

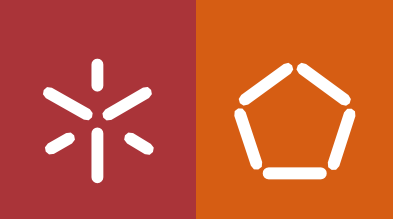


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**Motor effects of Cueing in Parkinson's
rehabilitation**

Escola de Engenharia

Universidade do Minho





Universidade do Minho
Escola de Engenharia

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Motor effects of Cueing in Parkinson's Rehabilitation

Master's Dissertation
Master Degree in Biomedical Engineering
Medical Electronics Branch

Dissertation supervised by
Professor Doctor Cristina Peixoto dos Santos

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AGRADECIMENTOS

Antes de mais, peço desculpa por destoar esta secção das restantes colocando-a em português, mas realmente só faria sentido se assim o fosse. Este ano foi um ano de muito crescimento pessoal. Escrever uma dissertação sem dúvida foi uma tarefa que posso descrever como complicada, não pelo projeto em si porque como se costuma dizer “quem corre por gosto não cansa”, mas por exigir momentos mais solitários que não combinam tanto comigo. No entanto, foi bastante menos complicada por ter tido a sorte de ser acompanhada pelas pessoas certas. E como este trabalho não teria sido possível realizar sem a ajuda direta ou indireta dessas pessoas, merecem também estar aqui mencionadas.

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RESUMO

A doença de *Parkinson (PD)*, é um distúrbio neurodegenerativo que afeta principalmente neurónios produtores de dopamina, traduzindo-se em sintomas motores incapacitantes como perturbações da marcha e *freezing of gait (FoG)* [1], [2]. O *Parkinson* impacta a autonomia dos pacientes ao realizar tarefas motoras diárias, diminuindo assim a sua qualidade de vida [2], [3]. Estratégias de aplicação de pistas sensoriais em dispositivos vestíveis, surgem como possibilidades promissoras para melhorar a qualidade de vida (*QoL*) [3]–[5]. Personalizadas para as necessidades dos pacientes de *PD*, permitem estimular diferentes caminhos neurológicos para gerar resposta motora [6]. As pistas podem assim ajudar os pacientes a restabelecer controlo motor e melhorar a mobilidade dos mesmos, surgindo como uma abordagem holística para os revigorar e restaurar a sua independência [5], [7].

Este projeto pretende avaliar o impacto das pistas sensoriais, focando-se no treino contínuo com a *+sensBand* em pacientes de *PD*, explorando o seu potencial para melhorar o controlo motor e reduzir episódios de *FoG*. A *+sensBand* é um dispositivo de *biofeedback* vestível, na forma de uma cinta, produzido pelo *BiRDLaB*, desenhado para potencializar reabilitação, monitorização motora e ainda administração de pistas táteis ou visuais, personalizada em pacientes de *PD*. O estudo tem como objetivo compreender os efeitos motores do uso de diferentes estratégias da *+sensBand*, implementando novas focadas em sintomas mais avançados como o *FoG*, e testando-as a longo prazo sobre os pacientes, através da estruturação e condução de um protocolo para um estudo longitudinal clínico, e consequente análise dos dados adquiridos.

Os estudos de validação realizados demonstraram que as pistas vibrotáteis tanto em *open* como *closed loop*, melhoraram eficazmente o desempenho da marcha, ao abordar os aspetos hipocinéticos e bradicinéticos em pacientes de *PD*. A combinação de pistas visuais e somatossensoriais, de ambos os métodos, numa nova estratégia focada na prevenção de *FoG*, foi validada com elevada aceitação em participantes saudáveis, tendo comprovado o potencial promissor para a reabilitação motora em diferentes cenários da vida diária. Estes resultados sustentaram a sua aplicação a longo prazo com os pacientes, tendo a sua eficácia dependido de um treino consistente. Adicionalmente, o treino contínuo com esta estratégia reduziu as ocorrências de *FoG*, melhorou o desempenho motor e a *QoL* dos pacientes de *PD*, destacando o impacto positivo desta estratégia no quotidiano destes pacientes.

Palavras-chave: Doença de Parkinson; estudo longitudinal; *Freezing of Gait*; pistas sensoriais; Qualidade de vida

ABSTRACT

Parkinson's Disease (PD) is a neurodegenerative disorder that affects dopaminergic neurons, leading to debilitating motor symptoms like gait disturbances and Freezing of Gait (FoG) [1], [2]. PD impacts patient's autonomy performing daily tasks, diminishing their overall quality of life (QoL) [2], [3]. Cueing strategies implemented on wearable devices, emerge as promising possibilities for enhancing QoL [3]–[5]. Tailored to the needs of PD patients, allow to explore different neurological pathways to generate motor response [6]. Cueing strategies can help PD patients regain motor control and improve mobility, offering a holistic approach that empowers patients and restores independence [5], [7].

This project aims to assess the impact of cueing strategies, focusing on the use of +sensBand by PD patients during several sessions, exploring its potential in improving motor control and reducing FoG episodes. The +sensBand is a wearable cueing system, an instrumented waistband from BiRDLab designed to enhance rehabilitation, motor assistance, and personalized clinical management on PD patients. The study aims to understand the motor effects of different +sensBand strategies, implement new strategies focused on targeting more advanced symptoms such as FoG, and testing the long-term rehabilitative potential of the system in PD patients by designing and conducting a protocol for a longitudinal clinical study and consequent analysis of collected data.

The validation studies conducted demonstrated that both open and closed loop vibrotactile approaches effectively improved gait performance by addressing hypokinetic and bradykinetic aspects in PD patients. Further combination of both visual and somatosensory cues at open and closed-loop, in a novel strategy focused in addressing FoG, was validated with high acceptability by healthy participants and promising potential for motor rehabilitation in different scenarios of daily living. These findings supported its long-term application with end-users, with effectiveness depending on consistent and appropriate use of cueing. Additionally, continuous training with the strategy allowed improvements in PD patients FoG occurrences, motor performance and quality of life, highlighting the positive impact of this strategy on daily living for PD patients.

Keywords: Cueing; Freezing of Gait; longitudinal study; Parkinson's Disease; Quality of Life

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LIST OF ACRONYMS AND ABBREVIATIONS

+sens – +sensBand system

2CA – Clinical Academic Center

A

APAs – Anticipatory Postural Adjustments

AS – Asymmetry

B

BS – Biofeedback System

BiRDLab – Biomedical Robotic Devices Laboratory

C

CMEMs – Center of MicroElectroMechanical Systems

D

DBS – Deep Brain Stimulation

F

FAB – Frontal Assessment Battery

FES-I - Falls Efficacy Scale

FoG – Freezing of Gait

FPRS – Face Pain Rating Scale

G

GDS-15 - Geriatric Depression Scale–15

GFQ – Gait and Falls Questionnaire

H

H&Y – Hoehn and Yahr

HC – Healthy Controls

I

IMUs – Inertial Measurement Units

J

JoLO – Judgement of Line Orientation

L

LEDD – Levodopa Equivalent Daily Dosage

M

MBEST – Mini Balance Evaluation Systems

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

MoCA - Montreal Cognitive Assessment

MMSE - Mini-Mental State Examination

N

NFOG-Q – New Freezing of Gait Questionnaire

P

PD – Parkinson’s Disease

PDQ-39 – Parkinson’s Disease Questionnaire

PIGD – Postural Instability and Gait Disorder

Q

QoL – Quality of Life

R

RAS – Rhythmic Auditory Stimulation

RCT – Randomized Controlled Trial

S

SD – Standard Deviation

SIP – Stepping-in-place

SNC – Senior Neurological Campus

STAI – State-Trait Anxiety Inventory

SUS – System Usability Scale

T

TEDD – Total Electrical Energy Delivered

U

UMinho - University of Minho

1. INTRODUCTION

The present report aims to outline the work established, along with respective findings, of a dissertation in the scope of the second year of the master's program in Biomedical Engineering – Medical Electronics field, at the University of Minho (UMinho), entitled “Motor effects of Biofeedback in Parkinson's rehabilitation”. This dissertation was designed to be accomplished during the academic year of 2023/2024, at the Biomedical Robotic Devices Laboratory (BiRDLab) – Center for MicroElectroMechanical Systems (CMEMS), research center of UMinho. Experimental trials were also executed in the scope of this dissertation, taking place in both the Clinical Academic Center (2CA) at the Hospital of Braga, and the Senior Neurological Campus (CNS), of Braga.

The work developed was supervised by a robotics professor at UMinho and principal investigator of BiRD Lab, Cristina Santos; and a Ph.D. biomedical engineer student also at BiRDLab, Cristiana Pinheiro. The project also counted with the support of a neurologist at Braga Hospital, Dr^a Ana Margarida Rodrigues, which partnered with the project recruiting PD patients for the clinical trials in the scope of this dissertation.

1.1. MOTIVATION

Parkinson's Disease (PD) stands as the second most prevalent neurodegenerative condition, following Alzheimer's, impacting particularly the aging population [8], [9]. Therefore, PD becomes an exacerbating concern as the world demographics continue to shift towards an increasingly aged population. This transition not only results in an increase in the prevalence of the disease but also elevates its economic implications, ultimately posing as a substantial burden on healthcare systems worldwide [1], [9].

PD is classified as a synucleinopathy, a neurodegenerative disorder characterized by the loss of dopamine-producing neurons within the nigra region of brain [1], [2]. Although the causes of Parkinson's disease (PD) remain a challenge to ascertain, it is known that abnormal alpha-synuclein protein buildup in the substantia nigra causes dopamine-producing neurons to degenerate, thereby lowering dopamine levels [1]. The direct and indirect channels that pass through the striatum are impacted by this decrease, which in turn affects an individual's motor response and, therefore, his motor activity [1], manifesting as debilitating motor symptoms such as Freezing of Gait (FoG), bradykinesia (slowness of movement), akinesia (inability to voluntarily perform a movement), tremors (involuntary repeated rhythmic movement of a body part), rigidity (continuous involuntary muscle contraction), and impaired motor

reflexes [1], [8]–[10]. Even though each patient affected may experience different motor symptoms, gait disturbances limit autonomy in carrying out everyday chores. As a result, become more dependent on help and Quality of Life (QoL) declines [7].

FoG is characterized by the sudden inability of generating movement, therefore freezing in place, and is one of the main symptoms that greatly affects QoL [3]. Not all PD patients' experience FoG, since it is a symptom that manifests in more advanced stages of the disease [11]. However, it is a frightening reality for patients to consider as the disease advances. FoG manifests spontaneously, being mainly triggered by certain tasks like turning or gait initiation, but also spatial constraint and stress situations, like staircases and passing through narrow paths, as for example door frames [3], [10]. The episodic nature of the symptom makes it one of the most challenging ones to understand, but also among the most dangerous for patients since it can result in falls [10].

However, studies have shown that these gait impairments in PD patients are not solely motor phenomena. Instead, they may arise from an intricate interplay among sensorimotor, cognitive, and emotional factors [11], [12]. This interaction between these domains leads to the expression of a broader spectrum of symptoms in PD, including sleep disturbances (insomnia), mood disorders (anxiety and depression), cognitive impairment (attention deficits), psychosis and confusion and even autonomic dysfunction (balance impairments and postural instability) [1], [13].

A thorough comprehension and research of these symptoms is essential to discover effective therapeutic solutions focused on enhancing patients' QoL.

Despite ongoing research efforts and advances in understanding the disease, the ethology and pathophysiology of PD remains enigmatic, making its management and treatment a formidable challenge. Therefore, the need for comprehensive research to uncover the underlying mechanisms and exploring potential therapeutic pathways has never been more crucial [3].

PD remains an incurable condition, underscoring the need to develop therapeutic interventions focused on enhancing patients' Quality of Life (QoL) [2], [3]. In the present days, pharmaceutical interventions with dopaminergic medication, such as drug delivery using levodopa to elevate dopamine levels in the brain, remains the primary treatment modality [4], [8]. A critical challenge in PD lies in the issues presented by certain symptoms, such as worsen FoG and inducing dyskinesias (abnormal involuntary movements) associated with dopaminergic medication usage [8], [14]. These motor fluctuations comprehend an obstacle to optimal treatment, limiting the efficacy of conventional therapies, hence, it is imperative to explore therapeutic alternatives that can mitigate these challenges.

Nevertheless, there is a growing interest in alternative and complementary therapies, such as Deep Brain Stimulation (DBS), occupational therapy, and physical therapy, which have gained prominence in recent years [4], [8]. However, these therapies also entail drawbacks, such as relatively high cost or long-term expenses [15]. Physical and occupational therapies, to be more effective require more experienced therapists, therefore being subjective which can also lead to slower progress, that can affect patients' motivation [15]. Both methods by depending on therapist don't allow patients to feel a sense of autonomy, which is also essential for motivating them to perform the treatments [16]. Some methods like DBS are invasive needing surgery, which entails associated risks. Additionally, there are patients that are not suitable for neither alternative due to the heterogeneous pathophysiology challenge of the disease, so it is necessary to give patients more options developed taking accountability of these lapses [3].

Cueing strategies are therapeutic approaches that emerge as promising alternatives which have great potential in treating PD [3], [4]. Cueing Systems (CSs) help patients executing motor tasks, providing external auditory, visual, or somatosensory cues delivered at a time or distance pace, for continuous enhancement of motor activity, dependent or independent of the end-user motor behaviour [5]. Cueing strategies can be categorized in two groups, depending on how they are delivered: open-loop or closed-loop. Open-loop cueing provides cues at a marked pace, independently of the users. On the other hand, closed-loop cueing is dependent of end-user, by adapting cueing rhythm to the end-users' behaviour [17]. Biofeedback is a type of closed-loop cueing strategies since provides the opportunity to monitor and control, offering real-time feedback, that assists patients in becoming aware and self-regulating their motor functions [7]. Both methods can be used separately and combined, allowing to monitor patients' reactions to cueing during gait, which arises great potential since provides a customized course of treatment for the patient [7].

Cueing stimulates a different pathway then the one affected by PD. Diverse cueing strategies, such as Rhythmic Auditory Stimulation (RAS), can activate channels from different brain regions not directly correlated with dopaminergic pathway's, including cerebellar and prefrontal channels [6]. Thus, since these alternative pathways are spared during the diseases' progression, retain potential for effective compensation and restoring of pace and rhythm during gait[6]

Wearable devices are the future of at-home or daily treatment options [7]. Motor tracking systems, such as wearable inertial sensors, allow the analysis of patients' gait, providing insights into different gait parameters such as spatiotemporal parameters, kinematic parameters, Anticipatory Postural Adjustments (APAs) and duration and number of FoG episodes [4], [5], [7]. Closed loop cueing systems,

by integrating motor tracking sensors with actuators capable of delivering auditory, visual or vibrotactile cues, arise the potential for guiding and correcting gait impairments or proactively addressing motor symptoms prior to their manifestation [4], [5], [7]. Therefore, closed loop cueing systems come to the forefront as a pioneering solution within this framework [7].

1.2. PROBLEM STATEMENT

Despite the availability already of existing therapeutics and technological solutions for treating Parkinson, it is imperative to explore novel options that can enhance patients QoL [3]. Therefore, long-term wearable devices are rising as a potential solution for a more convenient, low-cost, and portable at-home therapy [7]. However, it is essential to study and evaluate their efficacy and their impact on the disease to determine their viability as a potential treatment, since the training for daily tasks remains a challenge [7].

There are still gaps that need to be filled, regarding some cueing strategies, like vibrotactile cues [18]. Despite different types of cueing strategies already being tested, there is lack of information about: the types of cueing, and control strategies, that have better results in treating gait impairments of PD patients; and the long-term effects in enhancing PD patients motor effects and thus QoL [7], [18].

Since some cueing strategies, like vibrotactile cues, yield limited results also since benchmark has not been accomplished, resulting in lack of conclusions about their efficiency in treating PD symptoms, it is important to explore the potential of this type of cueing [18], [19]. Therefore, in this project it will be analysed the potential of the +sensBand, a wearable device, developed in BiRDLab, that uses vibrotactile cueing to enhance PD patients' rehabilitation [19].

To fully comprehend the potential of cueing strategies, it is crucial that clinical trials are conducted [7]. However, relying solely on single-use trials proves insufficient, given the abundance of existing results. The next step is to conduct long-term studies, designed to assess the viability of integrating these strategies for ongoing utilization and into daily tasks [7]. Only through such means will it be possible to innovate and start impacting patients QoL.

1.3. DISSERTATION GOALS AND RESEARCH QUESTIONS

The main goal of this dissertation is the development and consequent analysis of a longitudinal clinical study of Cueing strategies in PD patients, evaluating the long-term use motor and QoL impact and potential of wearable cueing systems, using +sensBand. The +sensBand is a plug-and-play wearable

cueing system created by BiRDLab. It integrates an inertial sensor and a miniaturized camera, to track and monitor users' movements, and features vibration sensors that provide somatosensory cueing, aiming to counteract any symptoms that may arise during gait tasks, such as FoG.

To achieve the main goal, several sub-objectives have been defined, with some respective key performance indicators (KPI's), to accomplish gradually along this dissertation:

- **Objective 1: Literature review and analysis focused on Parkinson clinical study, using cueing strategies.** This review will investigate how cueing strategies have been used (auditory, somatosensory, and visual) and applied (single use sessions or longitudinal studies) for combating motor symptoms of PD and their effectiveness (e.g., effects over clinical scales, APAs, step and stride length, cadence, velocity, number of FoG episodes). A clear summary of the main cueing strategies implemented, specifications and respective outcomes reviewed should be accomplished (**KPI 1**).
- **Objective 2: Familiarization with the +sensBand system and examination of control strategies suitable for long-term clinical trials with Parkinson.** Throughout the project, the intention is to leverage the pre-existing technology, +sensBand, and subsequently analyse its potential, alongside novel cueing strategies developed based on the conducted literature review. Therefore, it is imperative to consider an acquainting phase dedicated to understanding the device and its operation mode. Moreover, familiarization will include the participation on the conduction and data analysis of a currently in course cross-section clinical study with +sensBand in Parkinson. As for **KPI 2**, it included the summary of the different control strategies of +sensBand that should be considered for the further protocol development and included also data collection of 15 more patients gait metrics to complete the on-going cross-sectional study and its analysis.
- **Objective 3: Development and validation of a novel cueing strategy adequate to target FoG.** This strategy will be designed for PD patients in more advanced stages of the disease, based on the strategies already developed and literature conclusions, allowing a more complete and intense strategy targeting FoG. It is expected to perform a cross-sectional study, addressing the usability and workload of the strategy, to grant that should be suitable for use in scenarios of daily living. This objective will be measured by **KPI 3**: (i) implementation of a novel cueing strategy to assist PD patients with FoG;

(ii) implementation of both visual and somatosensory cues simultaneously; and (iii) granting that the strategy does not overstimulate patients with SUS scores above 65 points and according to the respective individual items reference benchmarks [20].

- **Objective 4: Development, validation and conduction of the proposed protocol with end-users.** This protocol will be designed for PD patients, based on the literature conclusions, functionalities of +sensBand, and by setting the necessary trade-offs with clinicians. It is expected to perform a longitudinal study, addressing the limitations but also potential of motor and QoL effects of long-term cueing use. This objective will be measured by the development of a continuous study circuit that will integrate different motor tasks susceptible of inducing FoG. To evaluate the different aspects of the device, it is imperative to perform the multiple training sessions (longitudinal study) using the +sensBand device and include evaluation time points for acquiring sensor based and clinical data, assessing the motor (FoG episodes and spatiotemporal parameters) and QoL effects of the training. During the protocol conduction it should be accomplished a reduction of patient's FoG episodes (**KPI 4**).
- **Objective 5: Data analysis and discussion regarding the motor and QoL effects of long-term cueing use in Parkinson.** The data collected from the protocol conduction should be examined and discussed, to draw conclusions about the cueing long-term use effects over PD patients' symptoms. This goal will be measured considering **KPI 5**, indicating that it should be accomplished spatiotemporal differences of at least 30% between study groups [21], PDQ-39 score minimal clinical improvements of at least 4.72 points [22], and minimal NFOG-Q score changes of at least 3 points [23].
- **Objective 6: Disseminate research by writing and presenting dissertation document, and articles (KPI6).**

Furthermore, to encourage the research for the literature review, this dissertation aimed to answer the following queries:

- **Research Question 1:** How have cueing strategies been used and applied for targeting motor symptoms of PD?

- **Research Question 2:** Which is the effectiveness of cueing strategies concerning motor effects and QoL?
- **Research Question 3:** How does +sensBand cueing system long-term use affect Parkinson's motor symptoms and QoL?

1.4. CONTRIBUTION TO KNOWLEDGE

The work done during this dissertation contributes with novel cueing solutions based on wearable devices to improve motor symptoms of PD patients. The main contributions outlined are:

- ❖ A literature review about clinical studies using sensory cueing solutions for PD motor rehabilitation, compiling information about: different cueing devices used, cueing modalities used and the way they were delivered, sensors used for data collection, sample sizes and study groups considered, protocol duration, training dosage and outcomes measured (**Chapter 2, Objective 1**).
- ❖ Finding how cueing strategies have been applied to target PD motor symptoms and their effectiveness regarding those effects but also QoL (**Chapter 2, Objective 1**).
- ❖ Implementation of a novel sensory cueing strategy (**FoG prevention cueing**) integrated on the +sensBand device designed to target FoG in PD patients (**Chapter 3, Objective 3**).
- ❖ Improvement of an ongoing study, resulting in a journal paper to be published, about the efficiency of using different somatosensory strategies in PD patients, comparing the efficiency of continuous rhythmic vibration with vibrations delivered at a personalized rate according to patients' final contacts of the right foot (**Chapter 4, Objective 2**).
- ❖ Validation of the usability and workload of the novel sensory cueing strategy, resulting in the publication of a conference paper (**Chapter 5, Objective 3**) and further validation of the strategy testing in PD patients (**Chapter 6, Objective 3**).
- ❖ A longitudinal study about the use of the novel cueing strategy in PD patients for motor rehabilitation and QoL improvements, regarding the long-term effects as a potential solution for mitigating FoG (**Chapter 6, Objectives 4 and 5**).

1.5. PUBLICATIONS AND ORAL COMMUNICATIONS [24]

This dissertation resulted in two articles: one conference paper as first author entitled “Robotic sensory cueing during gait: a usability study with scenarios of daily living”, IEEE International Conference

on Autonomous Robot Systems and Competitions, Paredes de Coura, Portugal, 2024, **Maria Pimenta**, Cristiana Pinheiro, Cristina P. Santos [24]; and one journal paper, as first author, currently under revision entitled “Gait event-driven biofeedback to improve gait impairments in Parkinson’s disease”, *Movement Disorders*, Official Journal of the International Parkinson and Movement Disorder Society (impact factor of 7.4), 2024, **Maria Pimenta**, Cristiana Pinheiro, Helena R. Gonçalves, Ana Margarida Rodrigues, Cristina P. Santos.

Following the “Robotic sensory cueing during gait: a usability study with scenarios of daily living”[24], besides the published conference article, this work also resulted in an oral presentation during the ICARSC 2024 conference.

1.6. MANUSCRIPT OUTLINE

This document is organized into seven chapters. **Chapter 1** presents the motivation for this dissertation, as well as the problem statement, objectives to accomplish, the contribution of this work for further research and the resulting publications and presentations. In the following chapter, **Chapter 2**, the state of art is outlined presenting the literature review found until the present moment. **Chapter 3** presents a conceptual overview of the main components, hardware and software, used during this dissertation.

Chapters 4, 5 and **6** contain the description and results of the three different studies done, respectively: a cross-sectional study that compared different cueing strategies in PD patients; a usability and mental workload study of a novel cueing strategy performed with healthy participants; and a longitudinal study using this novel strategy in PD patients with FoG.

Lastly, **Chapter 7** resembles the conclusions of all the work done for this project.

2. LITERATURE REVIEW ON CUEING STRATEGIES FOR PD PATIENT'S GAIT REHABILITATION

This chapter will present the literature review for this dissertation, focused on Cueing Systems (CSs) for gait rehabilitation of PD patients. The main focus of this literature review is to assemble and analyse recent studies using several cueing strategies, in order to comprehend the different cueing strategies being used to address motor symptoms of PD, and their consequent effects over patients QoL.

During the research for this chapter, two review papers were found with similar objectives. One paper consisted of a systematic review aiming to understand and evaluate the immediate effect, which means after only one single session using cueing strategies, of external cues provided during different gait tasks on FoG symptoms in individuals with PD [18]. The second review article found had essentially the same purpose, also aiming to understand the efficacy of diverse cueing strategies in improving PD patients motor parameters and clinical outcomes [25]. Nonetheless, this second paper only included Randomized Controlled Trials (RCTs) that trained for more weeks than single session training using cueing devices, therefore included longitudinal studies instead of cross-sectional.

Although both reviews providing insights about cueing motor effects in reducing PD symptoms, a thorough research was necessary to probe deeper into cueing assisted training effects in improving mobility but also, addressing motor symptoms such as FoG and improving QoL. Therefore, at the end of this literature review the Research Questions (RQ) 1 and 2 of the dissertation should be answered:

- **RQ1:** How have cueing strategies been used and applied for targeting motor symptoms of PD?
- **RQ2:** Which is the effectiveness of cueing strategies concerning motor effects and QoL?

2.1. METHODOLOGY

2.1.1. RESEARCH METHODOLOGY

The research for the studies presented in this review was made using two databases: Web of science and Scopus. Firstly, a search was made in Web of Science (search field: "Topic"; document type: "Review Article") to choose a recent research article that fitted the criteria. This search was made in September of 2023 using the keyword heading: "parkinson AND (biofeedback OR cueing)". Secondly, in Scopus database three additional searches were made, one (search field: "Article tile, Abstract, Keywords"; document type: "Review") focused on finding another review article but containing longitudinal clinical trials, other (search tip: "Article, Title, Abstract, Keywords"; document type: "Article";

Filter: “2022-2023”) filtered original articles from the ended date of the search of the previous reviews till now, and finally (search tip: “Article, Title, Abstract, Keywords”; document type: “Article”; Filter: “2013-2023”) in order to search more recent articles of longitudinal clinical studies. The research was made during October and November of 2023, using the keyword headings: “parkinson AND (biofeedback OR cueing)”, for the first two searches, and "parkinson AND (biofeedback OR cueing OR stimulus) AND (randomized control trial OR long-term OR longitudinal)" for the last. Of the results showed, the relevant studies as well as reference lists were examined.

2.1.2. SELECTION STRATEGY

The selection of the reviewed studies was made based on the following criteria: (i) clinical intervention in PD patients; (ii) cueing or biofeedback strategies in PD patients; (iii) cueing used in gait rehabilitation; (iv) clinical evaluation of motor effects; (v) evaluation of cueing strategies effects over FoG. Studies were excluded using the following criteria: (i) not having cueing; (ii) not having Parkinson patients; (iii) not addressing gait or motor activities; (iv) not presenting motor effects of therapy; (v) not presenting effects of therapy addressing FoG.

2.1.3. DATA EXTRACTION

After being selected, the papers were analysed and the following information was extracted: (i) the sensory cueing devices used, and respective cue location and mode; (ii) the sensor used to extract gait data, and respective location and parameters evaluated; (iii) assistive devices used to provide supplementary support during gait training; (iv) the number of participants for each sample group in each clinical study; (v) the training dosing and evaluation time points defined for each clinical assessment; (vi) the study types reviewed; (vii) the different motor tasks that participants executed; (viii) the medication state on which patients executed the clinical studies; (ix) the outcomes observed.

2.2. RESULTS

Firstly, in order to initiate this literature review, 2 review articles that meet the criteria, resulting from the first two searches, were selected and analysed. From these 2 review articles, a total of 37 original studies were selected to be included in this review.

Two secondary searches were then made in order to find more original studies to include in this review. This research reached 401 studies overall, leaving 29 studies after a first selection based on title and abstract, and counting and removing some repetitions. After that, 29 studies were screened and were evaluated for eligibility. These results eliminated 5 studies due to not having access to the full article,

and other 11 were eliminated essentially due to not referring cues effects on FoG or being focused on treatments without using cueing strategies. Ultimately, this review contained fifty (50) studies. Fig.1 shows a flowchart of the search strategy adopted.

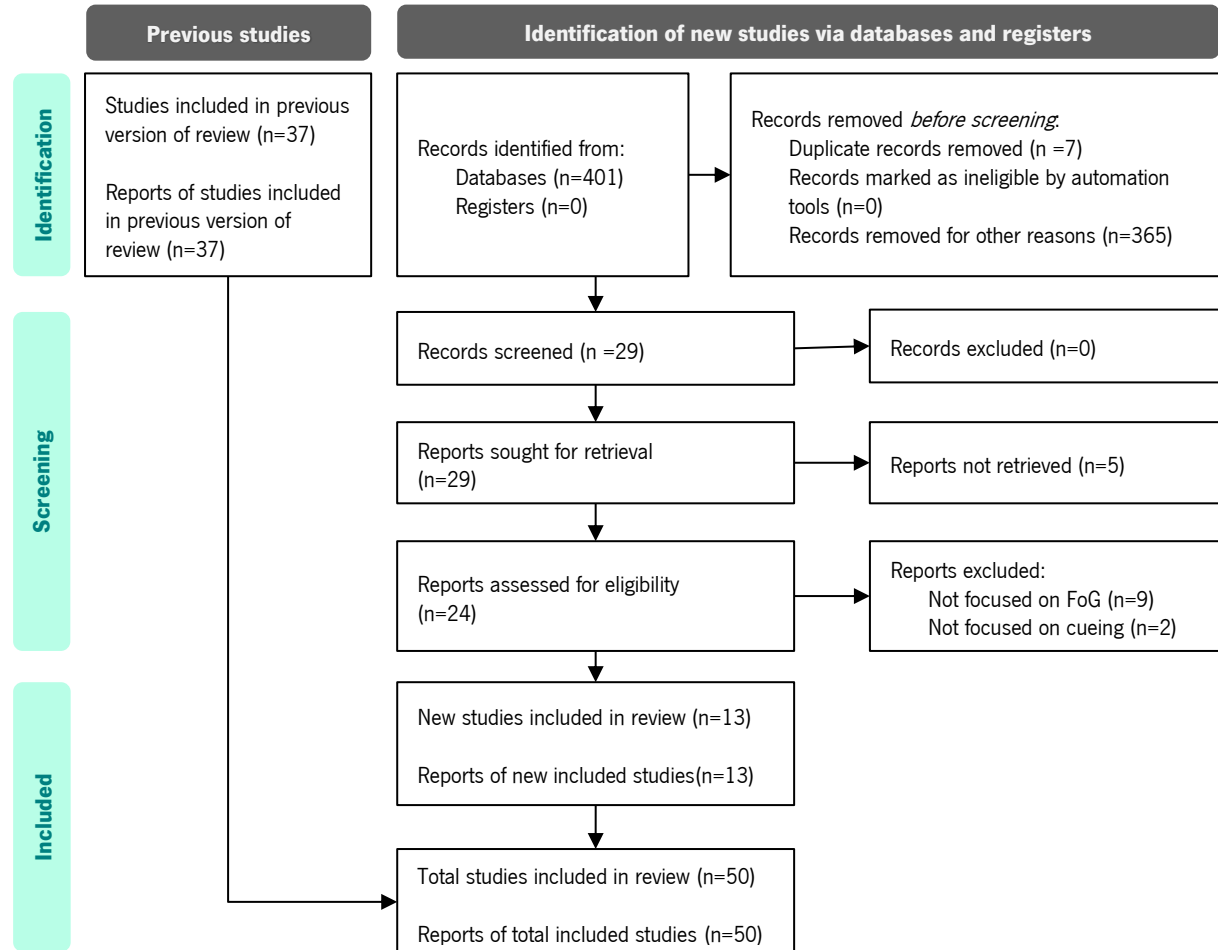


Fig.1. PRISMA representing the search strategy used.

2.2.1. TECHNICAL SPECIFICATIONS

In this section, to comprehend the reviewed technologies used to provide different types of cueing (sensory cue devices), but also for gait assessment to further evaluate motor effects (gait assessment sensor devices), Table 1 summarizes the main technical specifications to consider.

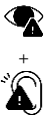
Table 1. Technical specifications of the different reviewed studies

Studies (year)	Sensory cues				Gait assessment sensors			
	Device type	Device description	Location	Mode	Device	Location	Parameter	
Das <i>et al.</i> (2022)[26]	Non-electronic	Star in black tape	Middle of the path		9 Opal IMU's (APDM Inc., USA)	Feet, calves, wrists, lumbar region, sternum, and head	Spatiotemporal (turning performance duration and velocity)	
Stuart <i>et al.</i> (2021)[27]		Stripe tape lines	120% of normal step length		32-channel mobile EEG system (Mobita, TMSi)	Eletrodes placed according to the international 10-20 system	Physiological (brain activity)	
					9 Opal IMU's (Opals Version 2, Mobility Lab Version 2, APDM Inc., Portland, OR, USA)	Feet, shanks, waist, sternum, wrists and head	Spatiotemporal (velocity and stride length)	
Russo <i>et al.</i> (2022)[28]		Stripe tape lines	Inter-strip distance of 120% of the baseline step length			6 IMU's (APDM Inc., USA)	Sternum, lumbar spine, bilaterally on the wrists, and feet	Spatiotemporal (stride length, step duration, velocity) Kinematic (APAs)
Polakova <i>et al.</i> (2020)[29]		16 square wooden rods	Inter-strip distance of 60cm			GaitRite Analysis System	Middle of the 10m marked path	Spatiotemporal (step length and variability; step time and variability, double support time, velocity, and cadence)
Beck et al. (2015)[30]		Stripe tape lines	6cm wide, inter-strip distance of 65cm			ProtoKinetics Movement Analysis Software™ (Zeno Walkway–ProtoKinetics, USA)	On the floor	Clinical (number of FoG and duration) Spatiotemporal (step length and variability, step time and variability, double support time, velocity)
Graham et al. (2023)[31]		Stripe tape lines	120% of patients step length		Wireless eye tracker	Eyes	Kinematic (gaze)	
					mobile infrared eye-tracker (Tobii Pro Glasses 2, Tobii, Inc.)	Eyes	Kinematic (saccade frequency, duration, peak velocity, amplitude, and fixation duration)	
					8 IMU's (APDM, Inc., USA)	Wrists, feet, shanks, sternum, and lumbar spine attached via straps	Spatiotemporal (velocity, stride length, stride time, and stride time variability)	
Gal <i>et al.</i> (2019)[32]	Electronic	3 Digital Light Processing projectors	Fixed on 5m high ceiling;			3 cameras (fixed bird's eye, moving leg zoom, and moving front lateral whole-body view; Answers in dual-task conditions recorded using portable microphone)	NM	Spatiotemporal (time of performing task, number of steps, velocity, step length, cadence) Clinical (number and total duration of FoG episodes)
Barthel <i>et al.</i> (2018)[33]		Laser beam projection	Orthogonally to the contralateral foot			NM (videotaped)	NM	Clinical (number of FOG episodes and duration occurring during standardized walking protocol)
Tang et al. (2017)[34]		Laser (2 modes: continuous (CL) or rhythmic (RL))	Attached on the sternum with elastic bandage, projected one step length in front of patient's feet			8-camera optical motion capture system (VICON from Oxford Metrics Ltd., UK)	6 markers: proximal end of the calcaneus, the first metatarsal head, the 5 th metatarsal head, lateral malleolus and medial malleolus	Clinical (Number of FoG episodes) Spatiotemporal (turning time, step time, gait arrhythmicity, asymmetry and discoordination)

Studies (year)	Sensory cues				Gait assessment sensors		
	Device type	Device description	Location	Mode	Device	Location	Parameter
Holmes et al. (2015)[35]	Eletronic	Laser wheeled walker (Mobilaser)	Projected on the floor		Zeno Electronic Walkway-C Model (Zenometrics, NY)	Floor	Spatiotemporal (step length and velocity)
Bryant et al. (2010)[36]		2 laser canes: 1 red and 1 green light laser beams	Projected laser line on the ground		Video camera	3 markers: 2 parallel on the walker frame and 1 on the harness over lateral aspect of patient's iliac crest	Spatiotemporal (walker positioning)
Bunting-Perry et al. (2013)[37]		Rolling laser walker	Projected at ankle level		Stopwatch	NM	Spatiotemporal (TUG task time)
Cubo et al. (2003)[38]		Wheeled laser walker	Projected perpendicular to the walker		GAITRite analysis system	NM	Spatiotemporal (velocity, cadence, and stride)
Ratanasutiranont et al. (2023)[39]		Smart ankle bracelet-laser device	Attached to tibial area, projected in front of contralateral foot		NM (recorded during a 50-foot walk and a 360 turn)	NM	Clinical (time and number of FoG episodes)
An et al. (2023)[40]		Laser shoes: PathFinder system (WalkWithPath Ltd, Denmark)	Projected in front, on the opposite side of the dorsum of each foot		NM (videotaped)	NM	Spatiotemporal (time to complete tasks, number of steps) Clinical (number of FOG episodes)
Geerse et al. (2022)[41]		HoloLens 1 mixed-reality headset	Headset		NM (videotaped)	NM	Clinical (duration and number of FoG episodes)
Byl et al. (2015)[42]		iPad: displays foot pressing indicators, step lengths, stride widths, and toe-out angles	NM		Single IMU	Ankle	Spatiotemporal (shank velocity) Clinical (number of FOG events)
Cao et al. (2020)[43]		Laser beam projection belt	Laser: Waist belt; Stripes: distance in between stripes of 40% of patient's height		Optoelectronic motion capture (marker-based) system (Optitrack PRIME 17 W)	NM	Spatiotemporal (velocity, stride length) Clinical (TUG test, duration of FoG)
					Video-cameras	NM	Clinical (total FoG occurrences, mean duration of each episode, total duration of three laps, and total duration of FOG)
					JAVA 1.53k (National Institutes of Health, USA)	NM	Spatiotemporal parameters (velocity, cadence, single/dual-limb support duration ratio)
					2 GoPro Hero 7 cameras (30 Hz): filmed session 1 and 3	1 attached to the chest of the participant and other of the researcher, both focusing on participant's feet	Clinical (number of FOG episodes and duration)
					goniometer	Measured angles at each joint in the lower extremity	Kinematic (range of motion)
					Microfet Dynamometer microFET2	NM	Kinetic (strength)
					10 inertial sensors – IMUs (GYENNO, China)	Lower back, chest, bilateral feet, ankles, thighs, and wrists by elastic belts	Spatiotemporal (step length, step duration)

Studies (year)	Sensory cues				Gait assessment sensors		
	Device type	Device description	Location	Mode	Device	Location	Parameter
	Non-eletronic	White transverse stripes					
Lebold et al. (2010)[44]	Non-eletronic	Stripe tape lines	65cm in-between stripes		GAITRite analysis system	On the floor	Spatiotemporal (velocity, step time and length, cadence, variability)
	Eletronic	Laser line projection	Projected 65cm in front of patient				
Kompoliti et al. (2000)[45]	Non-eletronic	Modified inverted cane	On the bottom of the rod, at a right angle and parallel to the floor		NM (videotaped)	NM	Spatiotemporal (total time to complete a trial) Clinical (number of FoG episodes, and ratio of walking time to the number of FoG episodes)
		Laser cane	Projected perpendicular to the cane				
Horin <i>et al.</i> (2020)[46]	Eletronic	Speakers (piano music arrangement)	NM		GAITRite Analysis System	Walking pathway	Spatiotemporal (step time, stride length, single support time; velocity, and cadence)
Spildoore n et al. (2017)[47]		Metronome	NM		8-camera VICON 3D capturing system	34 markers: front and back of head, shoulder, elbow, wrist, 2 nd metacarpal, anterior superior iliac spine, thigh, lateral epicondyle, tibia, lateral malleolus, 2 nd metatarsal and the calcaneus, C7, T10, clavicle, sternum, sacrum and middle of the left scapula	Clinical (Number of FoG episodes) Kinematic (axial rotation, COM deviation, knee-flexion amplitude) Spatiotemporal (total turn velocity)
Delval et al. (2014)[48]		Loudspeaker	Ceiling		2 force plates (AMTI, USA) Video motion analysis system (VICON from Oxford Metrics Ltd., UK)	Floor 6 markers: Lateral malleolus, heels and head of 2nd metatarsals	Kinematic (APA's) Spatiotemporal (step length, step time and velocity)
Willems et al. (2007)[49]		Metronome	NM		8-camera VICON motion analysis system	Markers: pelvis and anterior superior iliac spine, mid-thigh, lateral femoral condyle, mid-shank, lateral malleolus, dorsal aspect of the foot between second and third metatarsal head, and calcaneus	Kinematic (turn parameters) Spatiotemporal (step length and time, variability)
Chomiak et al. (2017)[50]		iPod: music or podcast	Headset		-	-	-

Studies (year)	Sensory cues				Gait assessment sensors		
	Device type	Device description	Location	Mode	Device	Location	Parameter
Ginis et al. (2016)[51]		CuPiD: audiobiofeedback (ABF-gait app) and FOG training (FOG-cue app) using a smartphone (Galaxy S3-mini, Samsung, South Korea),	Earphones or smartphone speaker		2 IMUs (EXLs3, Italy)	Shoes using ABF app, and above ankles using FOG app	Spatiotemporal (velocity, cadence, stride-length) Clinical (2-min Walk Test, MBEST, FSST, FES-I, PASE)
Tosserams et al. (2022)[52]		Metronome	NM		3-dimensional motion capture analysis (VICON from Oxford Metrics, UK)	16 markers placed following the Plug-in Gait Lower Body Model	Spatiotemporal (gait variability, stride time)
Capato et al. (2020)[53]		Speaker (JBL Go Portable Wireless Speaker): metronome sound	NM		Video cameras	NM	Clinical (MBEST, TUG dual task performance, UPDRS)
Chang et al. (2019)[54]		Metronome	NM		EMG through surface eletrodes Kistler force plate (Kistler AG, Switzerland) GAITRite Analysis System	Tibialis anterior muscle On the floor Pathway	Physiological (MEP, CSP, AMEP, SICI, ICF) Spatiotemporal (SIP performance) Spatiotemporal (gait speed, variability, cadence, and stride length)
Lirani-Silva et al. (2017)[55]	Non-electronic	Textured insoles: with semiesphered elevations	Distal phalanx of the hallux, heads of metatarsophalangeal joints and heel		optoelectronic tridimensional system (Nothern Digital Inc.)	4 markers: 5° right and 1°left metatarsal joints and lateral face of the right calcaneus and medial face of the left calcaneus	Spatiotemporal (stride length, duration and velocity, cadence, step width, stance phase duration and % of double-support phase duration)
Schlenstedt et al. (2020)[56]	Electronic	VibroGait	Wrists		3 Opal IMUs (APDM Inc., USA)	1 at posterior trunk (L5) and 1 at each shin	Kinematic (APAs)
Rosenthal et al. (2018)[57]		CueStim (custom-built electrical stimulator): worn on the waist with skin surface eletrods	Hamstrings or quadriceps of body side most affected		Surface eletromyography (EMG, Wave by Cometa)	Tibialis anterior and gastrocnemius mediali bilaterally	Physiological (TFL muscle activity)
Peppe et al. (2019)[58]		Equistasi®: wearable focal mechanical vibratory device	C7 vertebra and gastrocnemius		NM (recordings)	NM	Spatiotemporal (time of completing walking task) Clinical (VAS, FPR scale, number of FoG episodes)
El-Tamawy et al.		Vibratory devices (VDs) (OPTEC Co. Ltd., Japan)	Into-shoes		6-cameras stereophotogrammetric system synchronized to 8-channel sEMG system	4 muscles bilaterally: Rectus Femoris, Tibialis Anterior, Biceps Femoris and Gastrocnemius Lateralis	Physiological (Peak of the envelope and occurrence)
					Qualysis ProReflex motion analysis system (Qualysis Medical AB, Sweden)	NM	Spatiotemporal (cadence, stride length) Kinematic (hip, knee, and ankle joints' angular excursion)

Studies (year)	Sensory cues				Gait assessment sensors		
	Device type	Device description	Location	Mode	Device	Location	Parameter
(2012)[59]							
Zhao et al. (2016)[60]		Google Glass (Explorer version 2, XE 22.0, Android 4.0)	Headset		7 IMU's (MVN motion capture suit (Xsens, Netherlands))	Pelvis, upper legs, lower legs and feet	Spatiotemporal (velocity, cadence, stride length and variability)
Carpinella et al. (2017)[61]		Gamepad: 6 wearable inertial sensors (TMA) and PC with LCD screen (16")	NM		Video cameras	Start and midpoint of walkway	Clinical (presence and severity of FoG)
Yogev-Seligmann et al. (2023)[62]		Self Pro system: computer, projector and spatial camera (MS Kinect Azure camera & Software Developer Kit; SDK) Projected light stripes and metronome beats	Placed at 2m from the walking area (stripes projected at 110% of the user's step length)		6 IMUs (TMA)	Upper and lower trunk and lower limbs through elastic belts	Spatiotemporal (velocity, balance (BBS), 10-min walk test)
Lee et al. (2023)[63]		Google glass: custom-made auditory-visual cue applications "Walk With Me" and "Unfreeze Me"	Headset		Spatial camera	NM	Spatiotemporal (step length and time)
Janssen et al. (2017)[64]		Smartglasses	Headset		Video cameras	NM	Clinical (number and duration of FoG episodes)
		Metronome	NM		17 IMU's (XSens, Netherlands))	Feet, lower legs, upper legs, p��lvis, hands, forearms, upper arms, sternum, shoulders and head	Spatiotemporal (stride length, time, cadence and velocity)
Yang et al. (2022)[65]	Eletronic	Wireless-controlled commercial earphones: music with different rhythms	Ears		Smart insoles: with 6 PSUs	1 PSU set at the heel and 5 at the forefoot (3 at metatarsal heads and 2 to detect foot-inversion and foot-eversion)	Spatiotemporal (velocity, variability and stride length)
		Custom-made laser-light generator	Waist or top of shoes, projects line in front of patients				
Jiang et al. (2006)[66]		Piezo buzzer connected to a stimulator	NM		Optotrak 3020 system (Northern Digital Inc., Canada): with 3 IREDs:	1 to each heel and 1 over the zygomatic bone.	Spatiotemporal (step time and length, velocity)
	Non-eletronic	Stripe tape lines	Placed at patients step length or 40% of their height		Forceplate (Advanced Mechanical Technology Inc., USA)	Where patients stood	Kinetic (timing and magnitude of weight shift and push-off force)
Lee et al. (2012)[67]	Eletronic	Metronome	NM		3-dimensional computerized motion analyzer (Motion Analysis; CA)	19 markers: lower limbs and trunk, enabling 3D analysis of the foot, shank, thigh, pelvis, and trunk body segments	Spatiotemporal (velocity, cadence, stride length, step length, and double- and single-limb standing time); Kinematic (degrees of maximum pelvic tilt, hip flexion, knee flexion, and ankle dorsiflexion in the sagittal plane) Clinical (frequency of FoG episodes, total step numbers, and total time per walking cycle)
	Non-eletronic	Stripe tape lines	Placed at normalized step lengths distance				

Studies (year)	Sensory cues				Gait assessment sensors		
	Device type	Device description	Location	Mode	Device	Location	Parameter
Sijobert et al. (2017)[68]	Electronic	Eletrostimulator	Feet: anode (dorsum) cathode (arch)		Video cameras	NM	Clinical (number and duration of FoG episodes)
		Laser cane	Projected horizontally from cane tip on the floor				
Mancini et al. (2018)[69]		Speakers	NM		8 Opal IMUs (APDM Inc., USA)	Both shins, feet, wrists, on the sternum and posterior trunk (around L5)	Clinical (duration of FoG and FoG-ratio, smoothness)
		VibroGait vibration sensors	Wrist				
Klaver et al. (2023)[70]		Metronome (Natural metronome App)	NM		Video camera	NM	Clinical (number of FoG episodes and duration)
		Vibrating socks: flat mini vibration motor (Adafruit Mini Motor Disc 1201)	Below arch of both feet		17 IMU's (Xsens, Netherlands)	NM	Spatiotemporal (velocity and variability)
Silva-Batista et al. (2022)[71]		Speaker: delivered metronome beat	Center of laboratory		8 IMU's (APDM Inc., USA)	Both shins, feet, wrists, on the sternum and posterior trunk (around L5)	Clinical (FoG index)
		Vibrogait	Both wrists				
Lu et al. (2017)[72]		Vertical array of light emitting diodes (CREE)	3m in front of participants				
		Vibrotactile transducer (C-3 Tactor, Engineering)	Ankle (lateral malleolus) of initial stance leg		2 force plates (9260AA; Kistler)	On the floor, where patient starts task	Kinetic (ground reaction forces and CoP) Kinematic (APA's timing and amplitude)
		Speakers (HPG-100N, Atlas Sound)	NM				
McCandle ss et al. (2016)[73]		Metronome (Peterson BodyBeat Pulsing Metronome)	Belt, placed over right side of the pelvis	 + 	10 camera Qualisys motion analysis system	13 markers: feet, shanks, thighs, pelvis, trunk, head, arms and forearms	Clinical (number of FoG episodes) Spatiotemporal (first and 2nd step length)
		Laser cane (Laser Cane, U-Step)	Projected line on the floor		4 force plates (Advanced Mechanical Technology, Inc.)	NM	Kinetic (forward and sideways CoM velocity; forward and backward sways and number of sideways sways)
Nieuwboer et al.		Light emitting diode: flash	On glasses		Vitaport Activity Monitor (TEMEC Instruments Inc, Netherlands), with 5 accelerometers	1 on each leg (lateral thigh), 3 placed on the lower third of the sternum orientated	Spatiotemporal (turning speed and time during task)

Studies (year)	Sensory cues				Gait assessment sensors		
	Device type	Device description	Location	Mode	Device	Location	Parameter
(2009)[74]		Audio tone	Via earphone				
		Miniature cylinder: pulsed vibration	Wristband				
Suputtitad a et al. (2022)[75]		Waistbelt cueing device	LED laser	Projected line in front of patient	2m RS foot scan	Embedded in the center of walkway	Spatiotemporal (velocity, stride length, and cadence)
			Electronic buzzer	NM			
			Vibration motor	Waist			

IMUs: Inertial measurement units; **EEG:** Electroencephalography; **NM:** not mentioned; **TUG:** Timed Up and Go; **EMG:** electromyography; **ML APAs:** Medio lateral Antero posterial adjustments; **LED:** Light emitting diode; **VDs:** Vibratory devices; **PSU:** Pressure sensitive units; **CoM:** Center of Mass; **CoP:** Center of Pressure; **IREDS:** Infrareds;

 : Visual cues;  : Auditory cues;  : Somatosensory cues.

SENSORY CUES

This literature review intends to explore cueing strategies in PD patients. Therefore, one main topic to consider is the different devices used for cueing. By examining the present studies, it was possible to split the cueing devices in 2 categories: eletronic, considered when mentioned the use of at least an eletronic device providing the cueing mechanism (43 studies) [32]–[54], [56]–[75]; and non-eletronic, when it is not mentioned the device in itself used or the cue does not need a robotic device to be provided (14 studies) [26]–[32], [43]–[45], [52], [55], [66], [67]. It is worth noting that 7 studies, [32], [43]–[45], [52], [66], [67], used both types of cueing devices, one eletronic and another non-eletronic, and compared the motor effects of each cueing device in PD patients.

Cueing strategies can also be organized by the different cueing mode used. Essentially, there are 3 types of cueing modes: visual cues, auditory cues, and somatosensory cues; depending on the sense they act on, and it is possible to actuate using one single cueing mode or different modes combined. Visual cueing was the most used mode (33 studies) [26]–[45], [60]–[68], [72]–[75]; followed by auditory cueing (24 studies) [46]–[54], [60]–[67], [69]–[75]; and lastly somatosensory cueing (13 studies) [55]–[59], [68]–[75]. However, four different combinations were found within this studies, being the most common testing both Auditory and Visual cueing (8 studies) [60]–[67]; followed by testing all three Auditory, Visual and Somatosensory cueing (4 studies) [72]–[75], then testing Auditory and Somatosensory Cueing (3 studies) [69]–[71] and lastly Somatosensory and Visual cueing (1 study) [68].

Of the non-eletronic devices used for cueing, all studies used visual cues [26]–[32], [43]–[45], [66], [67] except one study that used somatosensory cueing [55] and another that used auditory cueing [52]. The non-eletronic visual cueing devices consisted of tape lines (8 studies) [27], [28], [30], [31], [43], [44], [66], [67] or tape stars arrangements (1 study) [26] to visually help patients perform the gait task by spatially marking the steps or the turning positions; checkered floor patterns to assist patients floor visualization, intending for the squares to assist foot placement during gait (1 study) [32], objects such as wooden rods to give a 3D spatial sensation of step positioning (1 study) [29], and an inverted wooden walking stick, with a slat of wood attached at the bottom to give a step line cue for spatial guidance and support, for patients when having FoG episodes (1 study) [45]. As for the non-eletronic somatosensory cueing device, Lirani-silva *et al.* [55], used textured insoles with 9mm of diameter sphere elevations, located under the distal phalanx of the hallux, heads of metatarsophalangeal joints and heel, to study the proprioceptive plantar effects in gait. Lastly, Tosserams *et al.* [52] used an internal cueing

technique that consisted of the patient self-counting and matching each step to the counting rhythm as a non-electronic cueing method for gait rehabilitation.

As for the electronic devices, 22 studies used auditory cues [46]–[51], [53], [54], [60]–[65], [67], [69]–[75], 21 studies used visual cues [33]–[42], [60]–[65], [68], [72]–[75] and 12 studies used somatosensory cues [56]–[59], [68]–[75]. Of that, 6 studies used both visual and auditory cueing electronic devices [60]–[65], 4 studies used all 3 modes of cueing [72]–[75], 3 studies used both somatosensory and auditory cue modes [69]–[71], and 1 used both visual and somatosensory cueing [68].

AUDITORY CUEING

The reviewed auditory cueing electronic devices consisted mainly of metronomes (11 studies) [47], [49], [52], [54], [62], [67], [70], [73], [53], [69], [71] to give temporal rhythmic input in PD patients by making them match each step to the metronome beats. Similarly, and with the same purpose, 3 studies used smart glasses with auditory rhythmic cues, 1 using Cinoptics (Cinoptics, Maastricht, the Netherlands) [64], and 2 using Google Glass (Explorer version 2, XE 22.0, Android 4.0) [60], [63]; 2 studies used buzzers that produced rhythmic beeps, 1 using a Piezo buzzer connected to a stimulator [66] and another using an electronic buzzer [75]; and 1 study used a rhythmic auditory tone delivered via earphones [74]. All auditory cueing devices reviewed delivered open-loop cueing.

As for other auditory cueing strategies used, 1 study used a piano arrangement of children's song "Row, Row, Row, Your boat", providing rhythm to help set the pace of the stride [46]; 1 study used speakers to deliver diverse timed tones [72]; other study used an iPod Touch playing music or podcasts as a reward when stepping correctly [50]; other used a Gamepad system that produced a sound alarm to guide patients when doing a wrong movement [61]; and lastly one study used a smartphone based system, called CuPiD, with an audiofeedback App (ABF-gait App) and an instrumented cueing App for FoG training (FOG-cue App) to give different auditory stimuli [51]. Although Horin *et al.* [46] being rather focused on the song choice and characteristics of the song to be used as a cueing strategy, it was considered that it used an electronic device, such as speakers or a computer, to provide the music arrangement.

Lu *et al.* [72] used speakers (HPG-100N, Atlas Sound) to deliver a warning and a go tone. The warning tone was set at 80dB and 1000Hz, and the go tone set at 90dB and 2000Hz, and patients were instructed to start walking only after hearing the go tone. The tones were delivered using 3 different timing protocols: a fixed delay; a countdown and a random delay. The countdown consisted of giving 3 warning

tones followed by a go tone, each 1s apart, giving patients the sensation of counting 3-2-1-go. The fixed delay was based on a similar principle but instead gave a warning cue followed 3s later with a go tone. As for the random delay cue, a warning cue was played and 4 to 12s later a go cue followed. Different timings were studied to analyse if had any implications in gait initiation for PD patients.

Note that in Chomiak *et al.* [50] an iPod Touch was strapped in patients' knee and paired to an earphones' headset. Patients were divided in two groups, one that received music stimuli and other that received podcast stimuli. In order to maintain the music or podcast playing, patients had to perform a stepping-in-place (SIP) task correctly, which means essentially, they had to stand on one leg while lifting the other. In this study the music and podcast cues were given as a reward for correct task performance, however since music provides rhythmic input, and podcasts provide information that need more of patients' attention, the two groups with different auditory stimuli were analysed and compared to understand the different impact in gait training.

VISUAL CUEING

The reviewed visual cueing electronic devices included: laser beam projection devices (15 studies), such as waist belts [43], [75], shoes [33], [40], laser canes [36], [45], [68], [73], wheeled laser walkers [35], [37], [38], laser ankle bracelets [39] or just laser generators [34], [44], [65] attached at different positions such as waist, chest or feet to project guide lines on the walking path, to help patients visualize each step position; smartglasses (4 studies) such as Cinoptics [64], Google Glass [60], [63] or HoloLens [41], providing augmented and mixed reality cues like stripe lines, warning light flashes, footsteps, 3D bars and staircases to analyse the effects of FoG inducing ambients and spatial awareness cues in mitigating FoG, and also comparing the effects of auditory and visual stimuli combined for better spatial and temporal orientation [60], [63], [64]; projectors (2 studies) such as Self Pro system [62], used to project stripe lines for stepping, or 3 Digital Light Processing projectors [32], used to project different checkered patterns on the floor of the walking path, and compare the motor effects in PD patients of this type of visual cue with the same non-electronic cueing strategy; and light emitting diodes (2 studies) providing a vertical array of lights [72] or attached to patients' glasses [74], to give warning cues for gait initiation or rhythmic flashes of light for step rhythmicity during walking. Other methods such as a Gamepad [61] or an iPad [42] were also used.

It is important to note that only 8 studies used closed-loop visual cueing strategies [33], [34], [37]–[39], [42], [45], [61], 3 of which compare open and closed-loop visual cueing modalities [34], [38], [45].

Barthel *et al.* [33], uses laser shoes as the cueing mechanism, to provide laser lines in front of patients during gait. The laser beam is activated by a switch located under the sole of the contralateral foot, therefore activating the laser during heel strike of the opposite foot, guiding the lifted foot where to step. When the foot is lifted laser is deactivated while simultaneously the opposite foot, now on the ground, activates the opposite laser beam. This cycle repeats itself during the gait cycle, providing cues only during certain gait-events (heel-strike), therefore using closed-loop mode. Ratanasutiranont *et al.* [39], similarly provided laser lines automatically at closed loop, but instead of using laser shoes it used an ankle bracelet with an inertial sensor to detect patients walking pattern and provide the laser line following each step.

Carpinella *et al.* [61] used a Gamepad, that combined both auditory and visual cueing, to give biofeedback during different motor tasks for patients to correct their movements. The Gamepad integrated an LCD screen that allowed patients to see bars filling or cartoons mirroring their movements, and when doing an incorrect movement (which means a movement bellow or above a certain threshold) the screen gave a red warning, a warning tone, or both, to indicate patients to repeat the movement correctly. Fig. 2 shows examples of the exercises included in the Gamepad.

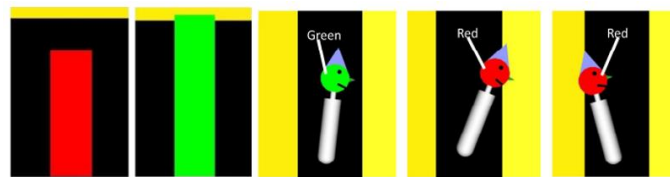


Fig. 2. Examples of Gamepad visual cueing exercises [61].

Similarly, Byl *et al.* [42] uses an iPad to display foot pressing indicators in green, yellow or red, during different mobility tasks, to let patients aware of their gait performance and correct their movements.

Lastly, as for the 3 studies that use both open and closed loop cueing, Tang *et al.* [34] compares laser lines provided continuously, i.e. fixed projection on the ground during walking (open-loop), with provided rhythmically, i.e. personalizing the frequency of laser lines projection according to patients stride cadence (closed-loop). Cubo *et al.* [38] and Kompoliti *et al.* [45] both used similar methods by comparing wheeled walker and laser cane, respectively, projection of laser lines continuously during gait (open-loop) with provided only when patients choose to, via switches on the handles that allowed them to activate and deactivate the cues (closed-loop). Bunting-Perry *et al.* [37], although not comparing with open-loop cue delivery, it used the same handle switch mechanism to provide closed-loop laser lines during gait.

SOMATOSENSORY CUEING

As for the somatosensory cueing devices, there can be essentially two types of devices: vibratory sensors or electrostimulation sensors. Therefore, 10 of the reviewed studies implemented vibratory systems, more specifically opted to provide closed-loop cueing using systems such as VibroGait [56], [69], [71], and vibratory socks [70]; or opted for open-loop cue delivery using devices such as a metronome in a vibratory mode [73], Equistasi [58], or other open-loop vibratory motors and transducers [59], [72], [74], [75]. Two studies opted for electrostimulation, using a wirelessly programmable electrostimulator (Phenix Neo Usb) [68] to deliver closed-loop cueing, or a custom-built electrical stimulator named cueStim [57] providing open-loop stimulation. As for the locations to position the devices to provide somatosensory cues were mainly applied at the wrists (4 studies) [56], [69], [71], [74]; waist (2 studies) [73], [75]; legs (2 studies) [57], [58]; feet (2 studies) [68], [70]; ankles (2 studies) [59], [72]; and neck (1 study) [58].

VibroGait is a vibrotactile cueing system, that integrates an inertial movement sensor (Opal IMUs), a controller unit, and a tactor unit, as shown in Fig. 3 a) [76]. Those components allow VibroGait to generate vibration on the user when detecting stance phase, which is a phase that usually can trigger FoG episodes. The actuator parts of the device consist only in the tactor unit since it is the part responsible for establishing the vibratory cue. This unit is placed on the wrists, where the vibration is applied [56], [69], following the setup shown in Fig. 3 b). The tactor unit, for optimal sensory cueing vibrates at 200-300 Hz range, similarly to the vibration of a cell phone in vibration mode [69].

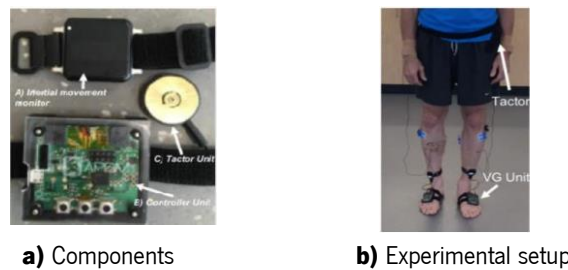


Fig. 3. VibroGait System characteristics [26].

Peppe *et al.* [58] used a different vibratory approach, with a wearable proprioceptive device based on focal mechanical vibration named Equistasi. Equistasi is made of nanotechnological fibers sensitive to temperature, able to transform body thermal energy into mechanical energy as a form of high frequency vibration. The Equistasi patch was placed in the C7, as shown in Fig. 4, and in the gastrocnemius, bilaterally, and as soon as it contacted with patients skin it started vibrating. Therefore, Equistasi provided open-loop cueing.



Fig. 4. Vertebral placement of Equistasi taken from [77].

Only two studies used electrical stimulation as somatosensory cueing strategy. Sijobert *et al.* [68] used a wirelessly programmable eletro-stimulator (Phenix Neo Usb, Montpellier, France). This stimulator was placed around the shank, and two eletrodes, an anode and a cathode, were placed on the dorsum and arch of the foot, respectively, where the stimulation was applied. The stimulation consisted of a closed-loop cueing pattern of five 500 ms/phase pulses at 200 Hz, repeated four times at 10 Hz. An IMU (HikoB) placed under the lateral malleolus on the sagital plane, was used to detect spatiotemporal outcomes and monitor gait events to provide the stimulation. When detecting heel-off, the stimulation was triggered and at swing phase stopped [68].

As for cueStim, it is a wearable two-channel electrical stimulator device, wireless controlled, that allows to monitor gait and FoG episodes in PD patients by using closed-loop electro stimulatory cues [57], [78]. The device is used as a waist belt, and integrates skin surface electrodes, placed in the hamstrings or quadriceps muscles of the body side most affected by the disease, as shown in Fig. 5 a) [57], [78]. The electrodes are responsible for inducing the electrostimulation. By controlling the voltage, a continuous series of electric bursts act on the muscles, delivering somatosensory cues for motor rehabilitation adjusted for each patient gait [57]. Each burst was delivered with 100ms of ramp-up time, then 500ms ON stimulation, followed by another 100ms of ramp-down time [57]. There was no interval following each burst, therefore OFF time was of 0ms [57]. Fig. 5 b) represents the cueing delivery strategies during gait [57], [78].

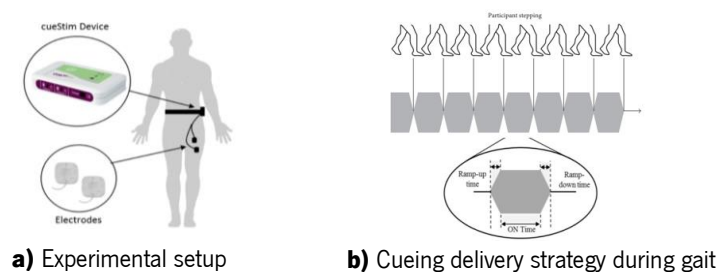


Fig. 5. cueStim System charatheristics [22], [27].

GAIT ASSESSMENT SENSORS

To assess the motor effects of the different cueing techniques in PD patients, it was imperative to collect data during each trained motor task, several sensors have been used to track motion data.

The most common strategy used for data collection were inertial sensors (16 studies) [26]–[28], [31], [39], [43], [51], [56], [60], [61], [64], [68]–[71], [74]. All these studies selected different numbers of sensors to implement, being the median placing 8 Inertial Measurement Units (IMUs) and the maximum number of IMU's used in one study was placing 17, using Xsens [64], [70]. In terms of location for sensor placement, the most frequent positions were sternum/chest (10 studies) [26]–[28], [31], [43], [61], [64], [69], [71], [74]; followed by feet (9 studies) [26]–[28], [31], [43], [60], [64], [69], [71]; then wrists (7 studies) [26]–[28], [31], [43], [69], [71]; then calves/shanks (6 studies) [26], [27], [31], [60], [61], [64]; then lower back, lumbar region or pelvis (8 studies) [26], [28], [31], [43], [61]; then thighs (5 studies) [43], [60], [61], [64], [74]; then ankles/lateral malleolus (4 studies) [39], [43], [51], [68]; then shins and and posterior trunk (level of L5) (both in the same 3 studies) [56], [69], [71]; [27], [60], [64] then head (3 studies) [26], [27], [64]; and lastly shoulders, upper arms, forearms and hands (in the same study) [64]. IMUs allow to measure acceleration and angular velocity along 3 axes, therefore were used essentially to evaluate spatiotemporal outcomes such as velocity [26]; step or stride time [28], length [28] and variability; cadence [64]; double and single support phase, and time to complete task [26].

The other sensors used for gait data collection were video cameras and camera analysis systems, (17 studies) [32], [34], [35], [39], [41], [47]–[49], [52], [55], [58], [59], [66], [67], [70], [71], [73]; pressure sensitivity walkways (7 studies), such as GAITRite Analysis System [29], [36], [44], [46], [54] and Zeno Walkway Gait Analysis System [30], [35]; force plates (5 studies) [48], [54], [66], [72], [73], being the maximum number of force platforms used 4 [73] and the mean was of 2; [32], [34], [35], [39], [41], [47]–[49], [52], [55], [58], [59], [66], [67], [70], [71], [73] electromyography (EMG) systems (3 studies) [54], [56], [58] to measure muscle activity primarily targeting tibialis anterior (all 3 studies), but also other muscles such as Gastrocnemius Medialis and Lateralis, Biceps Femoris and Rectus Femoris; eye trackers (2 studies) [30], [31]; a RS Foot Scan (1 study) [75]; an electroencephalography (EEG) system (1 study) [27] and a smart insoles device (1 study) [65], with pressure sensing units for gait monitoring. It is worth noting that IMUs were considered the main sensor used since the video cameras and camera analysis system are essentially 2 categories combined for a more synthesized literature review. Fifteen of the studies although not mentioning the specific sensors used, mention that the gait

evaluation strategy was videotaped or by recordings, that were afterward evaluated by researchers [33], [36]–[38], [40], [45], [50], [53], [57], [60], [62]–[65], [68], and Gál *et al.* [32] mentioned that a portable microphone device was used to record answers in dual-task conditions.

Pressure sensitive walkways and force plates, allowed to analyse mainly Kinetic parameters, such as force distribution during gait performance, and also evaluate positioning and postural aspects by monitoring patients Center of pressure [61]. Similarly, camera analysis systems used infrared markers placed on patients (mainly at the lower limbs) in order to track positioning, but instead using Kinematic parameters such as Center of Mass (CoM) and joint angles. These systems also allowed to evaluate spatiotemporal parameters and record time necessary to complete task. [28], [48], [56], [72]

As for the parameters evaluated by the different sensors, the most predominant outcomes evaluated were spatiotemporal (36 studies) [26]–[32], [34]–[36], [39], [40], [43], [44], [46]–[49], [51], [52], [54], [55], [57], [59]–[67], [70], [73]–[75]; then clinical (21 studies) [32], [33], [57], [69]; followed by kinematic (10 studies) [32], [33], [57], [69], [28], [42], [47]–[49], [56], [59], [67]; physiological (5 studies) [27], [30], [31], [40], [54], [56], [58] and lastly kinetic (4 studies) [42], [66], [72], [73].

The clinical parameters evaluated were only considered when the respective papers intended to evaluate those parameters alterations and used a sensor, even if indirectly, for that analysis. Although some of the studies evaluating clinical parameters such as clinical scales, those evaluations depended on sensors, mainly video cameras that videotaped patients' performance for researchers to evaluate [32], [33], [36]–[41], [45], [53], [57], [60], [64], [68], [70]. In the case of Chomiak *et al.* [50], clinical parameters were also evaluated. However, since those evaluations did not require any sensors, were not considered for this section.

As for kinematic outcomes, the parameters most predominantly analyzed were APAs, that give information about postural effects in PD patients. APA's were measured using mainly IMU's (2 studies) [23], [26] or force plates (2 studies) [34], [40].

It is also worth noting some supplementary sensors that were used to assist gait analysis. An *et al.* [40] and Yang *et al.* [65] suggest two different approaches. Yang *et al.* [65] used a 3-camera setup to gather gait data with the purpose of enhancing the accuracy of the main sensor, the smart insoles, therefore assisting the research. As for An *et al.* [40] it used a PET scan to assess the uptake of 18 F-FF-CT. This radiotracer binds to Dopamine Tracers (DAT) in different brain regions, therefore indirectly allowing to understand how PD progression might influence the compensatory effects of visual cueing in these patients.

Silva-Batista *et al.* [71] although using IMU's to detect patients' accelerations and angular velocities, it used those data to calculate FoG Index, therefore evaluating this clinical parameter indirectly.

Fig. 6 shows an overview of the different sensors used in the reviewed papers.

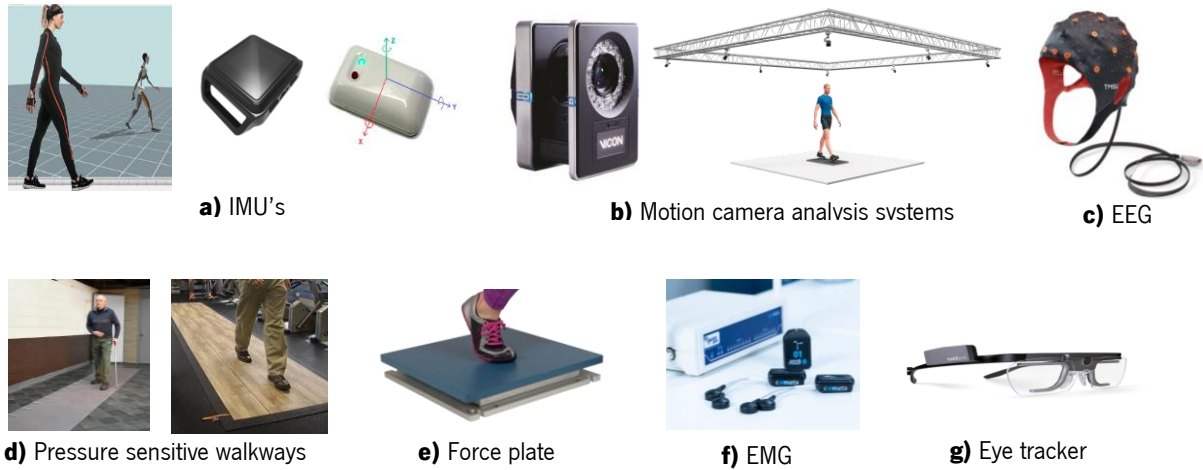


Fig. 6. Overview of the different sensors used.

ASSISTIVE DEVICES

Although being few, some papers required the use of assistive devices (6 studies) for motor task assistance [32], [33], [35], [36], [38], [45].

Motor task assistance devices consisted of walkers [38], walking sticks/canes [36], [45], safety harness systems [33], [35], or allowing the use of walk aids to perform the motor tasks [32], giving patients support during gait. Treadmills were also used in 2 studies [42], [59], for patients to perform walking exercises, therefore assisting motor tasks as supplementary devices. Beck *et al.* [30] used an alternative motor task assistance device that consisted of a cardboard device for occlusion task evaluation. The cardboard was attached to the front of patient's waist, therefore restricting their field of view of the lower limbs during gait performance on this condition.

2.2.2. CLINICAL SPECIFICATIONS

For better understanding the different clinical protocols described in the reviewed papers, Table 2 summarizes the main clinical specifications to consider.

Table 2. Clinical specifications of the different reviewed studies

	Studies (year)	Sample Size (PD, HC)	Training Dosing	Motor task	Evaluation Time points	Medication State	Outcomes	
							On-target cueing effects	Off-target cueing effects
Cross-sectional	Horin <i>et al.</i> (2020)[46][26]	68 (44*, 24) *20 PD+FoG; 24 PD-FoG	3 trials per patient (1 for each condition)	Walking	Pre: 5s quiet stance; During motor task	On	↑ velocity, stride length and cadence; ↓ step time.	-
	Russo <i>et al.</i> (2022)[28]	58(40*, 18) *20 PD+FoG; 20 PD-FoG	3 trials per each block (baseline and cueing), walking 9m		During motor task	On	↑ velocity and stride length; ↓ step latency; ↓ APA duration.	↓ ML APA was associated with larger UPDRS III score.
	Cao <i>et al.</i> (2020)[43]	35(35*, 0) *15 PD+FoG; 20 PD-FoG	3 trials per each condition (without cues, with laser, with stripes)		During motor task	On (end-of-dose state)	↑ step length; Stripe lines: Overall better improvements.	-
	Polakova <i>et al.</i> (2020)[29]	50(25, 25)	Gait tests in each condition were repeated twice		During motor tasks (assessed 90min after each change of DBS setting – relaxing state)	Off (but On and Off DBS)	↓ double-support phase.	-
	Rosenthal <i>et al.</i> (2018)[57]	9 (9, 0)	Performing task twice: with and without cueing		During motor task	On	↓ time to complete task; ↓ number of FoG episodes.	-
	Gal <i>et al.</i> (2019)[32]	32(32*, 0) *32 PD+FoG	1 trial per condition (6 conditions)		During motor task	On	Virtual large transverse floor pattern: ↑ velocity and step length; ↓ number of steps and time;	-
	Barthel <i>et al.</i> (2018)[33]	21(21*,0) *21 PD+FoG	10 trials, with and without cueing (2 laboratory assessments, Off and On medication, on 2 separate mornings)		Gait measures were recorded in between FoG episodes	Off and On	↓ Number of FoG episodes and % time FoG.	-
	Janssen <i>et al.</i> (2017)[64]	25 (25*,0) *25 PD+FoG	2 sessions, each with 5 blocks (1 per condition)		Single visit, lasting 2.5-3h on average	Off	↑ stride length; metronome preferred the most.	↓ cadence and velocity; ↑ stride variability and cycle time; AR cues were not beneficial for freezers.
	Lee <i>et al.</i> (2012)[67]	35 (25*,10) *15 PD+FoG; 10 PD-FoG	NM		NM	Off	<u>Visual cues:</u> ↓ Number of FoG episodes; ↑ stride length;	<u>Visual cues:</u> ↓ cadence and velocity;

	Studies (year)	Sample Size (PD, HC)	Training Dosing	Motor task	Evaluation Time points	Medication State	Outcomes	
							On-target cueing effects	Off-target cueing effects
							Auditory cues: ↑ Knee flexion and ankle dorsiflexion; ↑ Cadence and stride length;	
	Yogev-Seligmann et al. (2023)[62]	15 (15*,0) *15 PD+FoG	1 session of 1.5h		During motor task	On	↑ Confidence and stability; Preferred metronome; ↑ User satisfaction; <u>Light stripes:</u> ↑ step length; ↓ step time.	Light stripes: ↑ Gait variability.
	Graham et al. (2023)[31]	60 (43*,17) *22 PD+FoG 21 PD-FoG	2h session		During motor task	On	↑ Saccade frequency; ↓ Saccade peak velocity and amplitude; (related to foot strike time) Improved foot strike angle; ↑ stride length; ↓ stride time and stride variability.	-
	Tosserams et al. (2022)[52]	100 (100,0)	6 trials of 3min (total 4h completing questionnaires, clinical tests and gait assessment)		During motor task	On and Off	↑ Gait velocity; ↓ Variability; Lower MDS-UPDRS III scores, linked to improved gait variability; Higher MoCA scores linked to greater efficacy of external cueing.	-
	Yang et al. (2022)[65]	16 (16,0)	2h sessions, 6 walking tests (On and Off medication)		During motor task	On	↑ Gait velocity and stride length; ↓ Number of FoG episodes.	-
	Suputtitada et al. (2022)[75]	20 (20,0)	8 trials, at least 3 times each, 5 min break in-between		During motor task	Off	↑ Gait velocity and stride length.	-
	Beck et al. (2015)[30]	40 (40*,0) *20 PD+FoG; 20 PD-FoG	3 trials per each condition	Walking (passing through doorway)	Before passing doorway	On	↓ Number of FoG episodes; ↑ Gaze towards pathway; Improved gait with cues, despite lower limb occlusion and dual-task.	Worse gait during dual-task.
	Lebold et al. (2010)[44]	47 (31*,16) *15 PD+FoG; 16 PD-FoG	5 trials per condition		During motor task	On	Ground lines: Improved gait. ↑ Cadence and stride length.	Laser: ↑ Gait variability and double support time; ↓ Velocity.

	Studies (year)	Sample Size (PD, HC)	Training Dosing	Motor task	Evaluation Time points	Medication State	Outcomes	
							On-target cueing effects	Off-target cueing effects
	Cubo et al. (2003)[38]	19 (19*,0) *19 PD+FoG	Up to 3 trials per condition		During motor task	On	-	Laser had no effect in FoG.
	Kompoliti et al. (2000)[45]	28 (28*,0) *28 PD+FoG	3 trials per condition		During motor task	On	-	Didn't improve number of FoG episodes; No significant effects.
	Bunting-Perry et al. (2013)[37]	22 (22*,0) *22 PD+FoG	2 trials per condition		During motor task	On	-	No significant effects and laser did not improve FoG.
	Geerse et al. (2022)[41]	24 (24*,0) *24 PD+FoG	3 sessions: Session 1 and 3:4-10 trials per condition; Session 2: 3 trials continuous cues and 6 trials FoG provoking trail with on-demand cues	Walking (FoG provoking tasks)	Each session 1 week apart	On	Negative effects over FoG disappeared with habituation; ↓ % time, number and duration of FoG episodes initially;	↑ % time, number and duration of FoG episodes initially; Usability scale (SUS) rated below cut-off.
	Schlenstedt et al. (2020)[56]	36(36*, 0) *18 PD+FoG; 18 PD-FoG	2 blocks of testing (10–15min rest in between) performed in the following order: A) without any additional feedback and B) with closed-loop tactile vibration feedback	Gait initiation	Pre: 5s quiet stance; During motor task: walking 2min back and forward	Off	-	↑ first step duration; ↑ TFL contraction (in freezers);
	Lu et al. (2017)[72]	25 (25*,0) *11 PD+FoG; 14 PD-FoG	9 blocks of 6 trials per condition		During motor task	Off	↑ APA's amplitude; ↓ incidence of incomplete APA's; ↓ APA's duration (except somatosensory).	Didn't improve late push-off phase in freezers.
	Jiang et al. (2006)[66]	14 (14*,0) *7 PD+FoG; 7 PD-FoG	2 practice trials, then 10 trials per condition (3-5 min rest in between)		During motor task	On	<u>Visual cueing:</u> Greater push-off force; ↑ Velocity, first and second step length.	Neither cue had significant effects on timing.
	McCandless et al. (2016)[73]	20 (20*,0) *20 PD+FoG	At least 3 attempts at gait initiation		Start: while patient was seated; End: when patient had walked at least 3m	Off	↑ First and second step length; ↓ Number of FoG episodes; Improved forward COM velocity and number of COM sideways sways. Laser cane was most effective.	Vibration metronome disrupted movement.
	Delval et al. (2014)[48]	90 (60*,30) *30 PD+FoG; 30 PD-FoG	Number of trials depending on patient's ability to understand instructions (but at least 3 trials per condition)		During motor task	On and Off	Improved start hesitation in freezers; ↓ Step time; ↓ APA's duration; ↓ First step preparation.	↓ Step length; ↓ APA's amplitude.

	Studies (year)	Sample Size (PD, HC)	Training Dosing	Motor task	Evaluation Time points	Medication State	Outcomes	
							On-target cueing effects	Off-target cueing effects
	Mancini <i>et al.</i> (2018)[69]	43(43*,0) *25 PD+FoG; 18 PD-FoG	3 hours assessment (repeated 3 blocks of the same task under 3 different conditions)	Turning	While performing the different tasks, with a 10-15min break through each task	Off	Better turning smoothness; ↓ Number of FoG episodes.	↓ turning velocity and number of turns.
	Spildooren <i>et al.</i> (2017)[47]	29 (15*, 14) *15 PD+FoG	6 trials per condition (3 turning left and 3 right)		During motor task	Off	↓ Number of FoG episodes; Improved head rotation and head-pelvis separation.	Axial movement deficits did not improve.
	Das <i>et al.</i> (2022)[26]	63 (43*, 20) *22 PD+FoG; 21 PD-FoG	2h session		During motor task	On	↑ turning velocity (except PD+FOG).	-
	Tang <i>et al.</i> (2017)[34]	23 (23*,0) *23 PD+FoG	Few trials with 2-day interval between each condition		During motor task	On	Rhythmic laser cue: ↓ step time, turning time and gait arrhythmicity; ↓ Number of FoG episodes.	-
	Zhao <i>et al.</i> (2016)[60]	12 (12,0)	Each condition tested twice for each turning task		During motor task	Off	More stable gait pattern; Metronome was more effective and most preferred; Positive usability feedback of Google Glass.	-
	Willems <i>et al.</i> (2007)[49]	28 (19*,9) *9 PD+FoG; 10 PD-FoG	3 trials per condition		During motor task	On	-	Non-significant effects (similar results to noncued)
	Nieuwboer <i>et al.</i> (2009)[74]	133 (133*,0) *68 PD+FoG; 65 PD-FoG	8 trials per condition		During motor task	On	Auditory cueing was more effective; Improved turn times.	-
	Silva-Batista <i>et al.</i> (2022)[71]	13 (13,0)	2 rsfMRI scans consisting of 10 minutes		During motor task	Off	FoG Index improvements; Improved turning with both open and closed-loop cueing.	-
	Holmes <i>et al.</i> (2015)[35]	6 (6*,0) *6 PD+FoG	45-min session with 3 trials per condition	TUG	During motor task	On	Improved walker positioning.	-
	Stuart <i>et al.</i> (2021)[27]	63 (43*,20) *22 PD+FoG; 21 PD-FoG	2h session	Gait initiation and Walking	During motor task	On	↑ gait velocity and stride length; ↑ power spectral densities over sensory regions.	-
	Sijobert <i>et al.</i> (2017)[68]	13 (13*,0) *9 PD+FoG; 4 PD-FoG	5 trials per condition (3 last trials were analysed)		During motor tasks	NM	↓ time to complete task; ↓ Number of FoG episodes.	-
	Bryant <i>et al.</i> (2010)[36]	7 (7*,0) *7 PD+FoG	Rest periods between tasks	Walking and Turning	During motor task	On and Off	Green light: ↓ Number of FoG episodes;	-

	Studies (year)	Sample Size (PD, HC)	Training Dosing	Motor task	Evaluation Time points	Medication State	Outcomes	
							On-target cueing effects	Off-target cueing effects
	Ratanasutiranon t et al. (2023)[39]	4 (4*,0) *4 PD+FoG	2 sessions of TUG and walking; 10 min washout period between walking with laser on and off	Walking and TUG	Baseline; Tested again 1 week after	On	↓ Turn time and number of steps. ↑ stride length and velocity; ↓ TUG test time; ↓ % FoG time.	-
	Klaver et al. (2023)[70]	31 (31*,0) *31 PD+FoG	2 sessions on 2 separate days (1 On and other Off medication)	Walking (passing doorway) and Turning	During motor task	On and Off	>10% improvement in FOG; ↑ User satisfaction.	Closed-loop and open-loop tactile, and auditory cueing did not significantly impact the % time and number of FoG episodes, or spatiotemporal parameters
	Lee et al. (2023)[63]	10 (10*,0) *10 PD+FoG	3 trials per task		During motor task	On	“Walk with me” program: Better straight walk, dual task, and walk through doorway. “Unfreeze me” program: Only dual task improved.	UPDRS III did not had significant improvements; “Walk with me” program: Worse 180 degree turning.
	An et al. (2023)[40]	10 (10*,0) *10 PD+FoG	10 min familiarization; 3 trials per condition; 10 min break in between tasks	Gait initiation; Walking and Turning	During motor task	On	↓ Number, duration and proportion of FoG; Greater uptake of FP-CIT.	-
	Lirani-Silva et al. (2017)[55][50]	19 (19**,0) **10 textured insole; 9 conventional insole	5 trials without insoles	Walking	Pre-test; After 1 week wearing the groupspecific insoles (Post-test); After 1 week wearing conventional insoles (follow-up).	On	Post-test textured insoles: ↑ stride length and plantar sensation; Follow-up: Only plantar sensation improvements maintained.	-
Longitudinal	El-Tamawy et al. (2012)[59]	30 (30,0)	45-min session of low intensity physiotherapy program, 3 times a week, for 8 weeks; 5 min treadmill training at baseline and 25 min at the end of treatment		Before and after treatment	On	Improved lower limb joints' angles; ↑ Cadence and stride length.	-
	Ginis et al. (2016)[51]	40 (40**,0) **22 CuPiD; 18 CG	walk at least 3 times per week for 30 min, during 6 weeks FoG: additional 30 min, 3 times a week using the FOG-cue app		baseline; post-test (after 6 weeks); follow-up (following 4 weeks)	On	Post-test: ↓ MBEST score; Follow-up: Maintained SF-36 (while controls decreased).	MBEST not maintained at follow-up.

	Studies (year)	Sample Size (PD, HC)	Training Dosing	Motor task	Evaluation Time points	Medication State	Outcomes	
							On-target cueing effects	Off-target cueing effects
	Peppe et al. (2019)[58]	20 (20,0)	8 week training	Motor Balance	before and after first 8 weeks; before and after following 8 weeks	On	↓ Stance and double support time; ↑ Velocity and stride length; Severe patients (↑H&Y) had better improvements in MDS-UPDRS III; Placebo showed some improvements in MDS-UPDRS III.	-
	Carpinella et al. (2017)[61]	42 (42**,0) **22 EG; 20 CG	20 sessions of 45 min each, 3 per week		baseline; post-training; 1 month follow-up	On	Post-training: Better balance performance; ↓ CoP ML.	At 1-month improvements were not maintained.
	Capato et al. (2020)[53]	154 (154*,0) 56 RAS; 50 without RAS; 48 educational program	10 sessions of 45 min; 2 sessions per week, over 5 weeks		baseline (14 days prior to training); one day after the last 5th week training; 1-month follow-up; 6-months follow-up	On	↓ MBEST score; Retained improvements at 1 and 6-month follow-ups; Improved UPDRS.	-
	Chang et al. (2019)[54]	21 (21*,0) *10 PD+FoG; 11 PD-FoG	10 rounds of 50-step SIP movements	SIP	baseline and cued; (washout interval of at least 1 week between the 2 conditions)	Off	↑ Cadence; ↓ Step variability; ↑ Cortical Silent Period; Improved Short Interval Intracortical Inhibition	-
	Chomiak et al. (2017)[50]	11 (11**,0) **6 music; 5 podcast	3 times per week; 10-20 min training sessions		Before and after 4-week SIP at-home training	On	Improvement on dual-task step automaticity with music but not podcast	No significant effect of training on FES-I, MoCA, or FOG-Q
	Byl et al. (2015)[42]	24 (12**,0) **7 EG; 5 CG	6–8 weeks, 12 visits (90 min each) total of 18h of training	Mobility, range of motion, balance, and strength exercises	baseline; 6-weeks post-training	NM	↓ Number of falls; ↑ Step length; Improved strength, Berg balance and range of motion.	Non significant improvements in velocity and TUG time.

PD: Parkinson's Disease; **HC:** healthy controls; **PD+FoG:** PD patients with FoG; **PD-FoG:** PD patients without FoG; **EG:** experimental group; **CG:** Control group; **ML APAs:** Medio Lateral Antero Posterial Adjustments; **MDS-UPDRS:** Movement Disorder Society – Unified Parkinsons Disease; **MoCA:** Montreal Cognitive Assessment; **% time FoG:** percent time spent frozen; **TUG:** Timed Up an Go; **EMG:** eletromiography; **CoM:** Center of Mass; **MBEST:** Mini Balance Evaluation Systems test; **CoP:** Center of Pressure; **FOG-Q:** Freezing of Gait questionnaire

STUDY TYPES

Papers were classified as 2 different types: cross-sectional studies, when evaluating only single session short-term effects of cueing (41 studies) [26]–[41], [43]–[49], [52], [56], [57], [60], [62]–[75]; or longitudinal, when patients trained with cueing strategies for a continuous period, and multisession data analysis were performed in order to evaluate the long-term usage effects of cueing (9 studies) [42], [50], [51], [53]–[55], [58], [59], [61].

Ratanasutiranont *et al.* [39], although being longitudinal, it does not evaluate the long-term use of cueing strategies in motor rehabilitation, it only divides data collection during 2 sessions 1-week apart. Therefore, this paper outcomes were analysed as a cross-sectional study.

PD PATIENTS AND CONTROL GROUPS

The total number of PD patients summarized in this review, therefore the sum of all articles PD patients' samples, is 1543, being 43 the median sample size. Of the 50 articles analyzed, 18 studies [26]–[28], [30], [31], [43]–[46], [48], [49], [54], [56], [66]–[69], [72], [74] separated PD patients in both freezers (with FoG), and non-freezers (without FoG). Other 16 studies considered only freezers for the clinical protocol [32]–[35], [37]–[41], [45], [47], [62]–[64], [70], [73], and 1 study used compared one group of freezers with healthy controls [47]. Therefore, this resulted in a total of summing a total of 642 freezers and 378 non-freezers, with corresponding median sample sizes 20 and 20, respectively, and leaving 523 PD patients indiscriminate regarding suffering or not of FoG. The maximum sample size for PD patients was 154, found in Capato *et al.* [46] and the minimum was 4, found in Ratanasutiranont *et al.* [57].

The main factors reviewed to characterize PD patients were age (48 studies) [26]–[49], [52]–[75]; Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) (43 studies) [26]–[49], [52]–[75]; disease duration [26]–[49], [52]–[75]; and Hoehn and Yahr scale (H&Y) [26]–[49], [52]–[75] (both in 40 studies); gender (34 studies) [26]–[49], [52]–[75]; and New Freezing of Gait Questionnaire (NFOG-Q) or other FoG questionnaires (35 studies) [26]–[29], [31]–[37], [39]–[43], [46], [49]–[54], [56], [57], [60], [62]–[64], [67], [68], [70], [71], [73], [74].

Less than 50% of the studies characterized patients evaluating other clinical scales such as and Montreal Cognitive Assessment scale (MoCA) (15 studies) [26]–[28], [30]–[32], [41], [43], [50], [52], [56], [63], [68], [69], [73]; Mini-Mental State Examination (MMSE) (16 studies) [37], [38], [40], [43], [46]–[49], [54], [55], [57]–[59], [62], [64], [70]; Falls Efficacy Scale (FES-I) (9 studies) [26], [27], [29], [32], [46], [50], [53], [68], [74]; Parkinson's Disease Questionnaire (PDQ-39) (2 studies) [33], [43]; and Mini Balance Evaluation Systems test (MBEST) (2 studies) [52], [53]. Fewer studies also evaluated less

common scales such as Geriatric Depression Scale – 15 (GDS-15), Postural Instability and Gait Disorder (PIGD) Score, Frontal Assessment Battery (FAB) Total Score, Beck's Depression Inventory (BDI) Score, Royal's Clock Drawing task (CLOX 1&2), and State-Trait Anxiety Inventory (STAI) Scores.

Besides clinical scales, PD patients were characterized according to Levodopa Equivalent Daily Dosage (LEDD) (16 studies) [26], [27], [29], [32], [35], [36], [44], [46], [52], [60], [62]–[64], [66], [67], [73]; height (14 studies) [26]–[28], [34], [36], [43], [44], [49], [55], [59], [64]–[66], [75]; and weight (10 studies) [26]–[28], [34], [36], [49], [55], [59], [65], [75]. In some papers (4 studies) [63] usability questionnaires were also performed to analyze patients feedback about the cueing device.

It is important to note that these characteristics evaluations were not considered as clinical parameters analysed, since only provide information to characterize the population being studied.

As for medication state, the majority of the studies were assessed on medication (31 studies) [26]–[28], [30]–[32], [34], [35], [37]–[41], [43]–[46], [49]–[51], [53], [55], [57]–[59], [61]–[63], [65], [66], [74]. Alternatively, 12 studies [54], [71], [75], opted for assessing protocols during off medication, and 5 papers [33], [36], [48], [52], [70], tested both on and off states, to exclude bias of dopaminergic medication intake. Byl *et al.* [42] and Sijobert *et al.* [68] did not mention in which medication state patients were assessed.

Only 11 studies used healthy control groups to compare results with the PD populations being sampled [26]–[29], [31], [44], [46]–[49], [67]. This resulted in a total of 203 healthy controls, being the median sample size for healthy control groups 18. The maximum sample size for controls was found in Delval *et al.* [48], and the minimum, besides not having control group, was found in Willems *et al.* [49], with 30 and 9 healthy participants, respectively.

It is important to notice that 6 studies used only one group of PD patients to perform different cued and uncued tasks, in random order, to compare the cueing vs. non-cueing effects over mobility [52], [53], [57], [60], [65], [71], [75]; 2 studies distributed PD patients in two alternative groups being one cued and other Placebo, which meant patients used a similar device but without providing any type of cue [55], [58]; 4 other papers divided patients in experimental groups, receiving cueing, and control groups, that did not train with the cueing devices [42], [59], [61]; and 2 studies opted for other alternative sample groups organizations [50], [53].

Chomiak *et al.* [50] and Capato *et al.* [53] different group assignments are worth explaining separately. Chomiak *et al.* [50] divided patients in 2 groups, both receiving auditory stimuli in different manners: one group received music (5 patients) and other received stimuli in a form of a podcast (6 patients). These 2 groups were analysed for understanding the motor and FoG effects of a more rhythmic

induced auditory cue (music) when compared to an auditory cue that requires almost dual-task focus (podcast). Alternatively, Capato *et al.* [68] divided PD patients in 3 groups: one group that received Rhythmic Auditory Stimuli (RAS)-supported multimodal balance training (56 patients), one group that performed the same training but without cueing (50 patients) and a third control group that instead of performing the training, received an educational program explaining them the RAS training effects in addressing PD motor symptoms. These third group was assigned to compare the training and cueing effects with a group that although not being cue trained, is alerted of the intentions behind cue training. It is [53]also important to note that Byl *et al.* [42], besides evaluating PD patients also [42]evaluated patients that suffered from strokes, but for the purpose of this research that group of patients was excluded.

To summarize the different combinations and organizations of sample groups reviewed there were identified 9 studies that only divided freezers vs. non-freezers [30], [43], [54], [56], [66], [68], [69], [72], [74]; 9 studies that divided freezers, non-freezers and healthy controls [26]–[28], [31], [44], [46], [48], [49], [67]; a single study that compared a freezer group with healthy controls [47]; a single study that compared one PD group and one healthy control group [29]; 16 studies that only used one group of freezers [32]–[35], [37]–[41], [45], [47], [62]–[64], [70], [73]; 6 studies that only used one group of PD patients [52], [57], [60], [65], [71], [75]; 2 studies that analyzed one Placebo group vs. one experimental group [55], [58]; 4 studies designing one experimental vs. one control group of PD patients [42], [51], [59], [61]; and 2 studies opting for two different cued conditions [50], [53]. Ultimately, the mean number of experimental group participants was 19, 10 for Placebo group participants and 13 for control group with PD patients. The respective minimum and maximum numbers were 7 and 22 for experimental group sizes, 10 and 10 for Placebo group sizes; and 5 and 20 for control with PD patients group sizes.

INCLUSION AND EXCLUSION CRITERIA

Although not listed in the table, it was also important to analyse the most prevalent inclusion and exclusion criteria considered, for further consideration during the protocol design. It is important to note that not all studies presented these criteria. Four studies did not mention any exclusion criteria, but presented inclusion criteria [57], [62], [73], [75]; other four studies did not mention the inclusion criteria, but presented exclusion criteria [30], [44], [67], [72]; and five studies did not mention both [36], [38], [58], [63], [68].

The main and inherently present inclusion criteria considered was participants being diagnosed with PD, were 10 studies inclusively mentioned performing the diagnosis according to the UK brain bank criteria [26], [27], [31], [32], [40], [41], [53], [60], [64], [65]. The great majority of the studies only

included patients that were able to walk or stand independently (24 studies) [26], [27], [31], [34], [35], [37], [39], [42], [43], [46], [47], [49]–[51], [53]–[55], [59]–[62], [65], [66], [73], to grant that patients were able to perform the motor tasks; integrated a certain range of stages of H&Y scale (21 studies) [26]–[28], [31], [32], [34], [42], [47], [49], [51], [53]–[57], [61], [65], [69], [71], [74], [75], being the most prevalent including patients that ranged from stage 2 to 3 or patients ranging from stage 1 to 4; were evaluated with history or presence of FoG (19 studies) [32]–[35], [37], [39]–[41], [45], [47], [48], [57], [59], [60], [62], [64], [65], [70], [73], using for that purpose NFOG-Q or UPDRS-III; were able to perceive visual, auditory or vibratory stimuli (12 studies) [26], [27], [31], [35], [37], [46], [53], [54], [62], [70], [73], [75], mainly using Snellen chart to evaluate visual acuity; having a certain age (12 studies) [26]–[28], [31], [32], [35], [41], [46], [54], [64], [74], [75], being mostly common to consider patients that have at least 50 years; and absence of cognitive impairment or not being demented (11 studies) [29], [32], [37], [46], [47], [51], [53], [54], [57], [62], [74], frequently evaluated considering MoCA score or MMSE score larger than 24.

As for exclusion criteria, most of them complete the inclusion criteria by reinforcing determined aspects. Participants most predominantly were excluded if presented other neurodegenerative or health disorders (34 studies) [26]–[35], [39]–[44], [46], [48]–[52], [54], [56], [59], [60], [64]–[67], [69]–[72], such as Alzheimer's disease, stroke or gait disorders; if presented dementia or severe cognitive impairment making them unable to follow instructions (25 studies) [26]–[31], [37], [39], [41], [43], [44], [48]–[50], [54], [55], [59]–[61], [64], [65], [67], [69], [70], [72]; visual, hearing or somatosensory perception impairments (22 studies) [30], [32]–[35], [37], [39], [43], [44], [46], [50]–[52], [55], [59], [60], [64]–[66], [69], [70], [72]; and if patients were unable to walk or walk independently (10 studies) [26]–[28], [41], [45], [52], [56], [64], [69], [71]. It is also worth mentioning that 5 studies also considered to exclude patients that had DBS or other functional brain surgery, to prevent risk of bias [46], [47], [49], [64], [74].

MOTOR TASKS

To evaluate patients' motor performance using different cueing methodologies, it was essential to analyse different motor tasks. Essentially, motor tasks can be divided in 3 categories: walking tasks (34 studies) [27]–[33], [36]–[46], [51]–[53], [55], [57]–[59], [61]–[65], [67], [68], [70], [75]; turning tasks (13 studies) [26], [34], [36], [38], [40], [47], [49], [60], [63], [69]–[71], [74], such as 8-shaped turning task, 180° left U-turn, turning in place and 360° turns; [27]–[33], [36]–[46], [51]–[53], [55], [57]–[59], [61]–[65], [67], [68], [70], [75] gait initiation tasks (10 studies) [27], [28], [37], [40], [48],

[56], [66], [68], [72], [73], such as first step initiation, sitting-to-standing or stepping-in-place (SIP), and they can be performed individually or combined.

Different walking tasks were performed such as passing through a doorway (7 studies) [30], [37], [38], [44], [45], [63], [70], with the purpose of exposing patients to potential FoG triggering scenarios; range of motion tasks (1 study) [42] and balance training tasks (4 studies) [42], [53], [58], [61], that consist in walking or standing in different surfaces, or during conditions such as eyes closed, to analyse postural and motor control aspects. Timed Up and Go (TUG) task is an example of combining both gait initiation, walking and turning tasks. TUG task consists of evaluating gait performance when standing up from chair, walking, turn around, walk back and sit-down. In this research 7 studies performed TUG tasks [35], [39], [44], [52], [53], [61], [68], being Capato *et al.* [53] the only study that performed TUG dual-task.

Therefore, it is also important to highlight dual-task training (6 studies) [31], [35], [39], [44], [51]–[53], [56], [61], [63], [68]. Dual-task training consisted of simultaneously performing gait and attentional tasks. Three studies performed dual-task training by counting backwards by 7 [63] or by 3 [56], while walking (2 studies) [56], [63] or performing TUG dual-task test [53]. Similarly, Graham *et al.* [31] performed a forward digit span test while walking. As for Sijobert *et al.* [68] performed SIP dual-task test, by naming backwards the months of the year while stepping in place. Lastly, Ginis *et al.* [51] performed walking while reciting as many words from a letter as possible.

OUTCOMES

All 5 different parameters (Spatiotemporal, Kinetic, Kinematic, Physiological or Clinical) were analysed to evaluate cueing effects over PD patients gait performance and in mitigating motor symptoms, such as FoG. Different result outcomes were obtained, meaning positive (45 studies) [26]–[36], [39]–[44], [46]–[48], [50]–[55], [57]–[75], and negative (24 studies) [28], [30], [37], [38], [41], [42], [44], [45], [47]–[51], [56], [61]–[64], [66], [67], [69], [70], [72], [73], cueing effects over motor response were analysed.

Spatiotemporal parameters were the parameters that showed greater improvements with cueing (31 studies) [26]–[29], [31], [32], [34], [36], [39], [42]–[44], [46], [48], [52], [54], [55], [57]–[60], [62], [64]–[68], [72]–[75], mainly increasing patients' velocity while performing gait tasks [26]–[28], [32], [39], [46], [52], [58], [65], [66], [75], and cadence [44], [46], [54], [59], [67], therefore reducing time to complete tasks [34], [36], [39], [57], [68], [74]; increased step length [32], [42], [43], [62], [66], [73], and stride length [27], [28], [31], [39], [44], [46], [55], [58], [59], [64], [65], [67], [75]; decreased step

or stride time [31], [34], [46], [48], [62] , and variability [31], [52], [54]; allowing better task performance and more stable/smooth gait patterns [60], [69]. It is worth noting that in Mancini *et al.* [69] reducing the number and velocity of turns was not considered a real negative aspect, since it was hypothesized that this decrease was due to patients being more aware and focused during the turning tasks with cueing. Patients' smoothness during turning increased which indicated that they were more cautious during turning performance, making them slower but in alternative providing them an improved gait pattern and reducing FoG episodes.

As for Clinical parameters, the main improved outcome was the number and duration of FoG episodes (14 studies) [30], [33], [34], [36], [39]–[41], [47], [57], [65], [67]–[69], [73]. Geerse *et al.* [41] initially showed negative effects as the % time FoG and number of episodes increased at first. However, it was considered a habituation period, since as patients proceeded with training those negative effects were overcome.

Other clinical positive effects of cueing were reducing number of falls [42]; improved MBEST score [53], although at 4-week follow-up not maintained [51]; improved UPDRS [53], and better balance performance [42], [61].

Tosserams *et al.* [52] verified also a relationship between some clinical and spatiotemporal results, such as lower MDS-UPDRS III scores being linked to improved gait variability, meaning patients with less severe disease symptoms had better improvements in gait pattern; and higher MoCA scores linked to greater efficacy of external cueing, meaning less cognitive impaired patients showed better improvements when using cues. Another clinical outcomes worth mentioning are Peppe *et al.* [58] conclusions that showed that patients with higher H&Y score, therefore more severe disease stage, showed better improvements in MDS-UPDRS III, meaning their motor symptoms and disease perception may have improved. The Placebo group also showed some improvements in MDS-UPDRS III, meaning patients perception of the disease may have been also improved by the sense of having a 'false' cueing device even when it was not delivering cues.

As for Kinematic positive effects, the main improvements were improved APA's duration [28], [48], [72] and amplitude [72]; improved head rotation and head-pelvis separation during turning [47]; improved forward Center of Mass (CoM) velocity and sideways sways [73]; improved lower limbs joints and feet strike heads [31], [59]; and increased knee flexion and ankle dorsiflexion [67]. However, some studies showed that APA's amplitude did not increase amplitude in all patients, indicating that patients with higher UPDRS III scores decreased APA's amplitude [28], meaning APA's improvements may not be pronounced for all patients.

In other hand, kinetic outcomes gave information about pressure and forces effecting during different mobility tasks. The main improvements observed were improved positioning [35] and improved Center of Pressure (CoP) sways in the medio lateral plane [61]. Lastly, physiological outcomes mainly served as information to relate with other parameters. The main physiological results obtained were improved saccade, therefore improved rapid movement of the eyes between fixation points, using visual cues [31], meaning patients were more focused on preparing their movement when provided visual feedback; and greater uptake of FF-CT in the better cueing response group [40], which may indicate a potential connection between the compensatory effects of visual cueing and the dopaminergic function in specific brain regions in PD patients.

One study indicated improvements of Cortical Silent Period (CSP) and Short Interval Intracortical Inhibition (SICI), meaning that cortical inhibition may have been reduced by auditory cues, leading to better gait performance [54]. As for EMG results, Schlenstedt *et al.* [56] mentioned that, although first step decreasing when in dual-task performance, contraction of the tensor fasciae latae increased, therefore it was noticed an improvement of muscle activity using cueing.

2.3. DISCUSSION

2.3.1. RQ1: HOW HAVE CUEING STRATEGIES BEEN USED AND APPLIED FOR TARGETING MOTOR SYMPTOMS OF PD?

Cueing strategies have been employed to target PD motor symptoms by providing external stimuli to improve movement and gait. They can be divided essentially in 3 types according to the sensory aspect targeted: visual, auditory, or somatosensory cueing; and it was possible to understand their implementations separately or combined. Cues were delivered also via electronic devices, non-electronic strategies, or both methods combined. The great majority of the studies implemented Visual or Auditory cueing, essentially and respectively via laser devices to project laser lines for patients to step or metronomes to provide rhythm for patients to follow, while Somatosensory cueing was present in less than a third of the reviewed papers. Of this third, more than half combined Somatosensory cues with Visual and/or Auditory stimuli, which means that there are a lack of research evaluating Somatosensory cues alone in addressing motor symptoms such as FoG. The main somatosensory devices used were vibratory systems, such as VibroGait, to provide vibratory cues at a certain rhythm or when detecting a determined gait-event or phase.

Cues were delivered both open-loop [26]–[32], [34]–[36], [38], [40], [43]–[47], [49], [52]–[55], [57]–[60], [64]–[74], and/or closed-loop [33], [34], [37]–[39], [42], [45], [48], [50], [51], [56], [61], [65], [68]–[71], being open-loop the main strategy used. Open-loop cueing consisted of providing cues continuously or at a fixed time, non-dependent of user's performance, while closed-loop cueing offered a more patient tailored approach, providing cues when detecting certain patient gait events or an off-target performance. Both modes were used within the different cueing modalities and analysed.

Open-loop visual cues helped patients during motor tasks by providing them orientation, such as guidelines for them to step. This improved patients' spatial awareness of their surroundings while performing tasks, that become focused of where to step during gait. On other hand, auditory open-loop cues help patients by providing them with a sense of temporal rhythmicity. In other words, allows patients to focus on rhythm, which translates in improving their stepping rhythm during gait. Lastly, somatosensory cues delivered at open-loop also offer patients time awareness. Continuous but time-variant vibratory or auditory stimuli provides a gait rhythm, reminding patients when to step. Ultimately, these cueing strategies aim to bypass internal motor response mechanisms, helping patients maintain more controlled and smoother motor performances, reducing episodic symptoms such as FoG.

As for closed-loop cueing, essentially allowed the system to have into account the user's performance, that means visual, auditory or somatosensory stimuli is delivered synchronized with user's gait events and in some cases the patients can be aware of their performance and are encouraged to adjust their gait towards an healthy motor behavior. The main closed-loop cueing devices reviewed where laser devices and vibratory systems, that only provided the cue when patients were instructed or during certain gait phases. By using a personalized strategy, closed-loop cueing can act as a preventive strategy in addressing FoG while not imposing a gait pace to the user.

In which concerns the different clinical protocol designs reviewed to assess cueing training, the main motor task evaluated was walking. However, more than half of the studies that implemented walking courses, combined different FoG provoking tasks, such as passing through doorway, suddenly turning, or even stopping and restarting gait, indicating the importance of analyzing tasks of the daily patient's routine that elicit FoG and therefore reduce their autonomy. Cueing strategies during these tasks allow patients to alternate their focus on the cue perceived, therefore abstracting from the FoG inducing task while performing it.

Patients were mainly characterized by age, gender, disease duration and by evaluating some clinical scales. The prevalent trend reviewed was the evaluation of H&Y scale to identify patients severity degree of PD, MDS-UPDRS III used to evaluate patients' mobility impairment severity, and NFOG-Q to

determine the presence of FoG and respective severity. All of these scales were also used as inclusion criteria, being the most common criteria including patient's with less severe H&Y stages, ranging from 1 to 4; patient's needed to be able to walk independently without being aided, evaluated using H&Y or UPDRS-III; patient's couldn't have any other neurodegenerative disorders, dementia or cognitive impairments, evaluated using MMSE or MoCA; and had to have history or presence of FoG, evaluated using FOG-Q or NFOG-Q. More than half of the studies performed both training and gait assessment during On medication state, therefore it may also be considered the condition of being in On medication state as an inclusion criteria.

As for other parameters such as sample size and organization, training dose and evaluation time points, of the longitudinal studies it was mostly common to distribute patients into an experimental group, that receives the cueing strategies, and compare it with a control group, that performs the same train without cueing. Training sessions ranged from 1 to 8 weeks training, during 10-90 min. sessions, from 2 to 3 times per week; and with 1 week to 6 months follow-up for gait assessment. Some longitudinal studies opted for using a Placebo group instead of the normal control group, similarly, performing the same training as the cued group, but while wearing a placebo device to understand if patient's mindset using the devices even without providing any cue may also affect gait performance. Although being less than a fourth of the studies using this distribution, it is extremely interesting comparing mindset influence over gait performance and essentially patients' perception, which may potentially improve patients' perception of QoL.

2.3.2. RQ2: WHICH IS THE EFFECTIVENESS OF CUEING STRATEGIES CONCERNING MOTOR EFFECTS AND QOL?

In order to address the effectiveness of cueing strategies concerning motor effects and QoL it is important to consider the different outcomes obtained within this literature review, for short-term (cross-sectional) and long-term (longitudinal) studies.

Focusing first on cross-sectional studies results, different cueing strategies had diverse effects over Spatiotemporal (mainly evaluating velocity and stride length), Clinical (mainly evaluating FoG occurrences), Physiological (mainly evaluating muscle activity using EMG), Kinetic (mainly evaluating positioning of CoP) and Kinematic parameters (mainly evaluating patients' APA's). The predominant outcomes were Spatiotemporal followed by Clinical outcomes, indicating that these parameters should be considered when evaluating patients' mobility and motor symptoms.

Cosentino *et al.* [18] compiled the information of 31 of the reviewed papers within this research [17], [26]–[30], [32]–[38], [43]–[49], [56], [57], [60], [64], [66]–[69], [72]–[74]. It concluded that visual

and auditory cueing provided APA improvements when initiating gait, decreased number of FoG episodes and improved turning time. Visual cues were the main cueing strategies with walking improvements, addressing better cadence, gait speed, step time and step length. As for somatosensory cues the paper reviewed different results, ultimately concluding that the data available was not sufficient to draw significant results of this cue strategies over gait and FoG improvements.

By analysing the results found within the literature review for other cross-sectional studies, of the papers that used somatosensory cueing alone, showed overall improved FoG and gait performance [55], [57]–[59], which indicates great potential in overcoming debilitating motor symptoms and enhancing patients' QoL. Similarly, the same results were observed when used combined with auditory cueing and/or visual cueing. However, Nieuwboer et al. [74] showed better improvements using auditory cueing, when comparing all cueing methods, and in McCandless et al. [73] the vibratory metronome disrupted gait, which indicated that the vibratory mode confused patients' rhythmicity when compared to the normal metronome. This suggests that combining different cue methods may enhance the positive effects over mobility, however it is necessary to consider the mental and attentional effort of the tasks to not overstimulate patients.

As for longitudinal studies, upon observing the outcomes found within this research, it is noticeable the lack of this study types to evaluate the prolonged cueing systems usage effects in PD patients' mobility when comparing with cross-sectional studies. Despite the limited number of such studies, conclusions have been drawn concerning this longitudinal use aspect.

On another hand, when comparing the overall effects of electronic vs. non-eletronic devices, although being noted improvements in more than 80% of both studies, non-eletronic devices improvements were more consistent, mainly resulting in improvements in velocity, stride or step length, and cadence. It was also noted that, of the five studies that compared the use of both electronic and non-eletronic cueing strategies, only one study reported that electronic devices cueing strategies were more beneficial [67]. However, these results were not totally bias since compared different cueing mechanisms also (auditory cueing delivered via electronic device and visual cueing delivered using a non-eletronic cueing strategie), suggesting that more important to consider different devices is to analyse the efficiency of different cueing strategies.

The prevailing trend in the studies found suggests that although showing improvements in gait, FoG and clinical outcomes measures in the short term, these effects tend to disappear over the long-term usage [51], [55], [61]. The review article Zhang *et al.* [25] hypothesized that the plasticity of PD patients may inhibit them to maintain the positive immediate effects observed. This accentuates the imperative

need of larger-scale Randomized Control Trials (RCTs) to confirm the enduring usage efficacy of cueing systems in motor rehabilitation of PD. Therefore, this research purposes a clinical randomized control trial study to fill the gap in understanding the long-term utilization of cueing strategies in motor rehabilitation of PD patients.

However, Capato *et al.* [53] drawn divergent conclusions regarding the long-term utilization effects of cueing systems. In this study, RAS-supported multimodal balance training demonstrated sustained improvements in the MBEST, TUG dual-task performance, and UPDRS scores at 1 and 6-months follow-up. Consequently, the prolonged use of cueing strategies exhibits potential in motor rehabilitation of PD patients, mitigating motor symptoms such as FoG and enhancing self-reported health perception, thereby increasing QoL. It is also worth noticing the need of QoL clinical scales evaluations in these clinical studies for a more comprehensive understanding of the effects of long-term cueing training over the direct patient's perception of QoL.

Overall, it was shown that closed-loop cueing strategies had greater improvements, mainly in reducing number of FoG episodes and duration, but also in improving spatiotemporal gait metrics, suggesting that providing cueing strategies at a rhythm tailored to each patient's gait may be more benefic in addressing PD symptoms.

Some prevailing more negative effects observed on the long-term studies were not showing significant improvements of velocity [42], probably caused by the extensive training sessions duration, and use of too many different exercises which may overstimulated patients; not showing significant improvements of clinical evaluations such as MoCA, FES-I and FOG-Q [50]; and not maintaining results at follow-up [51], [61], which may indicate that the training dose to follow-up assessment ratio was not sufficient to maintain results, i.e. in order to maintain results using the defined training dosing, the follow-up should have been shorter than 1-month after.

Overall, when comparing with the review articles analyzed, Cosentino *et al.* [18] stated that the study had some limitations regarding the lack of direct measurements of FoG, and that since only included single-session studies, the results may alter at studies with long-term cue training. This confirms the need of evaluating more direct FoG parameters, such as NFOG-Q, but also enhances the importance of longitudinal studies evaluating patients' mobility and motor symptoms after long-term cue assisted training.

As for Zhang *et al.* [25], based on their findings concluded that although devices may have improved walking speed, overall did not cause significant effects on other gait parameters, which suggests the importance of evaluating gait speed as a potential primary outcome. It also suggests establishing a

more standardized training protocol, since more heterogeneous training regimens had poorer results and lacked comparability. This may also suggest the importance of defining one only continuous study design course instead of several separate exercises.

2.4. CONCLUSIONS

In order to guide future research, this section allows a conceptual overview of the main results obtained that are important to consider during the course of this dissertation. In which concerns patients' characteristics and inclusion criteria to be considered, it was noted the prevalence of characterizing patients by gender, age, disease duration, and by evaluating clinical scales such as H&Y stage, MDS-UPDRS III and NFOG-Q. To be included, it was prevalent the need of patient's being diagnosed with PD; be able to walk autonomously, therefore having less severe stages of H&Y; not having dementia or other neurodegenerative or cognitive disorders; being on ON medication state; and experiencing FoG episodes. These results reinforce the importance of evaluating these 3 clinical scales: H&Y, NFOG-Q and MDS-UPDRS III.

Somatosensory cueing systems are still being studied to understand their long-term usage effects in addressing mobility of PD patients, however present great results in reducing symptoms such as FoG. Closed-loop cueing delivery stands as the potential most effective control strategy, being also important to consider this type of patient tailored strategies for future research. Combining both somatosensory and visual cueing strategies may cause greater improvements than somatosensory alone, allowing better abstraction of patients' surroundings, focusing more on their motor task performance.

Although several different motor tasks being performed, it was concluded that FoG inducing tasks such as passing through doorways, turning and start-and-stop, while walking are essential to evaluate cueing effects addressing patients motor symptoms, such as FoG, therefore may be effective in improving patients QoL. By these means, PDQ-39 scale evaluation should be also considered for further protocol development.

For multiple session training and further gait assessment, it is important to consider not to overstimulate patients, neither to have long periods without follow-ups, since long-term cueing effects may be less significant and disappear without consistent training. Therefore, gait-assessments should be at not much more than 1-week follow-ups, and patients should train at least 2 to 3 times a week, approximately 30 to 45 min, during a mean of 4 weeks.

As for sample size and group distribution, it should be randomized considering one cued group as the experimental group to be analysed, and compare it with a control placebo group, using the same device but without providing any type of cue. The sample size of each group should be determined in the future during protocol design, by estimating the number needed for the study to present significant results of the primary outcome selected. In this context, spatiotemporal and clinical outcomes were reviewed as the main predominant improved parameters using cues, identifying velocity and FoG occurrences as primary outcomes to consider analysing on further research developments. By these means, Inertial systems such as Xsens should be considered for gait assessment, to evaluate spatiotemporal parameters.

3. SOLUTION OVERVIEW

This dissertation is the progress of several clinical studies that aim to analyse and compare different cueing strategies, to conclude which may cause better motor performance improvements in a cross-sectional study; develop a novel strategy; and practice a long-term protocol, in PD patients, using +sensBand and evaluating the motor effects of those strategies in gait rehabilitation, focusing on FoG and QoL. To achieve this, it is necessary to first consider the materials necessary to develop the novel solution. In this chapter, it is outlined: (i) an overview of the system focusing on the main hardware components, (ii) an introduction and description about the different strategies used and (iii) a description of the MATLAB App implemented for further data processing.

3.1. HARDWARE

In which concerns the technologies used in this project, it is important to take into account two different systems: the +sensBand system, responsible for providing both somatosensory cueing, visual cueing and for data collection (**Chapter 4, 5 and 6**), and the Xsens motion tracking system with Awinda, used for gait assessment validation in **Chapter 6**. Fig. 7 and Table 3 summarize the technologies used.

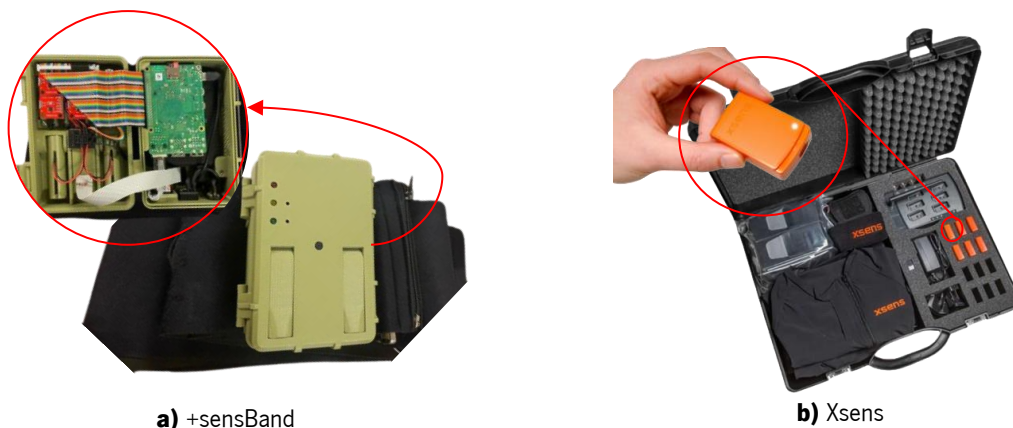


Fig. 7. Technology systems used.

Table 3. Technologies used during this dissertation

Technologies	Purpose	Data collected	Parameters evaluated
+sensBand	Provide different control strategies of somatosensory and visual cueing, during patients gait performance, and	Collects acceleration and angular velocity.	Allow to determine gait velocity, cadence, step length, step time, stride length, stride

	simultaneously collecting gait metrics.		time, asymmetry, and variability
Xsens	Validate +sensBand data collection and provide additional biomechanical outcomes	Collects motion data of each body segment position	

First, and since it is the main component to address in this project, it is important to start by understanding the +sensBand system and the different components integrated.

The +sensBand device itself includes **6 systems**: a **processing system**; an **actuation system**, that includes vibration motors responsible for somatosensory cueing and 2 laser projectors for visual cueing; a **sensory system**, including 4 IMU's responsible for data collection and a camera for door detection; a **memory system**; a **communication system**, responsible for communicating via Bluetooth with a smartphone App, designed for device configuration, and via SSH with the clinical desktop App, designed for data processing; and a **power supply**, that consists of a Charmast powerbank 10000. All 5 systems are located inside a 3D printed box, except for the sensory system, whose IMU's are located throughout the waistband textile itself, at 4 different locations around the waist: back; left side; right side and navel point. +sensBand allows to monitor axel accelerations and angular velocities on all these locations, simultaneously or not, to assess gait metrics, while the actuation system provides visual or vibrotactile cues according to the control strategy selected.

The Xsens system contains 6 wireless Motion Trackers (MTW), that consist of miniaturized IMU's that incorporate 3D accelerometers, gyroscopes, magnetometers and a barometer, therefore providing 3D orientations as well as linear acceleration, angular velocity, magnetic field and pressure data. This entails more detailed metrics than the +sensBand sensory system, allowing to validate the +sensBand collected data (acting as a ground truth) but also providing more information to assess patients motion outcomes. The IMU's are positioned on the patients' body (e.g. lower and upper legs, upper arms, wrists, and pelvis), using Velcro body straps. To charge and calibrate the MTW's, an Awinda Station is connected to an outlet, via DC power connector, and to a computer, or using an Awinda USB Dongle, via USB, allowing synchronization of data assessment when using the different MTW's simultaneously.

3.2. CONTROL AND MONITORING STRATEGIES

The +sensBand originally offered five possible control strategies, that can be selected using the smartphone App, including (i) **gait-event driven cueing**; (ii) context awareness cueing; (iii) turning

phase-dependent cueing; (iv) postural stability phase-dependent cueing and (v) **continuous cueing**. Based on the literature review conclusions, it was further developed a novel sensory cueing strategy, the (vi) **Fog prevention cueing**. For this project, only strategies (i), (ii) and (vi) were explored, therefore only those will be further discussed.

Besides providing different cueing strategies, the +sensband also provides a **motion monitoring** option.

All the different strategies can be selected to configure the +sensband device using a smartphone app, as shown in Fig. 8. In case the user pretends to not use any type of cueing, but rather only monitor the patient's gait, it should select the Motion monitoring option directly. When the Sensory cueing option is selected instead, a page with the different cueing strategies available will appear and the strategy pretended should be selected and then configured. Each of the strategies will be further explained in this section.

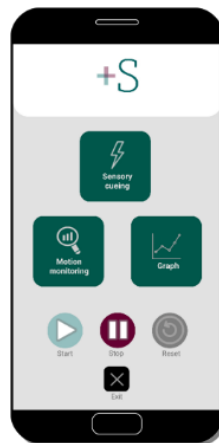


Fig. 8. +sensBand smartphone App.

3.2.1. MOTION MONITORING

PD motor symptoms are commonly present during patients' everyday tasks. Changes in patients' gait pattern such as reduced amplitude of movement, slowness, and shorter steps, can be an indicator for more severe symptoms such as FoG. Therefore it is of enormous importance to analyze patients' gait metrics.

By these means, the +sensBand was developed considering also the development of a **motion monitoring strategy**. This strategy activates only the IMU's of the +sensBand, to collect acceleration and angular velocity data, for further analysis of gait metrics.

Gait event detection requires the Back IMU data as a reference, so it is important to guarantee that the IMU is placed correctly at the lower back (approximately above L5). The +sensBand integrates a

gait event detection algorithm that receives the IMU data in real-time, then calibrates it to eliminate measurement errors, applies motion compensation to adjust for trunk rotations, and filters data to detect significant changes indicative of gait events. Then, the sensory data runs through a real-time adaptive algorithm, that allows to identify five key gait events: Heel strike (HS), the initial contact (IC) moment; Foot flat (FF); Mid stance (MSt); Heel off (HO); and Toe off or the final contact (FC) of the foot. This algorithm was developed specifically for PD patients, containing adaptive thresholds for each gait event, that are updated along the motion monitoring assessment. The adaptive thresholds are recalculated and updated periodically in sets of 10 gait cycles, considering the data of the previous gait cycle set.

The motion monitoring strategy is also automatically activated when using all the different cueing strategies, since it requires to activate motion monitoring to obtain the patient gait data file collected.

3.2.2. GAIT EVENT-DRIVEN CUEING

Several cueing strategies of +sensBand were explored, to comprehend each functionality but also to select which should be adapted and implemented in the clinical protocols.

Gait event-driven cueing consists in providing closed-loop vibratory stimulation, triggered every time a right-foot toe-off is detected. Toe-off gait event was selected since literature reports observation of inadequate swing phase before the occurrence of FoG episodes [79].

The vibratory frequency and time on which the cueing strategies are provided, which motors will apply the vibration, and the frequency on which the data will be collected are all selected/configured using the smartphone App for +sensBand. During the use of this strategy all motors were selected to provide vibrations around the waist, and were set at 200Hz to vibrate during 200ms, according to [19].



Fig. 9. Gait event-driven cueing delivery schematic.

The gait event detection algorithm plays an important role also in this cueing strategy. By segmenting the gait events, it is possible to detect the TO's of both feet, that are then distinguished considering that the right foot HS's presents angular velocity in the Antero Posterior plane (gyr_{AP}) below 0, and left HS's present gyr_{AP} above 0 [80].

When the TO's are detected and they correspond to the right foot TO's, the motors are activated, and the patient receives the vibrations set at the respective duration and frequency.

3.2.3. CONTINUOUS CUEING

Literature review as shown that one of the main strategies for temporal orientation of PD patients was the use of auditory cues set as metronomes, since it provides a fixed rhythm for patients to follow and try to match their pace. However, auditory cueing comprises several disadvantages concerning practical aspects, considering that audio can be intrusive. Somatosensory cueing, on the other hand, when applied at a fixed rhythm can be also used with the same purpose but in a more specific and discrete manner.

Continuous cueing, like a metronome, consists in providing continuous vibratory open loop cueing for a defined period of time and at a certain frequency. This strategy was configured in order to provide vibrations during 2s pulses, set at 200 Hz, according to [19]. Fig. 10 shows the schematic of this cueing mode delivery.

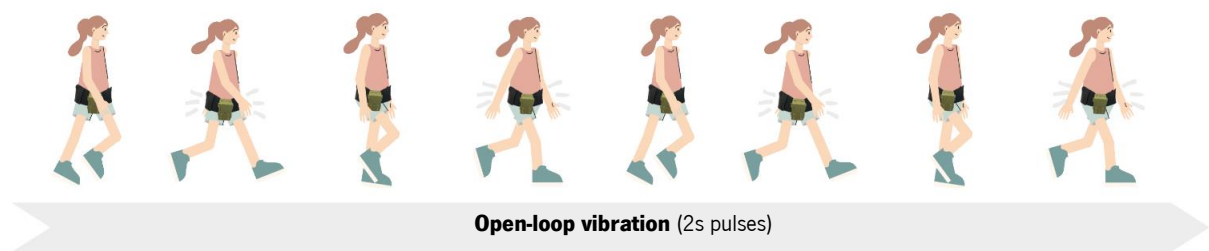


Fig. 10. Continuous feedback delivery schematic.

3.2.4. FOG PREVENTION CUEING

By analysing the literature review it was noted that, overall, the cueing strategies that predominantly resulted in higher gait improvements and in higher FoG episodes reduction were the visual cues. When applied at open loop providing patients spatial orientation on where to place each step, such as tape lines, acted as active strategies for patients to overcome FoG.

Somatosensory cues also had great potential for PD motor rehabilitation and in preventing FoG episodes, especially when applied at a closed loop rhythm, allowing to be personalized for each patient's gait performance to help them be more aware on when to step.

Combining both open loop visual cues with closed loop somatosensory cues, therefore, may have greater potential in targeting FoG, since it can act as both an active and preventive strategy, allowing a more complete sensory stimulation of the patients. Therefore, it was developed a novel sensory cueing

strategy using the +sensBand system that simultaneously provided both two cueing modalities, the **FoG prevention cueing**.

FoG prevention cueing initially provides vibration at a fixed continuous rate (open-loop) to help gait initiation, along with the projection of two fixed laser lines in front of the patient (also open-loop). After starting walking, the laser lines remain fixed and open-loop. However, the vibrotactile cues change to closed-loop after the first TO of the right foot being detected. Fig. 11 represents the cueing strategy delivery.

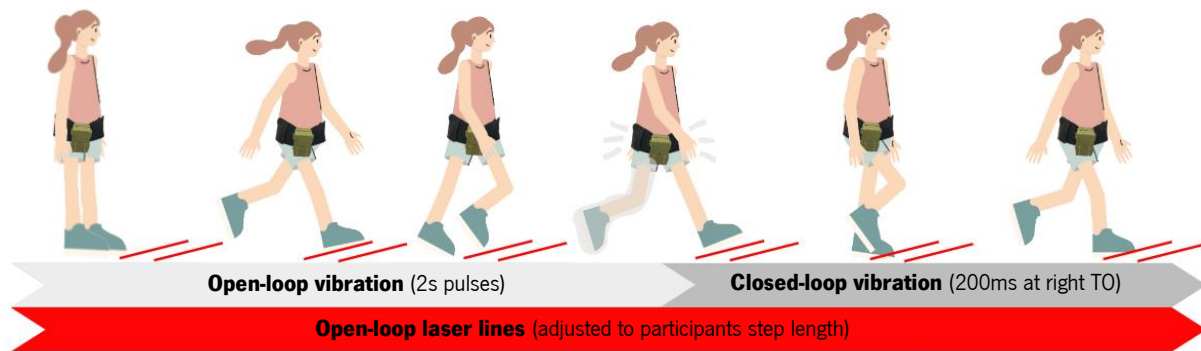


Fig. 11. FoG prevention cueing delivery schematic.

Closed-loop vibration is enabled at the right foot's toe-off gait event during 200 ms and is set at 200 Hz, using the same algorithm for gait event detection as the gait event-driven strategy. The vibration is set to 2s pulses. Since the start of walking usually elicits FoG, rhythmic open-loop vibration is enabled before gait initiation, reinforcing the first step execution [56], [73]. Therefore, after detecting the first toe-off, the control strategy switches to closed-loop vibration to personalize walking according to the users' self-selected pace.

Visual cues are continuously provided by activating the lasers to project two lines in front of the participants. These lines move along with users so they are always seeing the next two steps where the foot should be placed. Therefore, visual cues are applied to assist during a FoG episode, while vibrotactile cues also assist during gait initiation but during walking forward, turning, and passing through doors are applied also to prevent the occurrence of FoG episodes.

3.3. DESKTOP APP (MATLAB)

In order to further process and analyse the collected gait data, and calculate spatiotemporal gait metrics, it was developed a desktop clinical App using MatLAB (Fig. 12).

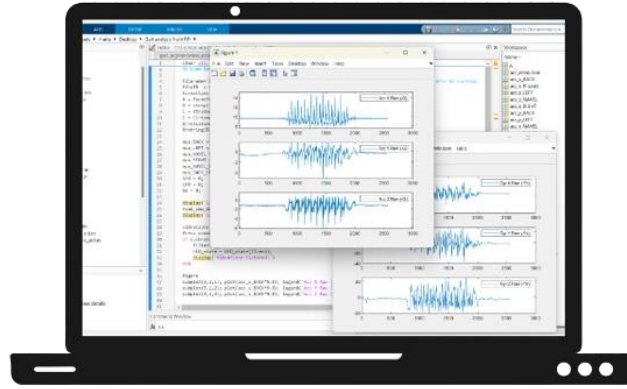


Fig. 12. Desktop clinical App.

This App was designed to read the IMU data files obtained using the +sensBand, process the data using several filters, and then running the data through a finite state machine (FSM) to detect IC's (HS) and FC's (TO) for each foot, to further calculate gait metrics. The FSM algorithm was developed to emulate the FSM of the +sensband itself. However, to avoid the accumulation of any errors, such as leg distinction errors, the Matlab FSM includes two additional conditions that ensure that after detecting a gait cycle of the right leg, the next gait cycle must be detected for the left leg, and vice versa. Instead of 5 states, the improved FSM contained a total of 10 states, corresponding to the different gait events in order but for both right and left feet (e.g. HS_right, FF_right, TO_left, MSt_right, HO_right, HS_left, FF_left, TO_right, MSt_left and HO_left). If the FSM detects consecutive gait cycles on the same leg, the state resets to correct any potential errors.

At TO it was inserted the gyr_AP condition for leg distinction. After detecting right or left HS, the subsequent events (FF, MSt, and HO) are associated to that same leg, except for the TO event that is associated to the opposite leg, in line with the descriptions of [81], [82]. Since it is important to ensure that after a right leg detection the following metrics should be of the opposite leg, and vice versa, the algorithm was set by first detecting the 5 events for the right leg gait cycle (HS_right, FF_right, TO_left, MSt_right and HO_right), and then following with the same sequence of gait events but for the left leg. If the events were detected with the gyr_AP condition for leg distinction detecting a right or left leg, and the following and previous legs were detected as the opposite legs, the gait events were correctly detected, therefore were inserted in the IC and FCs arrays for gait metrics calculation. Else, it meant that two gait cycles for the same leg were detected consecutively, presenting an error. In this case, the respective gait events detected in that gait cycle were removed, and Nans were added on those positions instead. This approach flags errors, with Nans marking cycles where the expected leg alternation failed, thus preventing inaccurate gait metrics from being calculated.

Depending on which foot the patient initiates gait, two FSM cycles were created: one starting with the left foot first and other starting with the right. For better understanding of the improved FSM algorithm, Fig. 13 presents a flowchart with the order of gait event detection highlighted by the color corresponding to the first foot detected in the FSM algorithm. When using the FSM_Right_first cycle, events are detected in the order indicated by the blue numbers, whereas in the FSM_Left_first cycle, events follow the order marked by the red numbers. Ultimately, the input acceleration and angular velocities components (acc_n, gyr_n), are processed through the FSM algorithm to identify the respective IC's and FC's for each foot (IC_R, FC_R, IC_L, FC_L).

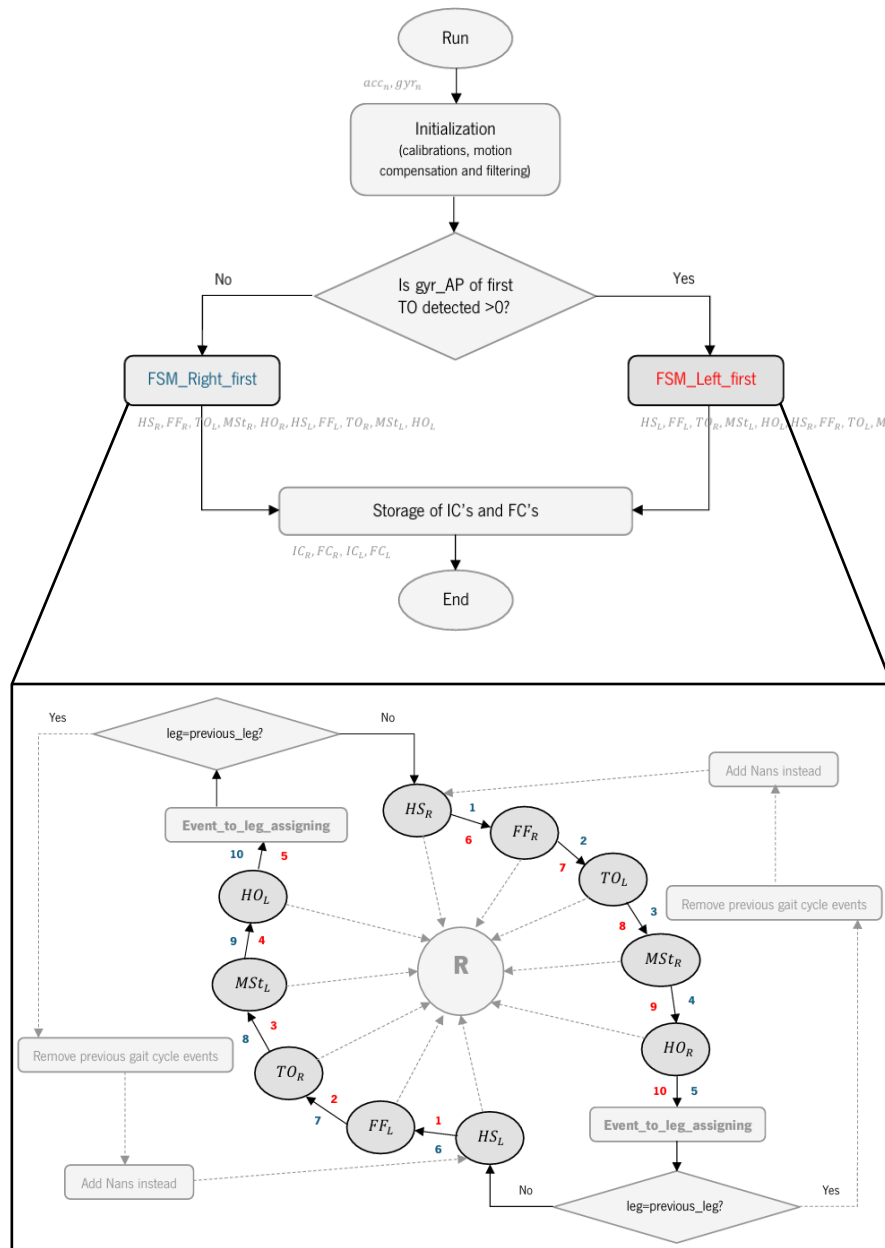


Fig. 13. Flowchart of the improved FSM for gait segmentation MatLab algorithm.

After processing and detecting ICs and FCs of each foot, gait metrics were calculated for both right and left legs, including step time and length; stride time and length; stance, swing and double support phase; gait speed; cadence and number of steps taken. Additionally, asymmetries and standard deviations were also computed by comparing metrics of both feet and analysing variability, respectively, for a more comprehensive understanding of the patient's gait characteristics. Table 4 presents the equations used to obtain each spatiotemporal gait metric calculated.

Table 4. Methods for estimating gait spatiotemporal metrics represented by domain, metric, formula and measurement units

Domain	Metric	Formula	Units
	Step length	$median\left(\left(2\sqrt{Lh - h^2}, h = \iint_{IC_{1i}}^{IC_{2i}} acc_V\right), \left(2\sqrt{Lh - h^2}, h = \iint_{IC_{2i}}^{IC_{1i+1}} acc_V\right)\right)$	Meters (m)
Pace	Velocity	$median\left(\frac{Step\ length_{1i}}{Step\ time_{1i}}, \frac{Step\ length_{2i}}{Step\ time_{2i}}\right)$	Meters per second (m/s)
	Cadence	$median\left(\frac{Velocity_{1i} \cdot 60}{Step\ length_{1i}}, \frac{Velocity_{2i} \cdot 60}{Step\ length_{2i}}\right)$	Steps per minute (step/min)
	Step time	$median((IC_{2i} - IC_{1i}), (IC_{1i+1} - IC_{2i}))$	Seconds (s)
Rhythm	Stance phase	$median((FC_{2i} - IC_{1i}), (FC_{1i+1} - IC_{2i}))$	Percentage (%)
	Swing phase	$median((100 - stancephase_1), (100 - stancephase_2))$	Percentage (%)
	SD step length	$SD(steplength_1, steplength_2)$	Meters (m)
Variability	SD velocity	$SD(velocity_1, velocity_2)$	Meters per second (m/s)
	SD step time	$SD(steptime_1, steptime_2)$	Seconds (s)
	AS step length	$ steplength_1 - steplength_2 $	Meters (m)
Assymetry	AS velocity	$ velocity_1 - velocity_2 $	Meters per second (m/s)
	AS step time	$ steptime_1 - steptime_2 $	Seconds (s)

1 and **2**: represent the first and second leg according to the order detected (right leg first or left leg first); **i**: instant; **L**: distance from floor to where the back IMU is placed in the user body; **h**: refers to the double integration of vertical acceleration; **acc_V**: refers to the vertical acceleration; **SD**: standard deviation; **AS**: asymmetry

3.4. CONCLUSIONS

Following an in-depth analysis of the current cueing strategies and technologies for gait rehabilitation in Parkinson's disease (PD) patients, it was found that the integration of advanced systems like the +sensBand and Xsens holds significant potential. These technologies not only provide diverse cueing modalities but also offer robust data collection and validation capabilities, which are essential for evaluating motor effects, particularly in addressing FoG and improving quality of life.

Thus, this dissertation focuses on exploring and implementing these technologies within the framework of ongoing clinical studies aimed at developing and assessing novel cueing strategies for PD. To this end, the dissertation provides a detailed overview of the system components, the control and

monitoring strategies employed, and the tools used for data processing and analysis. This work is part of the broader +sense project, contributing specifically to the advancement of gait rehabilitation techniques using state-of-the-art equipment such as the +sensBand system and the Xsens motion tracking system.

4. CROSS-SECTIONAL STUDY

To establish initial contact with end-users and compare the motor effects of closed vs. open loop somatosensory cueing in PD patients, single-session trials for improvements of an on-going clinical study were implemented. This study also aims to increase the sample number of the on-going study to reach scientific value. Therefore, more patients were evaluated using the pre-established protocol.

This study consisted of evaluating three different groups: one control group (CG) of PD patients training without cueing, using the +sensBand only for motion monitorization; one study group of PD patients training with +sensBand using the gait event-driven cueing strategy (SG1); and other of patients training with +sensBand with the continuous feedback strategy (SG2). All groups of the on-going study initially contained 10 participants, leading to a total of 30 participants overall. To accomplish a more significant sample size, 24 more patients (8 for each group: CG, SG1 and SG2) were added to the study.

Spatiotemporal parameters including step length, velocity, cadence, step time, stance phase, swing phase, gait variability (SD step length, SD velocity and SD step time) and asymmetry (AS step length, AS velocity and AS step time) were estimated based on the collected data and using the +sensBand desktop App. Clinical scales and questionnaires were also practised and collected for both results and demographics, such as MDS-UPDRS III, H&Y scale, NFOG-Q, PDQ-39 and SUS.

4.1. METHODOLOGY

4.1.1. PARTICIPANTS

A total of fifty-four PD patients (20 females and 34 males; 66.79 ± 10.67 years; 1.68 ± 0.06 m of height; 76.54 ± 14.39 Kg of weight; 6.5 ± 5.30 years diagnosed with PD; of which 19 patients were freezers) were recruited during their regular visits to the Neurology Service at the Hospital of Braga and included in this study. Table 5 presents patients' demographic data organized by the study group they were inserted in.

Table 5. Sociodemographics and clinical characteristics of study participants

Characteristics	SG1 (N=18)	SG2 (N=18)	CG (N=18)
Age [years] (mean $\pm$ SD)	65.78 $\pm$ 9.95	68.44 $\pm$ 8.49	64.83 $\pm$ 11.96
Height [cm] (mean $\pm$ SD)	164.22 $\pm$ 5.54	168.33 $\pm$ 8.07	165.22 $\pm$ 7.63
Weight [Kg] (mean $\pm$ SD)	75.61 $\pm$ 10.99	74.72 $\pm$ 17.73	73.33 $\pm$ 15.74
Gender	female	N=8	N=8
	male	N=10	N=10
H&Y (mean $\pm$ SD)	1.86 $\pm$ 0.76	1.47 $\pm$ 0.60	1.78 $\pm$ 0.81

UPDRS-III (mean±SD)	19.44±12.43	16.41±7.46	19.41±8.33
Number of freezers	5	5	9
NFOG-Q (mean±SD)	21.40±7.47	18.80±6.06	16.66±5.45
PDQ-39 (mean ± SD)	36±21	32±17	37±16

To be eligible to integrate this study, participants had to meet the following criteria: (i) diagnosed with PD; (ii) presented Hoehn & Yahr (H&Y) score lower than four, i.e. be able to walk independently or assisted by a walking aids device; and (iii) did not have cognitive impairment. Patients were evaluated by four different neurologists. The study took place at *Centro Clínico Académico* (2CA), in Hospital of Braga, and was approved by the Hospital of Braga Ethical Commission CEHB 36/2018, following the principles of the Declaration of Helsinki and the Oviedo Convention.

4.1.2. PROTOCOL

As the neurologists evaluated the patients and selected the ones that fitted the criteria, participants were randomly assigned into each group for the study, resulting in: (1) 18 participants in the control group (CG), which did not receive any sensory cueing and performed the experimental protocol while using the +sensBand only in motion monitoring mode; (2) 18 participants in study group 1 (SG1), which received gait event-driven cueing during the experimental protocol using the +sensBand; and (3) 18 participants in study group 2 (SG2), which received continuous feedback during the experimental protocol using the +sensBand. Table 6 summarizes the study groups and respective protocol characteristics.

Table 6. Summary of the study groups protocol characteristics (Number of participants, +sensBand strategy, cueing delivery configuration and data collection rate)

Group	Number of participants	+sensBand strategy	Cueing delivery	Data Collection Rate
Control Group (CG)	18	Motion monitoring	No sensory cueing	100 Hz
Study Group 1 (SG1)	18	Gait event-driven cueing	200ms vibrations at 200Hz	
Study Group 2 (SG2)	18	Continuous feedback	2s vibrotactile pulses	

After recruiting the participants and randomly assigning them to their respective groups, participants were instrumented with the +sensBand and the respective strategy was configured. Control group patients were programmed with the motion monitoring strategy collecting data at 100Hz. As for SG1 participants, the gait event-driven cueing was set at 200Hz and 200ms, while simultaneously

collecting data at 100Hz. Lastly, SG2 participants were set with the continuous feedback during 2s pulses, while also collecting data at 100Hz.

Then, participants were instructed to begin the walking trials. Each patient performed a total of 2 to 3 walking trials, to ensure data reproducibility, which consisted of walking at their normal gait, with self-selected speed, on a pre-defined course involving daily gait-related tasks that consisted of: (1) walking straight, (2) passing through a door, (3) walking straight again, (4) turning left 90 degrees, (5) turning 180 degrees left, (6) turning 90 degrees right, and (7) walking back, while passing through the door again and turning in the end 180 degrees, to reach the start position. Fig. 14 shows the schematic of the course taken during this study.

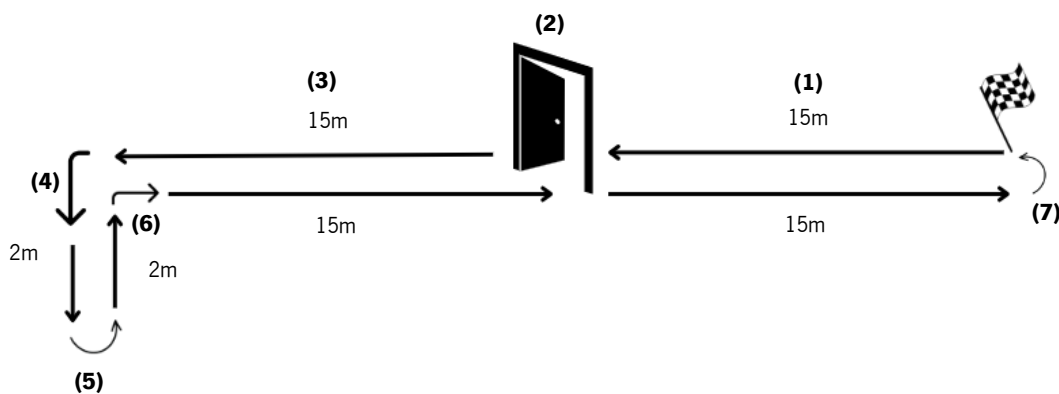


Fig. 14. Walking course schematic (cross-sectional).

4.1.3. DATA ACQUISITION

Kinematic data was collected by activating the motion monitoring strategy during the trials, while simultaneously receiving the respective cueing strategy for SG1 and SG2 patients. All trials were saved in the respective files for further processing. A total of 13099 steps were analyzed, with a mean of 102.85 ± 3.80 steps taken per trial and per patient in CG, 88.25 ± 3.32 steps for SG1, and 106.60 ± 4.77 steps for SG2.

Due to some errors during data storing, that lead to damaged files, and system failures in event detection preventing gait metric calculations, some trials had to be discarded. This resulted in a total of 51 trials analyzed for the CG, 41 trials for SG1, and 43 trials for SG2.

After completing the trials, the SUS questionnaire was also performed to be analyzed and discussed further the usability of the system. The SUS scores were obtained following the same method as in [83]. Considering that analyzing only the total usability score may lead to insufficient information since misunderstanding of certain questions can lead to poorer usability scores, it was opted to analyze also the mean and SDs of the score for each question.

4.1.4. DATA PROCESSING

The data was processed using the clinical desktop app in Matlab®2020a to estimate the gait-associated metrics across four domains: pace, rhythm, variability, and asymmetry. The pace domain variables consisted of the step length, velocity and cadence, and allowed to assess the amplitude of movement and hypokinetic character of gait. As for the rhythm domain variables assessed were the step time, stance phase and swing phase, and intend to evaluate the bradykinetic features of the gait cycle. The variability and asymmetry domains intended to measure gait deviations (standard deviations) and irregularities between the two feet (asymmetries), respectively, for metrics such as step length, velocity and step time.

Table 7 presents the pattern of these gait-associated metrics noted in PD patients, highlighting the prototypical parkinsonian gait, which is accentuated with disease severity. The application of cueing is expected to help PD patients counteract this typical motor behavior.

Table 7. Prototypical behavior of PD patients gait metrics

Domain	Variables	Prototypical behavior
Pace	Step length	↓
	Velocity	↓
	Cadence	↓
Rhythm	Step time	↑
	Stance phase	↑
	Swing phase	↓
Variability	SD Step length	↑
	SD Velocity	↑
	SD Step time	↑
Asymmetry	AS Step length	↑
	AS Velocity	↑
	AS Step time	↑

4.1.5. STATISTICAL ANALYSIS

Using the gait metrics obtained from data processing, a statistical analysis was performed in the IBM® SPSS 26.0 software for Windows. This statistical analysis aimed to (i) compare gait performance between the 3 study groups, and (ii) quantify variables of gait performance with the use of different sensory strategies.

Firstly, descriptive statistics were conducted to summarize the results and provide representative reference values, considering the means and standard deviations for each group. Simultaneously, data normalization was performed and examined using the **Kolmogorov-Smirnov test** since were analysed more than 50 samples (n=135 trials). If the significance value was lower than 0.05 (p-value<0.05), the data was considered not-normally distributed. By analyzing the resulting significances, all parameters were not normally distributed, except for the step length that was normally distributed along the 3 groups populations.

Since the majority of the **data was not normally distributed**, a non-parametric test was followed to compare these metrics of the groups. Furthermore, since this study presented 3 independent sample groups, the **Kruskal-Wallis test** was performed, considering a confidence level of 95% ($\alpha = 0.05$). As for the **step length**, since it **presented normality**, it was analysed using a **one-way ANOVA method**, using the same confidence level as the non-parametric data. The following **null hypothesis (H0)** was evaluated: **“The group distributions are the same for each group intervention”**. If the p-value was bellow 0.05, the H0 is rejected meaning that the groups presented significative differences of that variable.

Further, post-hoc tests were executed to identify and locate in between which groups were the significative differences of the variables. For the non-parametric data it was followed a **Dunn’s test**, and for the step length, it was used a **Scheffe method** after the ANOVA since the groups had different numbers of trials.

Table 8 presents a summary of the statistical analysis methods used.

Table 8. Statistical analysis methods used

Goal	Normality test	Type of data	Statistical method	Post-hoc test
Compare 3 independent sample groups	Kolmogorv-Smirnov test	Normal data	One-way ANOVA	Scheffe test
		Non-normal data	Kruskal-Wallis test	Dunn’s test

4.2. RESULTS

This section intends to analyse the results obtained from both gait metrics and SUS answers. Therefore, Table 9 presents the results for the gait metrics (mean±SD) and Table 10 the results of SUS individual questions (mean±SD).

Table 9. Gait metrics results (mean±SD) for each group, respective p-value (result of the statistical analysis), and r (result of Spearman correlation)

Domain	Gait metrics	CG Mean±SD	SG1 Mean±SD	SG2 Mean±SD	p-value	r
Pace	Step length [m] (↓)	0.570±0.013	0.593±0.021	0.678±0.033	0.003 CG vs SG2 (0.004) SG1 vs SG2(0.044)	0.228
	Velocity [m/s] (↓)	0.963±0.028	1.066±0.037	1.157±0.064	0.008 CG vs SG1 (0.034) CG vs SG2 (0.003)	0.263
	Cadence [steps/min] (↓)	102.046±2.237	110.263±3.381	105.501±4.013	0.033 CG vs SG1 (0.010)	0.093
Rhythm	Step time [s] (↑)	0.597±0.014	0.575±0.016	0.607±0.022	0.170	0.038
	Stance phase [%] (↑)	65.458±0.652	63.973±1.280	63.316±1.301	0.057	-0.150
	Swing phase [%] (↓)	34.168±0.652	35.999±1.296	37.231±1.304	0.044 CG vs SG1(0.004) CG vs SG2(0.044)	0.186
Variability	SD Step length [m] (↑)	0.200±0.020	0.218±0.019	0.320±0.036	0.011 CG vs SG2(0.004) SG1 vs SG2(0.029)	0.245
	SD Velocity [m/s] (↑)	0.333±0.025	0.367±0.026	0.486±0.050	0.008 CG vs SG2(0.002)	0.265
	SD Step time [s] (↑)	0.103±0.012	0.127±0.013	0.172±0.029	0.266	0.132
Asymmetry	AS Step length [m] (↑)	0.194±0.027	0.262±0.038	0.417±0.057	0.006 CG vs SG2(0.001)	0.278
	AS Velocity [m/s] (↑)	0.198±0.019	0.247±0.023	0.366±0.076	0.158	0.157
	AS Step time [s] (↑)	0.061±0.013	0.114±0.025	0.162±0.040	0.027 CG vs SG2(0.009)	0.229

(↑) and (↓) represents the PD prototypical increase/decrease, respectively, of the metric;

Bold highlights the metrics that improved.

Table 10. SUS results (mean±SD) for each individual question

SUS questions	Mean±SD
I think that I would like to use this system frequently.	3.77±1.20
I found the system unnecessarily complex.	1.32±0.94
I thought the system was easy to use.	4.77±0.46
I think that I would need the support of a technical person to be able to use this system.	2.00±1.23

I think the various functions of the system are very well integrated.	4.43±0.83
I thought there was too much inconsistency in this system.	1.48±0.92
I would imagine that most people would learn to use this system very quickly.	4.38±1.09
I found the system very cumbersome to use.	1.29±0.73
I felt very confident using the system.	4.34±0.76
I needed to learn a lot of things before I could get going with this system.	1.45±0.90

Likert scale: 1 – strongly disagree; 2 – disagree; 3 – indifferent; 4 – agree; 5 – strongly agree.

4.2.1. GAIT METRICS

Table 9 shows that pace was the domain that presented more significative differences. In this gait domain, step length increased the most in SG2 ($\approx 18.95\%$). Velocity only showed significant differences between the CG and each study group (SG1 or SG2), increasing with both cueing strategies in comparison to the CG ($\approx 10.70\%$ for SG1 and $\approx 20.14\%$ for SG2). No significant differences were noticed for velocity in between the two study groups (SG1 and SG2). As for cadence, only were noticed significant differences between CG and SG1, where SG1 showed a greater increase of this metric ($\approx 8.05\%$). Both study groups were able to counteract the prototypical pace behaviour of PD, improving pace metrics with cueing.

Similarly, the rhythm domain presented significant differences for the swing phase between the CG and each study group (SG1 or SG2). Both groups that used the two cueing modalities showed greater improvements of swing phase ($\approx 5.36\%$ for SG1 and $\approx 8.96\%$ for SG2), by presenting higher swing phases. No significant differences were observed for step time or stance phase. By considering the swing phase improvements, it is possible to understand that both cueing strategies were able to counteract the prototypical rhythm behaviour of PD.

As for the variability and asymmetry aspects of gait, different results were observed. For the variability domain, significant differences were noticed for SD step length and SD velocity. For both metrics it was noticed that cueing strategies worsened gait variability by following the prototypical behaviour of PD. However, in SD step length, SG1 presented significant differences when compared with SG2 indicating that gait event-driven cueing (SG1) had better results for SD step length than continuous cueing (SG2) ($\approx 46.79\%$ improvement between SG1 in comparison to SG2). No significant differences were noticed between CG and SG1. SD velocity, on the other hand, only presented significant differences between CG and SG2. Those differences resulted in worsened SD velocity for the SG2 ($\approx 45.94\%$). Similar results were noticed for AS step length and AS step time, where SG2 performed worse than CG (results worsened by almost twice the CG value). Therefore, it is possible to note that continuous cueing worsened

both variability and asymmetry aspects of gait performance. Gait event-driven cueing, when compared to the continuous cueing, provides less variability for step length during gait performance.

Overall, the CG presented less dispersion of the SD values, followed by SG1 and lastly SG2. SG2 was the group that presented higher dispersion of the SDs.

4.2.2. SYSTEM USABILITY SCALE (SUS)

Considering each patient's total SUS score, it was obtained a mean $\pm$ SD score of 86.32 $\pm$ 6.90%. This result indicates that the +sensBand was perceived with an excellent usability overall, being evaluated as an easy-to-use (4.77 $\pm$ 0.46% for question 3), cohesive (4.43 $\pm$ 0.83% for question 5), intuitive (4.38 $\pm$ 1.09 for question 7), and comfortable system (1.29 $\pm$ 0.73 for question 8). Overall, patients also felt safer and more confident about their gait performance when using the system (4.34 $\pm$ 0.76% for question 9).

However, some more neutral scores were noticed when answering the first question about if patients would like to use the system frequently (3.77 $\pm$ 1.20%). A good part of the patients was still capable of walking autonomously, without any major gait changes, therefore when asked this question, did not feel the need to use a system daily to improve their gait. Some comments were also noted regarding the design of the device not being the most appealing for day-to-day use, especially to use in public. The weight of the system was also commented about to be further improved, since it may not be the most comfortable for daily usage. On another hand, some patients also noted that although at first impact feeling a bit intimidated by the bulky design, they quickly adapted to it and accepted it. During the trials, it was not reported any discomfort while using the device.

4.3. DISCUSSION

Considering the prototypical motor behaviour of PD, this section intends to analyze and discuss the gait metrics results to understand if PD patients improved or not their gait performance. It is important to compare also both cued groups' results to provide insights about which of the two cueing methods may be more beneficial for PD patients' motor rehabilitation, and therefore achieve the main goal of this study.

The results obtained showed that overall, both cueing strategies were able to improve patients' gait performance by targeting the pace and rhythm aspects of gait, therefore mitigating the hypokinetic and bradykinetic gait patterns of PD. When comparing both cued groups with the control group it was possible to note improvements of step length ($\approx$ 18.95% for the SG2), velocity ($\approx$ 10.7% for the SG1 and

≈20.14% for the SG2), cadence (≈8.05% for the SG1), and swing time (≈5.36% for the SG1 and ≈8.96% for the SG2). Although both gait event-driven (SG1) and continuous (SG2) vibrotactile cueing presented improvements for both pace and rhythm, continuous feedback provided greater improvements overall (≈19.54% in mean for pace and ≈8.96% for rhythm) than gait event-driven cueing (≈9.38% in mean for pace and ≈5.36% for rhythm), that only showed greater improvements for cadence.

However, when comparing directly SG1 and SG2 results, mixed conclusions were taken depending on the metrics being analyzed. Only step length and SD step length metrics presented significant differences between the two study groups (SG1 and SG2), corresponding to two different aspects of gait (pace and variability, respectively). For step length, the group with continuous feedback (SG2) had greater improvements than the one receiving gait event-driven cueing (SG1). On the other hand, when considering the SD step length, gait event-driven cueing showed improvements when compared to the group receiving continuous feedback. Moreover, the SG2 group when compared to the CG group did not present any improvements of gait variability and asymmetry metrics, instead it was noticed an increase, therefore worsen, of SD step length (≈60%), SD velocity (≈45.94%), AS step length (≈114.95%) and AS step time (≈165.57%) with the use of open loop vibration.

Considering these results, it was hypothesized that continuous feedback, by delivering the vibrations at 2s pulses similarly to a metronome, caused more abrupt improvements in pace and rhythm than closed-loop vibration and also higher dispersion of SDs. Although SG2 presenting higher velocity and step length than the other groups, the resultant cadence is lower than the SG1. SG2 patients took approximately 3.41 steps per each 2s passed, meaning that completed approximately one gait cycle of one foot (from IC to the next IC of the same foot) during each 2s receiving the vibrations. This suggests that patients may unintentionally followed the rhythm of the vibrations and tried to fill the pulse duration by taking less steps but longer and slightly quicker. However, since these are more abrupt changes of pace than the changes noticed in the SG1, it caused higher instability of gait translated by worsened variability and asymmetry. Gait event-driven cueing, on the other hand, by providing the vibrations at a rhythm personalized to the patient's own pace, it consists of a more subtle strategy. Therefore, more subtle changes of the gait pattern were noticed, but less gait variability is noticed since patients perform an improved version of their own gait instead of forcing their gait to match the cues.

This highlights the potential of gait event-driven cueing which should not be discarded since it causes great improvements of pace and rhythm still and may surge as a better choice of strategy in preserving patients' gait variability. Also, since the study groups consisted in three independent populations the results may be affected by patients different clinical characteristics such as H&Y stage

and UPDRS III that was more advanced in SG1 when compared to both CG and SG2 (SG1 showed mean and SD of H&Y of 1.86 ± 0.76 points, indicating unilateral and axial towards bilateral involvement, and UPDRS III score of 19.44 ± 12.43 points, corresponding to a mild mobility stage). Also, although the CG group has more PD patients with FoG (9 freezers) than SG1 and SG2 (5 freezers each), the SG1 freezers showed higher scores of the NFOG-Q (21.40 ± 7.47). These clinical characteristics may indicate that patients receiving the gait event-driven cueing presented more advanced stages of the disease, therefore presenting worse mobility and gait patterns. Ultimately, patient variability may have affected the results of the study, and providing a cross-over analysis following the protocol in the future should be considered to improve the study conclusions.

Lastly, the SUS results of the usability aspects of the device have shown that overall, the +sensBand system was evaluated with an excellent usability score, being acceptable for further implementation in longer trials. However, in the future, the design should be improved to become more appealing for daily usage and less heavy to improve comfort for more extended periods of use.

4.4. CONCLUSIONS

Both open and closed-loop cueing strategies, as expected, improve gait performance by mitigating the hypokinetic and bradykinetic aspects of gait. Although overall continuous feedback causing greater improvements of pace and rhythm than gait event-driven cueing, it increased gait variability and asymmetry. Considering the different advantages of both cueing strategies, they both have great acceptability and potential for motor rehabilitation of PD patients, moreover if explored in a combined new strategy.

5. USABILITY STUDY

This study serves to introduce the FoG prevention cueing, with healthy participants for a primary validation of the usability and workload of this novel strategy, while simultaneously using the +sensBand device in different environments, to evaluate also the potentiality of being further used as a daily solution.

Therefore, the primary objective of this study is to validate the usability and workload of this new cueing strategy in healthy participants as a preliminary step before testing in the PD population. By evaluating the system's impact on gait temporal metrics and usability through the System Usability Scale, this research aims to ensure the device's effectiveness and comfort in daily use. Positive findings in this initial phase will pave the way for further trials focused on PD patients, ultimately aiming to improve their mobility and overall quality of life.

5.1. METHODOLOGY

5.1.1. PARTICIPANTS

A total of fifteen healthy participants (5 males and 10 females; 30.47 ± 14.09 years; higher education level; daily use of technologies) were included in this study. To be eligible to integrate this study, participants had to meet the following criteria: (i) not present any neurodegenerative disorders and gait impairments; (ii) be able to walk independently without any assistance; and (iii) sign informed consent to participate in the study. The study was approved by the ethical Ethics Committee CEICVS 006/2020, according to the Declaration of Helsinki and Oviedo Convention.

5.1.2. PROTOCOL

After instrumenting participants with the +sensBand waistband (Fig. 15 a)) and configuring the FoG prevention feedback strategy, a first calibration trial was executed, instructing them to take one step forward to adjust the +sensBand lasers to match the user's self-selected step length. After calibrating the lasers, three walking trials were performed, in one of three possible paths (in work or home-based scenarios). Fig. 15 b) shows the different environments used.



a) Instrumented subject

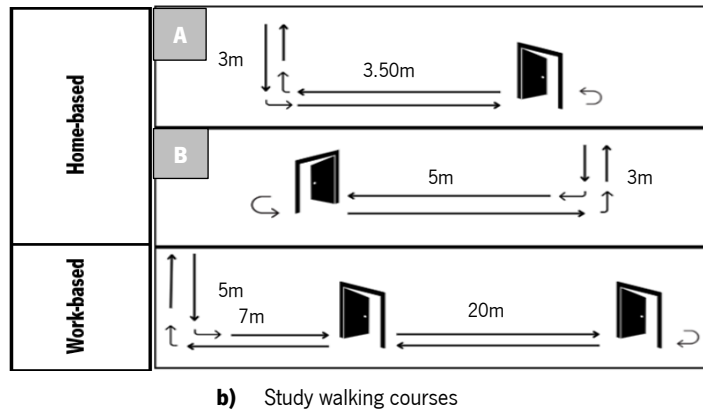


Fig. 15. FoG prevention feedback usability study test (a)) and courses (b)).

The work-based environment was a longer walking path (total of 64m) performed on a hallway of University of Minho, at Azurém Campus, and only 3 participants were selected for this scenario due to their availability to travel to the site and familiarization with the course. As for the home-based scenarios (A and B), they took place in two different houses, common to the participants. Considering space limitations of the different housings, shorter walking courses were considered (A: total of 13m; B: total of 16m). The purpose of at home trials was to assess participants in a secure and familiar setting, common to their daily routine, while using the device. By these means, participants were allocated to each course considering their day-to-day familiarization with environments A or B.

At the start of each trial, participants were instructed to stand in place for 20s, while receiving the open-loop vibrations and fixed laser lines. After those 20s, participants started walking and the vibrotactile mode changed to closed loop after detecting the first right foot TO. During the walking path, participants turned 90 degrees, passed through at least one door, turned 180 degrees and walked back to the start position. During each trial the researchers accompanied the participants to confirm that the +sensBand was providing the cues correctly.

5.1.3. DATA ACQUISITION

Each participant's demographic information was collected considering age, gender, education level, and technology usage.

To assess system's usability and workload, the System Usability Scale (SUS) and NASA Task Load Index (TLX) questionnaires were answered anonymously to reduce risk of bias. SUS questionnaire allowed to evaluate user experience aspects such as willingness to use the system often, complexity, ease of use, consistency, comfort and convenience. As for the NASA TLX questionnaire, three types of demands were evaluated (mental, physical, and temporal), but also performance, effort, and frustration felt. The

statements from the SUS and NASA TLX questionnaires were rated using a Likert scale, ranging from 1 (Strongly disagree) to 5 (Strongly agree) and 1 (Low) to 21 (High), respectively. Resulting SUS scores ranged from 0 to 100, allowing to be categorized as awful, poor, reasonable, good, or excellent for scores lower than 51, from 51 to 68, equal to 68, from 68 to 80.3, or greater than 80.3, respectively. Similarly, NASA TLX resulting scores ranged also from 0 to 100, categorizing workload as very high, high, somewhat high, medium, or light for scores higher than 80, from 50 to 80, from 30 to 50, from 10 to 30, or lower than 10, respectively.

5.1.4. DATA PROCESSING

Gait metrics were also assessed by the +sensBand during each trial, by activating the motion monitoring option while performing the FoG prevention feedback. The data files obtained were then processed using the desktop clinical App, to obtain the following temporal gait metrics: stride, step, stance, and swing times, and cadence.

Transitions from HS to FF, and from FF to TO were identified and stored in lists to detect Initial Contacts (IC) and Final Contacts (FC) during gait. Those lists were then used to calculate each temporal parameter as follows: step time and stride time were calculated as the temporal distance from IC of one foot to the following, and one IC to the next of the same foot, respectively; stance time was calculated as the temporal distance from IC to FC of the same foot; swing time was calculated as the difference between stride and stance time (respective phases were obtained by converting those times in percentages); and cadence was calculated by counting the number of steps, corresponding to the length of the list of IC, and dividing it by the gait duration, therefore time distance between first and last IC. The mean temporal gait metrics were calculated for each participant considering the gait cycles performed during the protocol. Finally, mean and standard deviation of the temporal gait metrics obtained from all participants were presented for the results section.

5.2. RESULTS

Table 11 presents both demographics and results obtained for each participant based on the questionnaire answers evaluating the usability and workload of the FoG prevention feedback using the +sensBand. Furthermore, mean and standard deviations (mean $\pm$ SD) of both SUS and NASA TLX scales are presented. Table 12 then presents the mean results of participants' temporal gait metrics.

Table 11. Healthy participants' age, gender (F – female; M – male), Education level, Technology usage, Walking course path (A – Home-based path A; B – Home-based path B; W – Work-based), SUS and NASA TLX scores, and corresponding qualitative levels (colored through green to red from better through worst usability, respectively)

ID	Age (years)	Gender	Walking path	SUS (score, level)		NASA TLX (score, level)	
P1	19	F	B	82.50	Excellent	18	Medium
P2		M	B	80	Good	11	Medium
P3			W	90	Excellent	9	Light
P4	22	F	A	75	Good	30	Somewhat high
P5			A	100	Excellent	18	Medium
P6			A	92.50	Excellent	11	Medium
P7	24	F	A	90	Excellent	15	Medium
P8	25	F	A	82.50	Excellent	15	Medium
P9	27	F	W	92.50	Excellent	21	Medium
P10		F	W	52.50	Poor	19	Medium
P11		M	B	77.50	Good	37	Somewhat high
P12	30	M	B	72.50	Good	21	Medium
P13	55	M	B	82.50	Excellent	8	Light
P14	57	F	B	97.50	Excellent	10	Medium
P15	59	M	B	77.50	Good	29	Medium
(mean±SD)	30.47±14.09	F	B	83±14.08	Excellent	18.1±9.36	Medium

Table 12. Healthy participants' mean step, stride, stance and swing times, stance and swing phases, and cadence, and respective total means and standard deviations

ID	Step time (s)	Stride time (s)	Stance time (s)	Stance phase (%)	Swing time (s)	Swing phase (%)	Cadence (steps/min)
P1	0.69	1.37	0.91	66.20	0.46	33.80	87.20
P2	0.68	1.34	0.91	68.20	0.43	31.80	88.24
P3	0.80	1.41	1.02	72.24	0.39	27.75	74.69
P4	0.63	1.25	0.77	61.66	0.48	38.33	95.15
P5	4.11	6.29	4.68	74.40	1.61	25.60	14.58

P6	1.10	1.95	1.44	73.46	0.52	26.54	56.31
P7	2.58	3.92	2.78	71.59	1.15	28.41	29.35
P8	1.14	1.94	1.29	66.52	0.65	33.48	54.27
P9	0.59	1.11	0.82	73.78	0.29	26.22	102.41
P10	1.05	2.06	1.33	64.40	0.74	35.60	56.85
P11	0.89	1.63	1.11	67.98	0.52	32.02	70.34
P12	1.78	3.16	2.24	70.60	0.92	29.40	33.61
P13	1.23	2.13	1.47	69.83	0.66	30.17	49.99
P14	2.48	4.63	2.83	61.72	1.80	38.28	25.19
P15	2.75	4.62	2.95	64.72	1.67	35.28	25.41
(mean±SD)	1.50±0.99	2.59±1.52	1.77±1.07	68.49±4.09	0.82±0.49	31.51±4.09	57.57±27.17

5.2.1. SYSTEM USABILITY SCALE (SUS)

SUS scores were predominantly excellent, with nine participants (8 females and 1 male) scoring between 82.50 and 100, aged 19-57 years, and predominantly training in home-based scenarios. Five participants (1 female and 4 males) scored good usability (72.50-80), with ages ranging from 19 to 59 years, and training mainly in home-based walking path B. Ultimately, one participant (female) scored poor usability (52.50), with 27 years and walking in work-based walking path. Overall, the results obtained were positive, considering an excellent average score (83 ± 14.08).

5.2.2. TASK LOAD INDEX (NASA TLX)

Only two participants (1 female and 1 male) scored the lowest workload level (light), ranging from 8 to 9, aged 22 and 55, and executing work and home-based B walking paths, respectively. Medium workload was the predominant score level, with eleven participants (8 females and 3 males) scoring between 10 and 29, aged 19-59 years, and predominantly training in both home-based courses. Two participants (1 female and 1 male) presented fewer positive results, scoring somewhat high (30 and 37), with ages 22 and 27 years, and training in home-based paths A and B, respectively. Although not reaching the best workload score level, the mental demand was still positive, with an overall medium average level (18.10 ± 9.36).

5.2.3. TEMPORAL GAIT METRICS

By processing the data metrics obtained, it was possible to calculate the mean and standard deviations considering all participants for step time ($1.50s \pm 0.99s$), stride time ($2.59s \pm 1.52s$), stance time ($1.77s \pm 1.07s$), swing time ($0.82s \pm 0.49s$) and cadence ($57.57\text{steps/min} \pm 27.17\text{steps/min}$).

Although not reaching the ideal stance and swing phases (60% and 40%, respectively) the means obtained were approximate of the expected resulting in $68.49\% \pm 4.09\%$ and $31.51\% \pm 4.09\%$, respectively [23].

5.3. DISCUSSION

Regarding usability, participants generally evaluated the cueing strategy and +sensBand with an excellent SUS score, therefore considering it as highly usable [20]. Ultimately, the system was well-received, considering it intuitive to use and user-friendly among the participants. However, it was reported one poor level of SUS score.

Although answering anonymously, most of the participants answered the questionnaires in the presence of the researchers so that they could be able to clarify any doubts that may arise. However, some participants couldn't answer right after the trials the questionnaires, answering further an online version without the researcher's presence. Ultimately, those cases reported difficulty in interpreting the questionnaire. Questions evaluating the necessity/likability of including this device in their daily routines were answered negatively in this case due to the participant focusing on their lack of need for the device rather than its usability. Also, questions about the performance and technological integration aspects of the device were not answered correctly, since some patients opted to give a neutral score since they didn't intend to comment on those aspects. All these misinterpretation errors ultimately may have affected the final score. In the future, clearer instructions should be considered to clarify the scales, as long as prioritizing answering the questionnaire immediately after the motor performance, with the researchers still present.

As for workload perception including both physical and mental demands, analysis of NASA TLX scores revealed varying levels of workload experienced by participants during the task. While most reported a medium workload level, some experienced lighter or somewhat higher demands. It is important to note that one participant, during the walking course reported that the laser projected lines, since were advancing as the participant also progressed, made the participant frustrated during the first trial trying to always step over them. This may have translated into a high score of workload perceived by this participant. However, the rest of the participants did not report any type of frustration and considered the laser lines an intuitive cueing modality, even more than the vibrations. When comparing home with work-based walking paths, the results of perceived workload tend to be positive in both environments. Home-based environments may present low mental demand due to familiarity and comfort. However, the two

worst scores for workload were both experienced in this scenario. This can potentially be explained by some of the participants who did not use the defined home-based walking path in a daily basis.

Demographic parameters such as age, gender, and activity level may also have affected perceived usability and workload. Since PD is mostly common in adults above 50 years of age, the usability and mental demand perceived by this age range adults may be a greater indicator. By analyzing the results for the group of healthy participants in this age range, it was possible to observe that were very positive, indicating the ease of use and intuitiveness that may promote user acceptance.

Upon analyzing the temporal data obtained, slower gait metrics appeared for some participants in comparison with literature (normal cadence ranging from 96 to 129 steps/min; stride, stance and swing time with mean and standard deviation of $1.20s \pm 0.11s$, $0.77s \pm 0.07s$ and $0.43s \pm 0.04s$, respectively, for young active women walking at low speed). Since participants were walking using an unfamiliar device, instructed that would be receiving cues and to use them the most convenient way possible, some participants opted to perform a slower gait, justifying these results. Also, the variability of participants characteristics may also contributed for these differences. However, the overall gait performance of each participant regarding temporal metrics was not compromised by using the device. Literature suggests that cueing, although not providing significant differences in healthy controls, may improve greatly these parameters in PD patients, leading to more stable gait and reducing the incidence of FoG episodes. Therefore, the results obtained prove the promising potential for the FoG prevention cueing in improving gait in PD patients. Participants in home-based courses also showed slower temporal metrics compared to those on the work-related courses, possibly due to the work-course, by being longer, allowing better performance of the +sensBand real-time gait-event detection algorithm. Therefore, the protocol to apply the strategy in PD patients should be adapted to allow longer use of the device during each trial, and to better simulate daily walking conditions. Overall, the study results allowed to validate the FoG prevention cueing strategy and supported further research to evaluate the effectiveness and feasibility of the strategy in preventing FoG episodes and improving QoL, directly with the end-users.

5.4. CONCLUSIONS

In conclusion, the study highlighted the potential of combining both visual and somatosensory cueing modalities, at open and closed-loop, in the developed FoG prevention cueing strategy for gait support without causing overstimulation of the users (excellent usability and medium workload). These

results were verified for both professional and home-based scenarios of daily living, therefore highlighting also the potential of this +sensBand strategy for daily usage.

Moreover, the gait temporal performance seemed not compromised by the use of the device in healthy participants. By these means, these findings provided sufficient insights to validate the strategy and test the effectiveness long-term in mitigating FoG directly with PD patients, as the next step.

6. LONGITUDINAL STUDY

To test the effectiveness of the FoG prevention cueing strategy directly with the end-users in mitigating FoG and assess the long-term use impact on patients' QoL and PD motor symptoms, a longitudinal study was followed.

By considering the SoA conclusions as well as other logistics, it was considered a protocol of 12 sessions of training, aimed to be accomplished with 2 to 3 sessions a week. To monitor and evaluate patients' overall performance before and after receiving cues, 3 main evaluation time points were considered: a pre-training assessment, a post-training assessment, and a follow-up assessment. Additionally, a mid-training assessment was also considered for a more detailed understanding of the intermediate effects of the cued training.

A total of 2 PD patients, with FoG, completed this study. Considering the main goals of the study, FoG was monitored during the sessions but also in between sessions, clinical scales were performed (NFOG-Q, H&Y, UPDRS III and PDQ-39), as well as training questionnaires (NASA TLX, cue perception Questionnaire, SUS). Gait metrics of each gait aspect (pace, rhythm, variability and asymmetry) were also monitored at each evaluation time point, for further details of long-term cued training motor effects in PD patients.

The following chapter presents the detailed methodology considered, as long as the obtained results and conclusions acquired.

6.1. METHODOLOGY

6.1.1. PARTICIPANTS

A total of two PD patients with FoG (2 females; both with 57 years; and with daily use of technologies) were included in this study. Participant P1 along with Parkinson medication reported taking also antidepressants. As for patient P2, along with the medication also reported performing surgery to implant DBS electrodes in February, and after the fourth session started testing new DBS modes. Both patients off-sessions performed physical therapies, such as pilates, 1 to 2 times per week, and patient P1 also performed speech therapy 1 time per week. Table 13 presents the characteristics of each participant (P1 and P2). Patients were assessed at the end of the ON-medication phase.

Table 13. Patients' individual characteristics

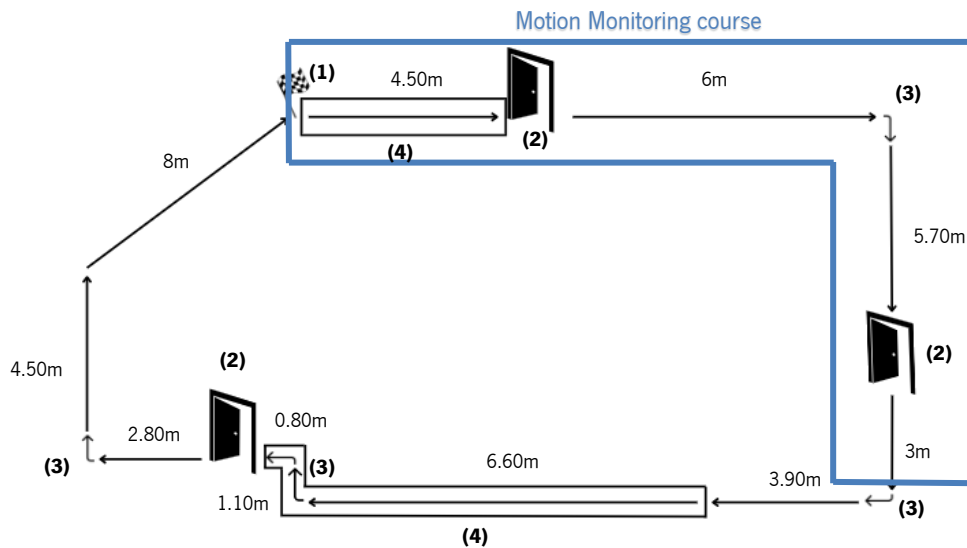
Characteristics	P1	P2
Gender	F	

Age (years)	57	
Height (m)	1.60	1.70
Weight (Kg)	90	76
Disease duration (years)	12	7
Education level	Basic	Higher
Use of technologies	Daily	

To be eligible to integrate this study, participants had to meet the following criteria: (i) diagnosed with PD; (ii) presence of FoG, assessed through NFOG-Q; (iii) not present any other neurodegenerative disorders or gait impairments; (iv) be able to walk independently without any assistance; and (v) availability to go to *Campus Neurológico Sénior (CNS)*, Braga, 2 to 3 times a week until completing the study protocol. The study was approved by the ethical Ethics Committee CES CNS 04_2024, according to the Declaration of Helsinki and Oviedo Convention.

6.1.2. PROTOCOL

As mentioned before, this clinical study took place at *CNS*, in Braga. The available space in the clinic allowed to create a continuous circular circuit, for walking in loop, that included several day-to-day FoG inducing tasks such as: (1) initiating gait; (2) passing through doorways; (3) turning; and (4) walking through narrow hallways. Fig. 16 shows the walking circuit representation, along with the respective measurements.



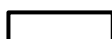
 : narrow aisles.

Fig. 16. Walking paths schematic (full course for training sessions and motion monitoring course for gait assessments).

After recruiting the patients eligible for the study, the protocol was assessed considering four major phases: the **pre-training phase**, using the Xsens and +sensBand but only for motion monitoring; the **training phase**, using the +sensBand FoG prevention strategy; the **post-training phase**, and the **follow-up phase**, only using the +sensBand for motion monitoring.

The **pre-training phase** occurred before the first training session and consisted of a first clinical and motion monitoring assessment, to evaluate clinical scales (NFOG-Q, PDQ-39, MDS-UPDRS III and H&Y) and gait performance at baseline, i.e. before receiving the cued training sessions. Gait assessment was performed using the +sensBand motion monitoring mode and simultaneously the Xsens Awinda on the lower limbs. After instrumenting patients with both systems, 3 trials were performed. Considering Xsens Awinda 10m range limitation, a shorter walking course was considered for motion monitoring (Fig. 16 blue segmented course). Each trial started and ended by instructing participants to lean forward and returning upright to trigger the synchronization of data from both systems.

After completing the pre-training session, participants started the **training phase**. Training phase comprised of a 12-session program, conducted 2-3 times per week according to patients' availability until reaching the total of the sessions. Each session included a total of 4 trials lasting 6 minutes each, where patients walked the course in a loop while receiving the FoG prevention cueing until the time was up (Fig. 16 complete course). Before each trial started, participants were asked to take one step forward, to adjust the lasers to the participants' step length. Then, the trials started by instructing the patients to stand still for 20s while receiving the open-loop vibration portion of the strategy. After 20s had passed, patients initiate gait at their normal pace while receiving the cueing strategy. During the first lap of the circuit, patients were instructed to perform the full lap while looking at the lasers, however after completing the first lap patients could use the cues as intuitively to them as possible, only if starting to freeze they were instructed to use the laser lines and try to step over them.

In between each trials patients had rest intervals, and during the trials could also rest at any point if needed. **Mid-training** (after the 6th session and before the 7th), patients underwent another monitoring session but without using the Xsens, only used the +sensBand in the motion monitoring mode (without receiving any cueing strategy) while following the same guidelines as the pre-training data collection. In each training session, participants answered the NASA TLX questionnaire; assessed their perception of the cues by answering from 1 to 5 how the vibrations were perceived during open-loop phase, and closed-loop phase, how visible was the laser during the first lap and with what frequency they

used the laser during the rest of the trial; report the frequency and duration of FoG episodes using the NFOG-Q; and the last time patients took medication.

After the final training session (12th session), patients also completed the SUS questionnaire and followed the **post-training phase**. This phase, similarly, to the **mid-training phase**, consisted on a single session of clinical and gait assessment following the same guidelines as previously.

Lastly, patients rested for a week, without receiving the cueing strategy. Afterwards, a **follow-up phase** followed, comprising a final follow-up clinical and gait assessment (same guidelines as the mid-training and post-training) to understand if the cueing effects were maintained.

Fig. 17 showcases a schematic of the protocol phases, and respective monitoring time-points (T1 to T4).

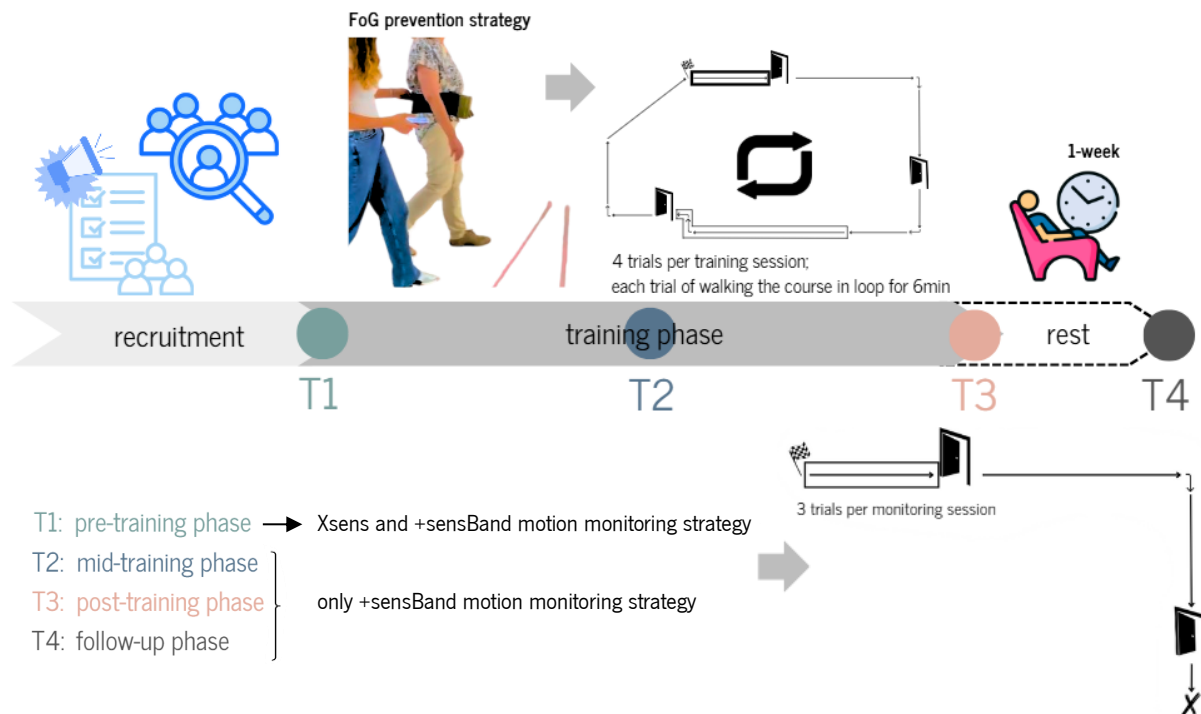


Fig. 17. Schematic of protocol summary, representing the phases and monitoring time-points.

6.1.3. DATA ACQUISITION

During the protocol execution, different types of data were collected such as **(i) FoG data, (ii) clinical data, (iii) training questionnaires data, and (iv) gait metrics.**

Since reducing FoG with the use of the +sensBand FoG prevention cueing strategy was the main goal of this study, FoG data was collected in several forms. In each session, patients' perception of the number of FoG occurrences in between sessions, i.e. FoG episodes occurring during their daily routine after the last session of training and before the next session, was collected as well as their perception of FoG episodes duration. During the trials, FoG episodes observed were also counted and noted. Any FoG

episodes occurring off the trials but during the sessions, i.e. during rest intervals or other moments, were not counted as FoG observations since were not present when using the strategy but were noted about the tasks done when occurring. During the evaluation time points established in the protocol, NFOG-Q answers were also collected to provide a clinical evaluation of FoG evolution before and after intervention, and if the results were maintained after a week (follow-up).

Clinical data was collected, evaluating H&Y, MDS-UPDRS III and PDQ-39 clinical scales at specific time points of the protocol (pre-training, post-training and follow-up), before the motion monitoring trials during each protocol time-point, to evaluate PD clinical evolution before and after receiving cues.

Similarly, some questionnaires were answered to evaluate different parameters of the cueing strategy used along the sessions. NASA TLX answers were collected at the end of each training session, to evaluate cognitive and physical demand of the strategy, as well as answering a personalized questionnaire about patients' perception of the different cues received during the trials, to evaluate how the cueing strategies were being used along the training sessions. The personalized questionnaire contained four questions, answered on a range from 1 to 5, as shown in Appendix B. At the end of the training protocol (after completing the session 12 cued training trials) patients answers of the SUS were also collected to provide end-users evaluation of the usability of the cueing strategy after long-term usage.

During pre-training, both Xsens and +sensBand allowed to acquire, at 100Hz, and collect acceleration, angular velocity and gait events data. The +sensBand also allowed to collect these metrics in the middle of training (session 6 or 7), at post-training and follow-up. These two systems were used at pre-training to compare both metrics obtained at baseline and therefore more thoroughly validate the +sensBand system performance for gait event detection. The +sensBand system was also used during the different time points to understand patients' gait performance evolution before and after using the cueing strategy.

6.1.4. DATA PROCESSING

Due to the reduced number of patients, for a better understanding of the results data processing consisted in performing descriptive analysis with the acquired data with the results varying along the respective protocol timeline. At first, it was important to analyze patients calendarized sessions and transform that calendar in a timeline.

Considering patients' availability and different starts of the protocol, the 12 sessions of training were spaced differently for each patient. Since the pre-training and the first session, which occurred on the same day, were the reference sessions starting at day 0, each session that followed was marked on a timeline by considering the number of days that passed since this reference. Ultimately, two protocol

timelines were obtained, a timeline ranging from 0 to 54 days for patient P1, and another ranging from 0 to 46 days for patient P2.

Overall, the protocol for patient P1 took 54 days to complete, where training took 47 days, and for patient P2 took 46 days to complete, where training took 39 days.

According to each type of acquired data and respective time points for data acquisition, the timeline of the respective graphic varied according to the sessions in between which the data were collected. This means that, data that was collected continuously along each session, such as number of FoG episodes perceived in-between sessions and number of FoG episodes observed in each session during trials, was graphically presented showing the results along each session of the full protocol (from pre-training to follow-up). Data that instead of being collected at each session was collected only at the protocol evaluation time points (pre-training, mid-training, post-training and follow-up), such as +sensBand motion monitoring resulting gait metrics, Xsens gait metrics, NFOG-Q results, MDS-UPDRS III results and PDQ-39 results, was graphically presented showing each result along the respective evaluation timepoint session. Lastly, data evaluated during the training sessions (+sensBand gait metrics acquired while receiving cues, NASA TLX results, and cue perception questionnaire results) was displayed graphically along a timeline ranging from the first training session to the last (session after pre-training to session before post-training).

It is important to note that H&Y, since it is a more specific scale designed to assess the overall stage of PD progression, was only evaluated before and after receiving the cued training (pre-training, post-training, and follow-up). This decision was made as the scale is not as sensitive to short-term changes throughout the intervention, unlike the other metrics. Therefore, given its relatively stable nature over time, the H&Y results were better suited to be displayed in a table format.

SUS results were also opted to be displayed in table format since were only assessed once, after completing the training sessions and therefore were not evaluated along a timeline.

Lastly, the +sensBand gait data was processed, similarly to **Chapters 4** and **5**, to obtain the following gait metrics: step length, velocity and cadence, for the pace domain; step time, stance phase and swing phase, for the rhythm domain; SD of step time, velocity and step time, for the variability domain; and AS of step time, velocity and step time, for the asymmetry domain of gait.

The Xsens data had to be imported from MVN, selecting acceleration, angular velocity but also foot contact to serve as ground truth for the gait event detection. Then the files had to be converted to *mat* type files, to be able to be read in Matlab. Lastly, using the Clinical Desktop App the Xsens foot contact data was processed obtaining the same gait metrics as the +sensBand gait data. Since it was

assessed three trials in each timepoint, it was calculated at each evaluation time points the mean and SD of the trials for each patient +sensBand resulting gait metrics. Similarly, at pre-training the mean and SD of the trials for each patient were calculated for both +sensBand and Xsens gait metrics. The +sensBand results, since are important to be analyzed along the different assessment moments, were then displayed graphically along the evaluation timepoints timeline.

6.2. RESULTS

For better comprehension of the results, this section is segmented in four subsections according to the different types of data acquired: **(i) FoG results**, where observed episodes during trials, perceived episodes in between sessions, episodes duration evolution along the protocol timeline and NFOG-Q results were considered; **(ii) clinical scales results**, including H&Y, UPDRS III and PDQ-39, evaluated only at protocol time-points; **(iii) training questionnaires results**, including questionnaires done continuously in each training session, such as NASA TLX and a custom-made perceived cues questionnaire, but also at the end of training such as SUS questionnaire; and **(iv) gait metrics results**, analyzing both Xsens and +sensBand gait collected data during the evaluation time-points but also continuously along the training sessions.

6.2.1. FOG

Fig. 18, Fig. 19 and Fig. 20 present the graphics obtained for the FoG results.

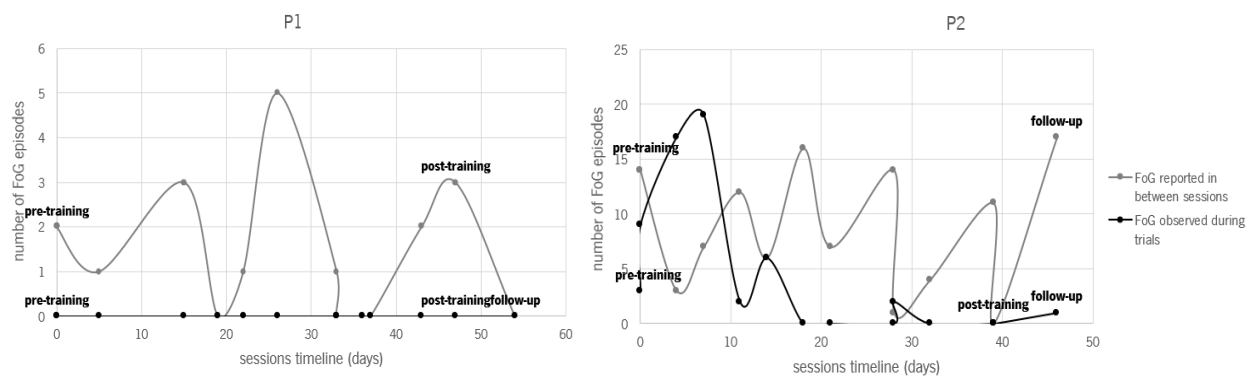


Fig. 18. Graphics of FoG perception in between sessions vs. FoG occurrences during trials, for patients P1 and P2.

When analysing the results of patients' perceived FoG in between sessions vs. FoG occurrences during trials (Fig. 18), it is noticeable that, for both patients, the perceived curve (black line points) tends to have unpredictable behaviour, but the observational curve (red line points) tends to decrease.

Patient P1 did not freeze during any trial along the protocol timeline. As for FoG episodes reported in between sessions, patient P1 perceived a maximum of 5 episodes in between sessions 5 and 6, that took place 4 days apart. When analysing only the evaluation time points, from pre-training to post-training the number of FoG episodes perceived increased ($\approx 50\%$), and from post-training to follow-up assessment the number of FoG episodes perceived improved greatly by decreasing to 0 episodes occurring in between post-training and follow-up assessments.

Patient P2 presented more cohesive observational results being noticeable a decrease of FoG during trials along the three main evaluation time points ($\approx 100\%$ in between pre-training and post-training, and $\approx 66.67\%$ in between pre-training and follow-up). From post-training to follow-up, however, it was observed an increase ($\approx 33.33\%$) of the number of FoG episodes occurring after 7 days without receiving cues.

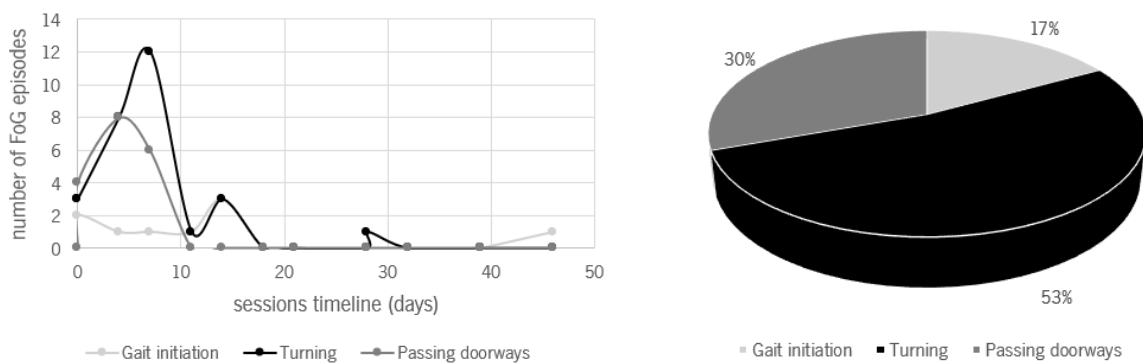


Fig. 19. Graphics of gait task responsible for FoG (Gait initiation, Turning, or Passing through doorways) along the sessions timeline and respective total percentage, both for patient P2.

It is important, to analyse also which tasks lead to freezing (Fig. 19). In pre-training the main FoG-inducing task was turning during the walking course ($\approx 100\%$ of FoG at session 0). Overall, counting all sessions, turning was the main FoG-inducing task ($\approx 53\%$ of all FoG episodes), followed by passing through doorways ($\approx 30\%$ of all FoG episodes), and lastly gait initiation ($\approx 17\%$ of all FoG episodes). However, at follow-up, the only FoG episode noticed occurred during gait initiation at the start of the first monitoring trial. The maximum number of FoG episodes observed during trials occurred in session 3, consisting of a total of 19 FoG episodes ($\approx 5.26\%$ during gait initiation, $\approx 63.16\%$ during turning, and $\approx 31.58\%$ while passing through doors). As for P2 perception of FoG in-between sessions, the maximum number of FoG episodes reported were 17 episodes at follow-up, after 7 days without receiving cueing. However, as far as considering the ratio between number of episodes reported and number of days passed, the maximum number of episodes between sessions was reported in between session 5 and 6 (≈ 4 ratio), reporting 16 FoG episodes along 4 days without cueing.

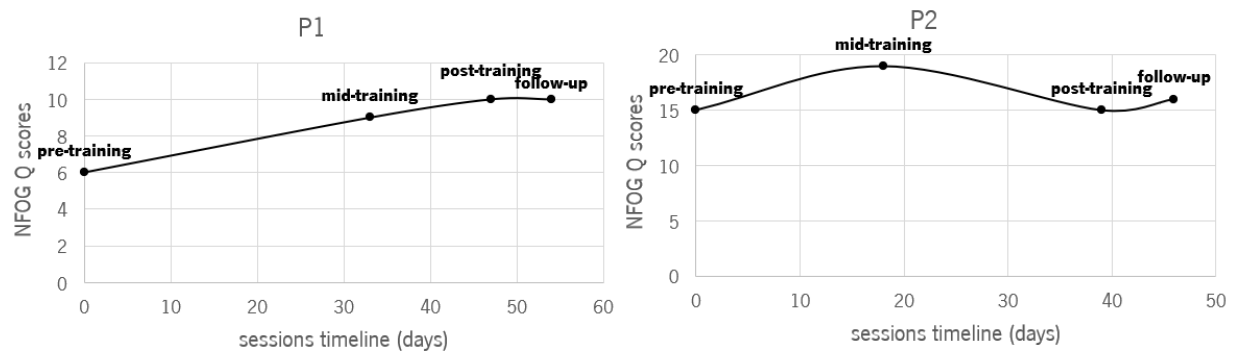


Fig. 20. Graphics of NFOG-Q scores along each time-point evaluation, for patients P1 and P2.

When analysing the NFOG-Q answers along the protocol time-points (Fig. 20), overall patient P2 reported higher scores than patient P1. Patient P1 along the protocol time points presented increasingly worse results of NFOG-Q, presenting a maximum score of 10 points at both post-training and follow-up. As for patient P2, the results varied along the time points, being noticed worst score results at mid-training, with 19 points. At both pre-training and post-training P2 obtained the same minimum NFOG-Q score of 15 points, however at follow-up the score increased by one point.

6.2.2. CLINICAL SCALES

Table 14, Fig. 21 and Fig. 22, show the table and graphics obtained for clinical scales results.

Table 14. H&Y score evolution before and after using the FoG prevention cueing, for patients P1 and P2

Stage	Description	Impairment	Pre-training	Post-training	Follow-up
0	Without any signs of the disease.				
1	Unilateral impairment.				
1.5	Axial and unilateral impairment.			P1	P1
2	Bilateral disease without balance deficit.		P1	P2	P2
2.5	Mild bilateral disease, with recovery in the 'push test'.	Mild to moderate	P2		
3	Mild to moderate bilateral disease; some postural instability; ability to live independently.				
4	Severe disability, still able to walk or stand without assistance.	Severe			

When considering the H&Y results (Table 14) it is possible to observe that for both patients, when comparing the moments before (pre-training) and after (post-training) receiving the cued training with the FoG prevention strategy, both patients improved their motor impairments. These score improvements were maintained at follow-up. Both patients showed an improvement of 0.5 score points, however, P2 presented still higher H&Y stage and, therefore worse PD symptom severity when compared to P1.

Both MDS-UPDRS III and PDQ-39 graphics (Fig. 21 and Fig. 22, respectively) showed an overall similar profile, with a tendency to take a U-shape format.

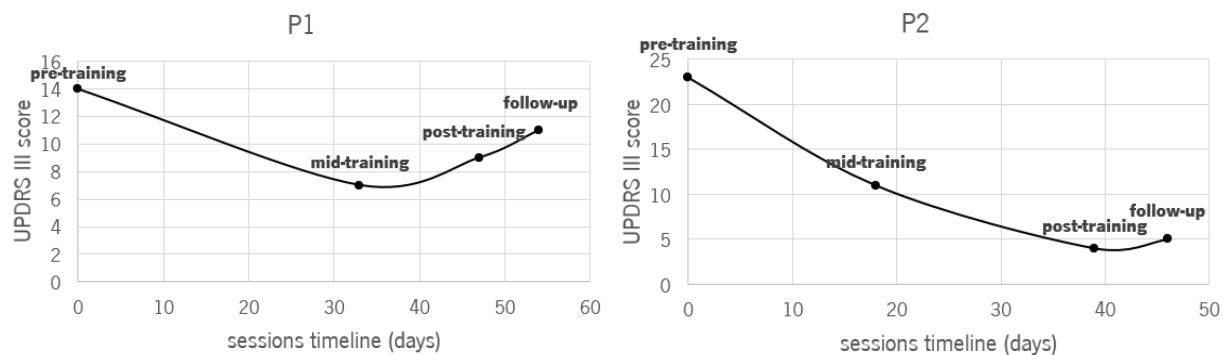


Fig. 21. UPDRS III scores evolution along each evaluation timepoint, for patients P1 and P2.

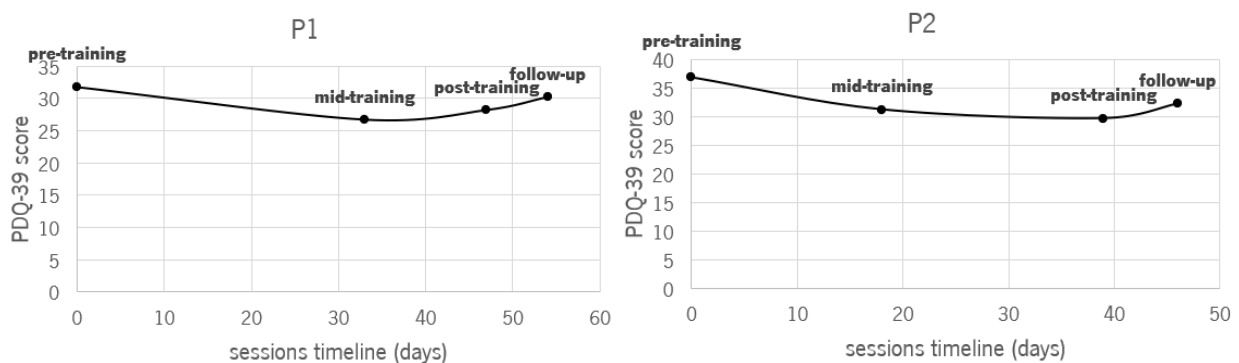


Fig. 22. PDQ-39 scores evolution along each evaluation timepoint, for patients P1 and P2.

When observing the MDS-UPDRS III results (Fig. 21) overall both patients decreased their scores, meaning improvements of motor function at each evaluation time point when compared to pre-training ($\approx 50\%$, $\approx 35.71\%$ and $\approx 21.43\%$ for P1, and $\approx 52.17\%$, $\approx 82.61\%$ and $\approx 78.26\%$ for P2, at mid-training, post-training and follow-up, respectively). However, both patients experienced a slight regression towards the end of the follow-up period ($\approx 22.22\%$ for P1 and $\approx 25\%$ for P2, regression from post-training). Patient P1 showed maximum improvements of UPDRS III scores at mid-training, while patient P2 showed maximum

improvements at post-training. Patient P2, although noting a regression at follow-up, presented a better MDS-UPDRS III score at follow-up than at mid-training, explaining the less prominent U-shape pattern of this graphic. Patient P1, although showing results at follow-up worse than mid-training, those results were still better than pre-training.

As for the PDQ-39 score results (Fig. 22) overall both patients also experienced an improvement in QoL over the evaluation time points. When comparing both patients, P1 showed greater variations along each timepoint's score, while P2 showed a less prominent improvement, with a more stable pattern overall. P1 achieved a minimum score, meaning maximum improvement felt of QoL, at mid-training ($\approx 16.10\%$ improvement from pre-training). At post-training, although having a small regression from the mid-training results ($\approx 5.74\%$ regression), still showed some degree of improvement when compared with the pre-training PDQ-39 score ($\approx 11.29\%$ improvement). A small regression towards the end of the follow-up period occurred, but without returning to pre-training levels. Patient P2 however showed maximum improvement at post-training ($\approx 19.45\%$ improvement from pre-training), improving gradually from pre-training to mid-training ($\approx 15.28\%$ improvement) and continuing to improve from mid-training to post-training ($\approx 4.92\%$ improvement) reaching its peak at this timepoint. At follow-up, for both patients although being noticed a regression of the results since post-training ($\approx 7.30\%$ regression for P1 and $\approx 8.64\%$ regression for P2), QoL improved since pre-training ($\approx 4.81\%$ improvement for P1 and $\approx 12.49\%$ improvement for P2). Overall, patient P2 although showing a more stable pattern, presented higher improvements of QoL from pre-training to both post-training and follow-up.

6.2.3. TRAINING QUESTIONNAIRES

Fig. 23, Fig. 24 and Table 15 present the graphics and table of the training questionnaires subsection.

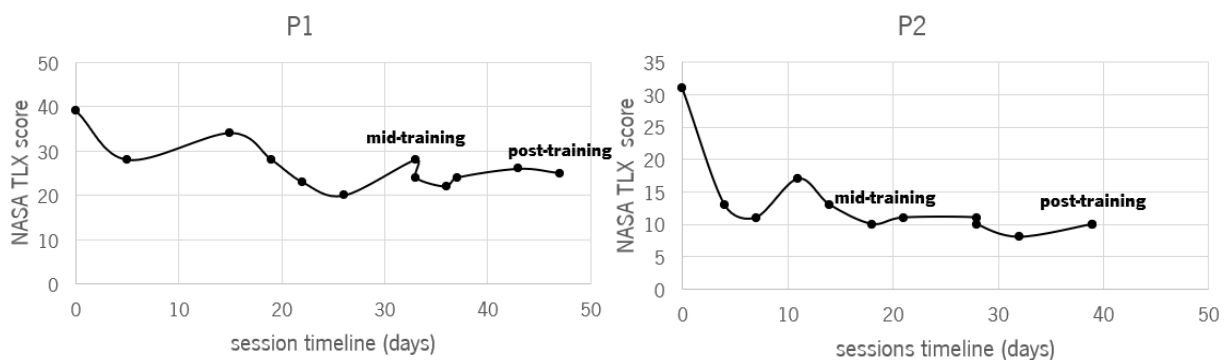


Fig. 23. NASA TLX scores evolution along each training session, for patients P1 and P2.

When analysing the mental and physical workload (Fig. 23) at the last training session both patients P1 and P2 reported lower NASA TLX scores, therefore improving along the sessions the mental effort felt during the cued training (improvements of $\approx 37.5\%$ for patient P1 and $\approx 67.74\%$ for P2). Patient P2 showed overall better results of NASA TLX scores along the training timeline, however both patients started the protocol considering the workload at a somewhat high level (39 score for P1 and 31 score for P2) but decreased it to a medium workload at both mid and post-training (28 and 25 scores, respectively, for patient P1, and 10 scores at both moments for P2).

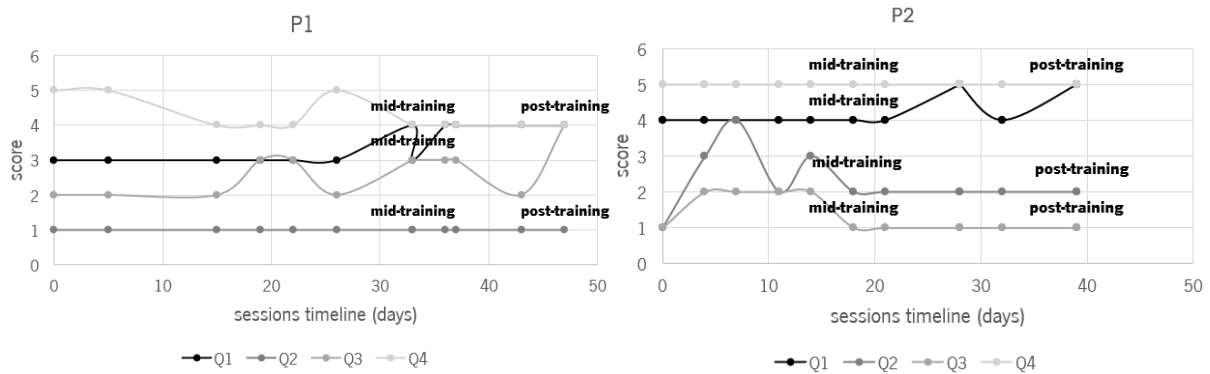


Fig. 24. Cue perception Questionnaire answers for each question (Q1: “How perceptible was the laser?”, Q2: “With what frequency did you use the laser cues?”, Q3: “How perceptible was the vibration during the trial?”, and Q4: “How perceptible was the vibration in the first 20s of the trial?”) evolution along each training session, for patients P1 and P2.

Cue perception results (Fig. 24) showed some variability across the two patients. Both patients reported high perception of vibration in the first 20 seconds of trials (Q4), however during the walking trials, the vibrations perceived at right toe-offs were lightly perceived (Q3). Overall, both patients could perceive the laser very well (Q1), however, only used it slightly (Q2). Patient P1 did not felt the need to use the laser and felt slightly confused by it. Patient P2 on the other hand reported using the laser lines right before FoG inducing tasks, to prevent from freezing. When the number of FoG episodes during the sessions started to diminish, this patient also started to report the need of using the laser less.

Table 15. SUS answers for each individual question, for patients P1 and P2

SUS Questions	P1	P2
I think that I would like to use this system frequently.	4	4
I found the system unnecessarily complex.	1	2
I thought the system was easy to use.	5	5
I think that I would need the support of a technical person to be able to use this system.	1	1
I think the various functions of the system are very well integrated.	4	3

I thought there was too much inconsistency in this system.	1	3
I would imagine that most people would learn to use this system very quickly.	5	5
I found the system very cumbersome to use.	1	1
I felt very confident using the system.	4	5
I needed to learn a lot of things before I could get going with this system.	1	1

Likert scale: 1 – strongly disagree; 2 – disagree; 3 – indifferent; 4 – agree; 5 – strongly agree.

As for the SUS results (Table 15) both patients showed overall excellent usability reaching total scores of 92.5 and 85, for patients P1 and P2, respectively.

6.2.4. GAIT METRICS

First, the metrics obtained at pre-training (baseline) with the +sensBand were compared with the ones captured by the Xsens that served as our ground truth. If the +sensBand resulting metrics fell within the range of the respective Xsens metrics were deemed acceptable, therefore validating those +sensBand results. Table 16 summarizes the resulting metrics obtained using both devices (Xsens and +sensBand) for each patient P1 and P2.

Table 16. Gait metrics obtained with the Xsens vs. +sensBand, for each patient P1 and P2 at pre-training

Gait metrics (pre-training)	Xsens		+sensBand	
	P1 Mean±SD	P2 Mean±SD	P1 Mean±SD	P2 Mean±SD
Step length [m]	0.565±0.021	0.484±0.035	0.515±0.015	0.604±0.047
Velocity [m/s]	0.974±0.009	0.988±0.114	0.950±0.075	1.062±0.089
Cadence [steps/min]	102.572±0.877	115.035±10.295	112.549±10.931	89.864±8.606
Step time [s]	0.585±0.005	0.513±0.032	0.550±0.050	0.597±0.030
Stance phase [%]	75.420±16.937	57.974±8.206	78.909±0.701	61.693±4.425
Swing phase [%]	24.580±16.937	47.050±8.206	21.091±0.701	38.307±4.425
SD Step length [m]	0.140±0.027	0.058±0.036	0.283±0.037	0.426±0.113
SD Velocity [m/s]	0.234±0.022	0.227±0.026	0.479±0.073	0.489±0.104
SD Step time [s]	0.901±0.147	0.113±0.062	0.228±0.155	0.137±0.022
AS Step length [m]	0.059±0.032	0.087±0.061	0.242±0.207	0.576±0.130
AS Velocity [m/s]	0.128±0.122	0.347±0.010	0.216±0.177	0.133±0.083
AS Step time [s]	0.038±0.012	0.148±0.107	0.167±0.110	0.177±0.051

Bold highlights the +sensBand metrics validated when compared with the Xsens metrics.

Overall, velocity, stance phase and swing phase were the only metrics validated for both patients. Patient P1, however, presented both cadence, AS step length and AS velocity within the respective XSens metrics range, therefore those +sensBand metrics were also validated for this patient. As for patient P2, only SD and AS of step time were further validated.

Lastly, Fig. 25, Fig. 26, Fig. 27, Fig. 28 and Fig. 29, present the graphics of the gait metrics results. When analysing the +sensBand gait metrics graphics along the protocol evaluation timepoints, it is possible to note different patterns along some metrics but also along each individual patient.

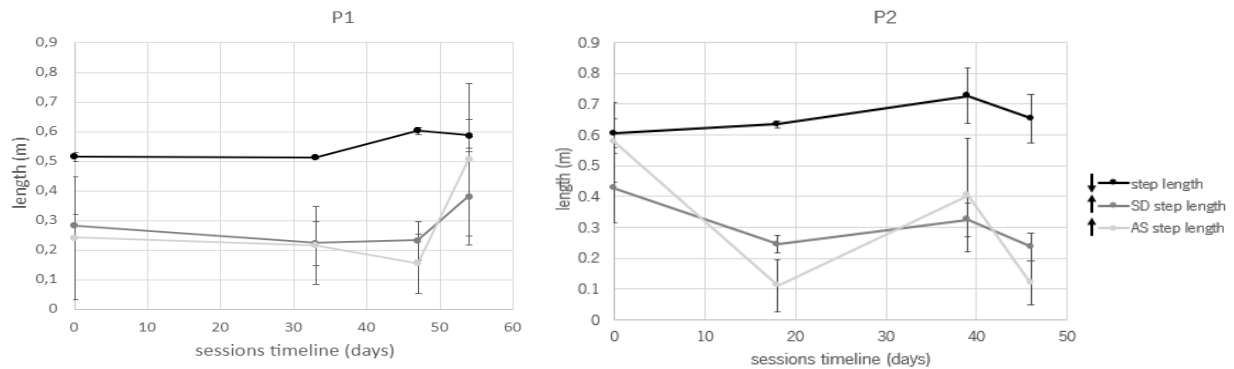


Fig. 25. Mean step length, respective SD and AS evolution along protocol evaluation timepoints, for each patient.

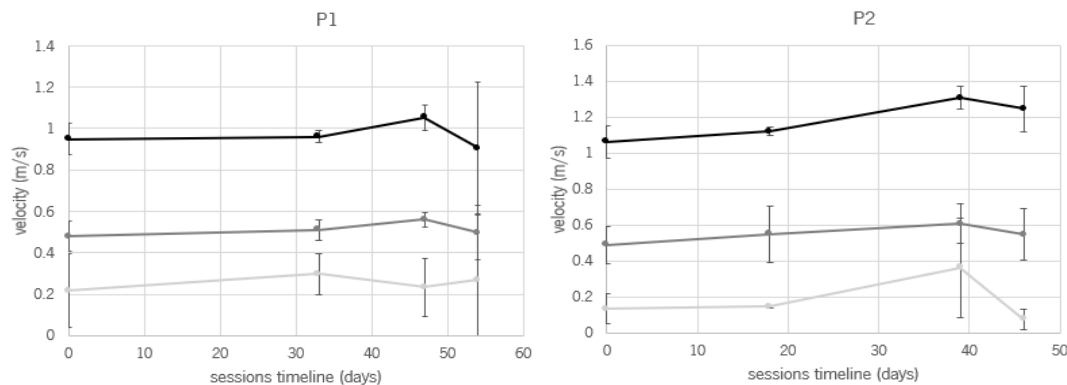


Fig. 26. Mean velocity, respective SD and AS evolution along protocol evaluation timepoints, for each patient.

Step length (Fig. 25) and velocity (Fig. 26) were the metrics that showed similar profiles for both patients, improving gradually as expected along the training sessions and reaching the max improvement peak at post-training ($\approx 17.13\%$ and $\approx 10.85\%$ for patient P1, and $\approx 20.39\%$ and $\approx 22.89\%$ for patient P2, improvements of step length and velocity, respectively, from pre-training to follow-up). At follow-up, the results showed a slight regression for both patients and both metrics, however, were still maintained improvements when compared to the pre-training assessment.

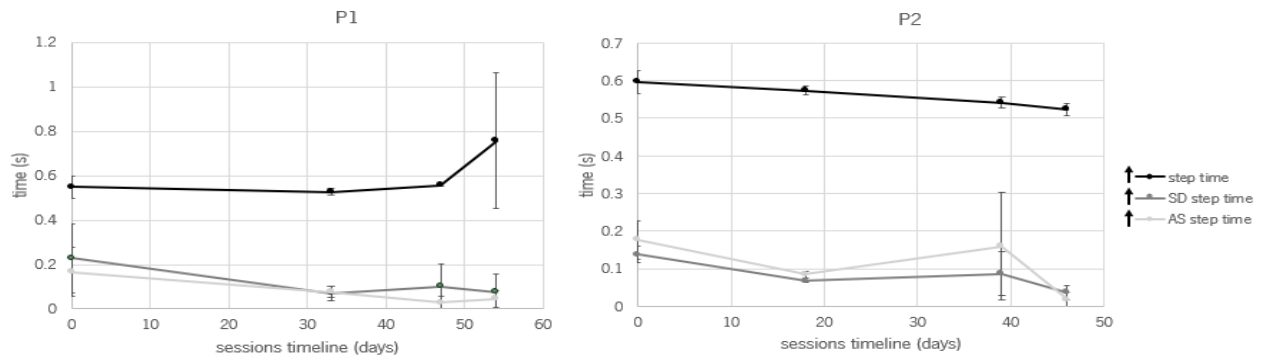


Fig. 27. Mean step time, respective SD and AS evolution along protocol evaluation timepoints, for each patient.

Step time (Fig. 27) although showing overall gradual improvements, it showed slightly different patterns when comparing patients P1 and P2. For patient P1 it was noted a max improvement at mid-training. However, at post-training it was observed a regression of the results ultimately noting no improvements when compared to pre-training. At follow-up, the step time continued to worsen for this patient. As for patient P2, an almost opposite behaviour was noted. Step time improved along the protocol time points, reaching its improvement peak at follow-up ($\approx 9.22\%$ at post-training and $\approx 12.30\%$ at follow-up).

Stance phase, swing phase (both at Fig. 28) and cadence (Fig. 29) were the metrics that showed mixed results in between the participants.

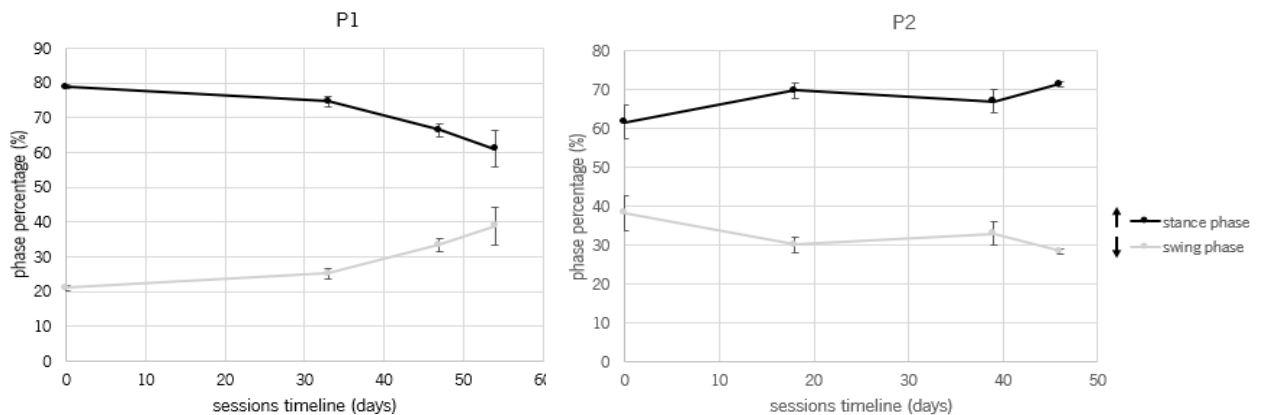


Fig. 28. Mean stance and swing phase evolution along protocol evaluation timepoints, for each patient.

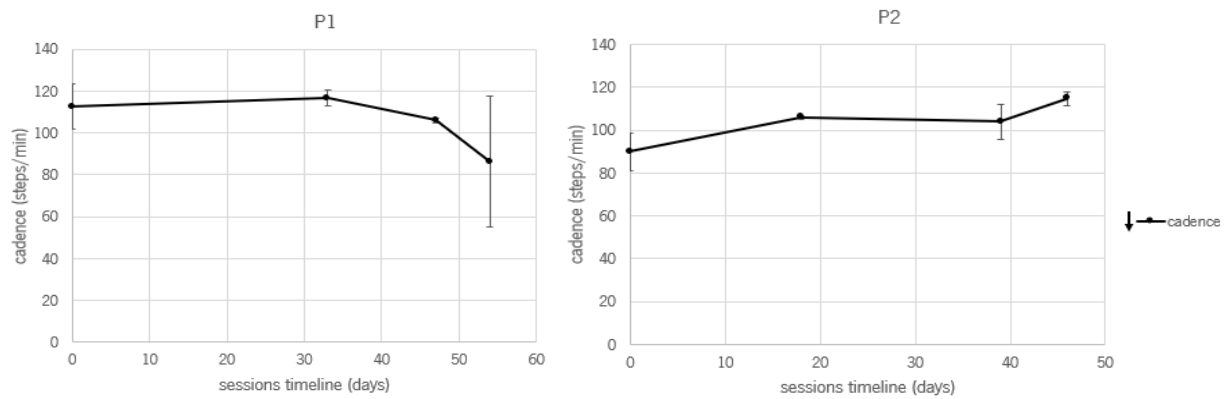


Fig. 29. Mean cadence evolution along protocol evaluation timepoints, for each patient.

For patient P1, there was noted a gradual improvement of both stance and swing phases, counteracting the prototypical behaviour of PD, and reaching the maximum improvement of both metrics at follow-up, although with higher SD dispersion (± 5.37 steps/min). However, P1 cadence only improved at mid-training. After this time point, it was observed a gradual decrease, resulting in worse cadence after training (at both post-training and follow-up) than at pre-training. It was also noted higher dispersion of SD values for cadence at follow-up for patient P1. P2, on the other hand showed continuous gradual improvements of cadence, reaching the maximum improvement at follow-up ($\approx 15.60\%$ at post-training and $\approx 27.65\%$ at follow-up). However, both stance and swing phases worsened along the protocol timepoints. After starting the training, at the mid-training session, the patient followed the prototypical PD behaviour, slightly increasing stance phase and decreasing swing phase. At post-training, however, patient P2 counteracted the prototypical behaviour showing some improvements from mid-training, but not enough to improve when compared directly to the start of the protocol (pre-training). At follow-up it was when the patient showed worse stance and swing phases.

It is also important to analyse both the variability and asymmetry aspects of gait.

When considering the gait variability aspects, both P1 and P2 showed similar profiles along each SD metrics. When considering both SD of step length and of step time, both patients showed gradual improvements along the protocol with slight regression from mid to post-training. At follow-up it was noted maximum improvement of the metrics with the exception of the patient's P1 SD of step length which showed a total regression, reaching the worst results in this evaluation time point. As for SD of velocity, an unexpected behaviour was noted for both patients. SD velocity worsened gradually from pre-training to post-training. However, from this point to follow-up, this variability metric improved, getting closer to the results before receiving the cued training (pre-training), therefore being necessary to analyse each case individually.

Regarding the AS of step length, P1's results gradually worsened as the training protocol progressed, with only a slight improvement between mid- and post-training. However, even at this time point, the results remained worse than pre-training. P2, on the other hand, gradually improved this metric, with only a slight regression of improvements from mid to post-training but maintaining better results overall after receiving the sensory cued training. In the AS of speed, both patients showed the same baseline pattern, worsening for both patients after starting the cued training. P1 showed slight improvements from mid- to post-training, however P2 showed the worst results in this time-point. At follow-up both patients seemed to improved greatly, noticing that P1 got closer to the pre-training results, and P2 reaching the maximum improvement in this moment, improving even from baseline (pre-training). Finally, with regard to AS of step-time, P1 gradually improved, with a slight regression from post-training to follow-up, as expected. On the other hand, although P2 also showed a gradual improvement, he regressed slightly from mid to post-training, but then maintained these improvements in follow-up.

6.3. DISCUSSION

The FoG results section indicates that for both patients, the FoG prevention cueing strategy resulted in reducing observed FoG episodes, therefore the results suggest that it has the potential to mitigate FoG in patients with PD. However, its effectiveness may vary according to the patient's profile and the type of task that triggers FoG.

For patient P1, since freezing was not observed during the trials nor during any moment of the sessions throughout the protocol, this patient observed FoG data was not considered to conclude about the training effectiveness. Patient P2, on another hand, showed a consistent pattern in the reduction of FoG episodes observed during the trials, with a 100% decrease from pre-training to post-training. However, the results were not maintained at follow-up, meaning that the FoG prevention cueing strategy may have more immediate improvements in targeting FoG than long-term benefits.

P2 NFOG-Q scores also showed positive results, with improvements from mid-training to post-training and slight regression at follow-up as expected. Although when comparing post-training directly with the pre-training not showing direct improvements, it was noticed that the patient at pre-training answered that only had freezing at gait initiation. This was noticed since the patient at this timepoint answered “[0] Never.” to the NFOG-Q question “With what frequency do you present FoG while turning?”, therefore ultimately not answering also the following question “How long does your greater FoG episode while turning last?”. However, this task was the most predominant FoG-inducing task during the sessions,

inducing more than half of the FoG episodes observed. All these findings may suggest that patients had worse FoG at pre-training than the first NFOG-Q score reported but were not as much aware of their FoG-inducing tasks. The training programme, with the continuous reports made patients more conscious of their own FoG. Therefore, self-reporting tools like the NFOG-Q scores may serve only to complement the more objective assessments such as the observed FoGs during sessions. Furthermore, the slight regression observed at follow-up is consistent with the expected decay of training effects over time, emphasizing the potential need for ongoing cued training to maintain the benefits at long term.

The literature review, based on the longitudinal studies identified, did not provide substantial conclusions regarding the potential of different cued-training protocols in mitigating FoG. However, a study using a similar 12-session training program, but with auditory cues delivered during at-home SIP training with music compared to a podcast, demonstrated no significant effect of cued training on the FOG-Q scores [50]. This highlights the importance of analyzing observational FoG data, which in this case showed positive trends, despite the not-so-significant findings from the NFOG-Q results in the study.

When analysing the other patient perception-based FoG parameter, the episodes perceived in between sessions, different conclusions were also taken. For patient P1 it was shown a more unexpected behaviour, with an increase after training ($\approx 50\%$) followed by a complete mitigation until follow-up (0 episodes). This suggests that, for P1, cueing could have caused a progressive impact, especially in the long term, since the patient experienced considerable improvements between post-training and follow-up counteracting the expected behaviour. However, it is important to consider that patient P1 had less intensive training, since this patient showed irregular time intervals in between sessions, resulting in more inconsistent cued-training dosage, which may have caused more irregularities of FoG in between sessions. Also, this patient reported changes of psychiatric medication at the end of the training protocol, that resulted in oscillations of patient stress levels. Since FoG occurred mainly when the patient was more stressed, those medication adjustments may also explain those abrupt changes of FoG in between sessions.

The clinical results also agree with these findings. It was noted that both patients, showed improvements in H&Y, MDS-UPDRS III and PDQ-39 scores at post-training, meaning that after completing the FoG prevention cueing training protocol, patients improved their overall motor function and perception of QoL. At follow-up, however, for both MDS-UPDRS III and PDQ-39 those clinical improvements slightly decreased but were still noticed improvements when compared to the pre-training assessments. This reinforces the efficacy of continuous cued-assisted training with this novel strategy in improving both PD

patients' mobility and perception of QoL. However, it also indicates that results may not be maintained after long periods without cueing, longer than 1-week.

The reduction in NASA TLX scores throughout the training sessions indicates that both patients experienced a significant decrease in perceived mental and physical workload. This suggests that the cued training became less mentally demanding over time, likely as a result of task familiarity and improved cognitive-motor integration. Patient P2, with greater overall improvement, may have adapted more efficiently to the training, possibly due to individual differences in cognitive capacity or baseline familiarity with the tasks. Despite both patients starting with relatively high workload perceptions, their scores dropped to moderate levels by mid-training, reflecting improved comfort and reduced effort as the sessions progressed. These findings highlight the potential for adaptive training programs to reduce perceived effort, improving engagement and performance over time.

The SUS scores results showed also excellent usability for both patients, reaching the individual items reference benchmarks [20], with the exception of item 5 ("I think the various functions of the system are very well integrated") and 6 ("I thought there was too much inconsistency in this system") for patient P2. This, however, may be explained by the comment noted of the patient answering neutrally as it perceived the questions from a more technical perspective and felt unable to provide an informed answer.

Lastly, the comparison between the results obtained from the +sensBand and the reference data captured by Xsens, although not validating some metrics (step length, SD of velocity and SD of step length), allowed to validate pace and rhythm gait metrics collected using the +sensBand. The asymmetry aspect of gait was also validated, however mixed results were obtained for the different AS metrics when comparing each patient's +sensBand gait event detection performance. For patient P1 the +sensBand allowed more similar results to the Xsens for both AS of step length and of velocity, whereas for patient P2 only for AS step time the +sensBand performed similarly to the Xsens as a monitoring system.

When analyzing the +sensBand gait metrics results evolution along the protocol timeline, positive improvements were noted after concluding the cued-training protocol (at post-training). Both patients, showed some unexpected behavior along gait metrics such as stance phase, swing phase, cadence, variability and asymmetry, however overall, both showed improvements of pace and rhythm after concluding the cued-training sessions, improving both step length, velocity and step time. At follow-up the majority of the results were lost, confirming once again the necessity of continuous use of the device and that it succeeded in acting as an assistive device.

As for comparing the results from the +sensBand gait metrics with those reported in the literature, three longitudinal studies were identified that used somatosensory cueing devices, though in an open-loop configuration. These studies demonstrated also post-training improvements in pace and rhythm metrics such as stride length [55], [58], [59], velocity [58], cadence [59], and stance [58]. Maximum improvements, from pre- to post-training, were noted of 11.28% for cadence [59] and 7.14% for velocity [58]. One of these studies included also a one-week without receiving cues for the follow-up period, ultimately reporting that the pace and rhythm improvements did not persist [55]. Therefore, the results of this study align with the expected outcomes from the literature, with slight improvements observed in some metrics. Although not all improvements were retained at follow-up, some positive effects on gait performance remained, which suggests a partial retention of the benefits.

Furthermore, since velocity was an impactful gait metric for this study, in the future it should be objectified to reach minimal improvements of velocity from 0.05m/s to 0.15m/s [84]. Therefore, the sample size should be projected to achieve a minimum of 22 patients [84]. Future research should consider following the protocol to achieve this target number of PD patients with FoG and increase the impact of these results. Another limitation comprises the absence of statistical analysis, which precludes determining if the observed results are statistically significant.

6.4. CONCLUSIONS

Based on the FoG results, it can be concluded that FoG prevention cueing strategy may have potential to reduce and mitigate freezing episodes observed in PD patients, even when executing challenging motor tasks more suitable to induce FoG. However, effectiveness depends not only on the strategy itself but also other factors such as the regularity of feedback training and the way patients use the cueing strategies (visual cues may have proven to be more effective in actively preventing FoG). Furthermore, there is evidence that the patient's subjective perception of FoG may not keep pace with motor performance, suggesting the need for better observational approaches to monitor FoG more precisely and provide greater detail on the benefits and durability of the treatment. The improvements observed, especially at post-training, demonstrate that feedback can be a valuable tool for mitigating FoG, but its application must be continuous.

Better QoL perception was also achieved right after completing the training protocol, accentuating the impact of targeting PD motor symptoms to improve patients' daily routines. Overall, the cued training

although being extensive was very well received, being perceived with excellent usability and medium workload.

Patients' motor performance was also improved at post-training, especially when considering improvements of pace (step length and velocity) but also rhythm (step time), reinforcing improvements of the hypokinetic and bradykinetic aspects of gait.

7. CONCLUSIONS

This chapter provides final reflections and research findings, highlighting the work contribution to knowledge. An overview of the results considered within each chapter is presented, and research questions are answered. Future steps to be considered are also discussed, enhancing the impact and further potential of this project research.

This dissertation relied on the +sensBand system project, aiming to improve its strategies, developing and validating a new one for mitigating FoG, and testing its long-term use potential for motor and QoL improvements. The work developed innovated by **overcoming some of the previous challenges** of the +sensBand research project, concluding research on the **efficiency of gait event-driven cueing and continuous feedback in PD patients**, providing a **novel strategy** suitable for more advanced stages of PD and performing its validation in a longitudinal protocol to allow insights on a rehabilitative perspective of the +sensBand system. This approach was based on gathering and analyzing, both patients' feedback and motor data, with the aim to enhance patients' motor performance and reduce motor symptoms of PD during daily activities, therefore improving their QoL. The research efforts, along with the encouraging results achieved through experimental methodologies with end-users, played a crucial role in achieving the dissertation goal, as outlined below.

The gathered knowledge in **Chapter 2**, was the motor for the project development, allowing an understanding of the different available cueing solutions being applied in PD patients, as well as how were being applied and their respective effects (**KPI1**). It was noticed that cueing strategies, particularly somatosensory and visual strategies, show promising results in reducing PD motor symptoms such as FoG. Closed-loop patient-tailored approaches highlighted their potential to significantly improve motor task performance. The literature review also allowed to understand that research should prioritize **spatiotemporal outcomes**, such as velocity and FoG occurrences, while incorporating **regular, consistent training protocols** and assessments to ensure sustained benefits with long-term cued training. Technological systems, along with the +sensBand solution components, considering the new implemented and developed strategy, were introduced and described in **Chapter 3**: (1) the hardware, considering both +sensBand and Xsens systems; (2) the cueing and monitoring +sensBand strategies used; and (3) the clinical desktop App improved for gait data processing.

The +sensBand allows with a single device to provide several cueing strategies, through laser line projection and/or vibrotactile motors, while simultaneously collecting patients gait data through an IMU-

based system. The Xsens system, by using high-tech IMU-based gait assessments, acts as a ground truth to validate the +sensBand gait assessments.

The +sensBand configuration is established via a smartphone app, which allows to select the respective strategy pretended. If it's intended to only monitor patients gait without providing cueing, the **motion monitoring** strategy allows to activate only the IMU sensors, collecting patients' angular velocity and acceleration data, and enabling real-time gait event detection. As for the cueing strategies, three modalities were considered. The **gait event-driven cueing** strategy consists on providing closed-loop vibratory cueing at right-foot toe-offs. The **continuous feedback**, alternatively, provides open-loop vibratory cueing, set to 2s on-and-off pulses. By considering that combining somatosensory closed-loop cueing and visual open-loop cueing may target FoG and enhance gait performance by instructing when and where to place the foot, respectively, the **FoG prevention cueing** was developed. Similarly to the gait event-driven cueing, it allows to provide vibrations at right-foot toe-offs, while simultaneously providing open-loop laser line projection set to patients' step length. Since gait initiation was identified as one of the main FoG-inducing tasks, the strategy was adapted to provide open-loop vibration as the continuous feedback strategy until the first right foot toe-off is detected. After detecting this event it automatically switches to the closed-loop mode.

It was also presented the **clinical desktop app**, developed in Matlab, that allows to transform the acquired data into the respective gait metrics being analyzed. The acceleration and angular velocity data run through calibration, filtering and gait segmentation processes (Finite State Machine algorithm) to obtain a list of ICs and FCs for each foot. By using these IC/FCs, gait metrics are calculated for both pace and rhythm domains, but also variability and asymmetry metrics.

The following three chapters comprise each of the three studies performed along this dissertation, regarding the respective protocol established, results obtained and conclusions.

Chapter 4 presented the on-going cross-sectional study executed in which was accomplished both the on-field familiarization with the +sensBand technologies but also the sample size goal to complete the study (**KPI2**). This study also allowed to understand the efficacy of both gait event-driven cueing and continuous feedback strategies in improving motor performance, being both capable of improving both pace and rhythm aspects of gait. Overall, there is potential of using both strategies combined, reinforcing the need of development of the FoG prevention cueing strategy.

Chapter 5 followed with the execution of a usability and workload study, performed in healthy individuals, for validation of the FoG prevention cueing strategy in different daily walking scenarios. From

this study, it was concluded that the strategy was perceived with excellent usability and low workload, therefore granting that it should not overstimulate patients (**KPI3**).

After the validation of the FoG prevention cueing strategy in healthy participants (**Chapter 5**), **Chapter 6** followed with the design and execution of the longitudinal study to address the long-term rehabilitative potential of the +sensBand directly with the end-users. The results, although showing some differences due to different patient characteristics, proved the potential of the FoG prevention cueing in mitigating FoG during training (**KPI4**). Its effectiveness, however, depends on consistent use. Improvements in motor performance and quality of life were also noted, as long as confirming the excellent usability of the strategy and mid-workload perceived (**KPI5**). Future work should consider targeting a larger number of FoG patients to participate in the study, to allow greater impact of spatiotemporal results.

Along with this dissertation document, the work developed resulted in 2 papers, a journal paper and a conference paper (**KPI6**).

In summary, the results obtained along this dissertation experimental assessments confirmed the effectiveness of the +sensBand system usage in improving PD patients motor performance, reducing motor symptoms and ultimately reaching better QoL, at both short and long-term uses. It was already possible to put the +sensBand to test in home-based scenarios and also at a longitudinal protocol setting. The findings obtained should serve as motivation to explore new approaches such as home-based long-term usage. Some adjustments mainly of design should still be considered. However, overall, this dissertation research project made a significant and grateful contribution to enhancing the daily lives of PD patients through the application of biomedical engineering solutions.

7.1. RESEARCH QUESTIONS

The resulting dissertation work presented allowed to answer the RQs outlined in **Chapter 1**. The concluding answers are presented in summary as followed.

RQ1: How have cueing strategies been used and applied for targeting motor symptoms of PD?

This RQ was answered in **Chapter 2**, by revising the literature available about different cueing applications designed to target several motor symptoms of PD. Cueing strategies applied to PD patients primarily involve external stimuli such as visual, auditory, and somatosensory cues, delivered through electronic and non-electronic methods. Visual cues, like laser lines, are mainly used to improve spatial

awareness, targeting mainly the pace aspects of gait (improve hypokinetic impairments), while auditory cues, like metronomes, enhance rhythm during gait (improve bradykinetic impairments). Somatosensory cues, often vibratory, are less researched and mostly used in combination with other stimuli. Cueing can be open-loop, providing the cue at a fixed rhythm, or closed-loop, synchronized with patients' gait performance for a more tailored approach. Studies have focused on using cueing during several walking tasks, often incorporating FoG triggers, to evaluate cueing efficacy using established clinical scales and collecting gait metrics.

RQ2: Which is the effectiveness of cueing strategies concerning motor effects and QoL?

Chapters 2 and **4**, through the literature review executed and the cross-sectional study developed with PD patients testing different cueing strategies, allowed to understand their efficacy in improving both motor symptoms and QoL. Considering the diverse range of cueing options, cueing strategies have shown varied effectiveness in addressing motor symptoms and improving QoL in PD. Short-term studies (cross-sectional studies) indicated that visual and auditory cues significantly improve gait parameters, targeting mainly pace aspects such as cadence, velocity, and step length, and can also reduce the number of FoG episodes in more advanced stages of the disease. Somatosensory cues, on another hand, also show potential, but their effectiveness is less consistent. Combining different cue types, for example, visual and somatosensory cues, can enhance both motor and QoL outcomes but may require attention in which concerns avoiding overstimulation. Long-term studies (longitudinal studies) suggest that while initial improvements in motor function and QoL occur, these effects may diminish over time without a continuous use of cueing. Closed-loop cueing appeared to provide better long-term benefits than open-loop methods, mainly in targeting FoG, improving pace (step length and velocity) and some aspects of rhythm (stance phase). Moreover, when comparing the use of open and closed-loop somatosensory cueing strategies in a cross-sectional study executed, it was proven that both cueing delivery methods are efficient in improving gait performance, however different aspects may be improved slightly differently with each method. Open loop cueing although showing greater overall improvements in pace, contributed to higher gait variability and asymmetry. In contrast, closed-loop cueing led to more subtle, stable improvements by aligning with the patient's natural rhythm, potentially preserving gait variability.

RQ3: How does +sensBand cueing system long-term use affect Parkinson's motor symptoms and QoL?

The final study chapter, **Chapter 6**, by addressing a longitudinal protocol in PD patients, allowed to answer this question considering the results obtained. The promising findings support the potential of

+sensBand cueing strategies, in the FoG prevention cueing form, in targeting more advanced symptoms of PD, such as FoG (mitigating FoG occurrences totally during training and reducing up to 66.67% after a week without receiving cued training) , improving mainly hypokinetic aspects of gait ($\approx 17.82\%$), and improving overall perceived QoL ($\approx 15.37\%$). However, the effectiveness for FoG mitigation depends also on the regularity of training using the FoG prevention cueing strategy, since the majority of the improvements were not maintained at follow-up, meaning that the strategy caused mainly immediate improvements during training that were not maintained at long-term. The improvements observed, especially at post-training, demonstrate that sensory cueing can be a valuable tool for mitigating FoG, but its application must be continuous. These findings, however, are not sufficient to guarantee the use of this sensory solution as a rehabilitative device instead of an assistive device for motor rehabilitation, therefore needing more evidence to conclude about these aspects.

7.2. FUTURE DIRECTIONS

Some limitations noticed along this dissertation work noticed consisted of: (i) high variability of PD patients, that may affect group and overall results; (ii) design limitations, regarding the bulkiness of the device; and (iii) small sample of PD patients available to participate in longitudinal studies.

These aspects should not discard, however, the potential of further investigation with the device. Furthermore, as patients often reported not perceiving the vibrotactile cues during walking, future work should explore alternative +sensBand cueing strategies, such as subliminal cues, to improve PD motor symptoms, as these may be more seamlessly integrated into patients' daily routine.

Lastly, the algorithm for gait-event detection proved to also have some limitations regarding patients gait variability due to the unpredictable nature of the disease. Therefore, to improve real-time gait-event detection and gait metrics calculation performance, the implementation of a machine learning algorithm able to adapt to different gait patterns should be considered instead of the developed FSM algorithm for IC/FC segmentation.

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9. APPENDICES

APPENDIX A – Statistical Analysis

Normality tests

		Kolmogorov-Smirnov ^a			Shapiro-Wilk		
	Study group	Statistics	DoF	Sig.	Statistics	DoF	Sig.
Step time [s]	1	.197	51	.000	.850	51	.000
	2	.250	41	.000	.736	41	.000
	3	.249	43	.000	.785	43	.000
Stance phase [%]	1	.128	51	.037	.900	51	.000
	2	.229	41	.000	.819	41	.000
	3	.236	43	.000	.759	43	.000
Swing phase [%]	1	.100	51	.200*	.974	51	.308
	2	.187	41	.001	.859	41	.000
	3	.232	43	.000	.779	43	.000
Step length [m]	1	.094	51	.200*	.973	51	.301
	2	.101	41	.200*	.976	41	.512
	3	.121	43	.123	.872	43	.000
Velocity [m/s]	1	.104	51	.200*	.961	51	.094
	2	.065	41	.200*	.986	41	.878
	3	.158	43	.009	.851	43	.000
Cadence [steps/min]	1	.114	51	.097	.925	51	.003
	2	.204	41	.000	.892	41	.001
	3	.140	43	.035	.922	43	.006
SD step length [m]	1	.201	51	.000	.659	51	.000
	2	.202	41	.000	.868	41	.000
	3	.158	43	.009	.840	43	.000
SD step time [s]	1	.220	51	.000	.637	51	.000
	2	.177	41	.002	.858	41	.000
	3	.294	43	.000	.665	43	.000
SD velocity [m/s]	1	.164	51	.001	.856	51	.000
	2	.208	41	.000	.877	41	.000
	3	.193	43	.000	.742	43	.000
AS step length [m]	1	.213	51	.000	.810	51	.000
	2	.266	41	.000	.804	41	.000
	3	.193	43	.000	.879	43	.000
AS step time [s]	1	.253	51	.000	.617	51	.000
	2	.279	41	.000	.696	41	.000
	3	.288	43	.000	.607	43	.000
AS velocity [m/s]	1	.082	51	.200*	.953	51	.042
	2	.097	41	.200*	.961	41	.167
	3	.248	43	.000	.583	43	.000

*. Este é um limite inferior da significância verdadeira.

a. Correlação de Significância de Lilliefors

Kruskal-Wallis

Null Hypothesis	Sig.	Decision
The distribution of Step time [s] is the same in the Study group categories	.170	Retain null hypothesis

The distribution of Stance phase [%] is the same in the Study group categories	.057	Retain null hypothesis
The distribution of Swing phase [%] is the same in the Study group categories	.044	Reject null hypothesis
The distribution of Velocity [m/s] is the same in the Study group categories	.008	Reject null hypothesis
The distribution of Cadence [steps/min] is the same in the Study group categories	.033	Reject null hypothesis
The distribution of SD step length [m] is the same in the Study group categories	.011	Reject null hypothesis
The distribution of SD step time [s] is the same in the Study group categories	.266	Retain null hypothesis
The distribution of SD velocity [m/s] is the same in the Study group categories	.008	Reject null hypothesis
The distribution of AS step length [m] is the same in the Study group categories	.006	Reject null hypothesis
The distribution of AS step time [s] is the same in the Study group categories	.027	Reject null hypothesis
The distribution of AS velocity [m/s] is the same in the Study group categories	.158	Retain null hypothesis

ANOVA

Step length [m]					
	Square sum	df	Mean square	Z	Sig.
Between groups	.291	2	.145	6.193	.003
In the groups	3.100	132	.023		
Total	3.391	134			

Scheffe test

Step length [m]

		Confidence level 95%				
(I) Study group	(J) Study group	Mean difference (I-J)	Error	Sig.	Minimum limit	Maximum limit
1	2	-.023061	.032143	.773	-.10264	.05652
	3	-.107813*	.031726	.004	-.18636	-.02927
2	1	.023061	.032143	.773	-.05652	.10264
	3	-.084752*	.033449	.044	-.16756	-.00194
3	1	.107813*	.031726	.004	.02927	.18636
	2	.084752*	.033449	.044	.00194	.16756

*. A diferença média é significativa no nível 0.05.

APPENDIX B – Custom-made cue perception Questionnaire

Questions
How perceptible was the laser?
With what frequency did you use the laser cues?
How perceptible was the vibration during the trial?
How perceptible was the vibration in the first 20s of the trial?
1 - Not perceptible at all/did not use at all; 5 – Always perceptible/used it always