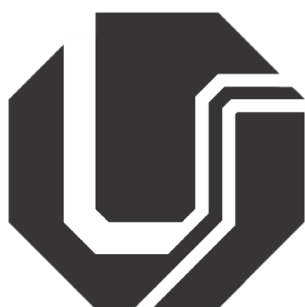


FEDERAL UNIVERSITY OF UBERLÂNDIA
UNIVERSITY OF LORRAINE
DOCTORAL THESIS – COTUTELLE PROGRAMME



LUANNE CARDOSO MENDES

DESIGN AND VALIDATION OF A SERIOUS GAME FOR
REHABILITATION AND MONITORING OF INDIVIDUALS WITH
PARKINSON'S DISEASE

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PARKINSON'S DISEASE

Thesis developed under a cotutelle programme between the Federal University of Uberlândia (UFU) and the University of Lorraine (UL). The thesis was submitted to both institutions as part of the requirements for obtaining the degree of PhD.

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Mendes, Luanne Cardoso, 1994-
DESIGN AND VALIDATION OF A SERIOUS GAME FOR
REHABILITATION AND MONITORING OF INDIVIDUALS WITH
PARKINSON'S DISEASE [recurso eletrônico] / Luanne
Cardoso Mendes. - 2024.

Orientador: Adriano de Oliveira Andrade.

Coorientador: Adriano Alves Pereira .

Tese (Doutorado) - Universidade Federal de Uberlândia,
Doutorado em Engenharia Biomédica.

Modo de acesso: Internet.

Disponível em: <http://doi.org/10.14393/ufu.te.2024.30>

Inclui bibliografia.

Inclui ilustrações.

1. Engenharia biomédica. I. Andrade, Adriano de
Oliveira, 1975-, (Orient.). II. , Adriano Alves Pereira,
1964-, (Coorient.). III. Universidade Federal de
Uberlândia. Doutorado em Engenharia Biomédica. IV.
Título.

CDU: 62:61

Bibliotecários responsáveis pela estrutura de acordo com o AACR2:

Gizele Cristine Nunes do Couto - CRB6/2091
Nelson Marcos Ferreira - CRB6/3074



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ATA DE DEFESA - PÓS-GRADUAÇÃO

Programa de Pós-Graduação em:	Engenharia Biomédica				
Defesa de:	Tese, 001, PPGEB				
Data:	vinte e dois de janeiro de dois mil e vinte e quatro	Hora de início:	13 horas	Hora de encerramento:	[15:54]
Matrícula do Discente:	11923EBI007				
Nome do Discente:	Luanne Cardoso Mendes				
Título do Trabalho:	Design and validation of a serious game for rehabilitation and monitoring of individuals with parkinson's disease				
Área de concentração:	Engenharia Biomédica				
Linha de pesquisa:	Engenharia de Reabilitação e Biomecânica				
Projeto de Pesquisa de vinculação:	CAPES-COFECUB Desenvolvimento de interface homem-máquina para a avaliação de sinais motores da doença de Parkinson				

Reuniu-se via plataforma ConferênciaWeb, a Banca Examinadora, designada pelo Colegiado do Programa de Pós-graduação em Engenharia Biomédica, assim composta: Professores Doutores: Edgard Afonso Lamounier Júnior - PPGEB/UFU; Thiago Ribeiro Teles dos Santos, FAEFI/UFU; Steffen Walter - Ulm University; François Cabestaing, Université de Lille; Adriano de Oliveira Andrade, PPGEB/UFU orientador da candidata.

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Documento assinado eletronicamente por **François Louis Jean Cabestaing, Usuário Externo**, em 22/01/2024, às 15:59, conforme horário oficial de Brasília, com fundamento no art. 6º, § 1º, do [Decreto nº 8.539, de 8 de outubro de 2015](#).



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ACKNOWLEDGEMENTS

A doctorate is a qualification that requires resilience and effort, and I get emotional when I remember every moment experienced during this period. Many things have happened since I started this journey, and today I understand that all of them contributed to my growth. Several people have shared this hard and pleasurable adventure with me, and I would like to express my gratitude to each one of them.

To God for His protection and for all blessings conceived throughout these years.

To my dear supervisor Adriano de Oliveira Andrade for guiding me with mastery, and for always motivating me to do my best. His love and dedication for his work is admirable and inspiring. Also, to my co-supervisor Adriano Alves Pereira for his patience and affection.

To my French tutors Yann Morère and Guy Bourhis, and to professor Pierre Pino, for all support I received during my studies in France.

To those who participated in the data collection and to the collaborators of the Parkinson's Association of the Triangle. Your help and participation were fundamental for the development of this research.

To my beloved husband Luiz Humberto Bonito Silvestrin for dreaming my dreams, fighting my battles and for always believing in my potential. His affection, care, comprehension, and partnership certainly contributed to my success. And to his family, who are also my family, Luiz Humberto Silvestrin, Rosuita Fratar Bonito, Pio Gustavo Bonito Silvestrin and Mayara Mafra Soares. Thank you for making this process lighter and easier.

To my parents, Marcos Antônio Mendes and Neide Aparecida Cardoso Mendes, my brother Lucas Cardoso Mendes and his fiancée Adriene Menezes Carrijo, for their immeasurable love, education, and patience. Thank you for always encouraging my studies and for understanding the moments when I was not present.

To the students of the Centre for Innovation and Technology Assessment in Health (NIATS) who always shared their knowledge and contributed to enrich my work. In special, I thank Isabela Alves Marques and Camille Marques Alves, great friends I had the pleasure of living with during my studies abroad and who became part of my family; and Ariana Moura Cabral, who never spared efforts to help me in the challenges I faced.

To all my uncles, cousins, and godchildren, who provide me joy and relaxation whenever we are together.

To my friends for always being present in my life. Special thanks for all your support and affection.

To my grandparents for the transmission of wisdom and unconditional love.

Thank you all so much! Without you I could not have achieved this mission!

“There will be obstacles. There will be doubters. There will be mistakes. But with hard work, there are no limits.” *Michael Phelps*

ABSTRACT

Introduction: Parkinson’s disease (PD) is a neurological disorder that affects body movements and causes symptoms such as bradykinesia and tremor. Bradykinesia, characterised as slowness of movement, is the main motor symptom of PD; while tremor, a rhythmic and involuntary oscillatory movement of a body part, is usually the first and the most troublesome motor symptom of the disease. Currently, Movement Disorder Society–Unified Parkinson’s Disease Rating Scale (MDS–UPDRS) is the most widely used clinical scale for assessing both symptoms. However, this type of assessment has limitations, such as subjectivity and dependence on experienced assessors. These problems can be overcome with the use of inertial sensors for objective measurements of movement, incorporated, for example, in control devices for serious games (SGs), increasingly promising tools for rehabilitation and movement assessment. **Objectives:** To develop a serious game with high usability and accessibility to individuals with PD, and, by using the signals recorded from the movements made during the game, to objectively assess bradykinesia and tremor. **Methods:** First, a literature review was carried out to identify existing technologies related to games for individuals with PD. Subsequently, a questionnaire was developed to assess multidimensional aspects of patients and guide the development of the game. Based on this research, a serious game about bees, so-called *RehaBEElitation*, was designed in Unity 3D. The game presents four phases, each one representing a bee’s task in the real world. The user has to control the movements of a bee in a 3D environment, executing the same movements found in the MDS–UPDRS. Fifteen individuals with PD and fifteen healthy individuals interacted with the game, constituting the experimental group (EG) and the control group (CG), respectively, with matched ages and sexes. Data was collected in the ON and OFF states of the medication for the EG. The usability of the game was assessed using the Nielsen-Shneiderman heuristics and user-centred approaches (evaluation questionnaires and semi-structured interview); and the accessibility, using the performance (scores) of the players in each phase. Bradykinesia was evaluated by detecting the trend of the gyroscope signals using Singular Spectrum Analysis (SSA), a time series decomposition method. The response time (RT) and angular velocity (AV) of the participants while playing *RehaBEElitation* were then estimated. Tremor was detected by removing the trend from the original signal and assessed by estimating the mean absolute value (MAV), root mean square (RMS) and power spectral density (PSD) of the gyroscope signals. In game usability evaluation, the paired-samples t-test and Wilcoxon test were used to confirm differences for questionnaire responses before and after game improvements. While assessing game accessibility and bradykinesia, one-way analysis of variance (ANOVA), t-test with Bonferroni correction, Kruskal-Wallis test and Wilcoxon test with Bonferroni correction were used to confirm the differences between groups. **Results and Discussion:** The heuristic evaluation contemplated all the 14 heuristics proposed by Shneiderman, which allowed the implementation of improvements

in the game. The questionnaires and the semi-structured interview also contributed to improve the usability of the game. The accessibility evaluation revealed no statistically significant differences ($p < 0.05$) between groups, except for the healthy group and the PD group in both states of medication during Phase 3. In bradykinesia assessment, significant differences were found between groups for all comparisons ($p < 0.05$). In most phases, CG participants obtained the best results for RT and AV, followed by EG in the ON state and EG in the OFF state. Regarding tremor, the probability that the peak frequencies of the PD-OFF signals fall within the frequency range of Parkinson's tremor (4-7 Hz) was higher than for the PD-ON group, which in turn was higher than for CG. For both MAV and RMS, the chance that the distribution having a bimodal aspect, which represents the presence of PD tremor, was higher for the EG in the ON and OFF states than for the CG. The PD-OFF group had the highest probability of having the highest peak power in the signal than the other groups. In summary, MAV and RMS showed strong correlation with MDS-UPDRS. **Conclusion:** The *RehaBEElitation* serious game is an alternative tool for assessing the main motor symptoms of PD in an objective and entertaining way. The game is compatible with the mental models of the target audience, which allowed users to easily interact with the developed system. In general, the EG participants in the OFF state showed increased bradykinesia and tremor compared to the ON state.

Keywords: Parkinson's disease; bradykinesia; tremor; objective evaluation; serious game

STUDY MOTIVATION

Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) is the most widely used clinical scale for assessing Parkinson's disease (PD) symptoms

LIMITATIONS: Subjectivity, dependence on experienced assessors, and on patient cooperation

SOLUTION: Assess PD symptoms by using inertial sensors integrated with a serious game

Multidimensional Assessment Questionnaire for Parkinson's Disease (MAQPD)

Initial version: 83 questions, 14 groups of questions

Answered by 302 individuals with PD

Factor analysis was used to validate its structure

The main motor limitations were driving and performing hand tasks

Final version: 71 questions, 3 groups of questions



Serious game for rehabilitation and monitoring of individuals with Parkinson's disease

Bee-themed game so-called *RehaBEElitation*

Four phases, each one representing a bee's task in the real world

Human machine interface device: glove with inertial and tactile sensors

Movements incorporated into the game: *hand opening-closing, wrist extension-flexion, wrist adduction-abduction, finger tapping and forearm supination-pronation*

The game presents high usability and accessibility

Objective assessment of bradykinesia

Voluntary movement detection: Singular Spectrum Analysis (SSA)

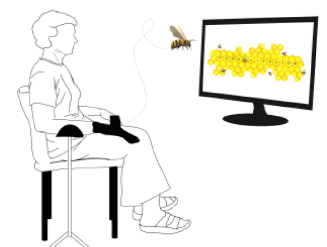
Bradykinesia assessment: MDS-UPDRS and by estimating players' response time (RT) and angular velocity (AV)

CG participants obtained the best results for RT and AV, followed by EG in the ON state and EG in the OFF state

DATA COLLECTION

Experimental Group (EG):
15 individuals with PD
ON and OFF medication states

Control Group (CG):
15 healthy individuals



Objective assessment of tremor

Tremor detection: original signal – trend

Tremor assessment: estimation of the mean absolute value (MAV), root mean square (RMS) and power spectral density (PSD) of the gyroscope signals

EG participants in the OFF state showed increased tremor compared to the ON state and to the healthy subjects

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List of Abbreviations and Acronyms

10WT 10 Meter Walk Test

ADL activities of daily living

AI Apathy Inventory

ANOVA one-way analysis of variance

AR augmented reality

ARAT Action Research Arm Test

AV angular velocity

BAASTA Battery for the Assessment of Auditory Sensorimotor and Timing Abilities

BBS Berg Balance Scale

BBT Box and Blocks Test

BPM Business Process Model

BPMN Business Process Model Notation

CG control group

CIT Constraint Induced Therapy

COVID–19 Coronavirus disease–19

CSQ Client Satisfaction Questionnaire

DBS deep brain stimulation

DGI Dynamic Gait Index

DNA deoxyribonucleic acid

DSST Digit Symbol Substitution Test

EG experimental group

EMD Empirical Mode Decomposition

FA factor analysis

FAB Frontal Assessment Battery

FGA Functional Gait Assessment

FMA Fugl–Meyer Assessment

GEQ Game Experience Questionnaire

HMD Head Mounted Display

HMI human machine interface

INPI National Institute of Industrial Property

IQCODE Informant Questionnaire on Cognitive Decline in the Elderly

KMO Kaiser—Meyer—Olkin

MAQPD Multidimensional Assessment Questionnaire for Individuals with Parkinson’s
Disease

MAS Motor Assessment Scale

MAV mean absolute value

MDRT Multi–Directional Reach Test

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

MFES Modified Falls Efficacy Scale

MINI–BES Mini–Balance Evaluation Systems

MMSE Mini Mental State Examination

MMT Manual Muscle Testing

MoCA Montreal Cognitive Assessment

MPI Multidimensional Pain Inventory

MSL Maximum Step Length

NHP Nottingham Health Profile

NPI Neuropsychiatric Inventory

OST–HMD Optical-See Through Head Mounted Display

PCA principal component analysis

PD Parkinson’s disease

PDQ–39 Parkinson’s Disease Questionnaire–39

PPT Purdue Pegboard Test

PRISMA Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PSD power spectral density

ReMoVes Remote Monitoring Validation Engineering System

RMS root mean square

RQ research questions

RT response time

SBEB Brazilian Society of Biomedical Engineering

Sd standard deviation

SEQ Suitability Evaluation Questionnaire

SF–36 Short-Form Health Survey

SFSS Short Flow State Scale

SGs serious games

SSA Singular Spectrum Analysis

SSD Singular Spectrum Decomposition

SST Sit-to-Stand Test

SUS System Usability Scale

TEMPA Test d’Évaluation des Membres Supérieurs de Personnes Âgées

TLX Task Load Index

TMT Trial Making Test

TUG Time Up and Go

UK United Kingdom

VHI Voice Handicap Index

VR virtual reality

WHO World Health Organization

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Introduction

1.1 Problem formulation

Individuals with Parkinson's disease (PD) need physical training to relieve the motor symptoms caused by the disease (107). However, the low levels of dopamine in the brain of these patients can cause demotivation, depression, and apathy, hindering their adherence to rehabilitation programs (130).

An alternative and more motivating way to perform physical training is by using serious games and virtual reality (77). Several games are currently developed, but most of them do not consider the experiences of the target audience. Many are not designed according to real needs of professionals and patients, and therefore may not present effective results when used for clinical purposes (93). Thus, the development of a user-centered tool capable of motivating players during motor exercises, as well as enabling the monitoring and objective assessment of the main motor symptoms of the disease, became necessary.

1.2 Relevance of the thesis

PD is the second most typical chronic neurodegenerative disorder among the elderly (after only Alzheimer's) (122). PD affects approximately 2-3 % of the population aged over 65 years (133), increasing to up to 5 % in people aged over 85 years (2). The crude incidence rate of PD ranges from 4.5 to 19 per 100,000 person-years. As it is a chronic disorder with a prolonged course, the prevalence is much higher than the incidence, being between 100 and 200 per 100,000 inhabitants (117). It is estimated that in Brazil there are approximately 220 thousand individuals with PD and this number may double by the year 2030 (26).

In recent years PD has become one of the leading causes of disability worldwide, and has shown the fastest growth in prevalence among all other neurological disorders (45). Disability reduces people's quality of life and generates substantial expenses in the world

health system with consultations, rehabilitation therapies, medications, and general care (118).

Studies aimed at understanding and evaluating motor symptoms of PD can contribute to technological advances in the health domain and improve the well-being of people suffering from the disease. The evaluation of cardinal signs of PD in an objective manner, for example, can assist health professionals to perform an accurate diagnosis of this disorder. Moreover, a playful and motivating interaction tool for motor training can provide a more pleasurable therapeutic experience for patients.

1.3 Research objectives

To develop and validate a serious game for rehabilitation and monitoring of individuals with Parkinson's disease; and, using the developed system, to evaluate bradykinesia and tremor, two motor symptoms of the disease.

1.4 Thesis objectives

To meet the research objectives, the following goals were formulated:

- To develop a literature review on the use of serious games for rehabilitation of individuals with PD
- To develop a questionnaire for multidimensional assessment of individuals with PD
- To design a serious game that presents a coherent and compatible narrative with the mental models of the target audience
- To define a data collection protocol with patients with PD and healthy individuals, allowing the comparison of results
- To evaluate the usability of the serious game at the design stage using the Nielsen-Shneiderman heuristics, and using user-centered approaches
- To evaluate the accessibility of the serious game comparing the players' performance (scores) in each phase of the game
- To objectively assess bradykinesia and tremor using the collected motor signals

1.5 Desired outcome of the thesis

It was expected that the serious game developed would be simple, smart, customizable, self-explanatory, easy to use, and that it would provide to users a playful and pleasant

experience. In addition, the game should be compatible with the mental models of the target audience to enable easy interaction. Thus, it would be possible to improve patients' motivation during a physiotherapy session and/or assessment of disease progression.

It was also intended that the signals recorded by the human machine interface (HMI) device, specifically developed for the interaction of players with the serious game described in this study, could be used for the evaluation of bradykinesia and tremor. As these signals represent information coming from the own neuromuscular system of the individuals, it would be possible to perform a robust and objective evaluation of these symptoms. No study was found in the literature that used the signals recorded by the HMI device during the interaction of users with a serious game to objectively evaluate motor symptoms of PD, being this a great differential of this research. The study of bradykinesia and tremor would be possible thanks to the use of signal processing techniques for extracting features sensitive to both symptoms.

Another important result would be finding correlation between the extracted characteristics and the clinical evaluations and difference between the control group (CG) and the experimental group (EG), proving the efficiency of the applied processing methods.

1.6 Research methodology

This study was divided into five stages. First, for a better understanding of the general aspects of PD, research was conducted in scientific databases and academic repositories. This stage was fundamental for comprehending the pathophysiology, etiology, diagnosis, main motor and non-motor symptoms of the disease, and also to understand how the clinical assessment of a patient performed by a doctor or therapist occurs.

Then, a literature review was conducted on the use of serious games focused on the rehabilitation of individuals with PD, which allowed a better understanding about the most current technologies aimed at this application. The searches were performed in eight different databases, and 38 articles were included in the review.

The third step consisted in the development of a questionnaire for multidimensional evaluation of individuals with Parkinson's disease. This instrument was created aiming at a better understanding of the real needs of patients and to guide the serious game development. The questionnaire was answered by 302 people with PD, and its structure was validated using the factor analysis (FA) method. The questionnaire responses revealed that domestic activities involving the use of the hands were one of the most difficult for people with PD to perform.

Based on the results of the literature review and the questionnaire, a serious game for hand and wrist training was designed. The game is about bee tasks, and the main movements required from patients during a clinical evaluation using the gold standard method of evaluating individuals with PD were incorporated into the game. Furthermore,

in this stage, the usability and accessibility of the system were evaluated. Five people with PD participated in the game usability evaluation; and 15 individuals with PD in the ON and OFF medication states and 15 healthy individuals participated in the game accessibility evaluation.

The fifth stage consisted in the evaluation of the main motor symptoms of PD: bradykinesia and tremor. They were objectively evaluated using the signals recorded by the HMI device. Fifteen individuals with PD in the ON and OFF medication states and 15 healthy people, age and sex matched, participated in this stage. For comparison purposes, the inertial data analyses of the individuals with PD were compared with those of the healthy individuals.

1.7 Scientific novelty of the thesis

The scientific novelties highlighted in this thesis are:

- Development and validation of a new multidimensional assessment tool for people with PD, the so-called "Multidimensional Assessment Questionnaire of Individuals with Parkinson's Disease". This questionnaire assesses multiple and important factors, such as motor, non-motor, and pain aspects. In addition, this questionnaire is able to identify activities that PD patients face more difficulties in executing, making it possible to direct research focused on improving the individual's performance when carrying out such activities.
- Design, implementation, and validation of an original serious game for training and monitoring individuals with PD. It was designed to meet real demands of professionals and patients, and presents simple and intuitive narrative and interface, different from the games described in published studies. These characteristics facilitate the interaction of players with the system, contributing to the high acceptance of the instrument.
- Innovation in the signal decomposition method used for the objective assessment of bradykinesia. This was the first study, as far as we know, that applied the Singular Spectrum Analysis (SSA) method to the collected signals for separating voluntary movements from involuntary movements (tremor).
- Objective assessment of motor symptoms of PD using the signals recorded by the HMI device during users' interaction with the game. Again, to our knowledge, no study described in the literature has used inertial sensor signals recorded during an interaction with a serious game to assess PD motor symptoms.

1.8 Practical value of the research findings

First, the serious game presented in this study can contribute to the advancement of technological innovations in games designed for health. The description of the game architecture and organization may facilitate the system reproduction and extend its application to other scenarios. Thus, healthcare professionals and patients can benefit from the use of increasingly robust and efficient technologies capable of providing a pleasant experience to users.

The experimental protocol executed in this study resulted in a large amount of data and information collected. In addition, new data collections using the game are currently being carried out. These data will be shared/made available worldwide (as approved by UFU's research ethics committee), contributing to the Open Science policy. Sharing and making scientific data available brings numerous advantages to science as a whole: (i) increases the impact and visibility of research internationally, (ii) promotes innovation and new potential uses of data, (iii) drives new collaborations between users, (iv) maximizes transparency and responsibility, (v) encourages validation of research methods, and (vi) reduces the cost of data collection (17, 129).

Furthermore, the study carried out to evaluate bradykinesia and tremor contributes to improving the reliability of the PD diagnosis. For an individual to be diagnosed with PD, he must necessarily present bradykinesia and another symptom (73). Thus, the objective evaluation of these cardinal signs helps the specialist in his decision making, ensuring a safe diagnosis of the disease.

1.9 Dissemination of the research results

The survey findings were published in nineteen scientific vehicles, five of which were papers in peer-reviewed journals and thirteen in conference proceedings. The developed technology was also disseminated in several digital media, listed below. In addition, the system was registered at the National Institute of Industrial Property (INPI).

Articles published in scientific journals:

1. **Mendes, L. C.** ; De Sá, A. A. R. ; Marques, I. A. ; Morère, Y. ; Andrade, A. de O. *RehaBEElitation: the architecture and organization of a serious game to evaluate motor signs in Parkinson's disease. PeerJ Computer Science (JCR 2.410)*, v. 9, p. e1267, 2023.
2. **Mendes, L. C.** ; Marques, I. A. ; Alves, C. M. ; Vieira, M. F. ; Júnior, E. A. L. ; Pereira, A. A. ; Naves, E. L. M. ; Oliveira, F. H. M. ; Bourhis, G. ; Pino, P. ; Morère, Y. ; Andrade, A. de O. Multidimensional Assessment of Individuals with

Parkinson's Disease: Development and Structure Validation of a Self-Assessment Questionnaire. *Healthcare* (JCR 3.160), v. 10, p. 1823, 2022.

3. Alves, C. M. ; Rezende, A. R. ; Marques, I. A. ; **Mendes, L. C.** ; Vieira, M. F. ; Júnior, E. A. L. ; Pereira, A. A. ; Oliveira, F. H. M. ; De Souza, L. P. S. ; Bourhis, G. ; Pino, P. ; Andrade, A. de O. ; Morère, Y. ; Naves, E. L. M. Wrist Rigidity Evaluation in Parkinson's Disease: A Scoping Review. *Healthcare* (JCR 3.160), v. 10, p. 2178, 2022.
4. Marques, I. A. ; Alves, C. M. ; Rezende, A. R. ; **Mendes, L. C.** ; Paiva, T. S. ; Cyrino, G. F. ; Souza, J. T. ; Silva, M. A. M. ; Souza, L. A. P. S. ; Naves, E. L. M. Virtual reality and serious game therapy for post-stroke individuals: A preliminary study with humanized rehabilitation approach protocol. *Complementary Therapies in Clinical Practice* (JCR 3.577), v. 49, p. 101681, 2022.
5. Oliveira, L. ; **Mendes, L. C.** ; Lopes, R. A. ; Carneiro, J. A. ; Cardoso, A. ; Junior, E. A. L. ; Andrade, A. de O. A systematic review of serious games used for rehabilitation of individuals with Parkinson's disease. *Research On Biomedical Engineering*, v. 35, p. 1-17, 2021.

Articles published in conferences:

1. **Mendes, L. C.** ; Cabral, A. M. ; Alves, C. M. ; Morere, Y. ; Andrade, A. de O. Objective Assessment of Tremor in Parkinson's Disease Using the *RehaBEElitation* Serious Game. In: 2023 IEEE International Conference on Metrology for eXtended Reality, Artificial Intelligence and Neural Engineering (IEEE MetroXRINE), 2023, Milan. 2023. p. 1-6.
2. **Mendes, L. C.** ; Cabral, A. M. ; Alves, C. M. ; Morere, Y. ; Marques, I. A. ; Andrade, A. de O. Objective Evaluation of Bradykinesia Using the *RehaBEElitation* Serious Game. In: 2022 IEEE Workshop on Complexity in Engineering (COMPENG), 2022, Florence. 2022 IEEE Workshop on Complexity in Engineering (COMPENG), 2022. p. 1-5.
3. **Mendes, L. C.** ; Alves, C. M. ; Marques, I. A. ; Pereira, A. A. ; Morere, Y. ; Andrade, A. de O. . Singular Spectrum Analysis: A Signal Decomposition Method Applied for Parkinson's Disease. In: XIV Simpósio de Engenharia Biomédica, 2022, Uberlândia. Anais do XIV Simpósio de Engenharia Biomédica, 2022.
4. Alves, C. M. ; **Mendes, L. C.** ; Rezende, A. R. ; Marques, I. A. ; Andrade, A. de O. ; Morere, Y. ; Naves, E. L. M. mlr3 Package in R to Classify and Interpret Data. In: XIV Simpósio de Engenharia Biomédica, 2022, Uberlândia. Anais do XIV Simpósio de Engenharia Biomédica, 2022.

5. Lima, K. R. ; Alves, C. M. ; **Mendes, L. C.** ; Marques, I. A. ; Rosa, R. R. ; Vieira, M. F. ; Oliveira, F. H. M. ; Morere, Y. ; Junior, E. A. L. ; Naves, E. L. M. ; Souza, L. P. S. ; Pereira, A. A. ; Sa, A. A. R. ; Andrade, A. de O. Avaliação da Destreza Manual de Indivíduos com Doença de Parkinson. In: XIV Simpósio de Engenharia Biomédica, 2022, Uberlândia. Anais do XIV Simpósio de Engenharia Biomédica, 2022.
6. Lima, K. R. ; **Mendes, L. C.** ; Alves, C. M. ; Moraes, C. R. ; Souza, L. P. S. ; Andrade, A. de O. Protocolo Experimental Baseado em Jogo Sérioso para a Melhora da Destreza Manual em Indivíduos com a Doença de Parkinson. In: XIV Simpósio de Engenharia Biomédica, 2022, Uberlândia. Anais do XIV Simpósio de Engenharia Biomédica, 2022.
7. **Mendes, L. C.** ; Marques, I. A. ; Alves, C. M. ; Sa, A. A. R. ; Rosa, R. R. ; Lima, K. R. ; Luiz, L. M. D. ; Vieira, M. F. ; Naves, E. L. M. ; Junior, E. A. L. ; Oliveira, F. H. M. ; Pereira, A. A. ; Bourhis, G. ; Pino, P. ; Morere, Y. ; Andrade, A. de O. Évaluation de l'utilisabilité d'un jeu sérieux pour la rééducation des personnes atteintes de la maladie de Parkinson. In: G. Thomann, Y. Morère. (Org.). Handicap 2022 Humaines et artificielles, les intelligences au service du handicap. 1ed.Paris: , 2022, v. , p. 40-45.
8. Marques, I. A. ; **Mendes, L. C.** ; Alves, C. M. ; Luiz, L. M. D. ; Rosa, R. R. ; Lima, K. R. ; Sa, A. A. R. ; Junior, E. A. L. ; Oliveira, F. H. M. ; Vieira, M. F. ; Bourhis, G. ; Pino, P. ; Pereira, A. A. ; Naves, E. L. M. ; Morere, Y. ; Andrade, A. de O. Évaluation de l'influence du professionnel de santé dans l'application du jeu sérieux *RehaBEElitation* pour les patients atteints de la maladie de Parkinson. In: G. Thomann, Y. Morère. (Org.). Handicap 2022 Humaines et artificielles, les intelligences au service du handicap. 1ed.Paris: , 2022, v. , p. 35-39.
9. Alves, C. M. ; Rosa, R. R. ; Souza, J. T. ; **Mendes, L. C.** ; Marques, I. A. ; Luiz, L. M. D. ; Junior, E. A. L. ; Oliveira, F. H. M. ; Vieira, M. F. ; Pereira, A. A. ; Bourhis, G. ; Pino, P. ; Andrade, A. de O. ; Naves, E. L. M. ; Morere, Y. Une nouvelle interface homme-machine pour la rééducation des personnes atteintes de la maladie de Parkinson. In: G. Thomann, Y. Morère. (Org.). Handicap 2022 Humaines et artificielles, les intelligences au service du handicap. 1ed.Paris: , 2022, v. , p. 81-86.
10. Rosa, R. R. ; Sá, A. A. R. de ; Alves, C. M. ; Marques, I. A. ; Lima, K. R. ; **Mendes, L. C.** ; Andrade, A. de O. A Human Machine Interface for Serious Games applied to the Rehabilitation of Individuals with Parkinson's Disease. In: XIII SEB; Simpósio de Engenharia Biomédica, 2021, Uberlândia. XIII SEB, 2021.

11. **Mendes, L. C.** ; Marques, I. A. ; Sá, A. A. R. de ; Alves, C. M. ; Rosa, R. R. ; Lima, K. R. ; Vieira, M. F. ; Oliveira, F. H. M. de ; Pino, P. ; Júnior, E. A. L. ; Naves, E. L. M. ; Morere, Y. ; Pereira, A. A. ; Andrade, A. de O. A Systematic Review of Serious Games Used for Upper-Limb Rehabilitation of Individuals with Parkinson's Disease. In: XIII SEB - Simpósio de Engenharia Biomédica, 2021, Uberlândia. XIII SEB, 2021.
12. **Mendes, L. C.** ; Marques, I. A. ; Sá, A. A. R. de ; Alves, C. M. ; Rosa, R. R. ; Lima, K. R. ; Pereira, A. A. ; Naves, E. L. M. ; Júnior, E. A. L. ; Morere, Y. ; Bourhis, G. ; Pino, P. ; Vieira, M. F. ; Oliveira, F. H. M. de ; Andrade, A. de O. Pain assessment of individuals with Parkinson's disease. In: Seventeenth International Symposium on Medical Information Processing and Analysis, 2021, Campinas. 17th International Symposium on Medical Information Processing and Analysis, 2021. p. 61.
13. **Mendes, L. C.** ; Marques, I. A. ; Sa, A. A. R. ; Alves, C. M. ; Rosa, R. R. ; Lima, K. R. ; Pereira, A. A. ; Naves, E. L. M. ; Junior, E. L. ; Oliveira, F. H. M. ; Vieira, M. F. ; Bourhis, G. ; Pino, P. ; Morere, Y. ; Andrade, A. de O. *RehaBEElitation* : Un Jeu Sérieux pour la Rééducation des Membres Supérieurs des Personnes Atteintes de la Maladie de Parkinson. In: Colloque « Jeunes Chercheuses, Jeunes Chercheurs », 2021, Paris. Handicap, Vieillissement, Autonomie, Insertion, Technologies. Lyon: AGG PRINT, 2021. p. 35-40.
14. Alves, C. M. ; Rezende, A. R. ; Marques, I. A. ; **Mendes, L. C.** ; Sa, A. A. R. ; Rosa, R. R. ; Lima, K. R. ; Oliveira, F. H. M. ; Pereira, A. A. ; Junior, E. L. ; Vieira, M. F. ; Bourhis, G. ; Pino, P. ; Andrade, A. de O. ; Morere, Y. ; Naves, E. L. M. Proposition d'une nouvelle méthode d'analyse quantitative de la rigidité du poignet dans la maladie de Parkinson. In: Colloque « Jeunes Chercheuses, Jeunes Chercheurs », 2021, Paris. Handicap, Vieillissement, Autonomie, Insertion, Technologies. Lyon: AGG PRINT, 2021. p. 41-47.

Research dissemination links:

1. O Globo (Brazilian newspaper)

Title: "Parkinson: Brazilian university creates game for patients with the disease; understand"

<https://oglobo.globo.com/saude/noticia/2023/07/parkinson-universidade-brasileira-cria-game-para-pacientes-com-a-doenca-entenda.ghtml>

2. Canal Tech (Brazilian multimedia platform)

Title: Brazilian game can help in the recovery of Parkinson's patients

<https://canaltech.com.br/saude/jogo-brasileiro-pode-ajudar-na-recuperacao-de-pacientes-com-parkinson-254724/>

3. Band Triângulo (Brazilian television broadcaster)

Title: “*RehaBEElitation* - Games help treat Parkinson’s disease”

<https://www.youtube.com/watch?v=jJRr7CkCPdo>

4. Filipe Deschamps (Brazilian newsletter)

Title: “Game developed by postgraduate students in Biomedical Engineering at the Federal University of Uberlândia promotes the treatment of patients with Parkinson’s disease”

<https://filipedeschamps.com.br/newsletter>

5. MGTV – MG TEC (Brazilian television broadcaster)

Title: “Treatment for Parkinson’s disease developed at the Federal University of Uberlândia”

<https://globoplay.globo.com/v/11813814/>

Received awards:

1. The developed serious game won the prize at the eleventh edition of the "Challenge Handicap & Technologie" event in Metz on 12 May 2023. The first-place prize was awarded in the "Autonomy" category, related to promoting the autonomy of people in situations of dependency.
2. The project also received the SBEB Boston Scientific Award for Innovation in Biomedical Engineering 2023. The award, created in a partnership between the Brazilian Society of Biomedical Engineering (SBEB) and Boston Scientific, aims to value and encourage the academic production of projects and work in biomedical engineering aimed at tackling the difficulties of the Brazilian health system and public health services in Latin America.

1.10 Thesis structure

This thesis is divided into seven chapters:

- Chapter 1: dedicated to present the introduction of this work, in which the formulation of the problem, relevance of the thesis, objectives, expected results, structure of the manuscript and vehicles for disseminating the thesis findings were described.

- Chapter 2: presents several aspects related to PD, such as the most common symptoms, and the methods used for diagnosis, assessment, and treatment.
- Chapter 3: presents the systematic review developed, whose objective was to identify and evaluate the scenario of the use of serious games for the rehabilitation of individuals with PD.
- Chapter 4: presents the development and validation of the multidimensional assessment questionnaire for individuals with PD.
- Chapter 5: describes in detail the architecture and organization of the designed serious game, as well as presents its usability and accessibility evaluation.
- Chapter 6: presents the objective evaluation of bradykinesia and tremor.
- Chapter 7: describes the final considerations of the study.

This thesis contains a section of bibliographical references and Appendices (A to G). The volume of the document is 143 pages, in which 38 figures and 23 tables are found. Additionally, 176 items are cited in the thesis.

1.11 Relevant considerations

This study was the result of a cotutelle doctorate between the Federal University of Uberlândia (Brazil) and the University of Lorraine (in Metz, France), funded by the CAPES—COFECUB programme. The doctoral student conducted her research at UFU from August/2019 – September/2021 and from February/2023 – December/2023, and at UL from September/2021 – February/2023.

The research was carried out with the support of the National Council for Scientific and Technological Development (CNPq), Coordination for the Improvement of Higher Education Personnel (CAPES) (CAPES - Program CAPES/DFATD-88887.159028/2017-00, Program CAPES/COFECUB-88881.370894/2019-01) and the Foundation for Research Support of the State of Minas Gerais (FAPEMIG). Adriano de Oliveira Andrade is fellow of CNPq, Brazil (302942/2022-0 and 304818/2018-6); and Luanne Cardoso Mendes and Yann Morère are fellow of the Program CAPES/COFECUB (88887.612297/2021-00 and MA957/20 2019-2023, respectively).

It is important to emphasise that this research was carried out as part of a collaborative project between undergraduate, master's, doctoral and post-doctoral students. Thus, each student acted more actively at different stages, for example: Rodrigo Ramos Rosa, a master's student, focused on developing the HMI device; Luanne Cardoso Mendes, the author of this thesis, worked more actively on creating the game's narrative, designing each phase, evaluating usability and accessibility, and objectively assessing bradykinesia

and tremor; Carlos Tobias Machado, an undergraduate student, developed the phases' scenarios and modelled the bee and other game objects; and Angela Abreu Rosa de Sá, a post-doctoral student, coded the game.

Parkinson's Disease

An overview of Parkinson's disease will be presented in this chapter.

Parkinson's disease (PD) was first defined in 1817 by the British physician James Parkinson (1755-1824) in a paper entitled "An Essay on the Shaking Palsy". The physician described the disease as an involuntary trembling movement with decreased muscle strength, with a propensity to bend the trunk forward, tending to change from a walking pace to a running pace. James Parkinson stated in his work that PD was a different form of paralysis, named "agitating paralysis", characterised by tremors and gait festination, but without any sensory impairment (124).

It is currently known that PD is a chronic neurodegenerative disorder caused by the progressive loss of dopaminergic neurons of the mesencephalon's substantia nigra (117). These neurons, under normal conditions, are responsible for producing and storing dopamine, a neurotransmitter that acts on a complex neuronal network regulating the execution of movements (133). As this neurotransmitter is responsible for conducting information for correct movement control, its deficiency predominantly affects the individual's motor function, with interference in cognitive systems (111). Figure 2.1 illustrates the mesencephalic substantia nigra degeneration in an individual with PD.

The main motor symptoms of the disease are: bradykinesia, which is manifested as slowness of movement; rest tremor, defined as a repetitive movement of any limb or body part, which occurs when it is not actively moving; muscle rigidity, defined as a muscle tone increase when the limb is moved passively; and postural instability, which refers to an impaired reaction when balance is disturbed (81, 134). Delayed onset motor symptoms include freezing of gait, speech difficulty, falls, and difficulty swallowing (117).

In addition to the motor symptoms of the disease, some non-motor symptoms can be manifested even before the motor symptoms. The main non-motor symptoms of PD are sleep behaviour disorder, constipation, pain, orthostatic hypotension (drop in blood pressure), paresthesia (abnormal sensory symptoms, characterised by itching, tingling, and burning), erectile dysfunction, depression, sleepiness, low olfactory sensitivity, rapid eye movements and changes in personality (117, 61). All these symptoms significantly

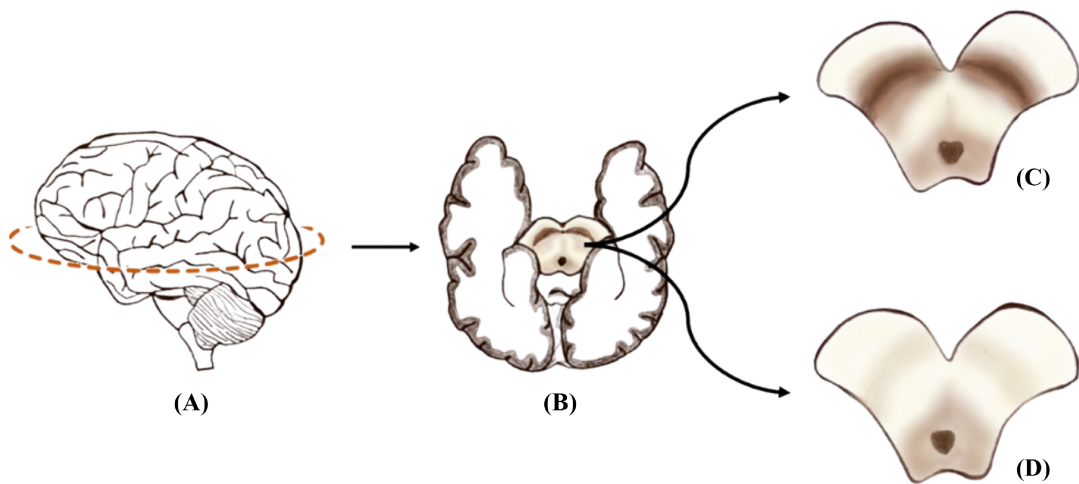


Figure 2.1 – Mesencephalon of healthy subjects and Parkinson’s disease patients. (A) Brain sectioned in the transverse plane. (B) Top view of the sectioned brain, with the mesencephalon at the centre. (C) Mesencephalon of a healthy individual, with preserved substantia nigra. (D) Mesencephalon of a patient with PD, with compromised substantia nigra.

affect the quality of life of those with the disease and increase individuals’ disability (2). Figure 2.2 characterises an individual with PD.

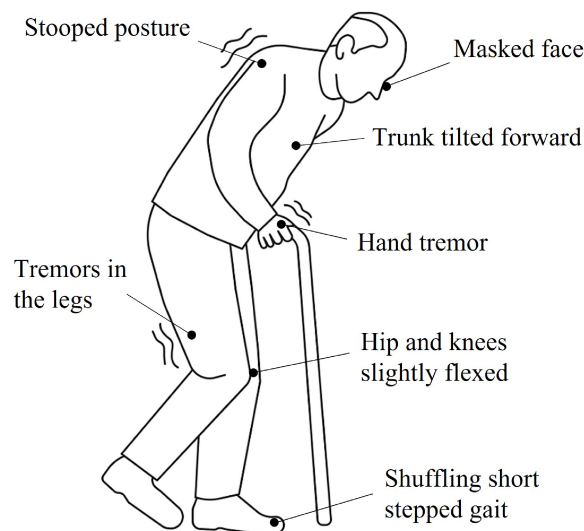


Figure 2.2 – Typical characteristics of a person with PD.

Current theories on the etiology and pathogenesis of PD consider this disorder multifactorial and of unknown origin. However, it is believed that this syndrome is the result of a genetic predisposition, possibly interacting with environmental factors (111).

Parkinsonian traits may be discrete and subtle at the onset of the disease, and therefore an incorrect diagnosis is very common (2). So far, there are no exams, definitive biological biomarkers or quantitative tests that can indicate the disease diagnosis. However, some criteria help in this process, such as anamnesis, observation, qualitative questionnaires,

and the organism's response to medications indicated to treat the motor symptoms of PD (164).

The most widely used clinical tool for assessing patients with PD is the Movement Disorders Society–Unified Parkinson's Disease Rating Scale (MDS–UPDRS) (101). It was introduced in 1987 by movement disorder experts and updated in 2008 (2, 111). The MDS–UPDRS was designed to follow the longitudinal course of the disease and assesses motor and non-motor characteristics of the patient. It is divided into four parts: Part I – non-motor experiences of daily living; Part II – motor experiences of daily living, Part III – motor condition; and Part IV – motor complications (58). In this type of assessment, the examiner analyses the patient and assigns a score between 0 (normal) and 4 (severe) to indicate the disease level of impairment, i.e., scores are given according to the visual perception of the examiner (110).

Another scale frequently used to assess PD is the Hoehn and Yahr (H&Y), created in 1967. This scale is a simple staging that evaluates the overall severity of the disease based on bilateral motor dysfunction, motor disability, gait impairment and balance impairment (2). Such features are assessed and rated from 1 to 5 to indicate the disease severity.

There is no cure for PD until now. However, the treatment of the symptoms is fundamental so that the functional independence of patients can be improved and/or maintained, besides reducing the discomfort suffered by these individuals. The motor symptoms of PD have been optimized using pharmacotherapy, neurosurgery, and supportive therapy (107).

The pharmacological treatments are mainly based on dopamine, and the most used drug is levodopa. Its use is recommended in all stages of the syndrome, and although it doesn't delay the progression of the disease, the medication has a very efficient action in reducing motor symptoms (3). It penetrates the haemato-encephalic barrier and is converted into dopamine by the dopa decarboxylase enzyme, exerting the effects of this neurotransmitter (133).

Deep brain stimulation (DBS) is the most common neurosurgical method for the treatment of PD symptoms and is very useful for individuals who do not respond to the effects of medication. DBS consists of implanting electrodes unilaterally or bilaterally in the subthalamic nucleus or in the inner globus pallidus, connected to a stimulator. This device produces electrical impulses that stimulate the region of the brain responsible for causing the motor symptoms of PD, instantly relieving symptoms such as tremor. DBS is an adjustable and reversible procedure (3).

Supportive therapies include physiotherapy, speech therapy, occupational therapy, dietary measures, among others (107). All these various approaches can benefit different motor aspects of PD and should be combined to achieve better results (3).

Rehabilitation for individuals with PD is important because, even with optimal medical treatment, patients suffer deterioration in body function. Therefore, the inclusion of

rehabilitation therapies to pharmacological and neurosurgical treatment is highly recommended (165).

Physiotherapy allows patients to maintain their mobility and independence. It involves posture, balance, strength, and gait exercises, using cognitive strategies to optimize the individual's well-being, improving their quality of life (107). These exercises stimulate the brain allowing neurons to create new connections to alleviate symptoms and overcome the difficulties imposed by the disease (24).

However, traditional physiotherapy exercises can be tiring, repetitive and time-consuming, causing lack of motivation in patients (who already suffer from depression and apathy due to low levels of dopamine in their brains) (130). Moreover, conventional training is only effective when the exercises are done daily and intensively (49, 160). These are the major problems of traditional physiotherapy and can contribute to a drop in patient adherence to treatment or even patient dropout from therapy programmes.

Thus, other approaches for movement rehabilitation are being increasingly explored, including the use of serious games (SGs) and virtual reality (VR) (160, 4). According to (14), SGs and VR favour the absorption of concepts and psychomotor skills in patients during rehabilitation. The ludic stimulates players' creativity and interaction, and associated with SGs and VR, enables the practice of activities considered impossible to be performed in a clinical environment (4, 65).

Serious Games for Individuals with Parkinson's Disease

The purpose of this chapter is to present a systematic review that aims to identify and evaluate the scenario of the use of serious games in the rehabilitation of individuals with Parkinson's disease.

3.1 Introduction

As previously mentioned, Parkinson's disease (PD) is one of the most common neurodegenerative diseases in individuals over 60 years of age (2). The motor symptoms of PD cause functional limitations and dependence in patients, which can lead to depression and isolation. Consequently, there is a need to conduct research that promotes patients' quality of life by providing them with greater independence to perform activities of daily living (116).

The use of serious games (SGs) and virtual reality (VR) to treat the motor symptoms of PD have been increasingly widespread in healthcare. SGs are games that combine serious intentions with educational, professional, or medical purposes (that are not primarily for entertainment), capable of generating some specific knowledge or skills (30). When used for rehabilitation, SGs can improve or train the movement and cognition of patients suffering from a variety of diseases, such as PD, stroke, spinal cord injury, among others (10).

As exercise through games is perceived as fun and not as therapy by the user (4), they are considered very promising and effective tools that can be exploited for rehabilitation (10). The use of game-based therapy does not simply enhance performance in tasks execution, but also positively affects the physical and mental condition of patients (160). This is because SGs enable a greater patient immersion in the activity and a greater sense of accomplishment and joy, improving their whole experience (160, 4). SGs strengthen patients' participation in rehabilitation programs because of the motivational and engagement aspects provided by the game (30).

VR is a 3D interface technology that involves simulation and real-time interactions using multiple sensory channels for acting or feedback (19). This technology allows navigation and manipulation of objects in a realistic 3D environment (21). Physical rehabilitation performed with the aid of VR has presented several advantages over conventional physical rehabilitation (65). VR can provide interactive feedback on patient performance, while giving to the patient a more stimulating and motivating experience than a traditional rehabilitation session (19). Moreover, studies that compared systems that used VR with systems without this technology for rehabilitation demonstrated that versions with VR present better results compared to versions without VR (38). This is because such technology facilitates motor learning and neuroplasticity, as well as exploiting users' cognitive abilities (65, 19, 109).

More recently, a deeper interest has been noted in developing alternative methods based on SGs for evaluation and monitoring of PD. However, the incorporation of this type of technology into the clinical scenario needs to be implemented more effectively. As a result, this review aims to identify and evaluate the scenario of the use of SGs in the motor rehabilitation of people with PD.

3.2 Methods

To develop this study, the methodology defined in (76) was adopted, which proposes comprehensive guidelines for creating a systematic literature review.

3.2.1 Planning the systematic literature review

The main research question in this study was "How have serious games contributed towards helping to treat the symptoms in individuals who suffer from Parkinson's disease?"

The specific research questions to guide the selection of primary studies were:

- RQ01 – What types of games were implemented to help in the treatment of symptoms associated with Parkinson's disease?
- RQ02 – What types of technologies (virtual reality – VR, augmented reality – AR, 3D, 2D) were identified in the games?
- RQ03 – Are the identified games currently used in conjunction with any multimodal device? Which one(s)?
- RQ04 – Were the identified games based on any protocol or treatment? Which one(s)?
- RQ05 – Did the proposed solutions present any instrument for assessing the game and monitoring the results obtained by the patient with Parkinson's disease? Which one(s)?

RQ06 – Did the games help in the treatment of any specific symptom presented by individuals with Parkinson’s disease? Which one(s)?

RQ07 – Did the assessment of the technologies consider experiments with patients?

3.2.2 Systematic literature review

The main stages for conducting the systematic review were:

- Stage 1 – Identification of keywords: The keywords were defined based on the guiding question of the study, namely: “Serious Game” and “Parkinson”.
- Stage 2 – Definition of the search string: The search strings were assembled through the association of keywords in English. String: (“Serious Game” and “Parkinson”).
- Stage 3 – Publication period: The searches were performed between February 2020 and February 2021. The publication period of the papers was from 2010 to 2021.
- Stage 4 – Databases: The review was performed considering papers belonging to the following indexed databases: Web of Science, Scopus, PubMed, Bireme, ScienceDirect, IEEE Digital Library, ACM Digital Library and Google Scholar.
- Stage 5 – Selection of primary studies: For this selection, inclusion and exclusion criteria were defined.
 - Inclusion Criteria (IC): [IC01] – Studies that addressed the development and/or use of a serious game capable of assisting people in the treatment of any symptoms caused by Parkinson’s disease.
 - Exclusion Criteria (EC): [EC01] – Studies that were not in English; [EC02] – Studies that presented only commercial aspects of the developed game; [EC03] – Studies that did not answer any of the research questions specific to this study; [EC04] – Duplicate or redundant papers (for studies of the same authorship or related to the same solution, only the most recent and/or most complete was included, unless it presented some complementary information); [EC05] – Studies that presented the development of games for entertainment only; [EC06] – Studies that did not have the full-text available with open access; [EC07] – Studies that did not address the development or use of a serious game as an aid in the treatment of symptoms of Parkinson’s disease; [EC08] – Studies that did not correspond to the publication of a full article (poster, book, technical note, patent, etc.).

The study selection process was conducted as follows:

1. After searching for primary studies in the databases, those considered not relevant to the questions under investigation were excluded. This first stage of exclusion was accomplished by reading study titles and keywords. If there was any doubt about the inclusion or exclusion of a study, it was decided that it should be retained.
2. Successively, the abstract, introduction and conclusion of the studies selected in the previous stage were read, performing a second filtering.
3. The studies were read thoroughly to filter those that were considered in this review.
4. Finally, data extraction and studies quality evaluation were performed.

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) tool was used for identification, selection, eligibility, and inclusion of studies. It presents preferred reporting items for systematic reviews and meta-analysis. As an initial result of the search, 169 studies were obtained by applying the inclusion criteria, and after applying the exclusion criteria, this number was reduced to 38. The systematic process for excluding papers at each stage is represented in Figure 3.1.

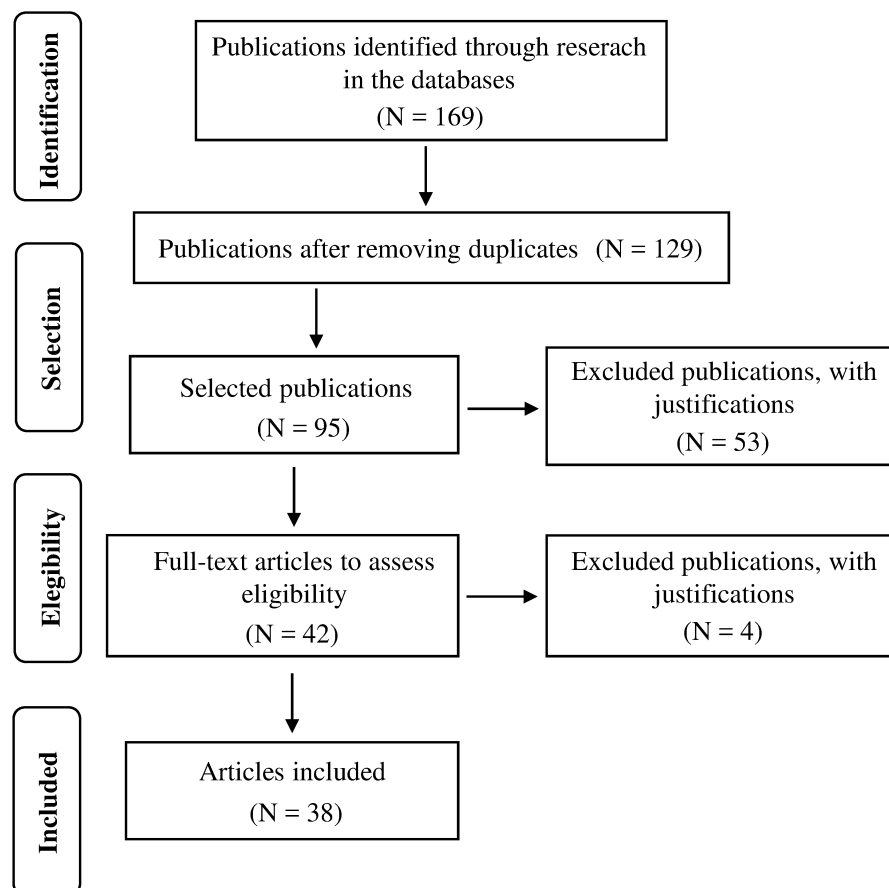


Figure 3.1 – Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), which shows the number of articles in each exclusion step.

- Stage 6 – Studies quality evaluation: In addition to the inclusion and exclusion criteria, the quality of the selected articles was also considered. This measure was obtained based on the recommendations indicated in (37), which suggests the following criteria to obtain a qualitative evaluation:

- A – Is the article based on research (or is it merely a lesson extracted based on expert opinion)?
- B – Is there a clear statement of the research objectives?
- C – Is there an adequate description of the context in which the research was conducted?
- D – Was the methodology used adequate in terms of meeting the research objectives?
- E – Was the participant recruitment strategy adequate for the research objectives?
- F – Was there a control group for comparing the results?
- G – Was data collected to address the research question?
- H – Was the data analysis sufficiently rigorous?
- I – Was the relationship between researcher and participants considered to an appropriate degree?
- J – Was there a clear statement of the results?
- L – What was developed in the study, can be applied in clinical practice?

The quality criteria were scored as follows: YES = 1 point; NO = 0 point; PARTIALLY = 0.5 point.

3.3 Profile of Selected Studies

After conducting database searches and reading the titles and keywords, 169 studies were selected. Of these, after applying the exclusion criteria, 38 papers were selected.

Most of the studies presented the development and evaluation of SGs as an auxiliary tool in the treatment of some symptoms caused by PD. These symptoms included difficulties in speech (79); gait with some disability (68, 155); motor weakness in upper limbs (46, 148) and lower limbs (4); loss of balance (155, 82, 135, 175); impairment of fine movements of fingers and hands (27, 115); cognitive problems (155, 47, 170); and low range of motion (152).

Some studies described projects that include more than one SG, as in (97), which presented the ReMoVes platform (Remote Monitoring Validation Engineering System)

with 60 variations of available games; and in (126), a study that applied four different games of Nintendo Wii Sports Resort, as well as Super Monkey Bool[®], Wii Play[®], Deca Sports[®] and Sports Resort[®]. Several of the above-mentioned issues were evaluated. On the other hand, although the study presented in (119) proposed the application of only one game, its objective was based on rehabilitation of upper and lower limbs at the same time; while the study developed by (147) dealt with both physical and mental rehabilitation. The other papers, in general, explored only the treatment of one symptom.

Some papers addressed specifically the development of one SG. These studies pointed out development guidelines (123), design elements (34) and framework (52) for creating SGs that assist in the rehabilitation process of individuals with PD.

Other explored themes were: evaluation of commercial rhythm games for training purposes (10); evaluation of a music-based SG for rhythmic skills training (30); comparison of technological approaches of two projects belonging to the European Union's largest research programme (158); assessment of the therapist-patient relationship (121); evaluation of motor functions (114); assessment of the motor dysfunction degree of patients (94); systematic review on the potential of exergames (games commanded by body movements, such as exercise) for PD rehabilitation (55); systematic review on the use of vision-based SGs and VR systems in motor rehabilitation programs (6); proposal of a fully immersive SG system to provide an interactive virtual environment in rehabilitation process (5); proposal of a new classification for SGs used in health (169); mapping the use of SGs for neuropsychological evaluation (166). Finally, there were studies not aimed directly at individuals with PD, however, the symptoms addressed in these papers also affect PD patients (38, 22, 153, 106, 143, 150).

Figure 3.2 shows the number of studies published in each year since 2011. Most were published between 2017 and 2020 (approximately 68.42%). This suggests a current and growing interest in research related to the development and/or use of SGs to assist in the treatment of symptoms of people with PD.

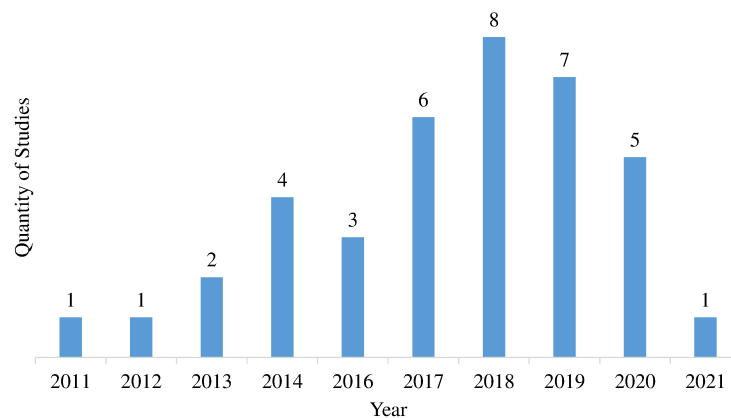


Figure 3.2 – Quantity of studies included in each year, ranging from 2011 to 2021. (This review was carried out in 2021, so studies up to this year were included.)

Figure 3.3 shows the distribution of the selected studies in each database. The articles from the Web of Science database were all excluded by the EC04 exclusion criteria, i.e., they were duplicated in other databases.

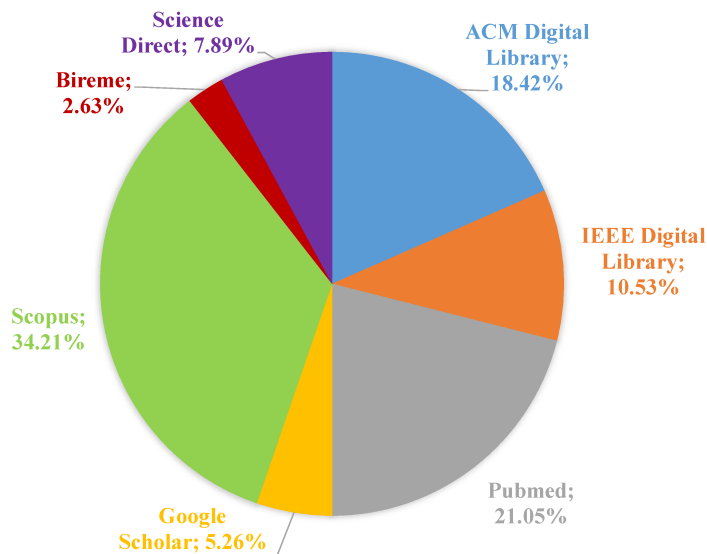


Figure 3.3 – Distribution of studies by database.

3.4 Results

3.4.1 Classification of studies regarding specific research questions

Each study was evaluated by the seven different research questions. For each one, a table listing the characteristic addressed by the question and the study reference was created. Articles that did not present/mention a specific characteristic were not indicated in the tables.

RQ01 – What types of games were implemented to help in the treatment of Parkinson’s disease symptoms?

The studies did not classify the type of games. They only described the game mechanics. Thus, the games were classified as shown in Table 3.1.

Type of game	Study
Exergame	(4); (5); (22); (27); (34); (38); (52); (82); (94); (97); (114); (115); (119); (123); (126); (135); (147); (152); (155); (175)
Musical/Rhythmic	(4); (10); (30); (79); (150)
Memory	(4); (46); (115); (121); (143); (147); (170)
Simulation	(46); (47); (148); (153); (170)

Reasoning	(46); (121); (126); (148); (155)
Haptic	(148)
Balance	(106); (175)
Race	(170)

Table 3.1 – Types of games.

Some studies are classified in more than one type of game. This fact occurs as the developed game presents phases, levels or approaches that fit in more than one classification. The game presented in (4), for example, is classified as exergame, musical/rhythmic and memory. In (155), the game is classified as exergame and reasoning; in (46), memory, simulation and reasoning games; in (148), simulation, reasoning, and haptic games; in (175), exergame and balance; in (170), memory, simulation and race; in (126), exergame and reasoning; in (147), exergame and memory; and in (121), memory and reasoning.

On the other hand, the studies (158, 55, 6, 169, 166) did not address the development of a game or did not present sufficient information about the games. Therefore, it was not possible to categorize them according to the type of game implemented.

RQ02 – What types of technologies (virtual reality - VR, augmented reality - AR, 3D, 2D) were identified in the games?

Table 3.2 presents the interfaces used in the games.

Type of interface	Study
2D	(4); (34); (52); (79); (106); (121); (150); (152); (170)
3D	(119); (135); (143); (153); (175)
VR	(5); (6); (22); (27); (38); (46); (97); (114); (115); (123); (126); (147); (148); (155)
AR	(47); (94)

Table 3.2 – Interfaces used in the games.

The studies (30, 10, 68, 82, 158, 55, 169, 166) did not present the development of a SG. Although the study (158) also did not address the development of a SG, it appears in Table 2 classified as VR as it presents a literature review on the use of SGs that employ VR.

RQ03 – Are the identified games currently used in conjunction with any multimodal device? Which one(s)?

The studies used several multimodal devices, as shown in Table 3.3.

Multimodal devices	Study
Leap Motion	(5); (46); (47); (52); (97); (114); (115); (148); (150)

Microsoft Kinect	(5); (97); (119); (135); (147); (152); (155); (158)
Microsoft Band	(97)
Nintendo Wii	(97); (123); (126)
RGB 360 cameras	(94); (158)
Smart bracelet	(158)
Binary sensors	(158)
Inertial sensors	(106); (126)
WSN sensors	(68); (153); (158)
HTC Vive	(38)
Optical-See Through Head Mounted Display (OST-HMD) with haptic controller	(94)
Oculus Rift	(114); (148)
Sony PlayStation Eye camera	(4)
Traditional devices (notebook, tablet, mouse and keyboard)	(30); (79); (121); (143); (170)
HMD	(5); (22); (27); (47)
XaviX (dance mat)	(175)

Table 3.3 – Multimodal devices used by the games.

Some studies used more than one device. In (148, 114), for example, Leap Motion and Oculus Rift were used. In (47), Leap Motion and HMD were used; in (97), Leap Motion, Microsoft Kinect, Microsoft Band and Nintendo Wii; in (126), Nintendo Wii and inertial sensors; in (158), Microsoft Kinect, RGB 360 cameras, smart bracelets, binary sensors and WSN sensors; in (94), RGB 360 cameras and Optical-See Through Head Mounted Display (OST-HMD) with haptic controller; and in (5), Leap Motion, Microsoft Kinect and HMD were used.

Other studies used only traditional devices, such as notebook and projector (79, 143); tablet (30, 121); and mouse and keyboard (170). Alternatively, in some studies specific devices were created, such as in (68, 153, 106). The studies (82, 34) did not mention the multimodal devices used. Finally, all studies that performed a systematic review (10, 55, 6, 169, 166) did not report or use multimodal devices.

RQ04 – Were the identified games based on any protocol or treatment? Which one(s)?

Table 3.4 presents the treatment protocols used.

Protocol	Study
Exercises based on traditional physiotherapy tasks	(22); (27); (46); (115); (143); (148)
Logopedic therapy	(79)
Multidirectional and target-directed stepping tasks	(175)

Training of daily activities	(47); (153)
Modified Constraint Induced Therapy (mCIT)	(38)
Guide for exercise and Parkinson's disease by the PD Society of UK	(123)
Box and Blocks Test (BBT)	(114)
Train BIG to move faster	(119)
Rhythmic training via rhythmic auditory stimulation	(30)

Table 3.4 – Protocols used by the games.

Several studies, although not reporting the use of a protocol, stated that the exercises proposed by the games were recommended/accompanied by doctors/therapists (97, 147, 52, 5). Moreover, the studies (46, 148, 27, 115, 22, 143) reported that the games tried to imitate exercises included in traditional physiotherapy, such as palm grip, finger flexion and extension, hand supination and pronation, and gait exercises. The other studies did not mention whether the games were based on any protocol or treatment.

RQ05 – Did the proposed solutions present any instrument for assessing the game and monitoring the results obtained by the patient with Parkinson's disease? Which one(s)?

Table 3.5 shows the instruments for evaluating games and monitoring patients.

Instrument	Study
Game Experience Questionnaire (GEQ)	(4); (79); (94)
VHI: 10 (Voice Handicap Index: 10)	(79)
Observation of occupational therapists	(27); (47); (153)
Recording of patients playing	(38); (47); (147); (152)
Mini Mental State Examination (MMSE)	(47); (143); (147)
Time Up and Go Test (TUG)	(22); (68); (82); (106)
10-Meter Walk Test (10WT)	(82); (155)
6 minute Walk test	(82)
Berg Balance Scale (BBS)	(68); (106); (175)
Short-Form Health Survey (SF-36)	(175)
Multi-Directional Reach Test (MDRT)	(175)
Maximum Step Length (MSL) test	(175)
Modified Falls Efficacy Scale (MFES)	(175)
Nottingham Health Profile (NHP)	(106)
Jamar® hydraulic hand dynamometer	(46); (115); (148)
Task Load Index (TLX)	(94)
System Usability Scale (SUS)	(4); (5); (27); (94)
Box and Blocks Test (BBT)	(46); (114); (115); (148)
Purdue Pegboard Test (PPT)	(46); (115); (148)

Client Satisfaction Questionnaire (CSQ-8)	(46); (148)
Action Research Arm Test (ARAT)	(148)
Movement Disorder Society–Unified Parkinson’s Disease Rating Scale (MDS–UPDRS)	(30); (126)
Suitability Evaluation Questionnaire (SEQ)	(30)
Battery for the Assessment of Auditory Sensorimotor and Timing Abilities (BAASTA)	(30)
Montreal Cognitive Assessment (MoCA)	(30); (155)
Parkinson’s Disease Questionnaire–39 (PDQ–39)	(30); (126); (155)
9 hole peg test	(46); (126)
Test d’Évaluation des Membres Supérieurs de Personnes Âgées (TEMPA)	(126)
Functional Gait Assessment (FGA)	(155)
Dynamic Gait Index (DGI)	(155)
Mini Balance Evaluation Systems Test (Mini-BESTest)	(155)
Five times Sit-to-Stand Test (SST)	(155)
Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)	(143)
Free and Cued Selective Reminding Test	(143)
Trial Making Test A (TMT A)	(143)
Stroop test	(143)
Digit Symbol Substitution Test (DSST)	(143)
Frontal Assessment Battery (FAB)	(143)
Neuropsychiatric Inventory (NPI)	(143)
Apathy Inventory (AI; clinician version)	(143)
Manual Muscle Testing (MMT)	(22)
Fugl-Meyer Assessment (FMA)	(22)
Motor Assessment Scale (MAS)	(22)
Barthel Index	(22)
Parameters of gait kinematics	(22)

Table 3.5 – Instruments for evaluation and monitoring.

Several studies presented more than one instrument for assessment and monitoring. This fact is quite coherent, as the assessment instrument refers to the game itself, while the monitoring instrument refers to the assessment of clinical and psychological/psychosocial aspects of patients. The other studies did not provide information on the use of an instrument for assessing the game and monitoring the patient.

RQ06 – Did the games help in the treatment of any specific symptom presented by individuals with Parkinson’s disease? Which one(s)?

Table 3.6 presents the symptoms addressed in the studies.

Symptom	Study
Bradykinesia	(6); (27); (46); (52); (68); (79); (94); (115); (119); (147); (148); (150); (152)

Postural instability	(82); (119); (135); (155); (158); (175)
Gait impairments	(22); (30); (68); (82); (119); (155); (158); (175)
Rest tremor	(27); (97); (126)
Rigidity	(27); (38); (46); (106); (148)
Cognitive impairments	(47); (135); (143); (147); (155); (166); (170)
Visuospatial disability	(166)

Table 3.6 – Symptoms treated by the games.

Some studies have proposed treating more than one symptom of PD, as in (68), which proposed the treatment of bradykinesia and gait impairments; in (155), postural instability, gait impairments and cognitive impairments; in (46, 148), bradykinesia and rigidity; in (82, 175, 158), postural instability and gait impairments; in (135), postural instability and cognitive impairments; in (27), bradykinesia, rest tremor and rigidity; in (119), bradykinesia, postural instability and gait impairments; in (147), bradykinesia and cognitive impairments; and in (166), cognitive impairments and visuospatial disability. The other studies did not specify which symptom the game was aimed at treating.

RQ07 - Did the assessment of the technologies consider experiments with patients?

Table 3.7 shows the studies' classification in terms of conducting experiments with real patients.

Experiments with patients	Study
Yes	(4); (5); (22); (27); (30); (38); (46); (47); (52); (68); (79); (82); (94); (97); (106); (114); (115); (121); (123); (126); (135); (143); (147); (148); (150); (152); (153); (155); (170); (175)
No/Not informed	(6); (10); (34); (55); (119); (158); (166); (169)

Table 3.7 – Experiments with patients.

3.4.2 Qualitative Evaluation

Table 3.8 shows the qualitative evaluation results of the studies, described in Stage 6 (Section 2.2). The “Total” column refers to the sum of scores for the evaluated items in each study, and the “Total” row refers to the sum of scores over all studies for each evaluated item.

Study (Reference)	Items for qualitative evaluation											Total
	A	B	C	D	E	F	G	H	I	J	L	
(4)	1	1	1	1	0.5	0	0.5	0.5	0	1	0.5	7.0
(5)	1	1	1	1	0.5	1	1	1	1	0.5	0.5	9.5
(6)	1	1	1	1	0.5	0	1	0.5	0	1	1	8.0

(10)	1	1	1	1	0	0	0.5	0	0	0.5	0	5.0
(22)	1	1	1	1	0.5	1	1	1	1	1	1	10.5
(27)	1	1	1	0.5	0.5	0	1	0.5	1	0.5	0.5	7.5
(30)	1	1	1	1	0.5	0	1	0.5	0	0.5	0.5	7.0
(34)	1	1	1	0.5	0.5	0	0.5	1	0	0.5	0.5	6.5
(38)	1	1	1	1	0.5	0	1	1	0	1	1	8.5
(46)	1	1	1	1	0.5	1	1	0.5	1	1	0.5	9.5
(47)	1	1	1	0.5	0.5	0	0.5	0.5	1	0.5	0.5	7.0
(52)	1	1	1	1	0.5	0	1	1	0	1	0.5	8.0
(55)	1	1	1	1	0	0	1	1	0	1	0	7.0
(68)	1	1	1	1	0.5	0	1	1	0.5	1	0.5	8.5
(79)	1	1	1	1	0.5	0	1	1	0	1	0.5	8.0
(82)	1	1	1	1	1	0	0.5	0.5	0.5	0.5	0.5	7.5
(94)	1	1	1	0.5	0.5	0	0.5	1	0	1	0.5	7.0
(97)	1	1	1	0.5	1	0	0.5	1	0	0.5	0.5	7.0
(106)	1	1	1	1	0.5	1	1	1	1	1	0.5	10.0
(114)	1	1	1	1	1	0	1	1	0	0.5	0.5	8.0
(115)	1	1	1	1	1	0	1	1	0	1	0.5	8.5
(119)	1	1	1	1	0	0	0	0	0	0.5	0.5	5.0
(121)	1	1	1	0.5	0.5	0	0.5	0	0	0	0	4.5
(123)	1	1	1	1	1	0	0.5	0.5	0	1	0.5	7.5
(126)	1	1	1	1	0.5	1	0.5	0.5	1	1	1	9.5
(135)	1	1	1	1	0.5	0.5	0.5	0	1	0.5	1	8.0
(143)	1	1	1	0.5	0.5	0.5	0.5	1	1	1	1	9.0
(147)	1	1	1	1	0.5	0	1	1	0	1	0.5	8.0
(148)	1	1	1	1	0.5	0	1	1	1	1	0.5	9.0
(150)	1	1	1	1	1	0.5	1	1	0	1	0.5	9.0
(152)	1	1	1	1	0.5	0	0.5	0.5	0	0.5	0	6.0
(153)	1	1	1	0.5	0.5	0	0.5	0	0	0.5	0.5	5.5
(155)	1	1	1	1	1	1	1	0.5	1	0.5	0.5	9.5
(158)	1	1	1	1	0.5	0	0.5	0.5	0	1	0.5	6.0
(166)	1	1	1	1	0.5	0.5	0.5	0.5	1	0.5	1	8.5
(169)	1	1	1	1	1	0.5	0.5	0.5	0.5	1	1	9.0
(170)	1	1	1	0.5	0.5	0	1	0	0	1	1	7.0
(175)	1	1	1	1	0.5	1	1	1	0.5	1	1	10.0
Total	38	38	38	33	21	9.5	28	25	14	29	22	

Table 3.8 – Qualitative evaluation results.

3.5 Discussion

This section presents a discussion of the results obtained from this study, which will be guided and separated according to the addressed research questions.

Table 3.1 shows the types of games presented in the studies included in this review.

The majority (52.63%) of the studies proposed the development and/or use of games that train players' physical movements (exergames). Keeping in mind information regarding the research questions RQ03 and RQ06 (Table 3.3 and Table 3.6, respectively), it is possible to establish a relationship between the type of the exergame with Kinect, Nintendo Wii and Leap Motion devices and the symptoms bradykinesia, postural instability, gait impairments and rest tremor. The availability of devices capable of capturing body movements combined with physical problems caused by PD may be factors that contribute to the preference in developing games classified as exergames.

According to (78), games can exercise the brain and as more patterns are learned, more novel approaches are needed to make a game attractive. Inevitably, at some point, a game can become boring and disposable. When this happens, it is necessary to change over to another game, highlighting the importance of having different games to treat a particular symptom. In this sense, by crossing the information presented in Table 3.1 and Table 3.6, one notes that by considering the type of game exergame, six studies were found that used different games for the treatment of the same symptom – bradykinesia. Thus, there is a need to have a wide variety of games with different characteristics and properties (scenarios, narratives, and mechanics) to support people with PD, when the desire or interest in a game is lost or diminished.

It is extremely important that games be developed considering some aspects related to the patients who will use them. Individuals affected by PD are, in general, elderly people. They are attracted by casual games that represent life experiences, rather than complex games with adventure and science fiction themes. Therefore, games based on themes such as country life and nature tend to be better accepted by these individuals, increasing the efficiency of the game for the treatment of symptoms (52).

In addition, games should be created specifically for people with PD, and it is very important to keep in mind the variations in cognitive and motor ability of patients (126). According to (149), depending on the demands of the game, people with PD show deficits compared to healthy elderly people. Thus, these games should not be difficult or complex, but rather present achievable challenges to the players.

Another important factor related to SGs for rehabilitation is the need to adapt and customize them to align with the target group's demands (9). The lack of customization and the need of engagement for sustainable use is one of the main issues existing in health oriented SGs. Different personalities are attracted to different games, and not just because of a particular problem in the brain (38, 52). Therefore, it is necessary to encourage the creation and availability of as many games as possible, to increase the number of people who can benefit from using games.

Table 3.2 shows that studies which used VR are more numerous (36.84%) compared to other interface technologies. This is certainly due to the positive potential demonstrated in using virtual technologies that keep the player immersed and engaged in healthy activities

(38, 126, 52). According to (126), VR increases the focus on tasks and requires cognitive interaction of the patient, thus contributing to the achievement of therapeutic benefits. As VR is an instrument that includes visual, auditory, and tactile feedback, it is able to meet the demands of PD patients and can be added to neurorehabilitation (126). Thus, physiotherapy based on VR is important for exploring not only motor skills of patients, but also cognitive skills, facilitating repetition and motor learning. Moreover, both VR and AR can create new scenarios, narratives, and mechanics for existing games. This reutilization can decrease the time needed to make a game available, compared to the time spent developing a new game from initial stages.

However, some negative factors may have contributed to 23.68% of the studies (a considerable proportion) featuring 2D interface technology. Many patients suffer from dizziness, headaches, mental confusion, and nausea when using virtual games with immersive characteristics (95); the exercise to be performed is prioritized, rather than the technology used; lack of technical knowledge to use VR or AR; and the development of 2D games is simpler than games with virtual interfaces.

Table 3.3 shows different devices and sensors that can be used to capture body movements in SGs for rehabilitation, especially Leap Motion and Microsoft Kinect. The physical impairment caused by PD can prevent people from being able to handle traditional game controls, contributing to the development of alternative types of input devices. As discussed in RQ01, this preference may be related to many games classified as exergames in this study.

Furthermore, there is an observed tendency for using traditional devices that already exist, i.e., devices that were not created considering the limitations of PD patients. Cost reduction may explain this choice. However, those with PD have severe limitations, especially in advanced stages of the disease. Therefore, the development of devices that improve player experience, while observing their limitations, can contribute to a better acceptance, as well as better results when using games. Only three studies (68, 153, 106) mentioned the creation of specific and adapted devices for individuals with PD.

The presence of a doctor or therapist accompanying the SGs development, as well as its use, was confirmed in most of studies. In contrast, the development of a game based on a rehabilitation protocol for people with PD was identified in only 15 studies (39.47%), as shown in Table 3.4. The use of a formal rehabilitation protocol can contribute positively towards evaluating and monitoring the results obtained by a SG in the treatment of PD symptoms.

The game evaluation and the monitoring of results obtained by patients are important for validating the solution. Some studies evaluated game usability and game experience, characteristics used to qualify and measure aspects related to games. However, the player can evaluate the game well, but not have satisfactory results in treating a symptom. Hence, it is important to use instruments to evaluate the results obtained by patients,

verifying whether the game was effective in treating a given symptom. As seen in Table 3.5, a wide variety of specific tools were used to assess patient outcomes regarding the treatment of a given symptom.

Table 3.6 presents the symptoms treated in the studies. The solutions used for physical rehabilitation were more numerous than for cognitive rehabilitation, and the two most treated symptoms were bradykinesia and gait impairments. Despite a wide variety of symptoms addressed in these papers, there is a lack of solutions that treat more than one symptom (only 12 studies treated two or more symptoms with the games). Among all studies included in this review, only (147) concluded that, although the addressed symptom (cognitive impairments) did not evolve, there was no improvement in its treatment using SG.

Most studies conducted experiments with real patients (78.95%). However, due to the small number of participants, the short follow-up time and the lack of experimental methodological rigidity, the authors did not provide any specification regarding the results obtained (they only described preliminary results). They only reported that a level of efficiency was achieved in treating the symptoms caused by PD. The need for long-term tests with a statistically representative population is evident to produce comprehensive results that can be validated with a high degree of precision.

Regarding qualitative evaluations, as illustrated in Table 3.8, the scores of each paper for the evaluated items ranged between 4.5 and 10.5 points. The mean score was 7.80 and standard deviation 1.48, showing that, in general, the studies presented approximately 3.20 points less than a total of 11 points for the quality factor. Only the studies (10, 119, 121, 153) obtained scores less than or equal to 50% of the total points distributed for quality evaluation, characterizing studies with more inconsistencies/failures when compared to the others. However, it is important to emphasize that, among these four studies, the ones (10, 119) did not perform experimental procedures. This is reflected in the final scores of the studies, since items E, F and I are related to the performing of an experiment.

The first three items evaluated in qualitative analysis (A, B and C) received the highest score in all included papers, presenting 38 points in the sum of the scores. However, two items (F and I) stood out for obtaining a sum of points below 50% of the total points added in relation to the other items. Therefore, in general, the selected studies presented two main deficiencies, a non-recruitment of people to form a control group, and a lack of care when dealing with possible bias that can affect the research regarding the relationship between researcher and participant. Two other items that obtained lower evaluation scores were those related to a recruitment strategy of individuals to perform the tests (E), and failure to apply what has been developed in practical situations (L).

3.6 Conclusions

This review evaluated the use of SGs for rehabilitation of individuals with PD. Several research initiatives proposed the use of these tools to assist in the treatment of symptoms arising from the disease. The solutions described in the studies assessed PD symptoms using physical tests such as the BBT, TEMPA, PPT and TUG; questionnaires/scales such as the PDQ-39, MDS-UPDRS, Barthel Index and MoCA; and observational analyses. No studies used recorded data of movements performed by players (provided by inertial sensors, for instance) during their interaction with the SG to assess any PD symptoms.

Designing SGs for health is a challenging process because they need to meet the demands of therapists and players, which are often complex and diverse. A successful game must be simple, enjoyable, customizable, have effectiveness in terms of therapy, and its design must consider the experiences of the users rather than the developers. Furthermore, the development of long-term studies with a statistically representative population is necessary for validating and generalizing the results obtained with the use of SGs. These characteristics are extremely important for the good acceptance of games by users and for the incorporation of these tools in outpatient settings.

Multidimensional Assessment Questionnaire for Individuals with Parkinson's Disease

The aim of this chapter is to present the development and structure validation of a self-assessment questionnaire that can be used remotely to assess the respondents' health condition. One of the objectives of this questionnaire was to identify the respondents' main motor limitations in order to guide the development of the serious game.

4.1 Introduction

Parkinson's disease (PD) has the potential to affect an individual on multiple levels, including motor, cognitive, social, and/or emotional aspects (134). As a result, individuals with PD should be evaluated on a regular basis (174).

Questionnaires are effective tools for multidimensional evaluation (56). They offer respondents the opportunity to reflect on themselves and provide information that contributes to a better understanding of their health status (75). Other advantages include: relatively low costs for both instrument development and data collection; the potential to be answered by a large number of people because they can be applied in person or remotely; no need for an interviewer; temporal flexibility for data collection (66); and the ability to measure and discriminate the actual needs of individuals, allowing for the development of new technologies designed to solve real problems (44).

Several instruments are being developed to assess general aspects of health and quality of life in people with PD. However, widely used questionnaires and scales, such as the Movement Disorder Society–Unified Parkinson's Disease Rating Scale (MDS–UPDRS) (58) cannot be conducted remotely because they require the physical presence of a clinician (146). Furthermore, in a pandemic situation, remote assessment would be useful for disease prevention, assessment, and patient condition monitoring. The study (57) emphasized the importance of using MDS–UPDRS to continuously assess individuals with PD, even in situations with limited physical contact. However, this and no other scales or questionnaires have yet been validated to be applied remotely.

The Parkinson’s Disease Questionnaire–39 (PDQ–39) (72) is another widely used questionnaire that has limitations in evaluating some aspects, such as pain, which is a symptom closely linked to quality of life and is present in approximately 85% of people with PD (31). Since PDQ–39 contains only 39 items, it may not favor a more in-depth assessment, particularly if used remotely.

The Barthel Index (99) and Katz Index (112) are two other scales used to assess people with PD. Nonetheless, aside from not evaluating different aspects, neither scale is specific for PD. The Barthel Index was created to assess post-stroke individuals (15), and the Katz Index to assess elderly people (112). Therefore, using these scales to assess people with PD may result in inaccurate assessments.

In summary, most of the instruments used to assess individuals with PD have the following limitations: they require the physical presence of a clinician to perform the assessment (which is impractical during emergency situations, such as COVID–19), were not designed specifically for patients with PD, and/or have not been validated to be self-administered or applied remotely. As a result, the need for developing a self-applied instrument capable of being used remotely, which can provide a detailed assessment of the overall health status of people with PD, was identified.

The goals of this study were to create and validate the structure of a multidimensional self-assessment questionnaire for people with PD that can be used remotely, to propose a model for calculating the final score and the respondents’ level of disability, to assess the scale’s accuracy, and to identify the most common limitations of individuals with PD. In short, this questionnaire was developed to allow the remote assessment of an individual with PD, and also to enable the identification of the main limitations of the respondents to direct the development of the game.

4.2 Methods

4.2.1 Questionnaire development

The questionnaire development and application were approved by the Ethics Committee for Human Research at the Federal University of Uberlândia.

Validated questionnaires and assessment scales such as MDS–UPDRS (58), PDQ–39 (72), Barthel Index (99), Katz Index (112), and Multidimensional Pain Inventory (MPI) (154) were used in the instrument development. Food, Mobility, Sanitation, Clothes, Miscellaneous, Memory/Concentration, Social and family conviviality, Personality, Energy, Emotion/Humor, Severity of pain, Interference, Perceived life control, and State of mood-affectivity were created as subgroups of questions.

The “Multidimensional Assessment Questionnaire for Individuals with Parkinson’s Disease” (MAQPD) questionnaire was proposed, with a total of 83 evaluation questions (Ap-

pendix A). The language of the questionnaire was Portuguese, it was created using Google Forms (a survey administration software), and it was applied to Portuguese speakers from Brazil. MAQPD was divided into three sections:

1. Section A – Research presentation. This section presents the aims of the research, describes the risks and benefits, as well as the importance of the participation of people with PD.
2. Section B – Questions about daily activities (Module 1), related to self-care and the capacity of individuals to live independently; and questions concerning cognitive aspects (Module 2), related to the individuals' feelings about life and society. This section presents 66 questions for evaluation by the respondents, of which 43 are distributed to the subgroups of Module 1 (7 for Food, 12 for Mobility, 7 for Sanitation, 7 for Clothes and 10 for Miscellaneous), and 23 distributed to the subgroups of Module 2 (2 for Memory/Concentration, 6 for Social and family conviviality, 3 for Personality, 6 for Energy and 6 for Emotion/Humor).
3. Section C – Multidimensional Pain Inventory. This section presents four subgroups of questions taken from the MPI (Portuguese version) (154), which refer to the impact of pain on the life of individuals. In this section there are 17 questions for assessment by the respondent, of which 3 are for the subgroup Severity of pain, 9 for Interference, 2 for Perceived life control, and 3 for State of mood-affectivity.

MAQPD uses two response scales: a LIKERT scale with five classification levels (0—Totally disagree; 1—Disagree; 2—Neutral; 3—Agree; and 4—Totally agree) used in Section B, and a LIKERT scale with seven classification levels ranging from 1 (little pain) to 7 (a lot of pain) used in Section C. In addition, the questionnaire presents optional open-ended questions so that respondents have the opportunity to express in detail complaints or aspects not mentioned in the questionnaire. The average time it took to respond to MAQPD was 18 minutes.

4.2.2 Questionnaire's structure validation

Research participants

People with PD were invited to participate in the study through a variety of channels, including email lists, discussion forums, PD webinars, interviews for local television stations, and WhatsApp groups. The inclusion criteria for the study were: having a confirmed diagnosis of PD from a neurologist or geriatrician; and being able to fill out the questionnaire independently. Individuals whose responses to the questionnaire were incomplete were excluded from the analysis. MAQPD was completed by 310 people, but 8 of them did not have PD. As a result, 302 answers were analyzed.

Factor analysis

Factor analysis (FA) was used to validate the structure of MAQPD. FA is a multivariate statistical method used to define underlying structures in data matrices. FA investigates the interrelationships between multiple variables to derive a reduced linear structure from the original data (168). As a result, in a questionnaire with many variables (83 in this study), FA seeks to group such variables into reduced sets described by factors (87).

In short, FA can be performed in two stages: factor extraction and factor rotation. Factor extraction involves choosing the number of factors to be extracted, and factor rotation aims to obtain a simple structure to improve data interpretability. One approach to factor extraction is principal component analysis (PCA), which explains correlations by explaining (common) variance (87).

PCA analyzes a data set in which observations are described by several quantitative dependent variables that are intercorrelated. The aim of this method is to express important information extracted from the data set as a set of new orthogonal variables. In addition, PCA represents the pattern of similarity of observations and variables (1).

PCA calculates new variables obtained as linear combinations of the original variables, called principal components. The first principal component is required to have the highest possible variance, and in this way, this component explains the largest part of the data set. The second and other components are computed under the restriction to have the biggest variance possible and to be orthogonal to the previous component. The values of these new variables for the observations are called factors scores, which can be interpreted in a geometric way as the observation's projections on the principal components (87). The number of factors retained can be observed using the Scree Plot (1).

First, the data were normalized to convert the response scale of Section C to the response scale of Section B. The normalization was done to satisfy the following relationship: a low score indicates severe impairment, whereas a high score indicates less impairment. Equation 4.1 was used to normalize questions 67 to 78 and 81 to 83, as these items have an inverse relationship with the response scale from 0 to 4. Equation 4.2 was applied to questions 79–80 because they are directly related to the response scale of 0–4. For both equations, X1 represents the normalized variable on a scale of 0 to 4, and X2 represents the variable on a scale of 1 to 7.

$$X1 = -4 * ((-X2 + 7)/6) \quad (4.1)$$

$$X1 = 4 * ((X2 - 1)/6) \quad (4.2)$$

The Bartlett sphericity and Kaiser–Meyer–Olkin (KMO) tests were used to determine whether the dataset met the requirements of FA. The Scree Plot was used to determine

the number of retained factors that were rotated (oblimin) to improve their interpretation and relationship with the original variables.

To improve the overall solution of FA, the following criteria were used to exclude irrelevant variables that satisfied at least one of the three criteria:

1. Variables with factor loadings less than 0.35 were considered insignificant based on the size of a sample between 250 and 349 individuals (87).
2. Variables with very similar factor loadings, i.e., difference between factor loadings less than 0.10, in more than one factor (62).
3. Variables with communality under 0.30 (89, 48). Low communality indicates they are not linearly correlated and, therefore, should not be included in FA.

After excluding variables that did not meet these criteria, FA was performed again to re-evaluate the need for additional variable exclusion.

4.2.3 Data analysis

Assessment of respondents' level of impairment

FA assigns a factor loading to each item of the questionnaire, which reflects the importance of the item in representing a given factor. To compute the final score for each respondent, the factor loadings were multiplied by the score given by the respondent in each question, and the sum of these values was calculated.

The Spearman's correlation coefficient between variables was estimated to determine whether the proposed model is consistent. The correlation coefficient was classified into four categories: very weak (0.00–0.19), weak (0.20–0.39), moderate (0.40–0.59), strong (0.60–0.79), and very strong (0.80–1.00) (110).

The final scores of individuals were analyzed using descriptive statistics such as mean, standard deviation, median, and minimum and maximum values. These measures were computed for the entire instrument as well as for each of the FA-defined factors. The violin plot was shown, which reveals additional details about the data distribution. To gain a better understanding of the distribution of the respondents' final scores, the histogram and cumulative distribution function of the entire instrument, as well as the measures of skewness and kurtosis, were examined.

Scale accuracy assessment

The floor and ceiling effects, as well as Cronbach's alpha, were used to assess the scale's precision. When a proportion of respondents achieves the lowest possible score across a given domain, the floor effect occurs, preventing the identification of changes in situations where the health condition deteriorates. The ceiling effect is interpreted in the

opposite way as the floor effect (11). When the floor and ceiling effect rates were less than 15%, they were considered satisfactory (64, 103).

Cronbach's alpha is a coefficient that can be used to determine whether the questionnaire items are homogeneous and whether the scale consistently measures the characteristic for which it was designed. If it was larger than 0.75 it was deemed adequate (80). Floor and ceiling effect rates, as well as Cronbach's alpha, were calculated for the entire instrument and for each domain.

Identification of motor difficulties and limitations related to cognition and pain

The most common answer (i.e., mode) for each question was identified to find the basic activities of daily living that the respondents had more difficulty performing, as well as the cognitive and pain aspects most affected in these individuals. The responses from the optional open-ended questions were also evaluated.

In addition, the main motor, cognitive, and pain limitations were identified and discriminated for each group of respondents according to their diagnosis time, also calculating the most common answer for each question.

4.3 Results

4.3.1 Questionnaire structure validation

As shown in Table 4.1, the majority of those who responded to the questionnaire (28.48%) had been diagnosed with PD for more than ten years, while the minority (4.30%) had been diagnosed for two to four years.

Diagnosis time	Number of respondents	Percentage of respondents(%)
less than 2 years	59	19.54
2 to 4 years	13	4.30
4 to 6 years	51	16.89
6 to 8 years	64	21.19
8 to 10 years	29	9.60
more than 10 years	86	28.48

Table 4.1 – Diagnosis time.

The adequacy of the data for the application of FA was verified. The results of the Bartlett's test of sphericity ($X^2 = 28247.25$; $df = 3403$ degrees of freedom; $p < 0.001$) and KMO test (overall Measure of Sampling Adequacy of 0.95) suggested a good adequacy of the data to FA. Figure 4.1 shows the data correlation matrix of the questionnaire.

PCA was used to confirm that three factors should be retained because the Scree Plot showed a linear decreasing trend at Component 3.

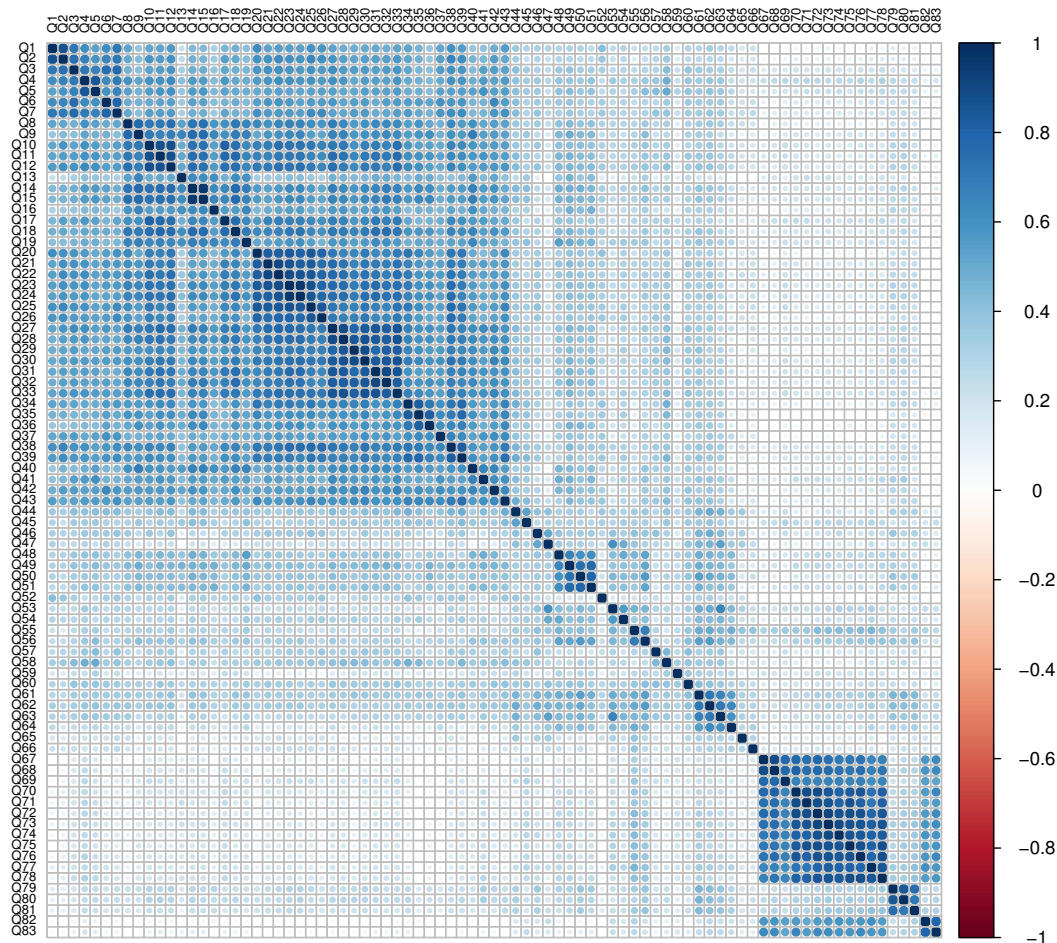


Figure 4.1 – Data correlation matrix before FA.

To improve the interpretation of the factors, the oblique rotation *oblimin* was used, and the factor loadings and communality were analyzed to eliminate twelve irrelevant variables. Question 45, 52, 57, 59, 66, and 80 had factor loadings less than 0.35; question 44 had factor loadings for two factors that were very similar; and questions 45, 52, 57, 58, 59, 60, 65, 66, 79, 80, and 81 had communalities less than 0.30. After these variables were removed, the questionnaire presented 71 items rather than 83.

FA was performed once more to ensure that the items in the new MAQPD (Appendix B) met any of the defined variable exclusion criteria. The results showed that the data was adequate for FA, as confirmed by the Bartlett's test of sphericity ($X^2 = 26020.98$; $df = 2485$ degrees of freedom; $p < 0.001$) and the KMO test (overall Measure of Sampling Adequacy of 0.95). Figure 4.2 depicts the new questionnaire's data correlation matrix.

Three factors should be retained because their proportion of variance explained was larger than 60% (62) and the Scree Plot showed a decreasing linear trend at Component 3. Oblique rotation *oblimin* was used to improve the interpretation of the factors, and the variables were reorganized into three different groups:

1. FACTOR 1: Comprised of 43 variables related to the activities of daily living (ADL).

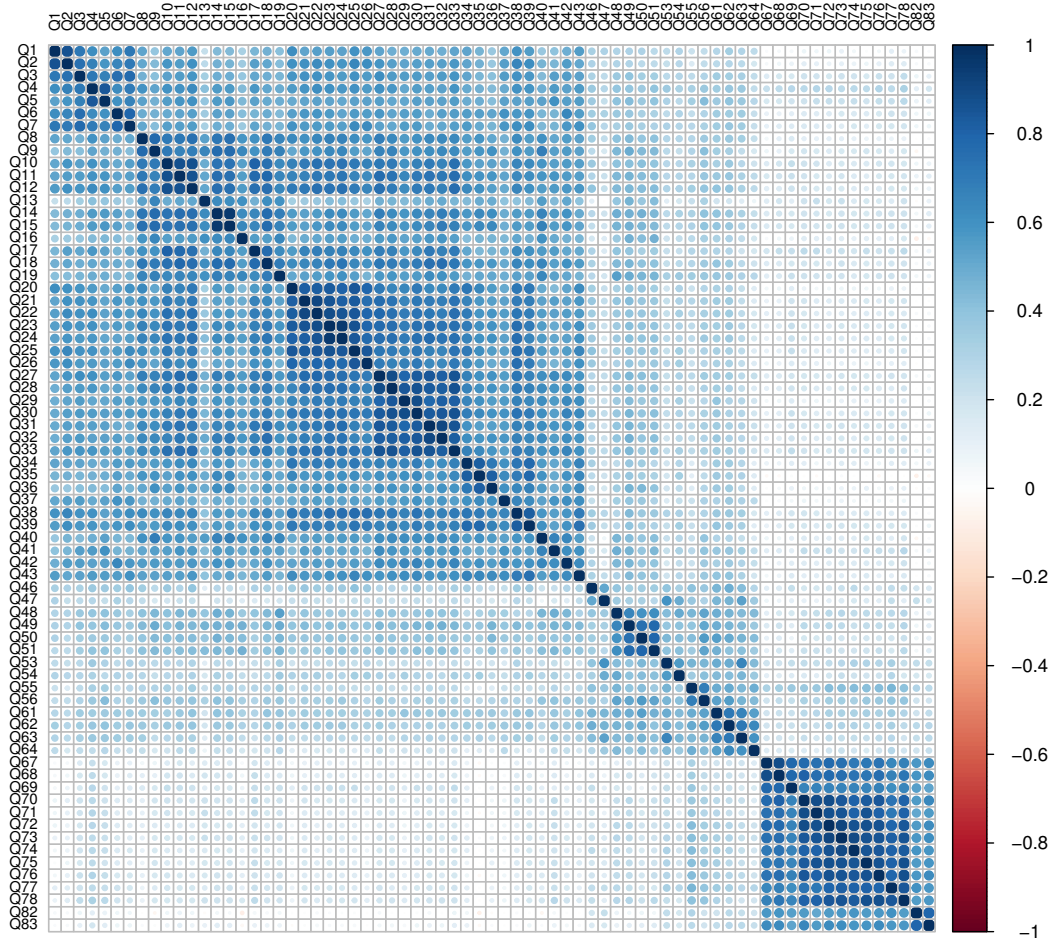


Figure 4.2 – Data correlation matrix after FA. The questions are numbered in accordance with the original questionnaire.

2. FACTOR 2: Comprised of 14 variables related to pain.
3. FACTOR 3: Comprised of 14 variables related to cognitive aspects.

No other variables needed to be excluded.

4.3.2 Assessment of respondents' level of impairment

The factor loadings of each questionnaire item are shown in Table 4.2.

The model in Equation 4.3 was used to compute the sum of each respondent's final score.

$$Final\ Score = 0.57S_{Q_1} + 0.63S_{Q_2} + 0.60S_{Q_3} + 0.57S_{Q_4} + \cdots + 0.64S_{Q_{83}} \quad (4.3)$$

where S_Q is the score given by the individual for each question.

Figure 4.3 shows the correlation plots for the variables of each factor and the total scores of each domain. The correlation between the total score of the entire questionnaire

Variable	Factor loadings	Variable	Factor loadings	Variable	Factor loadings	Variable	Factor loadings
Q1	0.57	Q19	0.57	Q37	0.59	Q62	0.72
Q2	0.63	Q20	0.91	Q38	0.80	Q63	0.79
Q3	0.60	Q21	0.91	Q39	0.78	Q64	0.72
Q4	0.57	Q22	0.92	Q40	0.65	Q67	0.84
Q5	0.50	Q23	0.94	Q41	0.55	Q68	0.85
Q6	0.57	Q24	0.91	Q42	0.65	Q69	0.75
Q7	0.59	Q25	0.92	Q43	0.62	Q70	0.92
Q8	0.71	Q26	0.87	Q46	0.48	Q71	0.93
Q9	0.65	Q27	0.88	Q47	0.60	Q72	0.94
Q10	0.84	Q28	0.89	Q48	0.60	Q73	0.93
Q11	0.83	Q29	0.82	Q49	0.56	Q74	0.89
Q12	0.84	Q30	0.88	Q50	0.66	Q75	0.92
Q13	0.50	Q31	0.87	Q51	0.60	Q76	0.71
Q14	0.67	Q32	0.84	Q53	0.69	Q77	0.80
Q15	0.68	Q33	0.91	Q54	0.55	Q78	0.90
Q16	0.60	Q34	0.80	Q55	0.55	Q82	0.61
Q17	0.76	Q35	0.70	Q56	0.61	Q83	0.64
Q18	0.80	Q36	0.63	Q61	0.69		

Table 4.2 – Factorial loadings of the 71 questionnaire items. The questions are numbered in accordance with the original questionnaire.

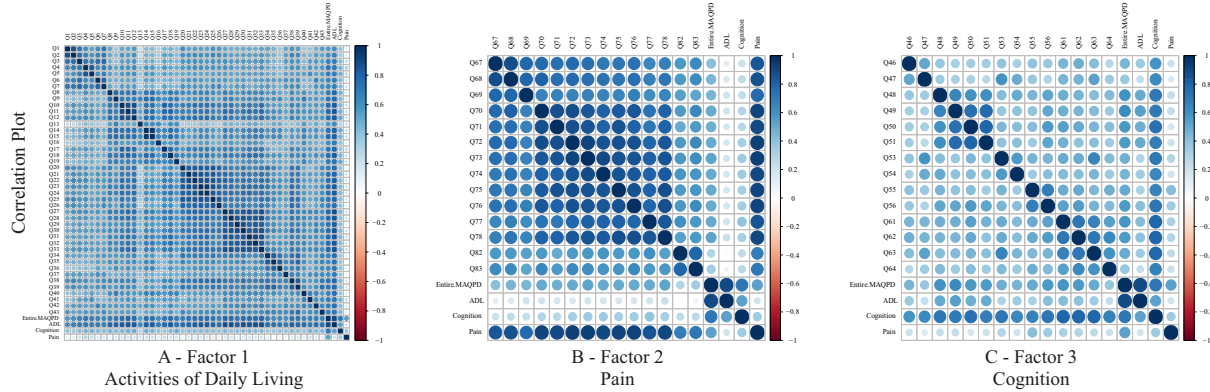


Figure 4.3 – Correlation plots showing the correlation between variables of Factor 1 (A), Factor 2 (B), and Factor 3 (C), and the final scores.

and the total score of each of the three domains was 0.89 (ADL), 0.54 (Pain), and 0.72 (Cognition).

Individuals' final scores could range from 0 to 209.36 points if they answered “0” and “4” to all questions, respectively, according to the model. In addition, the lower the score, the more impaired the individual is.

Table 4.3 shows the descriptive statistics of the final questionnaire scores for the entire questionnaire as well as for each domain.

Domain	Mean (Sd)	Median	Min–Max
Entire MAQPD (range: 0–209.36)	128.25 (43.60)	130.78	7.31–206.36
ADL (range: 0–126.84)	86.21 (32.91)	90.91	0–126.84
Cognition (range: 0–35.24)	16.16 (8.25)	15.57	0–35.24
Pain (range: 0–47.28)	25.87 (15.03)	25.71	0–47.28

Table 4.3 – Descriptive analysis of MAQPD scores.

Figure 4.4 presents the violin plot of the final scores.

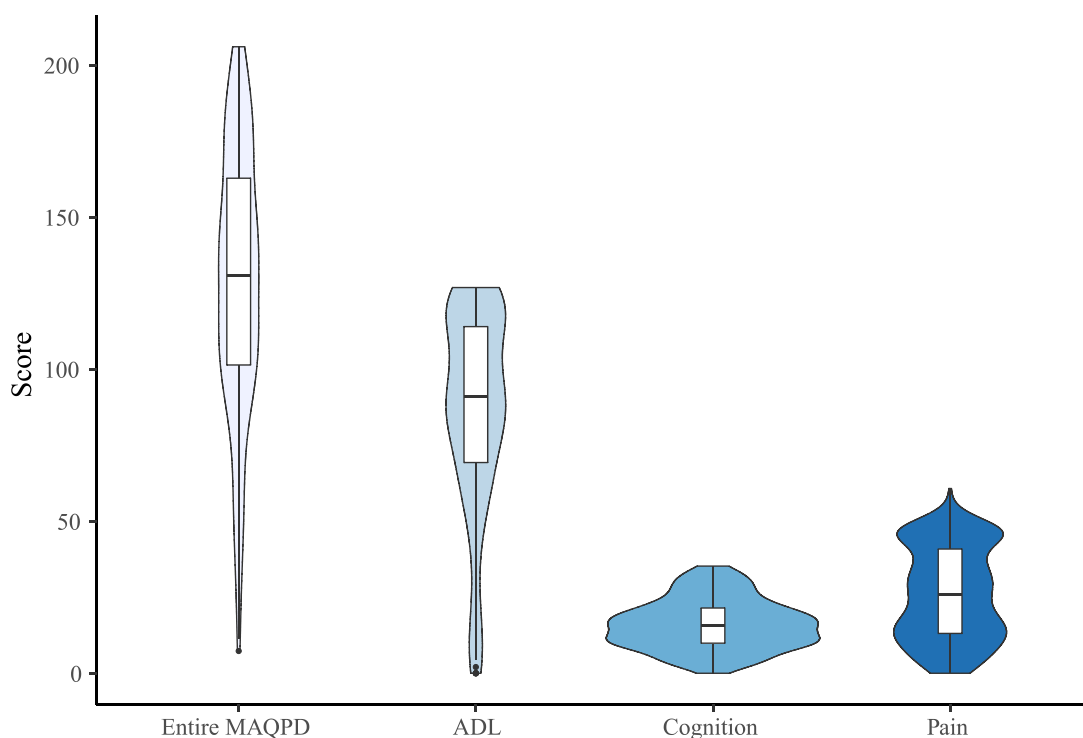


Figure 4.4 – Violin plot of the final scores.

The histogram and cumulative probability distribution function of the individuals' final scores are depicted in Figure 4.5.

The frequency distribution of the data is shown by the histogram. Most scores ranged from 100 to 180 points, and only a few people had low scores, i.e., less than 50 points. The cumulative distribution function expresses the likelihood that a random observation sampled from the population will be less than or equal to a given value. The probability of an individual's final score being between 100 and 180 points was approximately 62%, and the probability of the score being less than half of the possible score (approximately 105 points) was approximately 30%. The skewness was -0.37 and the kurtosis was -0.30 .

4.3.3 Scale accuracy assessment

Table 4.4 shows the estimated floor and ceiling effects of the final scores, as well as Cronbach's alpha, for the entire questionnaire and for each domain.

Domain	Floor effect(%)	Ceiling effect(%)	Cronbach's alpha
Entire MAQPD	0.28	3.77	0.9767
ADL	0.44	10.85	0.9839
Cognition	2.50	1.04	0.9270
Pain	4.32	8.20	0.9736

Table 4.4 – Analysis of the accuracy of the MAQPD scale.

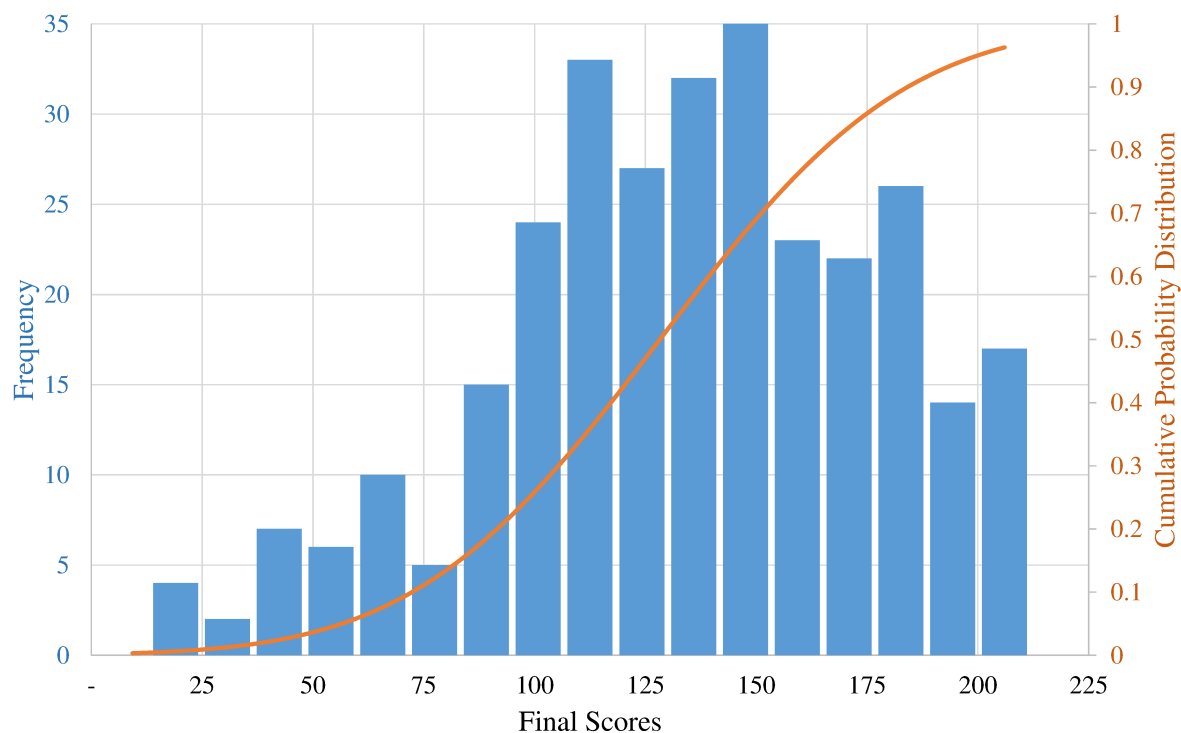


Figure 4.5 – Histogram and cumulative probability distribution function of final scores.

There were no significant floor or ceiling effects, with values ranging from 0.28% to 10.85%. Cronbach's alpha was larger than 0.90 for all dimensions, indicating that the proposed questionnaire has strong internal consistency.

4.3.4 Identification of motor difficulties and limitations related to cognition and pain

According to the responses, the activities of daily living that people with PD had more difficulty with were represented by Question 13 ("I drive without difficulty") with a prevalence of zero, indicated that most people completely disagree with the statement; and Question 16 ("I dance without difficulty") with a prevalence of one indicated that most people disagree with the statement.

The most affected cognitive aspects in patients are represented by the following questions: 48, 49, 50, and 51, which are about living with family and society; 53 and 54, which are about an individual's personality; 55 and 56, which are about energy and mood; and 63 and 64, which are about emotion and feeling. All these questions had a score prevalence of one.

In terms of pain, the following questions indicated the most impairment of the individual: 67, 68, 72, 76, and 83. All questions had a prevalence of scores equal to one.

Figure 4.6 depicts the questionnaire TreeMap. The color gradient corresponds to the most frequently assigned score for each question. The rectangles' sizes are proportional to the factor loading of the corresponding question. Each factor has its own set of questions.

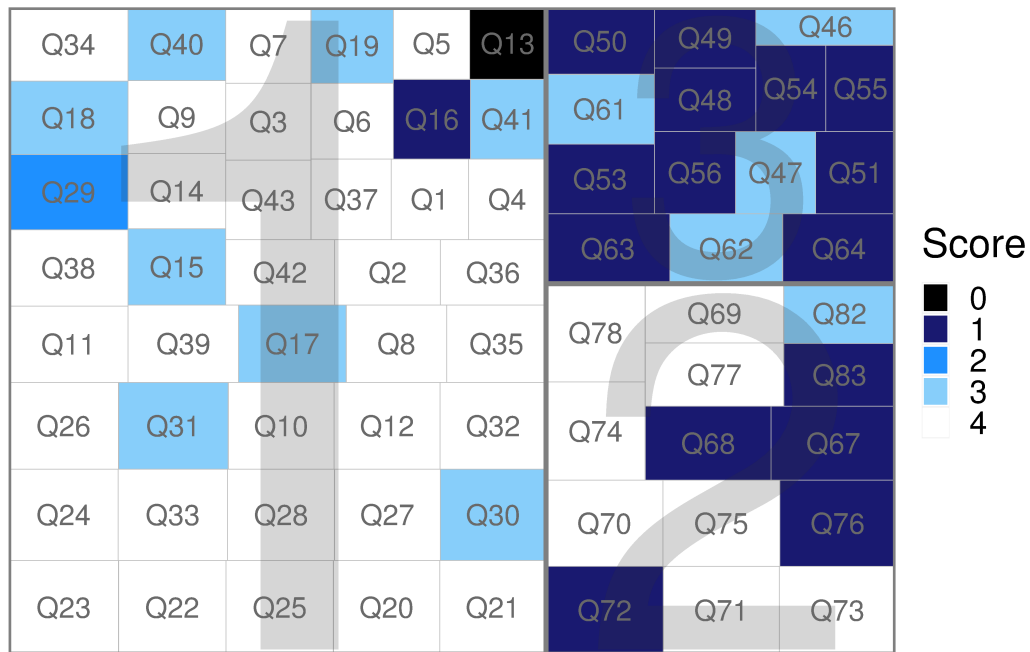


Figure 4.6 – TreeMap of the questionnaire. The colors represent the most common scoring for each question. The higher the factor loading, the larger the area of the rectangle. Each factor has its own set of questions (1, 2 or 3).

Additionally, 41.39% of the respondents answered the open-ended questions. Of these, most reported problems in performing household chores, such as washing dishes, cleaning the house, and cooking.

Table 4.5 shows the questions that most represent motor, cognitive, and pain limitations, discriminated according to the time of diagnosis of the respondents. Only the questions with a score equal to 0 (totally disagree) or 1 (disagree) were considered.

Diagnosis time	Main limitations – Question (Score)*		
	ADL	Cognition	Pain
Less than 2 years	Difficulty in dancing – Q16 (0)	Lack of social interaction and leisure – Q48 (1), Q49 (1), Q50 (1), Q51 (1); Mood changes – Q53 (1), Q54 (1); Lack of disposition – Q55 (1); Lack of happiness and future prospects – Q61 (1), Q62 (1), Q64 (1)	none

2 to 4 years	none	Mood changes – Q54 (1); Lack of disposition – Q55 (1); Lack of future prospects – Q64 (1)	Experiencing severe chronic pain – Q67 (1), Q68 (1); Interference of pain in different aspects of life (e.g., participation in social and leisure activities, ability to do housework) – Q70 (1), Q71 (1), Q72 (1), Q73 (1), Q75 (1); Mood changes – Q82 (1), Q83 (1)
4 to 6 years	Difficulty in driving – Q13 (0)	Lack of social interaction – Q51 (0)	none
6 to 8 years	Difficulty in driving – Q13 (0); Difficulty in dancing – Q16 (0)	Lack of social interaction – Q49 (0), Q51 (0)	Experiencing severe chronic pain – Q67 (1), Q68 (1); Interference of pain in different aspects of life (e.g., participation in social and leisure activities, ability to do housework) – Q70 (1), Q71 (1), Q72 (1), Q73 (1), Q75 (1), Q76 (1); Mood changes – Q83 (1)
8 to 10 years	Difficulty in walking – Q9 (1), Q19 (1); Difficulty in dressing oneself (loss of independence) – Q28 (1); Difficulty in holding a child – Q40 (1)	Lack of social interaction and leisure – Q48 (1), Q49 (1), Q50 (1), Q51 (1); Mood changes – Q53 (1), Q54 (1); Lack of disposition – Q55 (1), Q56 (1); Lack of future prospects – Q64 (1)	Experiencing severe chronic pain – Q67 (1), Q68 (1), Q69 (1); Mood changes – Q83 (1)
More than 10 years	Difficulty in driving – Q13 (0); Difficulty in dancing – Q16 (0)	Lack of social interaction and leisure – Q48 (1), Q49 (1), Q50 (1), Q51 (1); Mood changes – Q53 (1); Lack of disposition – Q55 (1), Q56 (1); Lack of happiness and future prospects – Q61 (1), Q64 (1)	Interference of pain in different aspects of life (e.g., participation in job, ability to do housework) – Q75 (0), Q76 (0)

Table 4.5 – Main motor, cognitive, and pain limitations of the groups defined by the diagnosis time of the disease.

* To simplify the interpretation and summarize the amount of information present in Table 13, when a given factor presented at least one question with a score equal to 0, the questions of the same factor with

a score equal to 1 were omitted from the table.

4.4 Discussion

This work was created in response to the lack of an instrument for remotely assessing the health of people with PD. No validated alternatives based on questionnaires or scales for remotely assessing individuals with PD have been fully validated so far.

Motolese et al. (100) aimed to monitor individuals with PD remotely, during the social isolation caused by COVID-19. To monitor the cognitive and motor performance of PD patients, Motolese et al. (100) applied five assessment questionnaires and proposed the use of a smartphone application. The five questionnaires totaled 91 items for evaluation that should be answered by the participants. Falla et al. (43) assessed, longitudinally, motor and non-motor aspects using nine structured questionnaires, which resulted in a total of 148 questions.

First, the questionnaires applied by Motolese et al. (100) were not developed and validated to be applied remotely. Furthermore, answering this large amount of questions may be unfeasible – especially if dealing with individuals with neurological disorders – and demands time from both study participants and researchers. In addition, these questionnaires were administered via telephone and remote web-based video calls by the researchers (they were not self-administered), i.e., participants did not have the opportunity to answer the questions privately. Thus, it is possible to note the importance of using a more concise instrument capable of assessing multidimensional aspects of the disease, which can be answered privately in an online version, and which can be used for remote monitoring of individuals, associated, for example, with the use of wearable sensors. As a result, we proposed developing and validating the structure of an online questionnaire for multidimensional assessment, as well as a model for estimating individuals' final score, which is related to their level of impairment.

MAQPD was developed based on existing assessment instruments. It was answered by many people with PD, which contributed to a more robust validation of the instrument structure using FA. This method was used to verify each question's contribution to the multidimensional evaluation and to group questions into latent dimensions, implying a better distribution and arrangement of the questions (168, 87). FA suggested removing 12 questions and categorizing them into three dimensions: ADL, cognition, and pain. The final version of MAQPD was validated for Portuguese speakers, and then it can be used for the remote assessment of individuals with PD in other studies.

The estimate of factor loadings from FA enabled weighing the final scores based on the relevance of the question to define the factor. Correlation coefficients ranging from 0.54 to 0.89 (Figure 4.3) were estimated between the overall questionnaire's final score and the scores for each domain, indicating a moderate to very strong correlation represented

by the model (Equation 4.3). The correlation between the final ADL domain scores and pain, on the other hand, was very weak (0.19). This could have happened because aspects of one domain may not interfere with the other, i.e., a person may have severe motor impairments but not feel pain.

The final scores for the entire MAQPD were higher than the measures for the three domains, as expected, because the instrument contains 71 questions in total, while the subgroups of questions related to ADL, cognition, and pain contained 43, 14, and 14 questions, respectively (Table 4.3). The relatively large standard deviation found for the scoring of all domains reveals that individuals with varying levels of impairment responded to the questionnaire, which can be explained by the respondents' varying diagnosis times.

When compared to pain, the scores for cognition questions were lower (Figure 4.4). This means that the individuals are more susceptible in cognitive aspects than in pain-related aspects. Since the questionnaire was completed during a period of social isolation, many of the respondents may have developed depression and negative feelings about life, society, and the future (Table 4.5).

The data distribution (Figure 4.5) reveals that most respondents scored between 100 and 180 points, and that the cumulative distribution function displayed a higher growth (steeper slope) between these values, indicating a high probability (62%) of an individual's score falling between these two values. These findings point to the absence of severe impairments in the individuals, which may be related to the fact that the individuals with PD were able to complete the questionnaire themselves.

The skewness and kurtosis coefficients of -0.37 and -0.30 , respectively, indicate that the final scores had higher values and were dispersed, indicating a sample with lower impairment but not homogeneous (various diagnosis times).

Floor and ceiling effects were not found in statistically significant proportions across the entire instrument or across any domain (Table 4.4). As a result, MAQPD has the potential to be a tool for measuring the worsening and improvement of a person's health. The ceiling effect in the ADL domain was relatively high (10.85%). An explanation for this is that the respondents may have answered the questionnaire soon after taking PD medication, which may have given them the false impression that they could perform the activities. Another possible explanation is that the individuals do not have severe motor impairment in comparison to the cognitive aspects. Cronbach's alpha was higher than 0.90 for all domains, implying the instrument's high reliability and internal consistency.

Question 13 – "I drive without difficulty" was the only one in the whole questionnaire that presented a prevalence of answer equal to zero, meaning that most individuals responded to this statement that they totally disagree. In this case, a physiotherapist can direct a rehabilitation session that focuses on specific exercises for alleviating the symptoms that prevent the patient from performing the activity, i.e., driving. Therapies may improve specific functions, allowing the activity to be performed again by the individuals.

Furthermore, it was determined that approximately 71.43% of the questions pertaining to cognitive aspects had a prevalence of answers equal to one. This indicates that most respondents had issues with social and family coexistence, lacked energy and motivation to develop routine activities, and struggled to control their emotions (Table 4.5). It is noted that more research in the areas covered by these questions is required.

Regarding pain, 35.71% of the questions presented prevalence of answers equal to one (a lot of pain), one of them being question 76 – “How much did your pain affect your ability to do housework?”. This result is associated with that obtained by the open-ended questions, for which most of the respondents answered that they had difficulties in performing housework, suggesting that one of the reasons why individuals feel difficulties in performing domestic chores is pain.

Table 4.5 shows the main limitation by the respondents according to their diagnosis time. As the diagnosis time is a concrete information (it is not subjective, such as the degree of disease impairment interpreted by the therapist when applying the MDS-UPDRS) closely associated with greater impairment and worse perceived quality of life (102), progression of motor disability and higher risk of dementia (40), and loss of independence (13), the diagnosis time may be an effective variable to guide specific treatments for individuals with PD.

Individuals with a diagnosis time of less than 2 years, for example, reported that they had great difficulty in dancing, and that they suffered from a variety of problems related to cognitive issues. For these individuals, doing activities that exercise balance, as well as therapy sessions, may be effective ways to solve these problems. In addition, individuals with a diagnosis time between 2 and 4 years reported that they had difficulty in driving and that they did not meet their friends as much as they would like. Possibly, training the body movements that affect driving – either by using a serious game in which the player is stimulated to drive virtually, or with conventional physiotherapy – may contribute toward the individual performing this activity more easily. Furthermore, promoting support groups with social activities in therapy centers, as well as informing friends and family members about the issue related to social interaction, may help to improve the conviviality of these individuals.

Additionally, as individuals with diagnosis time of less than 2 years, between 6 and 8 years and more than 10 years had lack of social interaction, mood changes, and/or lack of disposition, performing a physical activity that requires relating to other people, e.g., dancing, becomes an extremely complex task. These findings agree with those reported by Darweesh et al. (29). These may be the reasons why these individuals experience difficulties in dancing. Possibly, individuals diagnosed less than 2 years ago did not feel severe pain due to the short diagnosis time of the disease.

A different consideration that also should be highlighted is that all groups presented limitations related to cognitive aspects, which indicates that this domain needs a more

attentive and careful look by family members, health professionals and researchers. In addition, except for the group with diagnosis time of less than 2 years, all the other groups reported problems related to pain. Possibly, improving aspects related to cognition may contribute to reducing the pain experienced by individuals, since one may entail the other.

The results of an evaluation based on multidimensional questionnaires contribute to a comprehensive understanding of the individual's health status, as well as their true limitations and needs (56, 75). Understanding these characteristics is a critical step in the development of technologies or products that are centered on the needs of individuals.

4.5 Conclusions

A questionnaire, so-called MAQPD, was developed and its structure was validated by using FA, which allowed for grouping the questions into three domains: ADL, cognition, and pain. The final score for each respondent was calculated using the factor loadings as the weight of the questions. The respondents did not present an extremely severe level of impairment. As the instrument did not present substantial floor or ceiling effects, it can measure both the clinical worsening and improvement of the respondents. The ADLs that respondents had the most difficulty in performing were driving and household chores. Pain and cognition were also relevant aspects.

In conclusion, the MAQPD is the only self-administered questionnaire found in the literature capable of being used remotely, and which can provide a detailed assessment of the general health condition of people with PD.

Serious Game for Rehabilitation and Monitoring of Individuals with Parkinson's Disease

The purpose of this chapter is to describe the architecture and organisation of the developed serious game, as well as to present the evaluation of its usability and accessibility.

5.1 Introduction

In addition to allowing movement training for motor rehabilitation purposes, which is the most commonly found application in the literature for serious games (SGs) (109), patient monitoring and motor symptom assessment of a wide range of diseases, such as Parkinson's disease (PD), can be performed using SGs (171). Due to the variety and severity of PD symptoms, the importance of implementing technological resources such as SG as a valuable tool for clinical assessment and patient-centered monitoring is highlighted (109, 161).

One of the reasons that explain the scarcity of tools effectively used in clinical practice, not limited to controlled environments, is the lack of projects that actually meet the needs of professionals and patients. It is precisely in order to fill this gap that this study presents the design and implementation of a serious game, so-called *RehaBEElitation*. The game was designed considering a long experience of our research group in the evaluation of motor signs of PD (110, 109, 51, 50, 128, 86, 141, 39, 120).

The literature review presented in Chapter 3 showed that most studies related to the development of SGs for PD evaluation (109) do not concurrently address game architecture design, usability issues and game accessibility evaluation. Some studies mentioned the main modules and components of the game but did not present detailed and schematized information about the architecture and organization of the system. The lack of illustrative tools, such as diagrams and schemes, may hinder the understanding about the software framework as a whole. Thus, this research presents in a detailed way the game architecture design through Business Process Model Notation (BPMN), which uses

a set of graphical representations to facilitate the understanding and implementation of the game architecture (25).

In addition, once the game architecture is defined, it is relevant to validate it still at a design stage. This is an important step that we found to be neglected in most studies (148, 115, 47, 170, 5, 22). Thus, we proposed using the Heuristic Evaluation based on the Nielsen-Shneiderman heuristics to evaluate the system's usability (176). Heuristic evaluation is typically used after the system has been fully developed. In this study, we did an evaluation while the design is still in progress to predict and avoid usability issues. This is especially important in the development of SG for severe diseases such as PD, because a lack of understanding of potential usability issues may affect the patient's experience, contributing to clinical follow-up failure. After this first evaluation using the Nielsen-Shneiderman heuristics, we conducted another usability evaluation of the system, but this time focusing on the user experience when operating the game, i.e., using a user-centered approach. In this way, it is ensured the resolution of possible issues that may affect the user's interaction with the game.

Proving that a serious game is accessible is also crucial for ensuring the quality of the game design and for enhancing the player experience. Accessibility generally refers to the elimination of barriers that prevent individuals with various disabilities from accessing or utilising a product, such as a SG (90). This is a relevant assessment as it checks whether the disabled player can play the game similarly to a healthy individual, i.e., it assesses whether the game can be played at a competent level by anyone. According to (54), approximately 2% of the population, or approximately 6.3 million individuals, are unable to play computer games due to a disability. Consequently, this attribute was also considered.

In the literature review we also observed that the PD symptoms were not evaluated using recorded motor signals during users' interaction with the SG, but rather other instruments and/or subjective scales (e.g., Box and Blocks Test (BBT), Purdue Pegboard Test (PPT), Parkinson's Disease Questionnaire-39 (PDQ-39), and Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS)). Our proposal was to develop a serious game that can be used for both rehabilitation and monitoring symptoms of PD through game interaction and recording of inertial data.

The multidimensional assessment questionnaire (presented in Chapter 4) also contributed to the development of the *RehaBEElitation* serious game. The results revealed that carrying out domestic activities involving the use of hands was one of the biggest complaints from respondents in terms of motor limitations. The aim was therefore to develop a serious game capable of training hand movements, with the intention of improving the individuals' performance when executing these tasks.

We also developed a proprietary human machine interface (HMI) for serious game user interaction. The development of a specific instrument, as done in this study, can

be beneficial in several ways, including efficient detection of game's movements, ease in solving calibration problems, greater customization capacity (e.g., size, colours, etc.) to meet various demands, marketability, and a reduced cost HMI device.

In relation to other studies (109) the developed serious game is innovative in the following aspects: (i) the *RehaBEElitation* serious game is able to assess PD objectively, i.e., it is not only useful for rehabilitation but also for the assessment of motor symptoms; (ii) detailed provision of the game architecture through Business Process Model diagrams to facilitate the comprehension of the developed software framework; (iii) implementation of the system in a modularized way to allow future inclusion of processes and features and/or changes in the software; (iv) usability evaluation at the design stage, and using user-centred approaches; (v) evaluation of the game accessibility to ensure that individuals with PD are able to interact with the instrument; (vi) alignment between clinical and game design requirements; (vii) design of many events that enable the evaluation of clinical signs of PD at specific moments of the game; (viii) development of a human machine interface (HMI) device (glove) specific for this application; (ix) proposal of a game narrative that meets the efforts required to deal with the challenges of PD; (x) incorporation of the most relevant movements for clinical evaluation of hand motor signs in PD into the game; and (xi) possibility of longitudinal evaluation of the disease, which ensures long-term follow-up of patients.

5.2 Methods

5.2.1 Design principles of a serious game for rehabilitation and symptom assessment

The guidelines and design principles presented by (123) and (151) for the development of SGs used for rehabilitation and assessment of motor symptoms in people with PD were considered:

- Inclusion of a person with PD in the game refinement process to create a user-centered tool that actually meets the needs of patients while saving time and resources.
- Incorporation of specific motor assessment exercises for PD patients into the game.
- Presentation of a narrative that uses appealing graphics and scenarios, charming animations, and amusing sounds to provide playful experiences and increase player engagement.
- Presentation of clear and objective game instructions so that players understand exactly what they need to do to achieve the objectives of the phases.

- Inclusion of visual and auditory stimuli capable of providing the player with a playful and pleasurable experience while also aiding cognitive training.
- Automatic adaptation and calibration for each player to adjust the range of movement and exercise level required by the game, providing the best experience possible.
- Provision of player progress at each stage and in each game session to encourage competition with oneself and, as a result, motivation.
- Use of a commercially available and low-cost interface device for capturing player movements.

5.2.2 The *RehaBEElitation* serious game

RehaBEElitation is a serious game based on bees, developed for both rehabilitation and monitoring of individuals with PD. The bees represent hard work, effort and dedication, characteristics highly demanded of PD patients during their rehabilitation process. A multidisciplinary team from the fields of biomedical engineering, computer science (with experience in game design), physiotherapy and physical education collaborated in the design and development of the game. In addition, suggestions from a PD patient were considered.

The user must control the movements of a bee in a 3D environment. The game tasks were designed to mimic the following movements found in the gold-standard method tool (MDS-UPDRS Part III) (58) for the assessment of individuals with PD: hand opening and closing, wrist extension and flexion, wrist adduction and abduction, finger tapping, and forearm supination and pronation. These movements are shown in Figure 5.1.

The game presents four phases (Figure 5.2), each representing a bee worker's task in the real world. So that players understand the goal of each phase, four short videos were developed to explain to players the four tasks (each video for each task). Each video is executed before the beginning of each phase, with the option to interrupt it at any time for immediate start of the game. The objectives of the phases are:

- Phase 1: Pollinating the flowers – The objective is to collect pollen from one flower and pollinate another one. Flowers that have pollen to collect are indicated by yellow arcs around them, and those that need to be pollinated are indicated by green arcs. To move the bee up and down the player must perform the movements of wrist extension and flexion; and to move the bee to the left and right the movements of wrist adduction and abduction, if playing with the right hand. The player must move the bee to a flower containing pollen and close the hand to catch it. Then, with the hand closed, the player must move the bee to a flower that does not have pollen and open the hand to deposit it.

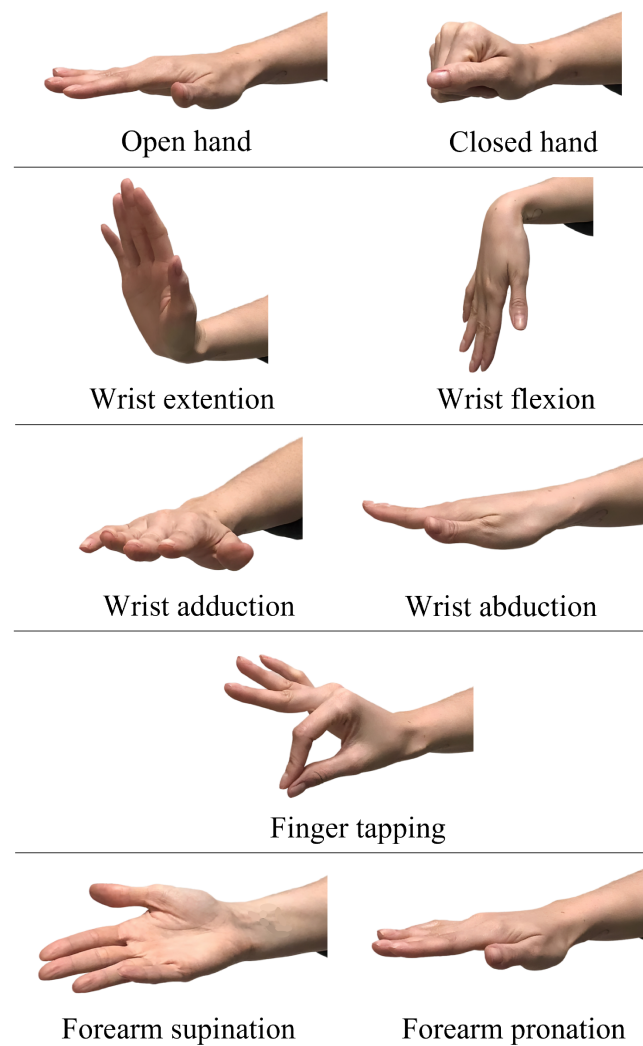


Figure 5.1 – Hand movements used to control the bee in the game and score points.

- Phase 2: Feeding the larvae – The aim is to feed the larvae. The bee moves through the scenario (up, down, left, and right) only if the player's hand is closed. When the player places the bee in front of a larva and opens his hand, the larva is fed.
- Phase 3: Collecting the nectar – The objective is to collect nectar from flowers. Flowers that have nectar are indicated by drops of water. The player must guide the bee to a flower that has nectar and perform the finger tapping movement to collect it.
- Phase 4: Drying the nectar – The aim is to dry the nectar to produce honey. The player must move the bee to the alveoli of the hive containing nectar (indicated by light reflections) and perform the forearm supination and pronation movements. The required movements enable the bee to flap its wings more quickly and dry the nectar.

There are nine different difficulty levels in the game. The characteristics that change

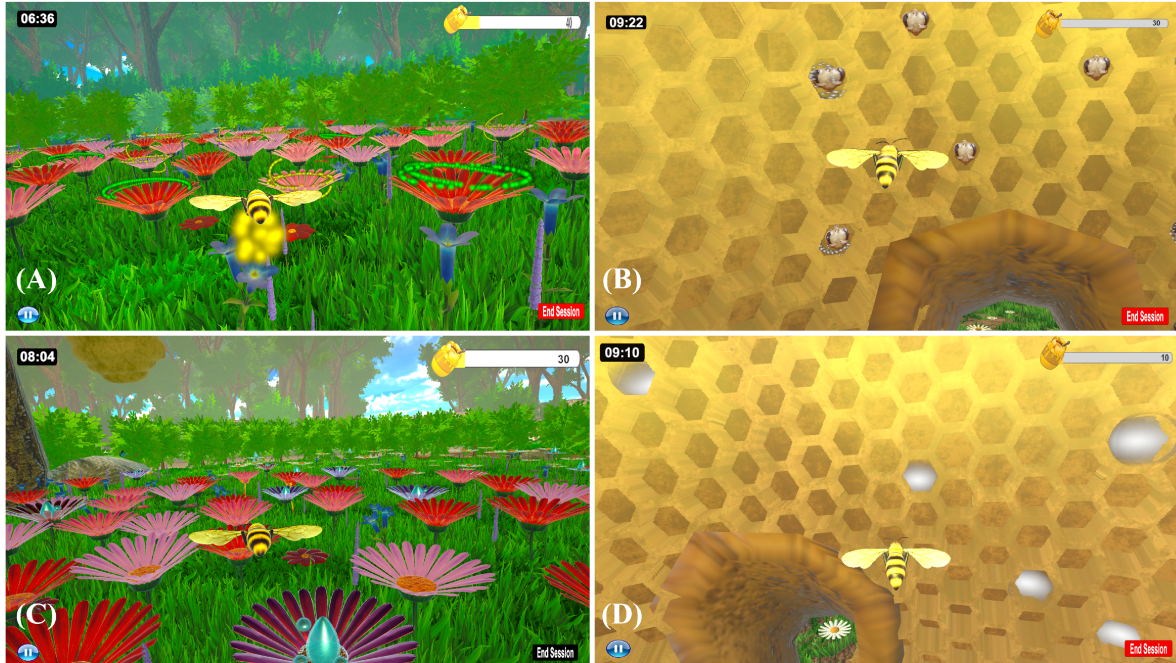


Figure 5.2 – Phases of the game – (A) Phase 1: Pollinating the flowers. (B) Phase 2: Feeding the larvae. (C) Phase 3: Collecting the nectar. (D) Phase 4: Drying the nectar.

according to the level of difficulty are the number of targets that should be reached by the player, the maximum time of the phase, and the speed of the bee movement (Table 5.1). The duration times of the phases in each difficulty level were determined to respect minimum conditions for playing the game, and, at the same time, to challenge the players.

Difficulty level	Number of targets	Maximum time(min)	Bee's speed
1	10	20	1
2	12	15	2
3	14	10	3
4	16	20	4
5	18	15	5
6	20	10	6
7	22	20	7
8	24	15	8
9	26	10	9

Table 5.1 – Game features at each difficulty level.

Each correct hit adds 10 points to the score. It is important to highlight that the player can evolve in the difficulty level independently, i.e., can increase the difficulty level in certain phases and not in others. The difficulty level is advanced for phases where the player reaches the objectives in the established time and maintained for those that this does not occur.

Brainstorming sessions were held to ensure that the game idea was accurately translated into the game design. These sessions were repeated, and the game design refined until a prototype was ready to be evaluated.

5.2.3 Interface device

To enable the communication between the game and the real environment, a HMI was developed (Figure 5.3). It consists of a glove composed of inertial sensors, located in a box attached to the glove on the back of the hand, capable of estimating hand orientation; and conductive thread sewn on the glove, towards the palm of the hand and the fingers, capable of estimating finger tapping movements and hand opening and closing (145).



Figure 5.3 – Two different perspectives of the wearable HMI.

The HMI is composed by a microprocessor (ESP32) which communicates with an inertial sensor (MPU6050). The inertial sensor is composed of an accelerometer and a gyroscope (MPU6050), and a magnetometer (QMC5883L). The microcontroller processes the information from the sensors and sends it to the game via Wi-Fi so that the user can control the bee and play the phases of the game. The device was validated through accuracy, precision, and performance tests, and was shown to be a feasible tool for collecting motor signals from PD patients (144).

There are 12 different states based on the data supplied by the glove to the game, each related to a bee movement. The relationships between states, hand movements and bee movements in the game are shown in Table 5.2.

State	HMI movement	Bee movement
1	Resting	Moves ahead / In place
2	Extension – Open hand	Up
3	Flexion – Open hand	Down
4	Adduction – Open hand	To the left
5	Abduction – Open hand	To the right
6	Finger tapping	Collect nectar
7	Extension – Closed hand	Up and carrying pollen
8	Flexion – Closed hand	Down and carrying pollen
9	Adduction – Closed hand	To the left and carrying pollen
10	Abduction – Closed hand	To the right and carrying pollen
11	Supination	Increases wing speed
12	Pronation	Decreases wing speed

Table 5.2 – Relationship between states, hand movements and bee movements in the game.

The state machine of the game (Figure 5.4) shows all the possible transitions between the 12 states. The player starts in state 1, and from there, can go to any other state.

There is always a return to state 1 before going to another state. For example, if the player wants to move the bee down and to the left, he/she must first perform wrist flexion, return to the resting state, and then, perform wrist adduction (if playing with the right hand).

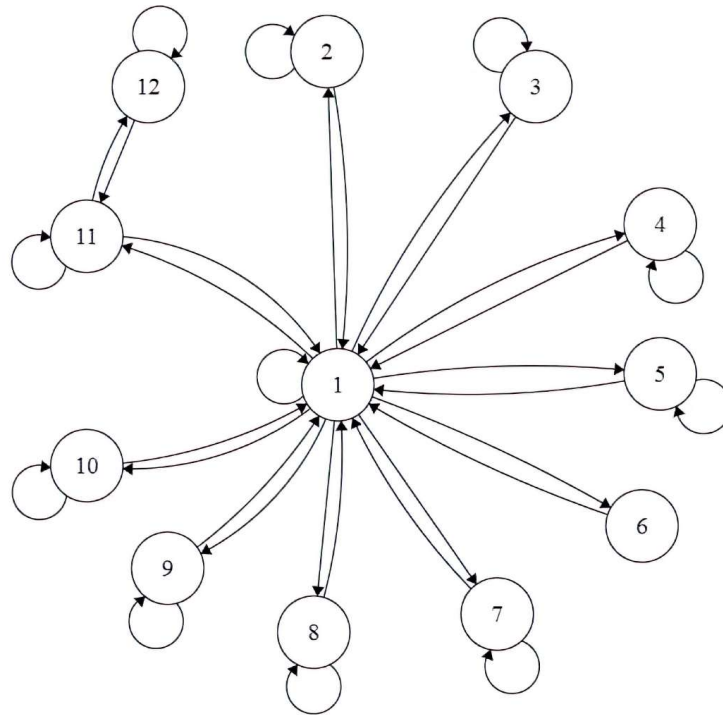


Figure 5.4 – State machine of the game.

5.2.4 Clinical assessment using the *RehaBEE* serious game

The serious game can be used to evaluate motor symptoms of PD, such as bradykinesia and tremor. Assessing these symptoms during a game session is an excellent alternative to monitor health status and disease progression of patients. For this, in addition to using signals collected by the HMI employing inertial measurement units, some markers were defined and incorporated into the game. Such markers are represented by events, responsible for characterizing specific occurrences. Totally, 23 events were defined, shown in Table 5.3.

Event id	Event description	Observations
1	Bee standing still without moving in the scenario	In phases 2 and 4
2	Bee moving forward	In phases 1 and 3
3	Collects pollen	Movement of closing the hand
4	Deposits pollen	Movement of opening the hand
5	Bee moves to the right	Player with open hand
6	Bee moves to the right	Player with closed hand
7	Bee moves to the left	Player with open hand

8	Bee moves to the left	Player with closed hand
9	Bee moves up	Player with open hand
10	Bee moves up	Player with closed hand
11	Bee moves down	Player with open hand
12	Bee moves down	Player with closed hand
13	Collects nectar	Finger tapping movement
14	Dries nectar	Supination movement
15	Dries nectar	Pronation movement
16	Releases/deposits pollen at the wrong time (player's failure)	Negative feedback
17	Player hits the target and can perform the required movement	Visual and audible feedback
18	Player scores a point (audible feedback)	Positive feedback
19	Player doesn't move the bee in the game for 30 seconds (visual and audible feedback)	Reinforcement feedback
20	Player doesn't score a point for one minute and 20 seconds (visual and audible feedback)	Reinforcement feedback
21	Game time is over (game over)	Negative feedback
22	Player completes the level (visual and audible feedback)	Positive feedback
23	Phase is paused	Glove data are not recorded

Table 5.3 – Events defined in the game.

5.2.5 Implementation of the architecture

Unity 3D was used to create the scenarios and interactions, and Blender 3D for the modelling of the game objects. The control panel was developed using Visual Studio 2019; and the database, using PostgreSQL. An overview of the general modules of the serious game is presented in Figure 5.5.

The glove detects hand movement, and a commercial wristband collects physiological signals (E4 – Empatica). The data recorded by the wristband and that recorded by the glove are synchronized to ensure the correct evaluation of the disorder's motor and non-motor symptoms.

5.2.6 Usability evaluation

Evaluation by Nielsen-Shneiderman heuristics

Heuristic evaluation is an evaluation technique used to identify major usability problems of a system that can be employed at a design stage. This technique requires three or more evaluators to apply usability heuristics to the system to identify violations and assess the severity of each violation (176).

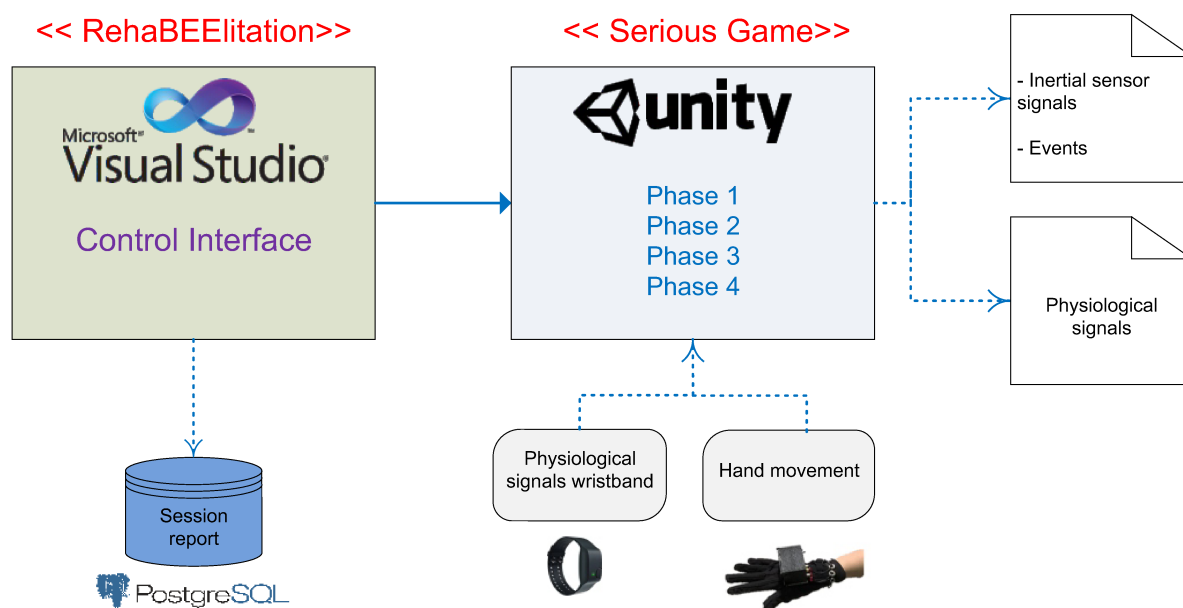


Figure 5.5 – General modules of the serious game.

The usability was assessed by four evaluators with experience in game development, computer science, biomedical engineering, and PD. The severity scores were defined as: 0 – No usability problem; 1 – Superficial problem. Does not need to be fixed unless extra time is available; 2 – Minor usability problem (low priority to fix); 3 – Major usability problem (high priority); and 4 – Usability catastrophe. Must be fixed prior to implementation.

As a result, a table was created detailing how the heuristic was contemplated in the project, besides presenting the description of the usability problem that could be generated if the heuristic was not satisfied, and the severity of each violation.

Evaluation by user-centered approaches

The evaluation of game usability using user-centered approaches was approved by the Ethics Committee for Human Research of the Federal University of Uberlândia. To conduct the assessment, we used the methodology described by Moreno-Ger et al. (98) and Paraskevopoulos et al. (123), which follows user-centered methods. These analyses are performed with two different approaches: using survey-based methods, in which the user fills out evaluation questionnaires after interacting with the system; and using observational analysis, in which the user interacts with the system while the developers observe and evaluate the interaction (69).

A group of five PD patients was involved in the study (one female, four males, 68 ± 5.83 years). This number of users meets the criteria suggested by (137), whereby five users are sufficient to detect more than 80% of usability problems. The eligibility criteria for participants were a confirmed diagnosis of PD performed by a neurologist or geriatrician; be aged between 40 and 100; have a mild to moderate stage of PD (H&Y levels I, II,

and III) (138); have a Mini Mental State Examination (MMSE) score > 22 (53); not have severe visual and hearing impairments; and not have a history of other neurological diseases. In contrast, individuals who did not sign the informed consent were excluded.

Initially, the individuals were instructed to sit on a chair positioned approximately one meter away from the screen on which the serious game was presented. Then, they wore the HMI device on the most affected limb (according to the clinical evaluation). The limb was positioned on a forearm support to isolate the required movements (Figure 5.6).

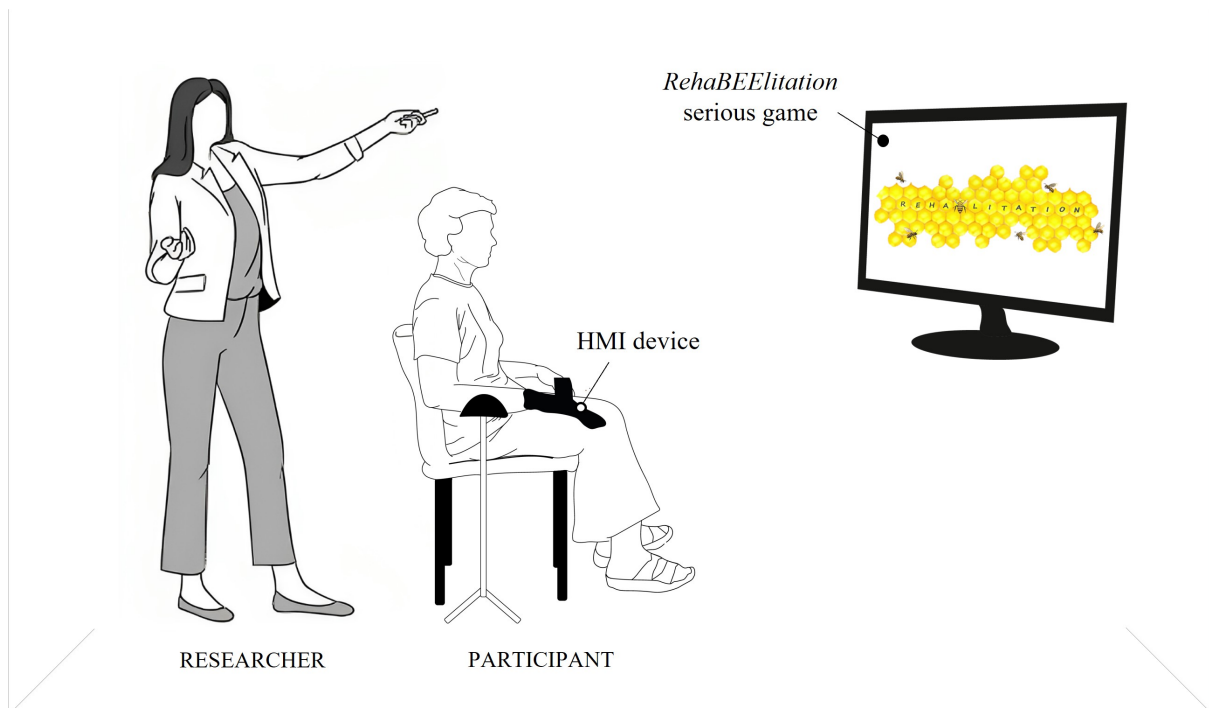


Figure 5.6 – Schematic of the experimental scenario (lateral view).

The participants received brief instructions about the context of the game and were asked to play the four phases for 20 minutes each, or until they complete the phases' objectives. Users were instructed to speak aloud during the interaction, expressing their thoughts and impressions. Participants' interactions with the game were recorded on video using a camera, which captured the user's hand and reactions; and the game screen was simultaneously recorded using OBS Studio software (7).

Immediately following the end of the session, each participant answered the System Usability Scale – SUS (Appendix C), one of the most reliable methods for assessing the usability of a system. This scale consists of ten questions, with five response options each, ranging from "strongly disagree" to "strongly agree" (18). To calculate participant's scores, the number 1 is subtracted from the score the user answered in the odd-numbered questions and the score the user answered in the even-numbered questions is subtracted from the number 5. Then, the values of all questions are added, and the sum is multiplied by 2.5, so that the total questionnaire score ranges from 0 to 100. For this questionnaire,

the overall average taken as reference is 68 points (18). Thus, a score lower than 68 points suggests that the developed serious game has usability problems.

However, since the SUS scale was not developed to specifically assess the usability of SGs (113), additional instruments that assess enjoyment and engagement, such as the Game Experience Questionnaire – GEQ (Appendix D) and the Short Flow State Scale – SFSS (Appendix E), were also used. The GEQ is an instrument that evaluates gaming experience through player’s perception (105). It consists of four modules: core, in-game, social and post-game. Responses to the questions are given on a Likert scale ranging from 0 (not at all) to 4 (extremely) (67). Only the core and post-game modules were applied. The in-game module should be applied during game breaks/intervals, and to avoid interrupting the user-game interaction, this module was not implemented. The social module was also not applied because it should only be enforced if the game had multiplayer features, and this was not desired.

For the core module, the component scores are calculated as the average value of their elements: immersion – questions 3, 12, 18, 19, 27, and 30; flow – 5, 13, 25, 28, and 31; competence – 2, 10, 15, 17, and 21; positive affect – 1, 4, 6, 14, and 20; negative affect – 7, 8, 9, and 16; tension – 22, 24, and 29; and challenge – 11, 23, 26, 32, and 33. For the post-game module, the component scores are also calculated as the average value of their items: positive experience – questions 1, 5, 7, 8, 12, and 16; negative experience – 2, 4, 6, 11, 14, and 15; tiredness – 10 and 13; and return to reality – 3, 9, and 17.

The SFSS assesses the player’s flow experience, i.e., their degree of engagement and immersion in the activity. It is composed of nine items, one for each dimension of flow: challenge-skill balance, action-conscience fusion, clear goals, unambiguous feedback, focus on task, sense of control, loss of self-awareness, time transformation, and autotelic experience. Each question presents five response options, ranging from "strongly disagree" (1) to "strongly agree" (5) (70). Participant’s scores are calculated by averaging their responses to all items.

In addition, volunteers answered a semi-structured interview of four questions: 1) Would you play this game more often?; 2) What did you consider easy in the game?; 2) What did you consider not easy in the game?; 4) Would you change something in the game?. These questions allow a more exploratory approach to detect possible usability problems (163).

After this first session, the recorded video showing the user was synchronized with the one showing the game screen (Figure 5.7). The synchronization was performed using Movavi Video Editor software (127). Next, the videos of the five participants were submitted to four evaluators, who composed a multidisciplinary team from the fields of game development and design, physical therapy, biomedical engineering, and physical education. The purpose of analysing the videos was to evaluate the participants’ interaction with the game, identifying and recording all significant events, which occur when the user

finds a problem or visibly reacts to the game.



Figure 5.7 – Synchronised video showing the participant performing the movements while playing, and the game screen. Participants’ identity was preserved.

Following the analysis of the videos, the questionnaires responses and the answers to the semi-structured interview, a list of game improvements was prepared. For each negative event observed, a corrective action was proposed. After making the changes in the game, the five PD patients interacted with the *RehaBEElitation* again and answered the questionnaires to validate the changes made.

Variables were described by mean, standard deviation, median, minimum, and maximum. The Shapiro-Wilk test was used to check whether the distribution of the data fits a normal distribution. The paired-samples t-test (for variables with normally distributed data) and Wilcoxon test (for variables with non-normally distributed data) were used to confirm differences for questionnaire responses before and after the game changes. A p-value of 0.05 was considered.

5.2.7 Game accessibility evaluation

An experimental session was conducted to assess the game accessibility, also approved by the Ethics Committee of the Federal University of Uberlândia. This was performed to assess whether the impaired group (experimental group – EG) can play as well as the healthy group (control group – CG), i.e., whether the serious game provides accessible gameplay.

In total, 30 participants were involved, being 15 healthy subjects and 15 individuals with PD, matched in age and gender (10 men and 5 women, 66.27 ± 9.13 years old). The criteria for participant eligibility were the same as those described above for the game usability evaluation.

Again, the individuals were instructed to sit on a chair positioned approximately one meter away from the television on which the serious game was presented (Figure 5.6). Then, they wore the HMI device on the most affected limb (according to the clinical evaluation). The limb was positioned on a forearm support to isolate the required movements.

The participants were asked to play each phase of the game for five minutes. Data collection was performed in the ON and OFF states of medication for EG, and the first session was performed with individuals in the OFF state, when they arrived at the data collection site, in the morning. The ON state occurs when disease symptoms are under medication control, and the OFF state occurs when symptoms are not being properly controlled by medication (23, 84). Following the first session, the EG participants took the medication and after feeling its effect on the body (approximately 90 minutes after ingestion), they interacted again with the game in a second session, as in the previous one. All participants played the game in the easiest difficulty level. The CG participants interacted with the *RehaBEElitation* serious game in a single session.

The game accessibility was assessed by estimating the final score of each game phase. In this way, it is possible to compare the performance of players in each group and verify whether players with PD have similar ability to play the game as healthy players.

One-way analysis of variance (ANOVA) and t-test with Bonferroni correction for pairwise comparisons between groups were used to compare group performance. When the ANOVA assumptions were not met, the non-parametric Kruskal-Wallis test was used. A p-value of 0.05 was considered. Data analysis was performed in R (139).

5.3 Results

5.3.1 The architecture of the *RehaBEElitation* serious game

The general BPM describing the interaction between the actors of the system (patient/player and therapist/researcher) and the game processes is shown in Figure 5.8.

Appendix F shows the BPM for the calibration of the game, the BPM for the operation of each phase and the BPM related to the data collection.

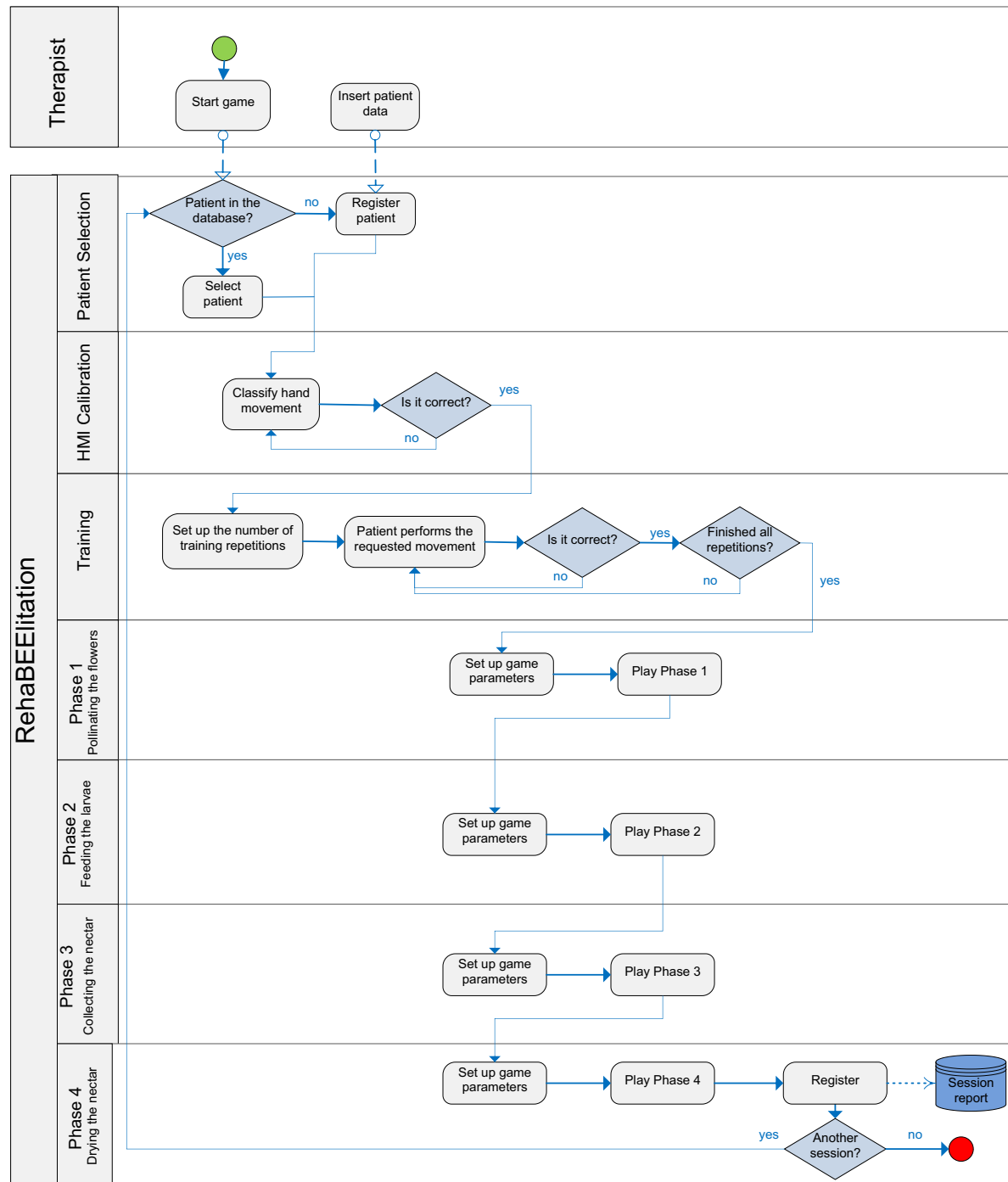


Figure 5.8 – Interaction between the actors of the system and the game processes.

5.3.2 Usability evaluation

Evaluation by Nielsen-Shneiderman heuristics

Table 5.4 presents the usability evaluation of the game at a design stage. The severity scores are based on the mean score estimated from four evaluators (designers) specialized in game designing, PD, and usability assessment. As mentioned above, this stage was crucial to avoid usability problems and ensure a good user interaction with the developed serious game.

Heuristics	How the heuristic was contemplated in the project	Description of the usability problem	Severity
H1. Consistency and patterns - Users should not have to worry about whether words, situations, or actions mean the same thing.	1 - The interface for game control was designed considering ergonomics and the positioning of sensors in pre-established regions for signal capture during clinical exams. The consistency consists of following the positioning already adopted in clinical studies.	1 - The health professional (researcher) has a mental model that comes from training. Changing the positioning of the sensor can generate confusion about the information acquired.	2.50
	2 - Perform game calibration considering clinical routine, clinical experience, and patient conditions.	2 - Do not ensure that the movement of the bee follows the movement of the hand, generating stress, demotivation, frustration, non-understanding of the activity.	3.50
	3 - Alignment between the tasks of the avatar (bee) with the tasks that the bees perform in the real world. For example, the bee pollinates in the real world as well as in the game.	3 - Problems interpreting the narrative of the game because it violates a mental model established according to the experiences of the participants about the role of bees in nature.	2.00
	4 - Direct relationship between the evaluations required in the clinic with those required for game control.	4 - Patients would not be stimulated to perform movements required for clinical assessment.	4.00
H2. Visibility of system state - The system should keep the user informed of what is occurring, through appropriate feedback.	1 - After the system calibration stage, with the objective of correctly identifying the hand movements, the system presents to the user the state in which the player's hand is, offering feedback to the user that the interface is functioning correctly.	1 - Difficulty in identifying problems related to game control. For example, the user (player) could move his hand to the right and the avatar does not obey the instruction given by the user.	3.25
	2 - Availability of real-time information showing that the physiological and inertial signals were effectively being collected.	2 - It may be impossible to control the avatar.	2.00
	3 - A light signal was available on the glove indicating that the device was on.	3 - It may be unable to control the avatar.	2.00
	4 - The targets were identified by the presence of markings such as arcs and light reflections to facilitate target identification and correct avatar positioning.	4 - As the game was built in three dimensions, the target location could be harmed by problems related to depth perception in the virtual scenario.	3.75
	5 - Presentation of a virtual object (hand in 3D) that showed the player the movement needed to perform the expected task.	5 - The player might not understand which movement should be done to execute the task.	3.00
	6 - Presentation of the players' score progress by a progress bar that is filled with honey.	6 - Misinformation about the game progress.	1.25
	7 - Visual and auditory feedback whenever the player reached the target, performed the correct movement, and met the phase's objectives.	7 - Loss of engagement of the player during the game.	2.25

H3. Correspondence between the system and the real world - The system must "speak" the same language as the user, making information natural and logical.	1 - Correspondence between the required task and the intuitive movement that the hand performs. In the real world the movement of closing the hand is intuitively associated with collecting things, and opening the hand is associated with depositing things. Then, in the real world the player closes his hand to collect the pollen and opens his hand to deposit it.	1 - Reduce player engagement, since using random, non-intuitive movements could interfere with the player's mental model and expectation.	3.00
	2 - The game narrative corresponds to the tasks the avatar performs in the real world, such as pollinating flowers, feeding larvae, collecting, and drying nectar.	2 - Reduce player engagement, since using random scenarios or activities could interfere with the player's mental model and expectation.	2.75
	3 - The movements used in the game are in accordance with those performed during clinical assessments, such as hand flexion and extension, finger tapping, pronation and supination, opening and closing of the hand.	3 - Ineffectiveness of the game for movement rehabilitation and motor symptom assessment in PD.	4.00
	4 - Insertion of the avatar in the expected environment in the real world, e.g., the avatar (bee) was inserted in scenarios such as garden with flowers and inside a hive.	4 - Reduce player engagement, since using random scenarios or activities could interfere with the player's mental model and expectation.	2.50
	5 - Correspondence of the virtual elements of the game, i.e., pollen, nectar, and larva, with their actual form found in the real world. The pollen in the game is represented by grains of the same form that is found in nature. The nectar is represented by water since in the real world 70% of its composition is water. The larva is represented by a real image of a bee larva.	5 - Difficult the player's immersion.	2.50

H4. Minimalist design - Dialogs should contain only the necessary information.	1 - Avoid excessive use of engagement reinforcement through virtual elements. In a preliminary version of the game, two virtual elements were incorporated, a butterfly and a bird, to reinforce the player's motivation. The butterfly appeared in the scenario whenever the player remained more than 30 seconds without making any movements. The bird would appear whenever the player did not score for about a minute. However, after a preliminary test, the designers verified that such elements were excessive, producing negative stimuli (i.e., irritation by the constant presence of stimuli).	1 - Increased stress and anxiety during the game, reducing immersion in the game.	2.00
	2 - Presence of few visual elements in the scenario. In phases 1 and 3 of the game the scenery is composed by flowers, grass, some insects, and the presence of a single tree with a beehive. In phases 2 and 4 the game takes place inside the beehive that has only the honeycomb with the targets (the larvae or the nectar).	2 - The increase of the number of elements in the scenario could cause distraction to the player, making it difficult to reach the game objectives.	1.00
H5. Recognize rather than remember - Users should have no need to remember information from one part of the system to another.	1 - The use of visual and auditory feedback to recognize relevant steps of the game. For example, when the user reaches the end of the scenario, a virtual hand is shown indicating the movement that should be performed by the player to continue the game.	1 - The user could imagine that the game was terminated early. The user might not execute the correct move at the correct time.	2.50
	2 - Movements already known and practiced during clinical assessment were incorporated into the game, thus facilitating recognition and intuitive execution of the movements.	2 - Overload the gameplay process, because besides learning the game rules, the player would have to learn how to execute the required moves.	3.00
H6. Informative feedback - Immediate and informative feedback should be given to users about their actions.	1 - Presence of visual elements in the interface that help the execution of movements at the moments in which they should occur. For example, the 3D hand indicates the movement that the player must perform when he reaches the target. In addition, the hand indicates to the player the exact way to execute the movement, effectively promoting the recording of motor signs of Parkinson's disease or improving the results of the application of the game as a rehabilitation tool. Another example is the use of target delimitations through visual elements that assist the correct positioning of the avatar.	1 - Difficulty to comprehend the game and its current state. The lack of visual elements on the interface hinders the learning process on how to actually play the game. In a preliminary version of the game, in phase 1, when the user reached the end of the scenario, a 3D hand always appeared open, indicating the adduction or abduction movement that the player should perform; however, if the player was holding the pollen (with a closed hand), when seeing the virtual open hand, the player automatically opened his hand releasing the pollen at the wrong moment.	3.00
	2 - Presence of sound feedback when the player scores, reaches a target, and completes the phase.	2 - Difficulty to establish a mental model that facilitates the understanding of the game state.	2.25

H7. Flexibility and efficiency of use - The system should satisfy both beginners and experienced users. The provision of shortcuts is a way to adjust to the various types of users.	1 - Nine difficulty levels were established with the intention of facilitating gameplay by people affected by distinct severity levels of motor signs of PD. In addition, the presence of nine levels of difficulty contributes to the development of rehabilitation protocols customized to the reality of the patient; and also, to evaluate pharmaceutical treatments, since it is expected that individuals with PD who are responding more adequately to treatment will find it easier to play the game at different levels of difficulty.	1 - People with distinct motor limitations, due to the severity of motor signs such as tremor and bradykinesia, might not be able to play the game. Moreover, players might not notice their progress in the game or even not be able to interact with the game. For some volunteers the interaction could be too easy and for others too complex, interfering with the flow experience. This could further impact adherence to the rehabilitation protocol.	3.50
	2 - The calibration of the system is done in a personalized way, respecting the motor limitations of people with Parkinson's disease. This way, people with a smaller range of movement can interact effectively with the game.	2 - The control of the avatar would be impaired. The number of people able to use the system would be reduced. This may produce negative feelings in the users, as they may have the feeling of being unable to perform the activities. In addition, since the calibration is done with the execution of the movements in their maximum amplitude, the absence of a personalized calibration makes the patient's movement be performed below what he really could execute, jeopardizing the result of treatments and evaluations.	3.00
	3 - The glove project was developed to allow the free execution of movements. The glove was projected in different sizes, respecting hand anatomic patterns. The glove material was merino wool, which enabled the development of a firm glove for the connection of the box with the electronic circuitry and provided comfort to the user. In addition, a conductive thread was used to make it possible to embed the electronic circuits directly into the fabric and at the same time ensure the execution of the movements.	3 - The absence of ergonomics could cause discomfort to the players and cause the discontinuity of the therapeutic process. For example, in a first version of the game it was used a glove with thicker fabric that made it difficult to close the hand.	2.50

H8. Assist users to recognize, diagnose and recover from errors - Error messages must be clear, objective and suggest solutions.	1 - Presence of auditory and visual feedbacks that indicate an action error caused by the player. In phase 1, when the player releases the pollen at the wrong moment the representation of the pollen on the screen disappears and a negative audio feedback is presented.	1 - The user does not notice the wrong execution of the movement and does not have the opportunity to correct the action. This, can leave him confused, affecting his learning in relation to the game.	2.25
	2 - When registering a user already in the system, an error message is presented to inform that that user is already registered.	2 - Causing duplication of the same user in the system.	2.00
	3 - An alert message informing that the data collected will not be saved if the user does not play all the phases in a single trial session.	3 - Lack of data to fully evaluate the motor signs of the person with PD. This does not guarantee that the patient will perform all the movements necessary for evaluation or rehabilitation.	3.00
	4 - Before starting the calibration process an alert message is presented to the player asking him to keep his hand in a stable position to ensure that the calibration is performed correctly.	4 - The avatar control will be affected, impairing the interaction.	3.50
H9. Error prevention - Preventing errors is better than providing good error messages.	1 - The data is automatically saved right after the execution of the four phases of the game.	1 - Data can be lost, impairing the assessment and recovery of patients with PD, loss of time and financial resources, discontinuation of periodic follow-up for medication adjustment and distrust of the process involved in the assessment. In cases of evaluation of patients on the OFF state of medication (when the patient's body is not under the effect of the drug) this loss of data is even more damaging since this situation produces great discomfort to the patient.	4.00
	2 - The game does not allow phases to be started without prior selection of a user and calibration of the glove.	2 - Absence of association between the registered data and the user identification.	3.75
H10. Clear closure - Every task has a beginning and an end.	1 - Visual and audible feedbacks are shown to the player when game tasks and phases are completed. A positive feedback message is presented whenever the player fulfills the phase objective in the established time.	1 - Lack of perception about the closure of game actions. This can cause distress, tension, irritation, and discontent.	3.00
	2 - At the end of the collection session, the system informs that the data was successfully saved.	2 - Doubts can be generated about the storage and availability of the data.	1.75

H11.	Reversible actions - Users should be allowed to recover from errors.	1 - Possibility of executing tasks in an indeterminate way. In phase 1, if the player cannot reach a target in the scenario, the game allows the player to naturally return to the lost target.	1 - The player does not complete the planned tasks, thus interfering on the therapeutic benefits of an effective assessment.	3.00
		2 - Users can make both correct and incorrect moves without the game interfering. In phase 1, if the player does not close his hand when collecting pollen, the game avatar remains on the target until the correct move is made. If the player makes an incorrect finger tapping movement (tapping all fingers together) in phase 3, the game avatar will remain on the target until the correct movement is made.	2 - If the game does not offer the opportunity for the player to repeat the movement, the user may become frustrated and not learn the correct movements for the use of the game. In addition, the user may make random movements that will not contribute to his clinical assessment.	2.75
H12.	User language - Language must always be presented in a way that it is understandable by the intended users.	1 - The textual and symbolic elements are simple and understandable. When the user finishes a phase satisfactorily a short text message appears on the screen ("Congratulations"). On the other hand, when he or she finishes the game phase unsatisfactorily, the message "Time Out" appears on the screen. In addition, the 3D model of the avatar (bee) and the hand were elaborated to represent reality, being easily understood by the users.	1 - Hinder the interaction between the user and the game, causing boredom, confusion regarding performance and demotivation.	2.00
		2 - Introductory videos for each phase were elaborated to contextualize the game narrative.	2 - If the player does not understand the tasks of a bee in the real world, he will not understand the narrative of the game.	2.75
H13.	User control - The system should be designed in such a way that users initiate actions, not respond to them.	1- Perform a calibration procedure that correctly identifies the movements required for controlling the game avatar.	1 - The lack of an adequate calibration may cause the user not to dominate the game, but rather to feel dominated by the game.	4.00
		2- Inclusion of standardized visual and audible feedback to facilitate memorization and learning of task execution.	2 - The absence of visual and sound feedback can lead to unexpected results and may result in the feeling that the user is not effectively controlling the system.	2.00
H14.	Help and documentation - The system must provide help and have a quick search form.	1 - The game includes training phases in which the user exercises and learns the movements required to control the avatar.	1 - The absence of the training phase can make learning more difficult, hindering the interaction and interfering in the rehabilitation and monitoring of PD symptoms.	2.75
		2 - The presence of virtual objects that aid in determining the proper movements to be performed.	2 - The absence of virtual objects can have an impact on movement execution, interfering with gameplay and clinical assessment.	3.00
		3 - The game has introductory videos that explain its narrative.	3 - The absence of videos about the game narrative can cause the player to become disconnected from the game, affecting gameplay.	2.75

Table 5.4 – Usability evaluation of the game at a design stage.

Evaluation by user-centered approaches

Table 5.5 presents the results comparing the responses to the applied questionnaires before (1st session) and after (2nd session) the changes. Significant differences are indicated by bold p-values.

Questionnaire	1st SESSION		2st SESSION		p-value
	Mean(SD)	Median (Min - Max)	Mean(SD)	Median (Min - Max)	
SUS	76 (9.62)	75 (62.5 - 87.5)	89.5 (4.11)	92.5 (85 - 92.5)	0.0111
GEQ - Immersion	2.87 (0.22)	2.83 (2.67-3.17)	3.53 (0.36)	3.67 (3 - 3.83)	0.0088
GEQ - Flow	2.84 (0.38)	2.8 (2.4 - 3.4)	3.5 (0.5)	3.4 (2.8 - 4)	0.0105
GEQ - Competence	2.16 (0.33)	2 (1.8 - 2.6)	3.84 (0.36)	4 (3.2 - 4)	0.0002
GEQ - Positive effect	3.56 (0.33)	3.6 (3 - 3.8)	3.88 (0.18)	4 (3.6 - 4)	0.0349
GEQ - Negative effect	0.35 (0.55)	0 (0 - 1.25)	0.3 (0.54)	0 (0 - 1.25)	0.8492
GEQ - Tension	0.07 (0.15)	0 (0 - 0.33)	0 (0)	0 (0 - 0)	0.7133
GEQ - Challenge	2.32 (0.39)	2.2 (2 - 3)	1.32 (0.36)	1.2 (1 - 1.8)	0.0008
GEQ - Positive Experience	3.33 (0.46)	3.33 (2.67 - 3.83)	3.8 (0.3)	4 (3.33 - 4)	0.0189
GEQ - Negative Experience	0.03 (0.07)	0 (0 - 1.67)	0 (0)	0 (0 - 0)	0.8986
GEQ - Tiredness	0.1 (0.22)	0 (0 - 0.5)	0.1 (0.22)	0 (0 - 0.5)	1
GEQ - Return to reality	1.07 (0.55)	1 (0.67 - 2)	1.87 (0.38)	2 (1.33 - 2.33)	0.0092
SFSS	3.89 (0.71)	4 (2.77 - 4.55)	4.33 (0.41)	4.33 (3.67 - 4.67)	0.0374

Table 5.5 – Statistical analysis of data.

Statistically significant differences were found for all questionnaires except for the GEQ "negative affect", "tension", "negative experience" and "tiredness" items. The mean scores of all questionnaires increased after the game modifications, indicating that the changes improved the game usability (except for the GEQ items with no significant differences, and the "challenge" item). The item showing the greatest difference after the game improvements was the users' competence to play ($p=0.0002$).

The analyses of the videos and the answers to the semi-structured interview allowed the identification of four problems which affected the game usability. For each issue detected, a solution action was proposed and implemented in the system. Table 5.6 shows the problems identified and the improvement actions applied.

Identified issues	Improvement actions
The glove did not correctly identify the movements of opening and closing the hand and finger tapping	Improve the ergonomics and structure of the glove. Use a thinner fabric glove and sew more conductive lines on the palm of the hand and fingers
The position of the targets in Phase 1 was not well adjusted	Turn the entire target area into the target itself in Phase 1

The 3D hand picture that appeared on the screen when the player reached the end of the scenario in Phase 1 still appeared open, even though the player was holding the pollen	Leave the 3D hand on the game screen in the same state as the player's hand is at the end of the scenario in Phase 1
As the game scenario is in three dimensions, targets in Phases 2 and 4 located closer to the edges of the screen appeared to be distorted	Remove targets from areas too close to the edges of the screen in Phases 2 and 4

Table 5.6 – Problems identified and the improvement actions applied.

5.3.3 Game accessibility evaluation

The main characteristics of the participants are given in Table 5.7.

Healthy group		Experimental group					
Id	Age	PD-ON				PD-OFF	
		Id	Age	MDS-UPDRS III	H&Y	MDS-UPDRS III	H&Y
1	82	1	57	25	2	61	3
2	64	2	80	25	2	49	2
3	80	3	64	26	2	58	2
4	66	4	77	31	2	44	2
5	51	5	59	24	2	47	3
6	56	6	64	39	2	48	2
7	77	7	70	20	2	41	2
8	62	8	73	42	3	45	3
9	60	9	60	12	1	29	2
10	80	10	66	16	1	29	1
11	69	11	69	37	2	70	3
12	59	12	60	31	2	54	2
13	62	13	50	35	3	59	4
14	55	14	68	38	2	52	2
15	71	15	77	11	1	38	1

Table 5.7 – Main characteristics of the participants of the study.

ANOVA was used to determine whether there was a difference in age between the healthy and PD groups. The test result confirmed that there was no statistical difference in age between the groups ($p > 0.05$). ANOVA was used to compare MDS-UPDRS III scores in the ON and OFF states of medication, and it revealed a statistical difference ($p < 0.05$) between the experimental conditions (ON and OFF). ANOVA was also used to compare Hoehn and Yahr scores in both states of medication and found no statistical difference ($p > 0.05$). Figure 5.9 shows the scores of the individuals for each group in each of the four phases of the game.

In Phases 1, 2, and 4, no statistically significant differences ($p > 0.05$) were found between the groups' scores, as confirmed by ANOVA (Phase 1) and Kruskal-Wallis rank

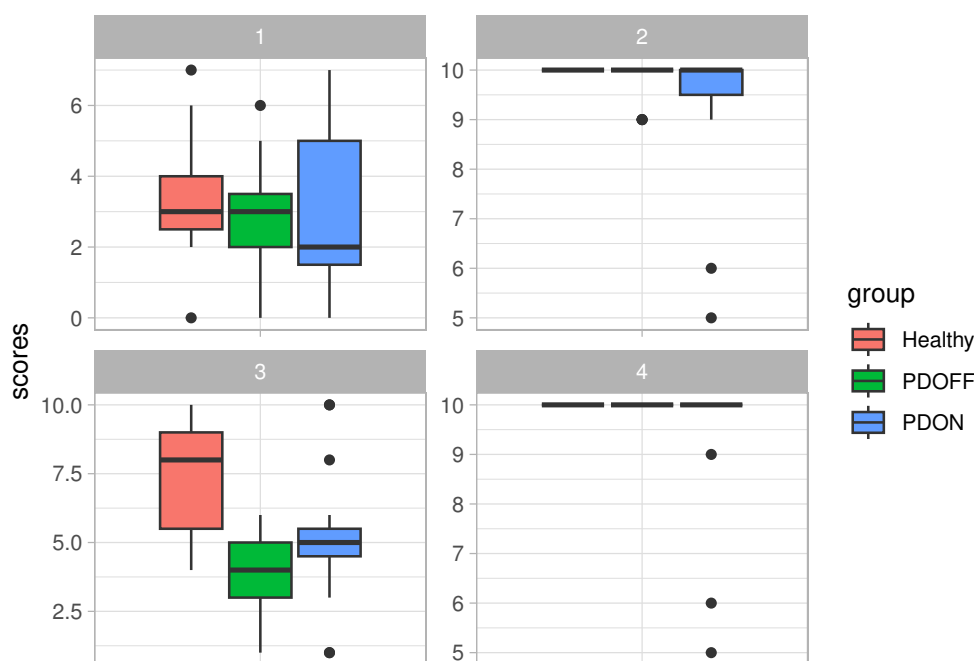


Figure 5.9 – Scores in each phase of the game.

sum test (Phases 2 and 4). This indicates that the scores of the participants were similar, suggesting that in these phases, all players can meet the phase objectives equally. In Phase 3, statistically significant differences in scores were found between groups of healthy participants and those with PD in the OFF state ($p=0.00027$), as well as between groups of healthy participants and those with PD in the ON state ($p=0.01351$), as indicated by the pairwise t test. These findings suggest that the movement required in Phase 3 (finger tapping) is difficult to perform for PD patients in both medication states, because it requires fine dexterity of the hand's fingers.

5.4 Discussion

The *RehaBEElitation* serious game was created to meet a real demand in the evaluation of upper limb motor signs in PD. The hand plays a fundamental role in our functional activities and its function can be severely affected in early stages of the disease, being of great relevance to evaluate motor signs in this region. Although there are initiatives in the literature for the assessment of upper limbs in PD using SG, there is a lack of development of methods that insert protocols from consolidated clinical tools, such as the MDS-UPDRS, in the game design. This is undoubtedly one of the great differentials of this study. By incorporating knowledge of clinical practice to the game, the game result will be more easily accepted by the clinical community, and the patient will have an easier interaction with the game since he is used to perform certain movements during clinical evaluation sessions.

By incorporating a wearable technology to monitor and record motor signs of PD, the healthcare professional or researcher has at his disposal a tool to visualize events that are imperceptible to the unaided eye, complementing and expanding the usual clinical evaluation. Thus, using sensors that allow the professional to identify nuances about the disease may be important, and may even be the differential factor for identifying the beginning of a serious disease or a change of trajectory in the disease treatment. From this perspective, i.e., a real demand to accurately monitor some PD symptoms (bradykinesia, tremor, or motor fluctuations), the *RehaBEElitation* emerges as an instrument that can be exactly useful in the clinical and even surgical environment, e.g., it can be used to evaluate the results of ablative surgeries and deep brain stimulation.

Several studies (43, 8, 96, 85) point to a high incidence of depression, anxiety and other negative emotional aspects that accompany PD. This contributes to the patient not having the necessary engagement in rehabilitation processes or even clinical assessment. Thus, the use of a playful assessment scenario, such as the one provided by the game, can be the difference between a successful or an inaccurate assessment. It is known that the mere fact that a person with PD is being monitored can instantly affect their motor signs (93). Thus, if the person is immersed in the virtual reality provided by the game, the influence of external factors can be reduced, contributing to a more accurate assessment of the effectiveness of treatments and the clinical condition of the individual.

The requirements gathering stage for the development of the *RehaBEElitation* serious game considered the participation of patients and professionals with experience in PD (e.g., biomedical engineers, physiotherapists, physical educator, researchers, neurologist, neurosurgeon, and experts in computer science, ergonomics, and human factors). Unlike several existing studies in the literature (46, 148, 28), the game was developed in such a way to place the end-user as the center of the development process. This may be fundamental for a good acceptability of the game.

The game architecture was designed having in mind two actors: the individual with PD (e.g., the player) and the professional who will be performing the assessment (e.g., physical therapist, neurologist, or a researcher). These actors can interact with the system at different times, and the game was modularized to customize interfaces for each type of actor. For instance, the therapist has exclusive access to glove calibration interfaces, user registration and experimental session customization. These modules are completely independent from other modules of the system, allowing future advances, such as the inclusion of modules for the generation of reports (e.g., for the presentation of the frequency of motor fluctuations, tremor, and bradykinesia) and connection with other data management systems for people with PD (51).

The system architecture considers the possibility of the user carrying out training sessions before experimental and clinical sessions. The independence of these steps is essential for the user to understand the game and execute the movements correctly, since it

is through the execution of such movements that the clinical assessment will be performed. At the same time, the system requires that during the clinical assessment the user performs all the processes related to the four phases of the game to ensure the execution of a protocol that allows the assessment in different contexts, as recommended by the MDS-UPDRS clinical scale.

The system was modularized to implement parallel and concurrent programming at different levels. For instance, the microcontroller responsible for interfacing the glove with the game estimates all parameters independently from other running processes. This requires less computational effort, which contributes to the use of more accessible hardware, since in countries like Brazil the cost of computers is still high and modern computers are not always available in clinical environments. Moreover, the independence between the processes contributes to the fluidity of the game and the control of the interface elements in real time.

Furthermore, the developed architecture allows the inclusion of new elements for monitoring the patient's state. For instance, in the current version of the game, there is a module which is responsible for collecting and storing data from a commercial device (e.g., E4 wristband). This feature is desirable since it extends the functionality of the developed tool without changing its fundamental characteristics. Thus, modularization also contributes to avoid obsolescence of the game, since other devices can be attached to it without compromising its basic operation. Finally, the inclusion of other sensors in the system enables the extension of the use of the game for the evaluation of new forms of motor and non-motor PD signs contemplated in its original design.

The developed system allows recording the biomedical and inertial signals of the participants. In addition, it records pre-defined events that can help the evaluation of the variability of biomedical signals during the period of the occurrence of the events. This functionality presents great clinical relevance, as it allows the assessment of the user in several contexts, for example, during the execution of different tasks and reception of different visual and sound stimuli.

The system design was developed in an incremental manner always considering the possibility of improvements due to unit test results (Figure F.6). Thus, even with the progress of the system development, new improvements were integrated into it according to the results of the usability evaluation performed at the design stage (Table 5.4). To evaluate the usability, the perception and experience of four evaluators were considered. In general, usability problems were identified with severity levels above 1 (that is, problems of medium, high or extremely high nature). By incorporating the necessary usability improvements to the game, we avoided players using a system that is still in an incipient stage (e.g., with basic usability problems), contributing to the good acceptance of the tool in the clinical scenario.

The heuristic evaluation performed contemplated all the 14 heuristics proposed by

Nielsen-Shneiderman. It was possible to identify improvements to be implemented due to each of them, emphasizing the relevance of the use of heuristic evaluation still at the design stage of SG development. In a recent literature review, which contemplated the use of SG for PD (109), it was not found any study that presented how the heuristics that aid the development of a game with good usability were contemplated. The application of this method in this study is also a contribution to the advancement of the design of SG for PD.

From the heuristic evaluation it was possible to identify the following usability issues classified as extremely serious (severity equal to 4): (i) the absence of a calibration step, enabling the adequacy of the game control to the motor impairment of the person with PD, could substantially affect the control of the game, causing serious gameplay problems; (ii) the meaning of a loss of data from an experimental session goes far beyond the loss of a file on a computer. This is a problem that can and should be seen as a usability problem. The loss of data may mean that the user is again exposed to a complex and long evaluation (since he may even be without the effect of medication) and that this previous experience may generate frustration and distrust in him, which totally interferes in the usability of the system; (iii) The lack of direct relationship between the evaluation performed by the game and that performed in a clinical scenario may generate problems related to the difficulty of understanding the tasks and performing movements, effectively jeopardizing the use of the game.

Under the perspective of user-centered usability evaluation, statistical analysis of the questionnaires was presented in Table 5.5. Considering the SUS and SFSS scales, it can be observed that the improvements made to the game contributed to raising game usability and participant engagement. The GEQ results showed that participants' competence in playing the game significantly increased. Although learning may have contributed to that, this result also suggests that the improvements actually enhanced the participant's interaction with the game. However, the characteristics "negative affect", "tension", "negative experience" and "tiredness" showed no changes before and after game modifications, probably because, even in need of improvements, the game did not generate negative feelings in the users since the first session. Moreover, participants perceived a lower level of challenge after the changes, indicating that the game's difficulty level decreased with the improvement actions. This result was already expected as the changes made in the game were aimed at correcting problems and improving player-game interaction.

Finally, Table 5.6 showed the four improvement actions carried out. The most significant improvement action in terms of frequency of problem occurrence was related to the glove used for player communication with the game. In the first session, the glove did not recognize well the closing and opening movements of the hand and the finger tapping movements, which significantly affected the game usability. For the second session, a new glove made with a thinner material and with more threads sewn on the palm of

the hand and fingers was developed, which solved the previously mentioned problems and thus considerably improved the participants' interaction with the game.

The game accessibility evaluation was performed to assess whether patients with PD were able to play the game in the same way as healthy patients (150). Statistical tests showed that the groups of healthy individuals and those with PD are homogeneous in terms of age. In general, as indicated by the MDS-UPDRS III and Hoehn and Yahr scores (Table 5.7), PD patients in the OFF medication state showed a higher degree of impairment compared to the ON state. However, despite all limitations, the assessment of the game accessibility revealed that *RehaBEElitation* can be played by individuals with PD in both medication states as well as by healthy individuals. Phase 3 was the only one that showed statistically significant differences between the scores of the healthy group with the PD group in both states of medication. As finger tapping is a movement that requires fine motor dexterity of the fingers, it is expected that a patient affected by a disease that causes limitations in the execution of movements, especially fine movements, will in fact feel more difficulty in performing the movement than an individual without impairment.

Due to situations such as the one imposed by the COVID-19 pandemic, the need to develop technologies for remote use was observed. In this context, the *RehaBEElitation* serious game could be used for remote assessments; however, the way the game was implemented does not allow its use in this scenario so far, being this one of the limitations of the game. It cannot yet be applied remotely at home, due to the following reasons: (i) The game must be played in the presence of a professional, who can clarify doubts and observe the execution of the tasks; (ii) In several countries, such as Brazil, there is still no legal regulation that allows the use of systems of this nature at home. Thus, we chose not to incorporate this possibility of use, although the game architecture is flexible enough to allow future incorporation; (iii) The use of SG involves the registration of biomedical data, and the use of the system at home may compromise the data security; (iv) The use of games at home requires the availability of connection to stable network systems, often not available to users.

Moreover, in the current version, the game cannot be played by hearing impaired patients, as they do not perceive important sound feedbacks emitted by the game. However, we are working to incorporate in the HMI device vibratory actuators to allow the delivery of tactile feedbacks to these individuals. Finally, the game cannot be played simultaneously by multiple players in the current version; however, the game architecture also enables the implementation of this feature.

In the future, we intend to incorporate into the game components that also allow the assessment of lower limbs of individuals with PD, enabling, for example, gait assessment. In this way, it would be possible to perform a complete and objective evaluation of patients by using the *RehaBEElitation* serious game.

The system described in this chapter was registered at the Brazilian National Institute of Industrial Property (INPI – registration number: BR 51 2021 001975 0). Appendix G provides supplementary information about the serious game, available in an open general-purpose repository (Zenodo).

5.5 Conclusions

This chapter presented the architecture and the usability evaluation of the *RehaBEElitation* serious game. The user-centered system was conceived from requirements of serious game projects, having in its conception the participation of a multidisciplinary team with experience in game development and PD.

The proposed architecture was presented using the BPM to facilitate the reproduction of the system, and to extend its application to other scenarios of use considering the evaluation of other diseases. In the same way, the heuristic evaluation presented can serve as a guide for the development of new SGs. The usability evaluation results showed that *RehaBEElitation* is a game that presents simple and intuitive narrative and interface, compatible with the players' mental models. This facilitated the interaction of individuals with the game and contributed with the great acceptance of the whole system.

In summary, the developed system allows the evaluation and monitoring of individuals with PD using an accessible serious game, objectively. The detailed description of the game architecture, as well as the evaluation of the game usability can help professionals from different areas to develop more efficient systems and technologies.

Objective Assessment of Bradykinesia and Tremor

The aim of this chapter is to present the objective assessment of the main motor symptoms of Parkinson's disease using the *RehaBEElitation* serious game.

6.1 Introduction

The loss of dopaminergic neurons caused by Parkinson's disease (PD) impairs the execution and control of body movements (167). The absence of dopamine in individuals with PD stimulates the manifestation of several motor symptoms, such as bradykinesia and tremor (122). Due to these symptoms, individuals affected by the disease are limited to perform simple daily tasks, which interferes in their quality of life (71, 91).

The pathophysiological explanation for the appearance of PD symptoms begins with the occurrence of oxidative stress, characterised as the imbalance between free radicals and antioxidants in the body. In general, this stress causes damage to cells of proteins, lipids, and DNA, contributing to the development of diseases such as PD (35).

For PD, oxidative stress damages dopaminergic neurons, i.e., it causes degeneration/loss of dopaminergic neurons in the substantia nigra of the mesencephalon. This reduces the concentration of dopamine in the striatum, a structure involved in motor learning and development of movement patterns (35, 20). As a result of this reduction in dopamine concentration, dysfunctions in neurotransmitter systems occur, such as abnormal synapses between neurons, which results in the appearance of symptoms such as akinesia and tremor. It is considered that the first motor signs of the disease occur when 70% or more of the dopamine in the striatum has been lost (20).

Bradykinesia is a symptom that must be present in an individual in order to be diagnosed with PD, i.e., bradykinesia affects all people who have PD (73). It is the main motor impairment observed in patients, characterised by the inability to plan, initiate, and perform movements (172). Basically, bradykinesia is manifested by the following features: slowness in the execution of voluntary movements; prolongation of reaction time, defined

as the interval between the stimulus' presentation and the beginning of the movement; prolongation of movement time, defined as the period of time between the beginning and the end of the movement; and, consequently, prolongation of response time (RT), which is the sum of reaction time and movement time (41). In short, RT represents the ability of an individual to detect relevant sources of information, process that information and use it to generate an appropriate movement response (156).

Tremor, often defined as the first, most obvious and most problematic motor symptom of PD, is a rhythmic and involuntary oscillatory movement of a body part (132, 140). The pathophysiology of tremor in PD is not yet fully understood and, unlike bradykinesia and rigidity, its severity is not related to the overall degree of dopaminergic denervation (132, 131). The classic tremor in PD is rest tremor, which affects the hands of approximately 70% of patients at the beginning of the disorder. It is an asymmetric tremor of 4 to 7 Hz in a body part not activated voluntarily, and which generally decreases with a voluntary movement (132, 140, 104).

The Movement Disorder Society–Unified Parkinson's Disease Rating Scale (MDS–UPDRS) is the most commonly used and considered the gold standard method for clinical assessment of bradykinesia and tremor (58). The clinical evaluation of bradykinesia is based on the analysis of the patient's ability to perform rapid, repetitive, and alternating hand movements, such as finger tapping, opening and closing the hand, and pronation and supination (74, 83). For clinical assessment of tremor, an examiner analyses the amplitude in centimetres of tremor and estimates the percentage of time the symptom is present in a patient's limb with the naked eye (157). Then, for both symptoms, the assessor assigns a score between 0 (normal) and 4 (severe) to indicate the level of impairment of the disease, i.e., scores are given according to his/her visual perception (110). Observational assessments such as this require experienced clinical professionals to minimize the effects of subjectivity and bias of the method, which can negatively influence both disease diagnosis and patient monitoring (86). In addition, the clinical assessment cannot accurately describe the amount of bradykinesia and tremor in a patient (110, 157).

As previously discussed, objective measurements of motion using inertial sensors can overcome the shortcomings of visual scoring-based scales (157). The objective assessment of motor signs of PD using wearable sensors has been widely studied. Rabelo et al. (141) discriminated groups of PD patients from healthy elderly by an objective assessment of bradykinesia using inertial sensors. Andrade et al. (110) observed that it is possible to study resting hand tremor and postural tremors using a single inertial measurement unit (IMU) placed on the back of the hand. As inertial sensors can measure voluntary and involuntary movements (74, 32), the use of tools with these devices is a promising alternative capable of identifying and quantifying motor signs of PD. In addition, assessing bradykinesia using time measurements is an accurate way to assess an individual's slowness. Because both reaction time and movement time are impaired in PD (41), RT may

be a good predictor of slowness severity. It is important to emphasize that the objective evaluation supplements the evaluation performed by clinical scales (12).

Therefore, the objective of this chapter was to assess in an objective way the bradykinesia and tremor of individuals with PD during their interaction with the *RehaBEElitation* serious game.

6.2 Methods

This study was approved by the Ethics Committee for Human Research at the Federal University of Uberlândia, and was composed of fifteen individuals with PD constituting the experimental group (EG) and fifteen healthy individuals constituting the control group (CG). The members of the groups were paired in age and sex. The eligibility criteria for participants and the data collection protocol were the same as those presented previously (section 5.2.7 Game accessibility evaluation). The data used to assess accessibility, bradykinesia and tremor were collected from the same experimental protocol. The PD group interacted with the game in both ON and OFF medication states. The MDS-UPDRS Part III was applied to the EG by a physiotherapist in each session, before starting the game, i.e., in both states of medication.

6.2.1 Bradykinesia evaluation

First, bradykinesia was clinically assessed using the scores related to items 3.4a to 3.6b of the MDS-UPDRS Part III for the EG in both ON and OFF states of medication. These items assess: 3.4a and 3.4b – tapping the fingers of the right and left hands, respectively; 3.5a and 3.5b – movements of the right and left hands, respectively; and 3.6a and 3.6b – pronation-supination movements of the right and left hands, respectively. The average scores of these items were considered for each medication state. In addition, bradykinesia was objectively assessed for all participants in two ways: by calculating the RT and by estimating the individuals' angular velocity (AV) of movement.

RT involves both reaction and movement time, and AV (in degrees per second) represents the speed of movement execution (125) (i.e., in relation to the RT variable, AV is linked to movement time). In this way, if AV increases in one section compared to another, it is understood that movement time decreases. Thus, if it is verified that the velocity of movement execution reduced after the use of medication, i.e., in the ON state compared to the OFF, the time to perform the movement increased, which may suggest a failure in the medication effect.

In addition, RT allows considering aspects related to the player's reaction time, such as the learning acquired after a first section of interaction with the game. The participant may, for example, decrease his reaction time by learning that immediately after receiving

the visual and sound stimuli, he should perform the movement required to score points in the game in the shortest possible time.

In this study, bootstrap was used to estimate the mean of RT and AV of each participant. The number of bootstrap samples was set to 1,000. As the Shapiro-Wilk test indicated that the distribution of the data does not fit a normal distribution (for both RT and AV variables), the non-parametric Kruskal-Wallis test was used, with Wilcoxon test with Bonferroni correction for pairwise comparisons between groups.

To compare the results of the two variables (RT and AV), descriptive statistics were used. Signal processing and statistical analyses were performed using The R Project for Statistical Computing (139) software.

Response time estimation

RT was measured by defining a binary event in the game that signals when the player approaches the target and executes the movement. This event begins when the player is supplied with visual and auditory stimuli indicating that he can do the movement, and ends when the player performs the movement and scores in the game. Figure 6.1 shows the game screen (during Phase 1) when the player reaches the target. RT was calculated by estimating the duration of this event.

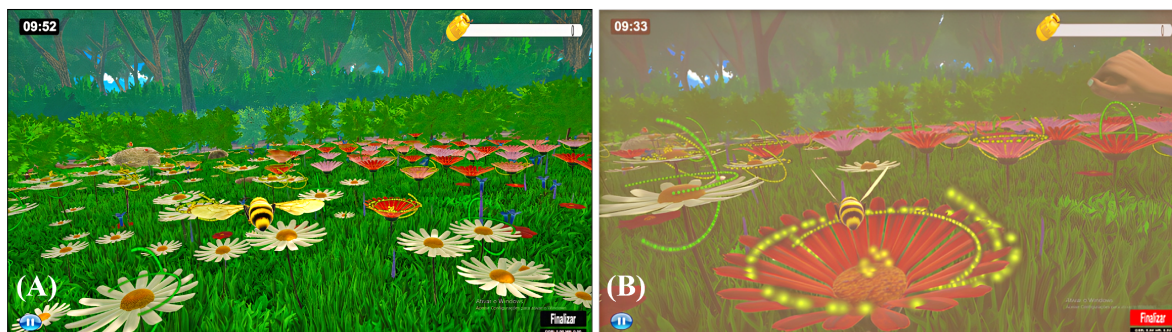


Figure 6.1 – (A) Game screen while the player freely controls the bee in the scenario. (B) Game screen when the player reaches the target and receives the visual and sound stimuli indicating that he/she can start executing the required movement. At this point (B), the bee remains static, the screen subtly changes colour, a virtual hand appears in the corner of the screen indicating to the player the movement to be performed, and a sound effect is emitted.

Figure 6.2 illustrates the occurrence of the described event of a volunteer from the EG in the OFF state during Phase 4. This player arrived at the target and executed the movement required ten times (ten occurrences of the binary event). The start and end indices of each event were identified to determine the start and end times of the event. The duration of each event was then estimated by calculating the difference between the end and start times.

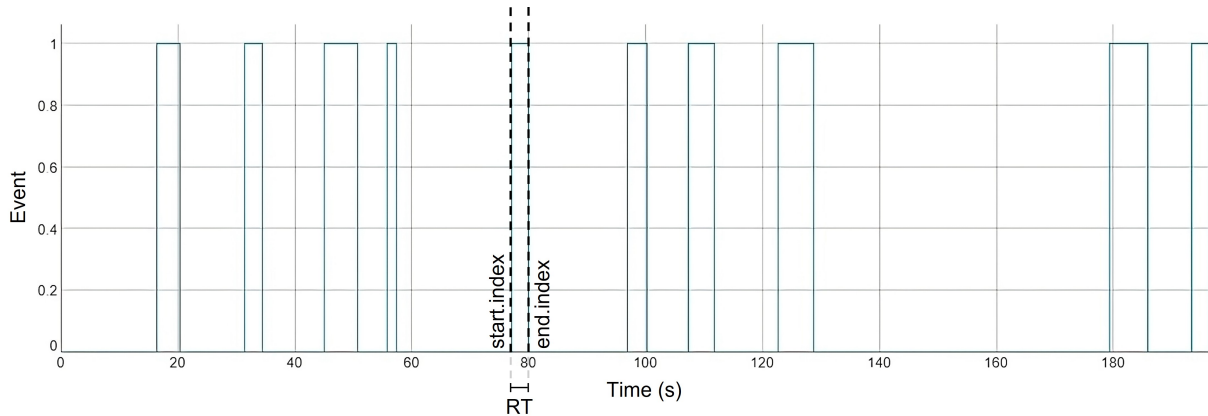


Figure 6.2 – RT estimation from the defined event.

Thus, as RT is the sum of reaction time and movement time, both reaction time and movement time were taken into consideration to estimate the slowness of the individuals (Figure 6.3). This evaluation was performed for the four phases of the game.

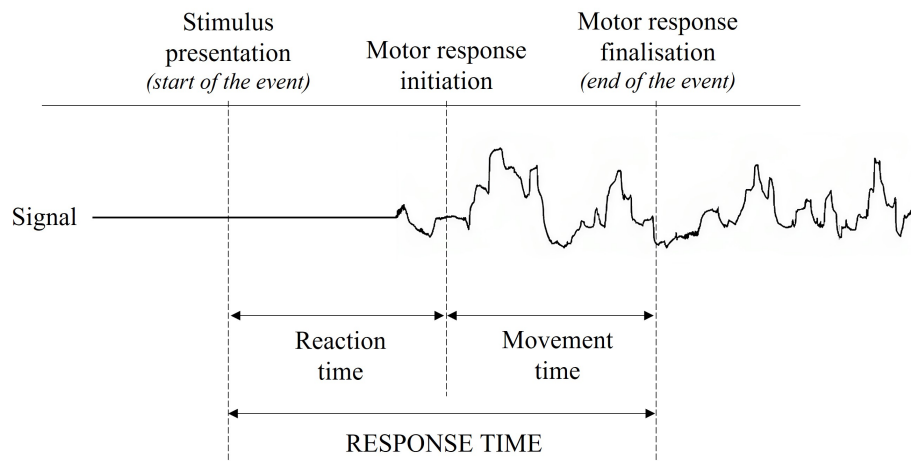


Figure 6.3 – Definition of RT, which includes both reaction time and movement time.

Angular velocity estimation

Gyroscope signals were used to measure the AV around a reference axis, which indicated how fast the movement was performed (125). This characteristic was estimated only for Phase 4 of the game because it is the only phase that requires the execution of a movement performed around one of the measurement axes of the inertial sensor (forearm supination and pronation).

As previously described, the motor symptoms of PD can be detected by inertial sensors, which are able to record the movements of individuals in the form of time series. These movement signals recorded by the sensors include both voluntary movements of the player to control the bee in the scenario and involuntary movements caused by the disease (represented by tremor). The presence of involuntary movements may interfere on the

estimation of bradykinesia; hence, they should be eliminated from the collected signals. Thus, to extract only information related to players' voluntary movements, it was necessary to use a signal processing method capable of performing time series decomposition.

Time series decomposition involves deconstructing a time series into several components, each representing one of the underlying categories of patterns in a signal. Several techniques can be used for time series decomposition, such as Fourier analysis, Empirical Mode Decomposition (EMD) and Singular Spectrum Decomposition (SSD). However, as the recorded signals are non-stationary time series, Fourier analysis is not the ideal option (88). Moreover, Fourier analysis and EMD can provide data decomposition results with limited physical sense, i.e., components with unclear physical meaning. The components retrieved by these techniques can also be affected by mode mixing, again interfering with the physical meaning of individual components (16). Regarding the SSD technique, it was first tested to decompose the original signal, but no successful results were obtained. The selection of the fundamental parameters in SSD (window length and elementary component indices) is completely automated, and this resulted in components with no physical meaning.

The Singular Spectrum Analysis (SSA) is a decomposition method frequently used in several fields, such as economics, physics, and geography (59); however, no study applying this method to signals collected from individuals with PD was found in the literature. For these reasons, the SSA method was used in this study.

Singular Spectrum Analysis (SSA) SSA is a non-parametric method for the analysis of time series and digital images. This method decomposes a time series into a set of components that are grouped and interpreted, and the original time series is recovered by summing all its components (59). SSA can be used to remove periodic and/or trend components from a time series, leaving only a particular component, which may have real and interpretable meaning (60, 59). In this study, the decomposition was performed so that bradykinesia could be evaluated objectively by using only the signals of voluntary movement, i.e., by analysing the trend component of the signals (without the influence of the tremor).

A general description of the method is presented below (60, 59, 63). SSA performs the four steps illustrated in Figure 6.4. The input X is an ordered collection of N real numbers (e.g., a time series or a digital image), and the output is a decomposition of X into a sum of identifiable components: $X = X_1 + \dots + X_m$.

- **Step 1 – Embedding:** The starting point of SSA is the embedding of the time series X into a vector space of dimension L . As an example, $X = (x_1, \dots, x_N)$ and $T = SSA$ maps R^N to the space of Hankel matrices $L \times K$ with equal values on the anti-diagonals. Thus, the embedding procedure constructs a sequence of vectors of

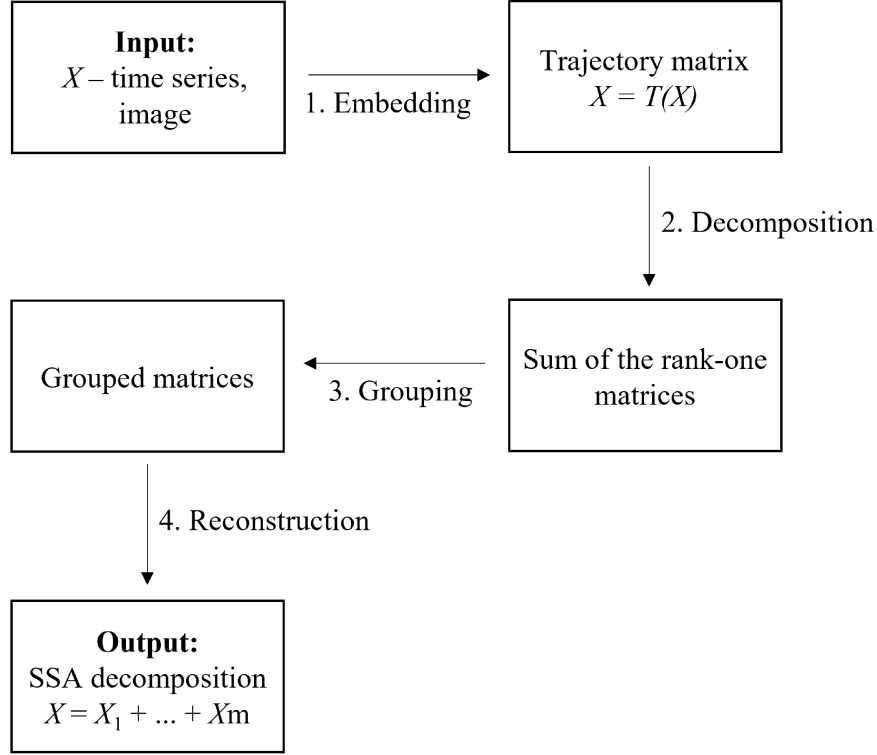


Figure 6.4 – Generic scheme of the SSA decomposition method.

the original time series using lagged copies of the scalar data. N is the length of the series, L is the length of the window (which is a parameter) and $K = N - L + 1$.

$$T(SSA)(X) = \begin{pmatrix} x_1 & x_2 & x_3 & \cdots & x_k \\ x_2 & x_3 & x_4 & \cdots & x_{k+1} \\ x_3 & x_4 & x_5 & \cdots & x_{k+2} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ x_L & x_{L+1} & x_{L+2} & \cdots & x_N \end{pmatrix}$$

- Step 2 – Decomposition: The result of this step is the decomposition $X = \sum_i X_i$, $X_i = \sigma_i U_i V_i^T$, where $U_i \in R^L$ and $V_i \in R^K$ are vectors such that $\|U_i\| = 1$ and $\|V_i\| = 1$ for all i and σ_i are non-negative numbers. This step performs the singular value decomposition (SVD) of the trajectory matrix and represents it as a sum of rank-one bi-orthogonal elementary matrices. Let $S = XX^T$, $\lambda_1 \geq \cdots \geq \lambda_L \geq 0$ be eigenvalues of the matrix S , $d = \text{rank} X = \max\{j : \lambda_j > 0\}$, $U_1, \dots, U_d$ be the corresponding eigenvectors, and $V_j = X^T U_j / \sqrt{\lambda_j}$, $j = 1, \dots, d$, be factor vectors. Denote $X_j = \sqrt{\lambda_j} U_j V_j^T$. Then the SVD of the trajectory matrix X can be written as $X = X_1 + \cdots + X_d$. The triple $(\sqrt{\lambda_j}, U_j, V_j)$ consisting of the singular value $\sigma_j = \sqrt{\lambda_j}$, the left singular vector U_j and the right singular vector V_j of X is called j_{th} eigentriple.

- Step 3 – Grouping: The grouping step corresponds to the division of the elementary matrices X_j into several groups and summing the matrices within each group. The grouping procedure partitions the set of indices $\{1, \dots, d\}$ into m disjoint subsets $\{I_1, \dots, I_m\}$, with each group I_k containing a set of principal components $\{i_1, \dots, i_p\}$ representing specific components of the signal. Let $I_k = \{i_1, \dots, i_p\}$. Then the resulting matrix XI_k corresponding to the group I_k is defined as $XI_k = Xi_1 + \dots + Xi_p$. These matrices are computed for $I_k = I_1, \dots, I_m$ and the SVD expansion leads to the decomposition $X = XI_1 + \dots + XI_m$. Each XI_k represents a set of eigentriples which describes a specific component series in the original time series.
- Step 4 – Reconstruction: The last step is to reconstruct the components of the original series. This is achieved by diagonal averaging of each XI_k to provide the k_{th} component of the series X , where the n_{th} sample is obtained by averaging over the cross-diagonal $i + j = const = n + 1$ of XI_k . This is because each XI_k can be seen as the Hankel matrix for the corresponding embedded component series. Then the resulting decomposition of the initial object X is $X = X_1 + \dots + X_m$.

The main R software function for the SSA method is `ssa`, which constructs the `ssa` object that holds the decomposition and various auxiliary information. The typical call of the `ssa` function in R is:

```
s <- ssa (x, L = (N + 1) %/% 2, neig = NULL)
```

The main arguments are (N is the length of the series):

- `x` is an object to be decomposed (e.g., time series).
- `L` is a window length, which by default is fixed to half the length of the series. However, it is also recommended to use a proportional value to the periodicity of the time series. Very high values of `L` may mix the trend component with the periodicity components. Therefore, `L = 250` was used (the sampling frequency of the data).
- `neig` is the number of eigentriples desired. If `neig = NULL`, a default value, which depends on `L` and `N`, will be used. It was considered `neig = NULL`.

The function returns a `ssa` object. The precise layout of the object is hidden, but identifying the indices of the elementary components is necessary for the next step (reconstruction). This identification is performed to find the selection parameters of the principal components to group the elementary time series. The indices of the elementary components can be identified by using the `$` operator, and by analysing the plots of the eigenvalues and the correlation matrix of the eigenvalues, namely:

- `s$sigma` returns the vector of single values.
- `(s$sigma)2` returns the vector of eigenvalues.
- `plot(s)` plots the eigenvalues.
- `plot(wcor(s))` plots the w-correlation matrix.

By definition, the first singular value (with highest eigenvalue) corresponds to the trend component of the series (59). Thus, the first elementary component indice will be used in the reconstruction step for the signal trend extraction.

The reconstruction step is performed with the `reconstruct` function. The typical call of this function in R is:

```
r <- reconstruct(s, groups = list(Trend = 1))
```

The main arguments are:

- `s` is a `ssa` object that holds the decomposition.
- `groups` is a list of numeric vectors consisting of the indices of the elementary components used for the reconstruction; the list entry can be named, and in this example it was called `Trend`. The elementary component of index 1 represents the trend of the time series, which characterises the voluntary movement of the player.

Thus, SSA was applied to the original signal collected during the experiment to extract the trend component of the signals (voluntary movement). Figure 6.5 illustrates the decomposition of a gyroscope signal from a participant of the EG.

After applying SSA for signal decomposition, the peaks of the signals representing the voluntary movement were identified and discriminated by using a threshold (`th`) of 0.5 to capture only the regions of interest and evaluate the participants' slowness of movement, as depicted in Figure 6.6. In this way, the influence of involuntary movement arising from PD was mitigated for the assessment of bradykinesia.

The SSA decomposition method was able to satisfactorily capture the trend of the time series. This method smoothed the peaks of the decomposed signal (attenuated the amplitude of the peaks), as shown in Figure 6.7, which was quite convenient for the detection of global peaks which describe the angular velocity of the players. This smoothing was important to avoid the detection of multiple local peaks, which could be related to the players' tremor, and which would require the application of several pre-processing steps, such as setting several thresholds, different for each analysed signal.

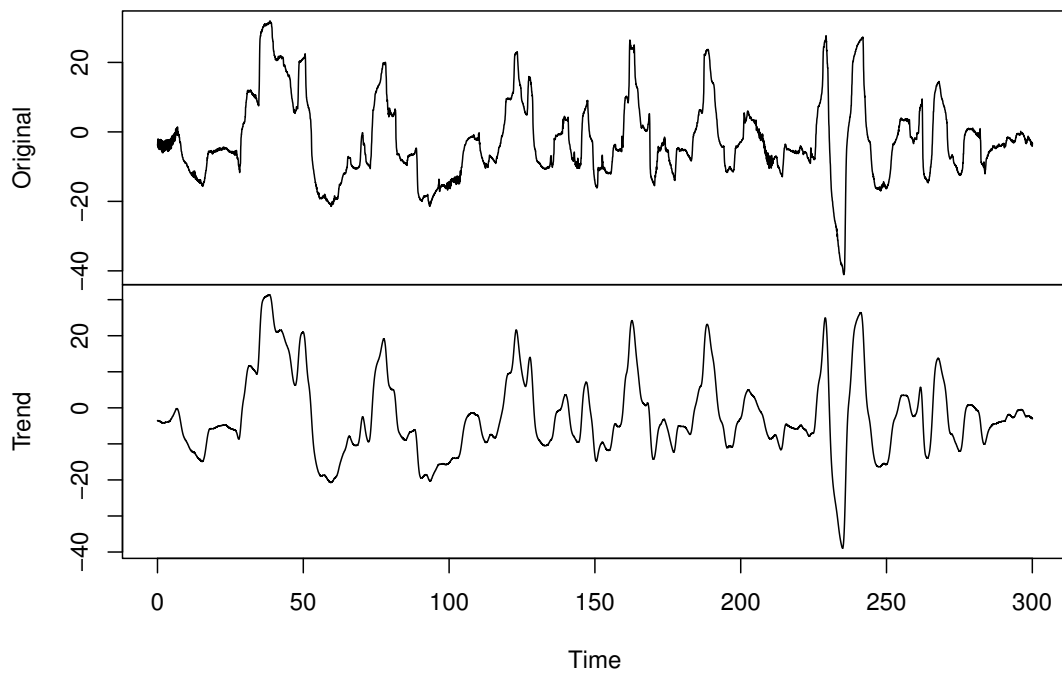


Figure 6.5 – Decomposition of a gyroscope signal from a EG participant. The first signal (on top) represents the original signal, and the second, the voluntary movement that the individual performs to play the game.

6.2.2 Tremor evaluation

Tremor was firstly assessed clinically using the scores related to items 3.15a to 3.17b of the MDS-UPDRS Part III. These items assess: 3.15a and 3.15b – postural tremor of the right and left hands, respectively; 3.16a and 3.16b – kinetic tremor of the right and

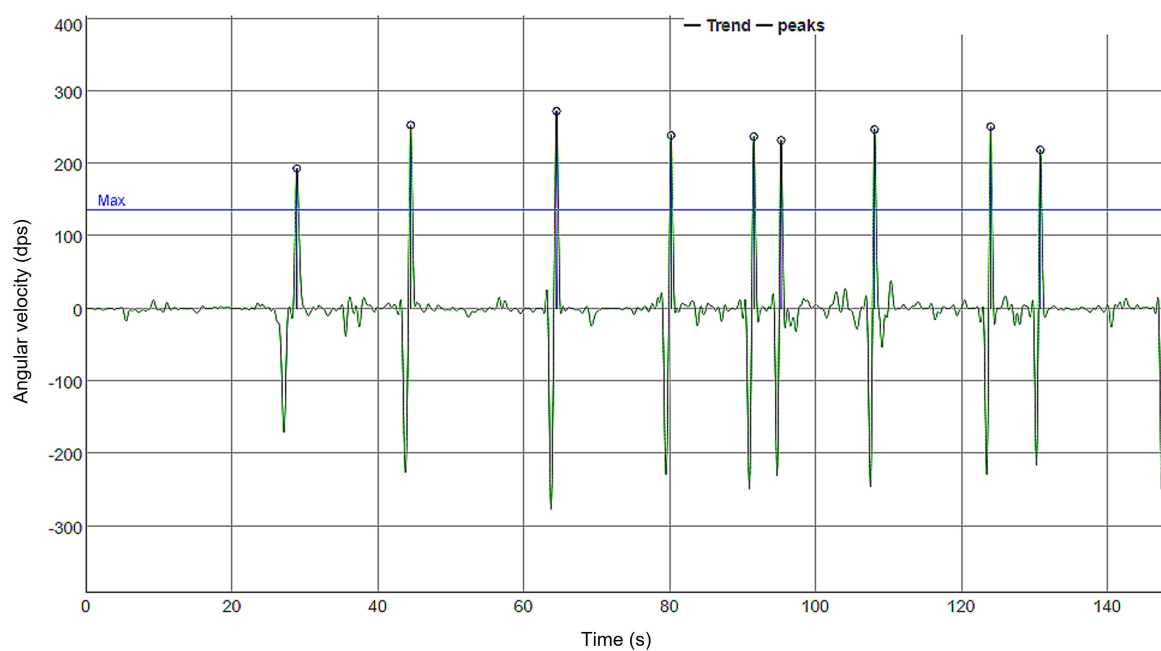


Figure 6.6 – Peak detection of the gyroscope signal, which represents the angular velocity of movement.

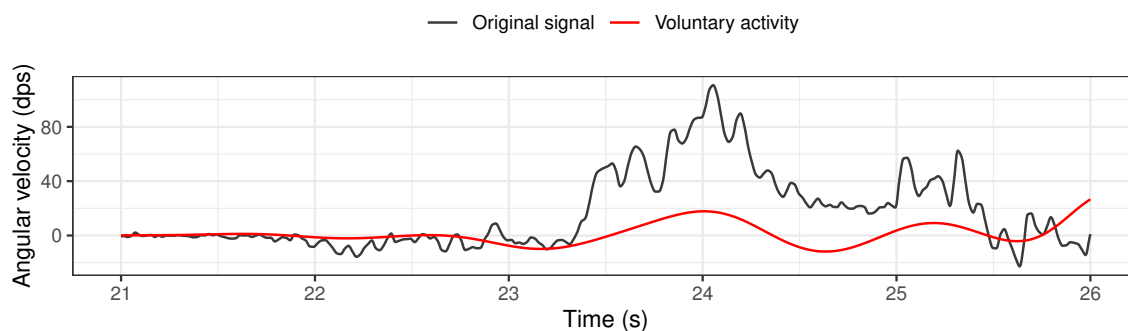


Figure 6.7 – Comparison between the original signal and the trend signal, emphasising the smoothing of the signal that represents voluntary activity.

left hands, respectively; and 3.17a and 3.17b – rest tremor amplitude of the right and left hands, respectively.

To objectively assess this symptom, gyroscope signals were also used (only for the Phase 4 of the game). Again, these signals present the voluntary movements of the player to control the avatar in the game and the involuntary movements caused by the disease (tremor). The tremor could be assessed by using SSA in two ways: (i) subtracting the original signal from the trend detected in the bradykinesia assessment, since the original time series is recovered from the sum of all its components; or (ii) directly detecting the periodic/oscillatory components of the original signal.

However, both approaches had limitations: (i) subtracting the estimated smoothed trend from the original signal invalidated the analysis of tremor, as the resulting signal would be contaminated by the interference of voluntary activity (subtraction would generate high amplitudes in the smoothed regions), thus hindering the analysis of tremor exclusively (Figure 6.8); and (ii) the direct extraction of oscillatory components from the original signal using SSA did not produce satisfactory results, as the method itself produced artefacts in the reconstructed signal when generating the components. For this reason, another signal processing method was used to detect the tremor.

First, the signals were visualised and resampled at 200 Hz (the original sampling frequency was 50 Hz). This pre-processing step was necessary to preserve the signal waveform over time and prevent the introduction of artefacts during the subsequent filtering step, which involves estimating the trends associated with the voluntary movements present in the signal. Then, to detect tremor-related information from these signals, the removal of the trend (associated with voluntary movements) from the original signal was performed. For this purpose, the mean was estimated for 200 ms rectangular windows, with an overlap of 50% of the window size (140, 162), and then interpolation of the mean values was performed (using splines) to estimate the voluntary trend of the signal. Thus, the involuntary signal activity, corresponding to the tremor, was obtained by subtracting the voluntary trend from the original signal.

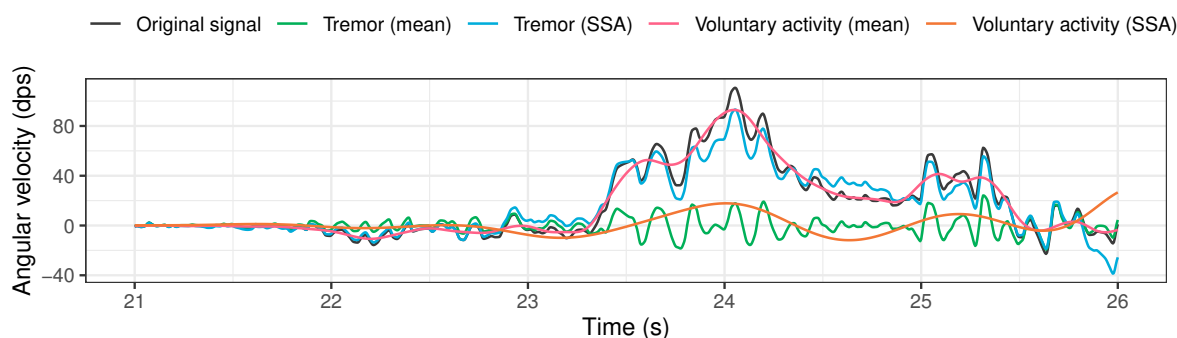


Figure 6.8 – Comparison between the methods used to detect/extract the signals for the assessment of each motor symptom (bradykinesia and tremor). Note that, if voluntary activity was detected by mean estimation, the resulting signal subsequently had to be smoothed for peak detection.

Then, amplitude-sensitive and frequency-sensitive features were extracted from the tremor signal, capable of accurately describing this symptom. For the time domain analysis, the signal was windowed, considering rectangular windows of 500 ms with 50% overlap (140, 162), and amplitude-sensitive features, the mean absolute value (MAV) and root mean square (RMS), were estimated for each window. For the frequency domain analysis, the power spectral density (PSD) was estimated, and the peak frequency and power were analysed.

To describe the set of values for each feature estimated across the different groups, a descriptive statistical analysis was conducted. This analysis involved estimating probability distribution functions for each feature and performing correlation analysis between the amplitude-sensitive features and the clinical scores.

Probability distribution functions describe the relative probability of the data, enabling the identification of patterns among the individuals of each group. Therefore, this type of analysis is valuable for understanding the motor sign profiles of individuals with PD and healthy individuals during interaction with serious game.

In correlation analysis, Spearman's correlation coefficients between amplitude-sensitive features and the assessed items of the MDS-UPDRS Part III were estimated to determine whether the objective assessment of tremor proposed in this study is correlated with the clinical assessment. The correlation coefficients were classified into four categories: very weak (0.00–0.19), weak (0.20–0.39), moderate (0.40–0.59), strong (0.60–0.79), and very strong (0.80–1.00) (110). Signal processing and statistical analyses were performed using R (139).

6.3 Results

6.3.1 Bradykinesia evaluation

The results of bradykinesia assessment for the EG and CG are shown in Table 6.1. The average RT and AV values for each participant considering the four phases of the game are presented.

Control group			Experimental group						
Id	RT (s)	AV (deg/s)	ON state				OFF state		
			Id	MDS-UPDRS III	RT (s)	AV (deg/s)	MDS-UPDRS III	RT (s)	AV (deg/s)
1	1.20	308.38	1	3	1.33	305.35	5	2.95	139.49
2	1.30	347.34	2	6	2.19	139.20	9	2.73	177.71
3	2.44	287.36	3	8	1.46	248.31	8	1.31	182.14
4	1.56	400.60	4	6	1.22	351.83	9	0.83	394.17
5	1.29	460.94	5	2	1.51	398.71	3	2.72	306.59
6	1.27	520.40	6	6	1.41	245.04	9	1.70	182.70
7	1.60	391.27	7	4	1.25	234.44	8	2.06	238.86
8	1.42	401.34	8	3	2.33	234.16	6	2.10	301.79
9	1.15	621.23	9	3	1.26	473.47	5	1.70	352.31
10	1.21	506.88	10	2	0.73	272.14	4	1.47	316.26
11	1.68	466.61	11	6	1.22	492.09	9	1.79	327.66
12	0.98	555.35	12	6	1.86	167.36	12	3.36	135.72
13	1.60	565.49	13	6	1.22	152.37	9	1.10	170.01
14	1.18	518.94	14	5	1.51	260.84	9	1.08	252.35
15	0.99	383.09	15	3	2.41	374.44	7	2.79	278.41

Table 6.1 – Results of bradykinesia evaluation.

The RT values were relatively lower for the CG than for the EG, and the AV values were relatively higher for the CG than for the EG, both in the ON and OFF states. It can be observed that the individual in the CG who presented the highest RT was also the one who presented the lowest AV (participant 3).

Regarding the EG, participants 1, 5, 6, 9, 11, 12 and 15 in the ON state of medication presented lower RT scores and higher AV scores compared to the OFF state. In the OFF state, the individual with the highest degree of disease impairment, according to the clinical evaluation, was also the one who presented the largest RT and the smallest AV (participant 12). Participants 3 and 14 increased their AV in the ON state compared to the OFF, but also increased their RT; and participants 2, 7 and 10 decreased their RT in the ON state compared to the OFF, but also decreased their AV. Participants 4, 8 and 13 increased their RT and decreased their AV in the ON state compared to the OFF state.

The distribution of RT data for all participants is shown in Figure 6.9. Except for Phase 1, in all other phases the CG had the lowest RT, followed by the EG in the ON state, and then by the EG in the OFF state. In Phase 1, the EG in the ON state showed the best results for RT, followed by the CG, and then by the EG in the OFF state.

The distribution of AV data for all participants is shown in Figure 6.10. Again, the CG was the one with the largest AV, followed by the EG in the ON state, and then by

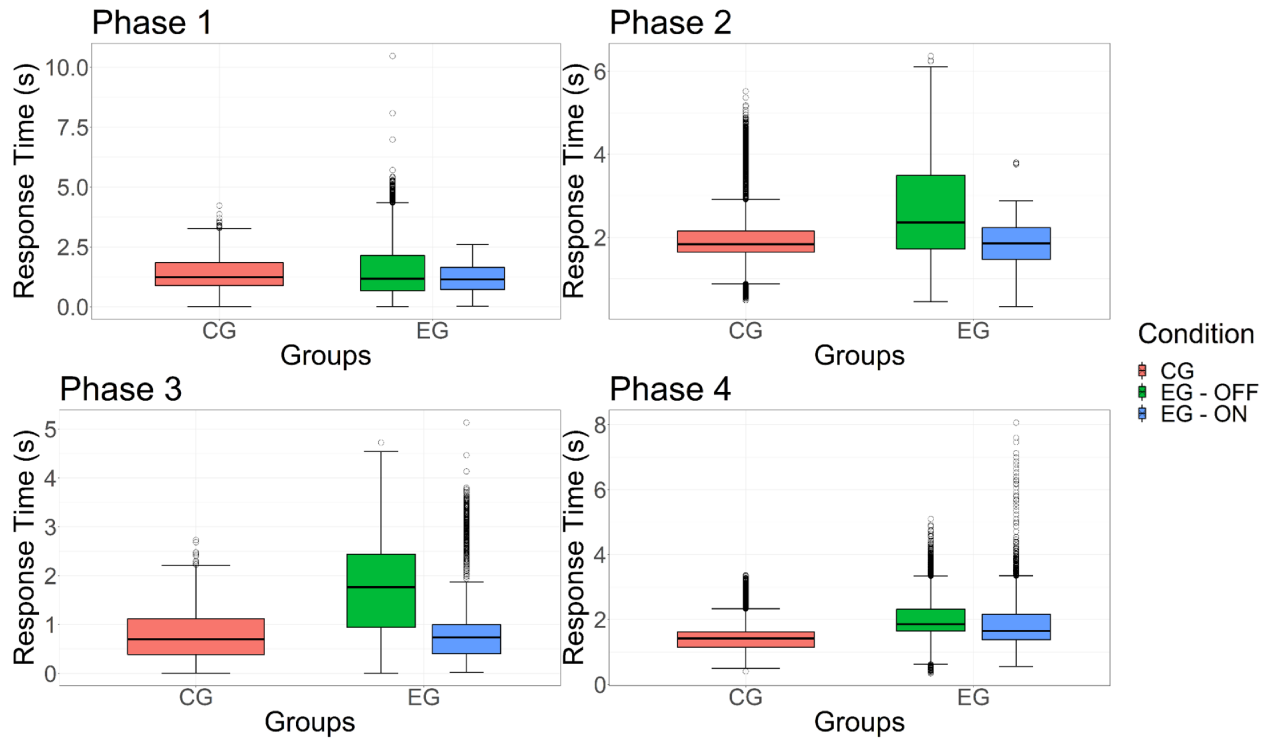


Figure 6.9 – Estimated RT of the participants for each of the four game phases.

the EG in the OFF state.

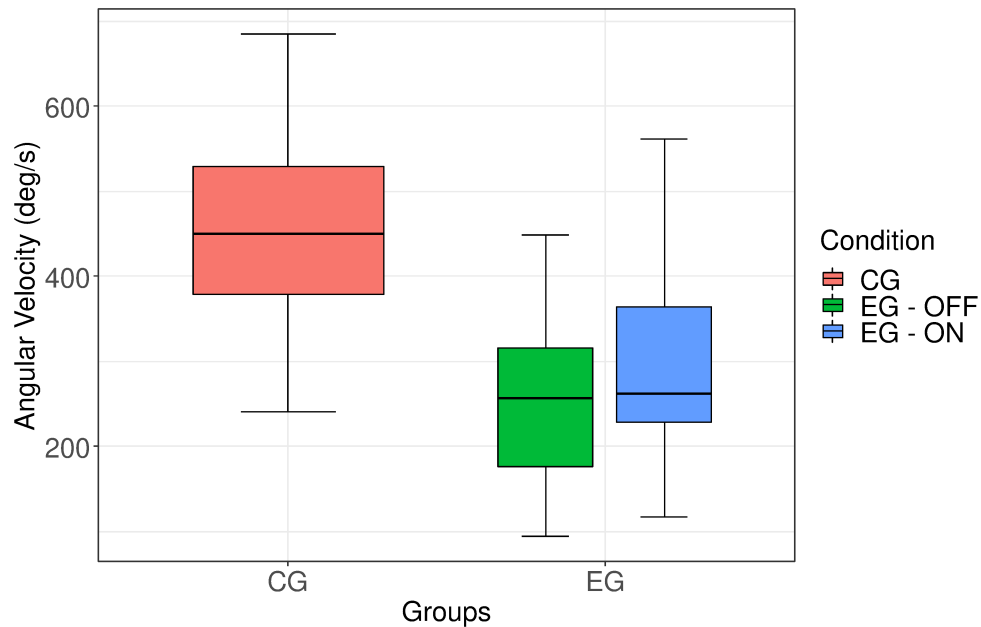


Figure 6.10 – AV of the participants. Note that AV was estimated only for Phase 4.

Table 6.2 shows the results of the statistical tests. Statistically significant results were found for all comparisons ($p < 0.05$).

Figure 6.11 shows the mean values of RT and AV for all groups. The CG presented the lowest RT and the highest AV compared to the EG-ON and EG-OFF. For the EG, the RTs decreased from the OFF state to the ON state, and AVs increased from the OFF

Comparisons	p-value (RT)				p-value (AV)
	Phase 1	Phase 2	Phase 3	Phase 4	Phase 4
CG and EG	<0.001	<0.001	<0.001	<0.001	<0.001
EG in the ON and EG in the OFF states	<0.001	<0.001	<0.001	<0.001	<0.001
CG and EG in the ON state	<0.001	<0.001	<0.001	<0.001	<0.001
CG and EG in the OFF state	0.03	<0.001	<0.001	<0.001	<0.001

Table 6.2 – Results of statistical evaluations.

state to the ON state.

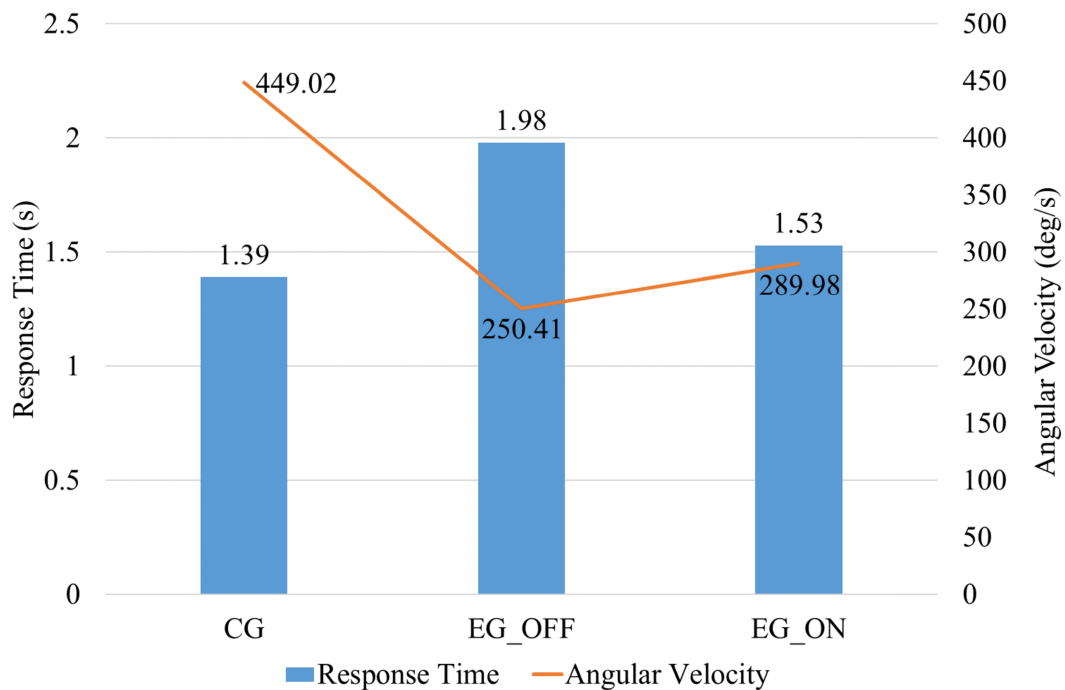


Figure 6.11 – Mean values of variables RT and AV, estimated for the objective assessment of bradykinesia.

6.3.2 Tremor evaluation

In Figure 6.12, the probability density function is depicted for each group and feature, regardless of subject, sensor, or axis.

For both MAV and RMS, the chance of the distribution having a bimodal aspect was greater for the PD-OFF and PD-ON groups than for the Healthy group. The probability that the peak frequencies of the PD-OFF signals fall within the frequency range of Parkinson's tremor (4-7 Hz) was higher than for the PD-ON group, which in turn was higher than for the Healthy group. The PD-OFF group had the highest probability of having the highest peak power in the signal (greater tremor energy) than the PD-ON group and the Healthy group.

Table 6.3 shows the correlation results of each clinically assessed item with the extracted amplitude-sensitive features. Most coefficients (83.33%) revealed a moderate to

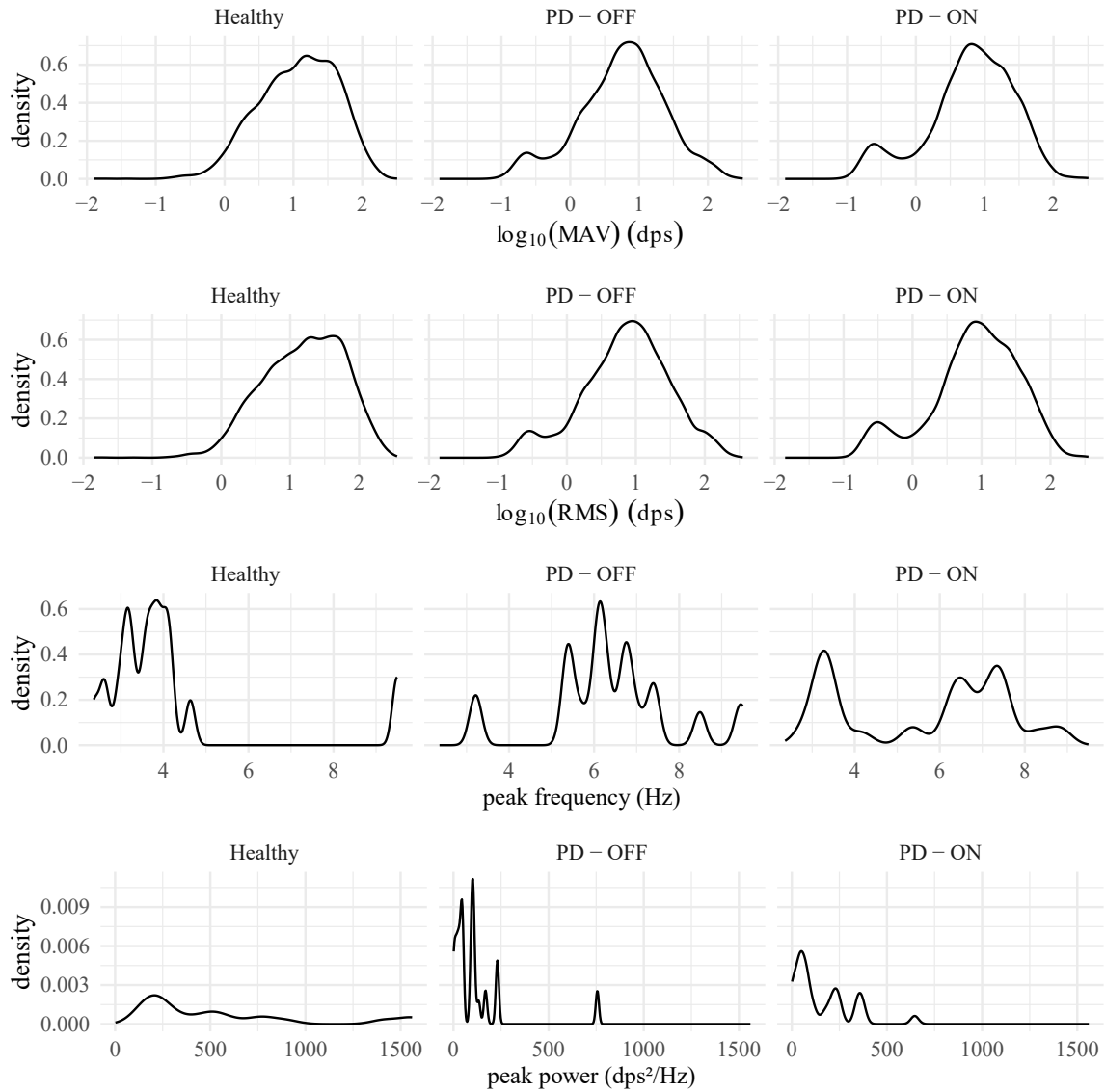


Figure 6.12 – Probability density function results for each feature extracted (peak frequency, MAV, RMS and peak power). Densities for MAV and RMS features are presented by a logarithmic transform in base 10.

very strong correlation between MDS–UPDRS scores with MAV and RMS variables. Only 4.16% of the coefficients showed very weak correlation, 12.5% showed weak correlation, 45.83% moderate correlation, 4.16% strong correlation and 33.33% of the coefficients showed very strong correlation.

The MDS–UPDRS item that showed the best correlation with MAV and RMS variables in both medication states was the amplitude of rest tremor in the left hand. The correlation was weak between kinetic tremor of the right hand in the ON state with MAV and RMS, and between amplitude of rest tremor of the right hand in the ON state with MAV. Only the correlation between amplitude of rest tremor of the right hand in the ON state with RMS was very weak.

	MDS-UPDRS											
	3.15a				3.16a				3.17a			
	OFF	ON	OFF	ON	OFF	ON	OFF	ON	OFF	ON	OFF	ON
MAV	0.494	0.640	0.447	0.866	0.809	0.342	0.447	0.577	0.562	0.213	0.866	0.866
RMS	0.494	0.569	0.447	0.866	0.809	0.266	0.447	0.577	0.562	0.142	0.866	0.866

Table 6.3 – Correlation results between MAV and RMS features and the MDS-UPDRS

6.4 Discussion

This chapter consisted in objectively evaluating bradykinesia and tremor in individuals with PD using the *RehaBEElitation* serious game. As previously mentioned, no studies have been found in the literature that use data recorded by inertial sensors during the interaction of PD patients with a serious game for an objective assessment of motor symptoms of the disease.

According to the World Health Organization (WHO), disability due to PD is increasing faster than for any other neurological disorder (173). A proper understanding of the cardinal signs of the disease, such as bradykinesia and tremor, can help diagnose the condition. Thus, the assessment of bradykinesia and hand tremor is a crucial step in the evaluation of a PD patient (50).

Although the MDS-UPDRS scale is the current gold standard method for the assessment of individuals with PD, it requires the presence of a qualified professional to carry out the evaluation; has high intra- and inter-examiner variability; and does not identify the fluctuations of symptoms during the day, capable of guiding the therapy (136, 36). In this way, recent studies point to the need for more reliable instruments that allow for a better understanding of the disease progression (142, 42). This motivated us to develop the *RehaBEElitation* serious game and the glove with inertial sensors, capable of registering the motor signs of the users. Such sensors can capture movement information coming directly from the neuromuscular system of individuals, which ensures a more accurate assessment of the main symptoms of the disease and the patient's level of impairment.

6.4.1 Bradykinesia evaluation

Bradykinesia was assessed using the individuals' RT, which was calculated by the duration of an event that indicates the moment when the player reaches the target and performs the movement, as well as using the gyroscope signal collected by the wearable HMI device, which represents the AV of movement. To obtain a reliable AV estimation, the SSA time series decomposition method was applied to the gyroscope signals collected from all participants to detect the voluntary activity (signal trend), which represents the movement the player makes to control the avatar in the game.

Time series decomposition allows extracting patterns and behaviours as components,

enabling an understanding of the mechanisms that constitute the time series. The decomposition using SSA was very satisfactory, and the smoothing of the resulting signal helped to detect global peaks to estimate the players' AV.

The results indicated in Table 6.1 showed that participants 1, 5, 6, 9, 11, 12 and 15 in the ON state of medication presented lower RT scores and higher AV scores compared to the OFF state. This result was already expected, since EG subjects in the ON state of medication have more reduced motor symptoms than in the OFF state (33). However, in the ON state, some situations also occurred: participants 2, 7 and 10 reduced RT but also reduced AV, participants 3 and 14 increased AV but also RT, and participants 4, 8 and 13 increased RT and reduced AV. It is known that RT is the sum of reaction time and movement time; AV is more related to movement time.

After taking the medication, participants 2, 7 and 10 had lower RT but performed the movements more slowly, i.e., they increased the movement time, which consequently results in a decrease in reaction time. Movement time may have increased because the medication is probably not bringing benefits regarding the improvement of motor symptoms in these individuals, which suggests the need to readjust the dosage of the medication or change it for another medication. The reaction time may have been reduced by the learning acquired in the first session of interaction with the game, i.e., the players learned that after reaching the target and receiving the visual and sound stimuli, they should perform the required movement. Thus, although the player performed the movements more slowly, he was able to initiate the execution of the movements earlier.

After participants 3 and 14 took the medication, the movements were performed faster, i.e., movement time was decreased, but RT increased, which consequently resulted in increased reaction time. Movement time may have been reduced due to the medication's effectiveness in reducing motor symptoms. The reaction time may have increased due to the lack of learning that could have been acquired in the first session, i.e., the participants did not understand that the visual and sound stimuli indicated the exact moment to start the execution of the movement. Thus, although the motor symptoms were reduced, the players did not learn enough, making them start the execution of the movements later.

And finally, after participants 4, 8 and 13 took the medication, their RT increased and they performed the movements more slowly, i.e., increased the movement time. It can be suggested that the medication is not reducing the motor symptoms of these individuals, and therefore, a readjustment of the medication dosage should be performed. Moreover, these individuals probably did not acquire learning in relation to the game.

Medication is the key treatment for the motor symptoms of PD, but the pharmacological response inevitably diminishes over time (108). Following these results, it is possible to identify the individuals who possibly need medication adjustments, as well as those who require additional training with the serious game to better understand its features and rules. These findings may provide a more personalised patient follow-up by healthcare

professionals, as well as assist them in assessing individuals and monitoring the disease.

In Phase 1, the RT of the EG participants in the ON state of medication was smaller than those in the CG. Probably, as most EG participants already had a first contact with the *RehaBEElitation* serious game (they already interacted with the game at least once), in the ON medication state they were less slow than the CG. Despite these considerations, there were no statistically significant differences between the groups.

Furthermore, the information indicated by Table 6.1 and Figure 6.5, Figure 6.10 and Figure 6.11 showed that, in general, the RT and AV scores for the CG participants were better than the EG in the ON state, which in turn were better than the EG in the OFF state, as already expected. In addition, EG participants in the OFF state of medication and CG participants who presented the worst results for RT also presented the worst results for AV, which reveals that the measures used for the assessment of bradykinesia were quite consistent.

Analysing Figure 6.9, Figure 6.10 and Table 6.2, it can be seen that Phase 4 is the most suitable for assessing bradykinesia using the *RehaBEElitation* serious game. Figure 6.9 shows that in this phase the differences between the groups were better detected, since the boxplots are less overlapped, and only in this phase it was possible to estimate the angular velocity of the participants. Phase 4 required the execution of the forearm supination and pronation movement, a more complex movement than the others and one that is not often performed during daily activities. This may have encouraged players to focus on the execution of the movement, which may have influenced a better estimation of the variables used in the study. These findings agree with those reported by Summa et al (159).

The correlation with the MDS-UPDRS (clinical assessment) was not performed because, in this study, bradykinesia was assessed considering reaction time and movement time. However, in the clinical assessment, reaction time is not considered to assess this symptom. Despite this, the individual with the highest degree of disease impairment, according to the MDS-UPDRS, was also the one with the highest RT and lowest AV in the OFF state of medication.

6.4.2 Tremor evaluation

The tremor was detected using signal processing techniques that involve removing trends from the signal. As the trend represents the voluntary movement of the player while controlling the movements of the bee, after its removal only the signal representing the involuntary movement of the user, characterised by tremor, remained. Thereafter, it was possible to extract information about the amplitude and frequency of this motor symptom.

The results presented in Figure 6.12 show the probability density function for each extracted feature. The MAV and RMS for the EG in both medication states had a

higher probability of presenting a distribution curve with a bimodal aspect (two peaks), which indicates the presence of two different modes, i.e., different statistical populations. The peak with lower amplitude represents involuntary movements (the PD tremor), not observed in the CG distribution curve.

In terms of frequency, the healthy individuals had a predominant frequency band between approximately 1 and 5 Hz. These frequencies, below 5 Hz, suggest that most individuals performed predominantly voluntary activities during the game, such as moving the bee or performing movements to score in the phase. On the other hand, the higher frequencies (8-10 Hz) suggest that some individuals had greater difficulty when playing, probably due to the presence of enhanced physiologic tremor. During the OFF state of the medication, individuals with PD presented a peak frequency between 5 and 10 Hz. However, these participants presented predominant peaks in two frequency bands during the ON state of the medication: between 1 and 5 Hz, as observed in healthy individuals; and between 5 and 9 Hz. This implies that participants with PD played more easily during the effect of the medication (i.e., ON state) and, furthermore, demonstrate the benefits of the medication in performing motor tasks.

The probability distribution functions of the peak power for each group support this idea. The shapes of the distributions are similar for the CG and the PD-ON group, i.e., both show a multimodal distribution with three predominant peaks, but with decreasing probabilities. However, the peak powers were higher for the healthy participants, probably because they can perform the movements more easily and many have no tremor. These three peaks in the peak power distributions may be related to the different actions performed by the player during the phase. For instance, the movements to raise and lower the bee on the scenario (wrist extension and flexion), the movements to move the bee to the right and left (wrist abduction and adduction) and the forearm supination and pronation movements to score points. This behaviour is not observed in the PD-OFF group, probably due to the presence of tremor, which hinders the execution of movements during the game. This occurs because the player in the OFF state cannot control the bee nor execute the movements in the time required to score points. This may justify the fact that the PD-OFF group has a lower peak power range than the PD-ON group.

In general, the MAV and RMS features estimated from the gyroscope signals showed strong correlation with the MDS-UPDRS. This validates the methodology applied for the detection and assessment of tremor in an objective way. As the highest correlation coefficient (considering both ON and OFF medication states) was observed in the comparison between rest tremor amplitude with the two extracted variables, it is suggested that rest tremor is the best and most faithfully assessed aspect using the signals collected from the game and applying the processing techniques used.

6.4.3 General considerations

In comparison to other methods, the use of serious games is an attractive option for the measurement of parkinsonian motor symptoms. This game can be applied frequently and easily in clinics and hospitals, which demonstrates excellent accessibility and is cost-effective. In addition, the methods applied can isolate voluntary activity from involuntary activity. Voluntary activity hinders the assessment of tremor, just as severe tremor or dyskinesia interferes with the classification of bradykinesia.

Some limitations of this study were the lack of previous training with the serious game for the CG, and the application of the game on the same day for the EG in the ON and OFF states of medication. This was done to avoid a possible bias in changing the day and time of data collection, however, some participants faced difficulties when they played the game in the ON state, possibly because they had been doing the exercises for some time, which was demonstrated by the results.

6.5 Conclusions

In this chapter, bradykinesia and tremor were assessed objectively using the *Re-haBEElitation* serious game. RT and AV proved to be very consistent variables to estimate the slowness of individuals. Patients in the ON medication state showed more reduced bradykinesia compared to patients in the OFF state. Regarding tremor evaluation, the participants of the EG in the OFF state of medication presented more tremor in comparison to the ON state, as expected. Moreover, the healthy individuals perceived less difficulty when playing as they had no or less tremor compared to the participants with PD.

Serious games are effective tools for the objective monitoring of PD symptoms, providing concrete information about the progression of the disease. In summary, it can be concluded that the developed system constitutes an alternative and quite complete tool capable of assessing the main motor symptoms of PD entertainingly and objectively.

Final Considerations

Parkinson's disease is characterised by various motor and non-motor symptoms that affect the quality of life and well-being of people who suffer from the condition. This disorder is difficult to diagnose, has no cure and uses a subjective scale as the gold standard assessment tool, which can produce incorrect conclusions about patients' health status. In this sense, it is important to develop new technologies that can help health professionals monitor and assess patients, as well as improve the rehabilitation process for individuals affected by the disease.

The literature review presented in Chapter 3 showed that several serious games have been developed for PD patients, but many do not take into account the experiences of the target audience, which is composed of elderly people who are not familiar with virtual technologies. Existing games generally present narratives that are incompatible with the players' mental models and are often not designed focusing on the real needs of professionals and patients (109).

To identify the main motor, cognitive and pain limitations of PD patients, a multi-dimensional assessment questionnaire was developed (92). The questionnaire enabled us to understand which types of daily tasks patients have most difficulty in performing, as well as which cognitive and pain aspects affect them the most. This has contributed to a better understanding of the real needs of individuals affected by the disease, as well as identifying considerable motor limitations experienced by patients.

The literature review and questionnaire results motivated us to develop a game considering the limitations and expectations of PD patients since the initial design stages. All of the game's features (such as the narrative, scenarios, interactions, visual and auditory feedback, and the movements required of the players) were entirely designed with the end users at the centre of the creation process. This has certainly contributed to the wide acceptance of the tool, and to the system's high usability and accessibility. We believe that *RehaBEElitation* is one of the best designed serious game for people with PD described in the literature.

As well as providing users with a fun and entertaining way of carrying out motor

rehabilitation, the serious game is also capable of objectively assessing bradykinesia and tremor. Using information collected by inertial sensors, it was possible to quantify the main symptoms of the disease, overcoming one of the main limitations of the MDS-UPDRS.

The developed system is a complete and effective alternative tool capable of objectively assessing the main motor symptoms of PD. Solutions such as this one can improve users' quality of life and help healthcare professionals diagnose, monitor, and assess the patient's motor condition.

The prospects for further studies include: implementing in the system the emission of reports with automated and simultaneous assessment of bradykinesia and tremor, providing real-time feedback to healthcare professionals; incorporating vibratory actuators in the glove to deliver sensory feedback to users, especially the hearing impaired, and thus improve the system's usability; and implementing new phases in the game to analyse and monitor other dimensions of PD, such as lower limb impairment, enabling a complete and objective assessment of patients using the developed system.

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Glossary

e.g.

an abbreviation of the latin expression *exempli gratia*, meaning “for example”.

i.e.

it means *id est*, which is the latin expression for “this is”.

MAV

is obtained by averaging the absolute value of the signal in a window.

PSD

is the measure of signal’s power content versus frequency.

RMS

square root of the mean square, which is the arithmetic mean of the squares of a group of values.

threshold (th)

is an amount, level, or limit on a scale.

UFU

Federal University of Uberlândia.

UL

University of Lorraine.

Appendix A - Multidimensional Assessment Questionnaire of Individuals with Parkinson's Disease

A.1 Section A – Presentation of the Survey and Sample Description

I declare that I have Parkinson's disease and that I am able to answer the questionnaire.

*

☐ Yes

☐ No

I was diagnosed with Parkinson's disease about: *

☐ Less than 2 years

☐ 2 to 4 years

☐ 4 to 6 years

☐ 6 to 8 years

☐ 8 to 10 years

☐ More than 10 years

The symbol * indicates that the participant must answer the question.

A.2 Section B – Individual Perception about Parkinson's Disease

The following statements refer to some aspects of your daily life. Please indicate how much you agree or disagree with each statement. To do this, please answer with one of the five rating levels below:

0 – Totally disagree

- 1 – Disagree
- 2 – Indifferent
- 3 – Agree
- 4 – Totally Agree

MODULE 1 – Activities of daily living (ADL)

This module refers to activities of daily living, that is, tasks related to self-care and your ability to live independently.

Food

- (1) I hold the flatware without assistance.
- (2) I handle the flatware without assistance.
- (3) I take the flatware with the food up to my mouth without help and without spilling it.
- (4) I chew the food without difficulty.
- (5) I have no difficulty swallowing food.
- (6) I serve liquid drinks without help and without spilling.
- (7) I drink liquids without help and without spilling.

Mobility

- (8) I walk short distances without help.
- (9) I walk long distances without help.
- (10) I lie in bed without help.
- (11) I get up from bed without help.
- (12) I sit without help.
- (13) I drive without difficulty.
- (14) I climb stairs without help.
- (15) I go downstairs without help.
- (16) I dance without difficulty.
- (17) I turn to bed at night without help.
- (18) I get up from the car seat without help.
- (19) I have balance when walking.

Sanitation

- (20) I turn on the shower without help.
- (21) I wash my body without help.
- (22) I dry myself with the towel without help.
- (23) I sit on the toilet without help.
- (24) I get up from the toilet without help.
- (25) I clean myself after evacuating without help.
- (26) I brush my teeth without help.

Clothes

- (27) I wear a pant/skirt without help.
- (28) I wear a shirt/blouse without help.
- (29) I button my clothes without help.
- (30) I open/close the zipper of my clothes without help.
- (31) I put on my shoes without help.
- (32) I tie the shoelaces without help.
- (33) I take off my clothes to shower without help.

Miscellaneous

- (34) I take my medicines without help.
- (35) I make phone calls without help.
- (36) I type messages on my cell phone without help.
- (37) I write on a sheet of paper without help.
- (38) I comb my hair without help.
- (39) I use the television remote control without assistance.
- (40) I hold a child in my arms without help.
- (41) I speak clearly and without difficulty.
- (42) I use Gillette without cutting myself.
- (43) I read texts without help.

Is there any other activity in your daily life that you have a lot of difficulty or desire to do that has not been mentioned in this questionnaire? _____

MODULE 2 – Cognitive aspects

This module refers to the cognitive aspects, that is, your feelings about life and society.

Memory/Concentration

- (44) I concentrate to accomplish the tasks.
- (45) I remember things without having to write them down.

Social and family conviviality

- (46) I feel close and welcomed by other people.
- (47) I am calm with other people.
- (48) My physical condition does not interfere with my social life.
- (49) I go out as often as I would like.
- (50) I dedicate time to my hobbies and leisure as much as I would like.

(51) I meet my friends as much as I would like.

Personality

(52) I feel interested in food.

(53) I feel calm/peaceful.

(54) My personality has not changed.

Energy

(55) I feel rested most of the time.

(56) I am willing to do the things I want.

(57) I do not feel nausea during the day.

(58) I do not have hallucinations and delusions often.

(59) I do not get much sleep during the day.

(60) I do not get dizzy when I am lying/sitting and getting up.

Emotion/Humor

(61) I have confidence in myself.

(62) I often feel happy.

(63) I often feel peaceful.

(64) I feel excited about my future.

(65) I have no desire to be alone.

(66) I sleep and do not wake up many times during the night.

Is there any other aspect that affects you mentally/psychologically that has not been mentioned in this questionnaire? _____

A.3 Section C – Multidimensional Pain Inventory – MPI

The following statements refer to the impact of pain on your life. Please indicate how much you agree or disagree with each one. To do this, answer with one of the seven levels, ranging from 1 (a little) to 7 (a lot). They are classified progressively, that is, level 1 is the lowest, followed by level 2 and so on, up to level 7, which represents the highest value of the scale.

Did you feel pain in the last week? *

() Yes

() No

* If the answer is yes, the participant will answer the MPI. The participant will be instructed to assign only one score on a LIKERT scale ranging from 1 (a little) to 7 (a lot).

Severity of pain

(67) On average, how severe has your pain been during the last week?

(68) How much suffering do you experience because of your pain?

(69) Estimate the level of your pain at this time.

Interference

(70) In general, how much does your pain interfere with your daily activities?

(71) From the moment your pain began, how much did your pain change your ability to work?

(72) How much did your pain change the amount of satisfaction or pleasure from your participation in social and leisure activities?

(73) How much did your pain change the amount of satisfaction or pleasure from your participation in family related activities?

(74) How much did your pain affect your relationship with your wife, family, or close people?

(75) How much did your pain change the amount of satisfaction or pleasure from your participation in job?

(76) How much did your pain affect your ability to do housework?

(77) How much did your pain change or interfere with your friendship with people other than your family?

(78) In general, how much did your pain affect your ability to participate in social activities?

Perceived life control

(79) During the last week, how much control did you feel you had over your life?

(80) During the last week, how much did you feel you were able to deal with everyday problems?

State of mood-affectivity

(81) Estimate your mood globally during the last week.

(82) During the last week, how irritable have you been?

(83) During the last week, how tense or anxious have you been?

Appendix B - Validated Questionnaire – Multidimensional Assessment Questionnaire of Individuals with Parkinson's Disease

B.1 Section A – Presentation of the Survey and Sample Description

I declare that I have Parkinson's disease and that I am able to answer the questionnaire.

*

☐ Yes

☐ No

I was diagnosed with Parkinson's disease about: *

☐ Less than 2 years

☐ 2 to 4 years

☐ 4 to 6 years

☐ 6 to 8 years

☐ 8 to 10 years

☐ More than 10 years

The symbol * indicates that the participant must answer the question.

B.2 Section B – Individual Perception about Parkinson's Disease

The following statements refer to some aspects of your daily life. Please indicate how much you agree or disagree with each statement. To do this, please answer with one of the five rating levels below:

0 – Totally disagree

- 1 – Disagree
- 2 – Indifferent
- 3 – Agree
- 4 – Totally Agree

MODULE 1 – Activities of daily living (ADL)

This module refers to activities of daily living, that is, tasks related to self-care and your ability to live independently.

- (1) I hold the flatware without assistance.
- (2) I handle the flatware without assistance.
- (3) I take the flatware with the food up to my mouth without help and without spilling it.
- (4) I chew the food without difficulty.
- (5) I have no difficulty swallowing food.
- (6) I serve liquid drinks without help and without spilling.
- (7) I drink liquids without help and without spilling.
- (8) I walk short distances without help.
- (9) I walk long distances without help.
- (10) I lie in bed without help.
- (11) I get up from bed without help.
- (12) I sit without help.
- (13) I drive without difficulty.
- (14) I climb stairs without help.
- (15) I go downstairs without help.
- (16) I dance without difficulty.
- (17) I turn to bed at night without help.
- (18) I get up from the car seat without help.
- (19) I have balance when walking.
- (20) I turn on the shower without help.
- (21) I wash my body without help.
- (22) I dry myself with the towel without help.
- (23) I sit on the toilet without help.
- (24) I get up from the toilet without help.
- (25) I clean myself after evacuating without help.
- (26) I brush my teeth without help.
- (27) I wear a pant/skirt without help.
- (28) I wear a shirt/blouse without help.
- (29) I button my clothes without help.
- (30) I open/close the zipper of my clothes without help.

- (31) I put on my shoes without help.
- (32) I tie the shoelaces without help.
- (33) I take off my clothes to shower without help.
- (34) I take my medicines without help.
- (35) I make phone calls without help.
- (36) I type messages on my cell phone without help.
- (37) I write on a sheet of paper without help.
- (38) I comb my hair without help.
- (39) I use the television remote control without assistance.
- (40) I hold a child in my arms without help.
- (41) I speak clearly and without difficulty.
- (42) I use Gillette without cutting myself.
- (43) I read texts without help.

Is there any other activity in your daily life that you have a lot of difficulty or desire to do that has not been mentioned in this questionnaire? _____

MODULE 2 – Cognitive aspects

This module refers to the cognitive aspects, that is, your feelings about life and society.

- (46) I feel close and welcomed by other people.
- (47) I am calm with other people.
- (48) My physical condition does not interfere with my social life.
- (49) I go out as often as I would like.
- (50) I dedicate time to my hobbies and leisure as much as I would like.
- (51) I meet my friends as much as I would like.
- (53) I feel calm/peaceful.
- (54) My personality has not changed.
- (55) I feel rested most of the time.
- (56) I am willing to do the things I want.
- (61) I have confidence in myself.
- (62) I often feel happy.
- (63) I often feel peaceful.
- (64) I feel excited about my future.

Is there any other aspect that affects you mentally/psychologically that has not been mentioned in this questionnaire? _____

B.3 Section C – Multidimensional Pain Inventory – MPI

The following statements refer to the impact of pain on your life. Please indicate how much you agree or disagree with each one. To do this, answer with one of the seven levels, ranging from 1 (a little) to 7 (a lot). They are classified progressively, that is, level 1 is the lowest, followed by level 2 and so on, up to level 7, which represents the highest value of the scale.

Did you feel pain in the last week? *

() Yes

() No

* If the answer is yes, the participant will answer the MPI. The participant will be instructed to assign only one score on a LIKERT scale ranging from 1 (a little) to 7 (a lot).

(67) On average, how severe has your pain been during the last week?

(68) How much suffering do you experience because of your pain?

(69) Estimate the level of your pain at this time.

(70) In general, how much does your pain interfere with your daily activities?

(71) From the moment your pain began, how much did your pain change your ability to work?

(72) How much did your pain change the amount of satisfaction or pleasure from your participation in social and leisure activities?

(73) How much did your pain change the amount of satisfaction or pleasure from your participation in family related activities?

(74) How much did your pain affect your relationship with your wife, family, or close people?

(75) How much did your pain change the amount of satisfaction or pleasure from your participation in job?

(76) How much did your pain affect your ability to do housework?

(77) How much did your pain change or interfere with your friendship with people other than your family?

(78) In general, how much did your pain affect your ability to participate in social activities?

(82) During the last week, how irritable have you been?

(83) During the last week, how tense or anxious have you been?

Appendix C – System Usability Scale, adapted

For each of the following statements, please give it a score from 1 to 5, in which 1 means that you totally disagree with the statement and 5 that you totally agree.

1. I think that I would like to use this game frequently.
2. I found this game unnecessarily complex.
3. I found this game easy to play.
4. I think I would need help from a therapist to play.
5. I found all the features of the game were well integrated.
6. I think the game has too many inconsistencies.
7. I believe that people will learn to use the game quickly.
8. I found the game too complicated/uncomfortable to play.
9. I felt confident playing the game.
10. I had to learn several new things before I could play.

Appendix D – Game Experience Questionnaire

Core module: Please indicate how you felt about the game for each of the elements on the following scale:

0 – not at all

1 – slightly

2 – moderately

3 – fairly

4 – extremely

1. I felt content.
2. I felt skilful.
3. I was interested in the game's story.
4. I thought it was fun.
5. I was fully occupied with the game.
6. I felt happy.
7. It gave me a bad mood.
8. I thought about other things.
9. I found it tiresome.
10. I felt competent.
11. I thought it was hard.
12. It was aesthetically pleasing.
13. I forgot everything around me.
14. I felt good.
15. I was good at it.
16. I felt bored.
17. I felt successful.
18. I felt imaginative.
19. I felt that I could explore things.
20. I enjoyed it.
21. I was fast at reaching the game's targets.

-
22. I felt annoyed.
 23. I felt pressured.
 24. I felt irritable.
 25. I lost track of time.
 26. I felt challenged.
 27. I found it impressive.
 28. I was deeply concentrated in the game.
 29. I felt frustrated.
 30. It felt like a rich experience.
 31. I lost connection with the outside world.
 32. I felt time pressure.
 33. I had to put a lot of effort into it.

Post-game module: Please indicate how you felt after you finished playing the game for each of the items, on the following scale:

0 – not at all

1 – slightly

2 – moderately

3 – fairly

4 – extremely

1. I felt revived.
2. I felt bad.
3. I found it hard to get back to reality.
4. I felt guilty.
5. It felt like a victory.
6. I found it a waste of time.
7. I felt energized.
8. I felt satisfied.
9. I felt disoriented.
10. I felt exhausted.
11. I felt that I could have done more useful things.
12. I felt powerful.
13. I felt weary.
14. I felt regret.
15. I felt ashamed.
16. I felt proud.
17. I had a sense that I had returned from a journey.

Appendix E – Short Flow State Scale

For each of the following statements, please give it a score from 1 to 5, where:

- 1 – Strongly disagree
- 2 – Disagree
- 3 – I do not agree nor disagree
- 4 – Agree
- 5 – Strongly agree

When I participate in this activity...

1. I feel competent enough to meet the high demands of the situation.
2. I do this spontaneously and automatically, without having to think.
3. I have a strong sense of what I want to do.
4. I have a good idea while I am performing about how well I am doing.
5. I am completely focused on the task at hand.
6. I have a feeling of total control.
7. I am not worried about what others may be thinking of me.
8. The way time passes seems to be different from normal.
9. The experience is extremely rewarding.

Appendix F – Data availability

BPM for the calibration of the game, the operation of phases 1, 2, 3 and 4, and the data collection.

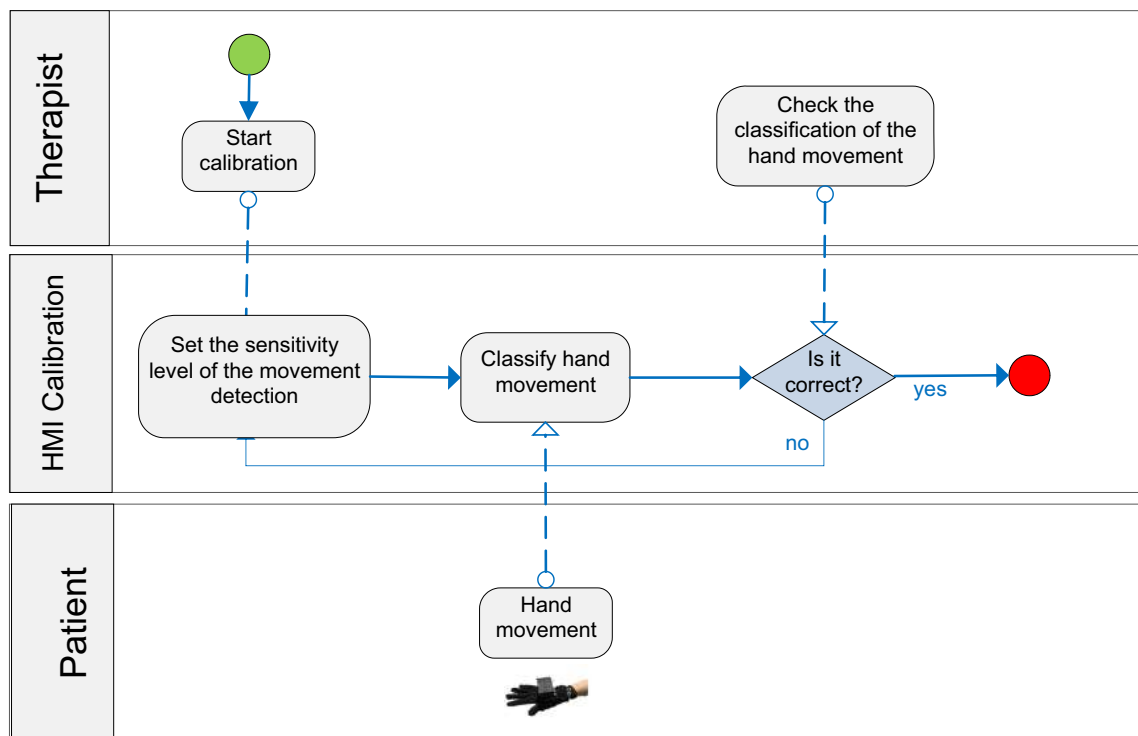


Figure F.1 – BPM representing the calibration process of the game.

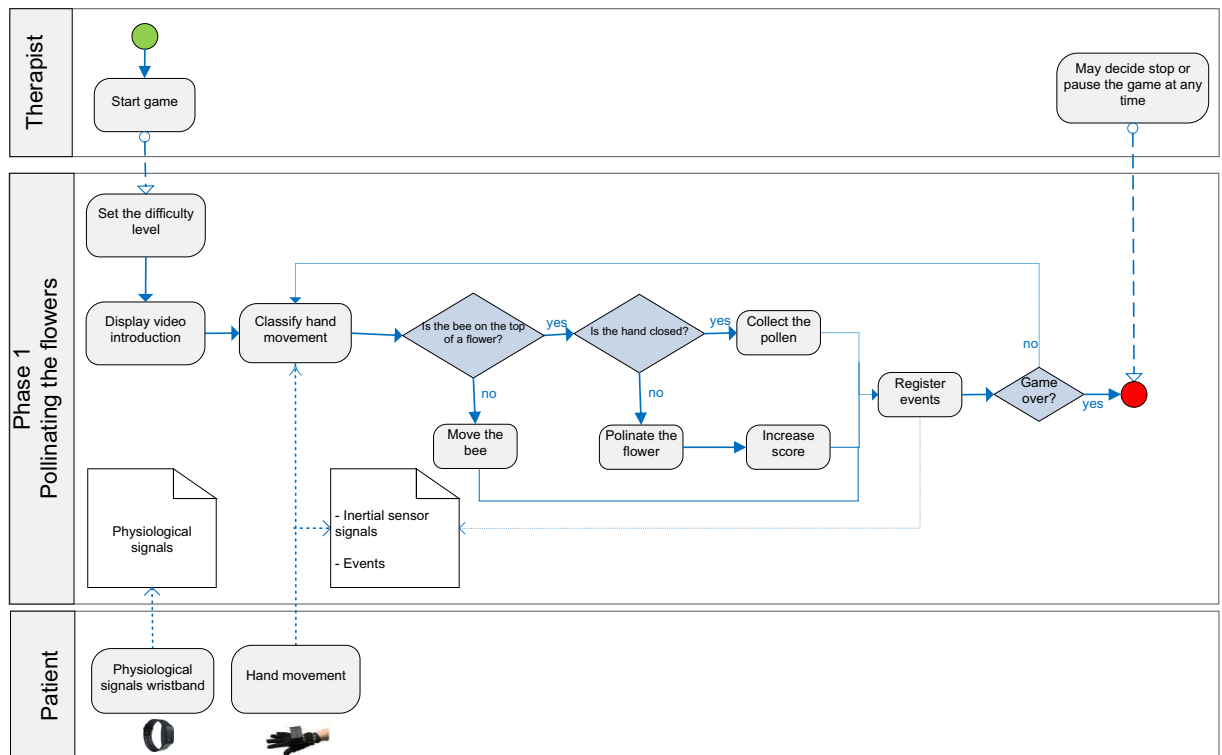
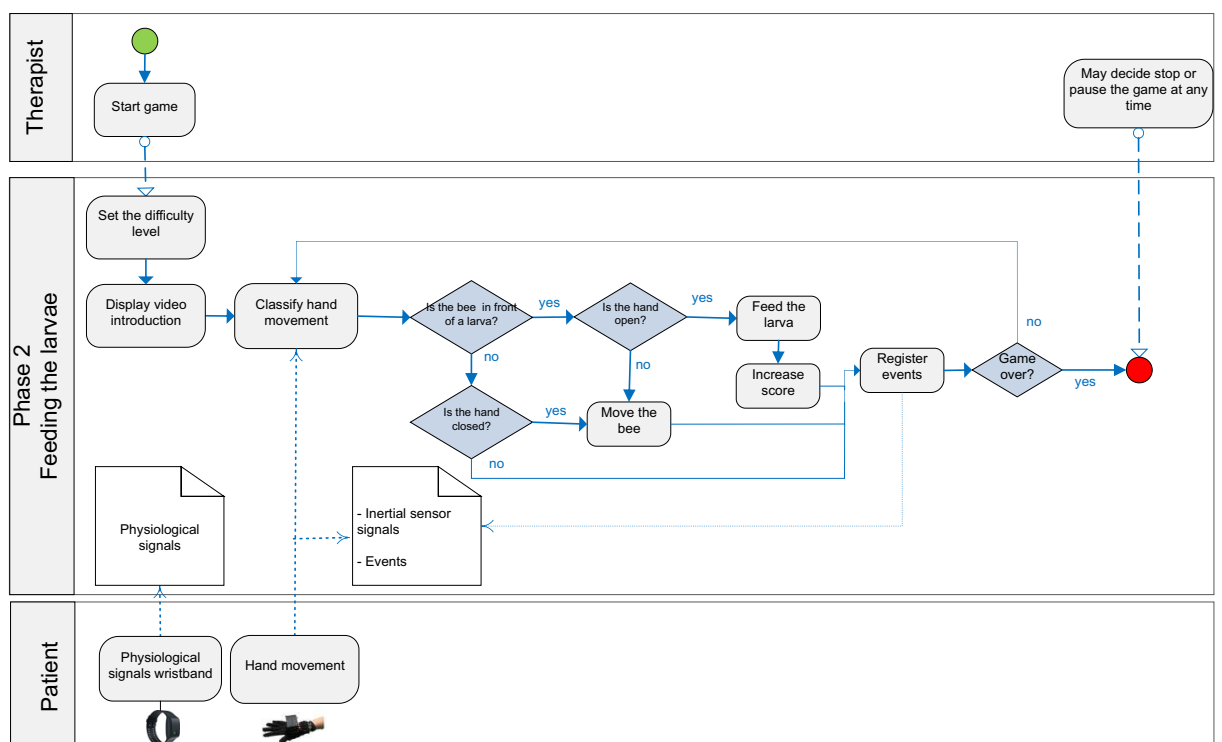


Figure F.2 – BPM representing the process of the Phase 1 of the game.

Figure F.3 – BPM representing the process of the Phase 2 of the game.



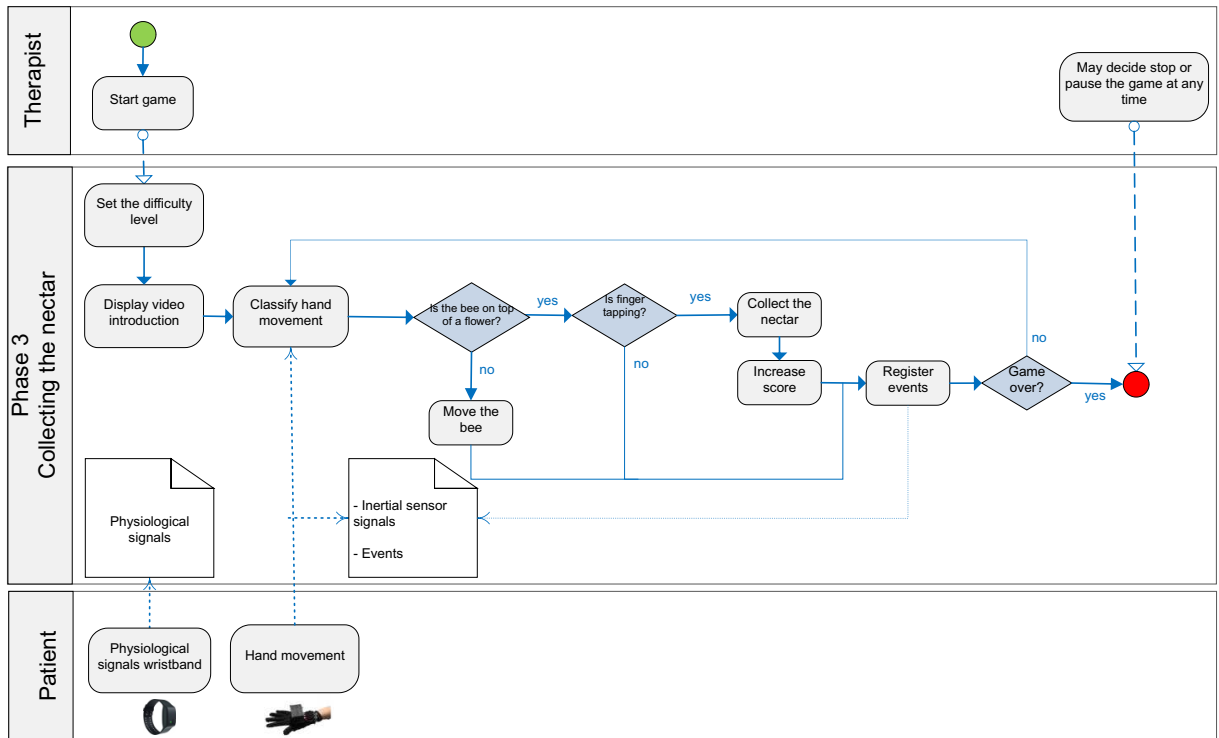


Figure F.4 – BPM representing the process of the Phase 3 of the game.

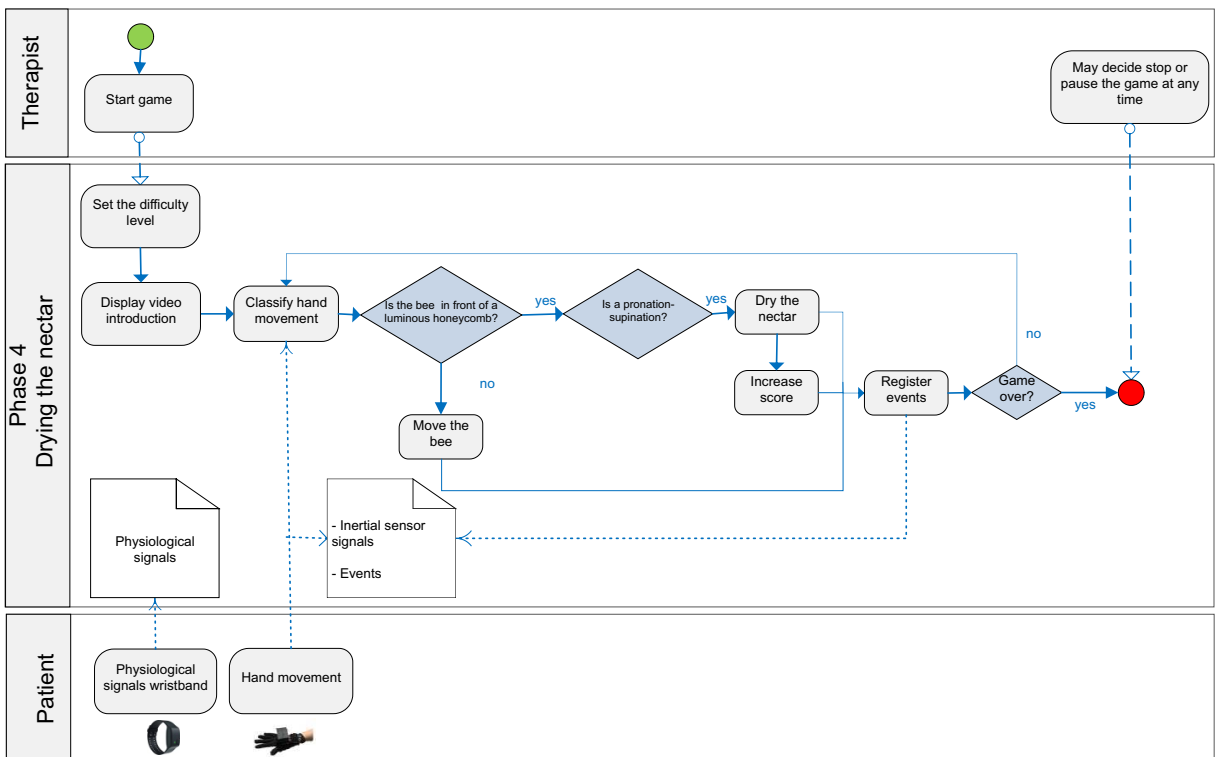


Figure F.5 – BPM representing the process of the Phase 4 of the game.

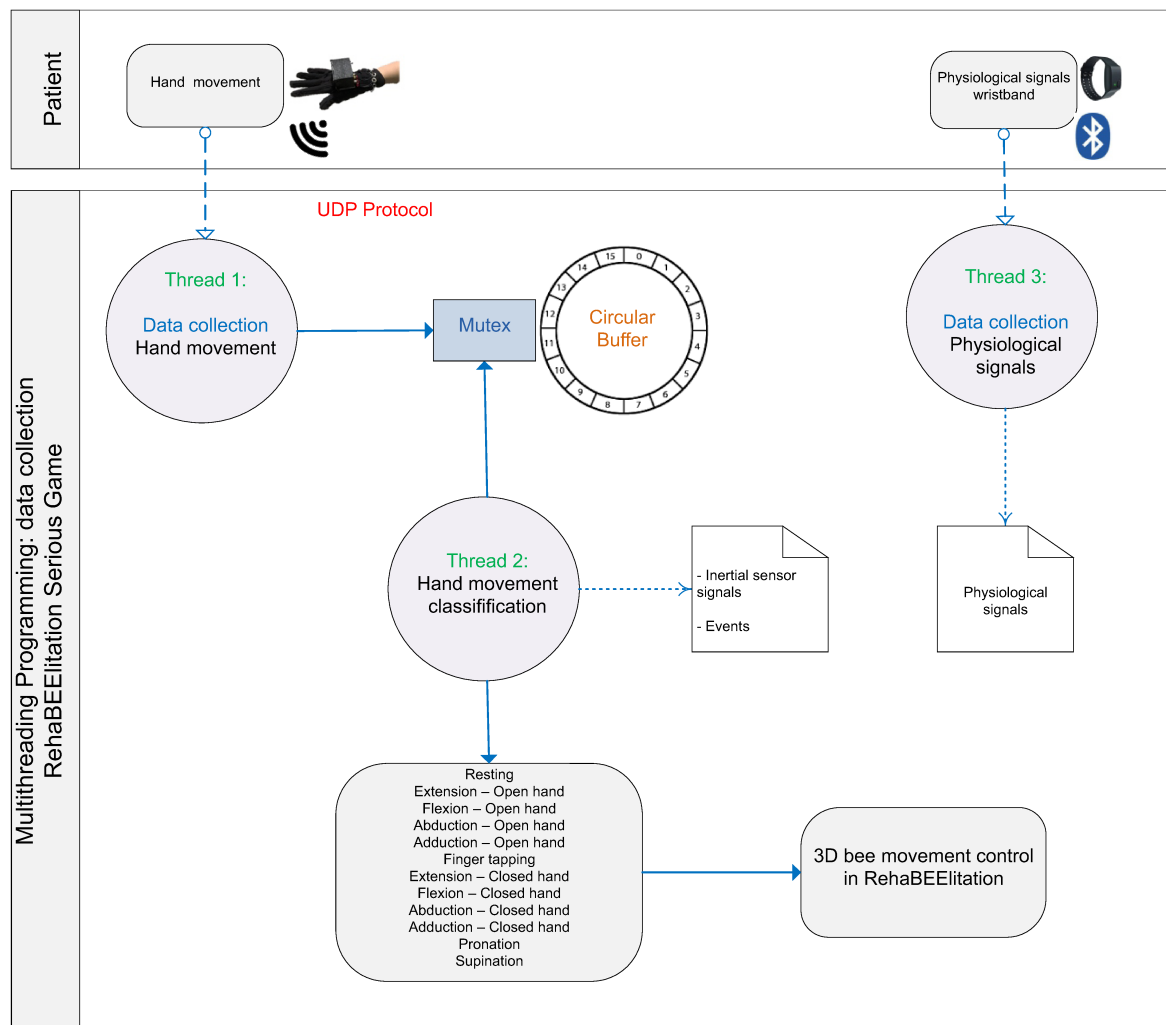


Figure F.6 – BPM representing the process of data collection.

Appendix G – Data availability

The following information can be accessed:

- **Mendes, L. C.** ; Marques, I. A. ; De Sá, A. A. R. ; Rosa, R. R ; Alves, C. M. ; Lima, K. R. ; Júnior, E. A. L. ; Naves, E. L. M. ; Vieira, M. F. ; Oliveira, F. H. M. ; Pino, P. ; Bourhis, G. ; Pereira, A. A. ; Machado, C. T. ; Morère, Y. ; Andrade, A. de O. (2022). *RehaBEElitation* - Source code. Zenodo. <https://doi.org/10.5281/zenodo.6985977>.
- **Mendes, L. C.** ; Marques, I. A. ; De Sá, A. A. R. ; Rosa, R. R ; Alves, C. M. ; Lima, K. R. ; Júnior, E. A. L. ; Naves, E. L. M. ; Vieira, M. F. ; Oliveira, F. H. M. ; Pino, P. ; Bourhis, G. ; Pereira, A. A. ; Machado, C. T. ; Morère, Y. ; Andrade, A. de O. (2022). *RehaBEElitation* serious game. Zenodo. <https://doi.org/10.5281/zenodo.6988572>.
- **Mendes, L. C.** ; De Sá, A. A. R. ; Marques, I. A. ; Morère, Y. ; Andrade, A. de O. (2022). Introductory videos and videos showing the functioning of each phase of the *RehaBEElitation* serious game. Zenodo. <https://doi.org/10.5281/zenodo.6977456>.