

École polytechnique de Louvain

Towards the development of a walking assist-as-needed protocol for patients with Parkinson's disease

Detection of freezing of gait episodes in real time

Authors: **Mélanie Colasse, Juliette Vanderhaeghen**

Supervisor: **Renaud Ronsse**

Readers: **Frédéric Crevecoeur, Greet Kerckhofs, Virginie Otlet**

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Abstract

Context The number of patients suffering from Parkinson’s disease continues to increase, primarily due to aging population but also to a growing exposure to environmental factors such as pesticides. The symptom of freezing of gait, affecting approximately half of individuals with Parkinson’s disease, is highly disabling and disrupts the walking ability of these patients. Treating this symptom is challenging, and traditional drug therapies such as levodopa does not always yield positive outcomes. Consequently, several studies, although somewhat limited, have investigated the potential of robotic gait assistance as a means to alleviate this disabling condition.

Objectives The objective of this work is to determine how freezing of gait episodes can be detected in real-time in order to enable future on-demand robotic assistance, therefore providing assistance only when needed.

Methods The effectiveness of three implementation methods (Freeze Index, surface electromyography-based method and K-index) is tested by comparing the results obtained with those reported in articles presenting these methods. This comparison is conducted in two ways. The first approach involves testing the algorithms developed on publicly available data. The second one involves testing the algorithms developed on data obtained experimentally as part of this study.

Results The obtained results concerning sensitivity and specificity diverged to some extent from the existing literature, displaying relatively inferior performances. Drawing conclusions about the superiority of one algorithm over another is challenging due to the variability between results across different datasets. Indeed, with the open access dataset, the K-index gives better performances followed by the Freeze Index. It is therefore the surface electromyography-based method which seems to be the weakest at detecting FOG episodes. On the other hand, testing the algorithms on the experimental data gives another ranking. The surface electromyography-based method becomes the better one, followed by the K-index and the Freeze Index. Although optimum performances are not achieved, this work effectively demonstrates the feasibility of developing a freezing of gait episode detection algorithm. It elucidates the influence of the studied algorithm parameters on performances and offers potential ideas for enhancement.

Table of contents

List of abbreviations	vi
Introduction	1
1 Context and theoretical background	3
1.1 Context	3
1.2 Neuropathology of Parkinson’s disease	4
1.3 Freezing of gait	6
1.4 Treatments of Parkinson’s disease	7
1.4.1 General treatments	7
1.4.2 Existing treatments for freezing of gait symptom	9
1.5 Theoretical background on normal gait cycle	10
1.6 Objectives of this work	12
2 State of the art of robotic gait assistance for Parkinson’s disease	13
2.1 General background	14
2.1.1 Robotic gait assistance in Parkinson’s disease	14
2.1.2 Evaluation tests	15
2.2 Clinical outcomes	16
2.2.1 General condition of the patient	16
2.2.2 Comparison between robotic-assisted gait training and other therapies	19
2.2.3 Freezing of gait	23
2.3 Conclusion	26
3 Detection of freezing of gait episodes	27
3.1 Statistical analysis	28
3.1.1 Sensitivity	28
3.1.2 Specificity	28
3.1.3 Compromise	28
3.2 Frequential domain	29
3.2.1 Freeze Index	29
3.2.2 Continuous Wavelet Transform	31
3.2.3 Anomaly Detection Technique	33

3.2.4	Entropy	35
3.2.5	Power spectral distribution analysis	36
3.3	Temporal domain	37
3.3.1	Surface electromyography-based method	37
3.3.2	K-index	39
3.3.3	Freezing of gait criterion	40
3.3.4	Pearson's correlation coefficient	41
3.3.5	Machine learning	42
3.4	Summary table	42
3.5	Selection of detection methods	42
4	Algorithms testing on open access data	45
4.1	Materials and methods	45
4.1.1	Open access dataset	45
4.1.2	Data processing	46
4.1.3	Freeze Index	46
4.1.4	Surface electromyography-based method	47
4.1.5	K-index	48
4.1.6	Statistical analysis	49
4.2	Results and interpretation	50
4.2.1	Freeze Index	50
4.2.2	Surface electromyography-based method	52
4.2.3	K-index	56
4.3	Summary	59
5	Algorithms testing on experimental data	61
5.1	Materials and methods	61
5.1.1	Subjects	61
5.1.2	Protocol	62
5.1.3	Visual analysis	63
5.1.4	Data treatment and analysis	64
5.2	Results and comparison with external data and author's performances	66
5.2.1	Freeze Index	66
5.2.2	Surface electromyography-based method	69
5.2.3	K-index	72
5.3	Summary	75
6	General discussion and perspectives	77
6.1	Discussion of the results	77
6.2	Limits of the study	79
6.3	Perspectives	81
	Conclusion	83

Appendices	85
A Types of tests	85
B Performances of the Freeze Index	87
B.1 Impact of parameters on performances in the open access dataset	87
B.2 Results of the mixed-effects models on the open access dataset	88
B.3 Impact of parameters on performances in experimental data .	89
C Performances of surface electromyography-based method	90
C.1 Impact of parameters on performances in the open access dataset	90
C.2 Results of the mixed-effects models on the open access dataset	91
C.3 Impact of parameters on performances in experimental data .	91
D Performances of the K-index	92
D.1 Person-dependent parameters and performances	92
D.2 Results of the mixed-effects models on the open access dataset	92
E Summary table of results	93
F Assist-as-needed	93
F.1 Impedance controller	94
F.2 Trajectory correction	95
F.3 Forgetting factor	95
F.4 Amplifier	96

List of abbreviations

CWT	Continuous wavelet transform
DBS	Deep brain stimulation
FFT	Fast fourier transform
FOG	Freezing of gait
H&Y	Hoehn and Yahr
IMUs	Inertial Measurements Units
PQ-39	Parkinson's disease questionnaire
sEMG	Surface electromyography
TUG	Timed Up and Go

Introduction

“I have just entered a different world.”

Parkinson’s disease, which is affecting an increasing number of people (especially due to the aging population), has a considerable impact on the quality of life of patients, as expressed in the above quote from a patient who participated in the experiments conducted in this work. It not only affects the physical aspect but also the mental well-being. One symptom that manifests itself in about half of Parkinson’s disease patients, known as freezing of gait (FOG), plays a significant role in the lives of certain patients. This symptom often leads to falls, which can be tremendously disabling and frightening for those who experience it. Unfortunately, Parkinson’s disease currently has no cure, and treating FOG episodes presents challenges. This symptom can be resistant to conventional drug therapies and is also dependent on individual patients. Consequently, it reveals an increasing need to find methods to enhance the everyday life of these individuals [1, 2, 3, 4].

Recently, researchers have turned their attention to robotic gait assistance in order to support and help motor symptoms of individuals with Parkinson’s disease. This treatment approach is gaining ground, although the studies conducted specifically for Parkinson’s disease and particularly regarding FOG episodes are limited. This work aims therefore to bring insight in potential benefits of robotic gait assistance. Furthermore, the long-term objective of this work also incorporates the principle of assist-as-needed. In a few words, assist-as-needed principle refers to providing robotic assistance only when the patient needs it. The objective of this master thesis is therefore to investigate how the detection of FOG episodes could be achieved in order to provide this robotic assistance only when the patient experiences this symptom. In addition, the goal is to analyze how effectively this detection can operate.

The structure of this master thesis is as follows. Chapter 1 provides the contextual background by explaining Parkinson’s disease, its symptoms, and the current treatment options. Special attention is given to the FOG symptom. The chapter also provides theoretical insights into the normal gait cycle to enhance understanding of how this condition affects individuals with Parkinson’s disease. Finally, the objectives of this work are defined.

In Chapter 2, a comprehensive review of the state of the art in robotic gait assistance for Parkinson’s disease is presented. It begins by explaining the concept of robotic gait assistance and provides a brief overview of the types of robots used in the studies reviewed. Next, three distinct categories of articles are presented, along with the various positive impacts they can have.

In Chapter 3, a non-exhaustive review of the methods developed to detect FOG episodes is conducted. In conclusion of this chapter, three methods are selected to be implemented and studied in this work.

In Chapter 4, the algorithms developed based on the methods from Chapter 3 are tested on publicly available external data. Methods used to process data and to implement specific parts of the algorithms are described. The results from the statistical analysis regarding the performance of these algorithms on this data are also presented. Furthermore, the impact of the algorithm’s parameters are interpreted.

In Chapter 5, the algorithms developed based on the methods from Chapter 3 are tested on data collected during the experiments carried out as part of this work. The results regarding the performance of the algorithms on these data are also presented and compared with the results of the authors of the methods as well as with those obtained with the open access data in Chapter 4. Finally, the results and limitations of Chapters 4 and 5 are discussed in Chapter 6, together with the perspectives offered by this master thesis.

Chapter 1

Context and theoretical background

This first chapter provides an overview of the context of this work and the neuropathological basis of Parkinson's disease. Special emphasis is placed on a prevalent and debilitating symptom of the disease known as FOG. Then, a discussion on the various existing treatments currently available is presented, with a section dedicated to FOG. Finally, the objective of this work is developed.

1.1 Context

According to the World Health Organization [5], Parkinson's disease affected 8.5 million people worldwide in 2019. In Belgium alone, the number of cases reached at least 30,000 in 2021 [6]. This incidence of cases is expected to continue to rise, as there were 2.4 times more cases in 2016 than in 1990. Indeed, the aging of the population is an important factor in this increase, as the risk of developing Parkinson's disease is significantly higher in the 40 to 75 age group, where 80% of cases occur. This aging trend is largely attributed to advances in medical care. Moreover, there is recognition that environmental factors, including exposure to specific pesticides and insecticides, contribute as additional risk factors. Our increasing exposure to these harmful substances amplifies the likelihood of developing this disease. In addition, there are also other risk factors such as male gender (with incidence and prevalence rates 1.5 to 2 times higher in men than in women [7]), previous head trauma and genetic factors. Finally, detection methods are becoming more accurate, allowing more patients to be diagnosed [2, 3, 4, 5].

Parkinson's disease is a disabling condition manifesting itself through motor and non-motor symptoms. The main motor symptoms are expressed by tremors at rest (with a tremor frequency between 4 Hz and 6 Hz), muscular rigidity, bradykinesia (*i.e.* reduction in the speed and amplitude of voluntary movements, mainly during repetitive tasks), akinesia (*i.e.* difficulty in initiating movements), postural instability

and festination (*i.e.* faster walking pace and shorter stride length). However, there is more to Parkinson’s disease than this. Indeed, more than half of patients with advanced Parkinson’s disease experience what is known as FOG episodes. It means that the patient’s feet are “stuck” to the ground and that the patient cannot start walking, even if he wishes to do so [8]. Moreover, as the disease progresses, FOG episodes often no longer respond to dopaminergic drug strategies [9]. Unfortunately, all the symptoms described appear gradually and worsen as the disease progresses leading to increased difficulty in activities of daily living such as walking and talking. Finally, non-motor symptoms such as depression, cognitive impairment, mental health problems and sleep disturbances also significantly impact the lives of Parkinson’s disease patients [2, 10].

Parkinson’s disease can be measured according to the Hoehn and Yahr (H&Y) scale, which was created to evaluate the clinical status of patients [11, 12]:

- Stage 1: Motor symptoms only impact one side of the body.
- Stage 1.5: Motor symptoms affect only one side of the body and axial disorders (posture, gait, speech and swallowing disorders) may occur [13].
- Stage 2: Motor symptoms impact both side of the body without balance impairment.
- Stage 2.5: The disease affects both sides of the body, resulting in mild disability. There is some recovery observed on the pull test, but slight impairment in balance (postural instability) begins to emerge [14].
- Stage 3: The disease affects both sides of the body, the disability is mild to moderate with postural instability. The patient remains physically independent.
- Stage 4: The disability is severe, but the patient is still able to walk or stand without assistance.
- Stage 5: The patient is no longer physically independent, must be in a wheelchair or bedridden unless assisted.

1.2 Neuropathology of Parkinson’s disease

Parkinson’s disease is defined by a loss of dopaminergic neurons in the substantia nigra pars compacta located in the midbrain. This degeneration leads to a decrease in dopamine transmission in the motor region of the striatum, which serves as the primary input to the basal ganglia. Therefore, the basal ganglia, consisting of a collection of interconnected subnuclei, experience dysfunction due to the neuronal loss associated with the disease [15]. Consequently, one of its functions, which is the control of movement, is affected. The basal ganglia have two main output nuclei,

the substantia nigra pars reticulata and the globus pallidus internus, which project to the thalamus. Different pathways are used by the basal ganglia to control the movement to be performed. To initiate the movement, an excitatory pathway, *i.e.* the direct pathway, activates the motor cortex which, in turn, activates the muscle. This direct pathway inhibits the activity of the two output nuclei mentioned above. These nuclei have an inhibitory activity on the thalamus, so that inhibition of the nuclei results in an increase in the excitation activity sent to the motor cortex. An inhibitory pathway, *i.e.* the indirect pathway, stops the movement. The indirect pathway, unlike the direct pathway, increases the activity of the two major basal ganglia nuclei, resulting in significant inhibition of the thalamus, thereby reducing the activity of the motor cortex [16]. Figure 1.1 shows these two pathways and their projections. However, when the substantia nigra pars compacta loses dopaminergic neurons, the direct and indirect pathways are reversed. This results in an increase in the activity of the indirect pathway and a decrease in the activity of the direct pathway, which in turn produces an increase in inhibitory activity in the thalamus. Consequently, the output activation of the motor cortex is reduced, as shown in Figure 1.1 [17]. This explains why the degeneration of dopaminergic neurons has such a negative impact on movement in Parkinson's disease [18].

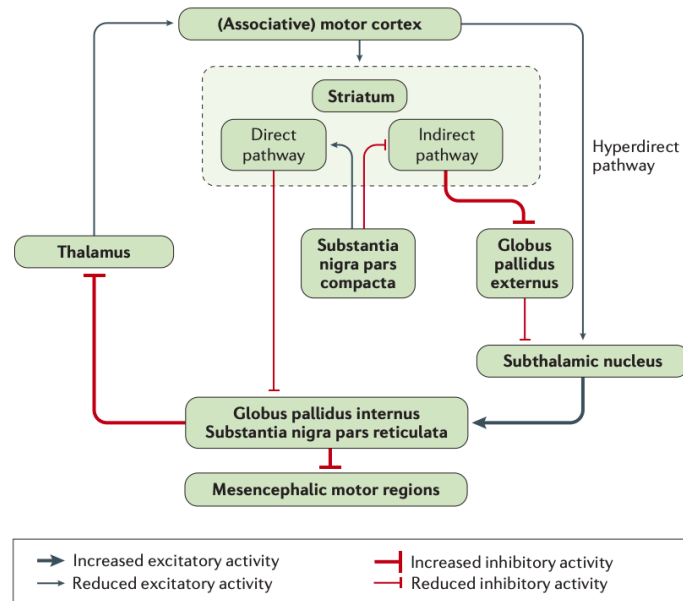


Figure 1.1: *Modifications of motor cortex circuit activity in Parkinson's disease*[17].

Parkinson's disease is also characterized by the existence of Lewy bodies in the neurons found in the midbrain. These are mainly composed of α -synuclein which form, as presented in Figure 1.2, intracellular inclusions via misfolding and the aggregation of β -sheet-rich amyloid. The intermediates produced during this aggregation process are toxic oligomeric and proto-fibrillar forms that damage lysosomal, mitochondrial and proteasomal functions, destroy biological membranes and the

cytoskeleton, modify synaptic functions and thus cause neuronal degeneration. However, Parkinson's disease is not limited to this, as it also extends to other areas of the brain and involves non-dopaminergic neurons, which is believed to cause non-motor symptoms [19, 20, 21].

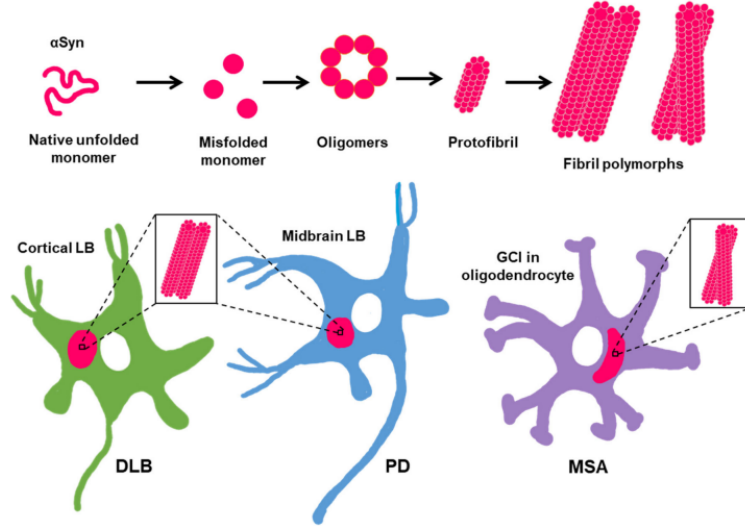


Figure 1.2: *The process of formation of Lewy Bodies, which are found in the midbrain in Parkinson's disease (indicated in blue) [19].*

1.3 Freezing of gait

FOG is a common and highly debilitating condition that affects up to 50% of individuals with Parkinson's disease, as previously mentioned. Patients who experience FOG episodes are commonly referred to as "freezers". Additionally, FOG is more frequently observed in men than in women, but its occurrence is less common when tremor is the primary symptom reported by the patient [22]. In 2011, FOG episodes have been described by Nutt and colleagues as "a brief and episodic absence or marked reduction in the forward progress of the feet despite the intention to walk" [8]. Also called motor blocks, FOG episodes are characterized by a period of a few seconds (usually) when the feet are "stuck" to the ground. This phenomenon can lead to a high number of falls and can impair patients' mobility and independence in activities of daily living [8].

FOG episodes and their treatment remain major challenges for both clinicians and researchers [23]. Indeed, the FOG symptom is a difficult aspect of the disease to treat, as the situations that trigger FOG episodes differ from person to person, requiring individualized solutions. Gait initiation, turns, confined spaces (such as doorways), cognitive and physical double-task or perceived stress can be triggers [24].

In addition, it may be asymmetric, *i.e.* it can affect only one foot. To address this symptom, an accurate and objective measure of FOG is essential, as outlined by Cui et al. [25].

FOG episodes can manifest as three different phenotypes: (i) shuffling in small steps, (ii) tremor in place or (iii) complete akinesia [25]. All three types can be detected during the "on" period, *i.e.* when other motor symptoms are decreased, and also during the "off" period, *i.e.* when the medication is no longer working, as explained in Section 1.4.

Various hypotheses have been raised in the form of models to explain the occurrence of these episodic FOG [23, 25]:

- According to the threshold model, when the accumulation of motor disabilities outgrowth a critical threshold, a FOG episode appears.
- The interference model suggests that the loss of dopaminergic neurons leads to an overload of the information processing capacity when combining a cognitive and a motor task. This dual task would therefore be the cause of FOG episodes.
- The cognitive model emphasizes the difficulty of freezers to resolve conflict. According to this explanation, patients respond too quickly and with inadequate coordination, triggering FOG episodes.
- The decoupling model describes a FOG episode as the fact that the intended motor control is no longer connected to the motor response.

These different models and their combinations are interesting, albeit incomplete, as they allow us to explore the understanding and characterization of FOG [23, 25].

1.4 Treatments of Parkinson's disease

1.4.1 General treatments

Currently, there is unfortunately no cure for Parkinson's disease. This induces palliative care as part of the treatment plan [2]. Therefore, existing treatments are only symptomatic, *i.e.* it focuses on improving motor and non-motor symptoms. Non-motor concerns require non-dopaminergic approaches such as cholinesterase inhibitors for cognition [2].

On the other hand, dopamine-based drug treatments are mainly used to reduce motor impairments. There are three types of drugs used with different mechanisms. Firstly, levodopa-based preparations aim to provide adequate dopamine concentrations during the day [2]. The small intestine absorbs the levodopa pills and the

blood carries them to the brain, where the levodopa is converted to dopamine [26]. This treatment is still considered the most effective in reducing the symptoms of Parkinson's disease. Moreover, almost all patients take it at some point in the disease [27]. Secondly, dopamine antagonists such as pramipexole are used to stimulate striatal dopamine receptors. The advantage of this drug is that it has a longer half-life than levodopa, resulting in less pulsatile stimulation of dopamine receptors. Finally, monoamine oxidase type B inhibitors have the effect of reducing the degradation of dopamine. In addition, they could delay the aggregation phase of α -synuclein, which could therefore reduce the progression of the disease [27].

Figure 1.3 illustrates the mode of action of levodopa, the most common and effective medication for motor symptoms. The mechanism explained here is applicable to all drugs. The OFF periods, *i.e.* when the drug dose is below the therapeutic window, represents when the effect of the drug has worn off. This period is also defined by the presence of motor symptoms. The patient is said to be in ON periods, *i.e.* when the drug dose is above the lower limit of the therapeutic window, when the drug continues to have an effect. During this period, motor symptoms are reduced or even disappear completely. The drug may also have side effects when the dose exceeds the upper limit of the therapeutic window. For example, episodes of dyskinesia (involuntary movements) in patients with Parkinson's disease may occur when the levodopa concentration in the brain peaks [2]. While levodopa is effective on most motor symptoms, FOG episodes can still occur during ON periods, albeit less frequently. According to Cui et al. [25], levodopa may even be responsible for triggering FOG episodes.

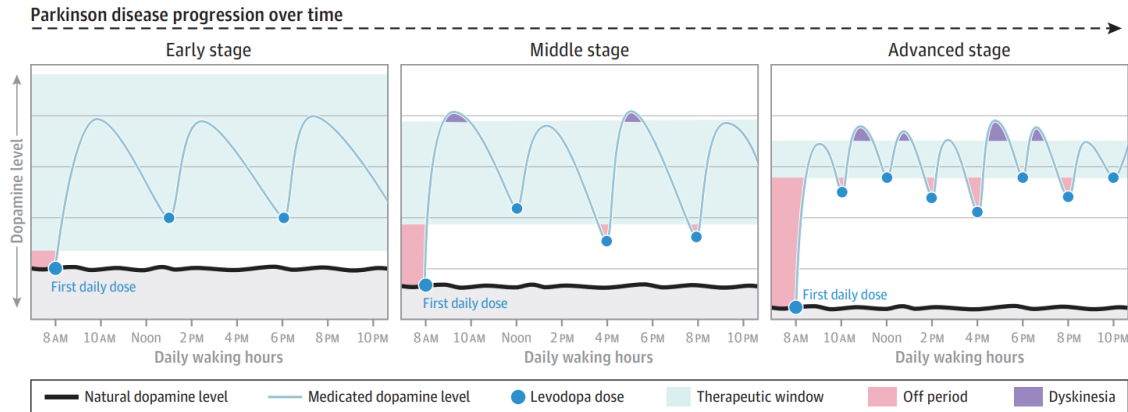


Figure 1.3: *The interaction between medication dosing, wearing off, and dyskinesias over time [2].*

With disease progression, it is common for patients to experience complications, such as the development of resistance to prescribed medications and the reduction of ON periods. In these cases, more advanced treatments such as deep brain stimula-

tion (DBS) can help to reduce tremors and the need for medication [2]. DBS consists of the insertion of electrodes in a certain area of the brain [28]. There are different possible locations, such as the subthalamic nucleus, the internal globus pallidus or the pedunculopontine nucleus [29]. In advanced stages of Parkinson’s disease, pumping devices such as Duodopa can be used. This is a method of treatment that involves the continuous administration of levodopa-carbidopa gel into the small intestine, the site of the body that best absorbs levodopa. This system avoids drug spikes and allows for a constant concentration of dopamine [30].

In addition to pharmacological treatments, rehabilitative therapies and exercises are widely used to manage symptoms at all disease stages. Indeed, gait, cognitive functions and quality of life of patients can be improved through various physical activities such as dancing or treadmill training [31]. Furthermore, ongoing studies are evaluating the benefits that robotic gait assistance could bring to Parkinson’s disease patients. Rehabilitation through the use of robots aims to enable patients to maintain but above all to improve their mobility and level of independence [32]. However, there are still many grey areas regarding this treatment method that remain unresolved [32]. This is why this treatment is chosen for study in this work because of its potential to treat symptoms affecting gait in Parkinson’s disease, and in particular its possible utility in treating the symptom of FOG. Chapter 2 is dedicated to providing a description of robotic gait assistance and its practical application in alleviating motor symptoms for patients with Parkinson’s disease.

1.4.2 Existing treatments for freezing of gait symptom

There are various treatments available to manage FOG episodes, with varying degrees of effectiveness. These treatments can be broadly classified into four categories, namely pharmacological treatments, surgical treatments, physical rehabilitation, and behavioral treatments.

The first category is medication, mainly dopaminergic medication, such as levodopa already explained in Section 1.4. This can reduce the severity of FOG episodes. However, there are dopamine-resistant FOG for which drugs that use other agents, *e.g.* amantadine, have been created, but with limited success [29, 33]. Additionally, the mental, emotional and cognitive state of the patient plays an important role in the occurrence of FOG episodes. Indeed, stress, anxiety, depression and dual-task situations (*e.g.*, talking and walking at the same time) can increase the occurrence of FOG episodes [34]. Therefore, drugs that improve mental problems such as depression or anxiety have also been found to be useful in managing FOG episodes [25].

The second category concerns implants. These implants are mainly DBS. The

duration of the disease, the responsiveness to levodopa during FOG episodes and the location of the DBS electrode have an impact on the quality of treatment. As FOG is a complex phenomenon involving several neuronal structures, there is also a multi-target strategy, such as pedunclopontine nucleus combined with subthalamic nucleus or subthalamic nucleus combined with substantia nigra pars reticulata. It is also possible to use an adaptive DBS that automatically adjusts the stimulation level according to neural activity in order to reduce the severity of FOG episodes and side effects as much as possible. In addition to DBS, there is also electrical stimulation of the spine that can help relieve FOG episodes. This suggests that the spinal cord could be used as a "pathway" to communicate therapeutic electrical signals to alter the state of the brain and thus reduce FOG [29, 35, 36].

The third category implies physical rehabilitation for which it has been shown to be crucial [37]. In research, physical activities such as walking, training with treadmill, curve walking and water aerobic have been shown to be more effective in comparison to standard physiotherapy and general exercises [25]. In addition, studies have been and are being conducted to evaluate the effectiveness of robotic gait assistance with and without training on FOG episodes, as detailed in Chapter 2. The review by Alwardat et al. [38] reveals that this treatment could have beneficial effects on this disease symptom, but that too few studies have been done to confirm it [38]. However, this solution seems promising.

The fourth and final category is based on cues and biofeedback. Auditory or visual cues can be used to help patients overcome FOG episodes. These cues can be provided through an online technique and given only when the patient needs them, which is known as an on-demand aid [29].

1.5 Theoretical background on normal gait cycle

In the gait cycle of an individual with Parkinson's disease, the following abnormalities are commonly observed: reduced gait speed, decreased swing phase duration, shortened step length and stride length, and increased cadence [39]. In addition, FOG episodes, as explained in Section 1.3, can take the form of small steps or tremors, or a complete halt in progress. This has a considerable impact on the person's gait cycle. Therefore, it is important to define the normal gait cycle in order to understand the implications of these abnormalities.

The normal gait cycle (see Figure 1.4) consists of two phases: the **stance phase**, which begins when the heel touches the ground and the **swing phase**, which begins when the foot is off the ground. The studied right leg will be referred as the ipsilateral leg and the opposite leg as the contralateral leg.

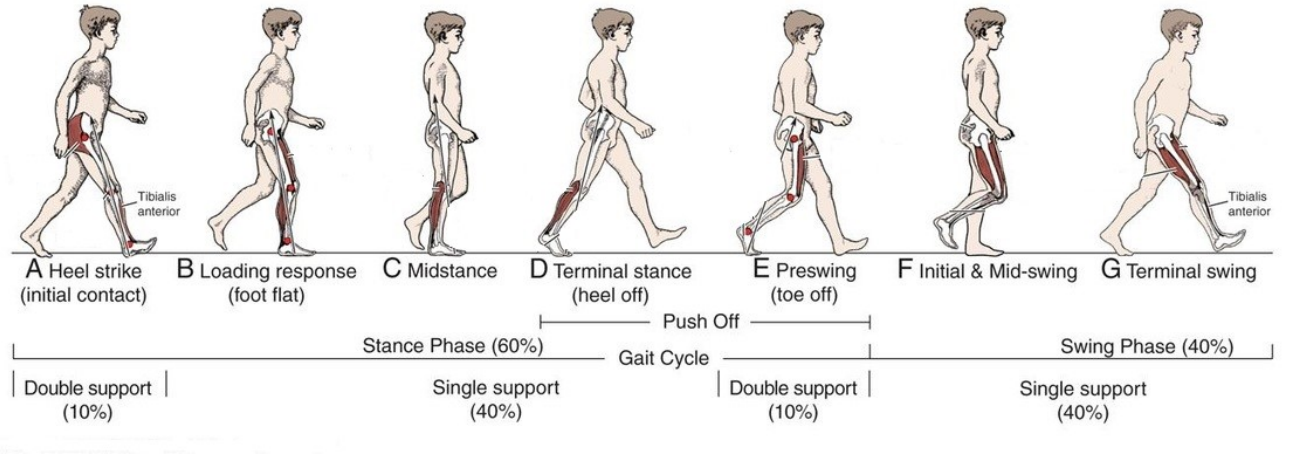


Figure 1.4: *Phases of the right leg gait cycle [40]*

Firstly, the stance phase, corresponding to approximately 60% of the gait cycle, can be divided into four sub-phases [41]:

1. The **loading response** is the interval during which the ipsilateral leg begins to bear the weight of the body while the contralateral leg enters its swing phase. It ends when the ipsilateral foot is flat on the ground. It is therefore a sub-phase during which both feet are in contact with the ground, and corresponds to the so-called double-support phase.
2. The **midstance** interval begins when the contralateral foot is off the ground and ends when the bodyweight is aligned with the ipsilateral foot.
3. The **terminal stance** begins when the heel of the ipsilateral leg lifts off the ground and continues until the contralateral foot hits the ground.
4. The **pre-swing** interval ends with the ipsilateral toe-off. During this time interval, the body weight is transferred from the ipsilateral leg to the contralateral leg. It is the other double-support sub-phase of the gait cycle, with both legs playing the dual role as compared to the loading response phase.

Next, the swing phase, corresponding to approximately 40% of the gait cycle, can be divided into three sub-phases [41]:

1. The **initial swing** ends when the ipsilateral foot is opposite to the contralateral foot.
2. The **mid swing** ends when the ipsilateral tibia is in a perpendicular position to the ground.
3. The **terminal swing** ends when the ipsilateral foot strikes the ground.

Moreover, the gait cycle can also be defined as the time interval between two consecutive heel strikes of the same foot, which is known as a stride. The step, on the other hand, refers to the distance between the feet during the terminal stance phase. Therefore, a stride is equal to two steps. Finally, cadence is defined as the

number of steps taken by a person in a certain period of time [39].

1.6 Objectives of this work

Upon examining the symptoms and current treatments available for Parkinson’s disease, a deficiency was found in addressing FOG symptom. Thus, it is necessary to find a solution that can fulfill the needs posed by this issue. Along with the progress already achieved through the pharmaceutical approach, robotic gait assistance appears to be a promising path to explore. In addition, one advantage of robotic gait assistance for Parkinson’s disease is its non-invasive nature, unlike DBS which involves surgical procedures.

The upcoming chapter showcases studies that demonstrate the potential benefits, or lack thereof, of robotic gait assistance for individuals with Parkinson’s disease. Regrettably, only a limited number of studies have explored the issue of FOG symptom. Furthermore, the current state of research shows that no tests have been carried out on on-demand assistance. The assist-as-needed (AAN) principle, which aims to provide robotic assistance based on the patient’s needs in real time, defined by their disability and effort at a given time, is a promising approach that deserves further exploration [42]. The idea behind this method is that the patient should gain as much as possible from the robotic rehabilitation. To do this, it is essential for the patient to be engaged in the activity. Too much assistance will not make him work at all, but too little assistance may discourage him because they will not be able to perform the task. Therefore, the advantage of this method is that it takes the patient’s intention into account and adapts to it, rather than imposing a control strategy [43, 44].

To conclude, this work is part of the long-term objective to provide a robotic gait assistance using the assist-as-needed principle for patients with Parkinson’s disease specifically affected by FOG episodes. The first step in this direction is to effectively detect the onset of a FOG episode in real time. Providing biofeedback, explained in the previous section, at the appropriate time would also require this, hence the multiple benefits of being able to detect FOG episodes exactly when they appear. The goal of this work is therefore to answer the following research question:

“How can a freezing of gait episode be detected in real time in order to provide on-demand assistance?”

Chapter 2

State of the art of robotic gait assistance for Parkinson's disease

In order to build upon existing research and gain insights into the effectiveness of robotic gait assistance for Parkinson's patients, it is crucial to first review the literature on the topic. Therefore, this chapter presents a state of the art that does not only provide an overview of what has already been done, but also identifies potential areas of interest for future studies.

Certain criteria were followed to select the articles included in this review. Only articles featuring robotic gait assistance for patients with Parkinson's disease were considered. These articles could encompass robotic gait assistance with or without training. Another crucial requirement was that the study involved robots that could be worn by the subjects, excluding devices such as canes, for instance. To the best of our knowledge, all articles meeting these criteria were included in this review of the state of the art.

First, background information is provided on robotic gait assistance and evaluation tests used in the reviewed literature. Moving forward, the list of articles is organized into three distinct categories, and for each category, the different possible clinical improvements/outcomes for the patient developed through robotic gait assistance are presented. The first category includes studies that specifically analyzed the effects of the robotic assistance on patients' gait and general physical condition. In the second category, articles that compared the effectiveness of robot-based rehabilitation, treadmill training and standard physical therapies can be found. The final category focuses primarily on the effects of these therapies on FOG episodes, which is the main topic of interest in this work. For each category, the authors' attempts to explain the origins of the different improvements are presented.

2.1 General background

2.1.1 Robotic gait assistance in Parkinson’s disease

Recently, numerous new rehabilitation technologies have emerged. Consequently, some studies have attempted to determine the improvements that robotic gait assistance can bring to patients with Parkinson’s disease [45]. A state of the art about robotic gait assistance for Parkinson’s disease is therefore presented in this chapter, and an overview of what involves this robotic assistance is described hereafter.

Robotic gait assistance is a therapy using electromechanical devices to assist walking by, for example, supporting the patient’s body weight [46]. In addition, the device makes it possible to impose symmetrical and consistent trajectories on the lower limbs, providing proprioceptive inputs to stimulate cortical activation and improve motor function [47]. Thanks to this assistance, the energy consumption required by patients would be reduced compared to conventional therapy and would allow more intensive and/or longer sessions [46]. In addition, the use of the robot during therapy would reduce the physical burden of the therapist [47].

Nowadays, several robots are being marketed or used in studies. They can be classified into three categories: end-effector devices, treadmill-based exoskeletons, and wearable devices. The first two categories can provide body weight support through a harness attached from above. These types of robots are fixed and must be used in a specific environment. Firstly, end-effector systems (Figure 2.1A) allow attachment only to the feet and can also simulate other types of walking such as walking on slopes and climbing stairs. Examples of such devices are the G-EO (Reha Technology AG, Olten, Switzerland) ([48, 49, 50, 51, 52]), the GTI (Reha-Stim, Berlin, Germany) ([53, 54, 55]) or the Morning Walk® (Curexo, Seoul, Korea) ([56]). Secondly, stationary treadmills exoskeletons (Figure 2.1B) simulate walking by providing a stable base and support for the legs. These include the Lokomat (Hocoma, Zurich, Switzerland) ([32, 45, 57, 58, 47, 59, 60, 61, 62]) and the Walkbot-S (P&S Mechanics, Seoul, Korea) ([63, 64, 65, 66]). The last category consists of robotic devices (Figure 2.1C) that can assist movement by providing support and stability to the legs. They have the advantage that they can be used overground on hard, flat surfaces and allow exercises to be performed in semi-ecological environments [46], *i.e* out of fixed footplates or treadmill. This category contains the hip orthosis SMA (Honda R&D, Tokyo, Japan) exoskeleton [67], the hip-knee-ankle orthosis EksoGT (EksoBionics, Richmond, CA, USA) [68], the knee orthosis Keeogo Rehab™ (B-Temia, Germany) [69], the UPS-PD based on the use of pneumatic muscles attached to the leg ([70, 71]), an ankle exoskeleton [72] and a hip-knee exoskeleton [73].

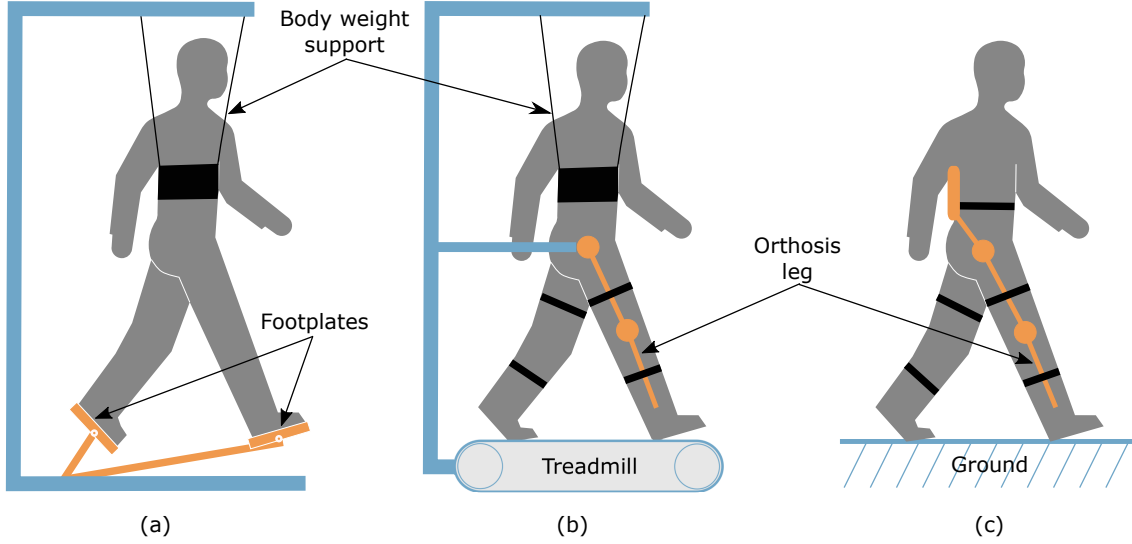


Figure 2.1: *Schematics of the different types of robots used for robotic gait assistance: (A) End-effector device; (B) Treadmill exoskeleton; (C) Wearable robotic device. The support (blue) and robotized parts (orange) are represented.*

2.1.2 Evaluation tests

The protocols of the different studies discussed in this chapter employ various tests to assess the effects and outcomes of robotic gait assistance on patients. These tests are mentioned in this section and are explained with more details in Appendix A.

Generally, the spatio-temporal variables of gait are assessed using the 10-meter Walk Test, which mainly measures gait speed, or with the performance of the Timed Up and Go (TUG) test. In the case of evaluating FOG episodes, these tests may be conducted with a dual-task paradigm. Other systems like GAITRite have been employed to measure stride length, cadence, and other gait-related measurements. Alternatively, some studies use simple overground walking for a specific distance.

Motor symptoms are typically assessed through various tests such as the Movement Disorder Society Unified Parkinson’s Disease Rating Scale (MDS-UPDRS), Functional Independence Measure, or even the PDQ-39. In most studies, patients’ balance is assessed using the Berg Balance Scale, Mini-BESTest, or Fear of Falling Efficacy Scale. Finally, studies focusing more in-depth on the effect of robotic gait assistance on FOG episodes uses questionnaires such as the Freezing Of Gait Questionnaire or the New Freezing Of Gait Questionnaire to assess the severity of these FOG episodes.

Generally, protocols consist of a predetermined number of sessions administered to patients, with regular recurrence of specific numbers. Indeed, out of the 26 articles, nine opted for a protocol consisting of 12 sessions distributed three days a week over

four weeks, with each session lasting between 30 and 45 minutes. Additionally, five other articles implemented a protocol of 20 sessions, spread over five days a week during a four-week period, with each session lasting 45 minutes. It should be noted that multiple authors may have contributed to these statistics, potentially introducing bias.

2.2 Clinical outcomes

Each study presented in each category compares the evaluation of patients before and after treatment. In some cases, one or more additional evaluations are conducted several weeks after the completion of treatment.

2.2.1 General condition of the patient

All the articles discussed in this section are summarized in Tables 2.1, which also include additional experimental details such as the number of patients or the number of sessions.

The studies have led to improvements in gait. These improvements include increasing average gait velocity, increasing step length, increasing average cadence, and reducing the metabolic cost of walking. The robots used in these studies are: the Lokomat, the Walkbot-S, the G-EO, the Morning Walk, the UPS-PD and an ankle exoskeleton.

Regarding spatio-temporal gait variables, several studies found an increase of the gait velocity ([45, 50, 57, 58, 63, 70, 71]), of the stride length ([45]), of the step length ([50, 71]) and of the cadence ([45, 50, 63]), after their corresponding robotic therapy. A decrease in the stance duration ([45, 70]), swing duration ([70]) and double limb support phase ([71]) was also reported. Galli et al. [50] offered an explanation for these improvements, suggesting that robotic gait assistance delivers intense and consistent somatosensory cues. They proposed that this stimulation could help in the functional recovery of gait automatism and velocity. In addition, another author explained that these improvements could be attributed, in part, to the delivery of a normal walking kinematics to the patient through assisted movements. This may help the patient in controlling inefficient gait synergies that they exhibit [61]. Gait synergies refer to the distinct patterns of temporal muscle activation that contribute to the execution of specific movements during walking. These synergies involve coordinated actions of different muscle groups working together to achieve the desired movement [74].

Lowering of the MDS-UPDRS part III score is a commonly reported finding

Table 2.1: Overview of robotic gait assistance used for Parkinson’s disease focusing on gait.

Source	Device	Patients (H&Y)	Duration	Evaluations	Results			
					Spatio-temporal variables	Motor symptoms	Kinematic variables	Balance
Paker et al. 2013 [57]	Treadmill: Lokomat	10 patients (1-3)	10 sessions (2x/w for 5w, 20 min)	5th week 12th week	↗ M	↗ M	na	na
Nardo et al. 2014 [45]	Treadmill: Lokomat	9 patients (na) with DBS	35 sessions (7x/w for 5w, 45 min)	5th week	↗	↗	≡	na
Galli et al. 2016 [50]	End-effector: G-EO	23 patients (na)	20 sessions (5x/w for 4w, 45 min)	4th week	↗	↗	≡	na
Fundarò et al. 2018 [58]	Treadmill: Lokomat	10 patients (na)	12 sessions (3x/w for 4w, 30 min)	4th week	↗	↗	na	na
Higuchi et al. 2019 [70]	End-effector: UPS-PD (Unplugged Powered Suit)	2 patients (3-4)	1 session	With UPS-PD	↗	na	na	na

↗: Improvements when there is no follow-up, ≡: Same as baseline, **M**: Improvements maintained at follow-up, **na**: Not available, **DBS**: Deep Brain Stimulation.

Table 2.1: Overview of robotic gait assistance used for Parkinson’s disease focusing on gait (continued).

Source	Device	Patients (<i>H&Y</i>)	Duration	Evaluations	Results			
					Spatio-temporal variables	Motor symptoms	Kinematic variables	Balance
Higuchi et al. 2020 [71]	End-effector: UPS-PD (Unplugged Powered Suit)	5 patients (2-3)	1 session	With UPS-PD	↗	na	na	na
Jain et al. 2020 [72]	Wearable: Ankle exoskeleton	1 patient (2.5)	3 sessions (4 weeks, 30 min)	With exoskeleton	na	na	na	↗
Choi et al. 2020 [56]	End-effector: Morning Walk	8 patients (na)	24 sessions (5x/w for 5w, 30min)	5th week	na	↗	na	na
Yun et al. 2021 [63]	Treadmill: Walkbot	11 patients (2,5-3)	12 sessions (3x/w for 4w, 45min)	4th week 8th week	↗ N	na	na	↗ M

↗: Improvements when there is no follow-up, **M**: Improvements maintained at follow-up, **N**: Improvements not maintained at follow-up, **na**: Not available.

in studies investigating the effect of robotic gait assistance on motor symptoms ([45, 50, 57]). An increase of the Functional Independence Measure, particularly for the motor component, was also demonstrated ([58]).

Some studies reported improved balance ([63, 72]). In contrast to articles that generally use basic tests to assess balance as described in Section 2.1.2, one of the studies analyzed this improvement by finding a reduced displacement of the anteroposterior pressure centre ([72]).

Only a few studies have analyzed longer-term outcomes of training sessions in this category. One study with a 7-week follow-up observed lasting improvements in spatio-temporal variables, but not in motor symptoms ([57]). Another, with a 1-month follow-up, found lasting improvements in balance, but a return to baseline in spatio-temporal variables at the end of the follow-up period ([63]).

Other improvements were also observed in walking abilities and metrics, including a reduction in the metabolic cost of walking ([72]), a decrease in the required body weight support and guiding force ([58]) as well as an increase in Functional Ambulation Category scale ([56]).

To conclude, eight studies focused solely on gait analysis. The use of robotic walking assistance for Parkinson’s disease patients appears to improve several gait variables. However, only two studies investigated the longer-term effects of these training sessions and not all the improved metrics were maintained.

2.2.2 Comparison between robotic-assisted gait training and other therapies

All the articles discussed in this section are summarized in Tables 2.2 which also include additional experimental details such as the number of patients or the number of training sessions.

In studies comparing robotic-assisted gait training, treadmill training and physiotherapy, several devices are used, including the Lokomat, the Walkbot-S, the G-EO but also the GT1, the SMA exoskeleton and the wearable EksoGT.

Multiple studies have demonstrated positive effects on spatio-temporal gait variables. Specifically, significant enhancements in gait velocity ([48, 49, 53, 67]), gait velocity under physical double-task ([65]), cadence ([48, 53]), step length ([48]), walking ability ([47]), and stride length ([53, 48]) have been reported favoring robotic-assisted gait training over physiotherapy or treadmill training. However, some studies have found significant improvement in gait velocity ([32, 66]) but no significant differ-

ence between the robotic-assisted gait training group and treadmill training. In some papers, greater improvements have even been observed in the group that followed conventional therapy ([59]).

Several studies showed better improvement, *i.e.* a decrease of the value, in the MDS-UPDRS part III score, which indicates a decrease in motor symptoms, in robotic-assisted gait training compared to treadmill training or physiotherapy groups ([53, 59, 67, 65]). However, some studies have concluded an improvement for each group analyzed, with no significant difference between the groups ([32, 47, 48, 49, 54]). The motor part of the Functional Independence Measure was also reported as improved no matter the group the patients were in ([59]). In contrast, other studies found no significant changes in the MDS-UPDRS part III score ([69]).

Out of the available studies, only five included follow-up assessments beyond the completion of treatment. Two studies conducted measurements several weeks after therapy and observed that the improvements were sustained only in the robotic-assisted gait training group ([47, 53]). Conversely, other studies demonstrated that improvements were maintained not only in the group using robotic gait assistance but also in the treadmill training or physiotherapy groups ([32, 54]). Additionally, one study found no significant difference between the baseline and one-month post-treatment values ([65]).

Several studies have examined the impact of robotic-assisted gait training on patients' balance. Specifically, three studies ([47, 54, 65, 67]) reported an increase in balance scores. In one of these studies, the improvement was found to be significantly better than that achieved through treadmill training ([54]), while another study observed this increase exclusively in the robotic-assisted gait training group ([67]). Lastly, one study did not show any significant improvement in balance ([69]).

Some studies have shown that robotic-assisted gait training leads to better outcomes than conventional physiotherapy training ([53, 54, 67, 69]) and than treadmill training ([48, 49, 66]). However, several studies did not demonstrate that robotic-assisted gait training was superior to treadmill training ([32, 59, 65]), although it was found in two of these studies that it improved the MDS-UPDRS part II score more effectively than treadmill training ([65]) and that it implied a greater decrease in the MDS-UPDRS part III score and MDS-UPDRS total score compared also to treadmill training ([59]). The authors tried to explain this through multiple reasons. On the first hand, according to Picelli et al. [53], robotic-assisted gait training may be superior to physiotherapy, particularly because it involves repeating movements that replicate a correct gait cycle. This repetition could provide external proprioceptive cues to gait function, reinforcing the neural circuits involved in gait rhythm. Furthermore, this difference could also arise from the fact that physiotherapy

Table 2.2: Overview of robotic gait assistance used for Parkinson’s disease focusing on comparison between robotic gait assistance and other physical therapies such as treadmill training (TT) and physiotherapy (PT).

Source	Device	Patients (H&Y)	Duration	Evaluations	Results				
					Spatio-temporal variables	Motor symptoms	Balance	RAGT over TT	RAGT over PT
Picelli et al. 2012 [53]	Treadmill: GT1	36 patients (2.5-3)	12 sessions (3x/w for 4w, 45 min)	4th week 8th week	↗ M	↗ M	na	na	✓
Carda et al. 2012[32]	Treadmill: Lokomat	30 patients (<3)	12 sessions (3x/w for 4w, 30 min)	4th week 16th week 28th week	↗ M	≡	na	✗	na
Picelli et al. 2013 [54]	Treadmill: GT1	60 patients (3)	12 sessions (3x/w for 4 w, 45 min)	4th week 16th week	↗ M	↗ M	↗ M	✗	✓
Sale et al. 2013 [49]	End-effector: G-EO system	20 patients (2.5-3)	20 sessions (5x/w for 4w, 45 min)	4th week	↗	↗	na	✓	
Galli et al. 2016 [48]	End-effector: G-EO system	50 patients (1-4)	20 sessions (5x/w for 4w, 45 min)	4th week	↗	↗	na	✓	na
Furnari et al. 2017 [47]	Treadmill: Lokomat	38 patients (2-3)	24 sessions (6x/w for 4w, 1 hour)	4th week 12th week	↗ M	↗ M	↗ M	na	✓

↗: Improvements when there is no follow-up, ≡: Same as baseline, **M**: Improvements maintained at follow-up, **na**: Not available.

Table 2.2: Overview of robotic-assisted gait training (RAGT) used for Parkinson’s disease focusing on comparison between robotic-assisted gait training (RAGT) and other physical therapies such as treadmill training (TT) and physiotherapy (PT) (continued).

Source	Device	Patients (H&Y)	Duration	Evaluations	Results				
					Spatio-temporal variables	Motor symptoms	Balance	RAGT over TT	RAGT over PT
Fundarò et al. 2019 [59]	Treadmill: Lokomat + virtual reality	20 patients (2-3)	20 sessions (5x/w for 4w, 30 min)	4th week	≡	↗	na	✗	na
Kawashima et al. 2022 [67]	Wearable: Stride Management Assist (SMA) exoskeleton	12 patients (2-4)	10 sessions (on 3 months, 30 min)	At the first six sessions	↗	↗	↗	na	✓
Kim et al. 2022 [65]	Treadmill: Walkbot-S	44 patients (2.5-3)	12 sessions (3 x/w for 4w, 45min)	4th week 8th week	↗ N	↗ N	↗ N	✗	na
Gryfe et al. 2022 [69]	Wearable: Keeogo Rehab™ exoskeleton	40 patients (1-4)	16 sessions (2x/w for 8w, 1 hour)	8th week	↗	↗	↗	na	✓
Kim et al. 2023 [66]	Treadmill: Walkbot-S	31 patients (2.5-3)	12 sessions (3x/w for 4w, 45min)	4th week	↗	↗	na	✓	na

↗: Improvements when there is no follow-up, ≡: Same as baseline, **N**: Improvements not maintained at follow-up, **na**: Not available.

treatment involved exercises performed in a non-physiological posture (*i.e.* lying down on a clinical bed) which, unlike robotic-assisted gait training, did not provide a walking model that would enable improvement in motor strategies [53]. On the other hand, Carda et al. [32] discussed why robotic-assisted gait training has not been showed superior to treadmill training in their study. One of their hypothesis is that the limited speed of the Lokomat (3.2 km/h) may have prevented patients from reaching higher exercise intensities, whereas the treadmill did not impose such a limitation. The therapeutic effects of the Lokomat on more severely affected patients may have been concealed by this inability to push the patients further. Another assumption is that the attention required for performing exercises with the Lokomat was lower compared to the treadmill, as the Lokomat provides support to the patient [32].

The protocols described in the two articles below have not been implemented yet and are therefore not included in Tables 2.2. Romanato et al. [68] introduced a wearable EksoGT, which they plan to compare with functional kinematic therapy, to investigate the impact of gait training on the relationship between brain activity and motor alterations caused by Parkinson’s disease. They assume that EksoGT training improves gait quality and balance more consistently than the other therapy [68]. Similarly, Kang et al. [64] aim to investigate the effects of Walkbot-S versus treadmill training on walking velocity, two-task interference, balance function, fall risk, and disease severity. The robotic-assisted gait training group in their study receives an auditory cue and visual feedback. Both protocols have a one-month follow-up, which is significant given the limited number of studies in this area [48, 68].

Eleven comparison papers that evaluated the effectiveness of robot-assisted gait training as compared to treadmill training and physiotherapy were identified. Studies concluded that robotic-assisted gait training can improve spatio-temporal gait variables, walking ability, motor symptoms, and balance in patients with Parkinson’s disease. Some studies found that robotic-assisted gait training did not necessarily lead to better outcomes than other physical therapies, as concluded in the review by Alwardat et al [75]. However, other studies, as reported by Smania et al. [76], found better improvements with robotic-assisted gait training than with the other therapies. It is important to note, however, that the follow-up periods of these studies were limited, and therefore, definitive conclusions cannot be drawn.

2.2.3 Freezing of gait

All the articles discussed in this section are summarized in Table 2.3, which also includes additional experimental details such as the number of patients or the number of training sessions.

Studies focusing on FOG symptom have made extensive use of robots such as the Lokomat, the GT1 or the G-EO end-effector system. Only one experiment used a portable hip-knee exoskeleton that enabled locomotion on various terrains.

Most studies have shown improvements in spatio-temporal variables through an increase in gait velocity ([51, 55, 60, 61, 62]), stride length ([60, 61]), step length ([55, 60, 62]) and cadence ([61]). Furthermore, a decrease in stride and swing time has been demonstrated ([60]). In conclusion, this shows that patients affected by FOG episodes present also gait abnormalities even in the absence of them ([60]). The results of the various gait measurements are therefore generally positive.

The results regarding motor symptoms are more mixed. While some studies have reported an improvement in the MDS-UPDRS total and Part III scores ([52, 60, 61]), two studies, on the other hand, did not observe any significant improvement in this regard ([55, 62]).

Papers that have focused on the effect of robotic rehabilitation on FOG symptom have generally shown a decrease in the occurrence of FOG episodes ([51, 60, 61]). Concerning their severity, an improvement of the FOG Questionnaire score has been revealed in majority of studies ([52, 55, 60, 62]). Ustinova et al. [61], as well as Barbe et al. [62], have attempted to explain these improvements as follows. The symptom of FOG is known to be improved through the use of visual or auditory cues and biofeedback, as presented in Section 1.4.2. Even though the Lokomat does not provide cues per se, it still acts as an external pacemaker by providing rhythmic input. In this way, the Lokomat's treadmill could contribute to the improvement of walking and indirectly reduce FOG episodes. Moreover, matching the steps to the Lokomat's rhythm generally leads to increased step length and walking speed. This, in turn, would also have an impact on reducing FOG episodes, which are often characterized by smaller step lengths.

Only two studies have evaluated the effects of therapy after several weeks. The first study reported a decline in the improvements observed in the MDS-UPDRS part III score at 15-week follow-up. However, improvements in spatio-temporal variables were still retained ([61]). On the other hand, the second study demonstrated that the therapeutic effect on FOG severity faded away at the six-week follow-up ([62]).

Two studies in this category assessed the impact of robotic gait assistance on balance. Both studies reported a significant improvement in balance ([51, 55]). Additionally, FOG episodes are frequently linked to a fear of falling. This fear was also evaluated and demonstrated a significant decrease, leading to a positive impact on everyday activities and quality of life ([55]).

Table 2.3: Overview of robotic gait assistance for patients affected by freezing of gait.

Source	Device	Patients ($H\&Y$)	Duration	Evaluations	Results				
					Spatio-temporal variables	Motor symptoms	FOG occurrence	FOG severity	Balance
Lo et al. 2010 [60]	Treadmill: Lokomat	4 patients (-)	10 sessions (2x/d for 5w, 30 min)	6th week	↗	na	↗	↗	na
Ustinova et al. 2011 [61]	Treadmill: Lokomat	1 patient (3)	6 sessions (3x/w for 2w, 25-40 min)	2th week 17th week	↗ M	↗ M	↗ M	na	na
Barbe et al. 2013 [62]	Treadmill: Lokomat	3 patients (1.5-4)	12 sessions (3x/w for 4w, lasting 30 min)	4th week 10th week	↗	≡	—	↗ N	na
Pilleri et al. 2015 [55]	Treadmill: GTI	18 patients (2.5-4)	15 sessions (5x/w for 3w, 30 min)	4th week	↗	≡	↗	↗	↗
Andrenelli et al. 2018 [51]	End-effector: G-EO	9 patients (na)	12 sessions (3x/w for 4w)	4th week	↗	na	↗	na	↗
Capecci et al. 2019 [52]	End-effector: G-EO	96 patients (≥ 2)	20 sessions (5x/w for 4w, 45min)	4th week	↗	↗	↗	↗	na

↗: Improvements when there is no follow-up, ≡: Same as baseline, **M**: Improvements maintained at follow-up, **N**: Improvements not maintained at follow-up, **na**: Not available.

Furthermore, a new device was presented by Changcheng et al. [73] in 2022. This is a robotic exoskeleton for the hips and knees. It has not yet been tested on patients, only on one healthy subject, so it was not included in Table 2.3. However, it is interesting to talk about it since its purpose is to relieve FOG episodes. Indeed, a FOG episode can be characterized by smaller steps and thus by a reduction of the normal gait cycle as presented in Section 1.5. If this reduction reaches 35%, then the device could be activated and help overcome the FOG episode.

In summary, a number of six papers on the effect of robotic rehabilitation with patients displaying FOG episodes have shown positive outcomes in terms of gait metrics, balance, and a decrease in the occurrence and severity of FOG episodes. The review of Alwardat et al. [38], written in 2019, states that due to the limited number of studies conducted and the limitations due to follow-up, it is difficult to draw definitive conclusions. However, robotic gait assistance seems to be a promising approach. Further research is needed to evaluate its long-term benefits [38].

2.3 Conclusion

To conclude, this state of the art illustrates that robotic gait assistance can improve walking in patients with Parkinson’s disease, although some authors do not seem to consider it superior to other more commonly used physical therapies. Nevertheless, the results of these studies seem promising. Future studies should also focus on a longer and more systematic follow-up, in order to analyze the long-term effects. Finally, this state of the art review highlights the absence of robots that enable on-demand assistance for patients. However, FOG episodes are an episodic symptom where it is necessary to assist the affected person only when it occurs. Therefore, the next chapter is dedicated to the search for methods to detect FOG episodes so that subsequently, this detection can facilitate the implementation of robotic assistance only when necessary.

Chapter 3

Detection of freezing of gait episodes

In this chapter, a comprehensive yet non-exhaustive overview of the methods used to detect FOG episodes is provided. To reach the total of 10 methods presented, they were identified and grouped based on a literature review on the subject written by Pardoel et al. [77]. These methods range from the simplest such as self-detection and visualisation to more complicated methods taking into account gait parameters and based on different types of cues which are explained below [77]. Methods that involved equipment too specific and not applicable to this work were excluded. For information, each method presented, unless specified, may only require signals from one leg. The choice of this leg is not indicated as specific for the methods described.

Firstly, general information on the statistical analysis carried out to obtain the algorithm's efficiency is provided. Each method is then described in detail. For these descriptions, four aspects are presented in order to have a common basis of comparison for these methods, summarized in Table 3.4. In first, the equipment and signals used are described, as well as if these methods can be used in real time and if they use computations in the time or frequency domain. The following presentation of the methods is based on their respective domains. Secondly, the experimental protocol(s) of the corresponding reference article(s) is briefly explained. Thirdly, the method algorithm is described in details. Finally, the performances reported by the article are mentioned. In terms of performance, all the methods presented below base their criteria on the comparison between the number of FOG episodes identified by the neurologists on the videos and the number of FOG episodes detected by the method. The two main performance parameters, specificity and sensitivity, are listed in the summary Table 3.4.

3.1 Statistical analysis

To perform the statistical analysis of the performance of the algorithms described in the following sections, the computation of sensitivity and specificity is used.

3.1.1 Sensitivity

Sensitivity is a commonly used metric to assess the ability of an algorithm to effectively detect positive cases. In other words, sensitivity is the probability of detecting a true case. Thus, high sensitivity indicates that true positives (TP) are correctly identified and the number of false negatives (FN) is minimized [78]. Sensitivity is calculated as follows:

$$Sensitivity(\%) = \frac{TP}{TP + FN} \quad (3.1)$$

In the context of this work, sensitivity is therefore the ability to effectively detect FOG episodes.

3.1.2 Specificity

Specificity is a complementary measure to sensitivity and assesses the ability of an algorithm to effectively detect negative cases. A high specificity indicates that true negative (TN) cases are correctly identified, and therefore the number of false positives (FP) is minimized. In other words, it indicates the discriminative power of the method [78]. Specificity is calculated as follows:

$$Specificity(\%) = \frac{TN}{TN + FP} \quad (3.2)$$

In the context of this work, specificity is the ability to report effectively the absence of FOG episodes.

3.1.3 Compromise

In general, when deciding on the best overall performance, a compromise is necessary. In many cases, as one performance value improves (such as sensitivity), the other tends to decrease (such as specificity). The aim is therefore to maximize both values as far as possible.

3.2 Frequential domain

This literature review has identified many ways to detect the occurrence of FOG episodes in the frequency domain. The methods that can be used in real time are presented before those that cannot.

3.2.1 Freeze Index

The Freeze Index is a **frequency-based**, possibly **real time**, method using inertial measurements units (IMUs) or accelerometers to acquire linear acceleration of joints in the frontal plane. The most effective results are obtained when sensors are positioned on the lateral side of the shanks according to Moore et al. [79].

Generally, the protocols used in the papers that implement this method consist of a TUG test, 180° or 360° turns, simulations of daily activities such as getting a glass of water from across the room and passing through narrow doorways [79, 80, 81, 82].

This solution is widely used and can be computed by comparing two bands, the locomotion one (0-3 Hz) and the little higher freeze one (3-8 Hz). The Freeze Index is computed using the following formula [83] :

$$FI = \frac{A_{freeze}^2}{A_{loco}^2} \quad (3.3)$$

where A_{freeze} is the area under the power spectrum of the freeze band, called the power in freeze band and A_{loco} is the area under the power spectrum of the locomotion band, called the power in the locomotion band.

In the equation 3.3, the square of these area is used because it allows to compensate for high frequency harmonics caused by normal walking and that could be wrongly associated to a FOG episode [83].

Figure 3.1 illustrates how the Freeze Index is obtained. The linear acceleration signal from one IMU placed on the shank is obtained. A 5-second sliding window centered at each point in time of the acceleration data is used, as illustrated in Figure 3.1A. The passage in the frequency domain, which consists in computing the power spectrum of the signal by the fast fourier transform (FFT) on the window, makes it possible to highlight two different bands representing a range of frequencies. As described by Moore et al. [80], the so-called “locomotio” band is characterized by walking events (stride, steps, ...) with frequencies not exceeding 3 Hz. However, the lower limb tremors that happen particularly during a FOG episode occur at frequencies between 3 and 8 Hz, which is why this particular band is called the

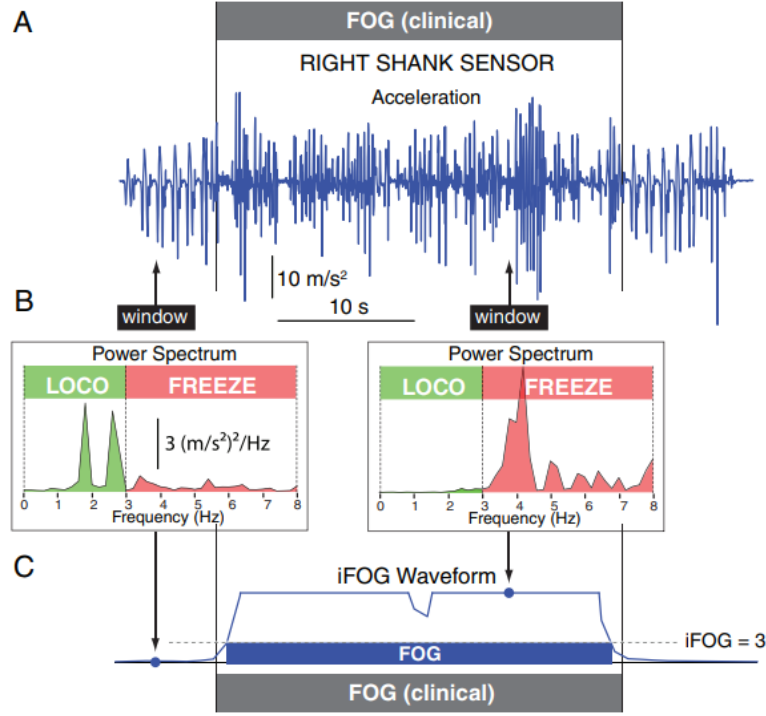


Figure 3.1: (A) Vertical linear acceleration data from the right shank in the frontal plane; (B) Acceleration data is analyzed using a 5-second sliding window centered in each point, and a power spectrum is computed for each window; (C) Index of FOG waveform, with a threshold set to three here [80].

“freeze” band. The difference between the two bands can be observed in Figure 3.1B with normal gait on the left and FOG on the right, where the power in the locomotion band has totally disappeared. The Freeze Index is then obtained by equation 3.3. If the index exceeds a pre-set threshold, a FOG event is declared. The FOG waveform in Figure 3.1C is obtained by dragging the window to cover the entire duration of the signal [80]. It is important to note that the choice of window width is important. Indeed, increasing it improve the specificity of the detection, but it could also smooth out the FOG events which would be shorter, thus reducing the sensitivity [80]. A window of 10s is defined as the upper limit by Moore et al [80]. In the paper by Bächlin et al. [81], a window of 4s and a step of 0.5s were used. In terms of thresholds, both global and patient-specific thresholds were tested, ranging from 1.32 to 4.4. Patient-specific thresholds have shown improvements in the algorithms developed in several papers [79, 80, 81] while some found no change [82].

Regarding performances, since the Freeze Index is a rather widely used method, many papers present different results. Table 3.1 lists some of them. Note that performances vary depending on whether the method is intended to be used in real time and where the IMUs are placed. Indeed, in 2013, Moore et al. [80] conducted tests and recommended several configurations, including one with an IMU at the

shank level and another with an IMU at the lower back. They found that using only the shank sensor produced similar FOG measurements to those obtained with an approach involving seven IMUs, placed on the feet, shanks, thighs, and lower back [79, 80, 81, 82].

Table 3.1: *Performance indices for the Freeze Index according to several publications.*

<i>Source</i>	<i>IMU placement</i>	<i>Sensitivity</i>	<i>Specificity</i>	<i>Real Time</i>
Moore et al. 2008 [79]	Shank	89.1%	90%	No
Bächlin et al. 2010 [81]	Shank	73.1%	81.6%	Yes
Moore et al. 2013 [80]	Shank	86.2%	66.7%	No
Moore et al. 2013 [80]	Lower back	86.8%	82.4%	No
Zach et al. 2015 [82]	Lower back	75%	76%	No

To go further in the use of this method, it is often combined with other tools such as the root mean square of acceleration [84] or spectral coherence features [85]. For example, Delval et al. [86] have described a method in which they use the Freeze Index in combination with another analysis (the sinusoidal wavelet transform, which, according to the authors, improves the detection time of frequency power changes) and with measures of kinematic parameters such as step duration and mean and minimum step amplitude. Through comparison with the video tapes and signals received during the experiments, they found that increased power of high frequencies or reduced step amplitude and duration allow the detection of subtler FOG episodes [86].

3.2.2 Continuous Wavelet Transform

The wavelet transform technique operates in the **frequential domain** and could be used **in real time**. Rezvanian et al. [87] evaluated this method using sagittal linear acceleration signals from 3D accelerometers placed on the anterior-posterior axis of the shanks [87].

The experience consisted in different walking conditions, *i.e.* random walk with several stops and 360° turns, walking simulating activities of daily living and walking back and forth in a straight line [87].

The FFT is often used to move into the frequency domain, as it is the case for the previous method. Unfortunately the smallest sampling window possible with this is too large for short duration FOG episodes. Consequently, the CWT, which provides information in terms of temporal and frequency components, could detect episodes of FOG (especially of short duration) more accurately. This makes it, indeed, possible to determine a transient change in the signal more precisely. For best performance,

a window size of 4s and a step size of 0.5s were chosen [87].

The continuous wavelet transform (CWT) is applied on the shank sagittal linear acceleration signal in order to extract some features able to indicate the presence of FOG [87]:

$$C(s, \tau) = \int_0^{window} a(t) \Psi^* \left(\frac{t - \tau}{s} \right) dt \quad (3.4)$$

where $a(t)$ is the acceleration signal and $\Psi^* \left(\frac{t - \tau}{s} \right)$ is the conjugate of mother wavelet which is shifted in temporal domain (τ) and scaled (s) in frequency domain. This way, the mother wavelet can be transferred to temporal domain and compressed or stretched [87].

The pseudo frequency, F_s , which corresponds to a specific scale s is computed as [87]:

$$F_s = \frac{F_c}{s\Delta} \quad (3.5)$$

where F_c is the center frequency of the mother wavelet and Δ is the sampling time.

The locomotor component is computed by [87]:

$$LC(\tau) = \sum_{i=0}^5 C \left(s = \frac{F_c}{0.5(1+i)\Delta}, \tau \right) \quad (3.6)$$

And the freeze component by [87]:

$$FC(\tau) = \sum_{i=5}^{15} C \left(s = \frac{F_c}{0.5(1+i)\Delta}, \tau \right) \quad (3.7)$$

where i selects the frequencies corresponding to the locomotor or freeze component. Each component is therefore computed as the sum of the CWT coefficient values of the scale ranges corresponding to each translation time τ [87].

Finally, the following ratio is computed [87]:

$$R(\tau) = 100 \frac{LC(\tau)}{LC(\tau) + FC(\tau)} \quad (3.8)$$

The average of $R(\tau)$ over the sampled window is used in order to define the FOG index. The principle is thus almost the same as the Freeze Index described previously, with the difference that this method uses the CWT instead of the FFT [87].

Figure 3.2 shows how this method is used in a practical way. On Figure 3.2A, the shank sagittal linear acceleration signal is represented, with the FOG episode (detected by the neurologists on the video recording) indicated by the dotted red

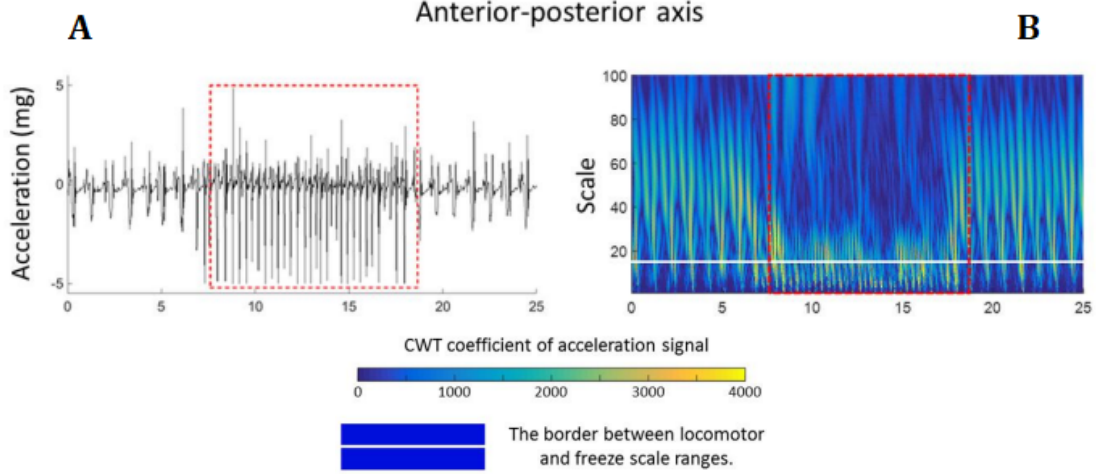


Figure 3.2: (A) Shank sagittal linear acceleration signal; (B) CWT coefficient values [87].

square. On Figure 3.2B, the CWT plot is shown together with a white line at scale 15.2 representing the frequency at 3 Hz. This delineation therefore makes the difference between the upper scale ranges representing the locomotion band (0.5-3 Hz) and lower scale ranges representing the freeze band (3-8 Hz). From the figure, it can be observed that higher CWT values indicate normal walking, whereas during freezing episodes, these values drop considerably [87].

The paper of Rezvanian et al. [87] compares different sensors locations, *i.e.* the lower back, thighs or shanks, and sensors orientations. They evaluated the method with the frontal, sagittal and transverse linear acceleration for each sensor placement and showed that those placed on the shanks in the sagittal axis give the best results as shown in Table 3.2 [87].

Table 3.2: Performance indexes for different location of the sensor for the wavelet transform method [87].

<i>Sensor Location</i>	<i>Sensitivity</i>	<i>Specificity</i>
Shank	84.9%	81%
Thigh	73.6%	79.6%
Lower back	83.5%	67.2%

3.2.3 Anomaly Detection Technique

The anomaly detection technique is another method that takes place in the **frequency domain** and can be used **in real time**. The knee sagittal linear acceleration signal is used to identify the occurrence of FOG episodes [88].

Pham et al. [88] conducted a test of their method on a freely available dataset that included signals from 10 advanced patients with Parkinson's disease experiencing regular FOG episodes. Patients were required to perform three walking tasks, each lasting 10 to 15 minutes [88].

An anomaly is defined as data that differs from previously observed patterns. From the first few seconds of the initial signal, the algorithm learns what normal behaviour is. In order to detect anomalies (in this case, FOG episodes), the patient's behaviour must therefore be normal at the time the data acquisition starts [88].

The data are analyzed window by window on the whole signal. For best performance, a window size of 0.6s and a step size from 0.6s to 0.7s were chosen. Each dataset is compared to the last window defined as normal behaviour. This comparison is based on spectral coherence. If this coherence is low, then the behaviour is identified as potentially abnormal [88].

To achieve this identification, an acceleration indicator is defined as follows [88]:

$$S_{AC} = \text{sgn}((X - (\bar{X} - \sigma))_+) \quad (3.9)$$

where X represents the acceleration dataset, σ and $\bar{X}$ the standard deviation and mean of X respectively, $\text{sgn}(\cdot)$ the sign function and the function $(a)_+$ returns 0 if a is less than 0 or the value of a if it is equal to or higher than 0 [88].

Two discrete signals (x and y) have a spectral coherence, C_{xy} defined as [88]:

$$C_{xy} = \frac{P_{xy}(\omega)}{\sqrt{P_{xx}(\omega)P_{yy}(\omega)}} \quad (3.10)$$

where the frequency is represented by ω , the power spectrum of the x -signal by P_{xx} and the cross power spectrum of the two signals by P_{xy} . If C_{xy} is small, it means that the correlation between the test and the non-freezing data is low, whereas if C_{xy} is quite large, it means that the correlation is high [88].

The score of spectral coherence, S_{speco} , is computed for a defined window as [88]:

$$S_{speco} = \begin{cases} 1 & \text{if } N_{peak} = 0 \\ 0 & \text{otherwise.} \end{cases} \quad (3.11)$$

where N_{peak} is the number of peak in $C_{xy}(\omega)$ that are greater than a specified correlation threshold θ_{speco} [88].

To identify a FOG event, the output of the algorithm, computed as $S_{AC}S_{speco}$, must be zero. Otherwise, it is considered to be a normal walk [88].

Performances depend on the sensors location as described in Table 3.3 [88]. This table, which compares average performances, includes two additional parameters compared to the tables of the other methods: the accuracy, defined as the closeness of a measured value to the true value, and the F_1 score, obtained by [88]:

$$F_1 = \frac{2TP}{2TP + FP + FN} \quad (3.12)$$

where TP is true positive which means that the FOG is well recognized, FP is false positive, means that a FOG is detected when there is none, and FN is false negative means that the algorithm does not detect the FOG while there is one.

Regarding performances, it can be noted that the ankle, knee, and hip positions give fairly similar results. However, the knee position has the best sensitivity and has a slightly higher accuracy and F_1 score than the ankle sensor.

Table 3.3: *Performance indexes for different location of the sensor for the anomaly detection technique [88].*

<i>Sensor</i>	<i>Sensitivity</i>	<i>Specificity</i>	<i>Accuracy</i>	<i>F1-score</i>
Ankle	86%	94%	91%	71%
Knee	88%	94%	92%	72%
Hip	87%	94%	92%	72%

3.2.4 Entropy

The method using entropy in the **frequency domain** requires the use of accelerometers and gyrometers. This method **cannot be used in real time**. According to Tripoliti et al. [89], four accelerometers can be placed on both wrists and both ankles (front of the leg), then two accelerometers/gyrometers can be placed on the chest and waist. They used the linear acceleration and angular velocity in each axis of each sensor [89].

Their protocol consisted of three tasks: lying down on a bed, getting out of bed and sitting on a chair, and getting up from this chair to perform typical activities of daily life. These activities are walking 5m, opening and closing a door, opening a door and walking 10m, walking back to the room, stopping to drink some water in a glass and returning to the chair [89].

For data preprocessing, a bandpass filter (2-10 Hz) is used. To analyze the entropy of the signal, the authors used a sliding window with a length of 1s and an overlap of 0.5s. These values were chosen in order to be sure to detect all FOG episodes as the

shortest FOG episode was 3s [89]. The calculation of the entropy is as follows [89]:

$$e_i(j) = \sum_{n=w(j)-f_s/2}^{w(j)+f_s/2} p(x_i(n)) \log(p(x_i(n))) \quad (3.13)$$

where $e_i(j)$ is the entropy of the j th window of the i th signal, f_s is the sampling frequency, $w(j)$ is the time position of the window used, $x_i(n)$ is the n th sample of the i th signal and $p(x_i(n))$ is the probability of that sample [89].

In order to detect FOG episodes, Tripoliti et al. [89] compared four classification algorithms: random forest, random trees, decision trees and naive bayes. The reader is referred to [89] for more details about these methods, which are beyond the scope of this work.

Random forests with the combination of all sensors was recognized as the best classifier. Its performance, in terms of sensitivity, specificity and accuracy, is 81.94%, 98.74% and 96.11% respectively [89].

3.2.5 Power spectral distribution analysis

Power spectral distribution analysis is a method in the **frequency domain** that **cannot be used in real time**. It uses IMUs signals. The paper written by Zabaleta and colleagues [90] showed that heels sagittal linear acceleration and angular velocity give better performance [90].

The protocol of this method consisted of a walking course, with a chair for sitting and standing, turns, zig-zags, doorways, and obstacle avoidance to trigger FOG episodes [90].

The acquired signals are transformed using the FFT to obtain their power spectral distributions. For this reason, this technique induces a slight delay due to the transformation of the signal. This delay is reflected throughout the process, increasing the number of false negatives at the beginning of FOG episodes and increasing the number of false positives at the end of them. The choice of sliding window used to calculate the FFT on the time domain signal allows to determine the length of the delay. To achieve the shortest delay while maintaining accurate detection of the FOG episode, the authors used a 3s sliding window [90].

Using the power spectral distribution graph, this algorithm decides, with the help of a linear classifier, in which group the signal falls, *i.e.* “normal gait” or “freezing gait”. The threshold that separates the two states depends on each person [90]. Concerning performances, none were clearly stated in the paper. However, they

tried using six accelerometers and gyroscopes placed on the thighs, shanks and heels. They concluded that the sensor placed on the heels would give better results [90].

3.3 Temporal domain

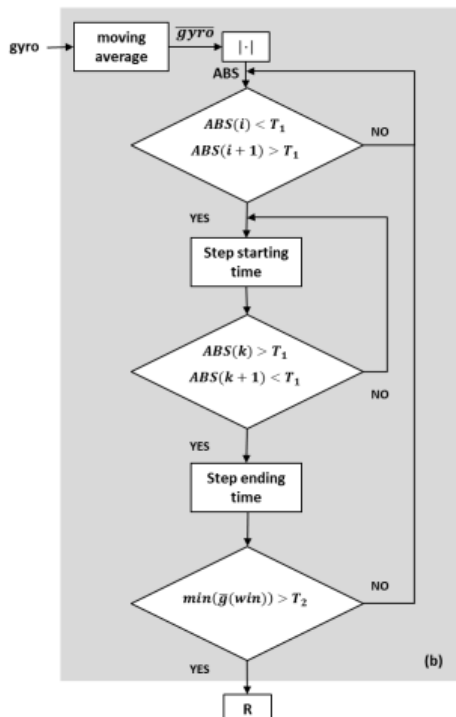
All the methods presented below base their calculations on the time domain. As for the frequency domain methods, the presentation starts with the methods that can be implemented in real time and ends with those that cannot.

3.3.1 Surface electromyography-based method

This method is a **real time** method in the **time domain**. To perform the analysis, the muscle activity of the tibialis anterior muscle as well as the shank sagittal angular velocity are required [91]. It therefore requires the presence of surface electromyography (sEMG) and IMUs, combined in a single sensor, placed at the shanks of the subjects at the level of the tibialis anterior muscle.

The experiment consisted in a 7m TUG test; the patient starts sitting in a chair, stands up, walks 7m, turns around and sits back in the chair. The experiment recreated a domestic environment with obstacles, passage reductions such as approaching doors or narrow corridors, all of which could cause FOG episodes [91].

The electrodes of the sEMG are placed on the tibialis anterior muscle according to standardized international criteria. The recording of activity of this muscle is quite tolerant of the placement of the electrodes, as it is a large muscle bundle. A wrong placement could only decrease the power of the recorded signal. The raw signals from the sEMG are conventionally pre-processed according to the literature [91].



Firstly, the absolute value of the average angular velocity, ABS , is computed. Next, a step time window is defined as well as a threshold T_1 which is compared to ABS for each index value i ($i = 1$ and $N =$ the last acquired sample). Once the threshold is passed, the step starting time is retained [91], as detailed in Figure 3.3.

The index $k = i + 1$ is used to calculate a new ABS . If it is below the threshold, it announces the step ending time. The time between the step start and the step end defines the step window.

Figure 3.3: *sEMG method algorithm [91]*

A negative threshold T_2 is introduced. The objective of this new threshold is to be able to ignore the stance phase that was inducing detection errors in regular steps. Thus, if the minimum value in the stance phase is less negative than T_2 , the step is classified as irregular and the R index is computed only in this case. Indeed, the angular velocity trace is less negative when there is a FOG than when the step is regular [91].

Finally, the ratio R is computed by the algorithm as following [91]:

$$R = \frac{\max(ABS)}{sEMG|_{t=\max(ABS)}} \quad (3.14)$$

A threshold equal to three is defined for the R index, below which the patient is said to experience a FOG episode. It is interesting to note that this algorithm takes into account resting time, recognize it and therefore does not calculate the R index for that time. Furthermore, Mazzetta et al. [91] improved this algorithm in order to differentiate between “shuffling” and “trembling in place” FOG phenotypes, the second one being a big risk of falling. The reader is referred to their paper for details.

Figure 3.4 illustrates how the method is used. When the R ratio falls below the threshold, FOG episode is detected. Moreover, during a well-detected rest period, the R ratio is not computed for this period [91].

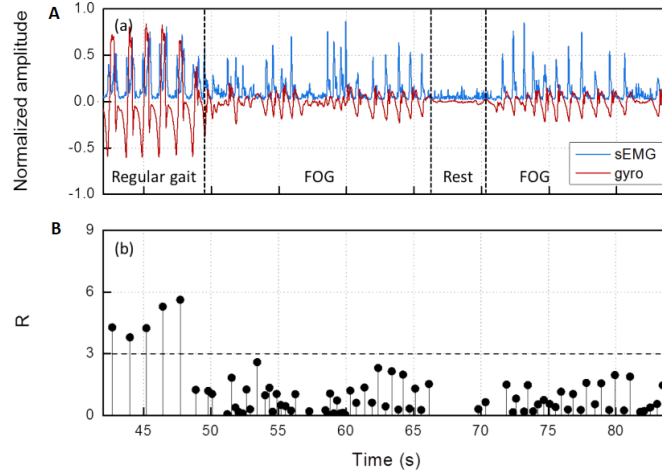


Figure 3.4: (A) An exemple of $sEMG$ and angular velocity traces is represented; (B) Corresponding R values on the same time scale.

The performances, in terms of sensitivity and specificity are 98% and 95% respectively [91].

3.3.2 K-index

This method is a **real time** method in the **temporal domain**, presented by Suppa et al. [92]. It requires both frontal and sagittal shanks angular velocities, acquired with IMUs.

Concerning the experimental protocol, the authors analyzed the gait of patients with Parkinson's disease in a modified 3m TUG test involving a doorway, which is meant to represent the everyday home environment [92].

This detection method is based on the variation of the angle β , shown in Figure 3.5. As an input, β is derived to find the angular velocities ω_{right} and ω_{left} . After taking the low-pass signal of these velocities, a variable K_t is computed as follows [92]:

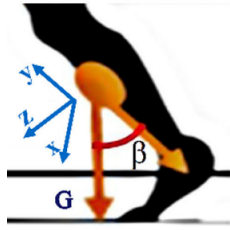


Figure 3.5:
Sensor reference
system [92]

$$K_t = (1 - \alpha)\omega_t + \alpha k_{t-1} \quad (3.15)$$

where $\alpha = (1 + 2\pi \frac{f_{cutoff}}{f_s})^{-1}$, ω_t is the right or left angular velocity and k_{t-1} is the value of k at the previous step. The index K is defined as the sum of K_{right} and K_{left} .

False positives can occur during turns, so the authors introduced the threshold T_{turn} and an index K_{turn} defined as follows [92]:

$$K_{turn} = \text{lowpass}(|\omega_y|) \quad (3.16)$$

$$K' = K + K_{turn} \text{ if } K_{turn} > T_{turn} \quad (3.17)$$

$$K' = K \text{ if } K_{turn} \leq T_{turn} \quad (3.18)$$

The particularity of this algorithm is the last index defined, K_{swing} , which differentiates between leg tremors during body swinging and during FOG episodes, defined as the absolute value of w_z which is low-pass filtered [92]. The authors also set two thresholds for the K index: T_1 and T_2 , which indicate the patient's gait state. The patient is in a regular gait if $K > T_2$, in a resting state if $K < T_1$ and in a FOG episode if $T_2 > K > T_1$, as shown on Figure 3.6A [92].

Figure 3.6B summarizes this algorithm. The first step is to compare K_{turn} to the threshold T_{turn} . If the index is higher than the threshold, then K' is computed. This index is then compared to K_{swing} and if K' is higher, then the algorithm rejects the hypothesis that this movement is a body swing and the movement is classified as irregular [92].

The performance of this method, in terms of sensitivity, specificity and accuracy,

is 93.41%, 98.51% and 98.51% respectively [92].

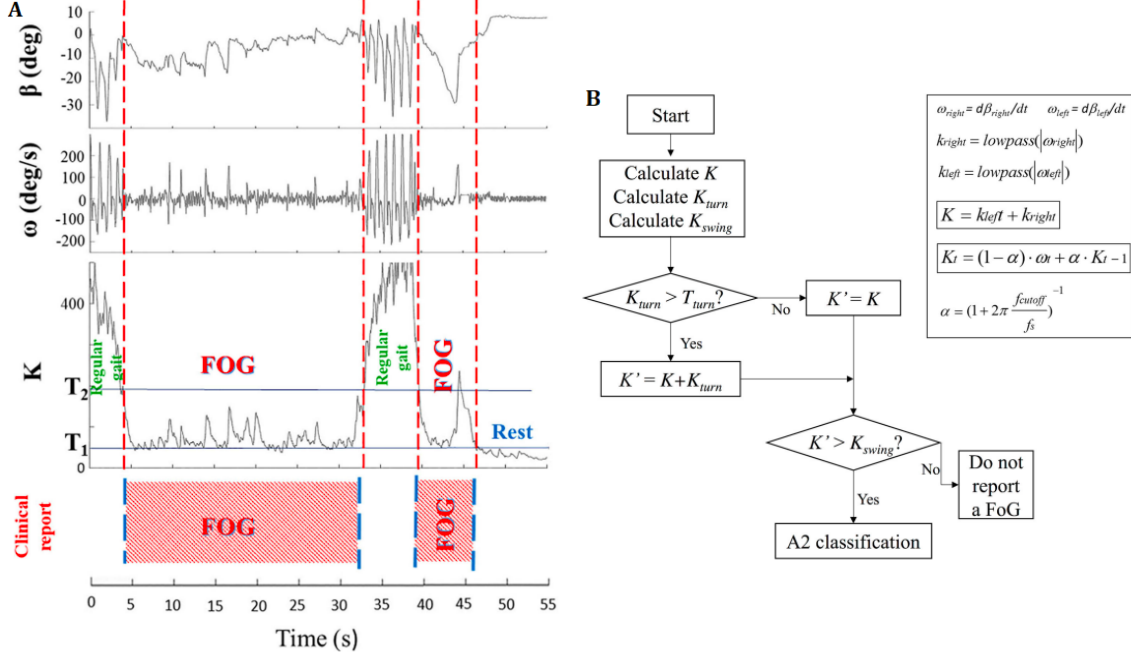


Figure 3.6: (A) FOG detection classification; (B) FOG detection algorithm [92].

3.3.3 Freezing of gait criterion

The index used to detect FOG episodes, called FOG criterion, operates in the **time domain** and requires the entire signal for detection, making it **unsuitable for real time use**. However, only one IMU is needed and it uses the sagittal shank angular velocity signal [93].

The patients were required to walk in a corridor on a distance of 10m while performing dual-tasks in order to trigger FOG episodes [93].

This FOG criterion is constructed on macroscopic gait data, using a continuous evaluation of stride length (L_n) and cadence (C_n) [93]:

$$FOG_{C_n} = \frac{C_n L_{min}}{C_{max}(L_n + L_{min})} \quad (3.19)$$

where $C_{max} = 5$ strides/s and $L_{min} = 5$ cm are predefined in order to bound the criterion to 1.

By integrating the acceleration signal, the forward displacement of the leg is estimated for each stride of the walk. To locate the boundaries of each stride, the gait is segmented using the shank angular velocities. The initial angular velocity of the leg is also captured for each stride. Afterwards, a correction is made to compare

the velocity estimated based on the accelerometer data with the values obtained from the angular velocity signal at the end of each stride. The higher the value of the FOG criterion, the more FOG episodes are expected. A threshold adapted to each patient is required to be able to compare it to values of FOG criterion [93].

Azevedo et al. [93] tested two algorithms (Freeze Index and FOG criterion) on the same data, and the result was a poorer sensitivity for the Freeze Index, being only 59%. The performance of the FOG criterion, by contrast, is 79.5% sensitive [93].

3.3.4 Pearson’s correlation coefficient

The Pearson’s correlation coefficient is a **time domain** technique that assesses the correlation between one section of a signal and the remaining portion. This method **cannot be computed in real time** as it needs the entire signal [94]. In the paper written by Popovic et al. [94], the Pearson’s correlation coefficient is applied on the signal acquired by force sensitive resistors.

Four force sensitive resistors were installed in the patient’s shoe while they were asked to walk back and forth along a corridor. The patient was also required to realize a TUG test passing through a doorway [94].

The idea behind this technique is to calculate the Pearson’s correlation coefficient between an estimated normal step and the rest of the steps recorded during the walk. The more irregular and therefore non-periodic the walk is, the weaker the correlation between a normal step and the measured step, and therefore the Pearson’s correlation coefficient decreases. The normal step used for the computation of the Pearson’s correlation coefficient is chosen by visual selection from a period of “normal” gait. Figure 3.7 illustrates the above explanations. The value of Pearson’s correlation coefficient oscillates between 1 and -1 during normal locomotion, but when various obstacles appear as shown with the black arrows, it decreases [94].

According to Popovic et al. [94], 100% of the FOG episodes are detected with this method. However, regarding the duration of each FOG episode, there is a difference between the actual FOG episode time detected on the video and the FOG episode duration computed by the method. This difference is approximately equal to $0.84 \pm 0.39\%$ of the actual FOG episode time in the best case. Furthermore, the sensitivity of the method regarding the evaluation of the duration of the FOG episode varies according to the threshold chosen for the Pearson’s correlation coefficient. If the coefficient is set to 0.85, the relative difference in the FOG duration estimate is $0.89 \pm 1.02\%$, if the coefficient is set to 0.9, the relative difference is $0.84 \pm 0.39\%$ and lastly, if the coefficient is set to 0.95 the relative difference is $1.7 \pm 1.45\%$ [94].

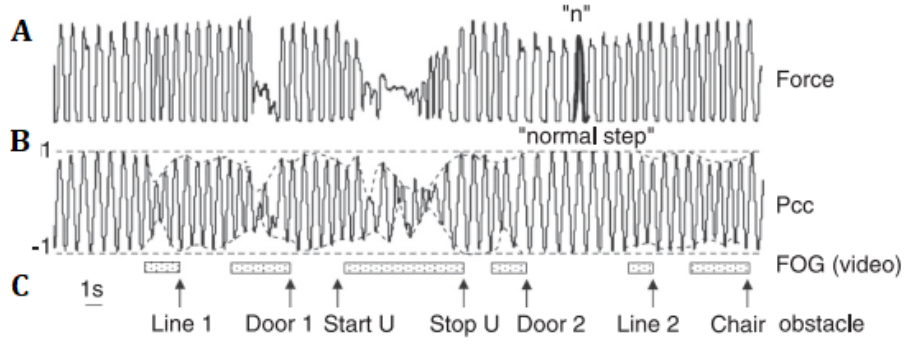


Figure 3.7: (A) Signal of the sum of forces of the four sensors with selection of a normal step (thick line); (B) Computation of Pearson's correlation coefficient between full record from A and the normal step; (C) Identification of FOG episodes from the video [94].

3.3.5 Machine learning

Many machine learning techniques are used to improve FOG detection performances. According to the review written by Pardoel et al. [77], neural networks, support vector machines, random forest and decision trees give the best results. The reader is referred to this paper for more information, since these methods are beyond the scope of this work [77].

3.4 Summary table

Table 3.4 summarizes all the methods explained previously. In this table, the position and type of sensors are those used in the studies to which it refers and which are described in the previous sections. A range of performances is given when several articles analyzed the same method.

3.5 Selection of detection methods

As a reminder, the goal of this work is to detect FOG episodes in real time to provide assistance as soon as an episode is detected. Thanks to the various methods discovered in this chapter, several solutions are available. Although around nine methods (excluding machine learning) were described, only three are selected and implemented to study their effectiveness. However, the choice of these methods must be relevant. Figure 3.8 illustrates the decision pathway performed. The first criterion for reducing the number of methods to explore is related to the possibility of using the technique in real time, which is essential. Secondly, the choice is based on whether the method operates in the time or frequency domain. Comparing these two domains in terms of delay, for example, would be interesting. The performance reported in the articles is the final factor in choosing one method over another.

Table 3.4: Summary table of FOG detection methods

[illegible]

However, some arbitrary aspects come also into play, such as wanting to test the most popular method found in the literature review conducted, *i.e* Freeze Index algorithm. Moreover, selecting methods that require the same equipment in the same location is another practical criterion to facilitate the conduct of experiments.

After applying all these criteria, the following methods are selected: the method using the Freeze Index, the one based on sEMG, and finally the one named K-index. The advantage of these three methods is that each requires the presence of accelerometers or gyroscopes found in IMUs, and each has better performance when the equipment is placed at the shank level. In addition, it is possible to combine sEMG with IMUs.

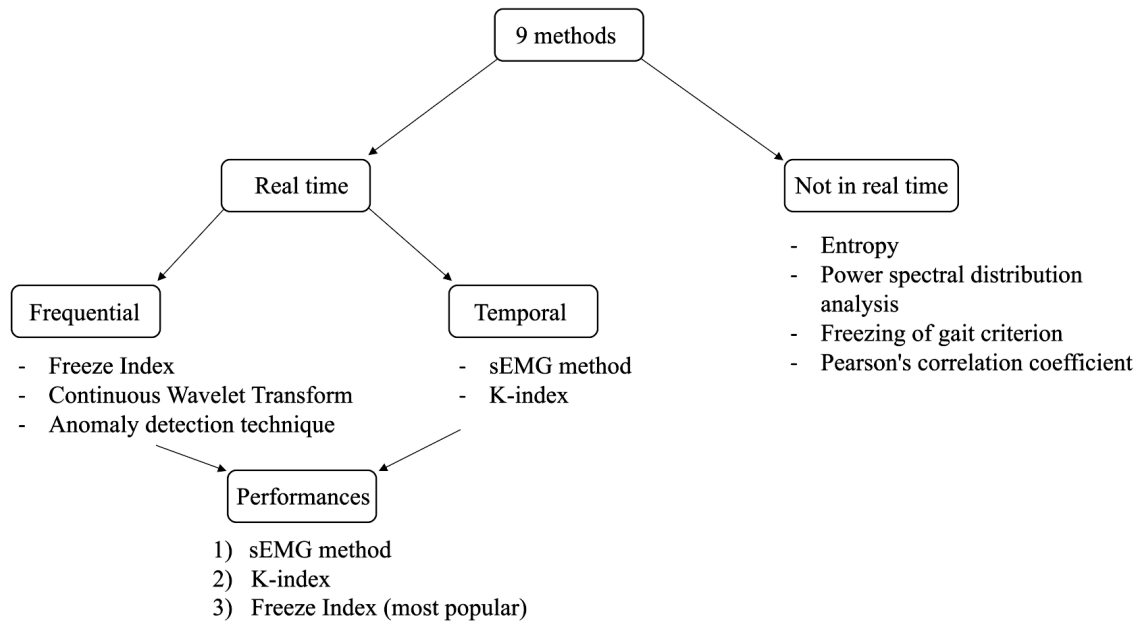


Figure 3.8: Selection diagram of three methods.

Chapter 4

Algorithms testing on open access data

This chapter covers the implementation of the three methods selected in the previous chapter as well as how the parameters influence performances. The aim of this section is to develop three algorithms for detecting FOG episodes with an open access dataset. This part therefore enables the implemented methods to be tested on already existing data before being used on data collected during experiments conducted as part of this work. The results of the algorithms tested on the experimental data can be found in Chapter 5. All the figures provided in this chapter were produced during the course of this work on the basis of external data.

Firstly, the chapter begins with a description of the equipment and methods used. Separate subsections are then devoted to the analysis of the performances, through measures such as sensitivity and specificity (detailed in Section 3.1), of the three algorithms.

4.1 Materials and methods

Each algorithm presented below was implemented in Python 3.10.

4.1.1 Open access dataset

The open access dataset¹ used was provided by Zhang et al. in 2022 [95]. This dataset contains the sagittal, frontal, and lateral linear acceleration, as well as angular velocity. Accelerometers (MPU6050) and gyroscopes (STM32) were placed on the lateral shank of the right and left legs. Additionally, recordings of the tibialis anterior muscle activity of both legs are included. The authors of the open access data used a 32-channel 'MOVE' wireless system (Brain Products GmbH, Gilching, Germany)

¹(<https://data.mendeley.com/datasets/r8gmbtv7w2/>)

to acquire sEMG. The acquisition frequency for all signals was 500 Hz. Next, the dataset encompasses two types of experiments aiming to induce FOG episodes, which were identified a posteriori by neurologists and indicated in the dataset. The first experiment involved walking through a corridor while navigating multiple obstacles. The second experiment entailed performing a 3m TUG test with a single round trip. Moreover, the experiment was conducted in the OFF state of patients. Finally, the dataset includes data from a total of 12 subjects (69.1 ± 7.9 years, 6 females) [95].

Signals from nine subjects could be used from the open access dataset as they exhibited FOG episodes. Subjects or tasks that did not manifest FOG episodes were discarded from the rest of the analysis. Only three of the nine subjects wore the sensors on both legs.

4.1.2 Data processing

The acceleration signals were filtered by a low-pass filter with a cut-off frequency of 16 Hz. In addition, sEMG data were filtered using a bandpass filter blocking frequencies below 10 Hz and above 500 Hz [95]. As the open source data was already supplied filtered, it was, in this work, only normalized so that all signals had the same scale. This was therefore the case for the linear acceleration, angular velocity and sEMG signals, as these are the signals required to implement the three methods below.

4.1.3 Freeze Index

As described in Section 3.2.1, the algorithm operates as follows. It analyzes the frontal linear acceleration signal in windows. Each window undergoes an FFT calculation and is transformed into its power spectral density. Only the power in the locomotion band (0.5 to 3 Hz) and the freezing band (3 to 8 Hz) is retained. Figure 4.1 shows that a normal gait is generally located in the locomotion band (Figure 4.1A), whereas during a FOG episode, the signal is no longer mainly located in this band and shows more power in the freeze band (Figure 4.1B). These bands are then divided to generate an index, which is then compared with a predetermined threshold. If the index exceeds this threshold, a FOG episode is detected.

In order to achieve this algorithm, an open access code² developed by Bähclin et al. was used [81, 96]. To this code, the possibility to modify the size of the window has been added. The window position parameter was also changed, with the analyzed point being considered as the center of the window, unlike the authors’

²(<https://archive.ics.uci.edu/ml/datasets/Daphnet+Freezing+of+Gait?fbclid=IwAR0R6puRux0RbAiiEHcLfNf52gPVixLJn5VYWHuh7s6RC0xkfrFhKYWPerE>)

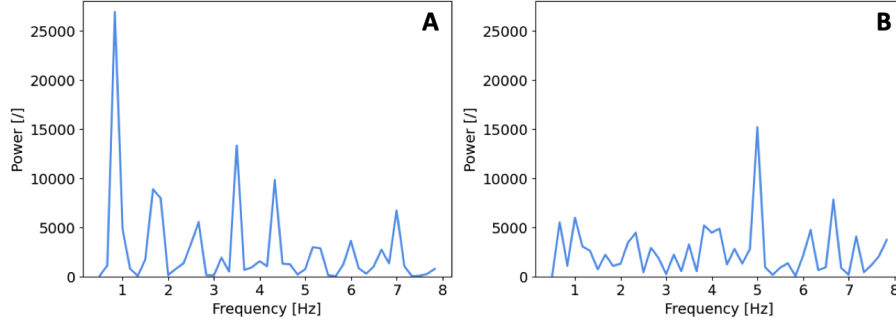


Figure 4.1: *Power spectral density on a window of 6s for : (A) a period of normal gait; (B) a period during which a FOG episode occurs.*

code [96] which used it as the last point. In the original code, the authors performed a 256-sample FFT on each signal window. Specifically, the authors originally used an acquisition frequency of 64 Hz and a 4s window for data analysis. In the modified version of this work, a different acquisition frequency was used and, to facilitate comparisons between different window sizes, the FFT was calculated as the product of the time window and the sampling frequency.

This method is designed for real time detection. However, a delay can be generated by the transition in the frequency domain, which generally requires a certain amount of computing time [92]. In addition, the size of the time window chosen has a direct impact on the delay, as it requires all points in the window to be recorded before proceeding.

4.1.4 Surface electromyography-based method

The method developed by Mazzetta et al. [91] was used to create an algorithm for detecting FOG episodes in real time (see Section 3.3.1). It requires the muscle activity value of the tibialis anterior muscle and the normalized absolute shank sagittal angular velocity. A R ratio between the maximum of the latter and the muscle activity at that moment is compared to a threshold for each window. If the value of this R ratio is below this threshold, the window is associated with a FOG episode. If the value exceeds this threshold, the window is associated with a regular step.

In this algorithm, time windows are identified in real time. They are defined each time the normalized absolute angular velocity falls below a T_1 threshold. This way of defining the window actually divides the step in two because during the stance phase, the angular velocity trace passes through zero. Therefore, for a regular step, there is typically a window corresponding to the swing phase and another corresponding to the stance phase as pictured in Figure 4.2. Then, in the paper [91], a second T_2 threshold is added and used to disregard the stance phase when it is regular.

Indeed, high muscle activity is recorded during stance phase, resulting in a low R ratio, which is consequently associated with a false positive and therefore a FOG episode [91]. The T_2 threshold thus minimizes these false positives. However, in this work, because it gave better performances, the R ratio is directly associated with a regular step and receives a random value higher than the threshold. The principle is the same, since this improvement is only supposed to occur during regular steps and therefore prevents the appearance of false positives. Finally, the delay for this method should be around the duration of a window, as stated in the article [91].

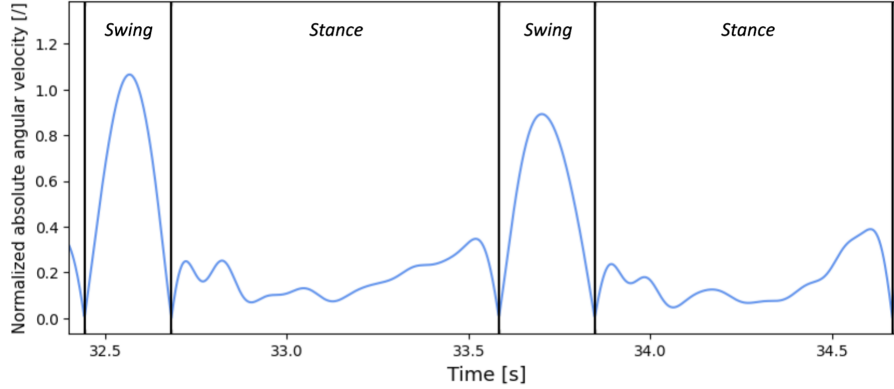


Figure 4.2: *Normalized absolute angular velocity of two regular steps and the division into computation windows.*

4.1.5 K-index

As detailed in Section 3.3.2, this FOG detection algorithm is based on the method developed by Suppa et al. [92]. The steps described by the paper [92] were followed to code this algorithm. For each point in the signal given by the gyroscope, the frontal and sagittal angular velocities of the subject's right and left shanks were analyzed. A variable K_t is computed on the basis of the low-pass filtered frontal velocity. This variable is then compared to a band threshold. If this variable is between a threshold T_1 and a threshold T_2 , a FOG episode is detected. Additionally, a T_{turn} threshold and a K_{swing} index was introduced. The former is used to differentiate turns from FOG episodes and the latter leg tremors during body swinging from leg tremors during FOG episodes. The K_{swing} index is defined as the absolute value of the low-pass filtered sagittal angular velocity. In order to be able to compare the subjects between them, the values of K_t were scaled from 0 to 1000.

In this work, to detect a FOG episode despite the fact that some points are sometimes slightly higher than T_2 or lower than T_1 , a detection improvement code has been created. Indeed, for each value of K_t , the average of the previous values is computed, this average becoming the value to be compared to the thresholds. If this average is between the two thresholds, then the algorithm defines it as a FOG episode.

On the other hand, if this average is outside the band created by the threshold, this value is declared as not being a FOG episode. By using the average, the delay of detection of a FOG episode is slightly increased. Furthermore, to avoid the algorithm detecting a false negative when the patient stops voluntarily, an additional step is necessary. Indeed, at this moment, the variable K_t crosses the interval defined by the two thresholds, as the resting state is below T_1 and normal walking is above T_2 . The algorithm checks whether the FOG episode lasts longer than one second, taking only these longer FOG episodes into account. In addition, the code checks whether the detected FOG episode is only followed by values outside the defined thresholds. In this case, the FOG event is not reported. However, if the following values include at least one instance reporting a FOG episode, the episode is indeed reported for the time analyzed.

4.1.6 Statistical analysis

In our particular case, the typical approach of using a paired t-test, which allows to compare groups with dependencies, is not feasible due to several drawbacks. The main issue is that if an observation is missing from a subject, the other observations from the same subject will automatically be deleted. This leads to a significant loss of information if this approach is used with the data obtained in this work. Indeed, as FOG episodes have not been detected in every tasks for each subject, some observations are missing.

To overcome these limitations, linear mixed-effects modelling was employed to assess the effectiveness of the algorithm studied as a function of the task performed, *i.e* short task or long task. Indeed, this model is chosen because it allows to use data for which some patients presented FOG episodes in both tasks, while others only in one of the two. In addition, it allows dealing with multiple repetitions per task for one subject. The predictor analyzed for this analysis is the task condition. This was done for the two statistical values explained previously (sensitivity/specificity), according to the following equation [97], performed in R version 4.3.0:

$$\text{statistical value} \sim 1 + \text{task} + (1|\text{participant}) \quad (4.1)$$

with both tasks as fixed effects and the participants as random effects. Fixed effects refer to effects that are expected to persist across experiments, in this case the short or long task. It captures the overall trend of the two tasks. Random effects model how these trends will vary across factors, e.g participants. This allows to take into account that behavior of some participants can deviate from the average [97].

4.2 Results and interpretation

For each method, in order to test its effectiveness, a calculation of sensitivity and specificity of the algorithm is performed, as described in Section 3.1. Additionally, the various parameters that can affect the algorithm's ability to detect FOG episodes are evaluated and an interpretation is given to determine how their modification impacts the algorithm.

4.2.1 Freeze Index

Figure 4.3 shows an example of the computation of the Freeze Index with a window size equal to 4s, a T threshold equal to 2 and a step size dt of 0.5s. The presented figure demonstrates that the occurrence of the clinical FOG episode is detected when there is a disruption in the normalized linear acceleration. Subsequently, the Freeze Index is computed, which generally aligns with the observed event, albeit with a few instances of false negatives.

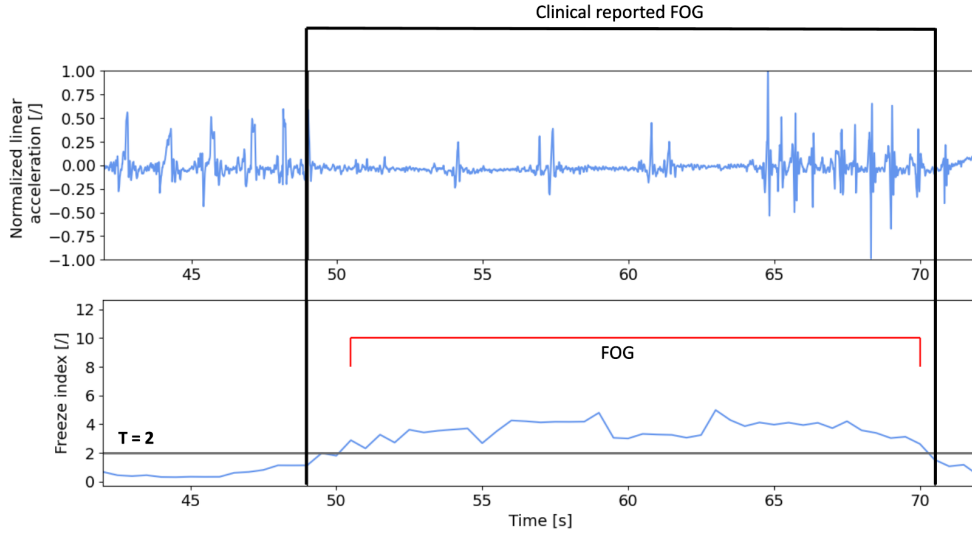


Figure 4.3: Representation of the operation of the Freeze Index algorithm. Normalized linear acceleration (top) and Freeze Index (bottom) for a period of time are represented. The red lines indicate FOG episodes determined by the algorithm.

As the method is not developed as person-dependent, boxplots of sensitivity and specificity over all subjects are drawn. Each box represents 50% of the subjects. The whiskers show the maximum and minimum observed in the subjects. The line drawn in the box represents the median of the values. Several parameters influence the detection capacity of the algorithm. Figure 4.4 mentioned here solely illustrates the influence of the window size, using the optimal threshold ($T = 2$) and optimal step size ($dt = 0.5$) that yielded the best results. Additional figures demonstrating the same relationship with threshold values of 2.5 and 3 and step size of 1 are included

in appendix Section B.1.

To begin, the first parameter having an impact on the efficiency of the algorithm is the size of the window used to calculate the Freeze Index. Figure 4.4 illustrates that the specificity of detection increases very slightly with the enlargement of the window size. However, it could also smooth out shorter events, thereby explaining the reduction in sensitivity. Secondly, upon examining Figure 4.4 with the figures in Section B.1, it becomes clear that decreasing the threshold T has a positive effect on sensitivity. This means that more FOG events are detected. However, this is associated with a decrease in specificity, as more normal events are likely to be associated with a FOG episode. Finally, the step size determines the magnitude by which the center point of the window is shifted to the subsequent position. The impact of the step size is relatively minimal since the smallest window considered is 4s, and the largest time interval tested, denoted as dt , is 1s. However, if the value of dt were to be increased, it would certainly exert a more substantial influence on the outcomes. Indeed, increasing the value of the step size dt could potentially skip over FOG episodes that are smaller in duration than the chosen time interval.

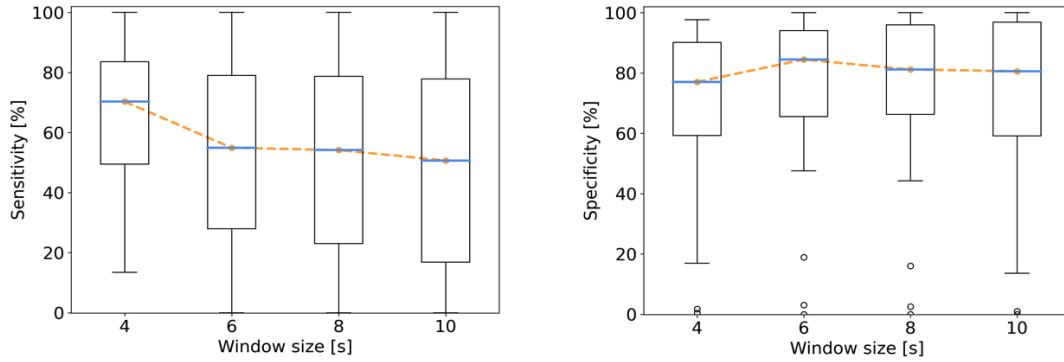


Figure 4.4: *Sensitivity (left) and specificity (right) of the Freeze Index algorithm for several window sizes, with the threshold $T = 2$ and step size $dt = 0.5$.*

In order to achieve the best trade-off between specificity and sensitivity, it has been determined that using a window size of 4s, a threshold value T of 2, and a step size dt of 0.5s yielded the highest median values for both specificity and sensitivity. That is 70.29% and 77.04% respectively. However, although these overall median performances give an idea of the detection capability of this algorithm, the range of boxplot whiskers is quite large. These findings suggest a considerable amount of variability among subjects, particularly in terms of sensitivity, which will be addressed in more details in Chapter 6. Moreover, certain sensitivity values indicate that the algorithm was not effective at all for some subjects. To achieve completeness and potentially performance improvement, it would be advisable to use an optimization

algorithm that encompasses all parameters.

Finally, a comparison of performances between obstacle avoidance walking (long task) and the TUG test (short task) is represented in Figure 4.5. Mixed-effects models is completed (appendix Table B.2.1), with parameters that give best sensitivity and specificity, and revealed no big distinction between the two tasks, neither in terms of sensitivity nor specificity ($p > 0.05$).

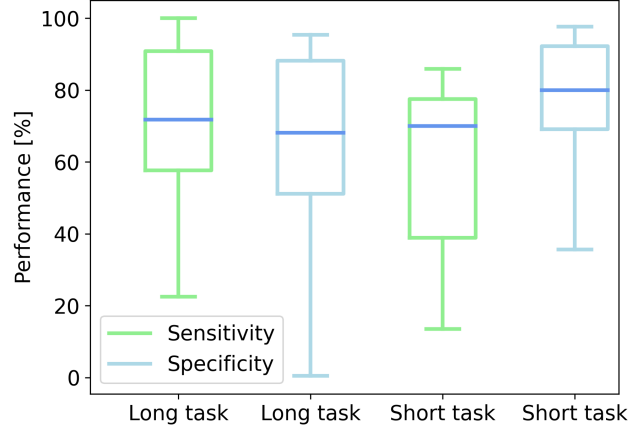


Figure 4.5: Comparison of performances between long and short tasks for the Freeze Index algorithm.

4.2.2 Surface electromyography-based method

Figure 4.6 is an example of a result obtained for a subject with a threshold T_R set to 3 and a window threshold T_1 set to 0.01. This figure demonstrates that indeed, when a FOG episode is detected by the algorithm, all R indices are below the threshold T_R .

It can also be observed that the R points are more spaced out when the gait cycle is regular, as the window is longer. Additionally, both the normalized angular velocity and the normalized trace of muscular activity respects a particular shape. During FOG episodes, the gait cycle is disrupted, resulting in definition of more smaller windows, and increasing the number of R ratios computed, which was thus expected. However, there are some false positives (outside the clinical reported FOG episode window) and false negatives (in the clinical reported FOG episode window) that need to be considered. The false positives are mainly due to incorrect window definition. Sometimes there are irregularities in the signal, so that during a regular step, very small windows are defined. In these small windows, the angular velocity signal is relatively low, resulting in a R ratio associated

with a FOG episode, even though this event was part of a regular step. The false negatives are due more to the signal itself. For example, on Figure 4.6, around 40s, a false negative can be spotted. However, at the same time, in the angular velocity, a peak is observed, increasing the value of R and leading to the false negative.

Finally, it can be confirmed that there is, most of the time, a correspondence between the disturbance of the normalized angular velocity signal and sEMG and the appearance of an episode of FOG. This is then translated by the algorithm into small values of R .

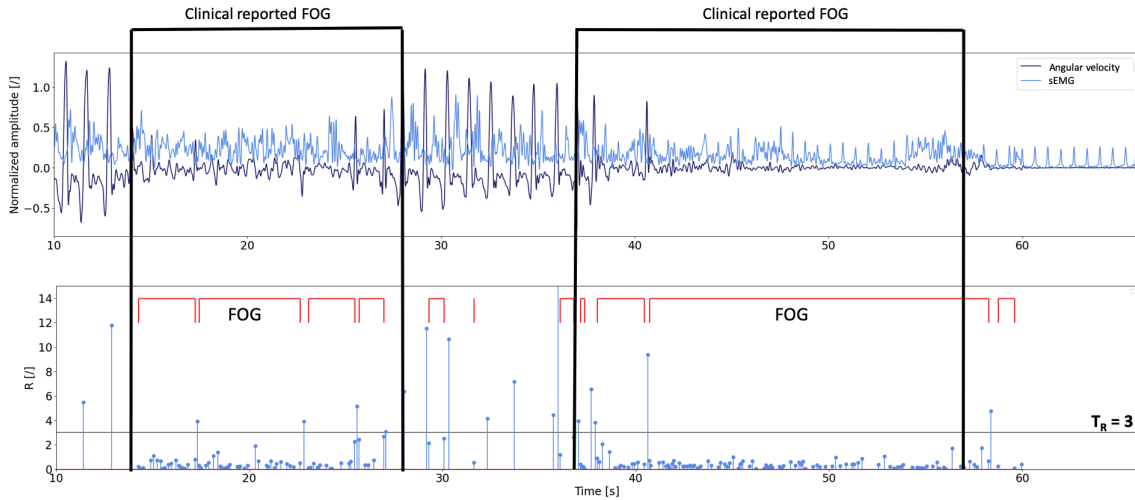


Figure 4.6: Representation of the operation of the sEMG method algorithm. The normalized sEMG (light blue) and angular velocity (dark blue) traces recorded on the tibialis anterior (top) and the corresponding R values on the same time scale (bottom) are represented.

Again, as the method does not depend on the person, boxplots of sensitivity and specificity are plotted. As explained in Section 4.1.4, a method has been used to minimize the number of false positives and thus the number of detection errors. This is possible thanks to the threshold T_2 which is proposed equal to -0.4 in the paper written by Mazzetta et al. [91]. However, to verify that it was indeed a good threshold value, different possibilities have been studied.

As shown in Figure 4.7, the choice is not obvious. By choosing a threshold $T_2 = -0.2$, the sensitivity is reduced. In fact, the algorithm is less sensitive because the angular velocity of FOG episodes could at times be lower than -0.2. This could thus be associated with a regular step, increasing the number of false negatives. On the other hand, specificity is increased because during regular steps, it is much less likely that the R ratio will be associated with a FOG episode, minimizing the false positives. Finally, when this threshold is increased, the trends reverse. Thus, a compromise must be made between the sensitivity and the specificity of the method.

It would again require an optimization algorithm to choose the best option. However, the threshold T_2 is set to -0.4 to align with the choice made by the authors of the method [91] and will be used for the remaining analysis. This option yields improved sensitivity at the expense of reduced specificity. Fortunately, further enhancements can still be achieved by adjusting the parameters described in the rest of this analysis.

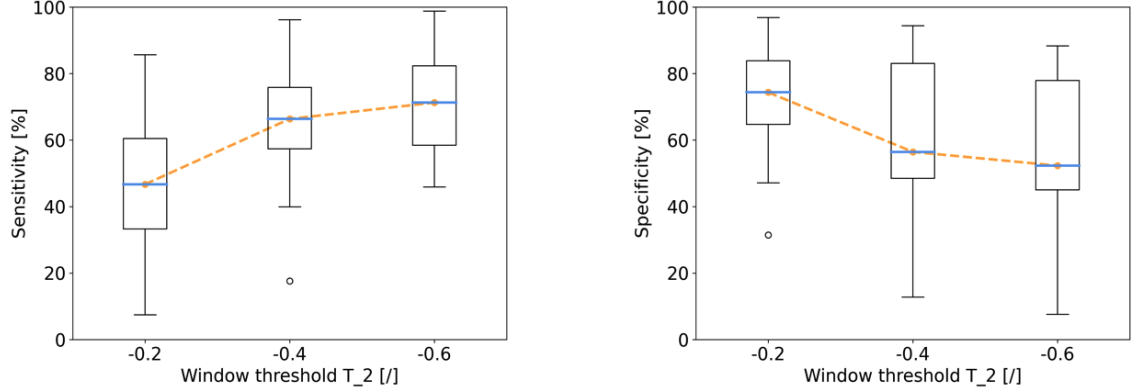


Figure 4.7: Influence of the threshold T_2 on sensitivity (left) and specificity (right) for all subjects with thresholds $T_R = 3$ and $T_1 = 0.01$.

After choosing the threshold $T_2 = -0.4$ for all subjects, the detection capability of the algorithm still depends on two factors. The first parameter is the threshold T_R (set to 3 in the paper by Mazzetta et al. [91]) below which R values are assigned to FOG episodes. Additionally, the parameter T_1 (set to 0.01 in the paper by Mazzetta et al. [91]), defining when a new window is identified, can also affect the detection ability. Figure 4.8 shows how these options influence the performances on all the analyzed subjects. Firstly, the threshold T_R chosen shows big differences. The sensitivity of the algorithm necessarily increases as the threshold gets bigger, since more points are likely to be associated with a FOG episode. On the other hand, the specificity necessarily decreases, as there is a greater chance that a regular step will be associated with a FOG episode. Secondly, the threshold T_1 used to define a new window has an influence, albeit slight. In general, a threshold of 0.01 gives a relatively higher specificity and a little lower sensitivity. In Figure 4.8, the sensitivity and specificity of the algorithm is shown for a threshold $T_1 = 0.01$ since it was the better, at least, for specificity. However, the other graph showing influence of threshold T_R with $T_1 = 0.015$ can be found in appendix Section C.1. It shows that the results between these two T_1 are very similar. The reason for the little difference that is observed is probably due to a slightly different initialization of the time windows.

Trying to take the best compromise, the parameters involving a threshold T_R set to 3 and a window definition threshold T_1 set to 0.01 give the best median performances over all subjects and tasks. That is 66.36% sensitivity and 56.44%

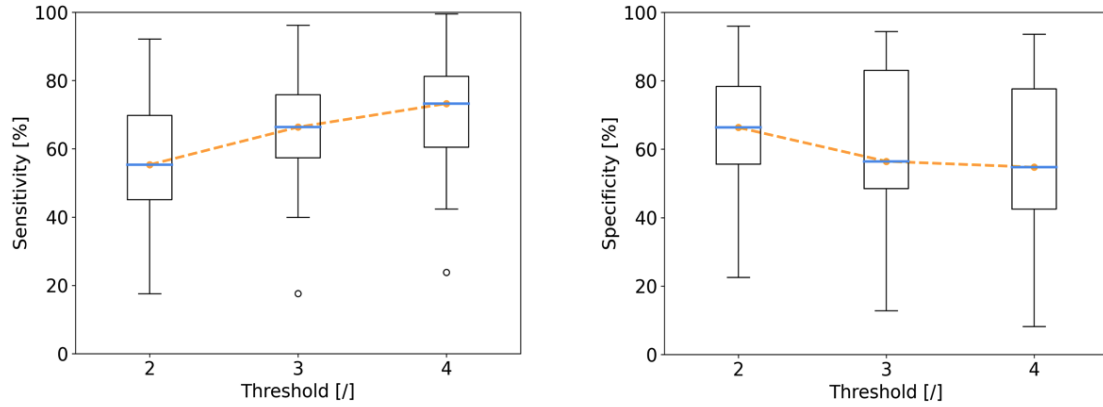


Figure 4.8: Influence of the threshold T_R on sensitivity (left) and specificity (right) for all subjects based on a specific window threshold $T_1 = 0.01$.

specificity. Once again, as observed with the Freeze Index algorithm, the significant variability depicted by the whiskers in Figure 4.8 indicates that the effectiveness of the method varies among the analyzed subjects. Furthermore, to ensure more precision, an optimization algorithm on the various parameters would also be required.

Finally, a comparison of performances between obstacle avoidance walking (long task) and the TUG test (short task) has been performed as shown by Figure 4.9. Mixed-effects models is completed (appendix Table C.2.1), with parameters that give best sensitivity and specificity, and revealed no big distinction between the two tasks, neither in terms of sensitivity nor specificity ($p > 0.05$), which was also concluded by the Freeze Index algorithm.

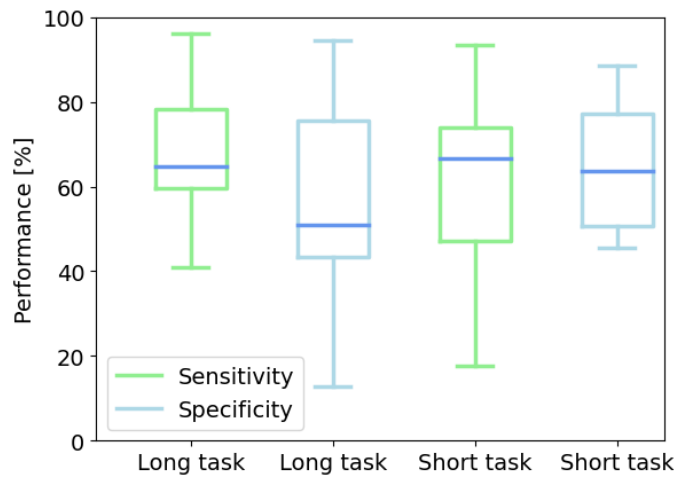


Figure 4.9: Comparison of performances between long and short tasks for the sEMG algorithm.

4.2.3 K-index

As previously mentioned, in the open access data, only three subjects wore the sensors on both legs and therefore only their signals can be analyzed with this method.

Figure 4.10 is an example of a result obtained for a subject with T_1 equal to 150 and T_2 to 400. On this figure, FOG episode, in the K-index signal, has a distinct pattern that clearly differs from normal gait, as expected. Normalized angular velocity also presents a different pattern, the amplitude is smaller and the signal is more irregular. However, in the K-index signal, some points are outside the predefined thresholds, which results in the FOG episode being detected in several episodes rather than a single one. It should also be noted that this algorithm has false negatives and false positives.

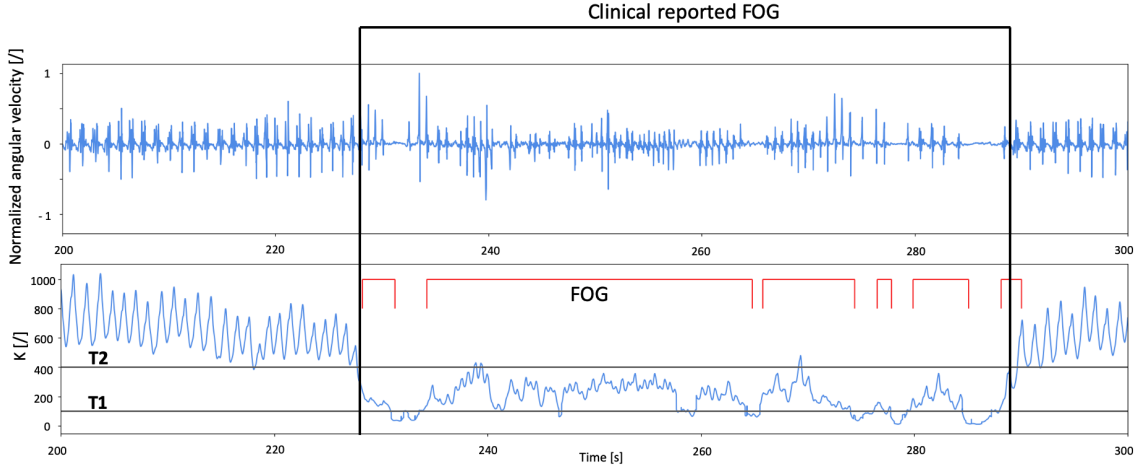


Figure 4.10: Representation of the operation of the algorithm. Angular velocity (top) and K-index (bottom) for a period of time are represented. The red lines indicate FOG episodes determined by the algorithm.

The algorithm aims to minimize false positives during turns, by defining a T_{turn} . Figure 4.11 shows the difference it can generate in terms of performances for a particular choice of thresholds and a particular number of neighbors analyzed. In the case of this figure, T_{turn} set to 0.5 gives the best results, although the threshold does not seem to have much impact. This is because the other parameters (the two thresholds and the number of values analyzed) are set to be the best for T_{turn} set at 0.5. Indeed, if T_{turn} is set to another value, the other chosen parameters will have to change, as they will no longer be optimal. Therefore, the best way to define the parameters in order to obtain the best results would be again an optimization algorithm.

In order to analyze the detection performances of this algorithm, other parameters need to be adjusted, including the choice of thresholds and the number of neighbors analyzed. These parameters have a direct impact on the algorithm's output.

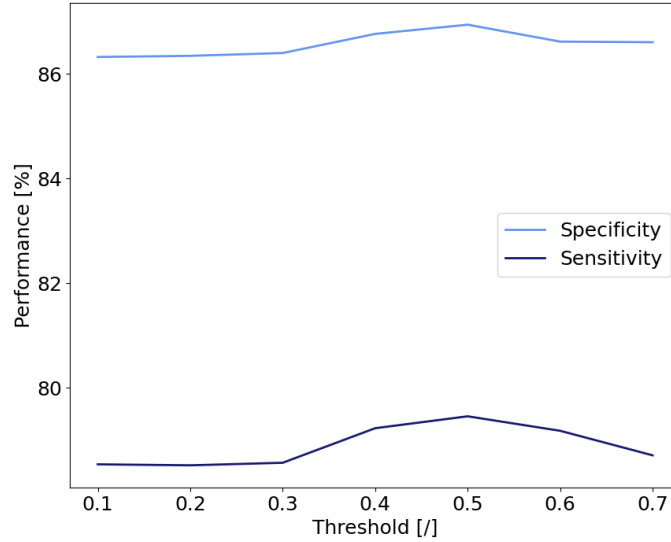


Figure 4.11: Influence of the threshold T_{turn} on performances for one subjects based on specific thresholds $T_1 = 150$ and $T_2 = 350$ and a specific number of 3 analyzed seconds.

Although the specific thresholds used are not mentioned in the article by Suppa et al. [92], it is stated that the thresholds depend on the individual. Hence, for this algorithm, the thresholds were set on an individual basis. Firstly, the differences in performances due to the choice of thresholds are illustrated by Figure 4.12. For the subject analyzed, the algorithm performs better when the threshold T_1 is set at 150 and T_2 at 350. However, it should be noted that the difference in performances between T_1 set at 150 and T_2 at 300 is not far from that obtained above. By reducing the threshold spacing, the algorithm becomes less sensitive but more accurate, as shown by the decrease of sensitivity and the increase of specificity for the 150-300 compared as the 150-350 thresholds. Figure 4.12 also shows that performances of the unimproved algorithm, represented by the orange and sand lines, have a lower sensitivity and specificity than the improved algorithm, indicated by the blue lines. The improved algorithm performs better overall. Secondly, as the detection delay depends on the number of neighbors analyzed, performances were evaluated considering data from 1s to 3s around the initial value, to avoid excessively long detection delays. For each subject, performances were best when considering 3s of data. It is important to note that analyzing a greater number of seconds offers greater confidence in the results. On the other hand, this can pose a problem if the FOG episode lasts less than the time analyzed. In this case, the signal may be between thresholds for less than the analysis time, leading to missed detection when averaging.

For each subject, performances were analyzed and trade-offs were made to obtain the best performances in terms of sensitivity and specificity. These results for each subject are presented in appendix Section D.1 where the parameters giving the best

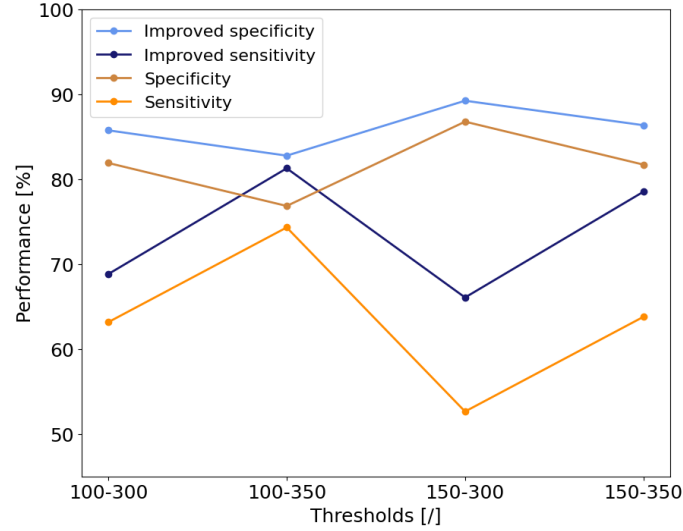


Figure 4.12: *K-index performances for the algorithm and its improvement based on the chosen thresholds for an analysis of 3s around each value.*

detection are indicated. Therefore, taking the best performances for each subject, the overall specificity and sensitivity are respectively 73.9% and 79.7%. This performances could perhaps be slightly improved by running an optimization algorithm on all parameters.

The blue line in the boxplots of the comparison between the long and short tasks presented in Figure 4.13 are the median of the results obtained with the best parameters for each subject. In contrast to the two previous methods, the comparison of the two tasks carried out for this dataset shows better results for the long tasks than for the short tasks, as shown in Figure 4.13. Indeed, mixed-effects models, completed with parameters that give best sensitivity and specificity, revealed a significant difference between the two tasks in terms of sensitivity ($p < 0.05$) (appendix Table D.2.1). However, difference in terms of specificity was not found significant by the mixed-effects models. This could be explained by the fact that the long task involves smoother turns and fewer 180° turns on oneself, unlike the short task. It may be that the K-index is more effective at detecting wide turns than tight ones. The difference observed between this method and the two others, the Freeze Index and sEMG methods, could be attributed to the fact that the K-index is designed to distinguish a turn from a FOG episode.

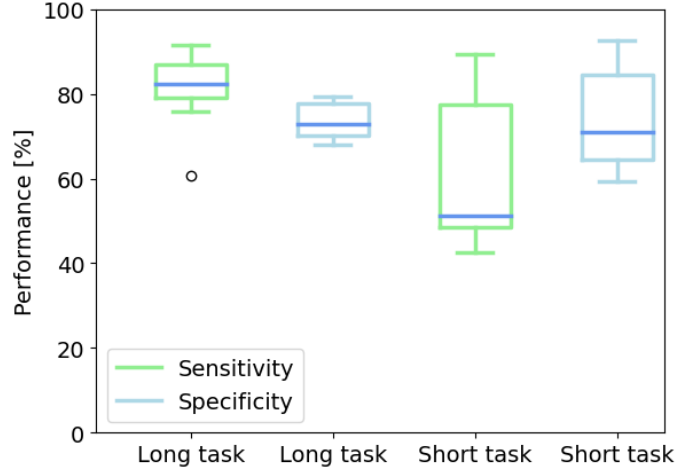


Figure 4.13: Comparison of performances between long and short tasks for the *K-index* algorithm.

4.3 Summary

The main results concern the three developed algorithm.

For the **Freeze Index** algorithm, the results are:

- Best parameters are window size equal to 4s, $T = 2$ and step size $dt = 0.5$.
- Overall sensitivity and specificity of 70.29% and 77.04% respectively.
- There is no significant difference in FOG detection between long and short tasks.

Secondly, for the **sEMG** algorithm, the results are:

- Best parameters are $T_R = 3$ and $T_1 = 0.01$ with $T_2 = -0.4$.
- Overall sensitivity and specificity of 66.36% and 56.45% respectively.
- There is no significant difference in FOG detection between long and short tasks.

Finally, for the **K-index** algorithm:

- $T_{turn} = 0.5$. Best results are obtained with an analysis of 3s of data. Person-dependent thresholds are set at 150-350, 60-400 and 25-300.
- Overall sensitivity and specificity of 73.90% and 79.70% respectively.
- Better results in terms of sensitivity of FOG detection for the long task than for the short task.

In conclusion, for the three techniques, what can be retained is that optimization algorithm would most probably be necessary to choose very precisely the parameters that give the best performances. However, it is beyond the scope of this work. In addition, the K-index seems to be the most effective algorithm despite the fact that sensitivity and specificity are still quite low for the type of application it is designed for. Next, the Freeze Index algorithm comes close in second position. Finally, the sEMG method seems to be the weakest at detecting FOG episodes.

Chapter 5

Algorithms testing on experimental data

This chapter provides a detailed account of how the experiments, aimed at testing the previously presented algorithms, were conducted. It begins with describing the subjects, the equipment used, the experimental protocol, the visual analysis of FOG episodes occurrence, and the data processing. Finally, an analysis of the results obtained by the algorithms on the experimental data is performed to conclude the chapter. In addition, a comparison is made with what was obtained in Chapter 4 and the authors' performances are reviewed.

5.1 Materials and methods

5.1.1 Subjects

Eight subjects were included in the study. Three were men with Parkinson's disease experiencing FOG episodes (69.7 ± 5.5 years), one of whom was treated with DBS. Five were healthy subjects (21 ± 1 years, three females). These subjects were used as controls.

Patients were excluded if they did not exhibit freezing, were unable to walk for three consecutive 10-minute periods, or required external assistance such as a cane to walk. All trials were conducted when the patient was in the ON state, meaning the last dose of levodopa they had taken was still active. A neurologist assessed the motor severity of Parkinson's disease in each patient using the MDS-UPDRS part III score. The MMSE was also carried out to assess each patient's cognitive state. A score above 24 is required for participation in this experiment, to ensure that the patient will understand the instructions. Finally, the questions from the New Freezing of gait Questionnaire were asked to each patient in order to determine the severity of their FOG episodes as well as their impact on the patient's daily life. Table 5.1 summarizes the patient's characteristics.

Table 5.1: *Characteristics of the study population: H&Y stands for the Hoehn and Yahr scale, NFOG-Q for the New Freezing of Gait Questionnaire and * for the patient implanted with Deep Brain Stimulation*

<i>Patient</i>	<i>Age</i>	<i>H&Y score</i>	<i>NFOG-Q score(/28)</i>	<i>Most affected side</i>
#1	64	3	22	Right
#2	70	2.5	18	Left
#3*	75	3	10	Right

5.1.2 Protocol

The development of the experimental protocol was carried out in collaboration with a neurologist. The experiment consisted of two major different exercises:

1. TUG test (see Figure 5.1A): the subject had to stand up from a chair, walk 3m, make a U-turn between two cones, and sit back down. For each condition, four round trips were performed, with two 180° turns to the left and two 180° turns to the right.
2. 10-Minute Circle Walk (see Figure 5.1B): the subject had to walk in a 7m diameter circle for 10 minutes for each condition.

Each of the previous exercises was achieved under three conditions. These three conditions were therefore the following:

- Control condition: the subject performed the exercises without any external influence. This condition serves as a reference for “normal” walking.
- Dual-task condition: the subject performed the exercises while engaging in a dual-task. For the TUG test, it involved a cognitive task of subtraction. For the circle walk, it involved walking while answering a prepared list of questions interspersed with cognitive tasks (subtractions or reciting letters of names backward). As described in Section 1.3, the dual-task imposes an information processing overload, which consequently can trigger a FOG episode.
- Metronome condition: the subject performed the exercises while synchronizing their movements to a metronome rhythm previously calculated according to the patient’s preferred cadence. This condition is chosen to observe if FOG episodes occurrence is reduced by providing the subject with an auditory cue. Indeed, as explained in Section 1.4.2, these aids can help patients overcome FOG episodes.

As the two previous exercises had not induced many FOG episodes in the first two patients, the last one performed an additional exercise, inserted at the end of the experimental protocol. This consisted in the doorway crossing and U-turn (see Figure 5.1C). The subject was asked to walk through a door and make a 180° turn around a cone. The gate was placed halfway between two cones, separated by a distance of

5m, and it was repeated a total of 10 times.

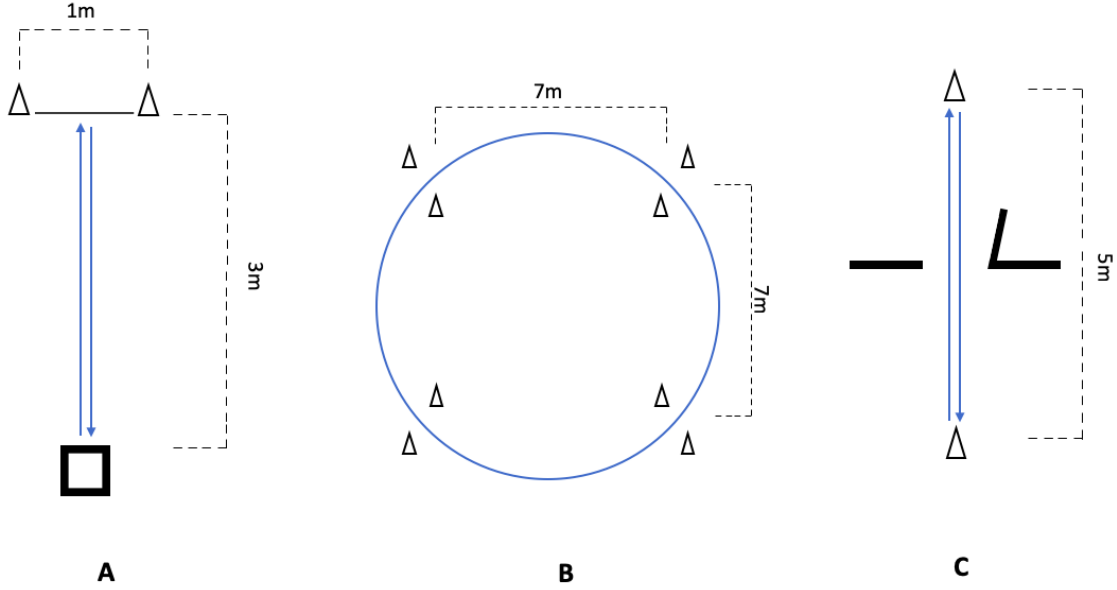


Figure 5.1: (A) TUG test; (B) 10-Minute Circle Walk; (C) Doorway crossing and U-turn.

During these exercises, the Trigno® Avanti Sensors (Delsys, Natick, MA, USA) were used to acquire the necessary signals. These sensors combine the functions of sEMG and IMUs, as they contain surface electrodes to measure muscle activity and accelerometers and gyroscopes to measure the 3D accelerations and angular speeds. The sampling frequency was set to 1260 Hz for sEMG and 148 Hz for IMUs [98]. These values could not be modified because they were imposed by the hardware. The sensors were placed on each leg on the tibialis anterior and lateralis gastrocnemius muscles following the standard usage [99] and as represented on Figure 5.2. Only the signal from the tibialis anterior were analyzed. A Lenovo ThinkPad laptop was used and connected through a cable with the sensor's box, which communicated by Bluetooth with the sensors. The Trigno Discover software was used to monitor the signals in real time. Finally, a smartphone camera was used to record the experiments.

5.1.3 Visual analysis

The video recordings of the experiments were reviewed by a neurologist from the *Cliniques Universitaires Saint-Luc*. The neurologist identified FOG episodes only in patients #2 and #3, specifically during the TUG exercise (control and dual-task condition) for patient #2, and during both the TUG exercise (control and metronome condition) and the doorway crossing exercise for patient #3. During the 10-Minute Circle Walk exercise, no FOG episodes were reported by the neurologist.

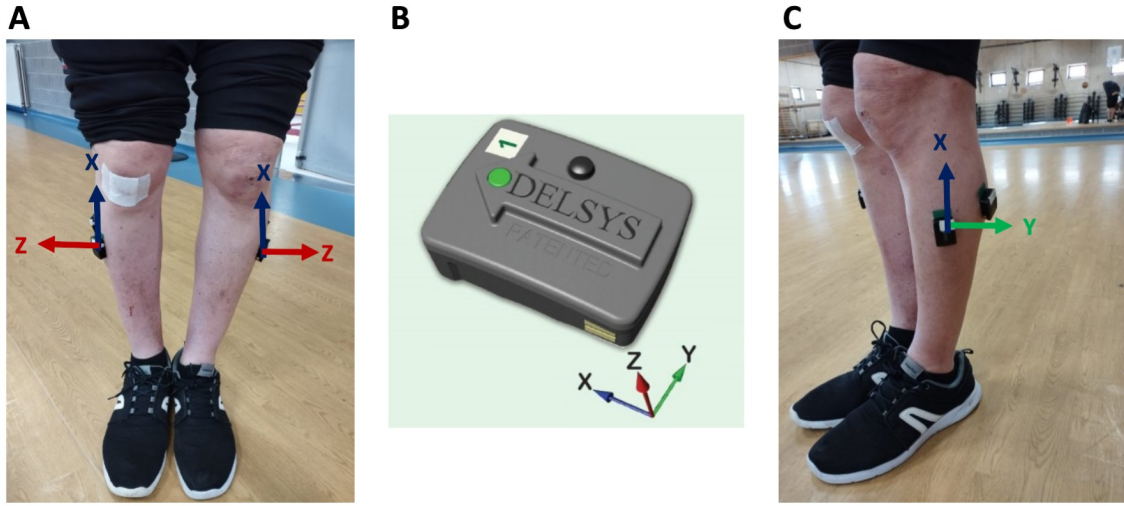


Figure 5.2: (A) Layout of the Trigno® Avanti Sensor on both legs of the subject; (B) Delsys Trigno® Avanti Sensor; (C) Layout of the Trigno® Avanti Sensor on left leg of the subject.

5.1.4 Data treatment and analysis

In order to use the data in the algorithms, they must be pre-processed. To do this, the raw data were filtered. Filters used in this work are Butterworth ones, since this type of filter is commonly used for data processing in gait analysis applications [100]. This filter was applied forward and backward to the signal to avoid the delay in the signal due to the digital filter.

The angular speed and acceleration signals were filtered using a low-pass filter with a cutoff frequency of 10 Hz to mitigate noise, as it typically occurs at high frequencies [100]. Figure 5.3 shows the results of the filtering process. The signal was then normalized and centered.

For the sEMG signals, the steps described in the paper by Mazzetta et al. [91] were followed. First, a high-pass filter was applied to the signal, with the cutoff frequency set at 3 Hz. This filter removes artifacts related to motion and background noise, as shown on Figure 5.4B. After this step, the signal was rectified (*i.e.* the absolute value of the signal is returned). This rectification is represented in Figure 5.4C. Next, a normalization to its maximum value was applied on the rectified signal. Finally, this signal was passed through a low-pass filter with a cut-off frequency of 10 Hz giving the signal plotted on Figure 5.4D. After all this, the sEMG signal was normalized.

Finally, to ensure synchronization between the video and the acquired signal, the experimental data were carefully aligned. During the experiments, subjects were asked to tap their feet at the beginning of each exercise. This tapping action was

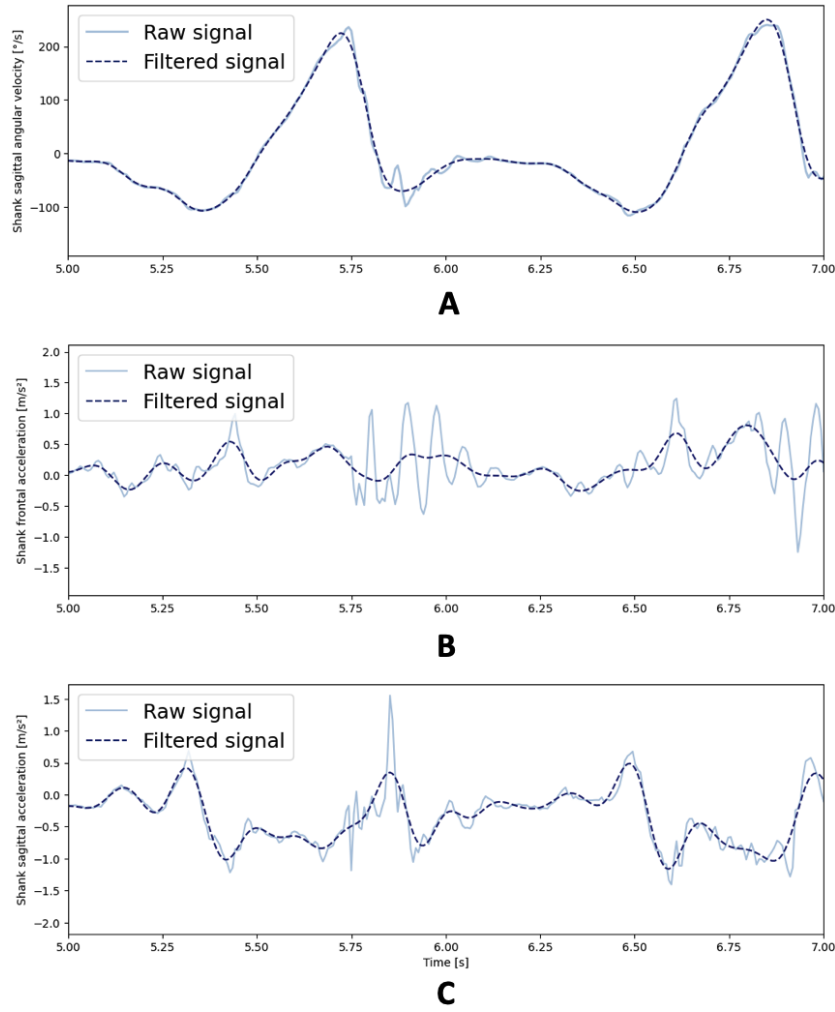


Figure 5.3: *Graphs of raw (light blue) and filtered (dark blue) signal for: (A) Angular velocity; (B) Sagittal acceleration; (C) Frontal acceleration.*

both visible in the signal data and captured in the video sequence. Therefore, the video was edited to begin precisely at the time of the foot tapping. Similarly, in the signal data, a significant peak of muscle activity or acceleration was observed at this precise moment. Therefore, the signal was cut to begin at zero at the precise moment of foot tapping. This precise timing is essential to accurately represent the occurrence of FOG episodes, as determined during video analysis, on the acquired signals.

After pre-processing the data, the algorithms detailed previously (see Sections 4.1.3, 4.1.4 and 4.1.5) were used to detect FOG episodes during these experiments. In the following section, the results and a comparison between these and what was obtained with the open access data are presented. In order to refer to the open access data, they will be mentioned as external data. The performances presented in the following section will be calculated on the signals from the exercises that induced

FOG episodes in patients #2 and #3.

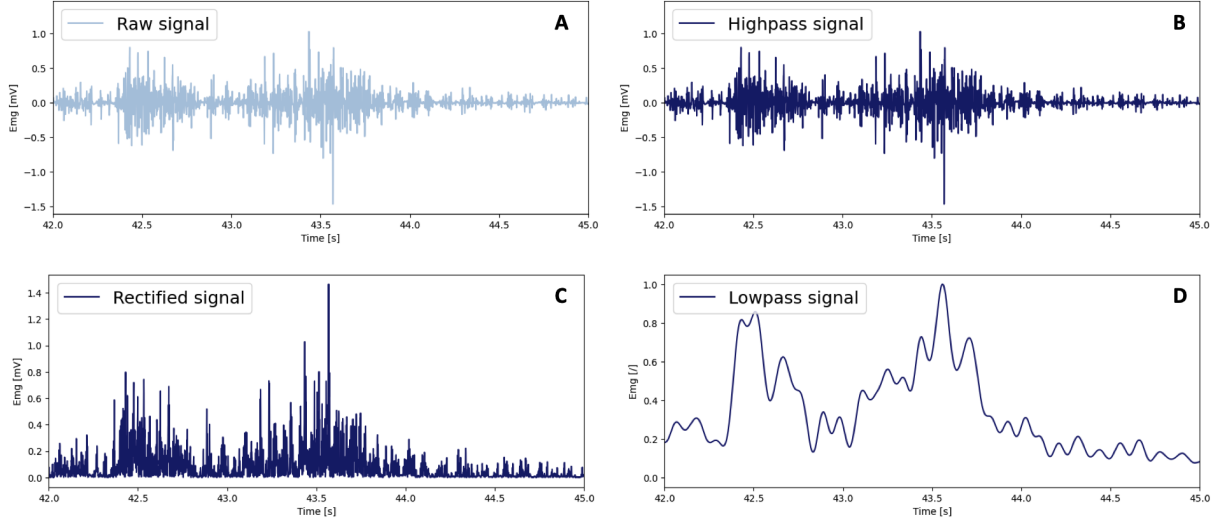


Figure 5.4: *Graphs of raw and filtered signal for sEMG signal: (A) Raw signal; (B) Signal through high-pass filter; (C) Signal after rectification; (D) Normalized signal through low-pass filter and again normalised.*

5.2 Results and comparison with external data and author's performances

5.2.1 Freeze Index

For this algorithm, the data obtained from the above experiments were analyzed in the same way as for the open access dataset. The most affected legs were selected on the basis of their ability to produce the best results. Various combinations of window size, step size and threshold were tested. They can be found in appendix Section B.3 The change in these parameters will induce some differences, as explained in Section 4.2.1. In contrast to the results obtained when analyzing external data, Figure 5.5 shows an increase in sensitivity with increasing window size. This could be explained by the low number of patients analyzed in this dataset. Indeed, analysis of a larger sample would provide a more representative result, which could lead to the opposite of the trend observed here. Specificity tends to be closer to the results obtained on external data, since it increases between the smallest and largest window sizes, although this increase is slight. Secondly, the threshold T has the same effect as for external data, as can be seen by analysing this figure and those in Section B.3. Decreasing it increases sensitivity and decreases specificity. Finally, the impact of dt is minimal and almost imperceptible, as for the external data.

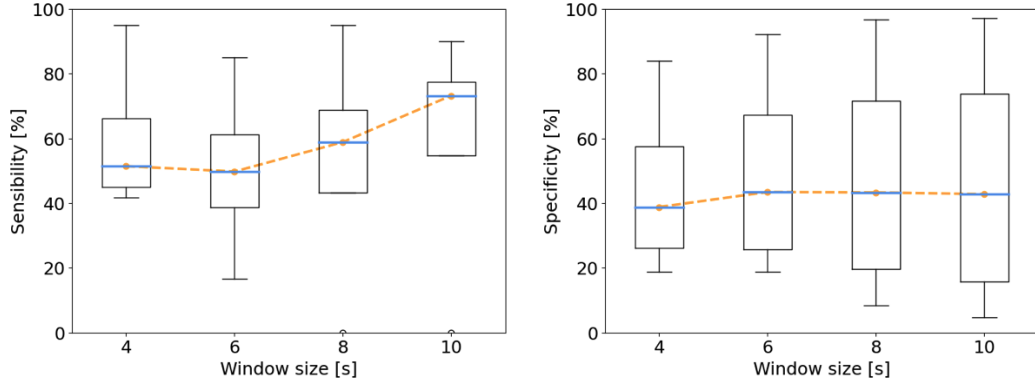


Figure 5.5: *Sensitivity (left) and specificity (right) of the Freeze Index algorithm for several window sizes, threshold set to 2 and step size set to 0.5s.*

The algorithm performed best with a window size of 10s, a threshold T of 2 and a step size dt of 0.5s. The window size parameter is not the same as for external data, which could be explained by the same reason as above, *i.e.* the number of patients. For these parameters, the overall sensitivity and specificity of the above-mentioned parameters are 73.21% and 42.77% respectively. The sensitivity obtained in this section is close to those obtained with this algorithm on external data. The specificity, on the other hand, is much lower than that achieved in Chapter 4. Moreover, the results for external data are close to the lower results found in the articles. Indeed, the articles' performances range from 73.1% to 89.1% for sensitivity and 76% to 90% for specificity [79, 80, 81, 82].

In order to analyze the difference between the two exercises that triggered FOG episodes, Figure 5.6 was obtained. It shows that for the Freeze Index algorithm, the results obtained are better for the TUG exercise than for the doorway exercise. It's important to highlight that in the case of one condition occurring during a patient's TUG exercise, the algorithm has a sensitivity of 0% and a specificity of 100%. This means that the algorithm did not detect any FOG episodes. Indeed, the threshold used by the algorithm appears to be excessively high compared with the signal. This data was therefore not taken into account in the previous analyses of all patients.

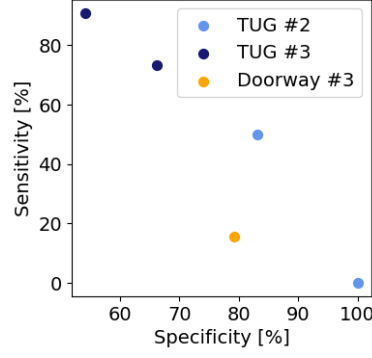


Figure 5.6: *Specificity and sensitivity of the Freeze Index for each subject and exercise.*

An analysis was then carried out on signals obtained from healthy subjects in the TUG exercise to study the occurrence of false positives. The video recordings were used to determine turns and sitting times. They were compared with the signal and with the results of the algorithm, in order to analyze when these false positives occur. The parameters used are those that give the best results in patients. The algorithm detects sometimes FOG episodes during the rotation period, as shown in Figure 5.7. There may also be other false positives that appear at random times. Their number does not depend on the condition. On the other hand, some papers [80] performing this method set a threshold of 3, which would remove a good number of these false positives.

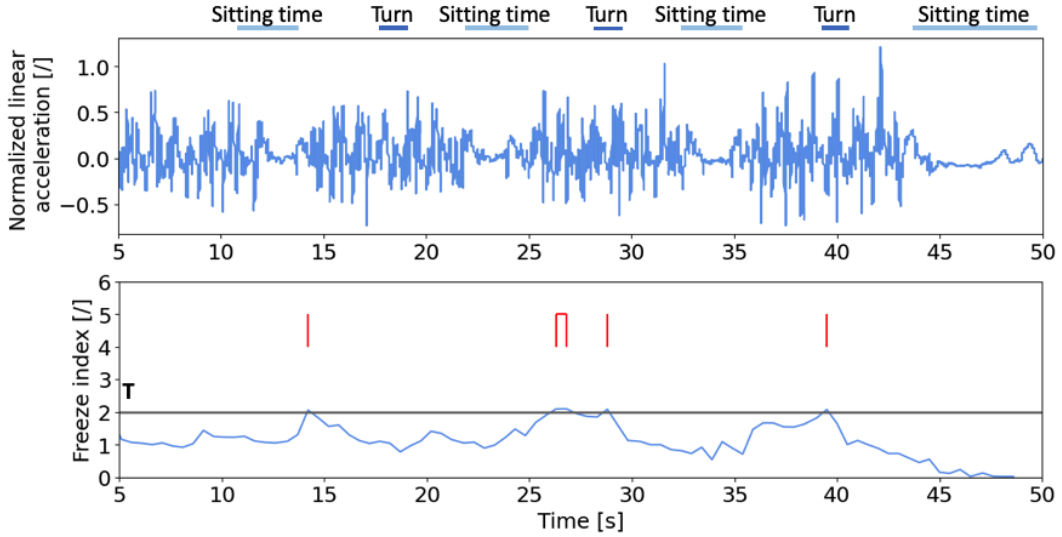


Figure 5.7: *Representation of the operation of the Freeze Index algorithm on the signal of a healthy subject. Linear acceleration (top) and Freeze Index (bottom) for a period of time are represented. The red lines indicate FOG episodes determined by the algorithm.*

In order to deeper analyze false positives, the 10-Minute Circle Walking exercise was also analyzed, this time for all subjects, *i.e.* healthy subjects and patients. It also tends to produce a certain number of false positives. As with the TUG, the number of false positives is also independent of condition. Figure 5.8 shows these false positives detected during 2.5 minutes of the 10-Minute Circle Walking exercise. It should be noted that when the person stops voluntarily (around 510 seconds), the algorithm does not detect a FOG episode.

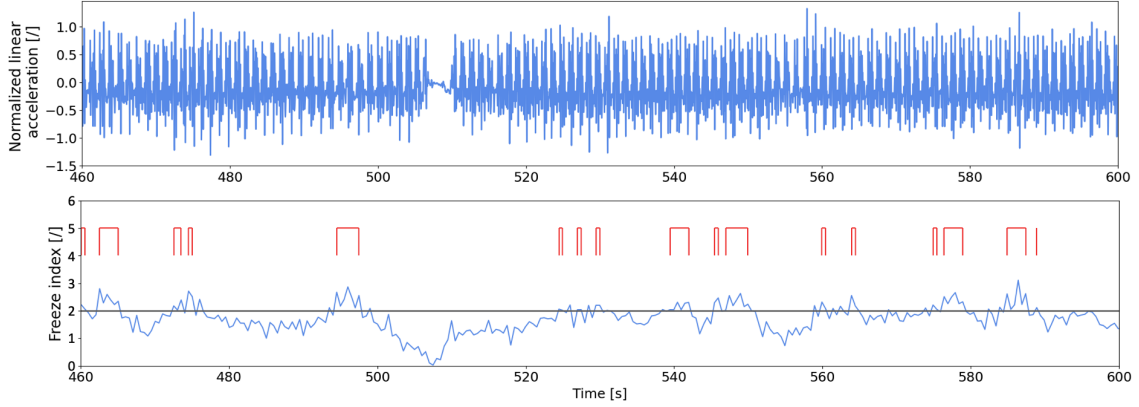


Figure 5.8: Representation of the operation of the algorithm on the signal of a 10-Minute Circle Walk of a patient. Linear acceleration (top) and Freeze Index (bottom) for a period of time are represented. The red lines indicate FOG episodes determined by the algorithm.

5.2.2 Surface electromyography-based method

Here, the same analysis is performed as for the open access dataset. Similarly to the Freeze Index algorithm, the selection of each analyzed leg is based on whether it yielded the best results or not. The threshold T_2 is still fixed at -0.4. Several combinations of T_R and T_1 are tested. They can all be found in appendix Section C.3. In Figure 5.9, the impact of the threshold T_R is illustrated, specifically for the optimal threshold value T_1 set to 0.01. The observations drawn from the figure align with the interpretations made in Chapter 4 regarding this particular parameter of the algorithm. However, the trend depicted in the figure is not as prominent, which could be attributed to the smaller sample size of only two patients compared to the larger external dataset of nine patients. Concerning the T_1 threshold, as for the external data, the difference is slight. As with the results observed in the external dataset, the overall performance is better when using the threshold value of T_1 set to 0.01.

Compared to what was obtained with the external data, results and conclusions on parameters are the same. Indeed, best performances are given by T_R set to 3 and T_1

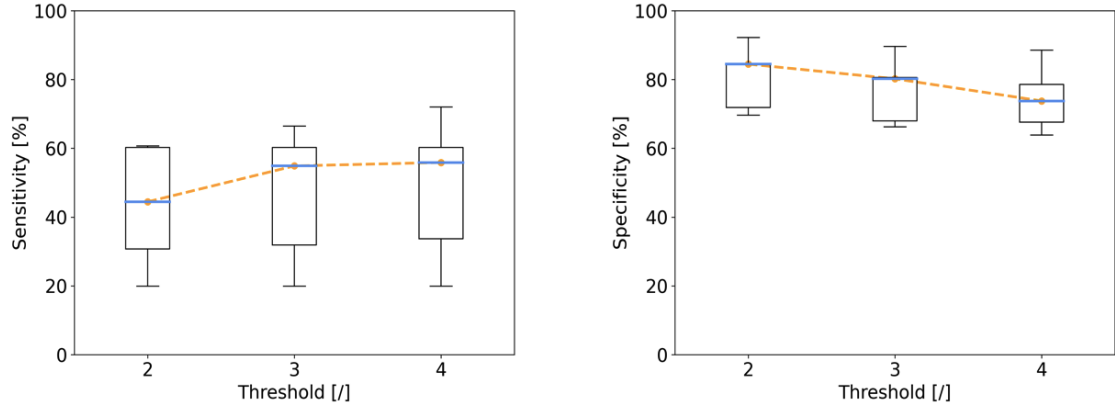


Figure 5.9: *sEMG method performance for the algorithm in function of the chosen threshold and based on a specific window threshold for patients of the experiment.*

set to 0.01 as revealed in Figure 5.9. Therefore, the overall sensitivity and specificity taking into account each patients are respectively 54.88% and 80.20%. On one hand, there is a decrease in sensitivity in comparison to external data. On the other hand, there is a significant increase in specificity. However, if the performances achieved by the authors of the article are observed, a clear difference is noticeable, whether it is for external or experimental data. Indeed, the sensitivities and specificities are considerably reduced, considering they were reported as 98% and 95% respectively in the paper [91].

Figure 5.10 depicts an analysis of the two exercises that induced FOG episodes on patients. The results demonstrate that the algorithm exhibits better performances during the doorway exercise compared to the TUG exercise. It could be explained by the fact that the doorway exercise could involve longer or more pronounced FOG episodes, making them easier to identify with this algorithm compared to the TUG exercise.

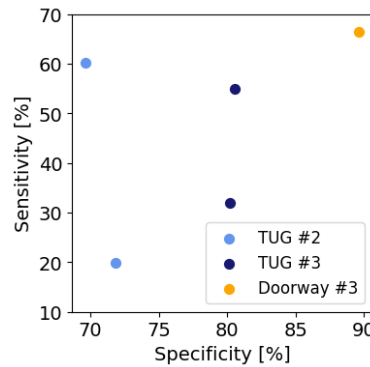


Figure 5.10: *Specificity and sensitivity of the sEMG method for each subject and each exercise.*

To compare results obtained with patients, only obtained on TUG exercise, an analysis of what happens with healthy subjects is conducted with parameters that gave best results with patients. It reveals that FOG episodes are detected in TUG exercise specifically when turning or sitting back in the chair as represented in Figure 5.11. The number of false positives rises when the metronome condition and dual-task are incorporated into the exercise, with a slightly more pronounced increase during the dual-task.

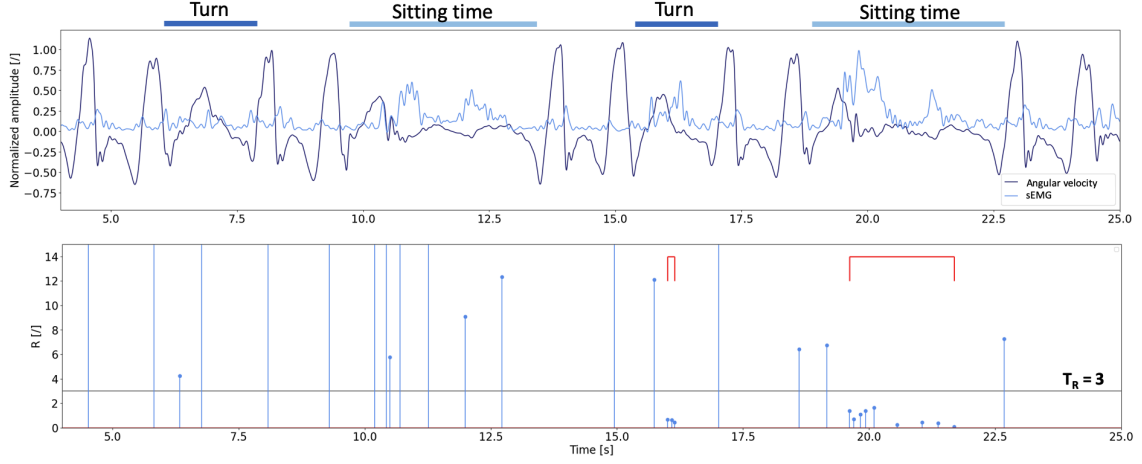


Figure 5.11: Representation of the operation of the surface electromyography-base algorithm on the signal of a healthy subject. Angular velocity and sEMG traces of the right shank (top) and R ratio (bottom) for a period of time are represented. The red lines indicate FOG episodes determined by the algorithm. The first FOG episode detected occurs during a turn in place while the second one happens during the return to the chair.

The same analysis to study the occurrence of false positives, has been made during the 10-Minute Circle Walk on all participants, *i.e* healthy subjects and patients. Almost every of them presented several false positives. However, the events detected were mostly really short (only one window associated with a FOG episode) as represented in Figure 5.12 just before 500s. Nevertheless, the voluntary stop observed at around 510s is detected as a FOG episode, even though this is not the case. Contrary to what was established in the article, the voluntary stop does not cause the computation of the R ratio to stop. This discrepancy could be explained by differences in the way the signal was smoothed. Specifically, they did not specify the extent to which it was done. Consequently, in our algorithm, it is possible that the signal retains excessive variability and falls below T_1 , leading to the computation of a R ratio, which was not observed in the article.

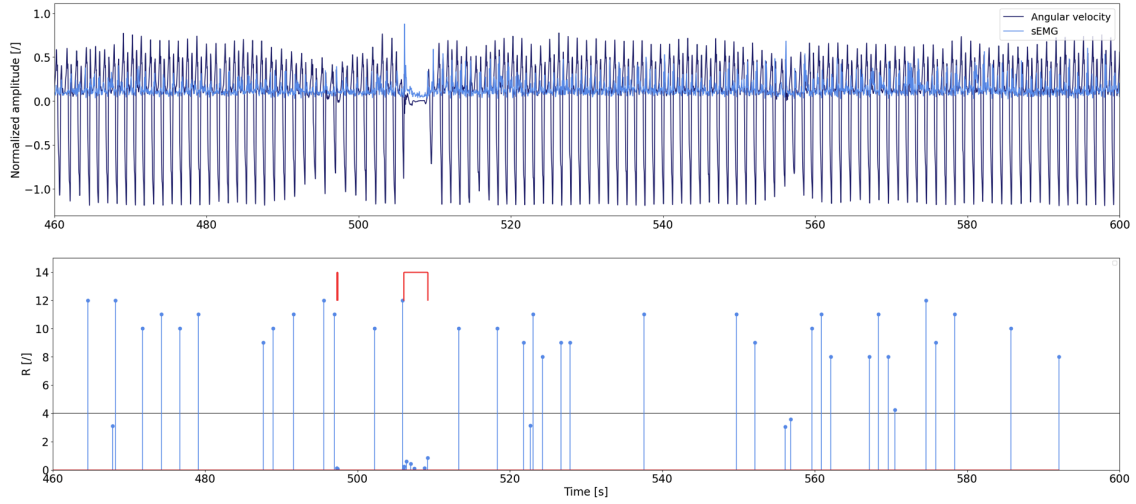


Figure 5.12: Representation of the operation of the sEMG algorithm on the signal of a 10-Minute Circle Walk of a patient. Normalized angular velocity and sEMG traces of the left shank (top) and R ratio (bottom) for a period of time are represented. The red lines indicate FOG episodes determined by the algorithm.

5.2.3 K-index

As with this algorithm on external data, T_{turn} has an impact on performance. Figure 5.13 shows the difference it can generate for a particular choice of thresholds and a particular number of neighbors analyzed. In the case of this figure, T_{turn} set between 0.3 and 0.7 gives better results. The choice of T_{turn} equal to 0.5 was therefore made, as for the external data. Again, if T_{turn} is changed, all the parameters will also change. An optimization algorithm is therefore necessary to find the best parameters.

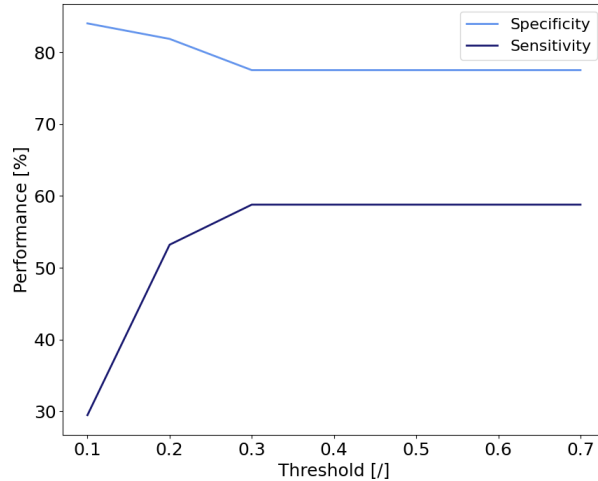


Figure 5.13: Influence of the threshold T_{turn} on performance for one subjects based on specific thresholds $T_1 = 100$ and $T_2 = 300$ and a specific number of 0.5s analyzed.

In this algorithm, the other modifiable parameters, as already mentioned, are

the thresholds and the number of analyzed neighbors. The thresholds were again analyzed based on the person and the performances change in function of them, as it can be seen on Figure 5.14. Based on this figure, the subject's performances are better when threshold T_1 is fixed at 40 and threshold T_2 is set at 350. The interpretation for these changes are already discussed in Section 4.2.3. For these data, because the FOG episodes were particularly short, the number of neighbors analyzed decreased compared to that employed for the external data. Indeed, here, the best results were obtained by analyzing neighbors over 0.5s.

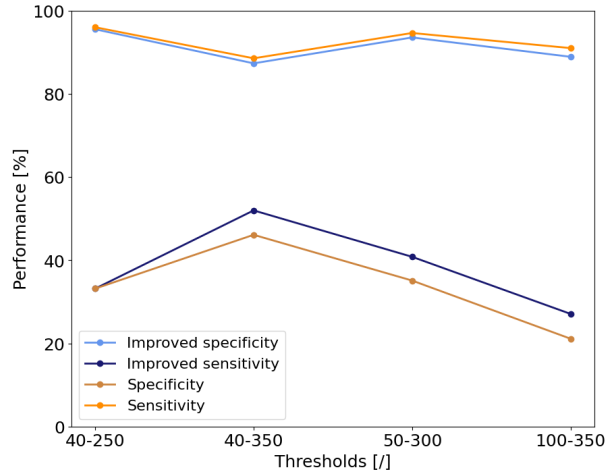


Figure 5.14: *K-index performance for the algorithm and its improvement based on the chosen thresholds for an analysis of 500ms around each value for a patient.*

The best performances of each subject can be found in appendix Table D.1.1 where the parameters giving the best detection are indicated. The overall performances, considering the best performances of each subject (which implies different thresholds for each), amount to 46.39% and 78.03% for sensitivity and specificity, respectively. These performances are decreased compared to those obtained on external data. And both performances obtained in this work are also decreased compared to those reported in the article by Suppa et al. [92], which are 93.4% for sensitivity and 98.5% for specificity.

The performances of each patient for each exercise are presented in Figure 5.15 to compare the results of the TUG exercise and the doorway exercise. The results indicate that the doorway exercise performs better, displaying the highest sensitivity and the second highest specificity. The reason for this could be that the doorway exercise might include longer or more noticeable FOG episodes, which makes them easier to identify using this algorithm compared to the TUG exercise, as already mentioned in the previous section. In addition, as the turns are less tight when passing through the door than those in the TUG, the explanation for this result could be similar to that given to justify the differences between the two exercises in

the external data. Indeed, the K-index is supposed to differentiate turns from FOG episodes, but this difference is obviously more difficult to observe during tight turns.

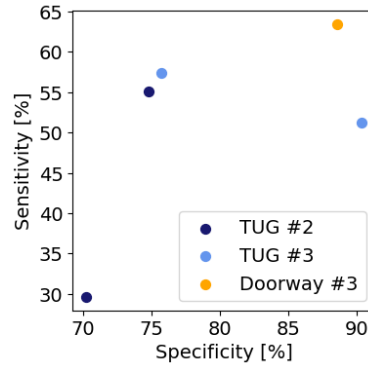


Figure 5.15: *Specificity and sensitivity of the K-index for each subject and each exercise.*

The data of the healthy subjects were analyzed in order to compare results obtained with patients. These signals triggered the detection of FOG episodes, during certain sharp turns as well as during the return to the sitting position on the chair, as presented in Figure 5.16.

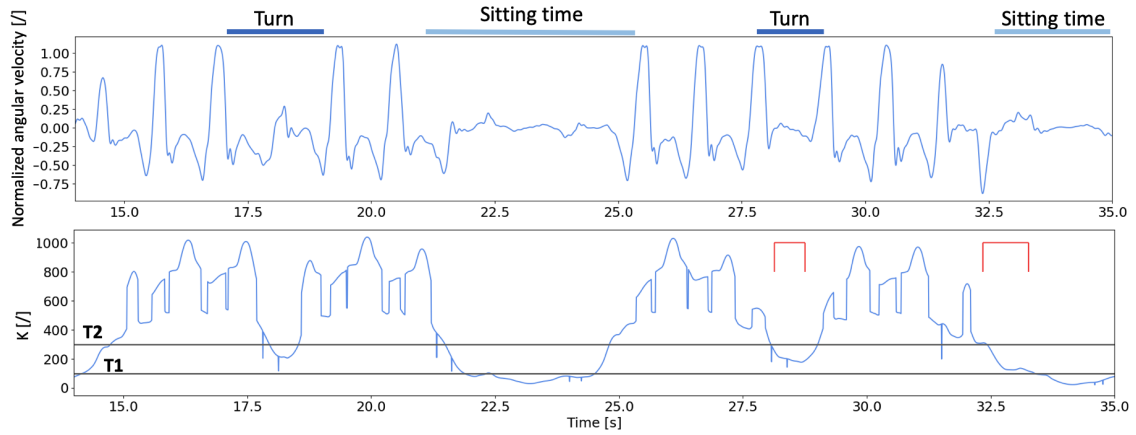


Figure 5.16: *Representation of the operation of the K-index algorithm on the signal of a healthy subject. Angular velocity (top) and K-index (bottom) for a period of time are represented. The red lines indicate FOG episodes determined by the algorithm. The first FOG episode detected occurs during a turn in place while the second one happens during the return to the chair.*

The algorithm did not detect any FOG during the 10-Minute Circle Walk exercise in all three patients and all healthy subjects. Even when the patients stopped voluntarily, no episode was detected. Figure 5.17 displays the K-index with voluntary stopping during this exercise, also showing that no FOG episode was detected.

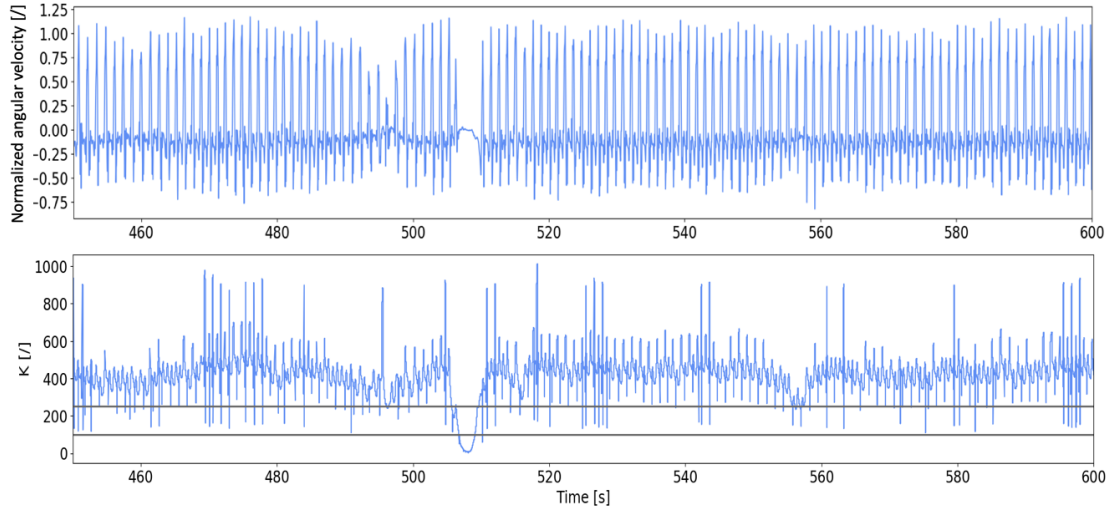


Figure 5.17: Representation of the operation of the algorithm on the signal of a 10-Minute Circle Walk of a patient. Angular velocity (top) and K-index (bottom) for a period of time are represented.

5.3 Summary

The main findings observed on the experimental data are as follows.

For the **Freeze Index** algorithm, the results are:

- Best parameters are window size equal to 10s, $T = 2$ and step size $dt = 0.5$.
- Overall sensitivity and specificity of 73.21% and 42.77% respectively.
- A performance difference is observed between the TUG exercise and the doorway exercise, with the former showing superior results in FOG detection.
- The 10-Minute Circle Walk induces false positives.

Secondly, **sEMG** algorithm:

- Best parameters are $T_R = 3$ and $T_1 = 0.01$ with $T_2 = -0.4$.
- Overall sensitivity and specificity of 54.88% and 80.20% respectively.
- A performance difference is observed between the TUG exercise and the doorway exercise, with the latter showing superior results in FOG detection.
- The 10-Minute Circle Walk induces false positives.

Finally, for the **K-index** algorithm:

- $T_{turn} = 0.5$. The best results are obtained with an analysis of 0.5 seconds of data. Person-dependent thresholds are set at 100-300 and 150-350.

- Overall sensitivity and specificity of 46.39% and 78.03% respectively.
- Performances differences are observed between the TUG exercise and the doorway exercise, with the latter showing superior results in FOG detection.
- The 10-Minute Circle Walk induces no false positives.

In conclusion, for all three techniques, an optimization algorithm would most probably be necessary, as already mentioned in the previous chapter. Furthermore, both healthy subjects and patients showed false positives mainly during the turning and sitting positions of the TUG exercise. In addition, all performances were reduced compared with those reported in the articles. In terms of sensitivity, the Freeze Index algorithm appears to be the best, followed by the sEMG method. In terms of specificity, the trend is reversed compared to what was obtained with external data, with first place going to the sEMG method, and second to the Freeze Index. Overall, taking the performance that maximizes both statistical values, sEMG method seems to be the winner, unlike in the previous chapter. It is followed by the K-index and finally the Freeze Index appears to be the weakest at detecting FOG episodes.

Chapter 6

General discussion and perspectives

In the previous two chapters, results of the algorithms developed as part of this work were presented, along with an interpretation of the influence of their parameters. In this chapter, a discussion is launched on why the algorithms developed in this work generally showed differences in performances compared with the results reported by the authors of the methods used. In addition, the limits of this work are identified and perspectives are explored.

6.1 Discussion of the results

To begin this discussion, a return on sensitivities and specificities of the developed algorithms is conducted. A summary table of the results obtained in Chapters 4 and 5, compared to the performance obtained by the authors of the methods, can be found in Appendix E. Firstly, differences are observed among the algorithms tested within the same dataset. For example, the K-index algorithm demonstrates the best trade-off in terms of sensitivity and specificity in the external data, but this is not observed in the experimental ones. In addition, comparing the methods proves to be challenging since the conclusions regarding performances and parameters differ between the external and experimental data. One possible explanation for these discrepancies is the number of patients involved, which is discussed in more depth in the limitations of this work. Additionally, it could be related to the protocols or the equipment used as described below.

Indeed, the experimental protocols were not similar. Regarding the Freeze Index, it is challenging to point a specific protocol since several articles discuss it. Generally, TUG test, 180° or 360° turns, simulations of daily activities such as getting a glass of water from across the room and passing through narrow doorways are used to trigger FOG episodes [79, 80, 81, 82]. On the other hand, as the K-index and

sEMG methods are presented in only one article each, comparison of the protocols is simpler. For the former, a modified 3m TUG test was used [92], while for the latter, the authors developed a 7m TUG test in an ecologically realistic environment [91], incorporating obstacles commonly encountered in everyday life and which must be avoided. Although the task was similar to that performed in the study carried out for this work, the realistic environment was not included. Another consequent difference lies in the patient's condition. Indeed, in the articles for all three algorithms, patients performed the experiments in both ON and OFF states. For the external data, the experiments were conducted only in the OFF state. Finally, in the present work, the experiments were carried out only in the ON condition, which reduced the number of FOG episode occurrences.

It should also be noted that the signals are acquired using different equipment, which may result in slight variations. Furthermore, the sensors are not set to the same acquisition frequency. This may lead to differences, as the number of data points analyzed may increase or decrease depending on the frequency chosen. For example, during a time window using the Freeze Index algorithm, the number of data points per window will not be identical. As a result, this variability in data sampling could affect the precision of the algorithm, leading to greater or lesser accuracy in its analysis.

It is important to realize that the performances of the algorithms developed in this master thesis are not satisfactory compared to what the authors of the various discussed articles have achieved. Although this decrease in sensitivity and specificity can be explained by the differences mentioned previously, it would likely be possible to improve the algorithms. The first proposed solution is to develop a parameter optimization algorithm. This would make it possible to test all possible combinations of parameters to find the best performance.

Another idea for improvement would be to personalize and determine these parameters on an individual basis. Indeed, as described in Chapters 4 and 5, the Freeze Index and the sEMG method show considerable variability, reflected by the whisker lengths of the boxplots. By performing a subject-by-subject analysis, it becomes clear that the variability observed stems from the algorithm's ability to deliver satisfactory results for some individuals while generating mediocre results for others. Therefore, although the methods have not been explicitly identified as patient-dependent, it would be desirable to consider person-dependent adaptation of parameters to improve results. This idea has been reported in several articles on the Freeze Index method. To achieve this, they analyzed the Freeze Index returned when each subject was standing or walking, and decided the value of the threshold on this basis. Some differences in results were noted between the global threshold and the person-based one, suggesting that the concept of person-dependent thresholds might be an alternative to give the algorithm better performances [79, 82]. These person-

dependent parameters could be found on the basis of the optimization algorithm mentioned previously, without preventing the algorithms from operating in real time. It would simply require running the optimization as a preliminary adjustment test. Once the parameters that yield the best performances are determined, they can be retained. However, periodic readjustments could be beneficial to monitor the progression of the disease.

Finally, another potential approach, as proposed by Bächlin et al. [81], is to consider information from both legs in order to enhance the outcome. This would be especially crucial for individuals who could exhibit distinct tremors in one leg compared to the other during a FOG episode.

Upon studying the effectiveness of the algorithms developed, it was observed that all three methods often detect FOG episodes in both patients and healthy individuals during turning and sitting, even when there were no actual instances of FOG episode. This phenomenon can likely be attributed to the definition of FOG for patients, which is discussed in the study’s limitations. In the case of healthy subjects, when they turned or sat down, they did so almost on a single foot, which is natural. However, this momentarily interrupts walking, disrupting the normal gait cycle, as illustrated by the angular velocity in the figures provided (Figures 5.11 and 5.16). It is possible that the algorithms capture this effect as abnormal and therefore associate these events with FOG episodes.

In conclusion, it would be valuable for future research to focus on improving the performances of the algorithms by further investigating the suggestions provided.

6.2 Limits of the study

There are several limitations to the study conducted for this work. Firstly, the small number of patients (and even fewer for those who developed FOG) involved in this study means that it is not possible to identify significant trends and compare them effectively with results obtained from freely available data, nor with those obtained from articles. As the patients were all men, despite the fact that men are more likely to develop the symptom of FOG, it is also not possible to draw any significant conclusions. In addition, only one patient has performed the doorway exercise.

Additionally to this small number of patients, the FOG episodes triggered in this experiment were also few in number. There may be several reasons for this. Firstly, the protocol could be improved to try to generate more FOG episodes. The TUG exercise could be retained, but a doorway passage (as in the case for the last patient in this study) or a passage from a room to a narrow corridor could be added. Furthermore, since the patients were instructed to tap their foot at the beginning

of each exercise, this could have provided them with a cue to avoid a FOG episode during the gait initiation. An alternative approach may be required to synchronize the signal and the video. One possible solution could involve tapping your foot and allowing a few more seconds of delay before initiating the task. Moreover, as described in Section 1.4.2, the onset of FOG episodes involves both the mind and the environment. Interestingly, one patient, despite having the highest NFOG-Q score and therefore being the most affected by FOG episodes, did not experience a single FOG episode throughout the entire duration of the experiment. This can be attributed to is strong motivation to perform well in the experiment. However, it is important to note that patients responded to this questionnaire based on their personal experiences, as well as their subjective estimation of the impact of these FOG episodes on their lives.

Another aspect that may have impacted the algorithm’s results during its evaluation on experimental data is the placement of the sensors. Indeed, they were positioned to track the muscle fibers of the tibialis anterior muscle. However, as can be observed in Figure 5.2 in Section 5.1.2, the sensors were slightly placed on the side of the leg, which disrupted the orientation of the X, Y and Z vectors. To address this properly, it would likely be necessary to perform calculations in order to determine, based on the sensor axes, new axes precisely oriented in the subject’s frontal, lateral and sagittal planes. Another potential solution would involve the use of separate sensors for measuring acceleration and muscle data. By employing this approach, the sensor placement can be optimized specifically for both signals. This separation of sensors would therefore offer flexibility in achieving accurate muscle data without compromising the accuracy of acceleration measurements. The method using sEMG would likely have an impact on patient comfort as it would require both sensors. However, for methods that only require linear acceleration or angular velocity, IMUs incorporating accelerometers and gyroscopes would be more than sufficient.

The definition of FOG is the subject of debate, even among specialists, as pointed out by the reference neurologist in this study. Consequently, this variation in definition can lead to discrepancies in data analysis and affect the algorithm’s performances. For example, in the experiments conducted in this study, when the patient returned to the chair during TUG exercises, the algorithms identified the patient as being in a FOG episode most of the time. This may be explained by the fact that patients often take small steps when turning to sit. However, the neurologist did not classify these moments as FOG episodes, considering this behavior as normal. Another neurologist might have analyzed this differently, classifying it as a FOG episode. This difference in the definition of FOG episodes therefore becomes crucial for understanding the results. In addition, the neurologist’s visual analysis is based on video sequences, and as FOG episodes are sometimes futile and difficult to see on video, the accuracy of detection may be reduced.

6.3 Perspectives

Ultimately, the development of these algorithms raises several questions. Is it truly necessary to use these methods to detect FOG episodes in real time and provide automatic assistance? Perhaps it would be “easier” to simply add a manual control button to the robot, so that when activated, it provides a push to help overcome the ongoing FOG episode. Indeed, as the patient’s feet would be blocked, but not his hands, he could activate it himself. This manual control would mitigate the security risks associated with the algorithm, given that it is not totally infallible. To achieve 100% reliability, the algorithm would need to have both 100% sensitivity and 100% specificity. This aspect is also not achieved by the authors of the described methods. However, an automatic assistance system can provide peace of mind to the patient and certainly improve their mental state. In such a scenario, once the algorithm detects a FOG episode, how should the type and intensity of assistance be provided? Additionally, what type of robot should be used to deliver this assistance?

Regarding the type of assistance, as this work aligns with the long-term project of providing on-demand assistance, research has been conducted on the principle of assist-as-needed. From this research, four concepts have emerged and are briefly explained in Appendix F.

As regards the intensity of the force applied, there are different ways of proceeding. Assistance can be increased gradually, starting with a small force, or it can be constant throughout the application. Indeed, the level of force administered to the patient must be carefully considered to avoid destabilizing him and increasing/equalizing the risk of falling compared to that due to FOG episodes. For example, in the sEMG algorithm, the results on external data, and particularly on experimental data, showed a high occurrence of false positives. Therefore, FOG episodes were detected while there was a priori none. However, a significant portion of these false positives lasted only for a single window, which is at most half a gait cycle. Considering that real time assistance is crucial, a possible approach would be to provide a light level of assistance until the FOG episode exceeds a certain duration. This way, the assistance would intervene if this very brief event is confirmed as a FOG episode. Otherwise, it would remain subtle enough not to disrupt the patient’s gait and mitigate any potential risks. It could be imagined that as long as the normal gait isn’t recovered, the assistance keeps to increase progressively. In addition, manifestation of FOG episodes is heterogeneous. Indeed, it can, even within a single subject, manifest as different phenotypes (as explained in Section 1.3), have different durations (half of episodes lasting less than 5s and 90% less than 20s) and have diverse triggering factors (environment, dual-task, emotional stress) [101]. This is clearly demonstrated

in Figure 6.1 presented in the paper by Mazetta et al. [91]. Consequently, the algorithm could be design to differentiate the phenotypes of FOG episodes, and the force delivered by the robot could be adapted accordingly.

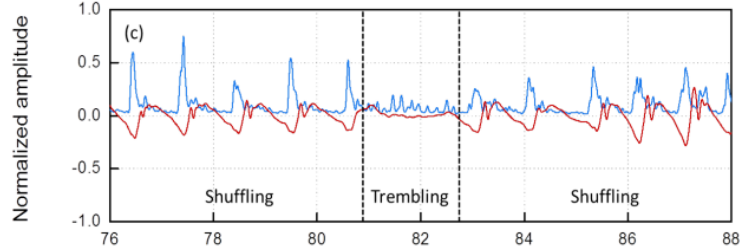


Figure 6.1: *Normalized angular velocity (red) and tibialis anterior muscle activity (blue) for shuffling and trembling FOG episodes.*

As discussed in Chapter 1, the progression of the disease leads to a worsening of both the severity of Parkinson’s disease and its symptoms over time. The ability to walk becomes increasingly challenging as the disease advances. Consequently, selecting the appropriate robot for providing assistance is crucial. Therefore, it becomes essential to have a robot capable of bearing part of the body’s weight. In this regard, exoskeletons like the EksoGT (briefly described in Section 2.1.1) can be a suitable option. However, for patients who can still walk relatively well, such a device may not be necessary. Additionally, it is important to consider that these machines are bulky and might startle or surprise people encountered along the way. Therefore, an alternative approach could involve opting for lighter and more discrete orthoses, such as the SMA (briefly described in Section 2.1.1), which can be attached to the hips.

The algorithms developed in this master thesis were intended to be used in real time. However, the delay between the occurrence of a FOG episode for the patient and the moment the algorithm detects the FOG episode needs to be investigated. The timing of the robotic assistance based on this detection should be as precise as possible, with an accurate duration, to ensure that the assistance is provided at the most appropriate moment. Within this work, practical analysis of this delay couldn’t be performed. Therefore, any assumptions about the timing of the method can only be provided in a theoretical manner. The estimations of the delay are indeed mentioned in each section dedicated to the implementation methods of the three algorithms in Chapter 4.

Conclusion

FOG episodes are widely recognized as a disabling symptom of Parkinson's disease. Therefore, this research specifically targeted patients who experienced FOG episodes, as this symptom was identified as a significant factor impacting gait. It is indeed described as a motor block, preventing the patient from moving his feet forward despite his intention to do so [8]. This master thesis is part of a research project aimed at developing a walking assistance protocol for patients with Parkinson's disease. The main aim was therefore to complete the first step by developing an algorithm to detect these episodes in real time. If it operates as expected, giving good performances, it could be used as a trigger for an on-demand assistance robot.

The state of the art indicates that the use of robotic rehabilitation has demonstrated positive effects on walking ability, as well as reduction in the occurrence and severity of FOG episodes. In addition, several studies showed that robotic rehabilitation outperformed other rehabilitation therapies. The review also pointed out that, to date, no studies of on-demand robotic assistance have been conducted on patients with Parkinson's disease. In response to this lack of research, the first step is to find a way of detecting FOG episodes. This is why methods for real time detection of these episodes were analyzed. After reviewing several, three were selected for development and evaluation in this work. These algorithms were the Freeze Index, the sEMG method and K-index.

To do this, data from two different sources were used. Firstly, the algorithms were tested on data from an open-source dataset. These data were collected during the OFF stage of the patients and on two different exercises, obstacle walking (long task) and TUG exercise (short task). Secondly, the algorithms were tested on data collected during experiments carried out as part of this work. Patients were in the ON stage and performed two exercises leading to FOG episodes, the TUG and the doorway exercises.

This led to relatively different results from those found in the literature. In fact, the results obtained in this research are relatively inferior. Firstly, when examining the Freeze Index, the parameters producing the best performances differ slightly between the two datasets. Indeed, the time window analysed varies, although the

other parameters remain the same. As far as the sEMG method is concerned, the parameters producing the most favorable results remained consistent in both datasets. Finally, it is difficult to draw conclusions for the K-index due to its person-dependent nature. The only perceptible difference between the different datasets lies in the number of seconds analyzed. Overall, the algorithms performed better on external data, except with the sEMG method. For external data, the sensitivity of the K-index as a function of the task performed (long vs. short) is the only performance that shows a significant difference. For the data collected as part of this work, the algorithms performed better during doorway exercise, except for the Freeze Index.

The results obtained were discussed and perspectives were presented. The limitations of the work were stated, including the small number of participants, the few FOG episodes generated, sensor placement and the debate surrounding the definition of a FOG episode. The perspectives of this work are quite numerous. They start with a big question: is this kind of robot with on-demand assistance really useful for this kind of problem? Indeed, a simple button that the patient presses when he is in a FOG episode could be considered, and perhaps safer. However, if such a robot is shown to be useful, and an algorithm with good enough performance is found, the type of assistance would need to be defined, as would the force applied by the robot. The latter could be changed according to the FOG episode duration, phenotype and certainly other parameters. Moreover, throughout this study, an opportunity to gain insights into the concept of on-demand assistance emerged, with an overview of the various approaches provided in Appendix F. Once all this has been defined, the choice of robot still has to be made, possibly depending on the progress of the disease.

To go further than the work already carried out, a number of ideas for improving the algorithms have been opened up, including the choice of parameters, which could be person-dependent, or the use of optimization algorithms to find the best parameters. The delay generated by the various techniques also should be analyzed. This is a very important parameter to take into account when working in real time.

In conclusion, this master thesis thus contributes to research by opening the door to detect when the assistance is needed by the patient. Indeed, it can be confirmed that real time detection of FOG episodes is possible. However, the integration of this detection capability into a robot to provide on-demand assistance has not yet been achieved, due to the demanding performance standards that must be met.

Appendices

A Types of tests

Table A.1: *Description of the different types of tests used to evaluate the effects and results of robotic gait assistance on patients.*

<i>Test name</i>	<i>Brief description</i>
Time Up and Go (TUG)	This test measures the time it takes for a person to stand up from a chair, walk a short distance, turn around, walk back to the chair and sit down again [102]. It allows to assess mobility, rated on a 1 (normal function) to 5 (severely abnormal function) scale [103].
10-meter Walk Test (10mWT)	This walking test measures gait speed of a person during a straight walk of ten meters [104].
Functional Independence Measure (FIM)	This measure is an assessment of the patient’s ability to perform daily activities. The test consists of a cognitive and a motor part. The higher the score, the more independent the person is in performing daily activities [105].
Mini Mental State Examination (MMSE)	This test measures the cognitive state of a person [106]. A score lower than 24 could indicate cognitive impairment [107].
Movement Disorder Society Unified Parkinson’s Disease Rating Scale (MDS-UPDRS)	The MDS-UPDRS is divided into four parts, which include: Part I, covering non-motor experiences of daily living; Part II, addressing motor experiences of daily living; Part III, focussing on motor examination; and Part IV, dedicated to motor complications [108]. The higher the score, the higher the impairments related to each part.

Table A.1: *Description of the different types of tests used to evaluate the effects and results of robotic gait assistance on patients (continued).*

<i>Test name</i>	<i>Brief description</i>
Berg Balance Scale	This test evaluates balance and consists in 14 items varying in difficulty from sitting in a chair to standing on one leg [109]. The lower the score, the higher the fall risk.
MiniBESTest	This test is composed of 14 items to assess the patient’s anticipatory postural adjustments, reactive postural control, sensory orientation and dynamic gait [110]. The lower the score, the worse the balance functions.
BriefBEST test	This test is a shorter version of the MiniBESTest, consisting in six sections to evaluate the patient’s balance [111]. The lower the score, the worse the balance functions.
Fear of Falling Efficacy Scale (FFES)	This test evaluates self perceived stability [55] and consists in 16 social and physical activities. The lower the score, the lower the concern about falling [112].
(New) Freezing Of Gait Questionnaire ((N)FOGQ)	This questionnaire consists in six items designed to assess severity and frequency of FOG episodes. The updated version of this questionnaire, the NFOGQ, is composed of nine items [113]. The higher the score of these tests, the more severe the FOG.
Functional Ambulation Category (FAC)	This test assesses the level of human support the patient requires during walking. It allows to assess the ability to ambulate on a scale from 1 (non-functional ambulation) to 5 (independent ambulation) [114].

B Performances of the Freeze Index

B.1 Impact of parameters on performances in the open access dataset

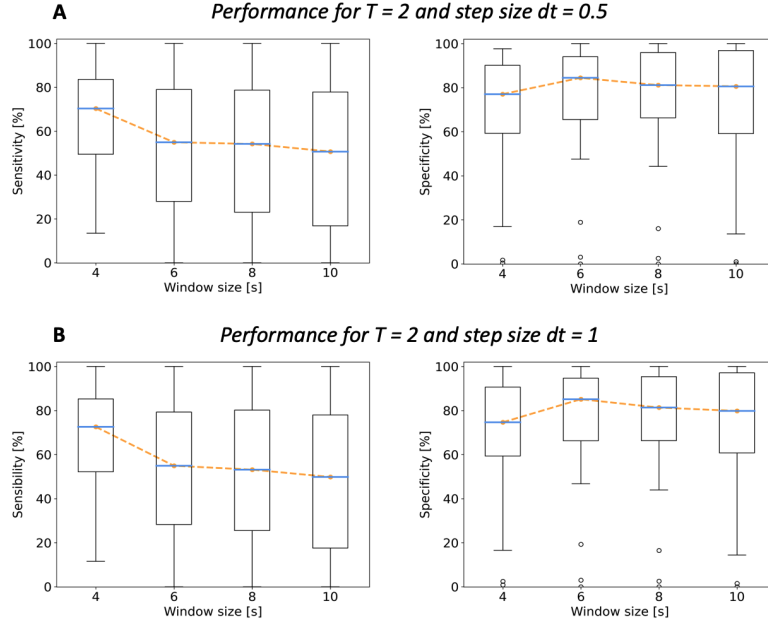


Figure B.1.1: Sensitivity and specificity for $T = 2$ and step size $dt = 1$.

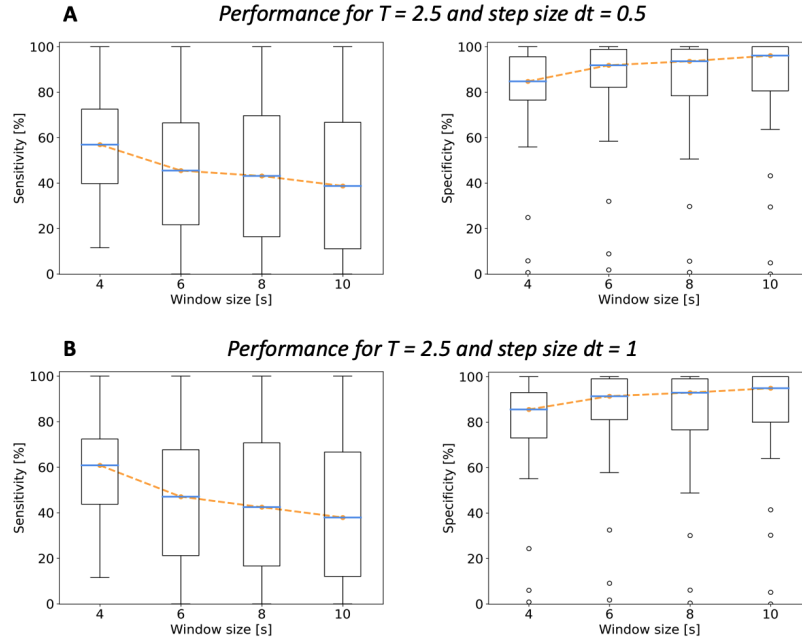


Figure B.1.2: (A) Sensitivity and specificity for $T = 2.5$ and step size $dt = 0.5$; (B) Sensitivity and specificity for $T = 2.5$ and step size $dt = 1$.

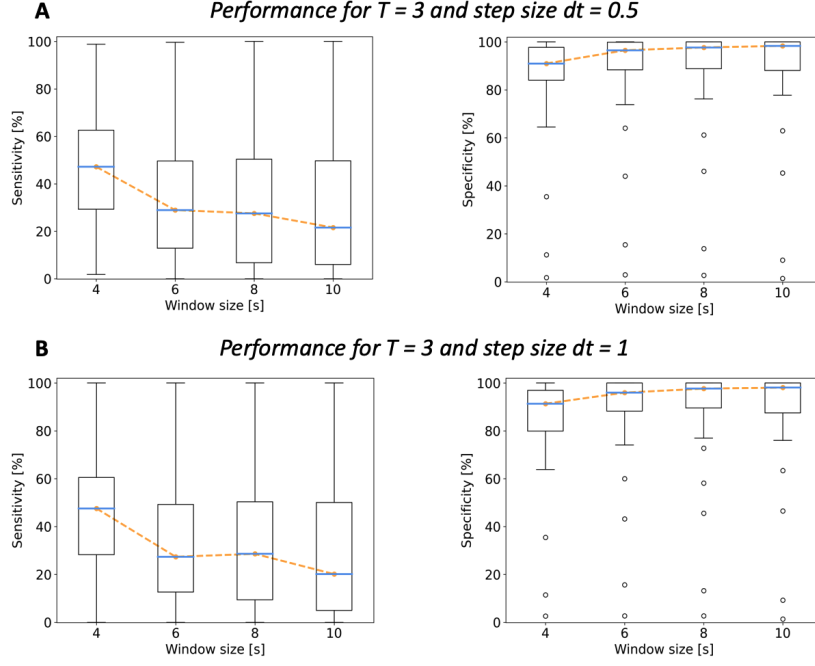


Figure B.1.3: (A) Sensitivity and specificity for $T = 3$ and step size $dt = 0.5$; (B) Sensitivity and specificity for $T = 3$ and step size $dt = 1$.

B.2 Results of the mixed-effects models on the open access dataset

Table B.2.1: Freeze Index algorithm p -values for the mixed-effects models on sensitivity and specificity of the condition short and long.

Pair of condition	p -value
Sensitivity for long tasks - Sensitivity for short tasks	0.187
Specificity for long tasks - Specificity for short tasks	0.078

B.3 Impact of parameters on performances in experimental data

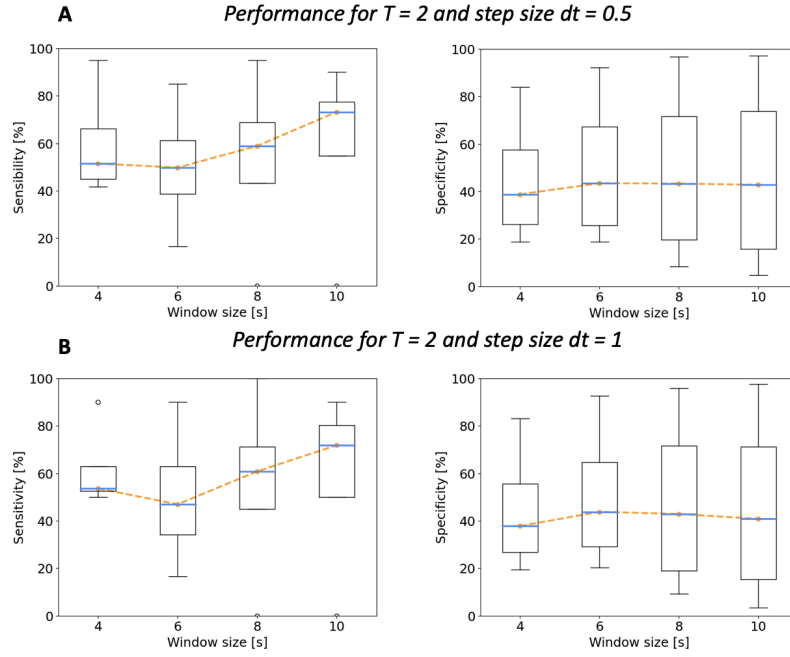


Figure B.3.1: (A) Sensitivity and specificity for $T = 2$ and step size $dt = 0.5$; (B) Sensitivity and specificity for $T = 2$ and step size $dt = 1$.

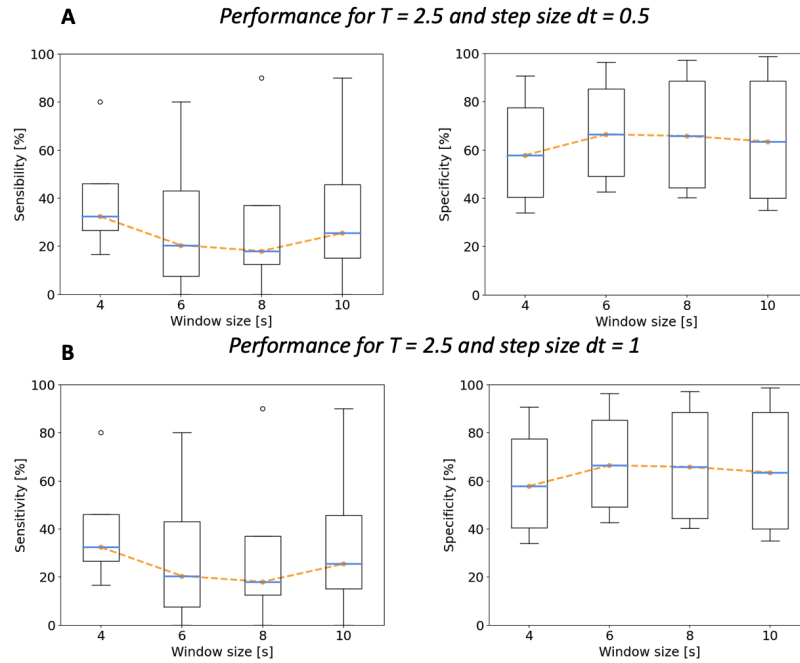


Figure B.3.2: (A) Sensitivity and specificity for $T = 2.5$ and step size $dt = 0.5$; (B) Sensitivity and specificity for $T = 2.5$ and step size $dt = 1$.

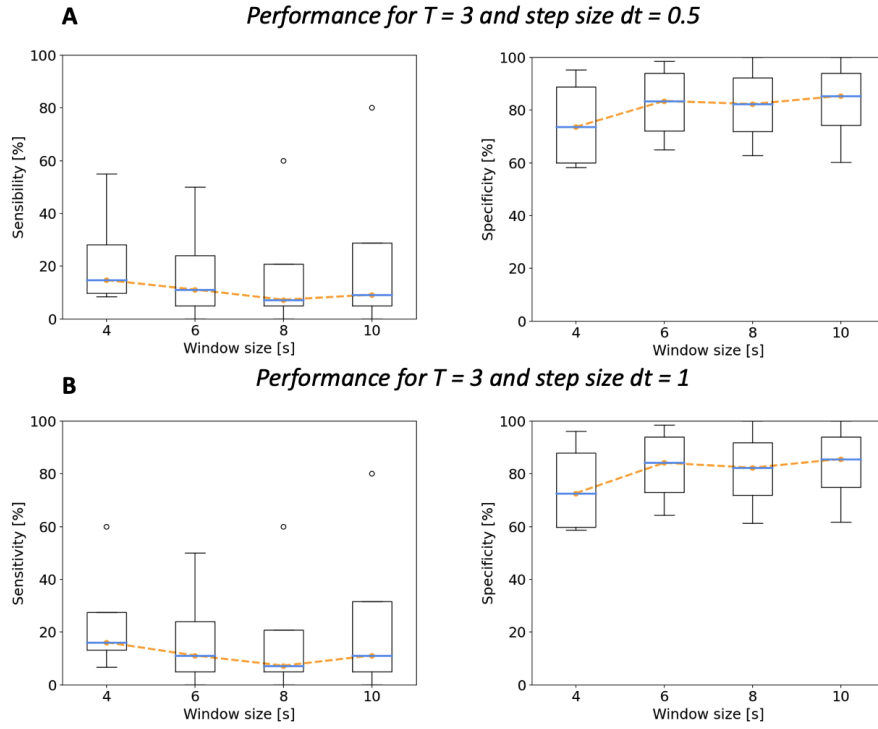


Figure B.3.3: (A) Sensitivity and specificity for $T = 3$ and step size $dt = 0.5$; (B) Sensitivity and specificity for $T = 3$ and step size $dt = 1$.

C Performances of surface electromyography-based method

C.1 Impact of parameters on performances in the open access dataset

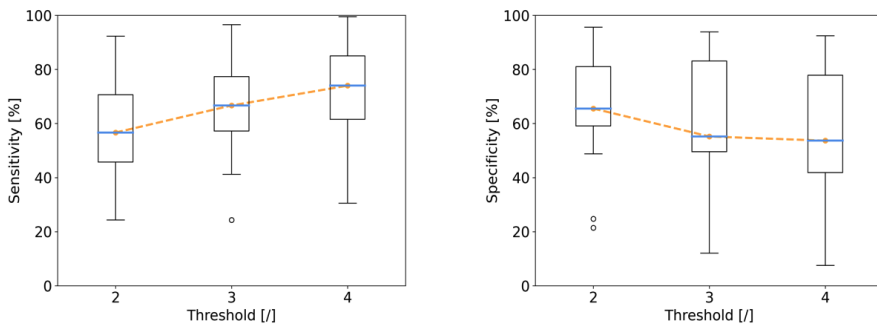


Figure C.1.1: Influence of the threshold T_R on sensitivity (left) and specificity (right) for all subjects based on a specific window threshold $T_1 = 0.01$.

C.2 Results of the mixed-effects models on the open access dataset

Table C.2.1: *sEMG* algorithm *p*-values for the mixed-effects models on sensitivity and specificity of the condition short and long.

<i>Pair of condition</i>	<i>p-value</i>
Sensitivity for long tasks - Sensitivity for short tasks	0.236
Specificity for long tasks - Specificity for short tasks	0.24

C.3 Impact of parameters on performances in experimental data

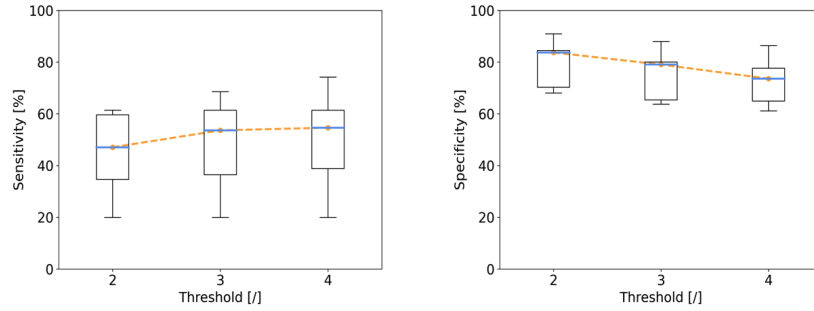


Figure C.3.1: Influence of the threshold T_R on sensitivity (left) and specificity (right) for two patients based on a specific window threshold $T_1 = 0.01$.

D Performances of the K-index

D.1 Person-dependent parameters and performances

Table D.1.1: *Performances of K-index method for each subject and different parameters.*

<i>Patient</i>	T_1	T_2	<i>Analyzed seconds</i>	<i>Sensitivity [%]</i>	<i>Specificity [%]</i>
Open access data					
#9	150	350	3	78.51	86.34
#10	60	400	3	93.72	66.47
#11	25	300	3	66.77	68.89
Experimental data					
#2	100	300	0.5	42.67	72.52
#3	150	350	0.5	57.37	83.54

D.2 Results of the mixed-effects models on the open access dataset

Table D.2.1: *K-index algorithm p-values for the mixed-effects models on sensitivity and specificity of the condition short and long. * stands for a significative result.*

<i>Pair of condition</i>	<i>p-value</i>
Sensitivity for long tasks - Sensitivity for short tasks	0.016*
Specificity for long tasks - Specificity for short tasks	0.891

E Summary table of results

Table D.2.2: *Summary and comparison of all results*

<i>Performance</i>	<i>Freeze Index</i>	<i>sEMG method</i>	<i>K-index</i>
Papers			
Sensitivity [%]	[73,1 - 89,1]	98	93,4
Specificity [%]	[76 - 90]	95	98,5
Open access data			
Sensitivity [%]	70.29	66.36	73.90
Specificity [%]	77.04	56.45	79.70
Experimental data			
Sensitivity [%]	73.21	54.88	46.39
Specificity [%]	42.77	80.20	78.03

F Assist-as-needed

The principle of assist-as-needed (AAN) aims to provide robotic assistance based on the patient's disability and effort level in real time [42]. The aim of this approach is to maximize the benefits of robotic rehabilitation for the patient by encouraging him to actively engage in the activity. Indeed, as the patient's performance increases, the assistance is gradually decreased to encourage the patient's improvement [115]. Unlike the imposition of a control strategy, the AAN method takes into account the patient's intention and adapts accordingly. In fact, robotic assistance would only intervene when the patient could not perform the task alone, enabling active participation while providing the minimum assistance necessary. To wrap up, the main aim is therefore to help the patient only when necessary, and to provide just the right amount of assistance [43, 44].

The initial impedance parameters can be changed manually by therapists or adapted by themselves. However, the former can lead to limitations as this adaptation is simply based on assumptions about the subject's abilities. A study conducted by Fricke et al. [116], demonstrated some advantages of automatic parameter adjustment, the main ones being that it reduces the time needed to adjust the assistance and increases the active participation of the user by using lower levels of assistance [116].

As shown in Chapter 2, robotic assistance has improved the gait of patients with Parkinson's disease. This is also the case for people with stroke and spinal cord injuries [117]. In this case, the patients were only passive. In contrast, this principle of need-based assistance, with not fully active assistance and voluntary movement

from the patient, can therefore lead to even better results in therapy, as it is the case for people with stroke and spinal cord injuries [118]. Unfortunately, to our knowledge, this principle has not yet been tested on patients suffering from Parkinson’s disease.

Different control strategies have been developed to provide this assistance on demand, each considering various parameters. The implementation of these strategies can vary, and they can also be combined. The following sections describe some commonly used concepts.

F.1 Impedance controller

Impedance control is the principle on which the majority of AAN algorithms are built. This principle is a method which modifies the assistance provided by the robot to achieve a certain objective, depending on the torque given by the patient or the position of the patient’s limbs [119, 120]. This type of control takes a position as input and gives a force as output [121].

In adaptive impedance control, the robot will apply an aid proportional to the effort provided by the patient. If patient effort is low, the impedance supplied by the robot will be high and, consequently, compliance (freedom of movement) will be low. This means that the patient will be forced to follow a defined trajectory. And conversely, the greater the effort made by the patient, the less assistance will be needed and therefore the impedance of the robot will be low. The robot impedance will define the robotic assistance provided to the patient’s limbs in order to follow a defined physiological walking trajectory. If the impedance is high, then the robot will not allow the patient to deviate much from the defined trajectory, while a low impedance will allow a greater deviation from the same trajectory. This impedance depends on the patient’s disability and the effort he puts in. The big challenge is to find a good balance between the compliance and the safety of the patient [119, 122, 123].

There are two different methods of implementing this control: joint space and end point space. The problem with the first method is that a small deviation in the knee joint can result in a large difference in foot placement. However, it does not depend on the kinematic configuration and can therefore be implemented in the stance or swing phase, as the actual joint trajectory and the reference trajectory are defined continuously throughout the gait cycle. Unlike the previous example, the end-point space depends on the gait cycle, and will need to be defined differently depending on whether you’re in the swing or stance phase. In this case, a stiffness and damping parameter is adapted to each step. This method is based on the error between the actual speed and position of the foot/ankle and those of the defined

trajectory [122].

F.2 Trajectory correction

Assistance based on trajectory correction consists of program-adjustable robotic rigidity and a virtual tunnel. It creates a compliant force field around a target motion to ensure tracking accuracy while allowing moderate kinematic errors [122]. In this configuration, the patient can control its gait. The patient's freedom stops when he passes the virtual tunnel, defined by a tolerance zone around a reference trajectory. The boundaries of the virtual tunnel are constraining forces that force the patient's leg to follow the physiologically correct pattern if it moves too far from it. Within the boundaries of the virtual tunnel, no force is applied, the subject is free, which allows for individual variability when walking, as it is represented in Figure E.1 [115] [124]. This principle is almost always coupled with the preceding principle of impedance control, since the principle is the same as the definition of this kind of control (*i.e.* to analyze the position of the patient's limb and apply a force if it is not in the expected zone). The force applied can be increasing. This means that, as the patient moves away from the center of the zone, the force applied becomes stronger. Generally, maximum force is applied at a certain distance from the zone, to prevent the patient from moving too far away [117]. In addition to these constraint forces applied in the form of normal forces, a tangential force is applied, allowing the limb to move forward correctly. This force decreases with distance from the center of the intended zone [117, 124].

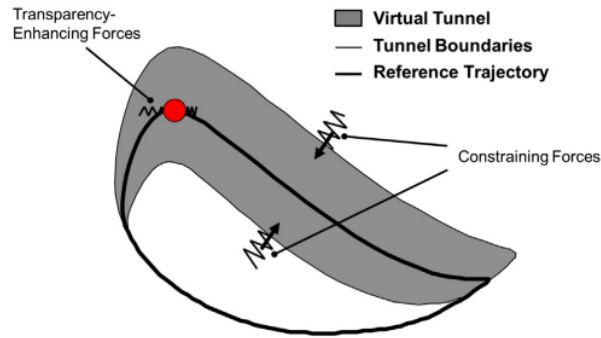


Figure E.1: *Schematic representation of the trajectory correction principle [115].*

F.3 Forgetting factor

This implementation method can be combined with the previously mentioned concepts (*i.e.* impedance and trajectory correction). In this approach, the focus is on whether the patient has successfully completed the previous movement. If they have, the assistance will slightly decrease. If the patient continues to perform the entire

movement correctly, the assistance will keep decreasing. However, if the patient is unable to perform the movement correctly at any point, the assistance coefficient will increase. By incorporating a forgetting factor, this method allows for more adaptability and variability with each step. Essentially, when the error is minimal, the assistance is reduced. This approach helps prevent the patient from becoming overly reliant on assistance and encourages them to contribute as much as possible. Consequently, the patient gains more freedom in their walking style, creating a more accommodating environment [125, 126, 127].

F.4 Amplifier

Amplifier method aims to produce assistance related to the subject’s motor intention captured by an electromyogram [128]. Once again, impedance is often a contributor. The use of electromyograms has developed in particular because it is non-invasive, requiring only electrodes on the surface of the skin. Furthermore, the signals acquired in this way precede the corresponding torque or force by 20 to 100ms [129].

The torque control is calculated by first estimating the voluntary torque of the ankle joint by an electromyogram-driven musculoskeletal model and then by multiplying it by an assistance ratio. This ratio is determined by the patient’s performance and by using a forgetting factor (as described in the previous section) as the patient improves. The error on which the forgetting factor is based is related to the trajectory of the patient’s movement. The error is therefore referred to as the difference between the desired angle and the actual angle [130]. This method is thus also linked to the trajectory correction method, described previously.

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École polytechnique de Louvain

Rue Archimède, 1 bte L6.11.01, 1348 Louvain-la-Neuve, Belgique | www.uclouvain.be/epl