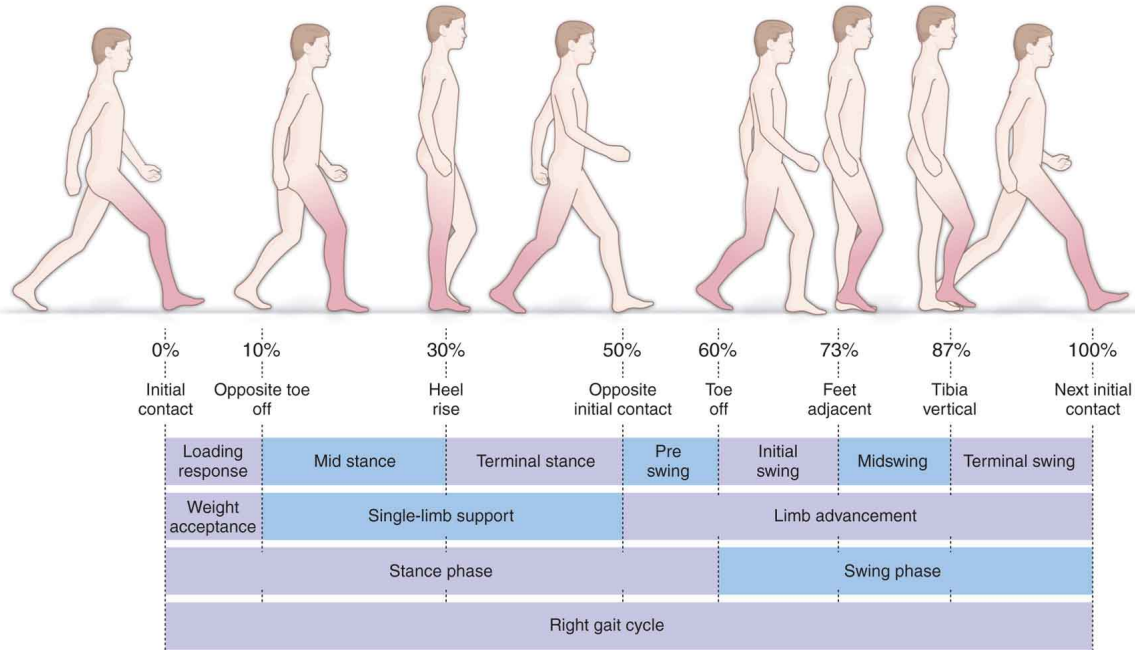


Figure 3.4: Gait cycle of the right leg decomposed into events, periods and phases [74].

The swing phase constitutes approximately 40% of the gait cycle and starts just after the stance phase when the foot leaves the ground. It ends when the ipsilateral foot's heel strikes the ground again. The swing phase is composed of the three consecutive intervals [73], [74]:

- **Initial swing:** starts with the ipsilateral toe-off and ends with both feet being opposite to each other.
- **Mid-swing:** ends when the ipsilateral limb is forward and has its tibia vertical with respect to the ground.
- **Terminal swing:** ends when the ipsilateral foot's heel strikes the ground again.

The heel strike and the toe-off both help to draw a clear line between the stance phase and the swing phase.

3.5.2 Finding the gait events

The IMUs' data were loaded into MATLAB. To investigate the patients' gait, the decision has been made to use the shank mediolateral angular velocity (Figures 3.5a and 3.5b) in order to identify the gait events, i.e., heel strikes, toe-offs and mid-swings, as defined above. In order to do that, multiple steps, which are presented hereunder, had to be performed on the signals before finding the gait events.

Signal processing

Once the raw data were obtained, the signals needed to be processed. It was done in two steps: the signals first went through a high-pass filter and then through a low-pass filter.

The high-pass filter was designed as an IIR filter (Equation 3.1). It allows to reduce the effect of drift on the signal. Drift is caused by bias instabilities which will, over time, cause drift due to the integration of inherent imperfections and noise within the device. These instabilities can be caused by temperature changes or by variations in the supply voltage [75].

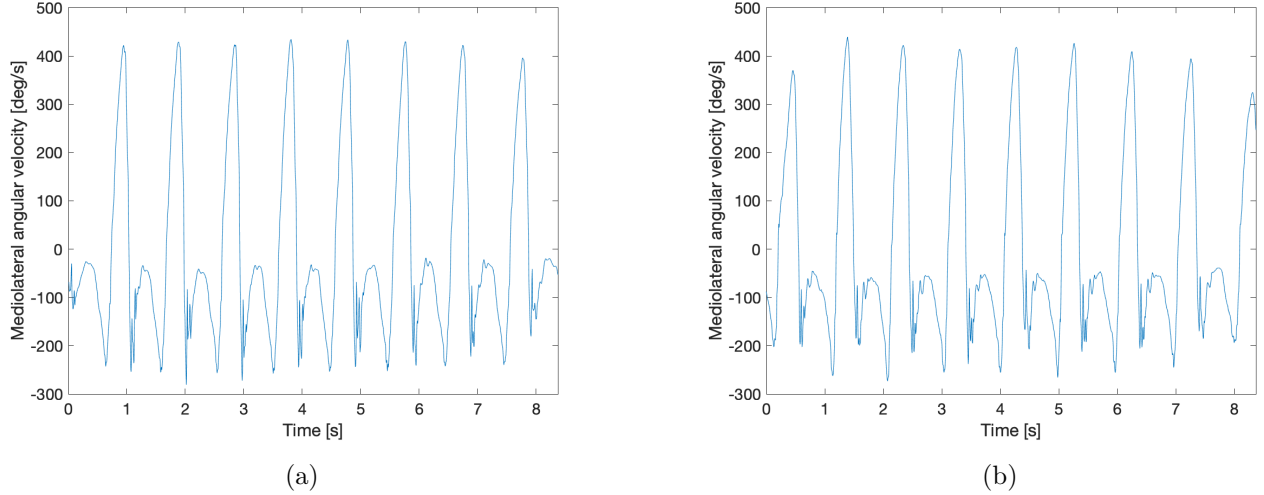


Figure 3.5: Raw signals from the mediolateral axis (Z-axis) of the gyroscope. First trial of the *control* condition for patient 1 with the IMU located at his (a) left and (b) right side.

The transfer function of the IIR filter is the following:

$$H(z) = \frac{1 - z^{-1}}{1 - \alpha \cdot z^{-1}} \quad (3.1)$$

The cutoff frequency was set to 0.25 Hz because the value of α was set to 0.995 [75].

The low-pass filter was designed by using a Butterworth filter with a cutoff frequency equal to 10 Hz [69]. The filter's order was determined after comparing the performances of 1th up to a 6th order's Butterworth filter (Figures 3.6a and 3.6b). When looking at the figures, their performances seem rather similar. However, the decision has been made to go with a 5th order's Butterworth filter. While it increased a bit the complexity of the filter compared to a lower order, it did not significantly increase the running time and allowed to detect less spurious peaks, which will be an advantage later on (section 3.5.2). This low-pass filter was applied to the signal to remove noise. The noise is due to the influence of devices and environmental interferences. Removing noise allowed to get a smoothed signal and to get rid of parasitic peaks [76].

Both filters were applied two times to avoid phase distortion by using the MATLAB function *filtfilt*: once in the forward direction and once in the backward direction. The signal has thus been filtered with a high-pass IIR filter and a low-pass 5th order's Butterworth filter (Figures 3.7a and 3.7b).

Heel strikes and toe-offs' identification

After being filtered, the mediolateral angular velocity can be used to detect the heel-strikes, the toe-offs and the mid-swings. The local maxima of the signal can be considered as the mid-swing area while the local minima can be considered as either a heel strike or a toe-off, depending on their positions. The local minimum that precedes the mid-swing is considered as the toe-off while the local minimum that occurs after the mid-swing is considered as the heel strike [77].

The next step was thus to detect the negative and positive peaks of the signal, which was done by using the MATLAB function *findpeaks*. It was combined with options such as *MinPeakHeight* to keep only peaks greater than a certain value and *MinPeakDistance* to avoid having two successive peaks that are too close, which would not be possible in real life. Once the peaks were identified and, even with

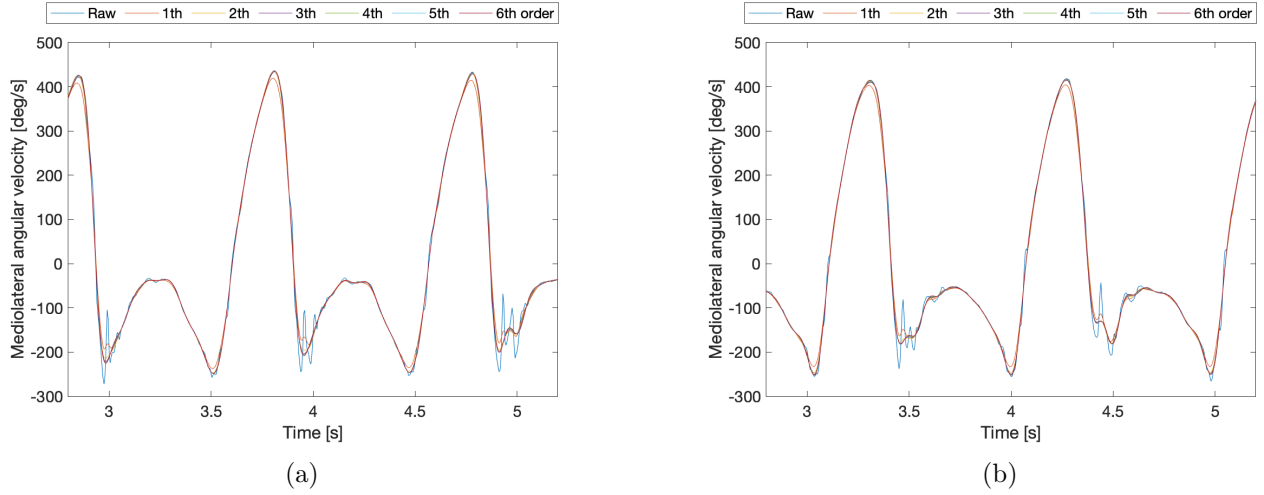


Figure 3.6: Signals from the mediolateral axis (Z-axis) of the gyroscope filtered with a Butterworth filter having different orders (1th to 6th) to compare their respective performances. Zoom on the first trial of the *Control* condition for patient 1 with the IMUs located at his (a) left and (b) right side.

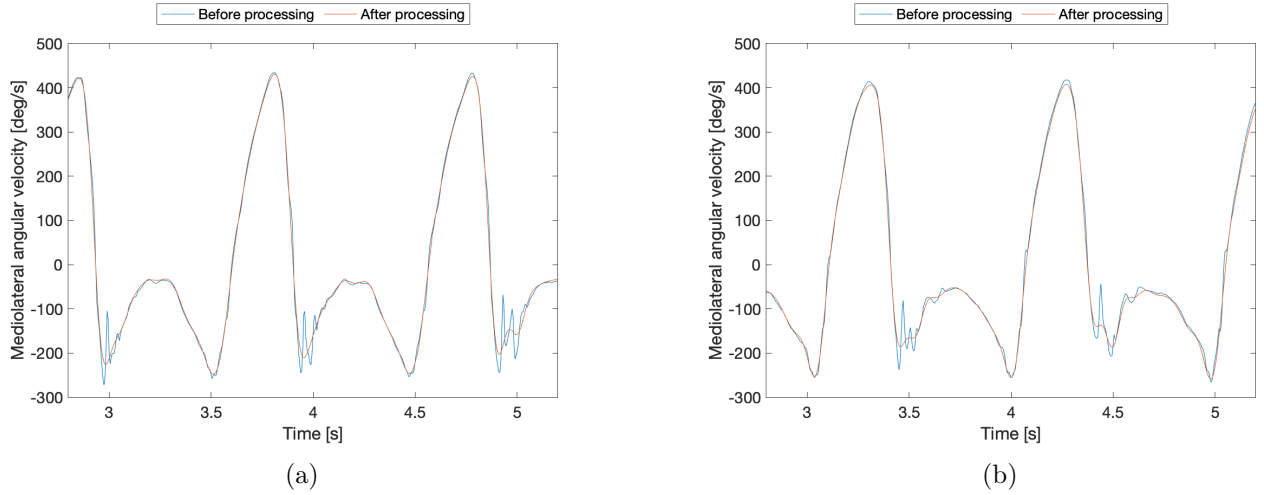


Figure 3.7: Comparison between the signals from the mediolateral axis (Z-axis) of the gyroscope before and after being filtered with a high-pass filter (IIR filter, $f_{cutoff} = 0.25$ Hz and with the transfer function described in Equation 3.1) and a low-pass filter (5th order Butterworth, $f_{cutoff} = 10$ Hz). Zoom on the first trial of the *Control* condition for patient 1 with the IMUs located at his (a) left and (b) right side.

the help of the options mentioned above, some unwanted peaks were identified by MATLAB (Figure 3.8a). Therefore, a manual removal of these unwanted peaks had to be performed. Knowing that a stride started with a heel strike and ended when the next heel strike started and that only complete strides were representative of the patient's gait, every peak in the stride other than the three successive local events (heel strike, toe-off and mid-swing) were deleted. Once only complete strides and their gait events were identified, the first and last stride were not taken into account to avoid having strides that could be influenced by the patient's starting or stopping. Finally, only the peaks that will be used later for analysis were kept (Figure 3.8b). The last step was to correctly identify and allocate the peaks between heel strikes and toe-offs (Figure 3.8c).

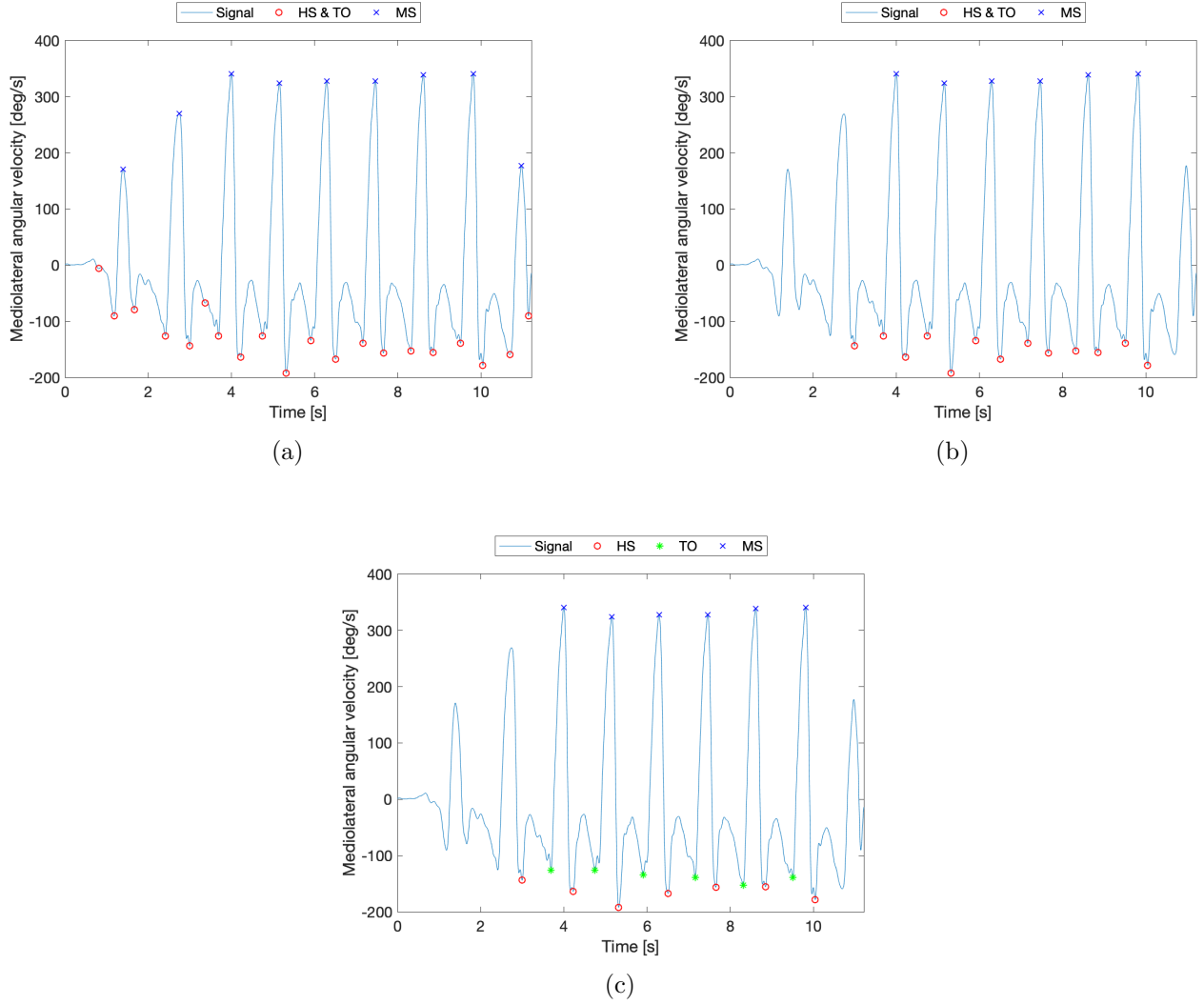


Figure 3.8: Gait events' detection (heel strikes, toe-offs and mid-swings) through negative and positive peak detection and distribution. Third trial of the *mats* condition for patient 4 and the IMU located at his right side. (a) Peaks' detection by using MATLAB's function *findpeaks*. Some of them are spurious and thus unwanted. (b) Removal of the unwanted peaks shown in Figure 3.8a. (c) Peaks' distribution between heel strikes and toe-offs after removal of the unwanted peaks.

Video matching for the *doorway* and *U-turn* conditions

The *doorway* and the *U-turn* conditions needed a last step in order to be analyzed. The videos filmed during the experiments had to be overlapped with the Left and Right shanks' signals to try and identify the exact moment when the patient crosses the doorway or makes his U-turn. The left and right strides corresponding to these exact moments needed to be identified in order to be able to precisely analyze the effect of the punctual change in the patient's gait.

For the *U-turn* condition, correctly identifying the turning stride has sometimes been proven somewhat difficult because each patient had his own way to perform the U-turn as efficiently as possible. This has been addressed by considering that the whole U-turn only consisted of one stride for each foot (Figures 3.9a and 3.9b).

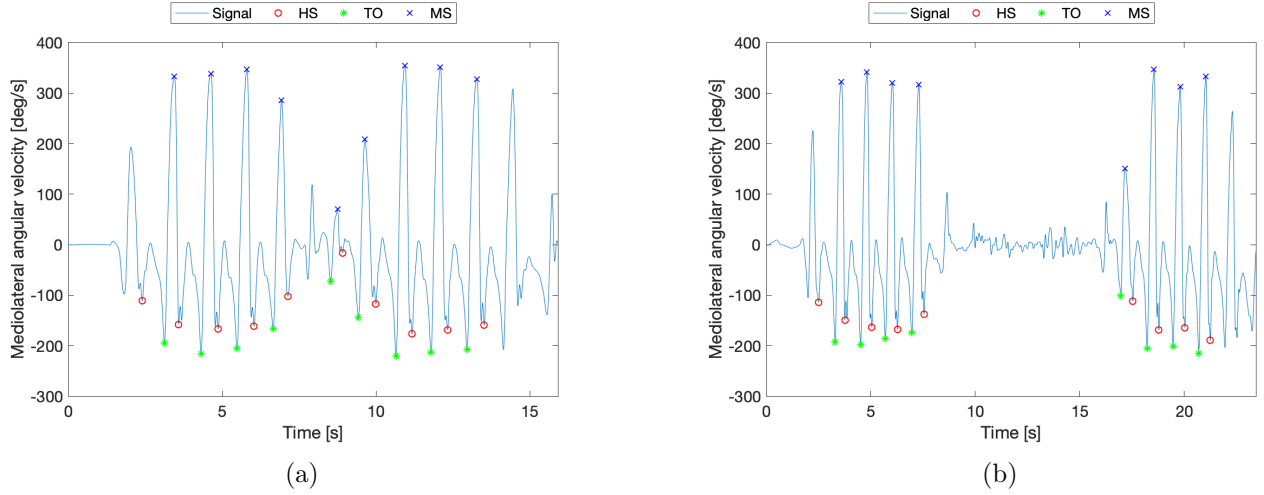


Figure 3.9: Matching between the videos and the signals to accurately find the stride at which the punctual event (doorway crossing or U-turn) happened. (a) Signal recorded during the U-turn when the patient made multiple small adjustment steps to properly turn. First trial of the *U-turn* condition for patient 5 and the IMU located at his right side. (b) Signal recorded during the U-turn when an episode of freezing occurred. Third trial of the *U-turn* condition for patient 5 and the IMU located at his right side.

Data acquisition's problems

Some problems were encountered when recording data by the IMUs during the experiments. Probably due to Wi-Fi connection problem, the IMUs sometimes stopped recording for a short period of time before starting to record again. This induced some gaps during data acquisition.

When the gap induced by the recording problem was small enough and did not hinder the identification of any of the three gait events the signal was kept intact (Figure 3.10).

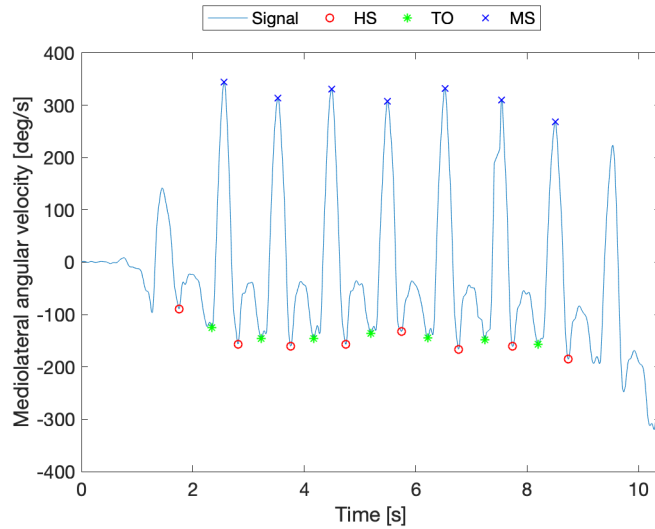


Figure 3.10: The gap in the data recording does not hinder the identification of any of the three gait events (heel strikes, mid-swings and toe-offs). First trial of the *doorway* condition for patient 6 and the IMU located at his right side.

However, some gaps were consequent and thus hindered the correct identification of complete strides.

Multiple possibilities arise and decisions were made depending on the situation :

Problem 1: The gap happened at the beginning of the signal which made it impossible to correctly identify either the heel strike, toe-off or mid-swing for the first stride(s) (Figure 3.11a).

Problem 2: The gap happened at the end of the signal which made it impossible to correctly identify either the heel strike, toe-off or mid-swing for the last stride(s) (Figure 3.11b).

Problem 3: The gap happened at the middle of the signal which made it impossible to correctly identify either the heel strike, toe-off or mid-swing for one or multiple strides while complete strides can be identified before and after the problem occurred (Figure 3.11c).

Problem 4: The gap was simply too large which makes it look like as if the IMU simply stopped recording too early (Figure 3.11d).

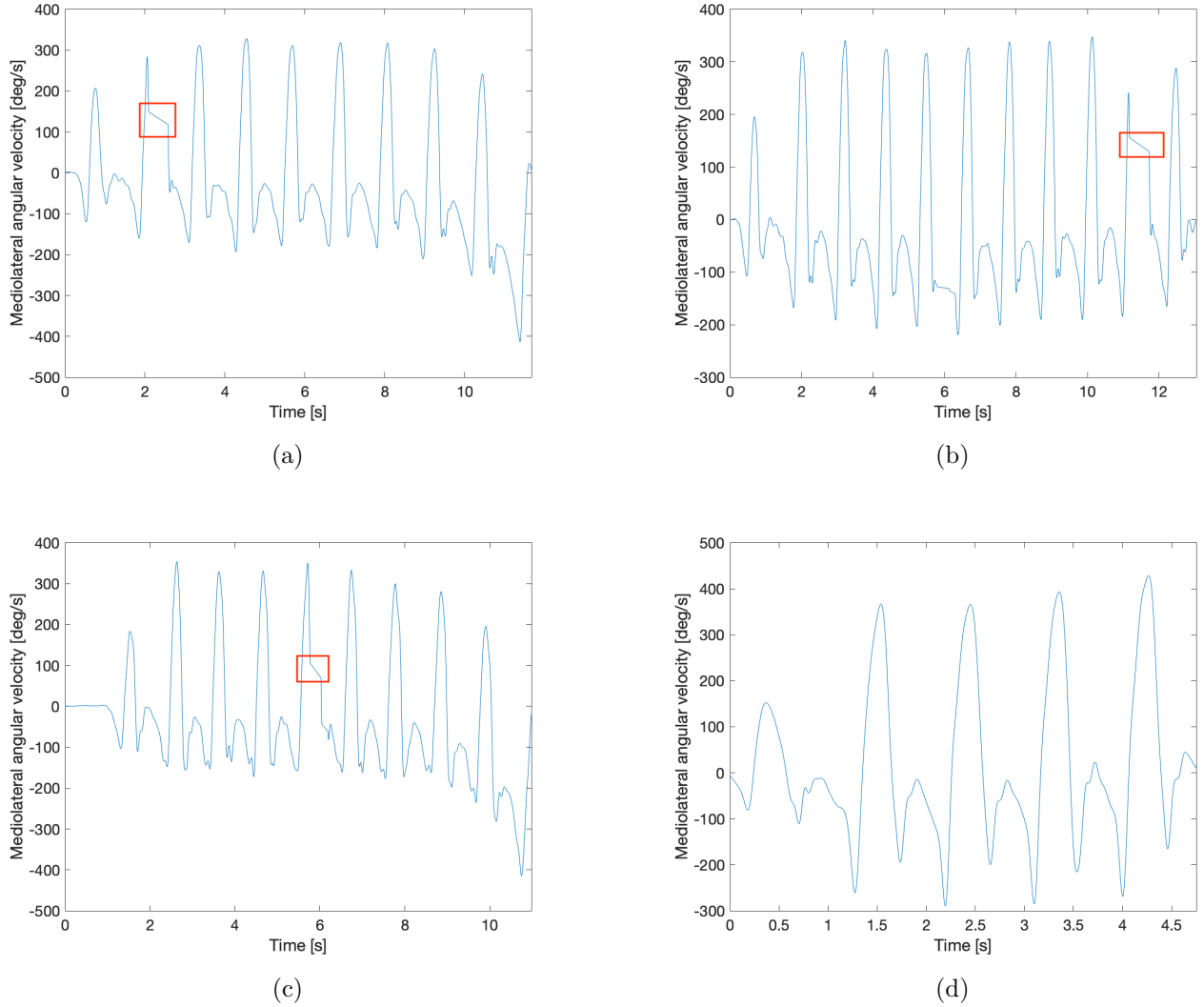


Figure 3.11: Examples of the four problems that occurred due to the gaps during the data recording with both left and right IMUs. (a) Example of *Problem 1*. First trial of the *mats* condition for patient 3 and the IMU located at his left side. (b) Example of *Problem 2*. Second trial of the *mats* condition for patient 3 and the IMU located at his left side. (c) Example of *Problem 3*. Second trial of the *mats* condition for patient 6 and the IMU located at his right side. (d) Example of *Problem 4*. Second trial of the *doorway* condition for patient 2 and the IMU located at his right side.

These problems had different implications depending whether it happened during the recording of the

control and *mats* conditions or the *doorway* and *U-turn* conditions.

Control and mats conditions

Since the *control* and *mats* conditions did not have any change during the 10 meters long walk, *Problem 1* could be solved by only starting the identification of the gait events when a first complete stride had been identified (Figure 3.12a). *Problem 2* was solved in the same way, simply by stopping identifying gait events once no complete stride could be found (Figure 3.12b). Solving *Problem 3* was a little bit more complicated. If the missing gait event was a toe-off (mid-swing), then the mid-swing (toe-off) of the same stride needed to be deleted but the heel strikes were kept to end the preceding stride and start the following stride. If the missing gait event was a heel strike, then both the preceding and following toe-offs and mid-swings needed to be deleted, which meant that two strides were not detected instead of one (Figure 3.12c). When *Problem 4* occurred, there were less complete strides identified compared to the signal from the other leg but the trials were still kept.

Doorway and U-turn conditions

Problem 1 and *2* never occurred for either the *doorway* or the *U-turn* condition. When *Problem 3* occurred, the gap in data either happened at the moment of the punctual event or right before/after. It thus made it impossible to use the signal because the important data were not recorded (Figure 3.13a). When *Problem 4* occurred, as for *Problem 3*, either the stride of the punctual event or the strides before/after were not recorded (Figure 3.13b). These problems occurred for several trials and the decision was made not to consider them since they would not be relevant anymore.

The discarded trials are the following: trials 1, 2 and 3 of the *doorway* condition for the right shank of patient 2; trial 1 of the *U-turn* condition for the right shank of patient 2; trial 3 of the *mats* condition for the left shank of patient 3; trial 2 of the *U-turn* condition for the right shank of patient 4; trial 3 of the *doorway* condition for the right shank of patient 5.

3.5.3 Studied metrics

Various metrics were computed based on the identification on the gait events above. The stride, stance and swing times as well as the phasing are represented on Figure 3.14.

Stride time

The stride time is defined as the time elapsed between the first contact of two consecutive footsteps of the same foot [78]. The stride time was computed in seconds as follows:

$$\text{Stride Time}(i) \text{ [s]} = HS(i+1) \text{ [s]} - HS(i) \text{ [s]} \quad (3.2)$$

where *HS* means *heel strike*.

Problem 3 has been solved when computing the stride time by not taking into account the distance between the heel strikes before and after the gap because it is not part of the same stride.

Stance time

The stance time is defined as the time duration between the heel strike and the toe-off of the same stride for the same foot [79]. The stance time was computed in seconds as follows:

$$\text{Stance Time}(i) \text{ [s]} = TO(i) \text{ [s]} - HS(i) \text{ [s]} \quad (3.3)$$

where *HS* and *TO* respectively mean *heel strike* and *toe-off*.

Problem 3 has been solved when computing the stance time by not taking into account the heel strike right before the gap happens because it is not part of the same stride as the next TO.

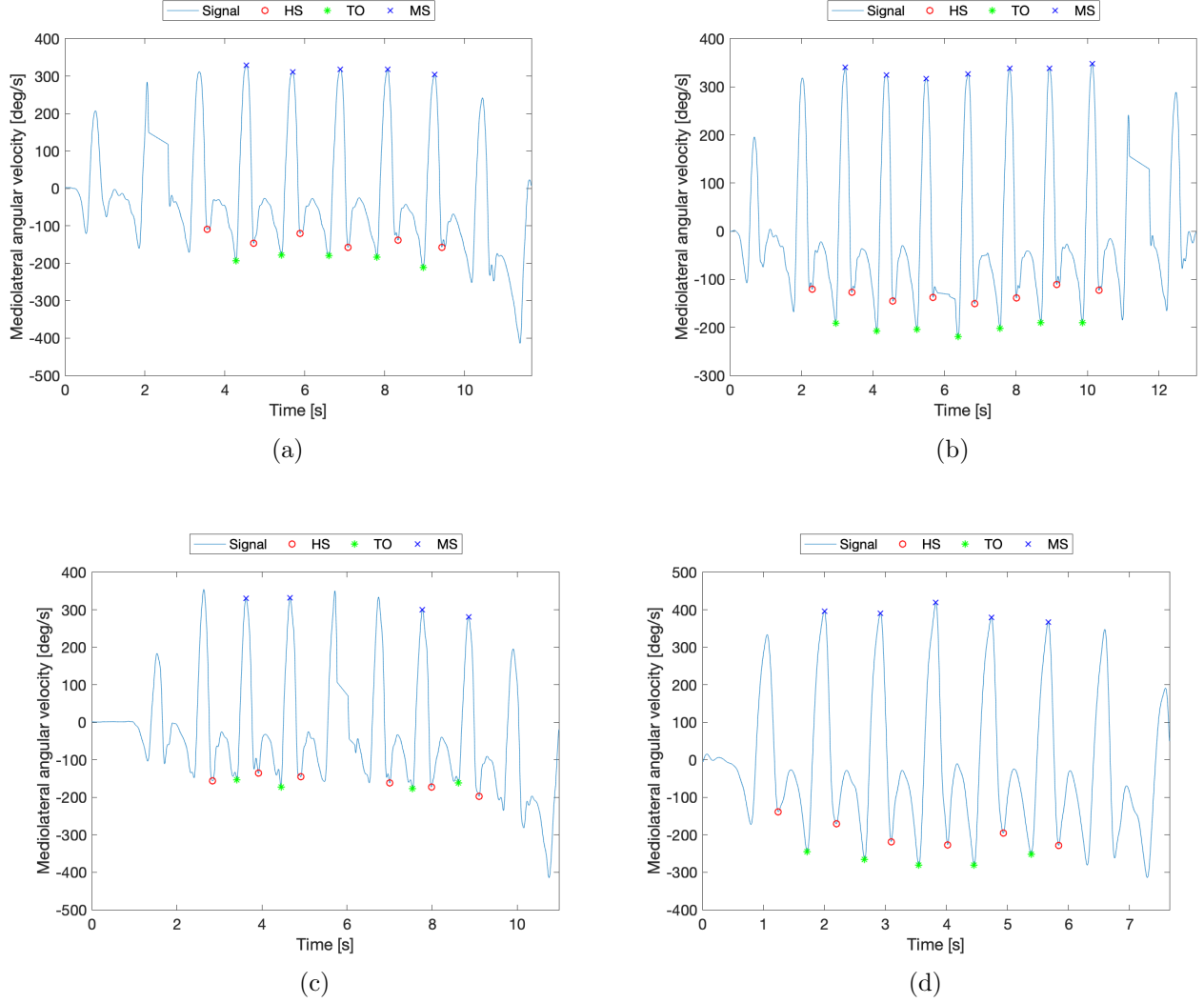


Figure 3.12: Examples of how the four problems that occurred due to the gaps during the data recording with both left and right IMUs were treated for the *control* and the *mats* conditions. (a) Example of how *Problem 1* was treated for the *control* and the *mats* conditions. First trial of the *mats* condition for patient 3 and the IMU located at his left side. (b) Example of how *Problem 2* was treated for the *control* and the *mats* conditions. Second trial of the *mats* condition for patient 3 and the IMU located at his left side. (c) Example of how *Problem 3* was treated for the *control* and the *mats* conditions. Second trial of the *mats* condition for patient 6 and the IMU located at his right side. (d) Example of how *Problem 4* was treated for the *control* and the *mats* conditions. Second trial of the *doorway* condition for patient 2 and the IMU located at his right side.

Swing time

The swing time is defined as the time duration between the toe-off of the current stride and the heel strike of the next stride for the same foot [79]. The swing time was computed in seconds as follows:

$$\text{Swing Time}(i) \text{ [s]} = HS(i+1) \text{ [s]} - TO(i) \text{ [s]} \quad (3.4)$$

where *HS* and *TO* respectively mean *heel strike* and *toe-off*.

Problem 3 has been solved when computing the swing time by not taking into account the heel strike right after the gap happens because it is part of the same stride as the next TO and not of the next stride.

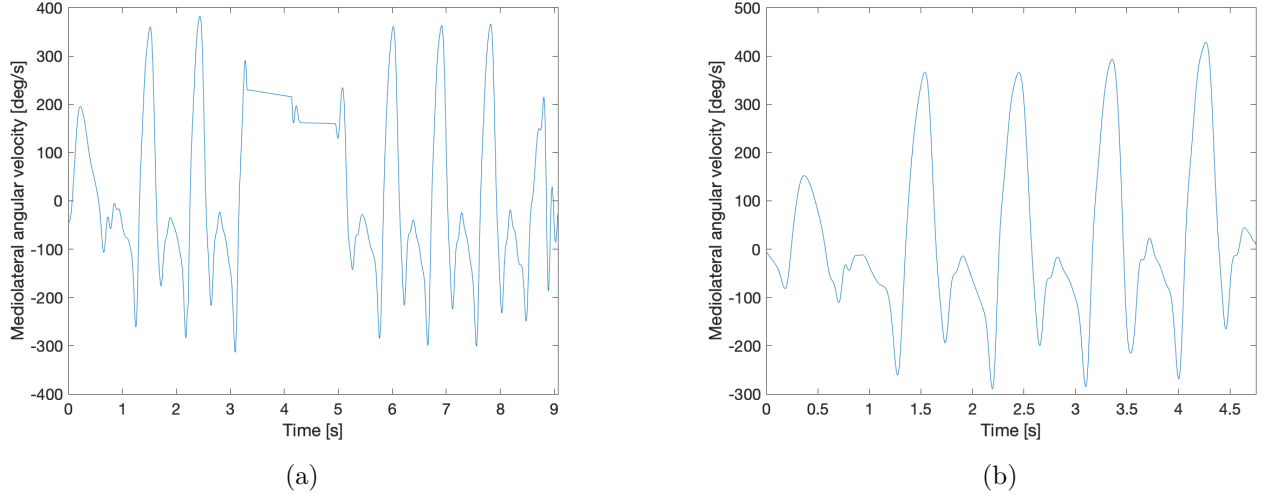


Figure 3.13: Examples of how the problems that occurred due to the gaps during the data recording with both left and right IMUs were treated for the *doorway* and the *U-turn* conditions. (a) Example of how *Problem 3* was treated for the *doorway* and the *U-turn* conditions. First trial of the *U-turn* condition for patient 2 and the IMU located at his right side. (b) Example of how *Problem 4* was treated for the *doorway* and the *U-turn* conditions. Second trial of the *doorway* condition for patient 2 and the IMU located at his right side.

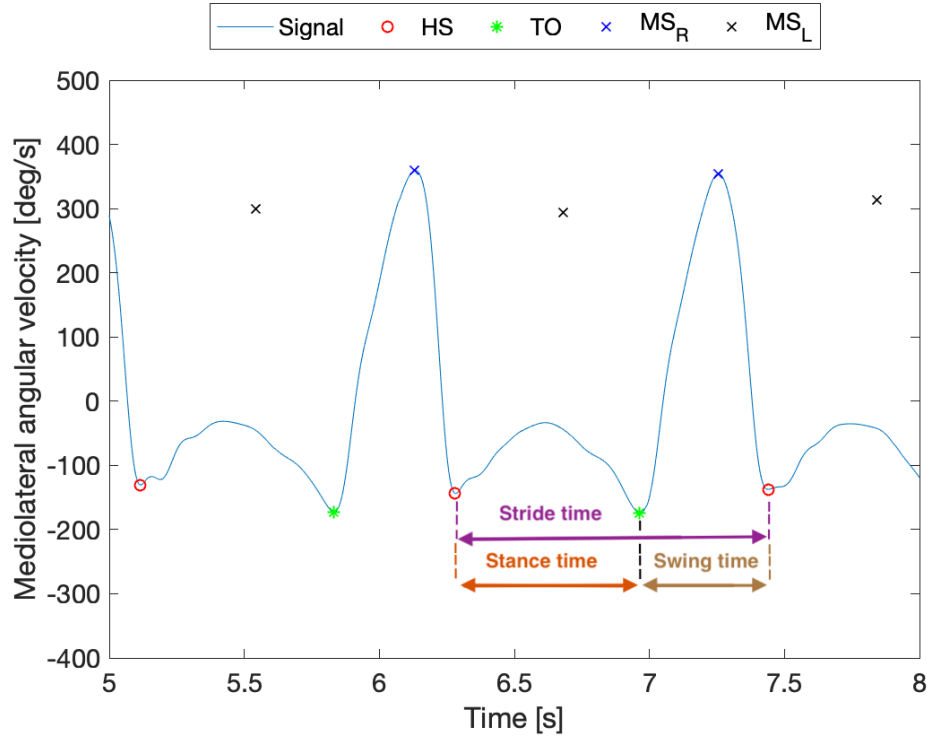


Figure 3.14: Representation of the stride time, stance time and swing time on the signal of the mediolateral angular velocity from the gyroscope. Zoom from the first trial of the *doorway* condition for patient 3 and the IMU located at his right shank.

Phasing

The phasing looks at the behavior of a leg compared to the other. The mid-swings of both legs were taken as comparison points. The phasing was computed as follows:

$$\text{Phasing}_{\text{Left}}(i) = \frac{MS_R(i) \text{ [s]} - MS_L(i) \text{ [s]}}{MS_L(i+1) \text{ [s]} - MS_L(i) \text{ [s]}} \quad (3.5)$$

$$\text{Phasing}_{\text{Right}}(i) = \frac{MS_L(i) \text{ [s]} - MS_R(i) \text{ [s]}}{MS_R(i+1) \text{ [s]} - MS_R(i) \text{ [s]}} \quad (3.6)$$

where MS_L and MS_R respectively mean *mid-swing of the left leg* and *mid-swing of the right leg*.

Take the right leg as reference for example, the first mid-swing from the left leg should take place halfway between the first and the second mid-swing of the right leg.

Signals that contained one of the four problems mentioned above (section 3.5.2) have been discarded since they could not properly be used together with the signal from the other IMU to look at the phasing between the legs.

Velocity

The velocity is the walking speed of the subject during each trial and has been normalized with the lengths of the patients' legs. The velocity has not been computed in real-time but has been taken as the average velocity over the whole trial. It was computed as follows:

$$\text{Velocity [L/s]} = \frac{\text{Total distance [m]}}{\text{Total time of acquisition [s]} \cdot \text{Leg length [m]}} \quad (3.7)$$

where Total time of acquisition is the duration of the recording.

Signals that contained *Problem 4* (section 3.5.2) have been treated separately so that the time of acquisition would be accurate even when there is a gap in the data.

Cadence

The cadence is the walking rate of the subject during each trial. The cadence has not been computed in real-time but has been taken as the average cadence over the whole trial. It was computed for both legs as follows:

$$\text{Cadence [steps/s]} = \frac{\text{Number of steps identified [steps]}}{\text{Time of acquisition [s]}} \quad (3.8)$$

where Time of acquisition [s] = $HS(end) \text{ [s]} - HS(1) \text{ [s]}$ to avoid the complications arising from *Problem 1* and *2*.

Signals that contained *Problem 3* (section 3.5.2) were treated separately to have an accurate time of acquisition even when a gap in the data recording occurred.

Step length

The step length is the distance between the heel strike of one foot and the heel strike of the opposite foot of the subject during each trial. In normal gait, right and left step lengths are similar. It was computed for both legs as follows:

$$\text{Step length [L/steps]} = \frac{\text{Velocity [L/s]}}{\text{Cadence [steps/s]}} \quad (3.9)$$

3.6 Data analysis

Two types of analysis were made: a statistical analysis for the *control* and *mats* conditions and a visual analysis for the *doorway* and *U-turn* conditions. The data from the healthy patients have not been used to compare their metrics to the ones of the patients with PD since only two of them participated to the experiments. This would not have been relevant due to the small number of healthy participants.

3.6.1 Statistical analysis

The statistical analysis was performed on *R Studio* (version 4.2.0) [80]. The statistical tools used here are a paired samples t-test and two-way repeated measures (RM) ANOVA since each subject was measured multiple times (environmental conditions) on the same variables (metrics). The repeated measures ANOVA will detect any overall differences between related means and will be used as a two-way ANOVA. a two-way RM ANOVA compares the mean differences between groups that have been split on two within-subjects factors. The two within-subjects factors are the environmental conditions (*control* and *mats* conditions) and the most or least affected side of the patient by PD. A certain number of assumptions need to be verified before using the two-way RM ANOVA. It has been done in Appendix A [81].

When the two-way RM ANOVA gives significant differences between the means of either factor or for the interaction between them, a pairwise t-test is applied on subsets of the data to learn between which conditions precisely the means are significantly different [82]. For example, if the environmental conditions are significant, the data are divided by the most and least affected side and t-tests are done on both subsets to see whether or not the environmental conditions are significantly different for each side. The pairwise t-test will also be applied on the mean velocity of the patient since it cannot be separated between the right or left side and there are thus only one factor (the environmental conditions) with two paired groups. The tested assumptions for it can be found in Appendix B [83].

For all statistical tests performed, the null hypothesis was rejected only when the p-value was lower than the significant threshold $\alpha = 0.05$.

Two-way repeated measures ANOVA

It allows to determine the effects of two factors and of their interaction on the variables. The variables are the metrics while the factors are the environmental conditions (*control* or *mats*) and the most affected side by PD. Since a two-way ANOVA considers the effects of two factors as well as the effect of the factors on each other, there are three pairs of null or alternative hypotheses [84]:

$$\begin{cases} H_{0a} : & \mu_{a,1} = \mu_{a,2} \\ H_{1a} : & \mu_{a,1} \neq \mu_{a,2} \end{cases} \quad (3.10)$$

with $\mu_{a,1}$ and $\mu_{a,2}$ the means of the factor corresponding to the most/least affected side.

$$\begin{cases} H_{0b} : & \mu_{b,1} = \mu_{b,2} \\ H_{1b} : & \mu_{b,1} \neq \mu_{b,2} \end{cases} \quad (3.11)$$

with $\mu_{b,1}$ and $\mu_{b,2}$ the means of the factor corresponding to the *control/mats* condition.

$$\begin{cases} H_{0c} : & \text{there is no interaction between both factors} \\ H_{1c} : & \text{there is an interaction between both factors} \end{cases} \quad (3.12)$$

This analysis is applied on the metrics computed as explained above in section 3.5.3. It was applied on three different subsets: all patients, freezers and non-freezers.

Pairwise t-test

A pairwise t-test is a statistical t-test performed on each pair of experimental conditions and used to determine if two paired groups are significantly different from each other with respect to the variable of interest. There is one pair of null hypotheses [85]:

$$\begin{cases} H_0 : & \mu_1 - \mu_2 = 0 \\ H_1 : & \mu_1 - \mu_2 \neq 0 \end{cases} \quad (3.13)$$

with μ_1 and μ_2 the means of the two conditions being compared.

A Bonferroni correction was applied during the pairwise t-tests to decrease the probability that errors of Type 1, which happens when a true null hypothesis is rejected, occur. The correction will adjust the significance level to reduce the probability of committing a Type 1 error [86].

3.6.2 Visual analysis

The *doorway* and *U-turn* conditions are transitional data since a punctual event happens once for each trial during the data recording. They will therefore be analyzed visually. Each metric is computed for every subject and then the means between all subjects are taken. The punctual event, i.e., going through the doorway or making a U-turn, is considered as position 0 while the time stride just before and after the event are respectively position -1 and 1. The data have been divided between the most and the least affected side while the metrics have been divided in three subgroups: all subjects, freezers and non-freezers.

As mentioned above, the data for the most affected side of one of the patient (one of the three freezer) during the *doorway condition* have been removed. When analyzing the behavior of the metrics for the freezers, for example, there will thus only be 2 sets of data instead of three for the most affected side's stride, stance and swing time. For the phasing, there will only be two sets of data for each side.

Chapter 4

Results

This chapter presents the results of the tests explained in section 3.6. The first part of the chapter analyzes the results of statistical tests performed on the metrics for the control and mats conditions. The second part is a visual analysis that looks at the metrics for the doorway and U-turn conditions.

4.1 Statistical analysis

The results of the ANOVAs can be found in Tables C1, C2 and C3 in Appendix C.

4.1.1 All subjects

Stride time - mean

The two-way repeated measures ANOVA revealed that the p-values for the effects of the environmental conditions, the most/least affected side and the interaction of both factors are respectively: 0.0053, 0.29 and 0.009. The null hypothesis can therefore not be rejected for the effects of the most/least affected side. Both the environmental conditions as well as the interaction of both factors have a significant effect on the stride time. The differences in means between sides for both conditions can be seen on Figure 4.1.

A pairwise t-test with Bonferroni correction is completed to determine if, for each side, the environmental conditions are significantly different or not (Table D1 in Appendix D). This is the case since the p-values for the most and the least affected side are respectively 0.0021 and 0.014. The participants' mean stride times were slightly smaller during the *control* condition than during the *mats* condition for the most (means of 1.049 for the *control* condition vs 1.1 for the *mats* condition) and least affected side (means of 1.058 for the *control* condition vs 1.098 for the *mats* condition).

Stance time - mean

The two-way repeated measures ANOVA revealed that both the environmental conditions (p-value = 0.037) and the affected sides (p-value = 0.037) have a significant effect on the participants' stance time. In contrast, the null hypothesis cannot be rejected for the interaction of both factors since its p-value is equal to 0.31. The differences in means between sides for both conditions and between conditions for both sides can be seen on Figure 4.2.

A first pairwise t-test with Bonferroni correction was completed to determine if, for each side, the environmental conditions are significantly different (Table D1 in Appendix D). This is only the case for the most affected side since its p-value is 0.039. On the other hand, the p-value for the least affected side is 0.052 and thus above the significant threshold. Moreover, another pairwise t-test with the same correction was realised to determine if, for each environmental condition, the most/least affected side are significantly different (Table D2 in Appendix D). This is not the case since the p-values for the *control* and *mats* conditions are respectively 0.66 and 0.86. It can be seen on Figure 4.2 that for both conditions,

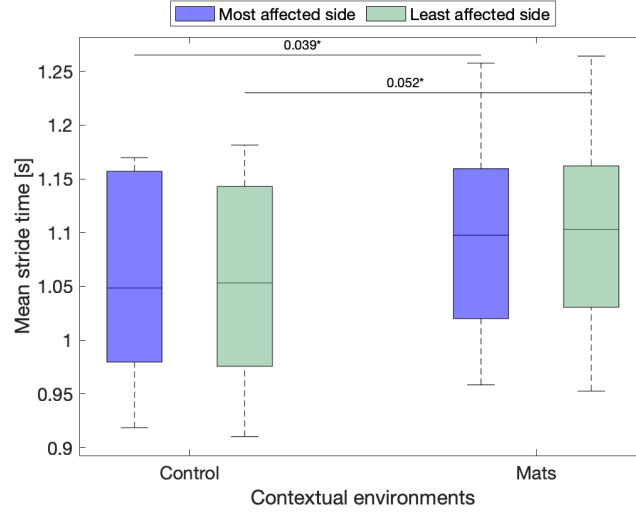


Figure 4.1: Comparison of the stride times [s] for both sides and both environmental conditions (*control* and *mats*) for all subjects.

the means of each side (respectively most affected vs least affected) are relatively similar: 0.55 vs 0.57 for the *control* and 0.61 vs 0.62 for the *mats* condition.

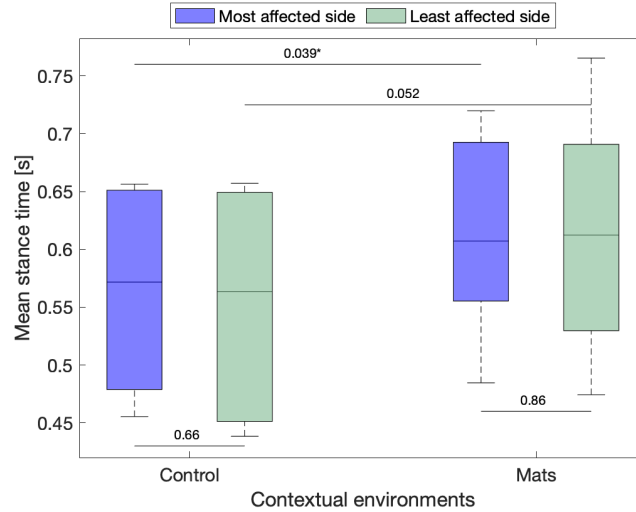


Figure 4.2: Comparison of the stance times [s] for both sides and both environmental conditions (*control* and *mats*) for all subjects.

Swing time - mean

For the swing time, the two-way repeated measures ANOVA showed that the affected side has a significant effect on it since its p-value is 0.03. The null hypothesis can however not be rejected for the environmental conditions' effect and the interaction between both factors because their p-values are equal to 0.714 and 0.699 respectively. The differences in means between sides for both conditions can be seen on Figure 4.3.

A pairwise t-test with a Bonferroni correction was thus realised to determine if, for each environmental

condition, the most/least affected side were significantly different (Table D2 in Appendix D). This is not the case since the p-values for the *control* and *mats* conditions are respectively 0.43 and 0.36.

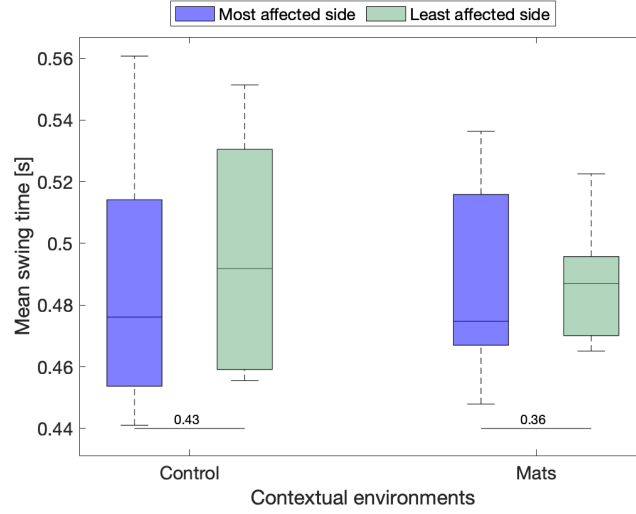


Figure 4.3: Comparison of the swing times [s] for both sides and both environmental conditions (*control* and *mats*) for all subjects.

Phasing - coefficient of variation

The two-way repeated measures ANOVA revealed that only the environmental conditions have a significant effect on the variability of the phasing since it gives a p-value equal to 0.023. Both the effects of the affected side and the interaction of the factors have respective p-values equal to 0.966 and 0.967. The null hypothesis can therefore not be rejected for them. The differences in means between sides for both conditions can be seen on Figure 4.4.

A pairwise t-test with Bonferroni correction was completed to determine if, for each side, the environmental conditions are significantly different (Table D1 in Appendix D). This is not the case since the p-values for the most and the least affected side are respectively 0.12 and 0.084.

Cadence - mean

The two-way repeated measures ANOVA showed that the p-value for the effect of the most/least affected side is 0.278, which means that its effect on the cadence is not significant. On the other hand, both the environmental conditions and the interaction between factors had a significant effect since their p-values are 0.002 and 0.006 respectively. The differences in means between sides for both conditions can be seen on Figure 4.5.

A pairwise t-test with Bonferroni correction was completed to determine if, for each side, the environmental conditions are significantly different (Table D1 in Appendix D). This was the case since the p-values for the most and the least affected side were respectively 0.00074 and 0.0061. The participants' mean cadences were higher during the *control* condition than during the *mats* condition for the most (means of 0.962 for the *control* condition vs 0.915 for the *mats* condition) and least affected side (means of 0.954 for the *control* condition vs 0.919 for the *mats* condition).

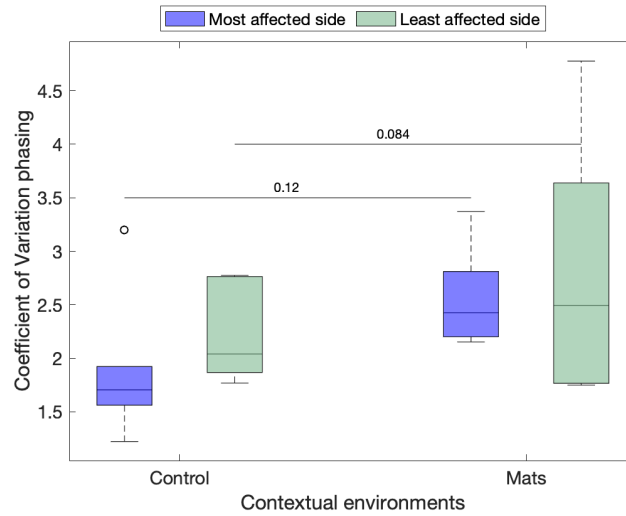


Figure 4.4: Comparison of the phasing for both sides and both environmental conditions (*control* and *mats*) for all subjects.

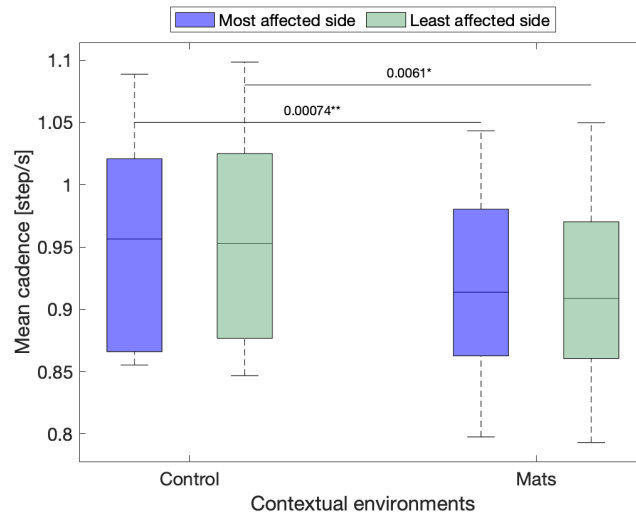


Figure 4.5: Comparison of the cadence [steps/s] for both sides and both environmental conditions (*control* and *mats*) for all subjects.

Velocity - mean

A pairwise t-test was applied to the velocity of the participants to see if there was any significant difference between their velocity during the *control* condition and during the *mats* condition. This was the case since the p-value is equal to 0.026 (see Table D5 in Appendix D). Participants were slightly faster when they walked during the *control* condition (1.09 L/s) compared to when they walked in the *mats* condition (1.04 L/s) which can also be seen on Figure 4.6.

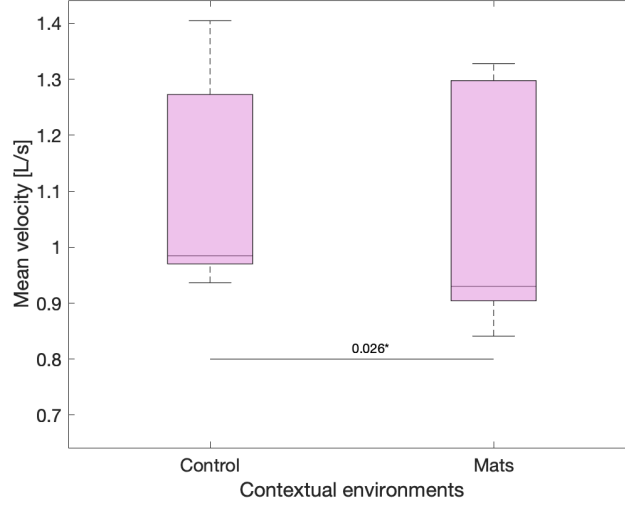


Figure 4.6: Comparison of the velocity [L/s] for both sides and both environmental conditions (*control* and *mats*) for all subjects.

4.1.2 Freezers

Phasing - mean

The two-way repeated measures ANOVA revealed that, for freezers, only the environmental conditions have a significant effect on the phasing since it gives a p-value equal to 0.003. Both the effects of the affected side and the interaction of the factors have respective p-values equal to 0.601 and 0.812, which is why the null hypothesis cannot be rejected for them. The differences in means between sides for both conditions can be seen on Figure 4.7.

A pairwise t-test with Bonferroni correction was done to determine if, for each side, the environmental conditions are significantly different (Table D3 in Appendix D). This is not the case since the p-values for the most and the least affected side are respectively 0.95 and 0.69. The participants' mean phasing were relatively similar during the *control* condition than during the *mats* condition for the most (means of 0.496 for the *control* condition vs 0.495 for the *mats* condition) and least affected side (means of 0.501 for the *control* condition vs 0.505 for the *mats* condition).

4.1.3 Non-freezers

Stride time - mean

The two-way repeated measures ANOVA showed that the p-value for the effect of the most/least affected side is 0.664, which means that its effect on the stride time is not significant. On the other hand, both the environmental conditions and the interaction between factors had a significant effect since their p-values are 0.00059 and 0.0087 respectively. The differences in means between sides for both conditions can be seen on Figure 4.8.

A pairwise t-test with Bonferroni correction is completed to determine if, for each side, the environmental conditions are significantly different (Table D4 in Appendix D). This is the case since the p-values for the most and the least affected side are respectively 0.00081 and 0.00084. The participants' mean stride times were slightly smaller during the *control* condition than during the *mats* condition for the most (means of 1.02 for the *control* condition vs 1.08 for the *mats* condition) and least affected side (means of

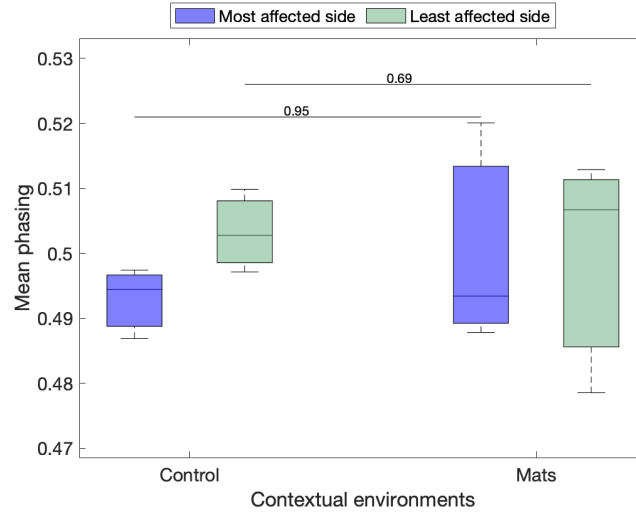


Figure 4.7: Comparison of the phasing for both sides and both environmental conditions (*control* and *mats*) for freezers.

1.03 for the *control* condition vs 1.07 for the *mats* condition).

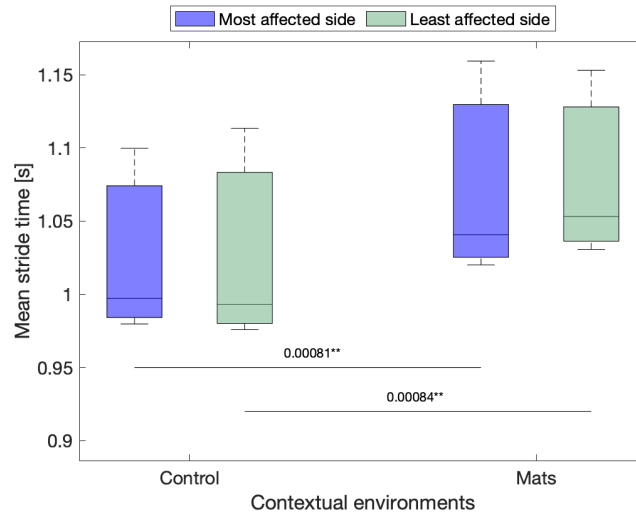


Figure 4.8: Comparison of the stride times [s] for both sides and both environmental conditions (*control* and *mats*) for non-freezers.

Cadence - mean

The two-way repeated measures ANOVA revealed that the p-values for the effects of the environmental conditions, the most/least affected side and the interaction of both factors are respectively: 0.0049, 0.693 and 0.0019. The null hypothesis can therefore not be rejected for the effects of the most/least affected side. On the other hand, both the environmental conditions as well as the interaction of both factors have a significant effect on the cadence. The differences in means between sides for both conditions can be seen on Figure 4.9.

A pairwise t-test with Bonferroni correction is completed to determine if, for each side, the environmental conditions are significantly different (Table D4 in Appendix D). This is the case since the p-values for the most and the least affected side are respectively 0.003 and 0.0082. The non-freezers' mean cadences were slightly higher during the *control* condition than during the *mats* condition for the most (means of 0.981 for the *control* condition vs 0.928 for the *mats* condition) and least affected side (means of 0.974 for the *control* condition vs 0.936 for the *mats* condition).

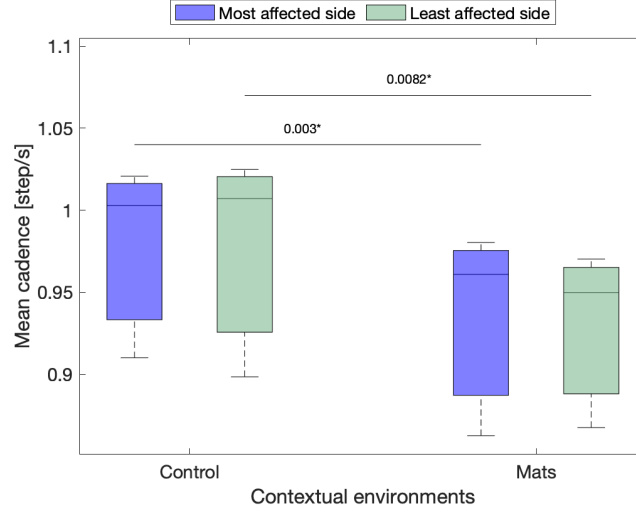


Figure 4.9: Comparison of the cadence [steps/s] for both sides and both environmental conditions (*control* and *mats*) for non-freezers.

Velocity - mean

A pairwise t-test was applied to the velocity of the participants without freezing of gait to see if there was any significant difference between their velocity during the *control* condition and during the *mats* condition. This was the case since the p-value is equal to 0.021 (see Table D5 in Appendix D). Participants were slightly faster when they walked during the *control* condition (1.12 L/s) compared to when they walked in the *mats* condition (1.06 L/s) which can also be seen on Figure 4.10.

Step length - mean

The two-way repeated measures ANOVA revealed that, for non-freezers, only the environmental conditions have a significant effect on the step length since it gives a p-value equal to 0.011. Both the effects of the affected side and the interaction of the factors have respective p-values equal to 0.709 and 0.309, which is why the null hypothesis cannot be rejected for them. The differences in means between sides for both conditions can be seen on Figure 4.11.

A pairwise t-test with Bonferroni correction was done to determine if, for each side, the environmental conditions are significantly different (Table D4 in Appendix D). This is not the case for the most affected side since its p-value is equal to 0.19. However, the least affected side has a p-value equal to 0.031, which means that the environmental conditions have a significant effect. The participants' mean step length were slightly more similar during the *control* condition than during the *mats* condition for the most affected side (means of 1.14 for the *control* condition vs 1.13 for the *mats* condition) than for the least affected side (means of 1.15 for the *control* condition vs 1.13 for the *mats* condition).

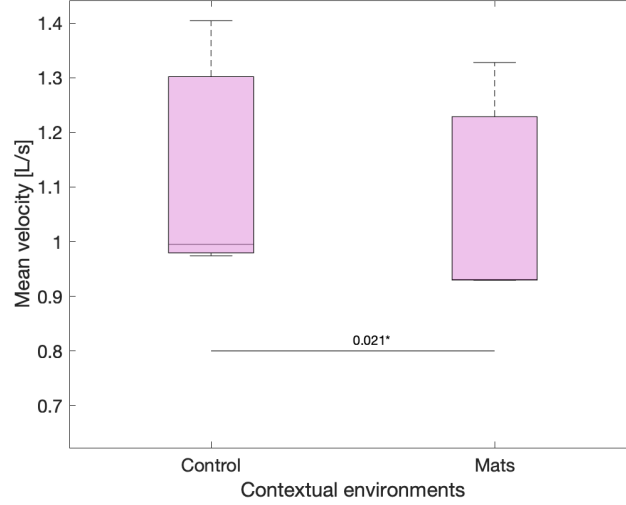


Figure 4.10: Comparison of the velocity [L/s] for both sides and both environmental conditions (*control* and *mats*) for non-freezers.

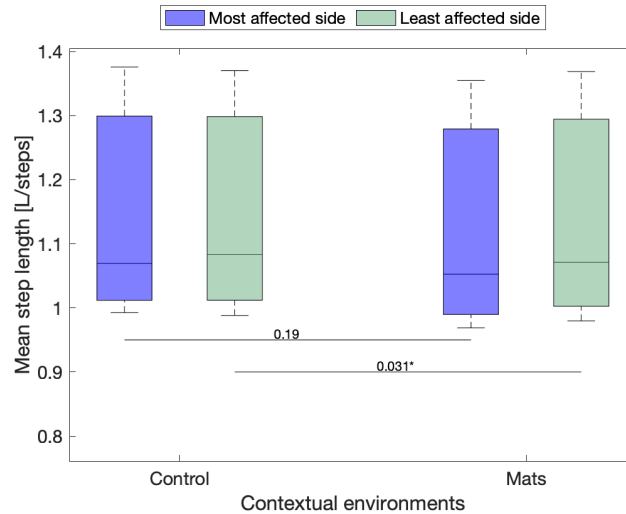


Figure 4.11: Comparison of the step length [L/steps] for both sides and both environmental conditions (*control* and *mats*) for non-freezers.

4.1.4 Comparison between freezers and non-freezers

The results of the comparison between the metrics for freezers and non-freezers are reported in Table 4.1. For each metric, the difference between freezers and non-freezers was calculated by subtracting the value of the metric for the non-freezers from the value of the metric for the freezers. First, it can be seen that freezers' stride, stance and swing times are longer for both the *control* and *mats* conditions. However, while the stance time increase more for the least affected side in both conditions, it was the opposite for swing time where the most affected side increase more compared to the least affected side. Second, freezers' phasing decrease in their most affected side but increase in their least affected side compared to non-freezers. Third, freezers' cadences, velocities and step lengths are smaller for both sides and during both environmental conditions compared to non-freezers. It can be seen that the step lengths decrease more for the most affected side than for the least affected side.

Table 4.1: Metrics' differences between freezers and non-freezers for *control* and *mats* conditions.

Metrics	<i>Control</i>		<i>Mats</i>	
	MA	LA	MA	LA
stride time [s]	0.051	0.056	0.043	0.054
stance time [s]	0.022	0.031	0.011	0.027
swing time [s]	0.029	0.025	0.032	0.027
phasing	-0.023	0.02	-0.026	0.027
cadence [steps/s]	-0.037	-0.04	-0.025	-0.035
velocity [L/s]	-0.065		-0.048	
step length [L/steps]	-0.024	-0.019	-0.019	-0.015

MA : Most Affected side; LA : Least Affected side;
Differences are computed as freezers - non-freezers

4.1.5 Summary

- All subjects:
 - *Control* and *mats* conditions have a significant effect on patients' stride time and cadence for both sides;
 - *Control* and *mats* conditions have a significant effect on patients' velocity;
 - *Control* and *mats* conditions have a significant effect on patients' stance time only for their most affected side.
- Freezers :
 - Neither the environmental conditions nor the most/least affected sides have significant effects on the metrics;
 - Compared to non-freezers, they have longer stride, stance and swing duration for both conditions and both sides;
 - Compared to non-freezers, they have a slower cadence and smaller step length for both conditions and sides;
 - Compared to non-freezers, they have a slower velocity for both conditions.
- Non-freezers :
 - *Control* and *mats* conditions have a significant effect on non-freezers' stride time and cadence for both sides;
 - *Control* and *mats* conditions have a significant effect on non-freezers' velocity;
 - *Control* and *mats* conditions have a significant effect on non-freezers' step length only for their least affected side.

4.2 Visual analysis

4.2.1 All subjects

Doorway condition

The most affected side's stride time (Figure 4.12a) follows the same trend for all patients: it increases at positions -1 and 0 before decreasing at position 1. For the least affected side, the stride time seems more variable. Most patients also increase their stride time at positions -1 and 0 and then decrease it at position 1. However, some of them either decrease it at position -1/0 or increase it at position 1.

The stance time (Figure 4.12b) on both sides follows the same trend for most of the patients: it increases at positions -1 and 0 before decreasing at position 1. However, some of them seem to either decrease their stance time at position -1 or increase it at position 1. Others also seem to decrease their stance time for their least affected side at position 0.

The swing time (Figure 4.12c) on both sides follows the same trend for most of the patients: it increases at positions -1 and 0 before decreasing at position 1. However, some of them seem to either decrease their swing time at positions -1 and 0 or increase it at position 1.

The phasing (Figure 4.12d) for the majority of the patients' most affected side decreases at position -1 and 1 and increases at position 0. However, the phasing of some of them seems to behave in the opposite way: it increases at position -1 and 1 and decreases at position 0. For their least affected side, most patients increase their phasing at positions -1 and 0 and decrease it at position 1. However, some of them seem to either decrease their phasing at position -1/0 or increase it at position 1. Figure 4.12d shows that the phasing at all three positions is out of sync, especially at positions -1 and 0 because both phasing are respectively below 0.5 and above 0.5. This tendency is less visible at position 1.

U-turn condition

The stride and stance time (Figure 4.13a-b) on both sides follow the same trend for most of the patients: they increase at positions -1 and 0 before decreasing at position 1. However, some of them seem to either slightly decrease their stride and stance time at position 0 or increase it at position 1.

The swing time (Figure 4.13c) on both sides follows the same trend for the majority of the patients: it increases at position -1 and stays constant at position 0. At position 1, it respectively increases or decreases for the most and least affected sides. However, this is not the case for all of them. Some patients, for example, decrease their swing time at position -1 or 1 for their most affected side. Others either increase or decrease it at position 0.

The phasing (Figure 4.13d) on the most affected side of the majority of the patients increases at positions -1 and 1 and decreases at position 0. However, the phasing of some of them behaves differently: it either decreases at position -1, increases at position 0 or decreases at position 1. For the least affected side, the phasing of most patients stays constant at position -1, increases at position 0 and then decreases at position 1. However, for some of them, it decreases or increases at position -1. For others, it decreases at position 0 instead of increasing or increases at position 1 instead of decreasing. Figure 4.13d shows that from position -1, the phasing is out of sync because both phasings are either below 0.5 (at position -1) or above 0.5 (starting from position 0).

Both the *doorway* and *U-turn* condition will be further investigated in sections 4.2.2 and 4.2.3.

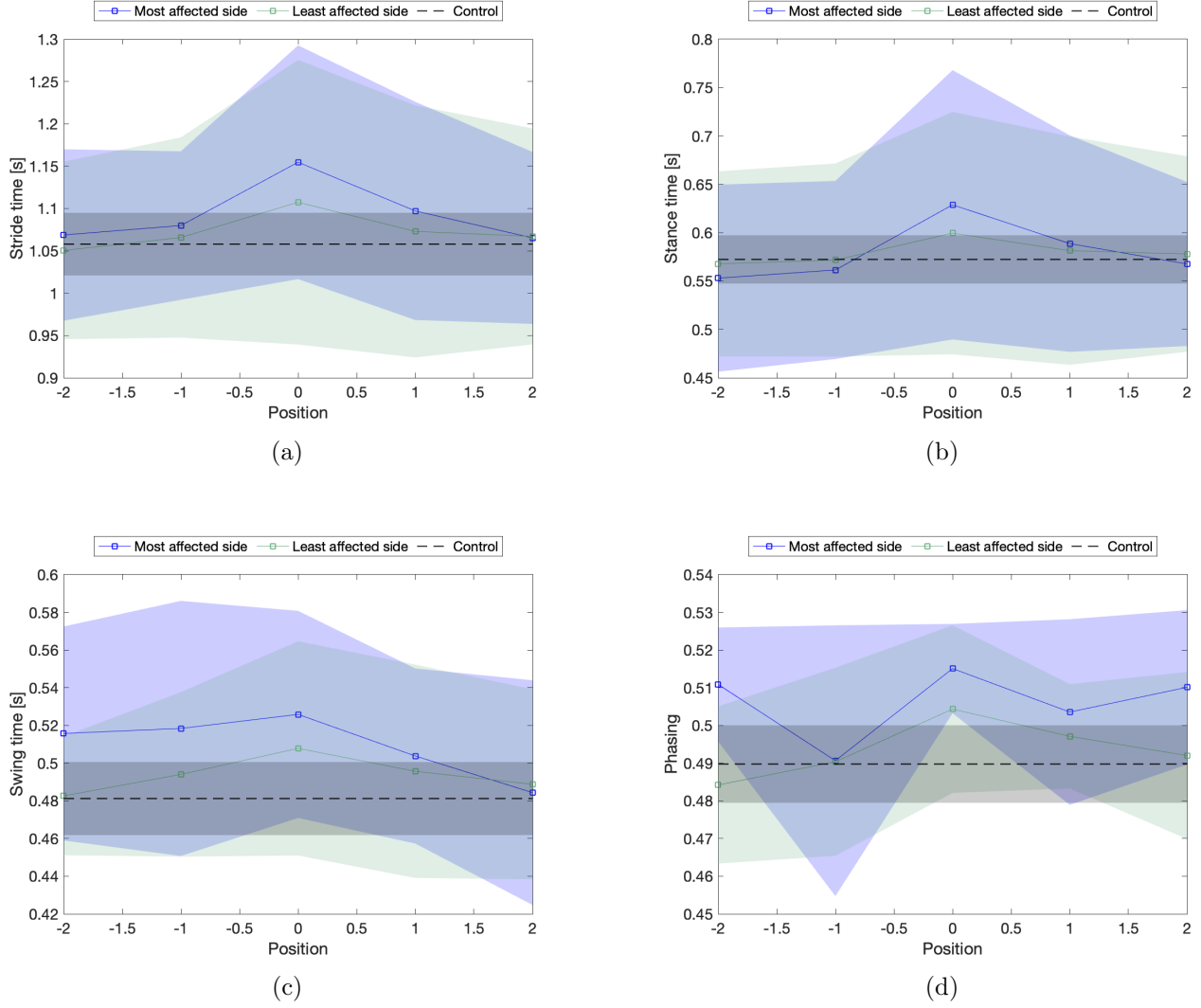


Figure 4.12: Metrics separated between most and least affected sides for all subjects during the *doorway* condition. The mean is represented by a line and the standard deviation is represented by the blue and green areas. (a) Stride time; (b) Stance time; (c) Swing time; (d) Phasing.

4.2.2 Freezers

Doorway condition

Two out of the three freezers have longer stride, stance and swing time for both sides compared to the control values. The last one has a shorter stride, stance and swing time for his least affected side while the data for his most affected side have been excluded from the analysis.

For the stride time (Figure 4.14a) of the most affected side, one freezer increases it while the other one decreases it at position -1. At position 0, both freezers increase their stride time. Afterwards, at position 1, the stride time of one of them decreases while the other one increases. For the least affected side, at position -1, two out of the three freezers increase their stride time while the last one decreases it. At position 0, all three freezers increase their stride time. Finally, at position 1, two freezers decrease their stride time while the last one increases it.

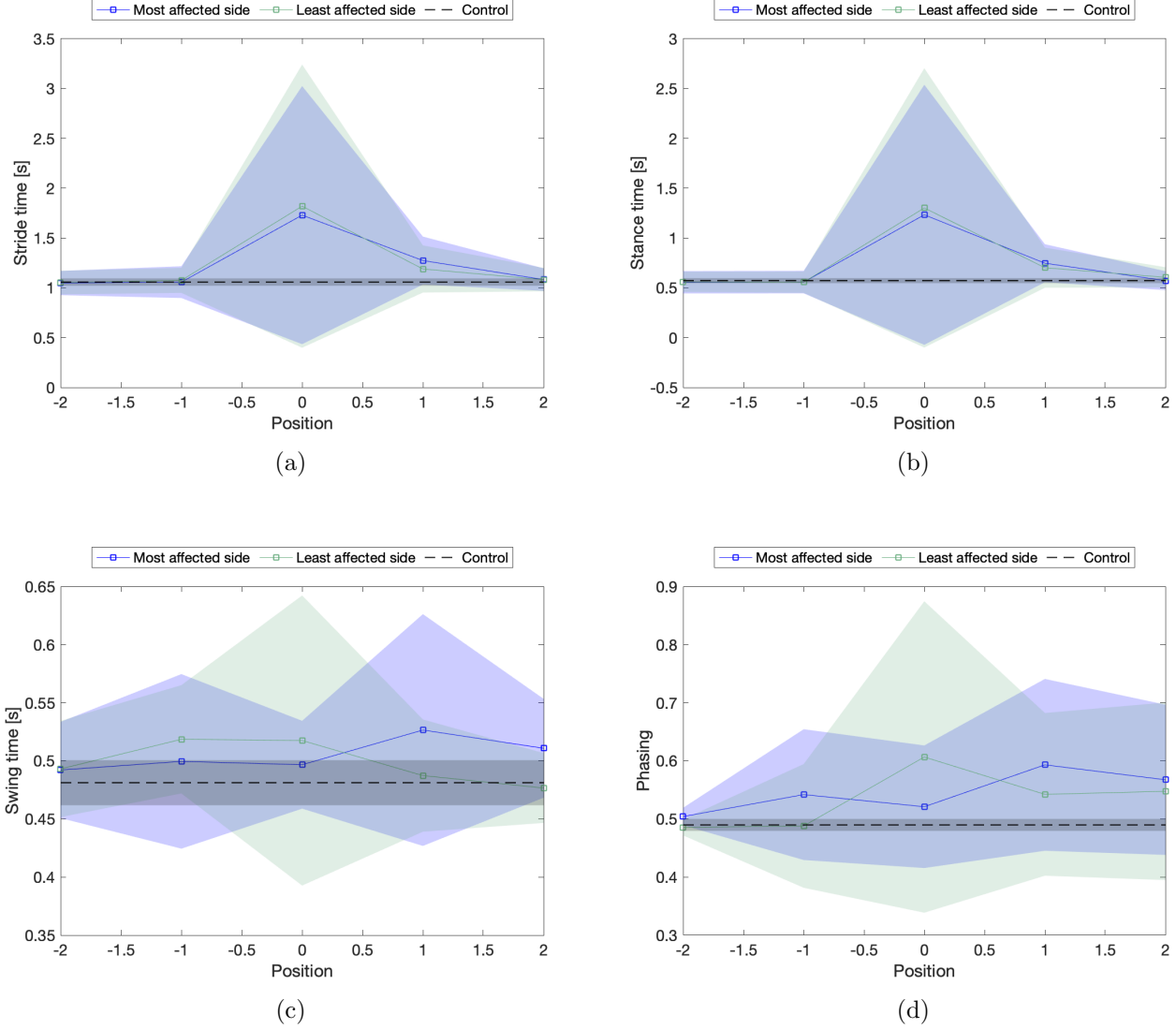


Figure 4.13: Metrics separated between most and least affected sides for all subjects during the *U-turn* condition. The mean is represented by a line and the standard deviation is represented by the blue and green areas. (a) Stride time; (b) Stance time; (c) Swing time; (d) Phasing.

For the stance time (Figure 4.14b) of the most affected side, one freezer decreases it while the other one increases it at position -1. At position 0, both of them increase their stance time. At position 1, one freezer continues to increase it while the other one decreases it. For the least affected side, out of the three freezers, two decrease their stance time at position -1 while the third one increases it. Afterwards, at position 0, two freezers increase their stance time and the last one keeps it constant. At position 1, two of them decrease it while the third one continues to increase it.

For the swing time (Figure 4.14c) of the most affected side, one freezer increases it while the second one decreases it at position -1. At position 0, both freezers decrease it. At position 1, one freezer increases its swing time while the other one decreases it. For the least affected side, at position -1, two freezers decrease their swing time while the third one increases it. All three freezers increase their swing time at position 0. Afterwards, at position 1, two of them decrease their swing time while the last one increases it.

For the phasing (Figure 4.14d) of the most affected side, both freezers have the same behavior: it decreases at position -1, increases at position 0 and decreases again at position 1. For the least affected side at position -1, both freezers increase their phasing. Afterwards, at position 0, one of them decreases it while the other one increases it. At position 1, both freezers decrease their phasing. Figure 4.14d shows that from position -1, the phasing varies greatly for the most affected side and is out of sync.

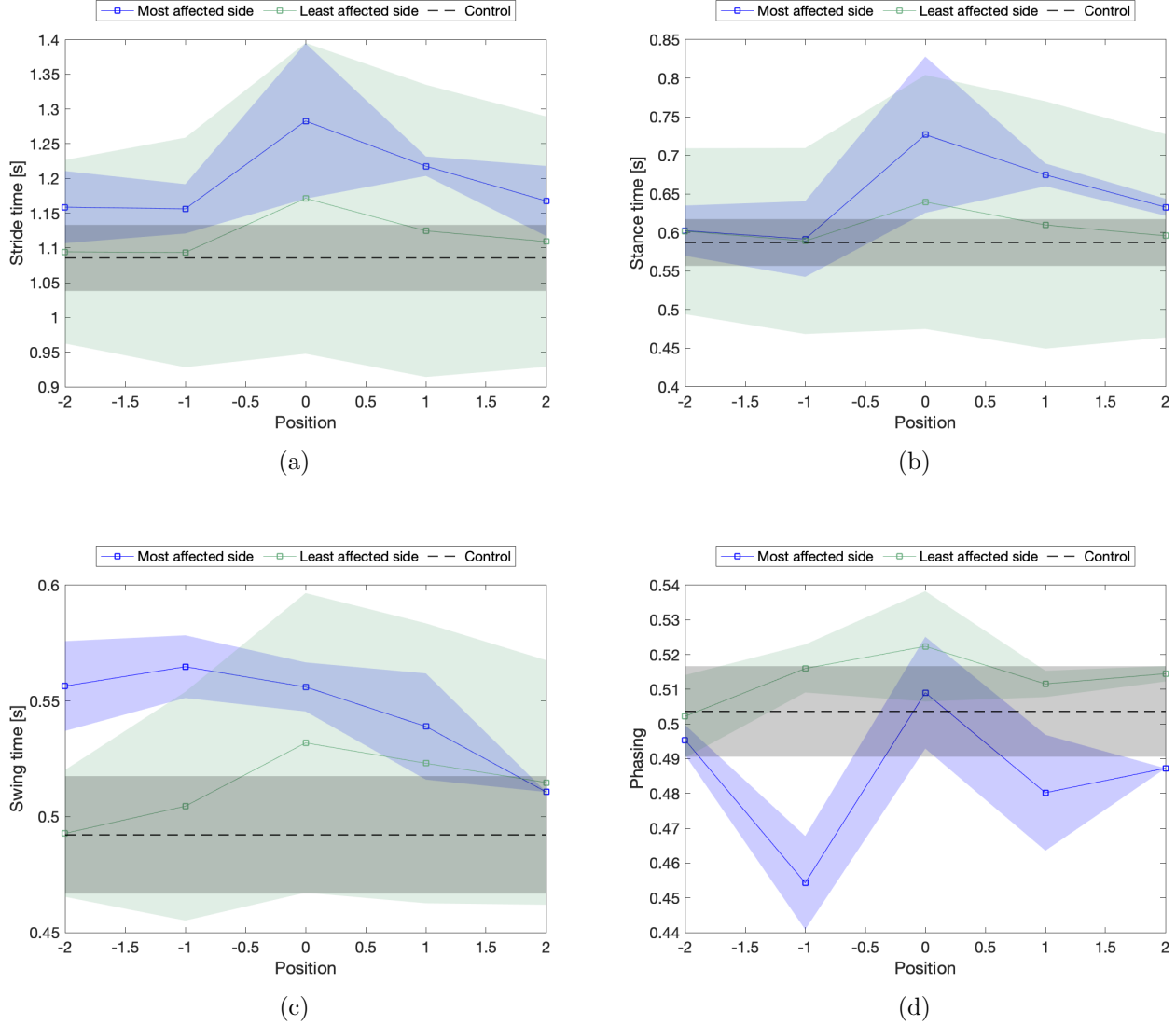


Figure 4.14: Metrics separated between most and least affected sides for freezers during the *doorway* condition. The mean is represented by a line and the standard deviation is represented by the blue and green areas. (a) Stride time; (b) Stance time; (c) Swing time; (d) Phasing.

***U-turn* condition**

Two out of the three freezers have longer stride, stance and swing time for both sides compared to the control values. In contrast, the third one has a shorter stride, stance and swing time for both sides.

The stride time (Figure 4.15a) for the most affected side of two freezers stays constant at position -1 while the last one shows a decrease in it. At position 0, two freezers have an increased stride time, one of which is particularly strong due to a freezing episode, while the last one has a decreased stride time.

At position 1, the two freezers who had an increase before now have a decrease in stride time while the third one has an increase in it. For the least affected side, the three freezers keep a constant stride time at position -1. At position 0, two of them have an increased stride time, one of which is particularly strong due to a freezing episode, while the last one has a decreased stride time. At position 1, there is an increase in stride time for two freezers while the last one has a decreased stride time.

For the most affected side, the stance time (Figure 4.15b) of all three freezers stays constant at position -1. At position 0, two freezers have an increased stance time, one of which is particularly strong due to a freezing episode, while the last one has a decreased stance time. At position 1, the two freezers who had an increase before now have a decreased stance time while the third one's stance time increases. For the least affected side, the three freezers keep a constant stance time at position -1. At position 0, two of them have an increased stance time, one of which is particularly strong due to a freezing episode, while the last one has a decreased stance time. At position 1, there is a decrease in stance time for two freezers while the last one has an increased stance time.

For the most affected side's swing time (Figure 4.15c), two freezers decrease it while the third one increases it at position -1. At position 0, two freezers decrease their swing time while the last one increases it. At position 1, the same freezers that had a decrease in swing time before now have an increase in it. The third freezer has a decrease in his swing time. For the least affected side, two out of the three freezers decrease their swing time at position -1 while the last one increases it. At position 0, all three of them decrease their swing time before increasing it back at position 1.

The most affected side's phasing (Figure 4.15d) respectively increases and decreases at positions -1 and 0 for all three freezers. At position 1, the phasing increases for two freezers while it decreases for the last one. For their least affected side, two freezers have an increase of phasing in position -1 while the third one has a decrease in it. At position 0, two freezers have an increased phasing, one of which is particularly strong, while the last one has a decreased phasing. At position 1, the phasing of two freezers decreases while the third one's phasing increases.

4.2.3 Non-freezers

Doorway condition

The stride and stance time are shorter than the control values for two non-freezers while longer for the third one. Another combination of two non-freezers has a shorter swing time than the control value while the other has a longer swing time.

The most affected side's stride time (Figure 4.16a) increases for all three non-freezers at positions -1 and 0 before decreasing at position 1. For the least affected side, all three non-freezers have an increased stride time at position -1. For only two of them does the stride time continue to increase at position 0 while it decreases for the third one. For the two non-freezers who had an increased stride time at position 0, the stride time decreases at position 1. For the third non-freezer, it increases.

The most affected side's stance time (Figure 4.16b) increases for all three non-freezers at positions -1 and 0. At position 1, it decreases for two of them and increases for the third one. For the least affected side, the stance time increases for all three non-freezers at position -1. At position 0, it decreases for one of them, increases for the second one and stays constant for the third one. Afterwards, at position 1, the stance time decreases for two non-freezers and increases for the last one.

The most affected side's swing time (Figure 4.16c) decreases at position -1 for two of the non-freezers and increases for the last one. At position 0 the swing time increases for two out of the three participants

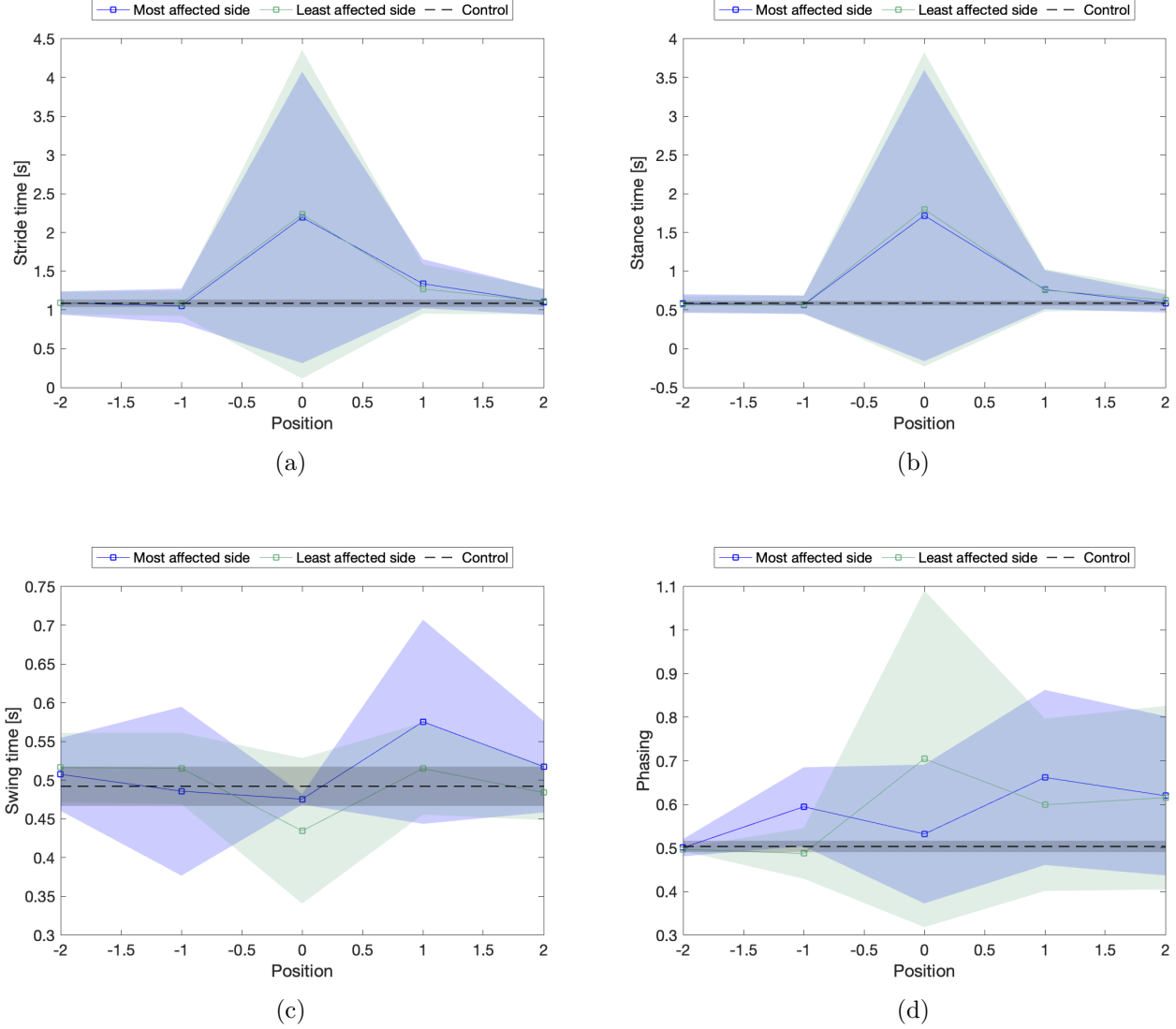


Figure 4.15: Metrics separated between most and least affected sides for freezers during the *U-turn* condition. The mean is represented by a line and the standard deviation is represented by the blue and green areas. (a) Stride time; (b) Stance time; (c) Swing time; (d) Phasing.

and decreases for the third one. Finally, at position 1, two non-freezers have a decrease in swing time while the other one has an increase in it. For the least affected side, the swing time increases at position -1 for all three non-freezers. At position 0, it then decreases for two of them and increases for the last one. Afterwards, at position 1, the swing time decreases for two of the non-freezers and increase for a third one.

The most affected side's phasing (Figure 4.16d) decreases at position -1 for two of the non-freezers and increases for a third one. The phasing then decreases for one of the non-freezer and increases for the two others at position 0. At position 1, it increases for two out of the three non-freezers and decreases for the other one. For the least affected side, out of the three non-freezers' phasing at position -1, one decreases, one increases and one stays constant. At position 0, for all three non-freezers, the phasing increases. It then continues to increase at position 1 for two of them and decreases for the last one.

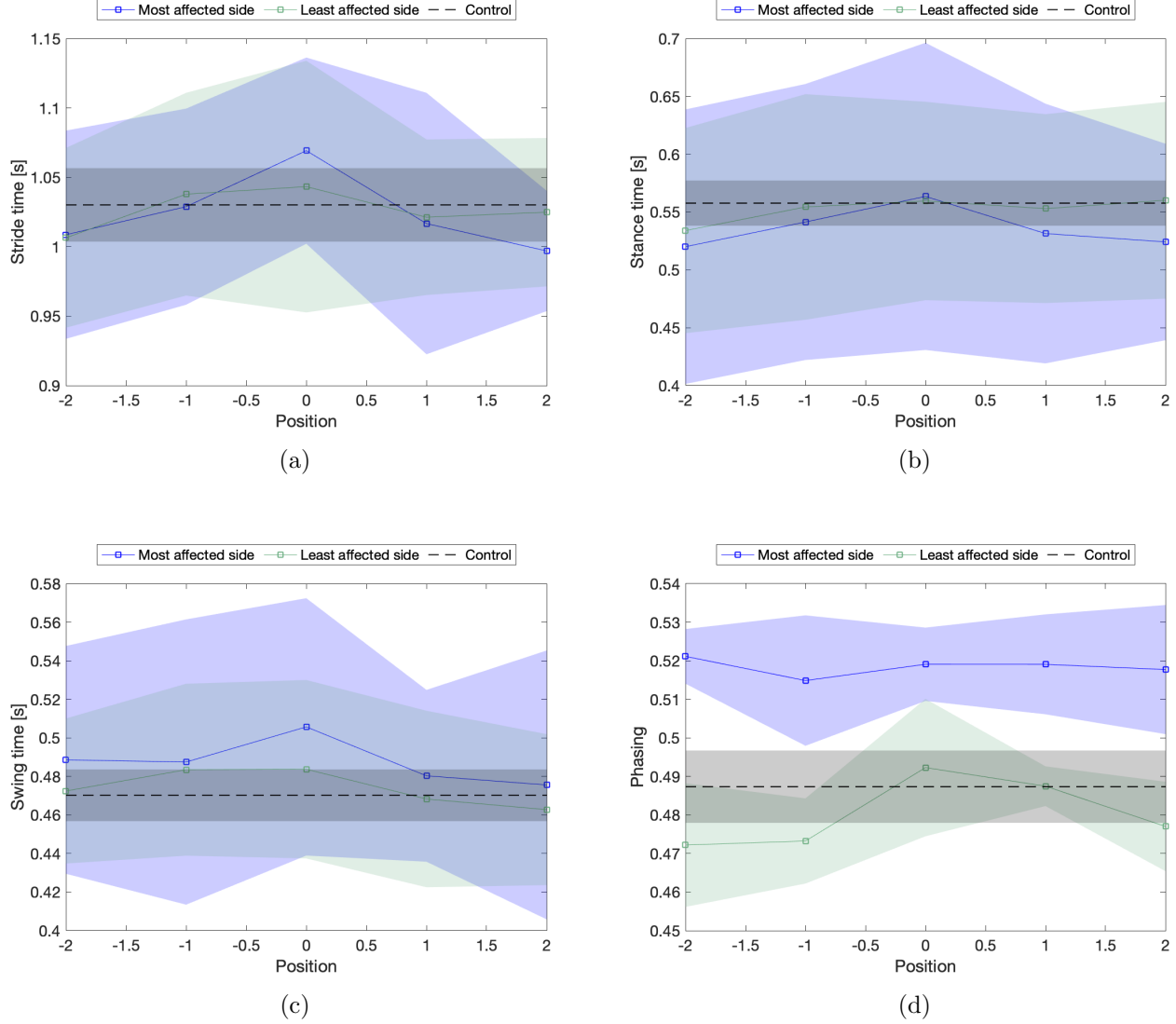


Figure 4.16: Metrics separated between most and least affected sides for non-freezers during the *doorway* condition. The mean is represented by a line and the standard deviation is represented by the blue and green areas. (a) Stride time; (b) Stance time; (c) Swing time; (d) Phasing.

U-turn condition

The most affected side's stride time (Figure 4.17a) increases for all three non-freezers at position -1. At position 0, the stride time of two of them increases while the stride of a third one decreases. At position 1, it decreases for two non-freezers out of the three, one of which is particularly small, and increases for the third one. For the least affected side, two out of the three non-freezers have an increased stride time at position -1 while the last one has a decrease in it. Afterwards, for all three non-freezers the stride time decreases at positions 0 and 1.

The most affected side's stance time (Figure 4.17b) increases for all three non-freezers at position -1. At position 0, it also increases for two out of the three and decreases for the last one. Afterwards, at position 1, the stance time increases for two non-freezers and decreases for the other one. For the least affected side, at position -1, the stance time decreases for two non-freezers and increases for the third one. At position 0, it increases for two of them and decreases for the other one. Finally, at position 1, it

increases for one non-freezer and decreases for the two others.

The most affected side's swing time (Figure 4.17b) increases for all three non-freezers at position -1. It then increases for one of them at position 0 while it decreases for the two others. At position 1, the swing time decreases for all three non-freezers. For the least affected side, the swing time also increases at position -1 for all three non-freezers. At position 0, it slightly decreases for two of them and increases for the other one. Finally, at position 1, the swing time decreases for all three non-freezers.

The most affected side's phasing (Figure 4.17d) increases for two non-freezers and decreases for the third one at position -1. At position 0, it increases for one of them and decreases for the two others. Finally, at position 1, the phasing increases for two non-freezers and decreases for the other one. For the most affected side, at position -1, the phasing increases for two out of the three non-freezers and decreases for the third one. Afterwards, at position 0, it decreases for two of them and increases for the other one. Finally, at position 1, the phasing increases for one non-freezer and decreases for the two other ones.

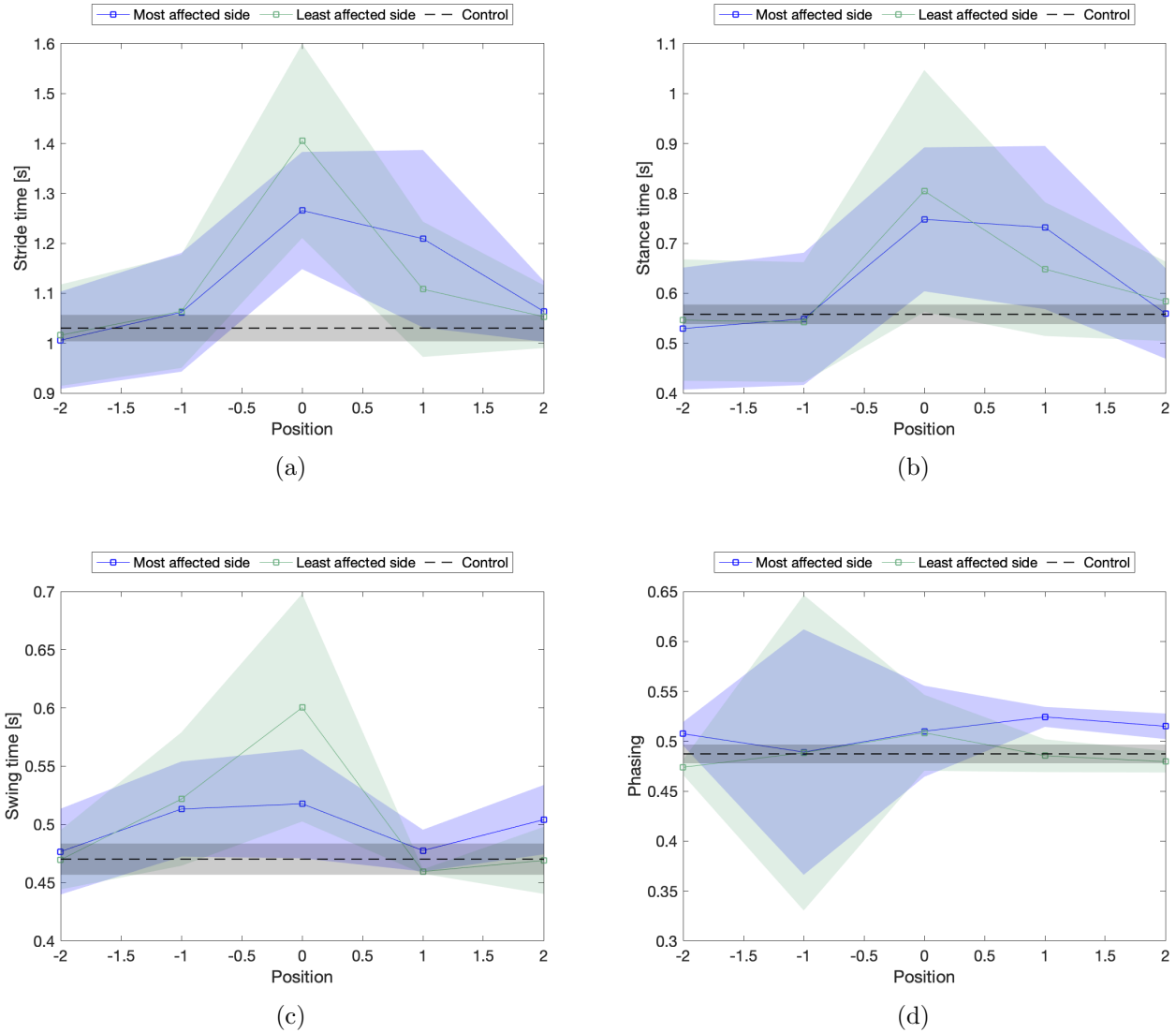


Figure 4.17: Metrics separated between most and least affected sides for non-freezers during the *U-turn* condition. The mean is represented by a line and the standard deviation is represented by the blue and green areas. (a) Stride time; (b) Stance time; (c) Swing time; (d) Phasing.

4.2.4 Summary

- All subjects:
 - *Doorway* condition
 - * Stride, stance and swing time on both sides: most patients increased them before and during the doorway and decreased them afterwards;
 - * Phasing: out of sync just before and during the crossing of the doorway for most patients.
 - *U-turn* condition
 - * Stride and stance time on both sides: most patients increased them before and during the turn. Afterwards, both metrics decreased;
 - * Swing time on both sides: increased before the turn and stayed constant during the turn for most patients;
 - * Phasing: out of sync starting from just before making the U-turn for most patients.
- Freezers:
 - *Doorway* condition
 - * Most freezers increased their stride, stance and swing time during the trial compared to the same metrics in the *control* condition;
 - * Stride and stance time: most freezers decreased them before the doorway for their least affected side. During the doorway, all freezers increased their stride and stance time on both sides. Most of them then decreased both metrics after having crossed the doorway;
 - * Swing time: all freezers decreased it during the crossing of the doorway for their most affected side. For their least affected side, most freezers decreased their swing time before and after crossing the door while all of them increased it during the doorway;
 - * Phasing: out of sync starting from just before crossing the doorway. It varied greatly for the most affected side.
 - *U-turn* condition
 - * Stride and stance time: on both sides, most freezers kept them constant before the turn and increased them during the turn. There was a particular large increase of stride and stance time during the turn due to a freezing episode for one of the freezer;
 - * Swing time: on both sides, most freezers decreased their swing time before and during the turn and increased it afterwards;
 - * Phasing: out of sync starting from just before freezers make the U-turn.
- Non-freezers:
 - *Doorway* condition
 - * Stride and stance time: for most non-freezers, the two metrics increased before and during the doorway while decreased after it;
 - * Swing time: for most non-freezers and their most affected side, it decreased before and after the passing through the door while it increased during the crossing of the doorway. For their least affected side, it increased before the doorway and decreased during and after the crossing of the doorway;
 - * Phasing: stayed more or less constant and in sync during the trial for all non-freezers.

– *U-turn* condition

- * Stride time: for their most affected side, most of the non-freezers increased their stride time before and during the turn and decreased it afterwards. For their least affected side, they increased their stride time before the turn and decreased it during and after the turn;
- * Stance time: for their most affected side, most of the non-freezers increased their stance time before, during and after the turn. For their least affected side, they decreased their stance time before and after the turn and increased it during the turn;
- * Swing time on both sides: most non-freezers increased it before the turn and decreased it during and after the turn;
- * Phasing: in sync for all non-freezers except when they make their U-turn where the phasing becomes out of sync.

Chapter 5

Discussion

This chapter discusses the results obtained in the previous chapter by distinguishing the three environmental conditions (i.e., the mats, doorway and U-turn conditions). It then explains the limits of the study and gives some perspectives for future works.

5.1 Discussion about previous results

5.1.1 Mats condition

The previous chapter showed that walking on gym mattresses, which represents an uneven terrain, significantly influenced the stride time, cadence and velocity for non-freezers' both sides. The same results were not found for freezers since the *mats* condition had no significant effect on their gait parameters. However, freezers had longer stride, stance and swing time as well as slower velocity and cadence and a smaller step length for the *control* condition compared to non-freezers. This was confirmed on an uneven terrain since they showed the same trend for their gait parameters during the *mats* condition compared to non-freezers. Xu *et al.* [37] showed that people with PD reduced their cadence when walking on irregular surfaces compared to regular surfaces. This could be explained by the fact that they adopted more conservative step patterns to cope with irregular surfaces. This thus confirms the findings that the cadence decreases for the *mats* condition. It also supports the findings that the stride time increases while the velocity decreases on irregular surfaces.

5.1.2 Doorway condition

Chapter 4 showed that freezers' least affected side had a smaller stride, stance and swing time before the doorway while non-freezers on both sides increased their stride and stance time but decreased their swing time before the doorway. During the doorway crossing, both groups increased their stride and stance time on both sides. However, freezers decreased their most affected side's swing time while the non-freezers increased it. The phasing for freezers started to be out of sync when they approached the doorway, especially for their most affected side. On the contrary, the doorway did not induce noticeable changes for non-freezers' phasing. These results do not validate those reported by Cowie *et al.* [30], which showed that freezers' stride time variability increased as the body approached the doorway. This could be due to the fact that the doorway was not narrow enough. However, Cowie *et al.* also showed that gait variability increased for freezers when approaching a doorway, which supports the results that the phasing of freezers' most affected side is completely out of sync before crossing the doorway.

5.1.3 U-turn condition

The previous chapter showed that the phasing of freezers and non-freezers were not the same. While both groups' phasing was out of sync during the turn, it was in sync before and after the turn for non-freezers while it already started to be out of sync before the turn for freezers and stayed out of sync until the end of the trial. The order of magnitude of this desynchronization was also larger for freezers compared to non-freezers. These results are consistent with Spildooren *et al.*'s findings that freezers had a worse

coordination during turning compared to non-freezers [28]. This can be due to the difference in turning techniques used by both groups or by the increased challenge that turning poses to lower limb coordination due to the inherent asymmetries of inner and outer legs during this task such as Courtine *et al.* suggested [87].

Chapter 4 showed that, before the turn, both freezers and non-freezers increased their swing time. During the turn, they increased their stride and stance time and decreased their swing time. To the best of our knowledge, no article studied how, for patients with PD, the stride, stance and swing time varied before a turn is made. Spildooren *et al.* [28] reported that turn duration was longer for freezers compared to non-freezers. However, no significant difference in turning time were noticed between both groups in this study. Before the turn, both groups increased their swing time, which may be due to a slight hesitation before performing a task that they know is more complicated for them than walking straight. During the turn, the stride and stance time increased, which seems logical since patients had to make the tightest possible 180° turn and the whole turn was considered as one stride. It can however be noticed that while the stride time increased on both sides for freezers during the turn, this was only the case for non-freezers' most affected side. This can be due to the difference in turning techniques used by both groups.

Out of the three freezers, only one of them had a noticeable episode of freezing during the nine trials. This is contradictory to what Spildooren *et al.* [28] showed, which is that FOG occurs for 38.2% of the freezers during a turn. This could be due to the patients being in the ON-state, which has a smaller occurrence rate of freezing episodes (11.1-40%) compared to freezers in the OFF-state (38.5-100%). Another reason might be that the selected environmental condition, which was a 180° turn, is not the most optimal one. Patients could, for example, have performed 360° or even 540° turns to increase the odds of provoking a freezing episode.

5.2 Limits of the study

The first limit of this study is the number of patients that took part in the experiments. A total of six patients participated in the experiments, which is a small number to perform a statistical analysis or to identify a trend on graphs such as the ones used in the visual analysis. Moreover, patients were divided equally between freezers and non-freezers which further reduced the number of data for either the statistical analysis or the visual analysis.

The second limit is that only the signals from the IMUs were analyzed whereas, during the experiments, a heart rate sensor and a motion capture system were also used to record data. The numbers of metrics that were obtained is thus limited, which reduced the range of the analysis performed for each environmental condition.

The third limit is that the experiments were made inside a sports room and are thus not representative of the real life of the patients. They do not perfectly reproduce the difficulties that patients will experience during their daily life. It would be more accurate to record data from a full day of patients' daily lives.

The fourth limit of the study is about the statistical analysis. It would have been better to use another statistical tool instead of a two-way repeated measures ANOVA. This statistical tool should allow the same analysis as the ANOVA as well as offer the possibility to compare freezers and non-freezers together directly instead of having to divide them manually as it was done in this study.

The fifth limit of the study is about the visual analysis. It would have been better to make the participants walk more before the *doorway* and *U-turn* conditions in order to obtain more complete

strides before and after the punctual events. This would have made the change in the patients' gait when nearing either the doorway or the U-turn clearer.

5.3 Perspectives

The results of this study are the first step towards the use of an APO with real-time assistance. It tested several metrics and determined how some of them might vary depending on the environmental context. First, a sudden increase in stride time or a sudden decrease in either cadence or velocity could be an indication that the patient is walking on an irregular surface. Second, if the patient is crossing a doorway, its stride and stance time will increase while its swing time will decrease. Moreover, for patients classified as freezers, these sudden changes will be preceded and followed by a desynchronization of the legs. Third, if the patient is going to make a turn, its swing time will increase beforehand. Furthermore, this increase will be coupled with a desynchronization of the legs that will continue during the turn for patients classified as freezers. All this information can be used as indicators for an APO coupled with assist-as-needed technology to provide real-time assistance to the patient when these complex environmental conditions are encountered.

To obtain a more complete understanding on how the environmental conditions influence the gait of people with PD, the data recorded by the motion capture system as well as the heart rate sensor have to be analyzed. The motion capture system provides many parameters such as the rotation, flexion and abduction angles of the hips, knees and ankles or the COM displacement. It is also important to quantify how the already studied metrics (e.g., stride time, phasing, etc.) and the upcoming metrics (e.g., rotation angles, COM displacement, etc.) vary. This will allow to define thresholds for every metric and thus adapt the level of real-time assistance provided to the patient according to its needs. Finally, recording data in patients' daily life and daily environment would allow to better understand the challenges that will have to be overcome in order to develop an APO with a real-time assistance.

Conclusion

Real-time assistance for people with Parkinson's disease is one of the challenges facing researchers in this field. It could significantly improve the quality of life of patients, as it will compensate for their gait impairment and thus improve their walking. This master thesis is part of the long-term objective to use an APO for assistive and rehabilitative natures and to develop a real-time assistance for the patient. Its goal was to identify how the gait parameters of people with PD would vary depending on specific environmental contexts. If trends can be observed for one or more parameters, they could then be used as thresholds to determine the level of assistance required by the patient depending on the environmental context.

The literature review showed that, depending on the environmental condition, the gait of people with Parkinson's disease can be influenced, resulting in difficulties in moving properly. Several factors have been identified such as turning, walking in narrow spaces or passing through doorways. These factors can also be more personal such as fatigue or anxiety. Several compensation strategies have been developed by patients and/or by researchers (e.g., external or internal cueing, action observation, etc.). They improve patients' gait and sometimes even prevent freezing episodes. Finally, research has been conducted on RAGT and assist-as-needed technologies for people with Parkinson's disease. While RAGT has been around for some time, assistive technology for people with Parkinson's disease is in its infancy.

The chapter about the materials and methods explained how the experiments were conducted. Six patients, three freezers and three non-freezers, took part in the experiments. They were asked to walk in four environmental conditions: (1) walking straight on for a distance of 10 meters on flat ground, (2) walking straight on for a distance of 10 meters on gym mattresses, (3) walking straight on for a distance of 10 meters on flat ground with a doorway at mid-way and (4) walking straight on for a distance of 5 meters, making a tight U-turn and walking back through the starting line. Videos of them were taken during the experiments and data were recorded by three equipment: (a) IMUs attached approximately 20 mm above each malleolus, (b) a motion capture system composed of six sensors placed on the lower part of the body and two sensors placed on the upper part and (c) a heart rate sensor placed on the torso under the sternum. The mediolateral velocity of both shanks was used to determine the following gait events: heel strikes, toe-offs and mid-swings. Afterwards, these gait events were used to compute several metrics: the stride, stance and swing time, the phasing, the velocity, the cadence and the step length. For the environmental conditions (3) and (4), the videos were used to identify the strides corresponding to either the crossing of the doorway or the U-turn.

The experiments showed that both the *control* and *mats* conditions had a significant effect on the stride time and cadence of parkinsonians for their most and least affected side. Both environmental conditions also had a significant effect on their velocity and their least affected side's step length. Freezers had a longer stride, stance and swing time as well as a slower cadence and smaller step length for both sides and both environmental conditions compared to non-freezers. Freezers' velocity is also slower for both environmental conditions. During the passage of the door, both freezers and non-freezers increased their stride and stance time while decreasing their swing time. Before performing a turn, patients increased their swing time. For both environmental conditions, freezers had desynchronized legs before the punctual event happened (i.e., doorway crossing or U-turn). This lasted during and after the punctual event occurrence. Surprisingly, the environmental conditions did not provoke many freezing episodes.

The information mentioned above can be used as indicators to provide real-time assistance to patients through an APO when they encounter complex environmental contexts.

To conclude this discussion, future directions were proposed. First, the data from the heart rate sensor and the motion capture system need to be analyzed to assess the behavior of other metrics. Second, the selected metrics that may be used for real-time assistance need to be studied more in depth to quantify how they vary and identify thresholds to provide the required level of assistance to the patient. Thirdly, studying the gait of freezers and non-freezers in their daily life would allow to better understand the challenges of providing them with the required real-time assistance.

Appendices

A Repeated measures ANOVA's assumptions

A.1 Continuity of the dependent variable

The dependent variables are the following : stride time [s], stance time [s], swing time [s], phasing, cadence [steps/s] and step length [L/s]. They are all continuous, which means that the assumption is respected.

A.2 Composition of the within-subjects factors

The two within-subjects factors, also called independent variables, must be composed of at least two categorical, related groups. This is the case the independent variables, which are the affected side and the environmental conditions are both composed of exactly two groups each. The affected side is composed of the least and the most affected side groups and the environmental conditions are composed of the *control* and the *mats* conditions.

A.3 The dependent variables are approximately normally distributed

The Shapiro-Wilk test is a test to determine whether a series of data follows a normal distribution. If the p-value is equal to or greater than 0.05 then the Shapiro-Wilk test did not show evidence of non-normality. W, which is the coefficient of determination (the square of the correlation coefficients) between the quantile series generated from the normal distribution and the empirical quantiles obtained from the data, is another indicator of the normal distribution. The higher W is, the more credible the compatibility with the normal distribution [88], [89]. The results of this normality test are given in Tables A1, A2 and A3. The data that are not normally distributed are highlighted in red.

Table A1: Results of the Shapiro-Wilk test on several metrics for all subjects

Metrics	Most affected side		Least affected side	
	p-value	W	p-value	W
stride time (mean)	0.791	0.961	0.624	0.949
stride time (cv)	0.0.448	0.0.936	0.0.292	0.0.921
stance time (mean)	0.672	0.952	0.585	0.946
stance time (cv)	0.712	0.955	0.782	0.959
swing time (mean)	0.112	0.888	0.452	0.936
swing time (cv)	0.784	0.96	0.067	0.871
phasing (mean)	0.884	0.968	0.838	0.964
phasing (cv)	0.031	0.844	0.107	0.887
cadence (mean)	0.739	0.957	0.617	0.949
step length (mean)	0.042	0.855	0.162	0.901

Table A2: Results of the Shapiro-Wilk test on several metrics for freezers

Metrics	Most affected side		Least affected side	
	p-value	W	p-value	W
stride time (mean)	0.262	0.878	0.259	0.878
stride time (cv)	0.572	0.929	0.186	0.859
stance time (mean)	0.506	0.92	0.353	0.896
stance time (cv)	0.354	0.897	0.534	0.924
swing time (mean)	0.578	0.929	0.619	0.935
swing time (cv)	0.482	0.917	0.049	0.791
phasing (mean)	0.999	0.998	0.929	0.976
phasing (cv)	0.223	0.869	0.182	0.858
cadence (mean)	0.158	0.85	0.155	0.849
step length (mean)	0.361	0.898	0.699	0.945

Table A3: Results of the Shapiro-Wilk test on several metrics for non-freezers

Metrics	Most affected side		Least affected side	
	p-value	W	p-value	W
stride time (mean)	0.781	0.955	0.448	0.912
stride time (cv)	0.558	0.927	0.536	0.924
stance time (mean)	0.916	0.974	0.716	0.947
stance time (cv)	0.655	0.939	0.663	0.941
swing time (mean)	0.064	0.804	0.447	0.912
swing time (cv)	0.04	0.782	0.284	0.883
phasing (mean)	0.413	0.906	0.269	0.879
phasing (cv)	0.396	0.904	0.189	0.859
cadence (mean)	0.868	0.967	0.545	0.925
step length (mean)	0.035	0.775	0.1	0.827

A.4 Sphericity

Mauchly's test is not necessary for sphericity because none of the repeated measures variables have more than two levels.

B Pairwise t-test's assumptions

B.1 Continuity of the variable

The assumption is respected since the variable is the velocity [L/s], which is continuous.

B.2 The variable is approximately normally distributed

The Shapiro-Wilk test is a test to determine whether a series of data follows a normal distribution. If the p-value is equal to or greater than 0.05 then the Shapiro-Wilk test did not show evidence of non-normality. W, which is the coefficient of determination (the square of the correlation coefficients) between the quantile series generated from the normal distribution and the empirical quantiles obtained from the data, is another indicator of the normal distribution. The higher W is, the more credible the compatibility with the normal distribution [88], [89]. The results of this normality test are given in Table B1. The data that are not normally distributed are highlighted in red.

Table B1: Results of the Shapiro-Wilk test on the mean velocity

Group	p-value	W
all subjects	0.016	0.819
freezers	0.096	0.824
non-freezers	0.029	0.766

B.3 Random sample

The data points from each group came from the experiments done for this thesis which were correctly acquired in a random way between trials.

B.4 Enough data

The sample size should be greater than five, which is the case here since there are 6 patients. The sample size decreases to three when the data are divided between freezers and non-freezers.

B.5 Homogeneity of variance

The velocity must be spread similarly between both environmental conditions, which is the case for these experiments.

C ANOVAs' results

Table C1: Results of the ANOVAs on several metrics for all subjects

Metrics	p-value		
	condition	side	interaction
stride time (mean)	0.005	0.285	0.009
stride time (cv)	0.36	0.938	0.909
stance time (mean)	0.037	0.037	0.311
stance time (cv)	0.237	0.637	0.885
swing time (mean)	0.714	0.03	0.699
swing time (cv)	0.164	0.99	0.643
phasing (mean)	0.082	0.279	0.985
phasing (cv)	0.023	0.966	0.967
cadence (mean)	0.002	0.278	0.006
step length (mean)	0.569	0.195	0.064

Table C2: Results of the ANOVAs on several metrics for freezers

Metrics	p-value		
	condition	side	interaction
stride time (mean)	0.182	0.065	0.248
stride time (cv)	0.905	0.137	0.892
stance time (mean)	0.266	0.146	0.544
stance time (cv)	0.575	0.757	0.613
swing time (mean)	0.896	0.142	0.769
swing time (cv)	0.528	0.676	0.789
phasing (mean)	0.003	0.601	0.812
phasing (cv)	0.085	0.783	0.413
cadence (mean)	0.129	0.078	0.208
step length (mean)	0.844	0.067	0.225

Table C3: Results of the ANOVAs on several metrics for non-freezers

Metrics	p-value		
	condition	side	interaction
stride time (mean)	0.00059	0.664	0.0087
stride time (cv)	0.272	0.341	0.76
stance time (mean)	0.167	0.279	0.534
stance time (cv)	0.386	0.354	0.75
swing time (mean)	0.781	0.255	0.839
swing time (cv)	0.305	0.596	0.742
phasing (mean)	0.998	0.108	0.689
phasing (cv)	0.265	0.855	0.06
cadence (mean)	0.0049	0.693	0.0019
step length (mean)	0.011	0.709	0.309

D Pairwise t-test’s results

Table D1: p-values for the pairwise t-test on the metrics for all subjects and the pair of conditions: *control* and *mats*

Metrics	most affected		least affected	
	p-value	effect size	p-value	effect size
stride time	0.002	0.505	0.014	0.37
stance time	0.039	0.661	0.052	0.471
phasing	0.12	0.747	0.084	1.01
cadence	0.00074	0.501	0.0061	0.373

Table D2: p-values for the pairwise t-test on the metrics for all subjects and the pair of sides: most affected and least affected

Metrics	<i>control</i> condition		<i>mats</i> condition	
	p-value	effect size	p-value	effect size
stance time	0.66	0.291	0.86	0.117
swing time	0.43	0.504	0.36	0.618

Table D3: p-values for the pairwise t-test on the metrics for freezers and the *control* and *mats* conditions

Metrics	most affected		least affected	
	p-value	effect size	p-value	effect size
phasing	0.95	0.051	0.69	0.353

Table D4: p-values for the pairwise t-test on the metrics for non-freezers and the *control* and *mats* conditions

Metrics	most affected		least affected	
	p-value	effect size	p-value	effect size
stride time	0.00081	0.856	0.00084	0.57
cadence	0.003	0.893	0.0082	0.598
step length	0.19	0.044	0.031	0.095

Table D5: p-values for the pairwise t-test on the mean velocity for the *control* and *mats* conditions

Group	p-value	effect size
all subjects	0.026	0.261
freezers	0.33	0.211
non-freezers	0.021	0.262

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