RESSALVA

Atendendo solicitação da autora, o texto completo deste documento será disponibilizado somente a partir de 18/06/2025.

Universidade Estadual Paulista
"Júlio de Mesquita Filho"
Faculdade de Ciências - Bauru

PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DO MOVIMENTO – INTERUNIDADES

ALINE PRIETO SILVEIRA CIOLA

ASYMMETRY, DUAL TASK AND INTERSEGMENTAL COORDINATION IN GAIT OF PEOPLE WITH PARKINSON'S DISEASE

Thesis presented to the Faculty of Sciences of the Bauru Campus, São Paulo State University, as part of the requirements for obtaining the title of Doctor of Movement Sciences.

Advisor: Fabio Augusto Barbieri

Bauru

2024

C576a

Ciola, Aline Prieto Silveira
Asymmetry, dual task and intersegmental coordination in gait of people with Parkinson's disease / Aline Prieto Silveira Ciola. -- Bauru, 2024
150 f.

Tese (doutorado) - Universidade Estadual Paulista (UNESP), Faculdade de Ciências, Bauru
Orientador: Fabio Augusto Barbieri

1. Motor control. 2. Asymmetry. 3. Movement disorders. 4. Cognition. 5. Electroencephalography. I. Título.

Sistema de geração automática de fichas catalográficas da Unesp. Dados fornecidos pelo autor(a).

UNIVERSIDADE ESTADUAL PAULISTA

Câmpus de Bauru

ATA DA DEFESA PÚBLICA DA TESE DE DOUTORADO DE ALINE PRIETO SILVEIRA CIOLA, DISCENTE DO PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DO MOVIMENTO, DA FACULDADE DE CIÊNCIAS - CÂMPUS DE BAURU.

Aos 18 dias do mês de dezembro do ano de 2024, às 13h, por meio de Videoconferência, realizou-se a defesa de TESE DE DOUTORADO de ALINE PRIETO SILVEIRA CIOLA, intitulada **ASYMMETRY, DUAL TASK AND INTERSEGMENTAL COORDINATION IN GAIT OF PEOPLE WITH PARKINSON'S DISEASE**. A Comissão Examinadora foi constituída pelos seguintes membros: Profa. Dra. PAULA FAVARO POLASTRI ZAGO (Participação Presencial) do(a) Departamento de Educação Física / UNESP - Faculdade de Ciências de Bauru - SP, Dra. CAMILA TORRIANI-PASIN (Participação Virtual) do(a) Physical Therapy and Movement Sciences / The University of Texas at El Paso (UTEP), Profa. Dra. NATALIA MADALENA RINALDI (Participação Virtual) do(a) Centro de Educação Física e Desportos / Universidade Federal do Espirito Santo - ES, Profa. Dra. ANA MARIA FORTI BARELA (Participação Virtual) do(a) Departamento de Educação Física / Universidade Cruzeiro do Sul de São Paulo - SP, Prof. Dr. RODRIGO VITORIO (Participação Virtual) do(a) Docente credenciado no Programa de Ciências da Motricidade / Northumbria University – Reino Unido. Após a exposição pela doutoranda e arguição pelos membros da Comissão Examinadora que participaram do ato, de forma presencial e/ou virtual, a discente recebeu o conceito final: APROVADA . Nada mais havendo, foi lavrada a presente ata, que após lida e aprovada, foi assinada pelo(a) Presidente(a) da Comissão Examinadora.

Profa. Dra. PAULA FAVARO POLASTRI ZAGO

Documento assinado digitalmente
gov.br
PAULA FAVARO POLASTRI ZAGO
Data: 19/12/2024 12:25:17-0300
Verifique em https://validar.iti.gov.br

POTENTIAL IMPACT OF THIS RESEARCH

This thesis contributes to the Sustainable Development Goal 3 (SDG-3) by addressing health and well-being. Through the investigation of asymmetry, intersegmental coordination, and dual-task effects on the gait of individuals with Parkinson's disease, this work aims to enhance our understanding of their motor behavior and identify tasks that pose significant risks. The findings can inform future research and guide rehabilitation professionals in developing targeted strategies to slow disease progression and mitigate related consequences, such as falls, thereby improving the quality of life for this population.

IMPACTO POTENCIAL DESTA PESQUISA

Essa tese contribui com os Objetivos de Desenvolvimento Sustentável (ODS - 3). Ao investigar os efeitos da assimetria, coordenação intersegmentar e duplas tarefas no andar de pessoas com doença de Parkinson, esperamos contribuir com a saúde e bem-estar desses indivíduos. Estabelecendo informações de como é o comportamento motor desses indivíduos e quais tarefas representam riscos, é possível que estudos futuros e profissionais da reabilitação usem tais informações para desenvolver estratégias de tratamento para frear a evolução da doença e prevenir consequências relacionadas, como as quedas.

Dedico este trabalho a todos os participantes do Ativa Parkinson, a minha família e a Deus.

AGRADECIMENTOS

Agradeço a Deus pelo dom da vida e por permitir que eu tivesse saúde e energia para realizar esse trabalho. Desejo que essas descobertas possam ajudar muitas pessoas e que toda a honra e glória seja destinada à Ele.

Agradeço meu esposo (Tobias) pelo amor e suporte no dia a dia, pelos incentivos quando eu estava fraca e pela sua paciência quando inúmeras vezes precisei dedicar minha atenção e tempo à tese.

Agradeço a meus pais (Paulo e Tânia) por sempre acreditarem em mim, incentivarem meu estudo e dar todo amor e apoio emocional necessário. Vocês são minha inspiração de perseverança, ética e trabalho.

Agradeço também ao meu irmão Bruno, meus sogros Carla e Beto e aos demais familiares e amigos queridos que me ajudaram em diferentes fases da tese. Não citarei todos os nomes, mas vocês também foram essenciais em diversos momentos. Poder compartilhar alegrias e angústias com vocês fez parte desse processo.

Agradeço imensamente ao meu orientador. Fabinho, obrigada por todo o conhecimento compartilhado e por inúmeras vezes me tirar da zona de conforto. Hoje vejo a grande evolução acadêmica e profissional que tive graças a tantas oportunidades que você fornece a nós, seus alunos. Espero ter contribuído e deixado minha marca no MOVI-LAB.

Agradeço aos meus amigos e companheiros de laboratório pelo auxílio nas atividades e por todas as conversas e momentos compartilhados. As risadas e desabafos sempre me deram forças para continuar.

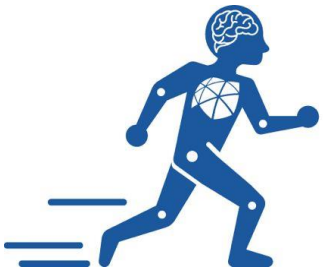
Agradeço aos participantes do Projeto Ativa Parkinson. Estar com vocês sempre foi um momento importante da minha semana. O “Ativa” não é só um projeto, ele se tornou uma família. Obrigada por todo o carinho nesses anos que acompanhei vocês de perto. Sentirei saudades.

Agradeço aos alunos da graduação que passaram pelo meu caminho. Poder ministrar aulas na graduação despertou o meu carinho pela docência e abriu uma porta que quero ultrapassar.

Não posso deixar de agradecer a Mauriceia, minha companheira quinzenal nesse processo. Estar com a mente saudável durante a pós-graduação, é um enorme privilégio atualmente.

Agradeço ao Prof. Christian Schenstedt e à Jana Seuthe por terem me recebido com acolhimento durante o período de intercâmbio na Alemanha.

Por fim, agradeço ao apoio da Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Código de Financiamento 001 que financiou o meu período de doutorado no Brasil e, também, na Alemanha. Essa foi uma experiência valiosa que não teria vivido se não fosse o incentivo da CAPES para a internacionalização dos alunos.



MOVI-LAB

Laboratório de Pesquisa em Movimento Humano



ativa PARKINSON

DEF - UNESP

ABSTRACT

Motor disorders caused by asymmetry in Parkinson's disease (PD) are not limited to classic motor symptoms; they are also evident in the gait of people with PD (pwPD). Gait asymmetry (GA) tends to intensify in scenarios involving obstacles or dual-task conditions, where increased cognitive demands can interfere with gait control and diminish its automaticity. As the disease progresses, disruptions in cortical connectivity may further exacerbate asymmetry and reduce coordination. These findings suggest that higher-level cognitive functions may influence specific aspects of gait. The primary goal of this thesis (study #1) was to examine the effects of asymmetry, dual-tasking, and intersegmental coordination on the gait of pwPD. To achieve this, three studies were conducted. The first study aimed to systematically review the current literature and perform a meta-analysis to compare GA in pwPD to neurologically healthy older individuals (NHI). Additionally, the study evaluated the impact of dopaminergic medication on GA. Study #2 investigated whether obstacle circumvention to the more or less affected side in pwPD, performed concomitantly with a dual task (DT), would lead to worse intersegmental coordination. Seventeen pwPD and 17 NHI were asked to avoid an obstacle while listening to an audio recording of random numbers. Before starting the task, participants were instructed to focus on a specific number. At the end of each trial, their response was recorded. A total of 20 trials were conducted—10 for each side—with half performed under DT conditions. Parameters of asymmetry and intersegmental coordination, including axial coordination and coordination between the lower limbs, were analyzed. Study #3 evaluated gait under various DT conditions in 15 pwPD and 15 NHI. The level of task difficulty was categorized into six conditions: no dual task, very easy, easy, moderate, reasonably difficult, and difficult task. Similar to Study #2, participants listened to an audio recording of random numbers and were asked to memorize how many times a specific number appeared. The level of difficulty increased with the number of digits to be memorized. Spatial-temporal asymmetry and cortical activity were analyzed during these tasks. The main findings are highlighted as follow: Study #1 revealed that pwPD exhibited greater gait asymmetry across most spatial-temporal variables compared to NHI. Swing time asymmetry was identified as the most sensitive indicator of gait asymmetry in PD. Study #2 demonstrated group differences, with pwPD displaying worse intersegmental coordination, particularly axial coordination, compared to NHI. However, the most affected side did not significantly impair coordination during obstacle circumvention. Study #3 revealed greater spatial-temporal and cortical asymmetry in pwPD compared to NHI. The effects of task difficulty on cortical asymmetry were observed exclusively in pwPD. This thesis confirms that pwPD are more asymmetric in both spatial-temporal and cortical parameters compared to NHI. Furthermore, intersegmental coordination, particularly axial coordination, is more affected in PD. However, the influence of challenging environments and dual-task conditions warrants further investigation.

Key words: Motor Control; Asymmetry; Movement Disorders; Cognition; Electroencephalography.

RESUMO

As alterações ocasionadas pela assimetria não se limitam aos sinais motores clássicos, ela também é verificada no andar de pessoas com DP. Em situações com a presença de obstáculos ou sob a condição de duplas tarefas, a assimetria no andar (GA) parece ser ainda mais intensificada. Em ambas as situações altas demandas cognitivas podem influenciar no controle da marcha, comprometendo sua automaticidade. Com o avanço da doença, alterações na conectividade de áreas corticais também podem ser comprometidas. Com isso, manifestações assimétricas e menos coordenadas podem ocorrer, sugerindo que alguns aspectos da marcha podem ser influenciados por funções cognitivas de nível superior. Sendo assim, o objetivo dessa tese foi verificar o efeito da assimetria, dupla tarefa e coordenação intersegmentar no andar de indivíduos com doença de Parkinson. Para isso, uma sequência de três estudos foi desenvolvida. O estudo #1 teve como objetivo verificar sistematicamente a literatura atual e realizar uma meta-análise para investigar as diferenças entre a GA em pwPD em comparação com idosos neurologicamente saudáveis (GC) e avaliar o efeito da medicação dopaminérgica na GA. O estudo #2 verificou se o desvio para o lado mais ou menos afetado pela DP concomitante a uma DT levaria a uma pior coordenação intersegmentar. Dezessete indivíduos com DP e 17 NHI realizaram o desvio de um obstáculo enquanto um áudio contendo números aleatórios era falado. Antes de iniciar a avaliação do andar, era dito ao indivíduo qual o número ele deveria prestar atenção. Ao final da tentativa, foi verificado contabilizada a resposta. Foram realizadas 20 tentativas no total, 10 para cada lado, sendo metade delas com a realização da dupla tarefa concomitante. Os parâmetros de assimetria e coordenação intersegmentar axial e entre membros inferiores foi verificado. No estudo #3, 15 indivíduos com DP e 15 GC realizaram a avaliação do andar livre sob várias condições de dupla tarefa. O grau de dificuldade foi caracterizado em 6 condições: sem dupla tarefa (ST), muito fácil, fácil, moderada, razoavelmente difícil e difícil. Assim como no estudo #2, os indivíduos deveriam escutar um áudio contendo números aleatórios e memorizar quantas vezes um número “x” era falado. Com o aumento do nível de dificuldade da tarefa, a quantidade de números a memorizar era aumentada. Durante a realização dessas tarefas, foi analisada a assimetria espaço-temporal e da atividade cortical. Os resultados do estudo #1 evidenciaram que indivíduos com DP apresentaram maior assimetria dos parâmetros espaço-temporais comparados ao GC. A variável mais sensível para detectar a assimetria no andar de indivíduos com DP é o tempo de balanço. O estudo #2 também revelou diferenças entre os grupos: pessoas com DP apresentaram pior coordenação intersegmentar axial e de membros inferiores que o GC. Entretanto, o lado mais afetado pela DP não comprometeu o padrão de coordenação com grandes impactos durante o desvio de um obstáculo. Por fim, no estudo #3, indivíduos com DP exibiram maior assimetria dos parâmetros espaço-temporais e corticais comparados ao GC. Embora, os efeitos da dificuldade da tarefa na assimetria cortical tenham sido exclusivos em indivíduos com DP. Como principal conclusão da tese, é possível assumir que indivíduos com DP são mais assimétricos que seus pares neurologicamente sadios para os parâmetros espaço-temporais e corticais. Além disso, a coordenação intersegmentar, especialmente a axial, é mais comprometida. Os efeitos de ambientes desafiadores e duplas tarefas precisam de mais investigações.

Palavras-chave: Controle Motor; Assimetria; Desordens do movimento; Cognição; Eletroencefalografia.

LIST OF FIGURES

Figure 1. Flowchart including literature search and selection steps following PRISMA statement 39

Figure 2. Cumulative amount of the included articles per year. 40

Figure 3. On the left there are the type of outcomes and the respective number of studies that investigated each one. On the right, the number of studies showing significant (or non-significant) results in GA when comparing pwPD vs NHI. The arrow graphic represents significant greater asymmetry in pwPD compared to NHI 62

Figure 4. Forest plots of GA for (a) step length asymmetry, (b) swing time asymmetry, and (c) step time asymmetry for the comparison between pwPD at OFF state vs. NHI. PD: people with Parkinson's disease; NHI: neurologically age-matched healthy individuals; SMD: Standardized mean difference; CI: Confidence interval. 65

Figure 5. Forest plots of GA for (a) step length asymmetry, (b) swing time asymmetry, (c) step time asymmetry, and (d) stance time asymmetry for the comparison between pwPD at ON state vs. NHI. PD: people with Parkinson's disease; NHI: neurologically age-matched healthy individuals; SMD: Standardized mean difference; CI: Confidence interval. 66

Figure 6. Forest plots of GA for (a) step length asymmetry, (b) swing time asymmetry, and (c) and step time asymmetry for the comparison between PD at ON vs. OFF state of dopaminergic medication. PD: people with Parkinson's disease; SMD: Standardized mean difference; CI: Confidence interval 67

Figure 7. A) illustration of the task performed by the individuals (two steps of aprroach and two steps of circumvention phases). B) and C) displays data captured by VICON cameras using Nexus software. The left panels (B) provide a lateral view, while the right panels (C) present a top-down view, illustrating the individual, the obstacle, and the walkway. 91

Figure 8. Intersegmental coordination between thighs, legs and feet during an obstacle cirvumvention with and without a dual task to the more and less affected side. *: indicates main effects of group; #: # Indicates main effects of task; Combination of continuous rectangles indicates interaction effects between Group x side 94

Figure 9. Intersegmental coordination between head-pelvis (1), head-trunk (2) and trunk-pelvis (3) during an obstacle cirvumvention with and without a dual task to the more and less affected side. *: indicates main effects of group; #: # Indicates main effects of task 95

Figure 10. Asymmetry of spatial-temporal variables during gait without a dual task (ST) and with different difficulties of dual task 115

Figure 11. The figure below presents the values of ΔPSD asymmetry index of theta, alpha, beta and gamma bands. Those values were calculated in three cortical regions: Prefrontal, Sensoriomotor and Occipital cortex during gait without a dual task (ST) and with different difficulties of dual task 117

LIST OF TABLES

Table 1. Demographic and clinical characteristics of the included studies 42

Table 2. Gait protocols, GA index and main findings of the studies included in the review . 48

Table 3. Gait variables investigated in each study according to kinematic, kinetic, muscular (EMG) and/or neural gait feature. The third column shows the results presented only for GA values when comparing NHI and pwPD or GA with correlate variables..... 55

Table 4. Table 4 shows the scores for the participants' anthropometric characteristics and clinical assessments 92

Table 5. Mean and standard deviation values for the sample's anthropometric and clinical data 113

Table 6. Absolute error values presented by both groups when performing the cognitive task while seated and while walking..... 114

Table 7. The table presents a synthesis of data from the current literature, highlighting the main findings of this thesis and offering recommendations for future studies 131

SUMMARY

CHAPTER 1 – Contextualization **16**
1.1 Introduction 17
1.1.1 Asymmetry in people with PD 18
1.1.2 Asymmetry on gait of people with PD 20
1.1.3 Dual task and gait asymmetry: what the literature shows and what we can do to move forward? 21
1.2 Objectives and design of the thesis 23
1.3 Hypotheses 24
References 26
CHAPTER 2 – Study 1: Gait Asymmetry in Parkinson's Disease – A systematic review and meta-analysis (AsymmGait-Parkinson study) 31
Abstract 32
2.1 Introduction 33
2.2 Methods 34
2.2.1 Protocol and registration 34
2.2.2 Search strategy 35
2.2.3 Study selection and eligibility 35
2.2.4 Quality assessment 36
2.2.5 Data extraction and analysis 37
2.2.6 Quantitative data synthesis and analysis 37
2.3 Results 38
2.3.1 Study selection 38
2.3.2 Quality assessment 39
2.3.3 Research paradigm 40
a) Distribution of studies published per year 40
b) Sample characteristics 40
c) GA studies' comparison 46
d) Walking task 46
e) GA index's calculation 46
f) Outcomes analyzed 47
2.3.4 Overview of main findings of the systematic review 62
a) kinematic outcomes 62
b) kinetic outcomes 63

c) muscular outcomes 63
d) neural outcomes 64
2.3.5 Meta-analysis 64
a) PD OFF vs. controls 64
a) PD ON vs. controls 64
a) PD ON vs. PD OFF 65
2.4 Discussion 68
2.4.1 Dopaminergic medication partly improves gait asymmetry 70
2.4.2 Methodological quality 70
Wide variability among experimental protocols to assess GA in pwPD 71
2.4.3 Clinical implications, study limitations and future directions 72
2.5 Conclusion 73
References 73

CHAPTER 3 – Study 2: Intersegmental coordination during an obstacle circumvention is not affected by side of symptoms and a dual task in people with Parkinson's disease 83
Abstract 84
3.1 Introduction 85
3.2 Methods 86
3.2.1 Participants 86
3.2.2 Experimental design 87
3.2.3 Clinical evaluations 87
3.2.4 Gait evaluation 88
3.2.5 Data analysis 89
3.2.6 Statistical analysis 90
3.3 Results 92
3.3.1 Sample characteristics and clinical parameters 92
3.3.2 Intersegmental coordination during OC to the most and least affected side with ir without a dual task 92
Coupling between left x right thigh 92
Coupling between left x right leg 92
Coupling between left x right foot 93
Coupling between head x pelvis 93
Coupling between head x trunk 93
Coupling between trunk x pélvis 93
3.4 Discussion 96

3.5 Conclusion 99
References 100
4. CHAPTER 4 – Study 3: Influence of the difficulty of the cognitive task during walking on the asymmetry of spatial-temporal parameters and cortical activity in individuals with Parkinson's disease **104**
Abstract 105
4.1 Introduction 106
4.2 Methods 107
4.2.1 Participants and experimental design 107
4.2.2 Clinical assessment 108
4.2.3 Gait assessment 109
4.2.4 Data Analysis 110
Spatial-temporal data 110
Cortical activity data 111
4.2.5 Análise estatística 112
4.3 Results 112
4.2.1 Clinical evaluation and performance in the cognitive dual task 112
4.2.1 Effects of dual task difficulty on asymmetry of spatial-temporal and cortical parameters 114
Spatial-temporal parameters 114
Cortical parameters 115
4.4 Discussion 117
4.5 Conclusion 120
References 121
5 CHAPTER 5 – Final remarks 127
5.1 Final remarks 128
a) Are individuals with PD always asymmetrical? 128
b) Dual task as a model to study gait asymmetry in PD 128
c) Intersegmental coordination and gait asymmetry in gait of pwPD 129
d) Limitations, future suggestions and practical applications 129
References 132
APPENDICES 133
Appendix A - Description of the terms used for paper searching in each database 134
Appendix B - Questions of appraisal tool adapted from Galna et al. (2015) 135
Appendix C - Basic information about the studies included at systematic review. 136

Appendix D - Methodological quality appraisal results. Each question is the average of the evaluation of three authors. The last column presents the total score for each paper. The last line presents the average for each question 139

Appendix E - Equations, indexes, and other methods employed to calculate asymmetry during gait 140

Appendix F - Funnel plots of step length asymmetry, swing time asymmetry, step time asymmetry and stance time asymmetry for the comparison between pwPD at ON state vs. NHI 144

Appendix G - Asymmetric spatial-temporal parameters of PG compared to CG during the approach and circumvention phases to the more and less affected side during the obstacle circumvention with and without a dual task 145

ANNEXES 146

Annex I - Ethics Committee approval 147

Annex II – PROSPERO registration number 150

CHAPTER 1 –
CONTEXTUALIZATION

1.1 INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disease in the world, affecting 1-2 out of every 1000 individuals (Tysnes; Storstein, 2017). In Brazil, estimates projected a prevalence of 340,000 people with the disease in the country by 2020 (Dorsey *et al*., 2006). Therefore, studies involving PD have been growing and are being highlighted by various research groups around the world, with the aim of helping with early diagnosis, understanding the mechanisms of the disease and possible treatments to mitigate its progression.

PD is characterized by the asymmetrical degeneration of dopaminergic cells in the substantia nigra of the midbrain (Lewis *et al.*, 2009). This degeneration causes motor signs/symptoms such as bradykinesia (slowness of movement), muscle rigidity, resting tremor and postural instability (Sant *et al*., 2008; Hughes, *et al.*, 2002; Hess, Hallett, 2017), which appear when there has already been a loss of 50-70% of the nigral neurons (Obeso *et al.*, 2000; Takakusaki *et al.*, 2004). At the beginning of the disease, signs and symptoms are present unilaterally (Djaldetti; Melamed, 2006; Segarra *et al.*, 2016; Kempster *et al.*, 1989; Uitti, 2005). As the disease progresses, symptoms can become bilateral, with changes predominating on the side where the disease began. In addition to motor impairments, changes in cortical activity are also present in PD, with patterns of cortical atrophy differing between the cerebral hemispheres throughout the course of the disease (Claassen *et al.*, 2016).

Locomotion, one of the main motor aspects affected in PD, can also manifest itself asymmetrically in tasks involving walking (Plotnik *et al*., 2008), for example during walking with crossing and avoiding obstacles (Barbieri *et al*., 2018a; Barbieri *et al*., 2018b). Asymmetrical gait in the elderly is directly related to a higher number of falls (Laroche; Cook; Mackala, 2012). Furthermore, in situations where tasks are concomitant with walking - dual tasks - the asymmetry seems to intensify even more (Yogev *et al*., 2007; Plotnik *et al*., 2005; Plotnik *et al*., 2009). Dual-tasking (DT) involves combining two tasks (each aimed at different goals), either motor or cognitive (Broeder *et al*., 2014). In PD, performing DTs in daily life impairs not only the spatial-temporal variables of gait (Yamada *et al*., 2020) but also bilateral symmetry and coordination during walking (Yogev *et al*., 2007). Asymmetry and reduced coordination during gait have been described as contributing to episodes of freezing (Plotnik *et al*., 2005; Plotnik; Giladi; Hausdorff, 2008), one of the most disabling signs of the disease.

However, in most studies, the DTs are performed under free walking conditions, without the major challenges of everyday life. There is considerable methodological variability in studies within the current literature (Kelly, Eusterbrock, Shumway-Cook, 2012), including a lack of standardization in the types of cognitive tasks used, their difficulty levels, and their effects on gait. Although cognitive deficits in PD and their impact on locomotor activities are well-documented (Raffegeau *et al*., 2019), the influence of task difficulty on gait dynamics remains a relatively unexplored area. Investigating cortical activity during cognitive dual tasks (DTs) offers valuable insights into capacity-sharing theories and the competition for attentional resources. Moreover, understanding the asymmetry in PD gait requires further exploration of contributing factors, such as reduced automaticity, altered cortical activity recruitment, and its impact on intersegmental coordination. This knowledge is essential for designing preventive measures to enhance safety and independence in individuals with PD. Furthermore, it can inform the development of locomotion-specific interventions, ultimately reducing hospitalization rates and associated healthcare costs from falls within this population.

The subsequent sections of this general introduction will provide an overview of asymmetry in Parkinson's disease (PD) and its implications for walking. Additionally, the topics will highlight current findings in the literature and explore areas where advancements can be made, particularly in understanding dual-tasking and asymmetry during gait in individuals with PD. Finally, the study's objectives and hypotheses will be presented.

1.1.1 Asymmetry in PD

Symmetry is often seen as a characteristic of a healthy system, while asymmetry can be indicative of harmful alterations to a system (McManus, 2005). Although the reason for the unilateral degenerative process in PD is unknown, possible genetic, structural, environmental, toxic and metabolic causes have been raised. Two main hypotheses have been proposed to explain the asymmetry: (I) the variation in the number of nigral dopaminergic cells between the hemispheres from birth and (II) the greater vulnerability of one side of the substantia nigra to neuronal death (Djaldetti; Melamed, 2006). According to the first hypothesis, the number of nigral neurons is different between the hemispheres from birth. With the degenerative process of PD,

both hemispheres are affected in a similar way; however, due to the baseline difference in the number of cells, one hemisphere reaches vulnerability first. The second hypothesis argues that as the degenerative process begins, one side of the substantia nigra is more susceptible to degeneration. Therefore, both sides are affected, but degeneration is more pronounced on one side. However, none of the hypotheses raised have been confirmed as a causal factor for the origin of the asymmetry.

Unilateral motor impairment in people with PD (pwPD) is present in more than half of all individuals (Uitti *et al*., 2005). This unilateral predominance of signs and symptoms affects people in the early stages and can persist throughout the progression of the disease, around 20 to 30 years (Djaldetti *et al*., 2006; Verreyt *et al*., 2011). The changes caused by asymmetry are not limited to the classic motor signs of the disease (Miller-Patterson *et al*., 2018); it extends to everyday locomotor activities (Barbieri *et al*., 2018a, Boonstra *et al*., 2014), as well as leading to functional and structural changes in the cerebral cortex (Claassen *et al*., 2016).

Cerebral asymmetry is defined by the functional, anatomical or neurochemical difference between the two hemispheres. In the early stages of PD, asymmetrical neurodegeneration of the nigrostriatal pathways occurs bilaterally (Wang *et al*., 2015). As the disease progresses, changes in the connectivity of cortical areas can also be compromised (Hawkes; Del Tredici; Braak, 2010). Contralateral structural and/or functional alterations in the nigrostriato-cortical circuit may be related to asymmetry in PD (De La Fuente-Fernandéz *et al*., 2000), which is one of the explanations for the asymmetrical negative effects on walking. The initial onset of symptoms in the right or left hemisphere may indicate a relationship between the laterality of motor symptoms and neural asymmetries. People with left-sided motor symptoms showed a “healthier” pattern of motor responses (Heinrichs-Graham *et al*., 2017). In addition, the laterality of symptoms can alter the response of cognitive functions, since the predominance of motor symptoms on the right is related to alterations in speech and verbal memory, while the predominant symptoms on the left reflect deficits in attention, visuospatial orientation and programming (Verreyt *et al*., 2011).

Moreover, cerebral atrophy in PD appears to be time-dependent, manifesting in different brain areas as the disease progresses. Specific cortical regions seem to experience atrophy with increasing disease duration, with frontal brain regions being more susceptible in the early stages, while posterior regions are more affected as the

disease advances (Kempster *et al*., 1989; Wang *et al*., 2015). Additionally, during the initial course of the disease, cortical atrophy is observed in regions of the left hemisphere, apparently independent of symptom dominance or severity. In later stages, this atrophy extends to the right hemisphere and posterior brain regions (Claassen *et al*., 2016). Despite these insights, significant gaps remain regarding the cortical effects, their relationship with gait asymmetry, and the specific walking functions affected.

1.1.2 Gait asymmetry among individuals with Parkinson's disease

Numerous studies have shown that gait is significantly impaired in individuals with Parkinson's disease, even in its early stages, characterized by reduced walking speed and shorter stride length, progressing to moderate levels of impairment (Yang *et al*., 2008). In advanced stages of the disease, individuals often lose the ability to walk independently, making it impossible to assess gait asymmetry. Consequently, individuals with PD experience compromised daily activities, as gait is essential for maintaining independence and quality of life (Viteckova *et al*., 2018). Therefore, gait alterations, such as asymmetry, may serve as indicators for early diagnosis of PD (Maetzler; Hausdorff, 2012) and can also be a useful tool for evaluating the benefits of training (Alam *et al*., 2017).

People with PD may exhibit asymmetry in arm swing (Roggendorf *et al*., 2012; KWON *et al*., 2014), step duration (Barbieri *et al*., 2018a), step length (ROEMMICH *et al*., 2014), and swing phase of the legs (Yogev *et al*., 2007). Additionally, impairments involving asymmetric postural control and motor coordination (Beretta *et al*., 2015; Frazzitta *et al*., 2013; Plotnik; Giladi; Hausdorff, 2008; Boonstra *et al*., 2014; Barbieri *et al*., 2018b) may further damage locomotion in individuals with PD. Greater asymmetry has also been linked to the occurrence of freezing episodes during walking (Plotnik *et al*., 2005).

The limitations induced by gait asymmetry range from unrestricted walking (Plotnik; Giladi; Hausdorff, 2008) to more complex activities, such as crossing horizontal obstacles (Barbieri *et al*., 2018b). Barbieri and colleagues (2018b) observed that during obstacle crossing, there is an increase in asymmetry in the leading foot. In another study, Barbieri and colleagues (2018a) also found an increase in asymmetry during avoidance of vertical obstacles. The latter study concluded that individuals with PD adopted riskier obstacle avoidance strategies on the more affected side compared to

the less affected side of the body. Similar results were observed in neurologically healthy older adults; however, the changes were more pronounced in individuals with PD.

Another critical factor is the relationship between spatial-temporal gait asymmetries and reduced integrity of corpus callosum tracts that connect the supplementary motor area (SMA) and pre-SMA (Fling; Curtze; Horak, 2018). A lack of integrity in these structures may further impair the conception and sequential planning of movements. Moreover, increased interhemispheric synchronization in the brain may accompany the asymmetric symptoms of PD during walking, potentially resulting from asymmetric neural degeneration (Miron-Shahar *et al*., 2019). Given that cortical-level impairments are present in PD, tasks requiring competition for cortical attentional resources, such as dual-task activities, may exacerbate gait execution difficulties.

1.1.3 Dual Task and Gait Asymmetry: What the Literature Presents and Possible Advances

The ability to perform two activities simultaneously is defined as a dual task (Sala *et al*., 1995). DTs are integrated into various everyday contexts, including locomotor activities such as walking while conversing (a cognitive task) or holding an object (a motor task). Their effects appear to impair the performance of spatial-temporal gait variables in elderly individuals with PD (Yamada *et al*., 2020); for instance, when walking while talking on a cellphone, this population exhibits reduced speed and cadence, shorter step length, and increased single and double support times. Individuals with PD, beyond the motor deficits caused by the disease, also experience cognitive impairments (Foltynie *et al*., 2004; Muslimovic *et al*., 2005), which are closely related to locomotor difficulties in PD patients (e.g., increased gait variability and reduced stability; Brauer *et al*., 2011).

Performing these simultaneous tasks can involve either parallel or competing cognitive processes. In the case of walking while performing a cognitive task, this process occurs concurrently, leading to competition for cognitive resources. This competition results in reduced automatization and increased reliance on cortical resources through attentional processes (Wu; Hallett; Chan, 2015), ultimately impairing walking performance (Yogev *et al*., 2007). Consequently, cortical resources necessary for gait adjustments are not optimized efficiently or in parallel (Clark, 2015; Gilat *et al*.,

2017). PD patients, in addition to motor deficits related to walking, often face significant cognitive impairments (e.g., executive function, memory, and attention). Notably, executive function and attention play crucial roles in gait regulation (Maruyama; Yanagisawa, 2006; Amboni *et al*., 2008). This combination of factors leads to considerable walking disabilities (Amboni; Barone; Hausdorff, 2013), which are further exacerbated in PD due to motor control asymmetry. Hence, gait asymmetry could be a potential impairment in dual-task scenarios (Plotnik *et al*., 2009).

Although the knowledge surrounding gait deficits in PD patients during DT scenarios is extensive (Kelly; Eusterbrock; Shumway-Cook, 2012), the effects of DT on gait asymmetry still require further investigation. Additionally, the relationship between gait symmetry and cognitive function needs to be better understood. The necessity to allocate sufficient cognitive resources simultaneously for walking and a DT (motor or cognitive) could explain the observed impairments in gait symmetry. According to the capacity-sharing theory (Tombu; Jolicoeur, 2003), when two functions requiring the same resources are performed simultaneously, the performance of one or both functions may be compromised. This cognitive resource competition may well exceed the available resources, increasing gait asymmetry. Some studies (Yogev *et al*., 2007; Plotnik *et al*., 2005; Plotnik *et al*., 2009) have demonstrated that DT negatively affects gait symmetry parameters in PD patients.

Yogev *et al*. (2007) investigated the effects of DT on PD patients, elderly fallers, and healthy older adults. Participants performed habitual walking and walking with a cognitive DT (arithmetic calculations – subtracting 7). In normal walking conditions, swing time asymmetry was significantly greater in both patient groups compared to controls. Furthermore, for both patient groups (PD and fallers), asymmetry increased under DT conditions compared to habitual walking, suggesting a relationship between asymmetry regulation and cognitive function. Cognitive abilities were mildly impaired in both PD patients and idiopathic elderly fallers. Based on this and the observation that gait deteriorates when these individuals are exposed to cognitive loads, it can be suggested that older adults with motor deficits, cognitive deficits, or both may struggle to regulate gait rhythm and coordinate symmetric leg movements while walking. In such scenarios, where cognitive demand increases, walking becomes less automatic and more asymmetrical, indicating that gait symmetry is sensitive to cognitive load.

According to Yang *et al*. (2006), gait symmetry in healthy individuals was not affected by DT, contrary to findings in neurologically impaired patients (post-stroke). The suggestion is that individuals with more automated gait are not sensitive to the cognitive load of DT, thus maintaining symmetric gait under lower-level control. However, when gait becomes less automated (as in PD), sensitivity to cognitive load increases, manifesting as asymmetrical walking and requiring additional cognitive input. Nonetheless, there is still a lack of information regarding the point at which cognitive DT begins to impair walking and whether the level of task difficulty reaches a threshold in cognitive processing capacity, "exhausting" cognitive reserves and consequently impairing gait. It is hypothesized that DT effects are difficulty-dependent. Previous studies have indicated that locomotion was more affected in situations involving more complex cognitive tasks performed concurrently with walking (Holtzer *et al*., 2011) compared to simpler dual tasks (Galletly; Brauer, 2005; Strouwen *et al*., 2016). However, despite previous studies providing relevant insights into the effect of cognitive DT difficulty on the locomotion of elderly individuals with PD, it remains controversial whether any cognitive DT affects locomotion or if there is a difficulty threshold for task limitations.

One potential method of analysis that could advance the discussion of the effect of cognitive TD on gait asymmetry in pwPD is inter-limb coordination. Asymmetry is a metric used to check the level of difference between sides, hemibodies or limbs. While intersegmental coordination can verify the association between segments, joints and limbs during a movement. Reduced asymmetry and coordination during gait have been described as contributing to episodes of gait freezing, especially in conditions of DT (Plotnik *et al*., 2005; Plotnik; Giladi; Hausdorff, 2008). In addition, coordination between the hemibodies during gait seems to be affected by cognitive attentional demand. In healthy individuals, gait coordination occurs automatically, but in PD this task may require greater control, reducing its automaticity and impairing task performance (Wu, Hallett, 2009).

1.2 Objectives and design

The general aim of this study is to investigate asymmetry in the gait of pwPD and to analyze the effect of PD on asymmetry in spatial-temporal parameters, intersegmental coordination and neural activity. In order to respond to the gaps in the

literature and advance knowledge on the topics covered, a sequence of three studies (one review and two experimental) is proposed.

The first study aims to systematically investigate the main deficits that asymmetry causes in the locomotion of individuals with PD. Since asymmetry is a limiting symptom in the gait of pwPD, the way in which asymmetry affects the parameters linked to locomotion (kinetic, kinematic, muscular and cortical) is extremely important for understanding the consequences of this motor manifestation.

The second study aimed to determine whether individuals exhibiting asymmetrical gait during a dual-task scenario involving obstacle avoidance also demonstrate poorer intersegmental coordination, depending on the side of the circumvention. Both variables may be affected by the reduced automaticity of movement observed during dual-tasking. However, the existing literature has yet to establish a direct relationship between these two factors. Identifying a common underlying mechanism could offer new approaches to mitigate the negative effects on locomotion.

The third study sought to explore how the difficulty of a concurrent cognitive dual task during walking influences spatial-temporal asymmetry and cortical activity in individuals with Parkinson's disease (PD). More complex cognitive tasks are likely to impose greater challenges on gait in individuals with PD compared to simpler tasks. Nonetheless, the wide variability in protocols across the literature makes it difficult to ascertain the specific impact of cognitive task difficulty on walking performance, particularly whether a plateau effect may occur at higher levels of task complexity.

1.3 Hypotheses

Based on the general objectives of the project, three main hypotheses were proposed:

i) The confirmation, through articles already available in the literature, of deficits caused by the presence of asymmetry in the locomotion of individuals with Parkinson's disease (PD). These deficits are expected to manifest as greater asymmetry in kinematic, kinetic, electromyographic, and/or cortical variables, with a more pronounced asymmetry observed in individuals with PD compared to their healthy pairs;

ii) Gait asymmetry during a cognitive DT with obstacle circumvention will be accompanied by changes in intersegmental coordination between the lower limbs,

characterized by more in-phase movements and a predominant contribution of the “less affected” limb. Although Plotnik, Giladi, and Hausdorff (2008) associate poorer bilateral gait coordination with the presence of freezing of gait, we hypothesize that such impaired coordination will also be observed in participants without freezing due to the inherently challenging nature of the task. Regarding axial coordination, it is expected that a more in-phase movement pattern will emerge when performing obstacle circumvention combined with a DT, especially toward the side most affected by the disease, as obstacle crossing in this direction presents a greater challenge.

iii) There will be a threshold of difficulty beyond which asymmetry begins to manifest in spatial-temporal parameters and cortical activity in individuals with PD. Additionally, greater cortical asymmetry is expected in the prefrontal and sensorimotor regions when compared to individuals without the disease.

REFERENCES

ALAM, M. N. et al. Vertical ground reaction force marker for Parkinson's disease. **PLoS ONE**, v. 12, n. 5, p. e0175951, 2017.

AMBONI, M. et al. Freezing of gait and executive functions in patients with Parkinson's disease. Movement Disorders, v. 23, n. 3, p. 395-400, 2008.

AMBONI, M.; BARONE, P.; HAUSDORFF, J. M. Cognitive contributions to gait and falls: Evidence and implications. **Movement Disorders**, v. 28, n. 11, p. 1520-33, 2013.

BARBIERI, F.A. et al. Obstacle circumvention and eye coordination during walking to least and most affected side in people with Parkinson's disease. **Behavioural Brain Research**, v. 346, p. 105-114, 2018[a].

BARBIERI, F. A. et al. Obstacle avoidance increases asymmetry of crossing step in individuals with Parkinson's disease and neurologically healthy individuals. **Journal of Motor Behaviour**, v. 50, n. 1, p. 17-25, 2018[b].

BERETTA, V. S. et al. Challenging Postural Tasks Increase Asymmetry in Patients with Parkinson's Disease. **PLoS One**, v. 10, n. 9, p. e0137722, 2015.

BOONSTRA, T. A. et al. Parkinson's disease patients compensate for balance control asymmetry. **Journal of Neurophysiology**, v. 112, n. 12, p. 3227-3239, 2014.

BRAUER, S. G. et al. Single and dual task gait training in people with Parkinson's Disease: A protocol for a randomised controlled trial. **BMC Neurol**, v. 11, p. 90, 2011.

BROEDER, S. et al. The effects of dual tasking on handwriting in patients with Parkinson´s disease. **Neuroscience**, v. 263, p. 193–202, 2014.

CLAASSEN, D. O. et al. Cortical asymmetry in Parkinson's disease: early susceptibility of the left hemisphere. **Brain and Behavior**, v. 6, n. 12, p. e00573, 2016.

CLARK, D. J. Automaticity of walking: functional significance, mechanisms, measurement and rehabilitation strategies. Frontiers in Human Neuroscience, v. 9, p. 246, 2015.

DE LA FUENTE-FERNÁNDEZ, R. et al. Nigrostriatal dopamine system and motor lateralization. Behavioural Brain Research, v. 112, n. 1–2, p. 63–68, 2000.

DJALDETTI, R.; ZIV, I.; MELAMED, E. The mystery of motor asymmetry in Parkinson's disease. **The Lancet Neurology**, v. 5, p. 796-802, 2006.

DORSEY, E. R. et al. Projected number of people with Parkinson disease in the most populous nations, 2005 through 2030. **Neurology**, v. 68, n. 5, p. 384–386, 2006.l

FLING, B. W.; CURTZE, C.; HORAK, F. B. Gait asymmetry in people with Parkinson's Disease is linked to reduced integrity of callosal sensorimotor regions. **Frontiers in Neurology**, v.9, p.215, 2018.

FOLTYNIE, T. et al. The cognitive ability of an incident cohort of Parkinson's patients in the UK. The CamPaIGN study. **Brain**, v. 127, p. 550-60, 2004.

FRAZZITTA, G. et al. Asymmetry and freezing of gait in parkinsonian patients. **Journal of Neurology**, v. 260, n.1, p. 71-76, 2013.

GALLETLY, R.; BRAUER, S. G. Does the type of concurrent task affect preferred and cued gait in people with Parkinson's disease? **Australian Journal of Physiotherapy**, v. 51, n. 3, p. 175–180, 2005.

GILAT, M. et al. Dopamine depletion impairs gait automaticity by altering cortico-striatal and cerebellar processing in Parkinson's disease. Neuroimage, v. 15, n. 152, p. 207-220, 2017.

HAWKES, C. H., DEL TREDICI, K.; BRAAK, H. A timeline for Parkinson's disease. **Parkinsonism & Related Disorders**, v. 16, p. 79–84, 2010.

HEINRICHS-GRAHAM, E. et al. The cortical signature of symptom laterality in Parkinson's disease. **NeuroImage: Clinical**, v. 14, p. 433-440, 2017.

HESS, C. W.; HALLETT, M. The Phenomenology of Parkinson's Disease. **Seminars in Neurology**, v. 37, n. 2, p. 109-117, 2017.

HOLTZER, R. et al. fNIRS study of walking and walking while talking in young and old individuals. **Journals of Gerontology - Series A Biological Sciences and Medical Sciences**, v. 66 A, n. 8, p. 879–887, 2011.

HUGHES, A. J. et al. The accuracy of diagnosis of parkinsonian syndromes in a specialist movement disorder service. **Brain**, v. 125, n. Pt 4, p. 861-70, 2002.

KELLY, V. E.; EUSTERBROCK, A. J.; SHUMWAY-COOK, A. A review of dual-task walking deficits in people with Parkinson's disease: motor and cognitive contributions, mechanisms, and clinical implications. **Parkinson's Disease**, v. 2012, p. 918719, 2012.

KEMPSTER, P. A. et al. Asymmetry of substantia nigra neuronal loss in Parkinson's disease and its relevance to the mechanism of levodopa related motor fluctuations. **Journal of Neurology, Neurosurgery, and Psychiatry**, v. 52, n. 1, p. 72–76, 1989.

KWON, K. et al. Is reduced arm and leg swing in Parkinson's disease associated with rigidity or bradykinesia? **Journal of the Neurological Sciences**, v. 341, p. 32-35, 2014.

LAROCHE, D. P.; COOK, S. B.; MACKALA, K. Strength asymmetry increases gait asymmetry and variability in older women. **Medice & Science in Sports & Exercise**, v. 44, n. 11, p. 2172–2181, 2012.

LEWIS, M. M. et al. **Asymmetrical lateral ventricular enlargement in Parkinson's disease. European Journal of Neurology**, v. 16, n. 4, p. 475-481, 2009.

MAETZLER, W.; HAUSDORFF, J. M. Motor Signs in the Prodromal Phase of Parkinson's Disease. **Movement Disorders**, v. 27, n. 5, p. 627-633, 2012.

MARUYAMA, T.; YANAGISAWA, N. Cognitive impact on freezing of gait in Parkinson's disease. Parkinsonism & Related Disorders, v. 12, p. S77-S82, 2006.

MCMANUS, I. C. Symmetry and asymmetry in aesthetics and the arts. **European Review**, v. 13, n. 2, p. 157–180, 2005.

MILLER-PATTERSON, C. et al. Motor asymmetry over time in Parkinson's disease. **Journal of the Neurological Sciences**, v. 393, p. 14-17, 2018.

MIRON-SHAHAR, Y. et al. Excessive phase synchronization in cortical activation during locomotion in persons with Parkinson's disease. **Parkinsonism & Related Disorders**, v. 65, p. 210-216, 2019.

MUSLIMOVIC, D. et al .Cognitive profile of patients with newly diagnosed Parkinson disease. **Neurology**, v. 25, p. 1239-45, 2005.
PLOTNIK, M. et al. Is freezing of gait in Parkinson's disease relates to asymmetric motor function? **Annals of Neurology**, v. 57, p. 656-663, 2005.

PLOTNIK, M.; HAUSDORFF, J. M. The role of gait rhythmicity and bilateral coordination of stepping in the pathophysiology of freezing of gait in Parkinson's disease. **Movement Disorders**, v. 23, n. S2, p. S444–S450, 2008.

PLOTNIK, M.; GILADI, N.; HAUSDORFF, J. M. Bilateral coordination of walking and freezing of gait in Parkinson's disease. **The European Journal of Neuroscience**, v. 27, p. 1999–2006, 2008.

PLOTNIK, M.; GILADI, N.; HAUSDORFF, J. M. Bilateral coordination of gait and Parkinson's disease: the effects of dual tasking. **Journal of neurology, neurosurgery, and psychiatry**, v. 80, n. 3, p. 347–350, 2009.

RAFFEGEAU, T. E. et al. A meta-analysis: Parkinson's disease and dual-task walking. **Parkinsonism & Related Disorders**, v. 62, p. 28-35, 2019.

ROEMMICH, R. T. et al. Locomotor adaptation and locomotor adaptive learning in Parkinson's disease and normal aging. **Clinical Neurophysiology**, v. 125, p. 313-319, 2014.

ROGGENDORF, J. et al. Arm swing asymmetry in Parkinson's disease measured with ultrasound based motion analysis during treadmill gait. **Gait & Posture**, v. 35, p. 116-20, 2012.

SALA, S. D. et al. Dual-Task Paradigm: A Means To Examine the Central Executive. **Annals of the New York Academy of Sciences**, v. 769, p. 161–172, 1995.

SANT, C. R. et al. Abordagem fisioterapêutica na doença de Parkinson. **Revista Brasileira de Ciências do Envelhecimento Humano**, v. 5, n. 1, p. 80-89, 2008.

SEGARRA, A. B. et al. Brain asymmetry and dopamine: beyond motor implications in Parkinson's disease and experimental hemiparkinsonism. **Revista de Neurologia**, v. 63, p. 415-421, 2016.

STROUWEN, C. et al. Are factors related to dual-task performance in people with Parkinson's disease dependent on the type of dual task? **Parkinsonism & Related Disorders**, v. 23, p. 23–30, 2016.

TAKAKUSAKI, K. et al. Role of basal ganglia-brainstem pathways in the control of motor behaviors. **Neuroscience Research**, v. 50, n. 2, p. 137-151, 2004.

TOMBU, M.; JOLICOEUR, P. A central capacity sharing model of dual-task performance. **Journal of Experimental Psychology: Human Perception and Performance**, v. 29, p. 3-18, 2003.
TYSNES, O. B.; STORSTEIN, A. Epidemiology of Parkinson's disease. **Journal of Neural Transmission**, v. 124, n. 8, p. 901–905, 2017.

VERREYT, N. et al. Cognitive differences between patients with left-sided and right-sided Parkinson's disease. A review. **Neuropsychology Review**, v. 21, n.4, p. 405-424. 2011.

VITECKOVA, S. et al. Gait symmetry measures:A review of current and prospective methods. **Biomedical Signal Processing and Control**, v. 42, p. 89-100, 2018.

UITTI, R. J. et al. Parkinson disease: handeness predicts asymmetry. **Neurology**, v. 64, p. 1925-1930, 2005.

WANG, J. et al. MRI evaluation of asymmetry of nigrostriatal damage in the early stage of early-onset Parkinson's disease. **Parkinsonism and Related Disorders**, v. 21, n. 6, p. 590-596, 2015.

WU, T.; HALLETT, M. Dual task interference in Parkinson's disease. **Touch Briefings**, p. 34–37, 2009.

WU, T.; HALLETT, M.; CHAN, P. Motor automaticity in Parkinson's disease. **Neurobiology of Disease**, v. 82, p. 226-234, 2015.

YAMADA, P. A. et al. Everyday tasks impair spatiotemporal variables of gait in olderadults with Parkinson's disease. **Human Movement Science**, v. 70, 102591.

YANG, B. et al. Feature extraction for EEG-based brain-computer interfaces by wavelet packet best basis decomposition. **Journal of Neural Engineering**, v. 3, n. 4, p. 251–6, 2006.

YANG, Y. R. et al. Relationships between gait and dynamic balance in early Parkinson's disease. **Gait and Posture**, v. 24, n. 4, p. 611-615, 2008.

YOGEV, G. et al. Gait asymmetry in patients with Parkinson's disease and elderly fallers: When does the bilateral coordination of gait require attention? **Experimental Brain Research**, v. 177, n. 3, p. 336-346, 2007.

CHAPTER 5

FINAL REMARKS

5.1 Final remarks

The thesis investigated asymmetry of gait in pwPD and analyzed the effect of PD on asymmetry of spatial-temporal parameters, intersegmental coordination and neural activity. Table 7 presents a synthesis of data from the current literature, highlighting the main findings of this thesis and offering recommendations for future studies.

We can draw some conclusions from the results obtained by the thesis:

a) Are individuals with PD always asymmetrical?

According to the studies included in the systematic review, gait is not always asymmetrical in individuals with Parkinson's disease (PD). However, the lack of standardization among these studies makes it difficult to identify the causes of the absence of asymmetry in gait. On the other hand, the meta-analysis carried out confirmed that the main variable for identifying gait asymmetry is swing time.

In all the three studies carried out in this thesis, it was found that the gait of pwPD showed asymmetrical characteristics when compared to the control group, both for spatial-temporal and cortical variables, and under the influence of a dual task. There is a gap in the literature regarding the asymmetrical manifestation of neural parameters in PD. This study contributes to the identification of this characteristic by showing that, even in the absence of a dual task, cortical activity was more asymmetrical in individuals with PD than in controls.

However, the addition of challenging activities in walking, such as obstacles and dual tasks, did not significantly increase asymmetry, contrary to initial expectations. Furthermore, performing the task of circumvention an obstacle on the most affected side by the disease did not worsen coordination deficits, although it did show greater asymmetry. This finding corroborates previous studies that have found no correlation between gait asymmetry and motor coordination (Plotnik; Giladi; Hausdorff, 2009).

b) Dual task as a model to study gait asymmetry in PD

The negative effects of a dual task (DT) on walking are widely reported in the literature. In people with Parkinson's disease (PD), DT is expected to intensify motor deficits due to competition for attentional resources. Previous studies have shown that DTs increase gait asymmetry in these individuals, worsen bilateral coordination between limbs and increase the risk of falls.

Unexpectedly, our findings did not confirm that increasing the level of difficulty intensified asymmetry. One possible bias identified was the lack of adequate leveling of difficulties according to individual abilities, which may have contributed to the lack of progression in asymmetry as the tasks became more complex. Even so, corroborating the literature, gait DTs proved to be good indicators of asymmetry between individuals with PD and their healthy peers.

c) Intersegmental coordination and gait asymmetry in gait of pwPD

Few studies have investigated the relationship between asymmetry and coordination in the gait of pwPD. Among the existing ones, two aspects stand out: gait was assessed in free walking situations, and the individuals had episodes of freezing. In these cases, greater asymmetry and worse bilateral coordination between the lower limbs were characteristics associated with more advanced stages of the disease and progressive gait impairment. However, the consensus on the relationship between asymmetry and coordination remains uncertain, suggesting that the mechanisms regulating these variables may be distinct.

Studies have often focused on bilateral coordination between lower limbs. However, the marked muscular rigidity in individuals with PD, especially axial rigidity, can compromise intersegmental coordination, which is relevant in contexts that simulate everyday challenges. For example, the task of circumvention an obstacle has been shown to be more challenging and potentially dangerous for the side most affected by the disease. This study found that people with PD had a lower coordination pattern compared to healthy individuals. Although the more impaired side intensified the asymmetry of spatial-temporal parameters, this asymmetry did not directly impact the coordination pattern. These findings corroborate previous studies which also failed to identify a clear relationship between worse bilateral coordination and increased symptoms of asymmetry during gait.

d) Limitations, future suggestions and practical applications

One limitation of this thesis was the inability to analyze gait asymmetry according to different phases of the gait cycle due to the lack of synchronization between the equipment used. To better understand the mechanisms underlying asymmetry, coordination, and cortical activity, examining each phase of the gait cycle could provide valuable insights.

Although the present study did not identify significant impairments caused by dual-tasking in gait asymmetry among individuals with PD, we recommend that future research investigates settings that simulate participants' daily lives. This would enable a more comprehensive understanding of how asymmetry impacts activities of daily living. Furthermore, we emphasize the importance of adjusting task difficulty levels to match each individual's cognitive abilities.

Finally, all three studies demonstrated the asymmetry-related deficits in individuals with PD compared to their healthy peers. We encourage health and rehabilitation professionals to focus on the challenges posed by asymmetry, developing strategies to mitigate its effects and improve the gait of these individuals.

Table 7. The table presents a synthesis of data from the current literature, highlighting the main findings of this thesis and offering recommendations for future studies.

Current literature	Main findings of the thesis	Future recommendations
• The motor symptoms of PD are asymmetrical (Sant et al., 2008; Hughes, et al., 2002), including walking (Plotnik et al., 2008). • Performing a DT compromises bilateral symmetry and coordination during walking in individuals with PD (Yogev et al., 2007). • No standardization of the type and difficulty of the task. • It is necessary to understand why the gait in PD asymmetrical and what factors may contribute to this.	**Study #1** • PwPD showed greater gait asymmetry in most spatial-temporal variables vs. NHI • Swing time asymmetry was most sensitive variable • Dopaminergic medication partly improved GA • Kinetic, EMG and brain activity parameters asymmetry need further studies • High variability in asymmetry measures across studies limited generalization **Study #2** • Side most affect by PD does not impairs the axial and lower limb coordination in a high extent during an obstacle circumvention. • A cognitive dual task minimally affected the coordination during OC. • PD and NHI present differences of axial and lower limbs intersegmental coordination. **Study #3** • The effects of task difficulty on asymmetry were exclusively in individuals with PD. • Individuals with PD exhibit greater asymmetry in spatial-temporal parameters and cortical activity compared to NHI. • Cognitive impairments on the errors of task were seeing since moderate task.	• GA in pwPD in free-living environments should be explored for future studies. • Define a measure that best represents gait asymmetry, due to the wide variety of indices. • To level the difficulty of the cognitive task for each participant in the study. •Verify the variables of spatial-temporal asymmetry, cortical activity and intersegmental coordination according to each phase of gait. • To check whether the strategies used to avoid an obstacle

REFERENCES

HUGHES, A. J. et al. The accuracy of diagnosis of parkinsonian syndromes in a specialist movement disorder service. **Brain**, v. 125, n. Pt 4, p. 861-70, 2002.

PLOTNIK, M.; GILADI, N.; HAUSDORFF, J. M. Bilateral coordination of walking and freezing of gait in Parkinson's disease. **The European Journal of Neuroscience**, v. 27, p. 1999–2006, 2008.

PLOTNIK, M.; GILADI, N.; HAUSDORFF, J. M. Bilateral coordination of gait and Parkinson's disease: the effects of dual tasking. **Journal of neurology, neurosurgery, and psychiatry**, v. 80, n. 3, p. 347–350, 2009.

SANT, C. R. et al. Abordagem fisioterapêutica na doença de Parkinson. **Revista Brasileira de Ciências do Envelhecimento Humano**, v. 5, n. 1, p. 80-89, 2008.

YOGEV, G. et al. Gait asymmetry in patients with Parkinson's disease and elderly fallers: When does the bilateral coordination of gait require attention? **Experimental Brain Research**, v. 177, n. 3, p. 336-346, 2007.

APPENDICES

APPENDIX A – Description of the terms used for paper searching in each database.

- PubMed

#1	(Parkin*[tw]) AND ((asymm*[tw]) OR symm*) AND ((((gait[tw]) OR walk*[tw]) OR locomotion[tw]) OR mobility[tw])

Note: tw = text words.

- Cochrane Library

#1	Parkin* AND (asymm* OR symm*) AND (gait OR walk* OR locomotion OR mobility)

- Lilacs

#1	(Parkin*) AND (asymm*) OR (symm*) AND (gait) OR (walk*) OR (locomotion) OR (mobility)

- SCOPUS – Science Direct

#1	Parkinson AND asymmetry (gait OR walk OR mobility OR locomotion)

- PEDro

#1	Parkin* asymm* gait
#2	Parkin* asymm* walk*
#3	Parkin* asymm* locomotion
#4	Parkin* asymm* mobility

APPENDIX B – Questions of appraisal tool adapted from Galna et al. (2015).

Question		Scoring criteria
1. Research aims or questions stated clearly		1 - Yes; 0,5 – yes, lacking detail or clarity; 0 – no
2. Participants detailed	Age	1 – Yes; 0 – No
	Sex	1 – Yes; 0 – No
	Height	1 – Yes; 0 – No
	Disease stage	1 – Yes; 0 – No
	UPDRS - Part III	1 – Yes; 0 – No
	Subtotal (average)	
3. Recruitment and sampling methods described		1 - Yes; 0.5 – yes, lacking detail or clarity; 0 – no
4. Inclusion and exclusion criteria detailed		1 - Yes; 0.5 – yes, lacking detail or clarity; 0 – no
5. Controlled co-variates	Medication status	1 – Yes; 0 – No
	Time of diagnosis	1 – Yes; 0 – No
	Disease stage	1 – Yes; 0 – No
	Walking Speed	1 – Yes; 0 – No
	Freezing of gait	1 – Yes; 0 – No
	Subtotal (average)	
6. Key outcome variables clearly described		1 – Yes; 0.5 – only some defined; 0.5 – yes, lacking detail or clarity; 0 – no
7. Adequate methodology able to repeat study	Participant sampling	1 – Yes; 0 – No
	Equipment	1 – Yes; 0 – No
	Procedure	1 – Yes; 0 – No
	Data processing	1 – Yes; 0 – No
	Statistical analysis	1 – Yes; 0 – No
	Subtotal (average)	
8. Methodology able to answer research question	Participant sampling	1 – Yes; 0 – No
	Equipment	1 – Yes; 0 – No
	Procedure	1 – Yes; 0 – No
	Data processing	1 – Yes; 0 – No
	Statistical analysis	1 – Yes; 0 – No
	Subtotal (average)	
9. Reliability of the methodology stated		1 – Yes; 0 – No
10. Internal validity of the methodology stated		1 – Yes; 0 – No
11. Research questions answered adequately in the discussion		1 – Yes; 0 – No
12. Key findings supported by the results		1 – Yes; 0 – No
13. Key findings interpreted in a logical manner which is supported by references		1 – Yes; 0 – No
14. Clinical implications stated		1 – Yes; 0.5 – yes, lacking detail or clarity; 0 - No

APPENDIX C – Table with basic information about the studies included at systematic review.

Authors (year)	Country*	Title	Journal
(Bailo *et al.*, 2024)	Italy	Characterization of walking in mild Parkinson's disease: Reliability, validity and discriminant ability of the six-minute walk test instrumented with a single inertial sensor	Sensors
(Baltadjieva *et al.*, 2006)	Israel	Marked alterations in the gait timing and rhythmicity of patients with de novo Parkinson's disease	European Journal of Neuroscience
(Barbieri *et al.*, 2018)	Brazil	Obstacle avoidance increases asymmetry of crossing step in individuals with Parkinson's disease and neurologically healthy individuals	Journal of Motor Behavior
(Barbosa *et al.*, 2024)	France	3D kinematics quantifies gait response to levodopa earlier and to a more comprehensive extent than the MDS-unified Parkinson's disease rating scale in patients with motor complications	Movement Disorders
(Brodie *et al.*, 2015)	Australia	Symmetry matched auditory cues improve gait steadiness in most people with Parkinson's disease but not in healthy older people	Journal of Parkinson's Disease
(Buckley *et al.*, 2019)	United Kingdom	Upper body accelerations as a biomarker of gait impairment in the early stages of Parkinson's disease	Gait & Posture
(Danoudis; Iansek; Simpson, 2012)	Australia	Freezing of gait in Parkinson's disease: Further insights into pathophysiological mechanisms	Parkinsonism & Related Disorders
(De Bartolo *et al.*, 2020)	Italy	Effect of different music genres on gait patterns in Parkinson's disease	Neurological Sciences
(Del Din; Godfrey; Rochester, 2016)	United Kingdom	Validation of an accelerometer to quantify a comprehensive battery of gait characteristics in healthy older adults and Parkinson's disease: Toward clinical and at home use	IEEE Journal of Biomedical and Health Informatics
(Del Din *et al.*, 2016)	United Kingdom	Free-living gait characteristics in ageing and Parkinson's disease: Impact of environment and ambulatory bout length	Journal of NeuroEngineering and Rehabilitation
(Djurić-Jovičić *et al.*, 2017)	Serbia	Selection of gait parameters for differential diagnostics of patients with de novo Parkinson's disease	Neurological Research
(Ferreira *et al.*, 2022)	Brazil	Machine learning models for Parkinson's disease detection and stage classification based on spatial-temporal gait parameters	Gait & Posture
(Fling; Curtze; Horak, 2018)	United States of America	Gait asymmetry in people with Parkinson's disease is linked to reduced integrity of callosal sensorimotor regions	Frontiers in Neurology

(Galna *et al.*, 2015)	United Kingdom	Progression of gait dysfunction in incident Parkinson's disease: Impact of medication and phenotype	Movement Disorders
(Grajić *et al.*, 2015)	Serbia	Gait in drug naïve patients with de novo Parkinson's disease--altered but symmetric	Neurological Research
(Gilmore *et al.*, 2019)	Canada	Forward and backward walking in Parkinson disease: A factor analysis	Gait & Posture
(Godi *et al.*, 2021)	Italy	A pathophysiological model of gait captures the details of the impairment of pace/rhythm, variability and asymmetry in Parkinsonian patients at distinct stages of the disease	Scientific Reports
(Hackney; Earhart, 2010)	United States of America	The effects of a secondary task on forward and backward walking in Parkinson's disease	Neurorehabilitation and Neural Repair
(Iosa *et al.*, 2016)	Italy	Loss of fractal gait harmony in Parkinson's Disease	Clinical Neurophysiology
(Keloth *et al.*, 2021)	Australia	Muscle activation strategies of people with early-stage Parkinson’s during walking	Journal of NeuroEngineering and Rehabilitation
(Kleiner *et al.*, 2018)	Italy	Analyzing gait variability and dual-task interference in patients with Parkinson’s disease and freezing by means of the word-color Stroop test	Aging Clinical and Experimental Research
(Koh *et al.*, 2019)	Republic of Korea	Influences of elbow, shoulder, trunk motion and temporospatial parameters on arm swing asymmetry of Parkinson's disease during walking	Human Movement Science
(Leavy *et al.*, 2018)	Sweden	Patient-reported and performance-based measures of walking in mild–moderate Parkinson's disease	Brain and Behavior
(Lee *et al.*, 2020)	Republic of Korea	Gait characteristics under imposed challenge speed conditions in patients with Parkinson’s disease during overground walking	Sensors
(Lencioni *et al.*, 2021)	Italy	Strategies for maintaining dynamic balance in persons with neurological disorders during overground walking	Journal of Engineering in Medicine
(Liu *et al.*, 2022)	China	Quantitative assessment of gait characteristics in patients with Parkinson's disease using 2D video	Parkinsonism and Related Disorders
(Martínez *et al.*, 2018)	Spain	Kinematic and kinetic patterns related to free-walking in Parkinson’s disease	Sensors
(Miller *et al.*, 1996)	United States of America	Components of EMG symmetry and variability in parkinsonian and healthy elderly gait	Electroencephalography and Clinical Neurophysiology

(Morris *et al.*, 2017)	United Kingdom	Gait rather than cognition predicts decline in specific cognitive domains in early Parkinson's disease	Journals of Gerontology: Medical Sciences
(Morris *et al.*, 2017)	United Kingdom	A model of free-living gait: A factor analysis in Parkinson's disease	Gait & Posture
(Nanhoe-Mahabier *et al.*, 2011)	Netherlands	Walking patterns in Parkinson's disease with and without freezing of gait	Neuroscience
(Pereira *et al.*, 2019)	Brazil	The effects of habitual footwear in gait outcomes in people with Parkinson’s disease	Gait & Posture
(Plotnik; Giladi; Hausdorff, 2007)	Israel	A new measure for quantifying the bilateral coordination of human gait: Effects of aging and Parkinson's disease	Experimental Brain Research
(Ren *et al.*, 2015)	United States of America	Veering in hemi-Parkinson's disease: Primacy of visual over motor contributions	Vision Research
(Seuthe *et al.*, 2024)	Germany	Gait asymmetry and symptom laterality in Parkinson’s disease: two of a kind?	Journal of Neurology
(Vervoort *et al.*, 2015)	Belgium	Distal motor deficit contributions to postural instability and gait disorder in Parkinson's disease	Behavioural Brain Research
(Vervoort, G *et al.*, 2016)	Belgium	Dual-task-related neural connectivity changes in patients with Parkinson' disease	Neuroscience
(Wu *et al.*, 2021)	China	Mild gait impairment and its potential diagnostic value in patients with early-stage Parkinson's disease	Behavioural Neurology
(Yogev *et al.*, 2007)	Israel	Gait asymmetry in patients with Parkinson's disease and elderly fallers: when does bilateral coordination of gait require attention?	Experimental Brain Research

*based on the information provided by the corresponding author.

APPENDIX D – Methodological quality appraisal results. Each question is the average of the evaluation of three authors. The last column presents the total score for each paper. The last line presents the average for each question.

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Total score
Bailo et al. (2024)	1	0.8	1	1	0	1	1	1	1	1	1	1	1	1	12.8
Baltadjieva et al. (2006)	1	0.8	1	1	0	1	1	1	0	0	1	1	1	0.5	10.3
Barbieri et al. (2018a)	1	0.8	1	1	0	1	0.9	1	0	0	1	1	1	0	9.7
Barbosa et al. (2024)	1	0.8	0.75	0.75	0	0.75	0.9	0.9	0	0	1	1	1	1	9.9
Brodie et al. (2015)	1	0.8	0.25	0.5	0	1	0.9	0.9	0	0	1	1	0.5	0.75	8.6
Buckley et al. (2019)	1	0.9	1	1	0	0.75	0.8	1	0	0	1	1	1	0.75	10.2
Danoudis et al. (2012)	1	0.9	0.5	0.75	0	1	0.7	0.9	0	0	0.5	1	0.5	0.25	8.0
De Bartolo et al. (2020)	1	0.6	0.25	0.75	0	1	1	1	0	0	1	1	1	1	9.6
Del Din et al. (2016)	1	0.9	1	0.5	0	1	0.9	1	0	1	1	1	1	1	11.3
Del Din et al. (2016)	1	0.9	1	0.5	0	1	0.9	1	0	0.5	1	1	1	0.75	10.5
Djurić-Jovičić et al. (2017)	1	0.8	0.75	0.5	0	1	0.9	1	0	0	1	1	1	1	9.9
Ferreira et al. (2022)	1	1	0.5	1	0	1	1	1	1	0	1	1	1	1	11.5
Fling, Curtze, Horak (2018)	1	0.8	0.25	0	0	0.75	0.8	0.8	0	0	1	1	1	0	7.4
Galna et al. (2015)	1	0.8	1	1	0	0.75	1	1	0	0	0.5	1	1	0	9.1
Grajić et al. (2015)	1	0.8	1	0.5	0	0.5	0.8	0.8	0	0	0.5	0.5	0.5	0	6.9
Gilmore et al. (2019)	1	0.7	1	0.5	0	1	0.9	0.8	0	0	1	1	0.5	1	9.4
Godi et al. (2021)	1	0.6	1	1	0	1	1	1	1	1	1	1	1	1	12.6
Hackney, Earhart (2010)	1	0.8	1	0.75	0	1	0.9	1	0	0	0	1	1	1	9.5
Iosa et al. (2016)	1	0.8	0.5	0.25	0	1	0.9	0.9	0	0	1	1	1	0.5	8.9
Keloth et al. (2021)	1	1	1	0.75	0	1	1	1	0	0	1	1	1	0.5	10.3
Kleiner et al. (2018)	1	0.9	0.75	1	0	1	1	0.9	0	0	0.5	1	0	0.5	8.6
Koh et al. (2019)	1	1	1	1	0.2	0.5	0.7	0.9	0	0	1	0.5	0.5	0.25	8.6
Leavy et al. (2018)	1	0.8	1	0.75	0	1	1	1	0	0	0.5	1	1	1	10.1
Lee et al. (2020)	1	1	1	1	0	1	1	1	1	0	1	1	1	1	12.0
Lencioni et al. (2021)	1	0.8	0.25	0.75	0	1	1	1	0	0	1	1	1	1	9.8
Liu et al. (2022)	1	1	0.5	1	0	1	1	1	0	1	1	1	1	0.75	11.3
Martínez et al. (2018)	1	0.9	1	0.5	0	1	1	1	1	1	1	1	1	1	12.4
Miller et al. (1996)	1	0.4	0.5	0.75	0	1	0.9	0.9	0	0	1	1	0	0	7.5
Morris et al. (2017a)	1	1	1	1	0	1	1	1	1	1	1	1	1	1	13.0
Morris et al. (2017b)	1	0.6	0.75	1	0	0.75	0.9	1	0	1	0.5	1	1	1	10.5
Nanhoe-Mahabier et al. (2011)	1	0.8	0.75	0.75	0.2	1	1	1	0	0	0.5	1	1	1	10.0
Pereira et al. (2019)	1	0.4	0.5	1	0	1	0.7	0.9	0	0	1	1	1	1	9.5
Plotnik et al. (2007)	1	0.8	1	1	0	1	0.9	0.9	0	0	1	1	1	1	10.6
Ren et al. (2015)	1	0.8	1	1	0	1	1	1	0	0	1	1	1	0.5	10.3
Seuthe et al. (2024)	1	0.8	0.25	1	0	1	1	1	0	0	1	1	1	1	10.1
Vervoort et al. (2015)	1	0.7	1	1	0	0.75	1	1	0.5	0.5	1	1	1	0.25	10.7
Vervoort et al. (2016)	1	0.8	0.5	1	0	1	1	1	0	0	1	1	1	0.5	9.8
Wu et al. (2021)	1	1	1	1	0	1	0.9	0.9	0	0	1	1	1	1	10.8
Yogev et al. (2007)	1	0.7	1	1	0	1	0.9	0.9	0	0	1	1	1	0.5	10.0
Means by item	**1**	**0.81**	**0.78**	**0.81**	**0.01**	**0.94**	**0.93**	**0.96**	**0.15**	**0.21**	**0.88**	**0.97**	**0.88**	**0.70**	**10.0**

APPENDIX E – Equations, indexes, and other methods employed to calculate asymmetry during gait

Authors	Method to calculate GA
Bailo et al. (2024)	**Harmonic Ratio (HR)** - Ratio between the sum of the amplitudes of the in-phase harmonics and the sum of the amplitudes of the out-of-phase harmonics; **Improved HR** - Ratio between the power of the in-phase harmonics and the sum of in-phase and out-of phase harmonics power.
Baltadjieva et al. (2006)	**Gait asymmetry** = 100 x |ln(SSWT/LSWT)|
Barbieri et al. (2018)	**Symmetric index** = $\frac{\text{(value of LAL - value of MAL)}}{\text{(value of LAL + value of MAL)}}$ x 100%
Barbosa et al. (2024)	**Asymmetry index** = (right side - left side)/(rigth side + left side)
Brodie et al. (2015)	**Mean asymmetry (MA)** **Absolute paired-step asymmetry (AA)**
Buckley et al. (2019)	**Spatiotemporal asymmetry -** (Step time asymmetry, Swing time asymmetry, Stance time asymmetry) - Lord, Galna, Rochester (2013) **Upper body acceleration symmetry** - Autocorrelation symmetry (Auto sym) and HR.
Danoudis, Iansek & Simpson (2012)	**Asymmetry =** |right measure - left measure|
De Bartolo et al. (2020)	**Symmetry index =** the percentage of overlapping between curve accelerations of right and left step
Del Din et al. (2016)	**Asymmetry =** | Average left (steps) - Average right (steps) |
Del Din, Godfrey & Rochester (2016)	**Asymmetry =** |Average left - Average right|

Djurić-Jovičić et al. (2017)	**Step time asymmetry** = left step time - right step **Stride time asymmetry =** left stride time - right stride time **Step length asymmetry** = right step length - left step length
Ferreira et al. (2022)	**Symmetric index** = $\frac{\text{(value of LAL - value of MAL)}}{\text{(value of LAL + value of MAL)}} \times 100\%$
Fling, Curtze & Horak (2018)	**Asymmetry** = |1 - left/right| x 100
Galna et al. (2015)	**Asymmetry =** |right measure - left measure|
Gilmore et al. (2019)	Extracted from the "PKMAS" Software
Godi et al. (2021)	**Asymmetry** = |ln(left/right)| x 100
Grajić et al. (2015)	**Asymmetry = statistical comparison considering:** Body sides: left leg X right leg Side of PD-onset: leg of the side of disease onset X contralateral leg
Hackney & Earhart (2010)	**Gait asymmetry =** 100 x |ln(SSWT/LSWT)|
Iosa et al. (2016)	**Symmetry ratio index** = ratio between longer step and shorter step within 1 stride; **Gai asymmetry index** = |ln (shorter swing time/longer swing time)|
Keloth et al. (2021)	**Asymmetry index** = 100 - ([higher value of sEMG RMS/lower value of sEMG RMS] x 100)

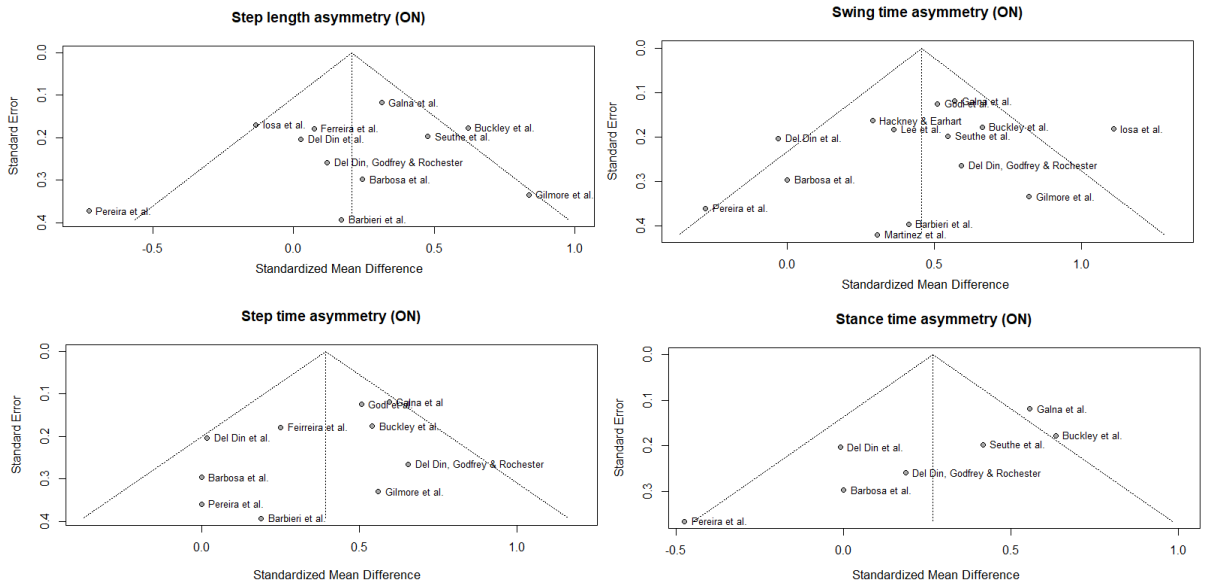
Kleiner et al. (2018)	**Step length asymmetry** = ([máx amplitude - min amplitude]/max amplitude) x 100%
Koh et al. (2019)	**Symmetry angle** = 100% x ((45° - arctan (small side / large side))/ 90°)
Leavy et al. (2018)	Based in Lord, Galna, Verghese et al. (2013)
Lee et al. (2020)	**Gait asymmetry =** 100 x |ln(SSWT/LSWT)|
Lencioni et al. (2021)	**Asymmetry: statistical comparison considering:** Lower limb (LL) as repeated measure factor (More/Less Affected and Non-Dominant/Dominant)
Liu et al. (2022)	**Symmetry angle** = 100% x ((45° - arctan (greater side/lesser side))/ 90°) Did not mention the step length asymmetry index
Martínez et al. (2018)	**Gait asymmetry** = 100 x |ln(SSWT/LSWT)|
Miller et al. (1996)	**Symmetry magnitude (Sm) and Symmetry phase (Sp) -** The bilateral symmetry for each muscle was computed from the LCEAs
Morris et al. (2017a)	Based in Lord, Galna, Verghese et al. (2013)
Morris et al. (2017b)	**Asymmetry** = |average left - average right|
Nanhoe-Mahabier et al. (2011)	**Step length asymmetry** = ([max amplitude - min amplitude]/max amplitude) x 100% **Step time asymmetry** = ([max time - min time]/max time) x 100%

Pereira et al. (2019)	Extracted from the "GAITRite" Software
Plotnik, Gilardi & Hausdorff (2007)	**Gait asymmetry** = 100 x |ln(SSWT/LSWT)|
Ren et al. (2015)	**Step asymmetry =** difference in the average stride lengths between the left and right legs
Seuthe et al. (2024)	**Asymmetry index** = (right side - left side)/(rigth side + left side)
Vervoort et al. (2015)	Based in Lord, Galna, Verghese et al. (2013)
Vervoort et al. (2016)	**Asymmetry** was calculated between the dominant (D) and non-dominant (ND) leg
Wu et al. (2021)	$\%AI = \frac{\max(\text{Left side value, Right side value}) - \min(\text{Left side value, Right side value})}{\max(\text{Left side value, Right side value})} \times 100$
Yogev et al., 2007	**Gait asymmetry =** 100 x |ln(SSWT/LSWT)|

SSWT: short swing time; LSWT: long swing time; LAL: least affected limb; MAL: most affected limb; EMG: eletromyography; RMS: root mean square; max: maximum; min: minimum.

Lord S, Galna B, Rochester L. Moving forward on gait measurement: toward a more refined approach. Mov Disord. 2013;28:1534–1543.
Lord S, Galna B, Verghese J, Coleman S, Burn D, Rochester L. Independent domains of gait in older adults and associated motor and nonmotor attributes: validation of a factor analysis approach. J Gerontol A Biol Sci Med Sci. 2013;68(7):820-827.

APPENDIX F – Funnel plots of step length asymmetry, swing time asymmetry, step time asymmetry and stance time asymmetry for the comparison between pwPD at ON state vs. NHI.



APPENDIX G – Asymmetric spatial-temporal parameters of PG compared to CG during the approach and circumvention phases to the more and less affected side during the obstacle circumvention with and without a dual task.

	OC				OC + DT				Main effects			Interaction effects			
Approach phase	**MORE AFFECTED SIDE**		**LESS AFFECTED SIDE**		**MORE AFFECTED SIDE**		**LESS AFFECTED SIDE**		Group (G)	Task (T)	Side (S)	G x T	G x S	T x S	G x T x S
	PG	**CG**	**PG**	**CG**	**PG**	**CG**	**PG**	**CG**							
SL asym	3.95 ± 4.50	3.58 ± 2.96	3.36 ± 3.75	4.08 ± 3.29	4.84 ± 7.22$^{*\#}$	2.35 ± 2.26	5.94 ± 5.78$^{*\#}$	2.78 ± 1.52	*ns*	*ns*	*ns*	$F_{1,30}$= 4.427, p=0.044, n^2=0.129	*ns*	*ns*	*ns*
SW asym	16.64 ± 16.34	17.29 ± 15.17	16.35 ± 15.62	18.41 ± 15.13	11.90 ± 12.64	11.14 ± 13.42	12.38 ± 8.22	17.12 ± 15.38	*ns*	*ns*	*ns*	*ns*	*ns*	*ns*	*ns*
ST asym	1.50 ± 1.21*	1.37 ± 1.42	2.22 ± 3.27*	0.92 ± 0.78	2.16 ± 1.64*	1.15 ± 0.84	2.26 ± 2.64*	0.98 ± 0.90	$F_{1,30}$= 4.843, p=0.036, n^2=0.139	*ns*	*ns*	*ns*	*ns*	*ns*	*ns*
SS asym	5.36 ± 8.21$^{£}$	3.15 ± 2.18$^{£}$	7.48 ± 7.03$^{£}$	4.62 ± 2.69$^{£}$	4.60 ± 6.18	2.42 ± 1.74	5.95 ± 6.34	2.61 ± 1.36	*ns*	$F_{1,30}$= 4.735, p=0.038, n^2=0.136	*ns*	*ns*	*ns*	*ns*	*ns*
DS asym	4.33 ± 4.64	2.64 ± 2.54	6.15 ± 5.31	5.06 ± 3.84	4.63 ± 3.02	3.73 ± 3.00	4.59 ± 5.50	3.12 ± 2.28	*ns*	*ns*	*ns*	*ns*	*ns*	*ns*	*ns*
Circumvention phase	**PG**	**CG**	**PG**	**CG**	**PG**	**CG**	**PG**	**CG**							
SL asym	2.63 ± 3.14	3.36 ± 3.89	3.18 ± 4.42	3.10 ± 1.42	5.16 ± 5.63$^{*\#}$	2.88 ± 2.77	4.64 ± 5.10$^{*\#}$	2.04 ± 1.86	*ns*	*ns*	*ns*	$F_{1,31}$= 9.982, p=0.004, n^2=0.244	*ns*	*ns*	*ns*
SW asym	10.51 ± 11.93	10.33 ± 9.88	14.26 ± 12.97	9.31 ± 13.89	11.74 ± 10.55	13.25 ± 16.96	17.64 ± 15.31	7.05 ± 6.79	*ns*	*ns*	*ns*	*ns*	*ns*	*ns*	*ns*
ST asym	1.79 ± 1.28*	1.18 ± 1.48	2.35 ± 2.38*	1.17 ± 0.84	1.98 ± 1.73*	1.14 ± 0.76	2.86 ± 2.57*	1.64 ± 1.54	$F_{1,31}$= 7.544, p=0.010, n^2=0.196	*ns*	*ns*	*ns*	*ns*	*ns*	*ns*
SS asym	3.10 ± 2.60$^{\$}$	3.84 ± 3.91$^{\$}$	5.33 ± 5.86$^{\$}$	3.84 ± 1.73$^{\$}$	4.44 ± 5.03*	2.70 ± 1.89	4.99 ± 5.09*	2.16 ± 1.83	*ns*	*ns*	*ns*	$F_{1,31}$= 6.547, p=0.016, n^2=0.174	*ns*	*ns*	*ns*
DS asym	7.41 ± 5.10$^{*£}$	3.56 ± 2.86$^{£}$	7.89 ± 6.68$^{*£}$	4.58 ± 3.74$^{£}$	5.65 ± 4.30*	3.01 ± 2.41	5.77 ± 6.54*	3.72 ± 3.17	$F_{1,31}$= 6.076, p=0.019, n^2=0.164	$F_{1,31}$= 4.577, p=0.04, n^2=0.129	*ns*	*ns*	*ns*	*ns*	*ns*

SL: step length; SW: step width; ST: step time; SS: step speed; DS: double support time; asym: asymmetry; PG: Parkinson's disease group; CG: control group; * GP > GC; $^{£}$ OC > OC + DT; $^{\#}$ GP = OC + DT > OC; $^{\$}$ GC = OC > OC+DT.

ANEXXES

ANNEX I – ETHICS COMMITTEE APPROVAL

UNESP - FACULDADE DE CIÊNCIAS CAMPUS BAURU - JÚLIO DE MESQUITA FILHO

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: EFEITO DA MEDICAÇÃO, TAREFA DUPLA E ASSIMETRIA NO COMPORTAMENTO DA ATIVIDADE DO CÓRTEX CEREBRAL DURANTE A LOCOMOÇÃO EM IDOSOS COM DOENÇA DE PARKINSON

Pesquisador: Fabio Augusto Barbieri

Área Temática:

Versão: 1

CAAE: 78660517.2.0000.5398

Instituição Proponente: UNIVERSIDADE ESTADUAL PAULISTA JULIO DE MESQUITA FILHO

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 2.422.821

Apresentação do Projeto:

O Projeto abarca três estudos sobre a locomoção em idosos com Doença de Parkinson (DP), para compreensão do efeito da medicação utilizada por tal população,realização de tarefa dupla ao andar e assimetria no comportamento da atividade do córtex durante a locomoção.

Objetivo da Pesquisa:

Compreensão de fatores que possam dificultar ou facilitar a atividade de locomoção de pessoas com Doença de Parkinson; compreender atividade cerebral e efeitos de medicamento e da assimetria na locomoção e na realização de tarefa concomitante.

Avaliação dos Riscos e Benefícios:

Há riscos de queda, mas a equipe prevê tais riscos e planeja acompanhar a atividade, com profissional próximo ao participante. Os achados dos estudos poderão contribuir de forma significativa para a população com DP, na medida em que puder favorecer a locomoção e a segurança ao mover-se.

Comentários e Considerações sobre a Pesquisa:

Pesquisa relevante, com projeto consistente e bem elaborado, que poderá melhorar a qualidade de vida de pessoas com DP.

Endereço: Av. Luiz Edmundo Carrijo Coube, nº 14-01
Bairro: CENTRO **CEP:** 17.033-360
UF: SP **Município:** BAURU
Telefone: (14)3103-9400 **Fax:** (14)3103-9400 **E-mail:** cepesquisa@fc.unesp.br

UNESP - FACULDADE DE CIÊNCIAS CAMPUS BAURU - JÚLIO DE MESQUITA FILHO

Continuação do Parecer: 2.422.821

Considerações sobre os Termos de apresentação obrigatória:

Termos bem elaborados e de acordo com a resolução 466.

Recomendações:

Orientar o participante e o cuidador sobre horários de início e de término de cada etapa do estudo e avaliar com os mesmos as necessidades relacionadas à permanência no laboratório para estudo. Aqueles cujo efeito da medicação será analisada precisam ser informados sobre horário e administração do remédio no dia de pesquisa.

Conclusões ou Pendências e Lista de Inadequações:

Estudo adequado e cuidadoso, que poderá ser aperfeiçoado se observadas as recomendações.

Considerações Finais a critério do CEP:

Projeto considerado aprovado por estar em conformidade com os parâmetros legais, metodológicos e éticos analisados pelo colegiado.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1000636.pdf	03/10/2017 10:10:19		Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE03_Is.doc	03/10/2017 10:07:57	Fabio Augusto Barbieri	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE02_Is.doc	03/10/2017 10:07:45	Fabio Augusto Barbieri	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE01_Is.doc	03/10/2017 10:07:32	Fabio Augusto Barbieri	Aceito
Projeto Detalhado / Brochura Investigador	Projeto_detalhado.docx	02/10/2017 17:46:17	Fabio Augusto Barbieri	Aceito
Folha de Rosto	folha_de_rosto.pdf	02/10/2017 17:45:34	Fabio Augusto Barbieri	Aceito

Situação do Parecer:

Aprovado

Endereço: Av. Luiz Edmundo Carrijo Coube, nº 14-01
Bairro: CENTRO **CEP:** 17.033-360
UF: SP **Município:** BAURU
Telefone: (14)3103-9400 **Fax:** (14)3103-9400 **E-mail:** cepesquisa@fc.unesp.br

UNESP - FACULDADE DE CIÊNCIAS CAMPUS BAURU - JÚLIO DE MESQUITA FILHO

Continuação do Parecer: 2.422.821

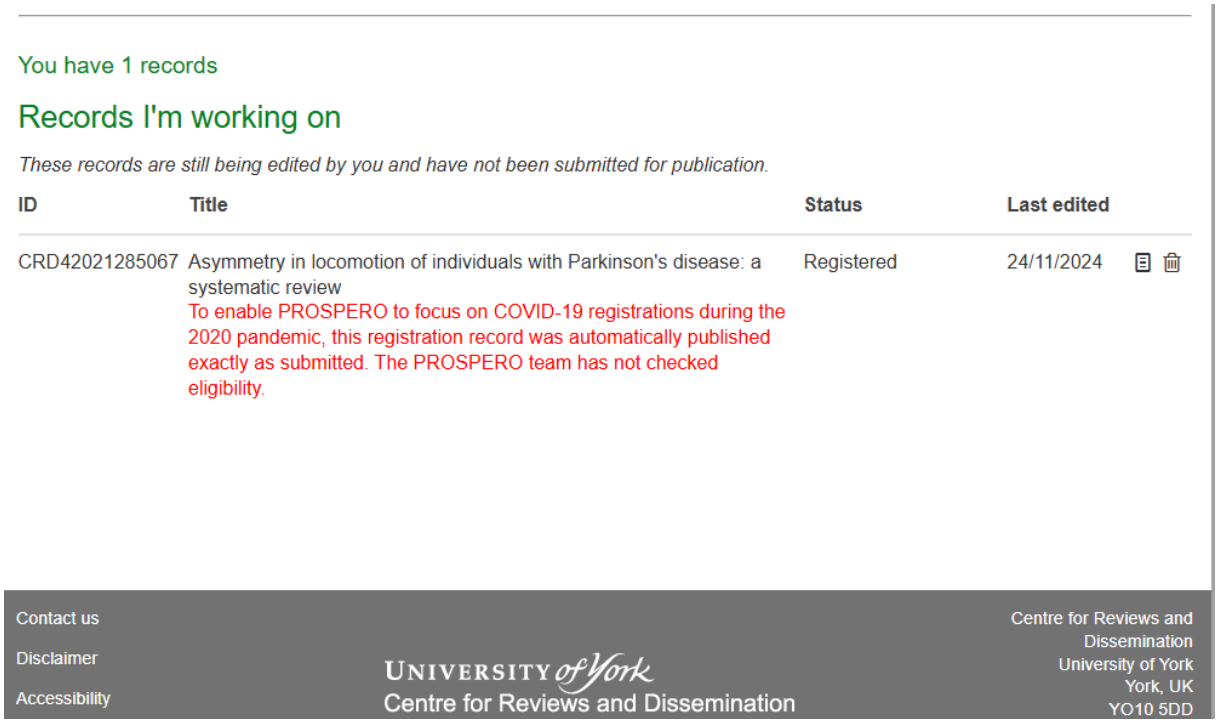
Necessita Apreciação da CONEP:
Não

BAURU, 07 de Dezembro de 2017

Assinado por:
Mário Lázaro Camargo
(Coordenador)

Endereço: Av. Luiz Edmundo Carrijo Coube, nº 14-01
Bairro: CENTRO **CEP:** 17.033-360
UF: SP **Município:** BAURU
Telefone: (14)3103-9400 **Fax:** (14)3103-9400 **E-mail:** cepesquisa@fc.unesp.br

ANNEX II – PROSPERO REGISTRATION NUMBER



You have 1 records

Records I'm working on

These records are still being edited by you and have not been submitted for publication.

ID	Title	Status	Last edited
CRD42021285067	Asymmetry in locomotion of individuals with Parkinson's disease: a systematic review To enable PROSPERO to focus on COVID-19 registrations during the 2020 pandemic, this registration record was automatically published exactly as submitted. The PROSPERO team has not checked eligibility.	Registered	24/11/2024

Contact us
Disclaimer
Accessibility

UNIVERSITY of York
Centre for Reviews and Dissemination

Centre for Reviews and Dissemination
University of York
York, UK
YO10 5DD