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São Paulo State University
“Júlio de Mesquita Filho”

Post Graduate Program in Human Movement Sciences – Interunit

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The effect of transcranial direct current stimulation and physical exercise on interlimb coordination during walking in people with Parkinson’s disease

Thesis submitted to the post Graduate Program in Human Movement Sciences – Interunit, Bauru Campus, São Paulo State University “Júlio de Mesquita Filho,” as part of the requirements for obtaining the Phd degree.

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Supervisor: Prof. Dr. Fabio Augusto Barbieri

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Bauru

2024

Z26e

Zampier, Vinicius Cavassano.
The effect of transcranial direct current stimulation and physical exercise on interlimb coordination during walking in people with Parkinson’s disease / Vinicius Cavassano zampier. -- Bauru, 2024 93 p. : il., tabs.

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

1. Desordens do movimento. 2. Estimulação transcraniana elétrica. 3. Coordenação intermembros. 4. EEG. 5. Intervenção. I. Título. Título.

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

ATA DA DEFESA PÚBLICA DA TESE DE DOUTORADO DE VINICIUS CAVASSANO ZAMPIER, DISCENTE DO PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DO MOVIMENTO, DA FACULDADE DE CIÊNCIAS - CÂMPUS DE BAURU.

Aos 17 dias do mês de dezembro do ano de 2024, às 14h, por meio de Videoconferência, realizou-se a defesa de TESE DE DOUTORADO de VINICIUS CAVASSANO ZAMPIER, intitulada **The effect of transcranial direct current stimulation and physical exercise on interlimb coordination during walking in 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, Prof. Dr. LUIS MOCHIZUKI (Participação Virtual) do(a) Escola de Artes, Ciências e Humanidades / Universidade de São Paulo - SP, Prof. Dr. ALEXANDRE HIDEKI OKANO (Participação Virtual) do(a) Centro de Matemática, Computação e Cognição / Universidade Federal do ABC - Santo André/SP, Dr. DIEGO ORCIOLI DA SILVA (Participação Virtual) do(a) Educação física / Universidade Estadual Paulista Júlio de Mesquita Filho Instituto de Biociências de Rio Claro, Prof. Dr. PAULO ROBERTO PEREIRA SANTIAGO (Participação Virtual) do(a) Escola de Educação Física e Esporte de Ribeirão Preto (Eeferp) / USP. Após a exposição pelo doutorando e arguição pelos membros da Comissão Examinadora que participaram do ato, de forma
presencial e/ou virtual, o discente recebeu o conceito final:_A_P_R_O_VA_ D_O_. 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

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Dedico este trabalho ao meu pai Pedro, a minha mãe Mara, ao meu irmão João Vitor, a minha namorada Gabriela e a minha mentora Lilian.

Agradecimentos

Gostaria de iniciar esta seção agradecendo aos meus pais Pedro e Mara, pelo apoio incondicional durante toda a minha trajetória acadêmica. Não tenho palavras para descrever a felicidade de poder compartilhar os momentos felizes com vocês e a gratidão pelo apoio em momentos difíceis. Esse título também é de vocês. Agradeço ao meu irmão João Vitor e a minha cunhada Julian pelo companheirismo durante todo esse tempo.

À minha namorada Gabriela por estar ao meu lado e me apoiar em todos os momentos. Eu sempre soube que poderia contar com você, eu te agradeço pelo companheirismo, compreensão, amor e paciência durante todos esses anos. Estar com você me trouxe felicidade e força para concluir essa etapa. Eu te amo muito!

À minha mentora Lilian Gobbi (*in memorian*) por todos os ensinamentos ao longo de toda a minha trajetória acadêmica. Foi uma honra ser o aluno dessa mulher incrível e a sua partida foi um dos momentos mais difíceis da minha vida. Levarei para sempre seus ensinamentos.

Ao meu orientador e amigo Fabio Barbieri. É uma honra ser seu aluno e poder aprender com você. Eu agradeço por se dispor a me ajudar em um momento difícil e por todas as oportunidades que você me proporcionou ao longo dos anos. Tenho muito orgulho de ter feito parte da equipe do Laboratório de Pesquisa em Movimento Humano (MOVI-LAB). Muito obrigado por tudo. Ao meu coorientador Anderson Oliveira. Eu agradeço a paciência e disponibilidade para me ensinar a realizar procedimentos extremamente relevantes para o desenvolvimento da minha tese. Agradeço por ter me recebido tão bem no seu grupo de pesquisa e pela parceria todos esses anos.

Aos meus amigos e colegas de laboratório do LEPLO, MOVI-LAB e do Departamento de Materiais e Produção da Universidade Aalborg na Dinamarca. Muito obrigado pelo companheirismo, pelas risadas e pela ajuda durante todos esses anos. Vou levar cada um de vocês no meu coração para sempre.

À Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES; Código de Financiamento 88887.598229/2021-00), pelo apoio financeiro, na forma de bolsa de estudo, para a realização desta tese e, também, por conceder uma bolsa de estudo para realização do Doutorado Sanduíche no Exterior, na Universidade de Aalborg, Dinamarca (processo: 88887.839166/2023-00).

Resumo

A estimulação transcraniana por corrente contínua (ETCC) e o exercício físico são terapias eficazes para melhorar a coordenação de movimentos e os parâmetros do andar em pessoas com doença de Parkinson (DP), geralmente acompanhadas por mudanças na atividade cortical. Contudo, a variabilidade nos protocolos de ETCC gera dúvidas sobre quais parâmetros são eficazes, e pouco se sabe sobre os efeitos da combinação de ETCC e exercício na locomoção e na atividade cortical em DP. Esta tese investigou essas lacunas em três estudos. O Estudo #1 sintetizou achados de estudos sobre protocolos de ETCC para melhorar a coordenação motora em parkinsonianos e idosos saudáveis por meio de uma revisão sistemática nas bases PubMed, Embase e Web of Science. O Estudo #2 investigou os efeitos agudos, e o Estudo #3 os efeitos crônicos, de um protocolo combinado de ETCC e exercício locomotor na coordenação intermembros, parâmetros do andar e atividade cortical de 22 indivíduos com DP. No protocolo de ETCC, o ânodo foi posicionado sobre o córtex motor contralateral ao lado mais afetado pela DP e o catodo na área supraorbital contralateral. A corrente elétrica de 2 mA foi aplicada por 20 minutos (ativo) ou 10 segundos (sham), concomitantemente ao exercício (20 minutos). No protocolo de exercício, os participantes percorreram um circuito de 18 m em duas condições: i) andar aumentando amplitude dos braços (10 min); ii) andar aumentando velocidade dos braços (10 min). No Estudo #2, os participantes realizaram ambas as condições de estimulação com sete dias de intervalo, sendo avaliados antes e após cada sessão. No Estudo #3, 22 participantes foram divididos em dois grupos (ativo, n = 12; sham, n = 10) e realizaram seis sessões em dias alternados. As avaliações ocorreram antes da primeira sessão, 48 horas após e 30 dias após a última sessão. O andar foi avaliado com o sistema GaitRite posicionado em uma passarela de 8 m. A coordenação intermembros foi analisada via fase relativa contínua entre sinais de acelerômetros nos punhos e tornozelos contralaterais. A atividade cortical foi analisada por EEG de 64 canais, considerando a densidade do poder espectral (alpha, beta e gamma) nos canais Fz, F3, F4, Cz, C3, C4, Pz, P3 e P4. O Estudo #1 mostrou que a ETCC melhora a coordenação motora, especialmente com protocolos de 20 min e 2 mA. O Estudo #2 revelou que uma sessão de ETCC combinada com exercício não potencializou os efeitos do exercício. O Estudo #3 mostrou que seis sessões potencializaram os efeitos do exercício, com menor variabilidade do ângulo de fase e redução do poder espectral na banda alfa do córtex pré-frontal no grupo ativo. Conclui-se que exercícios focados na amplitude e velocidade dos braços promovem melhorias na marcha e na atividade cortical em DP. Contudo, múltiplas sessões de ETCC são necessárias para potencializar esses efeitos, sugerindo que intervenções combinadas e repetidas são mais eficazes.

Palavras-Chave: Parkinson, Estimulação cortical, Locomoção, Eletroencefalograma.

Abstract

Transcranial direct current stimulation (tDCS) and physical exercise are effective therapies for improving motor coordination and gait parameters in people with Parkinson's disease (PD), often accompanied by changes in cortical activity. However, variability in tDCS protocols raises questions about which parameters are effective, and little is known about the effects of combining tDCS and exercise on locomotion and cortical activity in PD. This thesis investigated these gaps through three studies. Study #1 synthesized findings from studies on tDCS protocols aimed at improving motor coordination in individuals with parkinsonism and healthy older adults through a systematic review of PubMed, Embase, and Web of Science databases. Study #2 investigated the acute effects, and Study #3 the chronic effects, of a combined tDCS and locomotor exercise protocol on interlimb coordination, gait parameters, and cortical activity in 22 individuals with PD. In the tDCS protocol, the anode was positioned over the motor cortex contralateral to the most affected side and the cathode over the contralateral supraorbital area. A 2 mA current was applied for 20 minutes (active) or 10 seconds (sham) during 20 minutes of exercise. In the exercise protocol, participants walked an 18 m circuit under two conditions: i) walking with increased arm swing amplitude (10 min); ii) walking with increased arm swing speed (10 min). In Study #2, participants performed both stimulation conditions seven days apart, with assessments conducted before and after each session. In Study #3, 22 participants were divided into two groups (active, n = 12; sham, n = 10) and completed six sessions on alternate days. Assessments were performed before the first session, 48 hours after, and 30 days after the final session. Gait was assessed using the GaitRite system positioned on an 8 m walkway. Interlimb coordination was analyzed via continuous relative phase between signals from accelerometers placed on contralateral wrists and ankles. Cortical activity was analyzed using 64-channel EEG, considering spectral power density (alpha, beta, gamma) in channels Fz, F3, F4, Cz, C3, C4, Pz, P3, and P4. Study #1 showed that tDCS improves motor coordination, particularly with 20-minute, 2 mA protocols. Study #2 revealed that one tDCS session combined with exercise did not enhance exercise effects. Study #3 demonstrated that six sessions amplified exercise effects, with the active group showing lower phase angle variability and reduced alpha-band power in the prefrontal cortex. In conclusion, exercise protocols focusing on arm amplitude and speed improve gait and cortical activity in PD. However, multiple tDCS sessions are necessary to enhance these effects, suggesting that combined and repeated interventions are more effective.

Keywords: Parkinson, Cortical Stimulation, Locomotion, Electroencephalogram.

Summary

1. Chapter 1

General introduction

Locomotion is a type of motor behavior activated by signals sent from various cortical regions (Takakusaki, Tomita, & Yano, 2008). It requires visuomotor cognitive processing regulated by neural networks involving the cerebral cortex, basal ganglia, cerebellum, brainstem, and spinal cord (Takakusaki, 2017). The frontal areas of the cortex are responsible for visuospatial movement control, whereas motor areas, such as the supplementary motor area (SMA), premotor area, and primary motor cortex (M1), are involved in motor planning (Takakusaki, 2017). The cerebellum plays a role in executing cyclic movements following preestablished motor plans, controlled unconsciously (Linsberger & Thach, 2014). These regions are connected to basal ganglia structures such as the thalamus and substantia nigra pars reticulata (Takakusaki et al., 2004). The basal ganglia receive inputs from the cortex and send projections to brainstem structures, including the pedunculopontine nucleus, which regulates muscle tone, and the mesencephalic locomotor region, responsible for rhythmic movement control. Furthermore, they influence spinal cord structures such as the central pattern generator (CPG), which modulates rhythmicity by coordinating flexor and extensor muscle activity during gait (Pearson & Gordon, 2014; Takakusaki et al., 2003). When basal ganglia function is impaired, as in Parkinson's disease (PD), individuals exhibit movement execution impairments, including slowness (bradykinesia) and reduced amplitude (hypometria) (Takakusaki, 2017).

PD is characterized by progressive and asymmetric degeneration of dopaminergic neurons located in the substantia nigra pars compacta of the basal ganglia (Wichmann & DeLong, 2014). Dopamine is a critical neurotransmitter for regulating cortical activity. Its reduced production impairs inhibitory stimulus transmission from the substantia nigra pars compacta to the internal globus pallidus and substantia nigra pars reticulata, leading to increased inhibitory stimuli sent to the thalamus (Takakusaki, Tomita, & Yano, 2008). Consequently, there is greater inhibition of the thalamo-cortical pathway, reducing stimulus transmission to the cortex and decreasing basal ganglia activation (Blandini et al., 2000; Takakusaki, Tomita, & Yano, 2008). This dysfunction is associated with resting tremor, a hallmark symptom of PD. In gait-related circuitry deficits, inhibition of the pedunculopontine nucleus and mesencephalic locomotor region is reduced. With diminished dopaminergic activity, these structures, which typically receive inhibitory projections from the basal ganglia, increase inhibitory signals sent to the reticular formation (Takakusaki et al., 2004). As a result, gait deficits arise, including reduced stride length and speed, increased double support time, decreased and asymmetric arm swing, and impaired interlimb coordination (Huang et al., 2012; Lewek et al., 2010). The dense connectivity between the cortex and basal ganglia explains why, in the presence of motor dysfunction, individuals with PD exhibit altered cortical activity (Karimi et al., 2022; Stuart et al., 2021). Compared to healthy older adults, individuals with PD show increased alpha-band (8–12 Hz) and beta-band (13–30 Hz) power in frontal, motor, and parietal cortical regions (Karimi et al., 2022; Stuart et al., 2021). This increased cortical activity is interpreted as a compensatory mechanism for the basal ganglia's deficient circuitry, aimed at maintaining performance during motor tasks such as gait (Stuart et al., 2018).

Several studies have focused on treating gait characteristics in individuals with PD (Li et al., 2020; Luna et al., 2020; Nonnekes et al., 2016). The most commonly used therapy for managing PD signs and symptoms involves medications that compensate for dopamine deficits (Tarazi et al., 2014). This pharmacological approach effectively alleviates symptoms such as resting tremor and gait deficits, resulting in increased stride length and speed in older adults with PD (Nonnekes et al., 2016). Regarding cortical activity, medication reduces alpha-band spectral power in the frontal cortex of individuals with PD, reflecting decreased executive control demand and restoration of automatic gait patterns (Orcioli-Silva et al., 2021). However, continuous use of these medications can lead to side effects such as hallucinations and dyskinesia, while failing to improve static and dynamic balance (Nonnekes et al., 2016; Smulders et al., 2016). Consequently, other therapies that complement medication are gaining prominence in treating PD symptoms. Studies have shown that various physical exercise protocols improve gait parameters in individuals with PD, including increased stride length and speed, as well as enhanced strength in the lower and upper limbs (Ni et al., 2018). However, many exercise protocols developed to date focus on lower limb movement, disregarding upper limb movement and the interaction between these two body segments.

The Arm movement plays a crucial role in controlling key aspects of locomotion, such as dynamic balance and energy efficiency during walking, counterbalancing leg movement and reducing trunk rotation (Meyns et al., 2013; Pontzer et al., 2009). In neurodegenerative diseases such as PD, neural impairments affect arm movement, contributing to gait and movement coordination deficits (Espinosa et al., 2023). Ospinna et al. (2018) observed that individuals with PD exhibit reduced movement magnitude and speed and increased arm swing asymmetry compared to neurologically healthy older adults (Lewek et al., 2010). However, when individuals with PD are instructed to walk with increased arm movement amplitude and speed, improvements are observed in gait parameters such as stride length and speed (Zampier et al., 2018), interlimb coordination parameters such as decreased coordination pattern variability and increased arm-leg coupling (Zampier, 2019), accompanied by changes in alpha and beta bands in the supplementary motor area, indicating functional restoration of this region's activity (Wersink et al., 2020). Despite the relationship between upper and lower limb movements, the effects of exercise protocols targeting upper limb movement on gait parameters and interlimb coordination remain poorly understood.

In addition to physical exercise, other techniques have been explored to address gait deficits in older adults with PD, including invasive and non-invasive cortical stimulation techniques. Transcranial direct current stimulation (tDCS) (Beretta et al., 2020; Broeder et al., 2015; Lattari et al., 2017) is a non-invasive technique that applies low-intensity electrical currents (typically between 1–2 mA) through the scalp, altering neuronal membrane potentials and consequently increasing or decreasing excitability in specific cortical areas (Nitsche & Paulus, 2000). tDCS has gained popularity due to its ease of application, safety, and relatively low cost compared to other techniques, such as transcranial magnetic stimulation and deep brain stimulation (Broeder et al., 2015; Hanakawa, 2015). Studies suggest tDCS as a promising technique for improving movement coordination and gait in individuals with PD (Barreto et al., 2019; Pol et al., 2021). For instance, Leenus et al. (2014) reported that a 20-minute tDCS session over the prefrontal cortex reduced errors and increased accuracy in interlimb coordination tasks involving opposing arm and leg movements. Barreto et al. (2019) found that five consecutive sessions of cathodal tDCS over the motor cortex improved the coordination of rapid movements executed with a single limb. Additionally, Ferrucci et al. (2019) reported that a single tDCS session applied to the cerebellum improved coordination between movements of a single limb. In terms of gait, tDCS has been associated with increased step length and speed in older adults with PD (Pol et al., 2021). Although these findings demonstrate tDCS's efficacy in improving coordination-related characteristics, varying results, procedures, and stimulated areas suggest a need for studies that consolidate this information to facilitate understanding and exploration of tDCS effects on coordination.

Given the positive effects of tDCS on motor aspects, studies have examined the effects of combining tDCS with physical exercise on locomotor characteristics and cortical activity in individuals with PD (Beretta et al., 2020). When combined with aerobic exercise, tDCS enhances prefrontal cortex activity in the stimulated region (Conceição et al., 2021). This cortical activity alteration is accompanied by reduced variability in step duration and reaction time (Conceição et al., 2021). Beyond gait and cortical activity changes, combining tDCS with exercise protocols also shows synergistic effects on upper limb function and postural control in older adults with PD (Beretta et al., 2020). However, the wide variety of tDCS protocols used makes findings on the combined effects of tDCS and physical exercise on locomotor aspects and cortical activity in individuals with PD inconsistent, highlighting the need for further research. Additionally, most studies combining tDCS with physical exercise have employed exercise protocols focusing on lower limb movement, such as cycling (Conceição et al., 2021), without considering upper limb movement. To date, no studies have reported on the combined effects of tDCS and arm-focused locomotor exercises on gait parameters, interlimb coordination, and cortical electrical activity in individuals with PD.

Considering these points, this doctoral thesis aims to address three primary questions regarding the type of tDCS protocol that should be employed to improve movement coordination in individuals with PD: (1) How does tDCS alone influence gait parameters and interlimb coordination in older adults with PD? (2) How do exercise protocols involving the arms affect interlimb coordination and cortical activity in individuals with PD? (3) How does a combined tDCS and arm-focused locomotor exercise protocol affect gait parameters, interlimb coordination, and cortical activity in older adults with PD?

- Study #1: Effectiveness of transcranial direct and alternate current stimulation on movement coordination in older people and individuals with Parkinsonism: A systematic review.

- Study #2: The acute effects of transcranial direct current stimulation combined with locomotor exercise on people with Parkinson's disease locomotion and cortical activity.

- Study #3: The chronic effects of transcranial direct current stimulation combined with locomotor exercise on people with Parkinson's disease locomotion and cortical activity.

5. Chapter 5

5.1. Final Comentes

Table 1 summarizes the main findings e perspectives for further studies. The present thesis investigated the effects of transcranial direct current stimulation (tDCS) on gait parameters, interlimb coordination, and cortical activity in older adults with Parkinson's disease (PD). The study was guided by three key questions regarding the methods and effects of tDCS on locomotion and cortical activity in older adults with PD: i) What are the characteristics of tDCS protocols (number and duration of sessions, type of stimulation, and current intensity) that should be applied to improve movement coordination in individuals with and without neurodegenerative diseases? ii) What are the effects of a single session of tDCS combined with a locomotor exercise protocol focused on arm movements on gait parameters, interlimb coordination, and cortical activity in individuals with PD? iii) What are the effects of multiple sessions of tDCS combined with a locomotor exercise protocol focused on arm movements on gait parameters, interlimb coordination, and cortical activity in individuals with PD? Based on the findings of this thesis, it can be concluded that:

- The appropriate placement of tDCS electrodes should consider the specific brain regions affected by each pathology.

- A current intensity of 2mA is more effective than higher or lower intensities.

- Sessions lasting 20 minutes are more effective than shorter sessions.

- Multiple sessions of tDCS combined with locomotor exercises demonstrate greater efficacy in promoting synergistic and long-lasting effects on locomotion and cortical activity in individuals with PD compared to single sessions. These benefits include a reduction in alpha spectral power density in the prefrontal cortex and decreased variability in the coordination pattern between arms and legs, observed exclusively in the group that received active tDCS, 48 hours and 30 days after the last session.

- Locomotor exercises focused on increasing the amplitude and speed of arm movements are effective in promoting both acute and chronic improvements in gait parameters, interlimb coordination, and cortical activity in individuals with PD. Improvements in gait were evidenced by increased stride length and speed, as well as reduced double support phase, observed in both groups (active tDCS and sham tDCS) after a single session and after six sessions of arm-focused locomotor exercises. Improvements in coordination were demonstrated by increased phase angle and reduced variability in the coordination pattern between arm and contralateral leg movements after six non-consecutive sessions. Cortical activity changes included a reduction in gamma spectral power density in the motor cortex, as well as reductions in alpha, beta, and gamma spectral power densities in the occipital cortex, after a single session. After six sessions, reductions were also observed in beta spectral power density in the prefrontal cortex and alpha spectral power density in the motor cortex.

Studies have shown that both tDCS and locomotor exercise are promising, safe, and cost-effective tools for treating the signs and symptoms of PD (Ni et al., 2018; Broeder et al., 2015). Moreover, the combination of tDCS and physical exercise has been investigated, with evidence suggesting that tDCS can, in some cases, enhance the effects of exercise (Bereta et al., 2020; Conceição et al., 2021). However, findings on the effects of this combination remain inconsistent, raising questions about whether a single session of tDCS combined with exercise is sufficient to produce synergistic effects. Although there is a strong relationship between arm movements and gait parameters in individuals with PD (Zampieri et al., 2018; Ospina et al., 2018; Lewek et al., 2010; Ford et al., 2007), many studies investigating the effects of various exercise protocols on locomotor parameters in older adults with PD focus exclusively on modulating the lower limbs. Examples include interventions such as stationary cycling (Conceição et al., 2021) and visually guided walking (Ni et al., 2018), often neglecting the potential benefits of locomotor interventions focused on arm movements.

The results of this thesis support the literature highlighting the benefits of locomotor exercise on gait and motor coordination in older adults with PD. The study demonstrates that after engaging in a protocol of exercises aimed at increasing the amplitude and speed of arm movements, individuals with PD showed improvements in gait parameters and interlimb coordination. Furthermore, this work advances understanding of the neural mechanisms involved in gait control in individuals with PD by showing that these locomotor improvements are accompanied by reduced activity in motor and sensory cortical areas. Finally, the findings suggest that multiple sessions of tDCS are necessary to produce synergistic effects beyond those promoted by exercise alone on locomotion and cortical activity in individuals with PD. Thus, it can be concluded that locomotor exercises focused on increasing the amplitude and speed of arm movements are effective for improving locomotion in individuals with PD, and that combining this protocol with multiple sessions of tDCS amplifies these effects.

5.1.1. Practical Applications

The findings of this thesis are highly relevant for healthcare professionals, providing important insights into the application and effects of tDCS on locomotor characteristics and cortical activity in individuals with PD. This thesis demonstrates that tDCS protocols with a duration of 20 minutes and a current intensity of 2mA yield positive and consistent results in the literature. Moreover, more than one session of tDCS combined with locomotor exercise is required to produce synergistic effects on locomotor parameters and cortical activity in individuals with PD. Finally, this thesis shows that locomotor exercises focusing attention on increasing the amplitude and speed of arm movements can be considered an effective strategy for treating locomotor deficits caused by PD.

5.1.2. Limitations and Future Studies

Despite the significant findings, this thesis has some limitations. The facility where data were collected only allowed participants to walk a distance of 8 meters without making turns, limiting the assessment of gait parameters, interlimb coordination, and cortical activity. Future studies should consider using longer distances to evaluate changes in locomotor parameters and cortical activity in PD individuals during longer tasks. Additionally, the time required for patient preparation (e.g., EEG and accelerometer placement and removal) and the execution of the combined tDCS and locomotor exercise protocol limited the number of trials and the overall protocol length, as there was a risk of participants transitioning out of the ON-medication state. Future studies should consider using a tDCS system integrated with an EEG system, allowing the entire experimental protocol to be conducted without removing the EEG equipment during the procedure.

Table1. Summary of main findings and suggestions for future studies

<table>
<tr><th>Current Literature</th><th>Main Findings</th><th>Future Studies</th></tr>
<tr><th colspan="3">Study 1</th></tr>
<tr><td>tDCS has been suggested as a promising therapy to improve movement coordination (Alexoudi et al., 2019).</td><td rowspan="2">- The electrode placement should consider the participant individual status;
- The current intensity at 2mA seems to be more effective than lower or higher currents intensities; - Protocols lasting 20 minutes appear to be more effective than shorter protocols.</td><td rowspan="2">- Future studies should consider:
- investigating the effects of transcranial electrical stimulation on locomotor parameters (e.g. movement coordination and gait parameters) during complex tasks such as walking.</td></tr>
<tr><td>The vast number of available protocols makes it difficult to define the most appropriate protocol to improve motor coordination in older adults and people with Parkinsonism.</td></tr>
<tr><th colspan="3">Study 2</th></tr>
<tr><td>Locomotor exercise and tDCS have been show as effective alternative therapies to improve locomotion and to generate changes on cortical activity of PwPD (Broeder et al., 2015; Ni et al., 2018)</td><td rowspan="3">- Only one session of combined tDCS and locomotor exercise had no synergetic effect on PwPD walking, interlimb coordination and cortical activity parameters;
- One session of locomotor exercise protocol focused on the increase of arm swing amplitude and speed generated improvements on PwPD gait parameters, such as the increase in stride length and velocity and decrease double support time and a decrease on their occipital cortex activity.</td><td rowspan="3">Future studies should consider:
- investigate the effects of multiple sessions of a combined tDCS and locomotor exercise focused on arm swing amplitude and speed protocols on PwPD locomotor behavior
- Adopt longer walking distances to acquire data from PwPD locomotion and cortical activity.</td></tr>
<tr><td>Despite the strong relation between arm movement and walking performance, no study yet investigate the effects of locomotor exercise focused on arm swing amplitude and speed on PwPD locomotor behavior. (Zampier et al., 2018)</td></tr>
<tr><td>It has been suggested that tDCS generates synergetic effects on PwPD locomotor behavior when combined with physical exercise. However, no study yet investigated the acute effects of a combined tDCS and over ground locomotor exercise on PwPD interlimb coordination and cortical activity during walking. (Beretta et al., 2020; Conceição et al., 2021).</td></tr>
</table>

Study 3		
The literature suggest that when combined with other therapies tDCS generates synergetic effects on PwPD motor parameters (Beretta et al., 2020; Conceição et al., 2021). However the literature lacks the information regarding the effects of multiple sessions of combined tDCS with over ground locomotor exercise on PwPD locomotor behavior and cortical activity.	The combination between tDCS and locomotor exercise focused on the increase of arm swing amplitude and speed had synergetic effects on PwPD locomotor behavior and cortical activity. The a-tDCS group presented a decrease on arm-leg movement coordination followed by a decrease in PFC alpha band PSD.	Future studies should consider: - Adopt longer walking distances to acquire data from PwPD locomotion and cortical activity. - Perform gait event related EEG analysis to verify the brain activity changes in different moments during the walking task

6. General References

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