Journal of Integrative Neuroscience

J. Integr. Neurosci. **2024**; 23(2): 25
https://doi.org/10.31083/j.jin2302025

Original Research

Effects of Transcranial Direct Current Stimulation on Potential P300-Related Events and Alpha and Beta EEG Band Rhythms in Parkinson's Disease

Rosa Angela Fabio[1], Rossella Suriano[2,*], Antonio Gangemi[3]

[1]Department of Economics, University of Messina, 98100 Messina, Italy
[2]Department of Cognitive, Psychological and Pedagogical Sciences and Cultural Studies, University of Messina, 98100 Messina, Italy
[3]Polyclinic Madonna della Consolazione, 89124 Reggio Calabria, Italy
*Correspondence: suriano.rossellaz@gmail.com (Rossella Suriano)

Academic Editor: Yoshihiro Noda
Submitted: 24 September 2023 Revised: 23 November 2023 Accepted: 27 November 2023 Published: 31 January 2024

Abstract

Background: Parkinson's disease is one of the most common neurodegenerative disorders. While a definitive cure for Parkinson's disease remains elusive, a range of treatments are available to slow its progression and counteract its symptoms. Transcranial direct current stimulation (tDCS) represents a non-invasive method to induce brain plasticity. The aim of this study was to examine the effects of two weeks of tDCS on the left dorsolateral prefrontal cortex (DLPFC) on the neurophysiological functioning of Parkinson's patients. **Methods**: Thirty patients aged between 67 and 82 years with Parkinson's disease participated to the experiment. Fifteen underwent tDCS on the left DLPFC, while fifteen underwent sham tDCS. Neurophysiological functions were assessed before and after tDCS using electroencephalogram methods for alpha and beta band rhythms and P300 event-related potential latency. **Results**: tDCS led to a reduction in the onset latency of the P300 response and an increase in the power spectrum of the alpha and beta band rhythms. **Conclusions**: This research enhances our understanding of the potential effects of tDCS in the context of Parkinson's disease treatment, as the reduction in P300 latency and the increase in alpha and beta bands are associated with improvements in cognitive aspects.

Keywords: Parkinson's disease; transcranial direct current stimulation (tDCS); electroencephalogram (EEG); P300 event-related potential; alpha and beta band rhythms

1. Introduction

Parkinson's disease (PD) is one of the most common neurodegenerative conditions, affecting about 1% of individuals over 60 years of age, with standardized incidence rates of 8–18 cases per 100,000 person-years [1,2]. This condition is characterized by the progressive loss of dopaminergic neurons within the substantia nigra pars compacta in the brain, causing a wide range of both motor and non-motor symptoms [3–5]. The motor symptoms constitute the distinctive symptomatic ensemble that forms the basis of the clinical diagnosis of the disease, including tremors, rigidity, bradykinesia, and postural instability [6]. Regarding non-motor symptoms, cognitive deficits affect approximately 30–40% of patients and represent the most debilitating complication of PD [7,8]. These deficits arise from the reduced availability of dopamine in the brain, particularly in the frontal domains and the attentional system, giving rise to a fronto-striatal syndrome [9]. Cognitive deficits can manifest from the early stages of the disease and are primarily characterized by involvement of executive functions, visuospatial abilities, and memory [10,11]. The cognitive dysfunctions of PD encompass various nuances, ranging from mild cognitive impairment in PD (PD-MCI) to Parkinson's disease dementia (PDD) [12,13].

1.1 Non-Pharmacological Treatments

Currently, there are few pharmacological treatments that effectively and comprehensively address the symptoms of PD [14]. These treatments only target the motor symptoms, while non-motor symptoms such as cognition remain unaffected and continue to negatively impact the quality of life of patients [15–17]. Consequently, the possibility of resorting to non-pharmacological treatments, including non-invasive brain stimulation (NIBS) targeting affected cortical areas, has been considered [18–20]. Among these, transcranial direct current stimulation (tDCS) could promote synaptic plasticity and reinforce compensatory brain networks [21–23]. It involves a method of non-invasive neurostimulation through a low-intensity electric current applied to the scalp's surface using one or two stimulation electrodes positioned over specific brain regions [24–27]. The direction and intensity of the current influence neuronal activity. Anodal stimulation increases the excitability of brain areas near the electrode, while cathodal stimulation decreases it [28,29]. The short-term effects of tDCS are caused by depolarization of the membrane potential, while the long-term effects are linked to mechanisms involving N-methyl-D-aspartate (NMDA) receptors and synaptic plasticity [30,31]. Despite possible adverse effects, such as tingling, itching, mild headache, and skin burns, tDCS is gen-

erally considered a safe rehabilitative strategy that offers several advantages, including painless application, few side effects, cost-effectiveness, and the potential for at-home administration with remote expert supervision [32–34]. As a result, tDCS has been adopted with significant success, demonstrating promising results in addressing brain degenerative processes, encompassing both physiological processes related to aging and pathological processes, covering a wide range of neurological disorders [35–38] and neuropsychiatric conditions [39–42]. The application of tDCS has raised new prospects for the treatment of mild cognitive impairments and dementia [43–46]. tDCS appears to be particularly effective in cases of mild cognitive impairment, showing more promising results compared with its application in Alzheimer's dementia [47]. Therefore, the use of tDCS should be considered during the phase of PD-MCI, when effectiveness seems particularly likely [48]. Considering all this, there is a growing need for randomized placebo-controlled trials that assess both the efficacy and specific neural mechanisms of the exclusive use of tDCS in individuals affected by PD-MCI. Despite the established evidence for tDCS, conflicting results have emerged from studies examining the effects of tDCS in combination with other treatments [49–51]. These studies have reported improvements in various cognitive domains, but whether these improvements can be solely attributed to tDCS or whether there has been adjunct effect—an enhancement of the effects of additional therapies—remains ambiguous [52–55]. This point is of considerable significance and requires further investigation.

1.2 Evaluating Cognitive Functions Through Electroencephalography Parameters in PD

Cognitive deficits in PD encompass various aspects, including executive functions, visuospatial abilities, and memory [10,11]. Event-related potentials (ERPs) represent an objective quantifier of cognitive functions, providing an opportunity to monitor cognitive changes without the apparent influence of motor deficits in PD [56]. ERPs are a valuable tool in cognitive neuroscience that allow researchers to measure and analyze brain activity in response to specific stimuli or events. ERPs are obtained through electroencephalography (EEG), a non-invasive technique that records the electrical activity of the brain over time. EEG involves placing electrodes on the scalp, which detect and record electrical signals generated by neural activity. ERPs are time-locked to a specific event, such as the presentation of a stimulus, and provide a way to assess neural processing associated with sensory, motor, or cognitive functions. In our study, the P300 ERP is of particular importance [57]. The P300 component is a positive deflection in the ERP waveform that typically occurs around 300 ms after the presentation of a rare or unexpected stimulus. P300 is associated with cognitive processes related to attention, memory, and decision-making. The onset latency of the P300 component, which is the time it takes for the P300 response to appear after a stimulus, is an essential measure as it reflects the speed and efficiency of cognitive processing. In addition to ERPs, the present study investigated the role of alpha and beta band rhythms in PD. These neural oscillations, measured through EEG, are critical in understanding the motor and cognitive aspects of PD. The alpha band is associated with the inhibition of sensory information processing. When the brain is at rest or not engaged in a specific cognitive task, alpha rhythms are dominant. They are typically recorded over posterior brain regions and are believed to be involved in inhibiting irrelevant sensory information, thereby promoting focused attention and cognitive stability. Beta rhythms are associated with motor control and motor planning. They are often recorded over motor-related areas of the brain, such as the sensorimotor cortex. These rhythms are implicated in the coordination of muscle movements, and their modulation is linked to changes in motor function [58]. In PD, aberrations in alpha and beta band rhythms, coupled with alterations in P300 oscillatory dynamics, may collectively serve as critical neurophysiological markers. These markers potentially underlie the intricate interplay observed between motor dysfunction and cognitive impairment in individuals with PD [59]. The rationale for their utilization lies in the well-established involvement of alpha and beta band rhythms in motor control, as evidenced by Hammond *et al.* [59], which is closely intertwined with the cognitive deficits witnessed in PD. Concurrently, abnormalities in P300 oscillations have been linked to cognitive decline in PD [60]. Consequently, we posit that investigating the convergence of alpha and beta band rhythms with P300 oscillations in PD could illuminate the mechanistic underpinnings of both the motor and cognitive manifestations of the disease.

1.3 Study Significance and Hypotheses

Although a body of evidence suggests that ERPs could be a sensitive method to investigate mechanisms of symptomatic improvement due to tDCS [61], and while some studies have investigated the neurophysiological effects of tDCS in samples with mild cognitive decline [62,63], few studies have investigated the effects of tDCS on ERPs in PD [64–68]. The primary objective of this research was to assess the effects of tDCS on the left dorsolateral prefrontal cortex (DLPFC) in patients with PD concerning neurophysiological functions measured through EEG. Our hypothesis posited that tDCS on the left DLPFC would lead to a reduction in the onset latency of the P300 event-related potential, accompanied by an increase in alpha and beta band rhythms within the neural oscillatory activity. This hypothesis is grounded in prior research findings that have demonstrated the modulatory effects of tDCS on cortical excitability and neural oscillations [69–71]. Specifically, studies have shown that tDCS can influence neuronal membrane potentials and enhance cortical synchronization, which are

associated with alterations in event-related potentials and alpha and beta band rhythms. Furthermore, the left DLPFC is a region known to be involved in the cognitive processes of interest, including those related to P300 latency [72,73]. Preliminary studies and research on deep brain stimulation (DBS) in PD have suggested that modulating the left DLPFC could lead to improvements in both motor and cognitive symptoms [74]. These prior findings have justified further investigation into DLPFC stimulation in the context of PD. In fact, the left DLPFC is implicated in high-level cognitive functions such as attention, working memory, and decision-making [75]. Cognitive deficits are common in PD [76]. Stimulating the left DLPFC may potentially enhance these compromised cognitive functions. Stimulation of the left DLPFC may have a dual effect, improving both motor and cognitive symptoms because this brain region is involved in both types of functions [14,77]. DLPFC stimulation can influence brain circuits, including those connecting the DLPFC to other brain regions involved in PD symptoms. This modulation may help regulate brain activity and enhance function in affected areas. Furthermore, in this study, we hypothesized that (a) patients undergoing tDCS would exhibit a significant reduction in the onset latency of the P300 event-related potential compared with the group undergoing sham tDCS and (b) patients undergoing tDCS would demonstrate a significant increase in the power spectrum of alpha and beta band rhythms compared with the group undergoing sham tDCS.

2. Materials and Methods

2.1 Experimental Design

The study employed an ABA experimental design, consisting of a pre-test, an intervention, and a post-test or both groups. It was double-blinded, on the part of both the researcher and the evaluator. A matching procedure was implemented for the assignment. The tDCS group was initially recruited and, subsequently, the sham group was matched to them based on key demographic and clinical variables, ensuring baseline comparability between the two groups. This approach was chosen to minimize potential confounding factors and enhance the internal validity of our study.

2.2 Participants

Based on the sample size commonly reported in the literature and the estimated sample dimension [78,79], 30 patients diagnosed with PD were recruited from the Madonna della Consolazione Polyclinic Nursing Home in Reggio Calabria, a region in Southern Italy. All participants were aged between 67 and 82 years (mean age [M] = 74.5 years, standard deviation [SD] = 7.2 years). Among these patients, a group of 15 individuals received anodal tDCS, while the other group of 15 age- and sex-matched subjects received simulated tDCS.

Inclusion criteria required a diagnosis of PD based on the guidelines of the United Kingdom Parkinson's Disease Society (UKPDS) and the clinical diagnostic criteria of the Brain Bank [80,81]. Additionally, the diagnosis of PD-MCI aligned with Level 2 (comprehensive) criteria for PD-MCI [82], which involved a performance that was 1.5 SDs below normative data in at least two tests within a single domain or in one or two tests across distinct domains [83]. Selected participants exhibited scores ranging from 22 to 26 points on the Mini-Mental State Examination (MMSE), which was adjusted for the educational level of this population [84,85]. The clinical data related to the Unified Parkinson's Disease Rating Scale (UPDRS) [86] of patients who underwent anodal tDCS and sham procedure were extracted from medical records. Furthermore, a detailed clinical assessment of the patients was conducted, and they presented motor symptoms ranging from stage I to III on the Hoehn and Yahr (H&Y) scale [87]. Right-hand laterality was assessed using the Edinburgh Handedness Inventory (EHI). All patients had been maintained on stable and optimal dopaminergic medication therapy for at least one month prior to the start of the study and were required to maintain this regimen throughout the study's duration.

Exclusion criteria included a diagnosis or evidence of secondary or atypical parkinsonism, previous clinically significant neurological disorders, prior neurosurgical interventions, head traumas, brain injuries, epilepsy, stroke, or multiple sclerosis. Additionally, patients with a diagnosis of major depressive disorder, psychotic disorders, bipolar disorder, or alcohol and substance use disorders were excluded.

2.3 Procedure

This study was conducted in accordance with the Declaration of Helsinki and received approval from the Ethics Committee of Madonna della Consolazione Polyclinic Nursing Home (protocol approval number 2021-198). Clinically documented data, already available at the healthcare facility and provided by healthcare professionals within a timeframe not exceeding one month (MMSE, UPDRS, DD [Duration of Disease], LEV [Levodopa Equivalent Dose], H&Y score), were utilized for the present study. Before participating, each participant received detailed information about the study's purpose and data collection procedures. This information was presented clearly and comprehensibly, enabling participants to make an informed decision about their involvement. Subsequently, each participant provided written informed consent. Prior to the intervention, participants were thoroughly briefed on the stimulation procedure employed in the study. This explanation included details about the functioning of tDCS, as well as the associated practical procedures. Additionally, a clear illustration of potential side effects related to the intervention was provided. Each participant was informed of their right to withdraw from the study at any time without incurring

any negative consequences. At the start of the stimulation, participants were asked about their tolerance to the 2 mA or if they experienced any discomfort. Subjects tolerated the treatment well, and no adverse effects associated with tDCS were observed.

2.4 Measurements

In this research, the electroencephalogram was employed as the measuring instrument to explore neurophysiological parameters. More precisely, the analysis focused on the P300 component through an auditory oddball paradigm, while also examining the rhythms within the alpha and beta bands from the DLPFC.

2.4.1 EEG Recording

EEG recordings were captured at a sampling rate of 500 Hz, employing a band-pass filter set between 0.1 Hz and 70 Hz. SCAN software (version 4.3, Neuroscan, Compumedics, El Paso, TX, USA) along with NuAMP amplifiers were used for the recording. Eighteen scalp electrodes (Ag/AgCl) were positioned according to the standard 10/20 system outlined by Jasper [88]. The reference electrode was placed in the midline derivations, such as Fz, FCz, Cz, and Pz, and the ground electrode between Cz and Pz. All positions were referenced to a common Cz reference and later re-referenced offline to average mastoids. Electrode impedances were maintained at or below 10 kΩ. EEG data intended for ERP analysis underwent offline processing. This involved the application of a 20 Hz low-pass filter, baseline correction, and division of waveforms into epochs centered around stimulus presentation. Trials deviating in amplitude beyond $\pm$100 μV were excluded. A minimum of 20 trials for each stimulus were deemed necessary for the inclusion of individual average ERP waveforms. Epochs spanning from 200 ms to 1000 ms were generated offline, centered around low and high tones along with novel noises. The key components of interest, namely P1, N2, and P3a, were automatically detected within specific time intervals (70–110 ms, 210–270 ms, and 270–370 ms, respectively) from midline positions (Fz, FCz, Cz, and Pz) where these peaks exhibit maximum activity [89]. Frequent stimuli immediately preceding each infrequent stimulus were selected for averaging, ensuring comparable signal-to-noise ratios.

2.4.2 Auditory Oddball Paradigm

This study utilized an auditory oddball task, where participants were exposed to auditory stimuli without needing to provide overt responses. The stimuli were presented using specialized presentation software from Neurobehavioral Systems Inc. (Berkeley, CA, USA). Each participant was seated in a partially illuminated and soundproofed room, positioned in front of a computer monitor situated approximately 70 cm away. Adjacent to the monitor, two speakers were set up for audio presentation. The auditory paradigm encompassed three distinct sound categories: frequent pure sinusoidal tones, infrequent pure sinusoidal tones, and novel sounds. Within this framework, 10% of the stimuli consisted of infrequent tones (2 kHz, 200 ms duration, 5 ms rise and fall time, 70 dB sound pressure level [SPL]). Another 10% constituted novel noises, while the remaining 80% were frequent tones (1.5 kHz, 200 ms duration, 5 ms rise and fall time, 70 dB SPL). The duration of each tone or noise was 200 ms, with a stimulus onset asynchrony of 700 ms. The presentation consisted of two blocks, each containing 700 stimuli (560 frequent, 70 infrequent, and 70 novel). The intensity of novel sounds was digitally adjusted to ensure they did not surpass 70 dB SPL, as measured by a Bruel and Kjaer sound pressure meter. Fourteen distinct novel stimuli were employed, each repeated a maximum of five times during the experiment. Overall, the task completion time amounted to approximately 20 minutes.

2.4.3 Alpha and Beta Band Rhythms

Quantitative analysis of EEG data was conducted using customized algorithms developed in MATLAB code (The MathWorks Inc., Natick, MA, USA) [90]. The assessment of power spectral density (PSD) involved converting the signal from the time domain to the frequency domain through the utilization of the Welch method [91]. PSD values were determined for individual epochs, with subsequent computation of their averages. Initial calculations encompassed the absolute power of the entire signal and the absolute power within designated frequency bands for each electrode. PSD was calculated for 5-s windows after rejecting an initial 50 s out of total duration of 200 s for which the rhythmic tones were played. This study specifically focused on the alpha band (8–13 Hz) and beta band (14–29 Hz) from the DLPFC.

2.4.4 UPDRS

The UPDRS was used to integrate elements from existing scales and provide a comprehensive tool for capturing and assessing various aspects of PD, including motor disability, movement impairment, cognitive issues, emotional aspects, and treatment-related complications [87]. The UPDRS is divided into four parts. Part I focuses on non-motor symptoms, such as dementia, depression, and psychosis. Part II assesses the patient's ability to perform daily activities like dressing, grooming, and using utensils. Part III is evaluated by a physician and measures motor symptoms like speech, facial expression, tremors, muscle tone, speed of hand and leg movements, walking, and balance. Part IV assesses treatment complications. The response scale is five-point, with choices ranging from 0 to 4.

2.5 Intervention

The tDCS device utilized in this study was the BRAINDEE stimulator, manufactured by Omicron-t S.r.l., based in Naples, Italy. Stimulation was conducted using a

pair of sponge electrodes, each with a diameter of 25 mm, previously saturated with a saline solution. A constant current was delivered by a battery-powered stimulator. The decision was made to target the left DLPFC due to its involvement in high-level cognitive functions such as attention, working memory, and decision-making. These cognitive functions are frequently impaired in patients with PD. By modulating the DLPFC, this stimulation may contribute to improvements in both motor and cognitive symptoms. Given the DLPFC's dual role in motor and cognitive functions, stimulating this region could potentially have a dual effect, enhancing compromised cognitive functions as well [92,93]. To activate the left DLPFC, the anode was positioned over the F7 region, while the cathodic reference electrode was located above the right supraorbital area. The precise electrode placement was determined following the EEG 10–20 system. Stimulation intensity was set at 2 mA (with a current density of 2.5 mA/cm^2) for 20 minutes, administered five times a week for two consecutive weeks, both in the study group and the placebo group. The decision to use 2 mA was based on the safety and comfort of our participants. We opted for the 2 mA intensity as it is considered safe and well-tolerated, which is particularly crucial when dealing with individuals who may have various health conditions or sensitivities. Safety is paramount in human research, and a 2 mA intensity level is widely accepted [79,94].

In the simulated sham condition, the electrodes were placed in the same manner as in actual stimulation, but the stimulation automatically ceased after 10 s from the beginning of the session. This time interval is insufficient to induce a significant stimulation effect on the brain. A stimulation ramp was incorporated to ensure that participants would experience the typical tingling sensations near the electrodes, creating the illusion of receiving stimulation even during the simulated sham condition when no actual stimulation was applied. This procedure was implemented to maintain participants' unawareness of whether they were receiving real stimulation or the sham condition.

2.6 Statistical Analysis

All statistical analyses were conducted using SPSS 24.0 software (SPSS Inc., Chicago, IL, USA). The main objective of the analyses was to explore potential differences between the experimental group (i.e., anodal stimulation) and the sham group (i.e., sham stimulation) in neurophysiological parameters such as P300 latency and the alpha and beta band rhythms. To verify the causal relationship between UPDRS as a predictive variable and the P300 latency and the alpha and beta band rhythms, separate linear regressions were conducted. Repeated-measures (RM) analysis of variances (ANOVAs) were performed, employing the experimental groups as a between-subjects factor, and the phases—pre- and post-tests—as within-subjects factors. Furthermore, if the RM ANOVAs revealed significance, a post hoc analysis was conducted to identify which group exhibited changes between the pre- and post-test phases. Post hoc pairwise comparisons were executed using the Student's paired *t*-test. To address the issue of multiple comparisons, significance was attributed solely to the level $p < 0.005$. Regarding effect size, we employed Cohen's d for *t*-test comparisons, Eta-squared (η^2) for ANOVA, and R-squared (R^2) for regression analysis.

Table 1. Demographic data of participants.

Characteristic	Experimental Group	Sham Group
	Mean (SD)	Mean (SD)
Age (years)	73.27 (±5.64)	73.73 (±5.20)
Sex (ratio)	F:M = 2:3	F:M = 2:3
Education (years)	6.87 (±1.85)	7.13 (±1.64)
MMSE core	22.87 (±1.85)	23.73 (±1.62)
UPDRS* Part I score	8.76 (±1.89)	7.46 (±2.11)
UPDRS Part II score	13.74 (±3.89)	12.74 (±5.13)
UPDRS Part III score	29.00 (±11.45)	28.40 (±9.88)
DD (years)	3.67 (±1.05)	3.53 (±0.99)
LED (mg)	870.45 (±122.12)	899.87 (±134.76)
H&Y score	2.80 (±0.80)	2.70 (±0.70)

*Higher score means more severe symptoms. SD, standard deviation; F, female; M, male; MMSE, Mini-Mental State Examination; UPDRS, Unified Parkinson's Disease Rating Scale; DD, disease duration; LED, levodopa equivalent dose; H&Y, Hoehn and Yahr.

3. Results

Table 1 summarizes the demographic characteristics of the participants.

Table 2 shows descriptive statistics of the alpha and beta band rhythms and P300 latency. To verify the relationship between the scores pertaining to the UPDRS scores and the P300 latency, the alpha and beta band rhythms, linear regression analyses were conducted. UPDRS scores did not show statistical significance as predictors of the differences between the pre-test and post-test phases in P300 latency (–0.02 ± 0.03, $\beta \pm$ standard error [SE], $p = 0.06$), nor did they significantly predict the differences between the pre-test and post-test phases in the alpha band rhythm (–0.04 ± 0.05, $\beta \pm$ SE, $p = 0.05$) or the beta band rhythm (0.04 ± 0.03, $\beta \pm$ SE, $p = 0.08$).

Fig. 1 shows the pre- and post-test alpha band rhythms for both groups. RM-ANOVA with one between-subject factor group and one within-subject factor phase was conducted. RM-ANOVA showed again that the effect of group was not significant ($F(1, 28) = 1.99$; $p = 0.22$, $\eta^2 = 0.08$). The phase factor also shows no significant differences ($F(1, 28) = 1.34$, $p = 0.34$), but the effect of the group x phase interaction was significant ($F(1, 28) = 16.51$; $p < 0.01$, $\eta^2 = 0.09$). Paired *t*-tests show statistical differences in the alpha band only for PD patients with anodal tDCS. Alpha bands had higher values in the post-test than in the pre-test phase

Table 2. Alpha and beta band rhythms and P300 latency.

Test	Experimental Group Pre-Test Phase	Sham Group Pre-Test Phase	Experimental Group Post-Test Phase	Sham Group Post-Test Phase
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Alpha band power	8.64 (±0.29)	8.53 (±0.94)	9.52 (±0.74)	8.46 (±0.68)
Beta band power	15.58 (±1.06)	15.24 (±1.42)	17.71 (±1.07)	15.19 (±1.40)
P300 Latency	310.40 (±3.48)	310.60 (±3.74)	305.61 (±2.24)	309.60 (±3.46)

SD, standard deviation.

(post = 9.52 ± 0.74, pre = 8.64 ± 0.29; t (14) = 4.34, $p < 0.001$, d = 0.80). An independent *t*-test was also applied to analyze the post-test means of the two groups (experimental = 9.52 ± 0.74, sham = 8.46 ± 0.68; t (28) = 6.11, $p < 0.001$, d = 0.78).

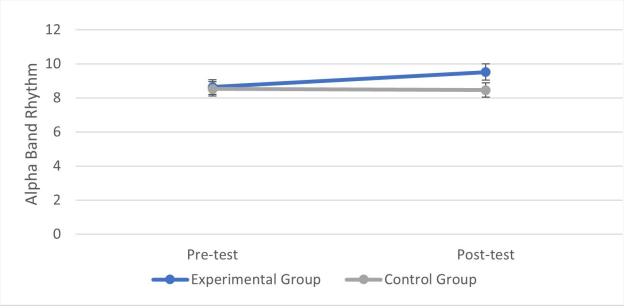

Fig. 1. Alpha band rhythms in the pre- and post-test phases for the experimental and sham groups. Plots show mean and whiskers show standard deviation.

Fig. 2 shows the pre- and post-test beta band rhythms for both groups. RM-ANOVA showed again that the effect of group was not significant (F (1, 28) = 1.32; $p = 0.27$, $\eta^2 = 0.10$) and the phase group was also not significant (F (1, 28) = 0.76; $p = 0.56$, η^2=0.09). The effect of the group x phase interaction was significant (F (1, 28) = 48.94; $p < 0.01$, $\eta^2 = 0.09$). Paired *t*-tests show statistical differences in beta band only for PD patients with anodal tDCS. Beta bands had higher values in the post-test than in the pre-test phase (post = 17.71 ± 1.07, pre = 15.58 ± 1.06; t (14) = 5.21, $p < 0.001$, d = 0.90). An independent *t*-test was also applied to analyze the post-test means of the two groups (experimental = 17.71 ± 1.07, sham = 15.19 ± 1.40; t (28) = 6.11, $p < 0.001$, d = 0.86).

Fig. 3 shows the pre- and post-test P300 latency in both groups. RM-ANOVA showed that the group had no significant effect (F (1, 28) = 2.46; $p = 0.126$, $\eta^2 = 0.08$) and the phase factor also did not show significant differences (F (1, 28) = 2.1; $p = 0.09$, $\eta^2 = 0.09$). The results revealed again a significant effect of the interaction group x phases (F (1, 28) = 30.56; $p < 0.01$, $\eta^2 = 0.09$). This significant interaction indicates that P300 latency was lower in the post-test phase than in the pre-test phase only for PD patients with anodal tDCS. Post-hoc analysis was conducted

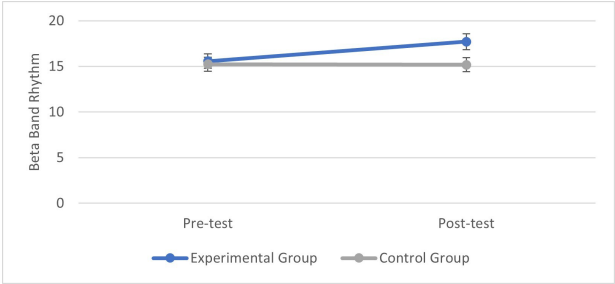

Fig. 2. Beta band rhythms in the pre- and post-test phases for the experimental and sham groups. Plots show mean and whiskers show standard deviation.

separately for the two groups. With reference to PD patients with anodal tDCS, paired *t*-tests showed statistical differences in P300 (t (14) = 4.23, $p < 0.001$, d = 0.84), while this was not seen in the sham group. An independent *t*-test was also applied to analyze the post-test means of the two groups (t (28) = 4.56, $p < 0.001$, d = 0.81). These results indicated that sham tDCS did not significantly change measures of P300 latency in the post-test phase.

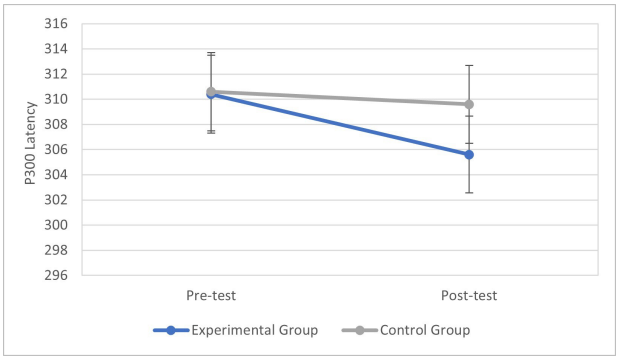

Fig. 3. P300 latency in the pre- and post-test phases for the experimental and sham groups. Plots show mean and whiskers show standard deviation.

Fig. 4 shows comparisons of the absolute spectral power in central electrodes between the experimental and sham groups. There were significant differences in the spectral power in the alpha and beta band rhythms between the pre- and post-test phases (respectively, 8–14 Hz, F = 8.23, $p < 0.01$; 14–30 Hz, F = 6.83, $p < 0.01$).

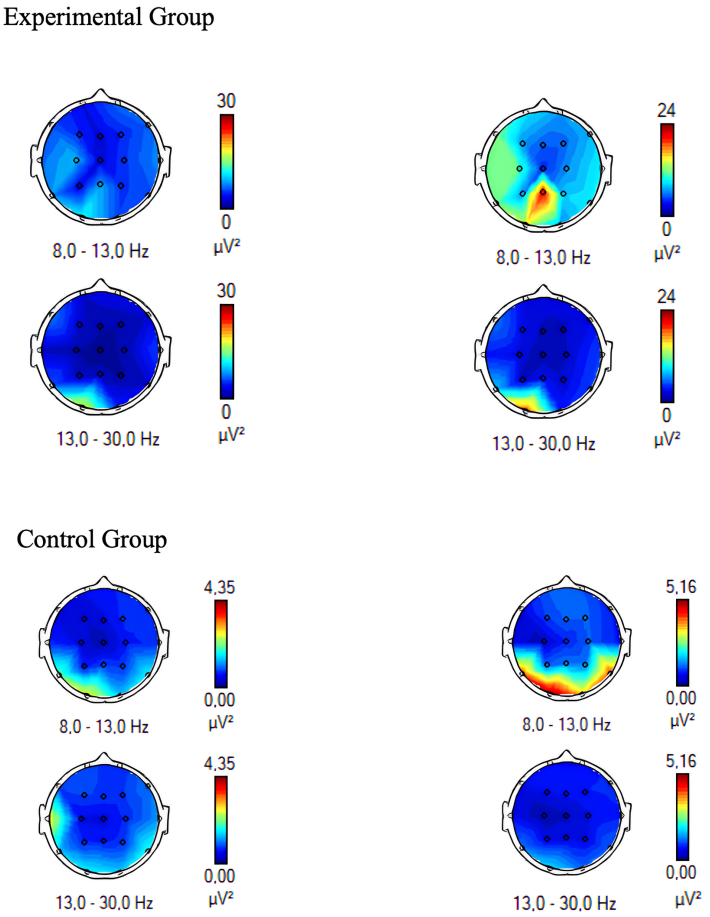

Fig. 4. Spectral power difference and grand average of spectral power across all sensors in the pre- and post-test phases.

4. Discussion

The present study aimed to investigate the effects of anodal tDCS on the left frontotemporal cortex in patients with PD, focusing on the analysis of neurophysiological functions through EEG. The focus was on evaluating ERPs and alpha and beta brain frequencies as indicators of possible changes in brain activity. The overarching goal was to enhance the understanding of how tDCS could influence these aspects in patients with PD-MCI.

Summarizing our results, alpha and beta band rhythms, as well as spectral power, were higher in the post-test phase compared with the pre-test phase for PD patients with anodal tDCS. P300 latency was lower in the post-test phase than in the pre-test phase, specifically for PD patients with anodal tDCS.

The confirmation of the first hypothesis, which posited that patients undergoing tDCS would exhibit a significant reduction in the onset latency of the P300 event-related potential, aligns with the findings of a prior study conducted by Aksu *et al.* [64]. The consistency between our results and theirs contributes to the consolidation and expansion of current knowledge in this field. The second hypothesis, suggesting that patients undergoing tDCS would show a significant increase in the power spectrum of the alpha and beta bands, was also confirmed.

Through a comprehensive analysis of the neurophysiological functions involved, this research makes a significant contribution to expanding our understanding of the potential effects of tDCS in the context of PD treatment. Furthermore, it provides essential insights for designing new investigative paths aimed at optimizing therapeutic strategies for PD patients with mild cognitive impairment. Numerous studies, including those by Hadoush *et al.* [65] and Fregni *et al.* [66], have explored the effects of stimulating the DLPFC in PD, primarily focusing on the cognitive domain. Our findings, which show a reduction in P300 latency and improved cognitive functioning in PD patients following anodal tDCS over the left DLPFC, are consistent with these studies. This suggests a coherent pattern of cognitive improvement associated with DLPFC tDCS. Studies concentrating on stimulating the primary motor cortex (M1), such as those by Lu *et al.* [67] and Pol *et al.* [68], have predominantly investigated motor improvements in PD patients. Although our study primarily assessed cognitive outcomes, the observed cognitive enhancements with anodal

tDCS align with the motor improvements reported in these studies. This indicates a potential dual impact of tDCS on both cognitive and motor functions in PD.

With reference to cerebellar tDCS in PD, its role in balance and motor control has been examined in studies conducted by Lu *et al*. [67] and Pol *et al*. [68]. Although our study did not specifically concentrate on balance control, the observed increase in alpha and beta band rhythms aligns with findings from studies targeting the cerebellum. This resonance suggests a broader impact of tDCS on neural modulation, further supporting the potential multifaceted effects of tDCS in PD. However, the severity of clinical symptoms measured by the UPDRS were not related to the empowerment of neurophysiological measures; in fact, the UPDRS scores does not predict the differences between the pre and post-test measures.

The observed changes in P300 latency and alpha and beta band rhythms could reflect neuroplasticity [95–99]. If these changes are sustained over time, they might have positive long-term effects on patients' cognitive and motor abilities. Moreover, the reduction in P300 latency suggests that patients may experience an improvement in cognitive processing speed and responsiveness [100,101]. PD often leads to cognitive deficits, including slowed processing and attention difficulties [102]. By enhancing cognitive processing, patients might find it easier to engage in daily activities, communicate, and maintain mental clarity [103]. Therefore, a shorter P300 latency could indicate an improvement in attention and the ability to identify relevant stimuli more rapidly [104,105]. This improvement could translate into better focus, concentration, and attention control for individuals with PD, thereby aiding in tasks that require sustained attention. Conversely, an increase in alpha and beta band rhythms could be associated with motor symptoms [106,107]. Studies investigating this association have reported conflicting results. While some have suggested that an increase in beta was associated with the presence of motor symptoms, others have proposed that an increase in beta was associated with the improvement of these symptoms [108–110]. Furthermore, it has been emphasized that the positive or negative nature of this association is linked to the specific symptoms considered [111]. While in the advanced stages of PD, excessive activity in the beta band is well-documented and correlated with motor symptoms [112,113], early-stage PD, characterized by mild cognitive deficits, shows baseline levels of activity in the beta band. In fact, our sample showed an increase in baseline beta band levels only after tDCS. Taken together, the results of this research provide interesting insights into the effect of tDCS on alpha and beta band rhythms in the early stages of PD-MCI.

The integrated approach that combined tDCS with the analysis of neurophysiological parameters, such as ERPs and alpha and beta brain rhythms, constitutes one of the significant strengths that emerged from this research. As emphasized, these parameters represent objective measures of cognitive functioning. Other positive aspects include the exclusive use of tDCS, without the combination of other treatments that could influence the attribution of observed improvements. Additionally, a comparison was conducted with a sham group, which received a tDCS simulation, in order to exclude possible placebo-related effects.

It should be noted that this study has some limitations. Among these is the small sample size, the absence of long-term follow-up to assess the persistence of effects over time, and the absence of a post-treatment UPDRS assessment. The assessment of the tolerability of stimulation was carried out through the collection of direct feedback from participants. While this approach provided us with specific and qualitative information, we acknowledge that the use of a standardized scale could have offered more structured and comparative data [114,115]. We acknowledge the importance of examining P300 amplitude as well as P300 latency, and future research should address this issue. It would be advisable for future studies to involve larger clinical trials, following standardized protocols and including long-term assessments, to establish the duration of the observed effects in patients with mild cognitive decline associated with PD.

5. Conclusions

The current research provides evidence of the efficacy of tDCS on crucial neurophysiological parameters, such as P300 brain response latency and alpha and beta frequency rhythms, in individuals exhibiting PD-MCI. Our results can be summarized in the following key points: (a) tDCS demonstrates a significant effect in reducing P300 response latency and (b) tDCS induces a significant increase in alpha and beta band rhythms.

Availability of Data and Materials

The data and materials are available upon request.

Author Contributions

RAF, RS & AG conceived and designed this research. RAF, RS & AG conducted the experiments and led statistical. RAF& RS wrote the manuscript, revised manuscript, and supervised the project. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Madonna della Consolazione Polyclinic Nursing Home (process approval number prot. 2021-198). Prior to participating in the study, each participant was provided

with detailed information about the study's purpose and data collection procedures. This information was presented clearly and comprehensibly so that participants could make an informed decision about their participation. After receiving these explanations, each participant have provided their informed consent in written form.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Cherian A, K P D, Vijayaraghavan A. Parkinson's disease - genetic cause. Current Opinion in Neurology. 2023; 36: 292–301.

[2] Ortega Moreno L, Bagues A, Martínez V, Abalo R. New Pieces for an Old Puzzle: Approaching Parkinson's Disease from Translatable Animal Models, Gut Microbiota Modulation, and Lipidomics. Nutrients. 2023; 15: 2775.

[3] Weintraub D, Aarsland D, Chaudhuri KR, Dobkin RD, Leentjens AF, Rodriguez-Violante M, *et al*. The neuropsychiatry of Parkinson's disease: advances and challenges. The Lancet. Neurology. 2022; 21: 89–102.

[4] Chopade P, Chopade N, Zhao Z, Mitragotri S, Liao R, Chandran Suja V. Alzheimer's and Parkinson's disease therapies in the clinic. Bioengineering & Translational Medicine. 2022; 8: e10367.

[5] Gopinath A, Mackie PM, Phan LT, Tansey MG, Khoshbouei H. The complex role of inflammation and gliotransmitters in Parkinson's disease. Neurobiology of Disease. 2023; 176: 105940.

[6] Moustafa AA, Chakravarthy S, Phillips JR, Gupta A, Keri S, Polner B, *et al*. Motor symptoms in Parkinson's disease: A unified framework. Neuroscience and Biobehavioral Reviews. 2016; 68: 727–740.

[7] Weil RS, Costantini AA, Schrag AE. Mild Cognitive Impairment in Parkinson's Disease-What Is It? Current Neurology and Neuroscience Reports. 2018; 18: 17.

[8] Wojtala J, Heber IA, Neuser P, Heller J, Kalbe E, Rehberg SP, *et al*. Cognitive decline in Parkinson's disease: the impact of the motor phenotype on cognition. Journal of Neurology, Neurosurgery, and Psychiatry. 2019; 90: 171–179.

[9] Cammisuli DM, Cignoni F, Ceravolo R, Bonuccelli U, Castelnuovo G. Transcranial Direct Current Stimulation (tDCS) as a Useful Rehabilitation Strategy to Improve Cognition in Patients With Alzheimer's Disease and Parkinson's Disease: An Updated Systematic Review of Randomized Controlled Trials. Frontiers in Neurology. 2022; 12: 798191.

[10] Hoogland J, van Wanrooij LL, Boel JA, Goldman JG, Stebbins GT, Dalrymple-Alford JC, *et al*. Detecting Mild Cognitive Deficits in Parkinson's Disease: Comparison of Neuropsychological Tests. Movement Disorders. 2018; 33: 1750–1759.

[11] Cammisuli DM, Cammisuli SM, Fusi J, Franzoni F, Pruneti C. Parkinson's Disease-Mild Cognitive Impairment (PD-MCI): A Useful Summary of Update Knowledge. Frontiers in Aging Neuroscience. 2019; 11: 303.

[12] Jellinger KA. Morphological basis of Parkinson disease-associated cognitive impairment: an update. Journal of Neural Transmission. 2022; 129: 977–999.

[13] Yang J, Pourzinal D, Byrne GJ, McMahon KL, Copland DA, O'Sullivan JD, *et al*. Global assessment, cognitive profile, and characteristics of mild cognitive impairment in Parkinson's disease. International Journal of Geriatric Psychiatry. 2023; 38: e5955.

[14] Mishra RK, Thrasher AT. Effect of concurrent transcranial direct current stimulation on instrumented timed up and go task performance in people with Parkinson's disease: A double-blind and cross-over study. Journal of Clinical Neuroscience. 2022; 100: 184–191.

[15] Tsuboi T, Satake Y, Hiraga K, Yokoi K, Hattori M, Suzuki M, *et al*. Effects of MAO-B inhibitors on non-motor symptoms and quality of life in Parkinson's disease: A systematic review. NPJ Parkinson's Disease. 2022; 8: 75.

[16] Poewe W, Mahlknecht P. Pharmacologic Treatment of Motor Symptoms Associated with Parkinson Disease. Neurologic Clinics. 2020; 38: 255–267.

[17] Zeuner KE, Schäffer E, Hopfner F, Brüggemann N, Berg D. Progress of Pharmacological Approaches in Parkinson's Disease. Clinical Pharmacology and Therapeutics. 2019; 105: 1106–1120.

[18] Sun C, Armstrong MJ. Treatment of Parkinson's Disease with Cognitive Impairment: Current Approaches and Future Directions. Behavioral Sciences. 2021; 11: 54.

[19] Schneider JS, Kortagere S. Current concepts in treating mild cognitive impairment in Parkinson's disease. Neuropharmacology. 2022; 203: 108880.

[20] Broeder S, Vandendoorent B, Hermans P, Nackaerts E, Verheyden G, Meesen R, *et al*. Transcranial direct current stimulation enhances motor learning in Parkinson's disease: a randomized controlled trial. Journal of Neurology. 2023; 270: 3442–3450.

[21] Gangemi A, Caprí T, Fabio RA, Puggioni P, Falzone AM, Martino G. Transcranial direct current stimulation (tDCS) and cognitive empowerment for the functional recovery of diseases with chronic impairment and genetic etiopathogenesis. Advances in Genetic Research. 2018; 18: 179–196.

[22] Şirin TC, Aksu S, Kurt A, Karamursel S, Baykan B. Efficacy and mechanisms of transcranial electrical stimulation in headache disorders. Neurological Sciences and Neurophysiology. 2019; 36: 57–68.

[23] Firouzi M, Baetens K, Swinnen E, Baeken C, Van Overwalle F, Deroost N. Does transcranial direct current stimulation of the primary motor cortex improve implicit motor sequence learning in Parkinson's disease? Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation. 2023; 16: 8.

[24] Fabio RA, Gangemi A, Capri T, Budden S, Falzone A. Neurophysiological and cognitive effects of Transcranial Direct Current Stimulation in three girls with Rett Syndrome with chronic language impairments. Research in Developmental Disabilities. 2018; 76: 76–87.

[25] Caulfield KA, Indahlastari A, Nissim NR, Lopez JW, Fleischmann HH, Woods AJ, *et al*. Electric Field Strength From Prefrontal Transcranial Direct Current Stimulation Determines Degree of Working Memory Response: A Potential Application of Reverse-Calculation Modeling? Neuromodulation. 2022; 25: 578–587.

[26] Majdi A, van Boekholdt L, Sadigh-Eteghad S, Mc Laughlin M. A systematic review and meta-analysis of transcranial direct-current stimulation effects on cognitive function in patients with Alzheimer's disease. Molecular Psychiatry. 2022; 27: 2000–2009.

[27] Ko MH, Yoon JY, Jo YJ, Son MN, Kim DS, Kim GW, *et al*. Home-Based Transcranial Direct Current Stimulation to Enhance Cognition in Stroke: Randomized Controlled Trial. Stroke. 2022; 53: 2992–3001.

[28] Beretta VS, Santos PCR, Orcioli-Silva D, Zampier VC, Vitório R, Gobbi LTB. Transcranial direct current stimulation for balance rehabilitation in neurological disorders: A systematic review and meta-analysis. Ageing Research Reviews. 2022; 81: 101736.
[29] Rezaei B, Khorrami Banaraki A, Yadegari F, Mazdeh M. Comparison of the Effect of Four Transcranial Direct Current Stimulation Configurations on Picture-Naming Improvement in Non-Fluent Aphasia: A Randomized Clinical Trial. Iranian Journal of Medical Sciences. 2023; 48: 292–301.
[30] Damercheli S, Ramne M, Ortiz-Catalan M. Transcranial direct current stimulation (tDCS) for the treatment and investigation of phantom limb pain (PLP). Psychoradiology. 2022; 2: 23–31.
[31] Ghanavati E, Salehinejad MA, De Melo L, Nitsche MA, Kuo MF. NMDA receptor–related mechanisms of dopaminergic modulation of tDCS-induced neuroplasticity. Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation. 2023; 16: 405.
[32] Gangemi A, Colombo B, Fabio RA. Effects of short- and long-term neurostimulation (tDCS) on Alzheimer's disease patients: two randomized studies. Aging Clinical and Experimental Research. 2021; 33: 383–390.
[33] Kumpf U, Palm U, Eder J, Ezim H, Stadler M, Burkhardt G, *et al*. TDCS at home for depressive disorders: an updated systematic review and lessons learned from a prematurely terminated randomized controlled pilot study. European Archives of Psychiatry and Clinical Neuroscience. 2023; 273: 1403–1420.
[34] Day P, Twiddy J, Dubljević V. Present and emerging ethical issues with tDCS use: A summary and review. Neuroethics. 2023; 16: 1.
[35] Beumer S, Boon P, Klooster DCW, van Ee R, Carrette E, Paulides MM, *et al*. Personalized tDCS for Focal Epilepsy-A Narrative Review: A Data-Driven Workflow Based on Imaging and EEG Data. Brain Sciences. 2022; 12: 610.
[36] Corominas-Teruel X, Mozo RMSS, Simó MF, Colomina Fosch MT, Valero-Cabré A. Transcranial direct current stimulation for gait recovery following stroke: A systematic review of current literature and beyond. Frontiers in Neurology. 2022; 13: 953939.
[37] Sanches C, Amzallag F, Dubois B, Lévy R, Truong DQ, Bikson M, *et al*. Evaluation of the effect of transcranial direct current stimulation on language impairments in the behavioural variant of frontotemporal dementia. Brain Communications. 2022; 4: fcac050.
[38] Licata AE, Zhao Y, Herrmann O, Hillis AE, Desmond J, Onyike C, *et al*. Sex differences in effects of tDCS and language treatments on brain functional connectivity in primary progressive aphasia. NeuroImage. Clinical. 2023; 37: 103329.
[39] DaSilva AF, Datta A, Swami J, Kim DJ, Patil PG, Bikson M. The Concept, Development, and Application of a Home-Based High-Definition tDCS for Bilateral Motor Cortex Modulation in Migraine and Pain. Frontiers in Pain Research. 2022; 3: 798056.
[40] Hu Y, Jia Y, Sun Y, Ding Y, Huang Z, Liu C, *et al*. Efficacy and safety of simultaneous rTMS-tDCS over bilateral angular gyrus on neuropsychiatric symptoms in patients with moderate Alzheimer's disease: A prospective, randomized, sham-controlled pilot study. Brain Stimulation. 2022; 15: 1530–1537.
[41] Daniel AA, De Souza S. Safety of repeated neuromodulation by transcranial direct current stimulation (tDCS) in dementia: A narrative review. European Psychiatry. 2023; 66: S248.
[42] Turnbull A, Anthony M, Tadin D, Porsteinsson AP, Heffner K, Lin FV. Effect of online tDCS to left somatomotor cortex on neuropsychiatric symptoms among older adults at risk for dementia. Cortex. 2023; 159: 131–141.
[43] Garcia S, Nalven M, Ault A, Eskenazi MA. tDCS as a treatment for anxiety and related cognitive deficits. International Journal of Psychophysiology. 2020; 158: 172–177.
[44] Beheshti I, Ko JH. Modulating brain networks associated with cognitive deficits in Parkinson's disease. Molecular Medicine. 2021; 27: 24.
[45] Murphy K, Khan A, Bachu A, Tampi R. Treatment of behavioral and psychological symptoms of dementia using transcranial magnetic stimulation: a systematic review. International Psychogeriatrics. 2023; 35: 611–622.
[46] Tseng PT, Chen YW, Zeng BY, Zeng BS, Hung CM, Sun CK, *et al*. The beneficial effect on cognition of noninvasive brain stimulation intervention in patients with dementia: a network meta-analysis of randomized controlled trials. Alzheimer's Research & Therapy. 2023; 15: 20.
[47] Cruz Gonzalez P, Fong KNK, Chung RCK, Ting KH, Law LLF, Brown T. Can Transcranial Direct-Current Stimulation Alone or Combined With Cognitive Training Be Used as a Clinical Intervention to Improve Cognitive Functioning in Persons With Mild Cognitive Impairment and Dementia? A Systematic Review and Meta-Analysis. Frontiers in Human Neuroscience. 2018; 12: 416.
[48] Biundo R, Weis L, Antonini A. Cognitive decline in Parkinson's disease: the complex picture. NPJ Parkinson's Disease. 2016; 2: 16018.
[49] Baroni A, Magro G, Martinuzzi C, Brondi L, Masiero S, Milani G, *et al*. Combined effects of cerebellar tDCS and task-oriented circuit training in people with multiple sclerosis: A pilot randomized control trial. Restorative Neurology and Neuroscience. 2022; 40: 85–95.
[50] Chow AMD, Shin J, Wang H, Kellawan JM, Pereira HM. Influence of Transcranial Direct Current Stimulation Dosage and Associated Therapy on Motor Recovery Post-stroke: A Systematic Review and Meta-Analysis. Frontiers in Aging Neuroscience. 2022; 14: 821915.
[51] Jung J, Salazar Fajardo JC, Kim S, Kim B, Oh S, Yoon B. Effect of tDCS Combined With Physical Training on Physical Performance in a Healthy Population. Research Quarterly for Exercise and Sport. 2023; 1–8.
[52] Andrade SM, Machado DGDS, Silva-Sauerc LD, Regis CT, Mendes CKTT, de Araújo JSS, *et al*. Effects of multisite anodal transcranial direct current stimulation combined with cognitive stimulation in patients with Alzheimer's disease and its neurophysiological correlates: A double-blind randomized clinical trial. Neurophysiologie Clinique. 2022; 52: 117–127.
[53] Talar K, Vetrovsky T, van Haren M, Négyesi J, Granacher U, Váczi M, *et al*. The effects of aerobic exercise and transcranial direct current stimulation on cognitive function in older adults with and without cognitive impairment: A systematic review and meta-analysis. Ageing Research Reviews. 2022; 81: 101738.
[54] Ulrichsen KM, Kolskår KK, Richard G, Pedersen ML, Alnaes D, Dørum ES, *et al*. No add-on effect of tDCS on fatigue and depression in chronic stroke patients: A randomized sham-controlled trial combining tDCS with computerized cognitive training. Brain and Behavior. 2022; 12: e2643.
[55] Westwood SJ, Criaud M, Lam SL, Lukito S, Wallace-Hanlon S, Kowalczyk OS, *et al*. Transcranial direct current stimulation (tDCS) combined with cognitive training in adolescent boys with ADHD: a double-blind, randomised, sham-controlled trial. Psychological Medicine. 2023; 53: 497–512.
[56] Seer C, Lange F, Georgiev D, Jahanshahi M, Kopp B. Event-related potentials and cognition in Parkinson's disease: An integrative review. Neuroscience and Biobehavioral Reviews. 2016; 71: 691–714.
[57] Singh A, Cole RC, Espinoza AI, Brown D, Cavanagh JF, Narayanan NS. Frontal theta and beta oscillations during lower-limb movement in Parkinson's disease. Clinical Neurophysiology. 2020; 131: 694–702.

[58] Davis NJ, Tomlinson SP, Morgan HM. The role of β-frequency neural oscillations in motor control. The Journal of Neuroscience. 2012; 32: 403–404.
[59] Hammond C, Bergman H, Brown P. Pathological synchronization in Parkinson's disease: networks, models and treatments. Trends in Neurosciences. 2007; 30: 357–364.
[60] Olde Dubbelink KTE, Stoffers D, Deijen JB, Twisk JWR, Stam CJ, Berendse HW. Cognitive decline in Parkinson's disease is associated with slowing of resting-state brain activity: a longitudinal study. Neurobiology of Aging. 2013; 34: 408–418.
[61] Kim M, Kwak YB, Lee TY, Kwon JS. Modulation of Electrophysiology by Transcranial Direct Current Stimulation in Psychiatric Disorders: A Systematic Review. Psychiatry Investigation. 2018; 15: 434–444.
[62] Emonson MRL, Fitzgerald PB, Rogasch NC, Hoy KE. Neurobiological effects of transcranial direct current stimulation in younger adults, older adults and mild cognitive impairment. Neuropsychologia. 2019; 125: 51–61.
[63] Gu J, Li D, Li Z, Guo Y, Qian F, Wang Y, *et al*. The Effect and Mechanism of Transcranial Direct Current Stimulation on Episodic Memory in Patients With Mild Cognitive Impairment. Frontiers in Neuroscience. 2022; 16: 811403.
[64] Aksu S, Uslu A, İşçen P, Tülay EE, Barham H, Soyata AZ, *et al*. Does transcranial direct current stimulation enhance cognitive performance in Parkinson's disease mild cognitive impairment? An event-related potentials and neuropsychological assessment study. Neurological Sciences. 2022; 43: 4029–4044.
[65] Hadoush H, Al-Sharman A, Khalil H, Banihani SA, Al-Jarrah M. Sleep Quality, Depression, and Quality of Life After Bilateral Anodal Transcranial Direct Current Stimulation in Patients with Parkinson's Disease. Medical Science Monitor Basic Research. 2018; 24: 198–205.
[66] Fregni F, Boggio PS, Santos MC, Lima M, Vieira AL, Rigonatti SP, *et al*. Noninvasive cortical stimulation with transcranial direct current stimulation in Parkinson's disease. Movement Disorders. 2006; 21: 1693–1702.
[67] Lu C, Amundsen Huffmaster SL, Tuite PJ, MacKinnon CD. The effects of anodal tDCS over the supplementary motor area on gait initiation in Parkinson's disease with freezing of gait: a pilot study. Journal of Neurology. 2018; 265: 2023–2032.
[68] Pol F, Salehinejad MA, Baharlouei H, Nitsche MA. The effects of transcranial direct current stimulation on gait in patients with Parkinson's disease: a systematic review. Translational Neurodegeneration. 2021; 10: 22.
[69] Nitsche MA, Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. The Journal of Physiology. 2000; 527 Pt 3: 633–639.
[70] Kuo MF, Paulus W, Nitsche MA. Boosting focally-induced brain plasticity by dopamine. Cerebral Cortex. 2008; 18: 648–651.
[71] Zaehle T, Rach S, Herrmann CS. Transcranial alternating current stimulation enhances individual alpha activity in human EEG. PLoS ONE. 2010; 5: e13766.
[72] Dubreuil-Vall L, Chau P, Ruffini G, Widge AS, Camprodon JA. tDCS to the left DLPFC modulates cognitive and physiological correlates of executive function in a state-dependent manner. Brain Stimulation. 2019; 12: 1456–1463.
[73] Karton I, Bachmann T. Disrupting dorsolateral prefrontal cortex by rTMS reduces the P300 based marker of deception. Brain and Behavior. 2017; 7: e00656.
[74] Lu H, Li J, Zhang L, Meng L, Ning Y, Jiang T. Pinpointing the precise stimulation targets for brain rehabilitation in early-stage Parkinson's disease. BMC Neuroscience. 2023; 24: 24.
[75] Asgarinejad M, Saviz M, Sadjadi SM, Saliminia S, Kakaei A, Esmaeili P, *et al*. Effectiveness of Repetitive Transcranial Magnetic Stimulation (rTMS) on DLPFC for Enhancing Cognitive Function in Healthy Adults: A Review. SSRN. 2023. (preprint)
[76] Austgen G, Marsh L. Cognitive dysfunction and neuropsychiatric aspects of Parkinson's disease. Progress in Brain Research. 2022; 269: 59–90.
[77] Jiang S, Zhan C, He P, Feng S, Gao Y, Zhao J, *et al*. Neuronavigated repetitive transcranial magnetic stimulation improves depression, anxiety and motor symptoms in Parkinson's disease. Heliyon. 2023; 9: e18364.
[78] de Oliveira PCA, de Araújo TAB, Machado DGDS, Rodrigues AC, Bikson M, Andrade SM, *et al*. Transcranial Direct Current Stimulation on Parkinson's Disease: Systematic Review and Meta-Analysis. Frontiers in Neurology. 2022; 12: 794784.
[79] Wong PL, Yang YR, Tang SC, Huang SF, Wang RY. Comparing different montages of transcranial direct current stimulation on dual-task walking and cortical activity in chronic stroke: double-blinded randomized controlled trial. BMC Neurology. 2022; 22: 119.
[80] Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. Journal of Neurology, Neurosurgery, and Psychiatry. 1992; 55: 181–184.
[81] Racette BA, Rundle M, Parsian A, Perlmutter JS. Evaluation of a screening questionnaire for genetic studies of Parkinson's disease. American Journal of Medical Genetics. 1999; 88: 539–543.
[82] Litvan I, Goldman JG, Tröster AI, Schmand BA, Weintraub D, Petersen RC, *et al*. Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. Movement Disorders. 2012; 27: 349–356.
[83] Uysal-Cantürk P, Hanağası HA, Bilgiç B, Gürvit H, Emre M. An assessment of Movement Disorder Society Task Force diagnostic criteria for mild cognitive impairment in Parkinson's disease. European Journal of Neurology. 2018; 25: 148–153.
[84] Foley JA, Dore C, Cipolotti L. Correspondence between MMSE and detailed neuropsychological testing in Parkinson's disease. Neuropsychologist. 2022; 13: 9–14.
[85] Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research. 1975; 12: 189–198.
[86] Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. The Unified Parkinson's Disease Rating Scale (UPDRS): status and recommendations. Movement Disorders. 2003; 18: 738–750.
[87] Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology. 1967; 17: 427–442.
[88] Jasper HH, Radmussen T. Studies of clinical and electrical responses to deep temporal stimulation in men with some considerations of functional anatomy. Research Publications - Association for Research in Nervous and Mental Disease. 1958; 36: 316–334.
[89] Fjell AM, Walhovd KB. Life-span changes in P3a. Psychophysiology. 2004; 41: 575–583.
[90] Fabio RA, Gangemi A, Semino M, Vignoli A, Canevini MP, Priori A, *et al*. Effects of Combined Transcranial Direct Current Stimulation with Cognitive Training in Girls with Rett Syndrome. Brain Sciences. 2020; 10: 276.
[91] Welch P. The use of fast Fourier transforms for the estimation of power spectra: A method based on time averaging over short, modified periodograms. IEEE Transactions on Audio and Electroacoustics. 1967; 15: 70–73.
[92] Rektorova I, Sedlackova S, Telecka S, Hlubocky A, Rektor I. Dorsolateral prefrontal cortex: a possible target for modulating dyskinesias in Parkinson's disease by repetitive transcranial magnetic stimulation. International Journal of Biomedical Imaging. 2008; 2008: 372125.
[93] Lattari E, Costa SS, Campos C, de Oliveira AJ, Machado S,

Maranhao Neto GA. Can transcranial direct current stimulation on the dorsolateral prefrontal cortex improves balance and functional mobility in Parkinson's disease? Neuroscience Letters. 2017; 636: 165–169.
[94] Workman CD, Fietsam AC, Uc EY, Rudroff T. Cerebellar Transcranial Direct Current Stimulation in People with Parkinson's Disease: A Pilot Study. Brain Sciences. 2020; 10: 96.
[95] Bayram MB, Suviseshamuthu ES, Plow EB, Forrest GF, Yue GH. Aging-induced alterations in EEG spectral power associated with graded force motor tasks. Experimental Brain Research. 2023; 241: 905–915.
[96] Sciacca G, Mostile G, Disilvestro I, Donzuso G, Nicoletti A, Zappia M. Long-Duration Response to Levodopa, Motor Learning, and Neuroplasticity in Early Parkinson's Disease. Movement Disorders. 2023; 38: 626–635.
[97] Tapper A, Staines WR, Niechwiej-Szwedo E. EEG reveals deficits in sensory gating and cognitive processing in asymptomatic adults with a history of concussion. Brain Injury. 2022; 36: 1266–1279.
[98] Suarez-García DMA, Grisales-Cárdenas JS, Zimerman M, Cardona JF. Transcranial Direct Current Stimulation to Enhance Cognitive Impairment in Parkinson's Disease: A Systematic Review and Meta-Analysis. Frontiers in Neurology. 2020; 11: 597955.
[99] Liu X, Liu H, Liu Z, Rao J, Wang J, Wang P, *et al*. Transcranial Direct Current Stimulation for Parkinson's Disease: A Systematic Review and Meta-Analysis. Frontiers in Aging Neuroscience. 2021; 13: 746797.
[100] Firouzi M, Van Herk K, Kerckhofs E, Swinnen E, Baeken C, Van Overwalle F, *et al*. Transcranial direct-current stimulation enhances implicit motor sequence learning in persons with Parkinson's disease with mild cognitive impairment. Journal of Neuropsychology. 2021; 15: 363–378.
[101] Lima NC, Kirov R, de Almondes KM. Impairment of executive functions due to sleep alterations: An integrative review on the use of P300. Frontiers in Neuroscience. 2022; 16: 906492.
[102] Aarsland D, Batzu L, Halliday GM, Geurtsen GJ, Ballard C, Ray Chaudhuri K, *et al*. Parkinson disease-associated cognitive impairment. Nature Reviews. Disease Primers. 2021; 7: 47.
[103] Baiano C, Barone P, Trojano L, Santangelo G. Prevalence and clinical aspects of mild cognitive impairment in Parkinson's disease: A meta-analysis. Movement Disorders. 2020; 35: 45–54.
[104] Herzog ND, Steinfath TP, Tarrasch R. Critical Dynamics in Spontaneous Resting-State Oscillations Are Associated With the Attention-Related P300 ERP in a Go/Nogo Task. Frontiers in Neuroscience. 2021; 15: 632922.
[105] Seçen Yazıcı M, Serdengeçti N, Dikmen M, Koyuncu Z, Sandıkçı B, Arslan B, *et al*. Evaluation of p300 and spectral resolution in children with attention deficit hyperactivity disorder and specific learning disorder. Psychiatry Research. Neuroimaging. 2023; 334: 111688.
[106] McAuliffe D, Hirabayashi K, Adamek JH, Luo Y, Crocetti D, Pillai AS, *et al*. Increased mirror overflow movements in ADHD are associated with altered EEG alpha/beta band desynchronization. The European Journal of Neuroscience. 2020; 51: 1815–1826.
[107] Athanasiou A, Klados MA, Styliadis C, Foroglou N, Polyzoidis K, Bamidis PD. Investigating the Role of Alpha and Beta Rhythms in Functional Motor Networks. Neuroscience. 2018; 378: 54–70.
[108] Michmizos KP, Frangou P, Stathis P, Sakas D, Nikita KS. Beta-band frequency peaks inside the subthalamic nucleus as a biomarker for motor improvement after deep brain stimulation in Parkinson's disease. IEEE Journal of Biomedical and Health Informatics. 2015; 19: 174–180.
[109] Schwerdt HN, Amemori K, Gibson DJ, Stanwicks LL, Yoshida T, Bichot NP, *et al*. Dopamine and beta-band oscillations differentially link to striatal value and motor control. Science Advances. 2020; 6: eabb9226.
[110] van Rheede JJ, Feldmann LK, Busch JL, Fleming JE, Mathiopoulou V, Denison T, *et al*. Diurnal modulation of subthalamic beta oscillatory power in Parkinson's disease patients during deep brain stimulation. NPJ Parkinson's Disease. 2022; 8: 88.
[111] Boon LI, Hillebrand A, Potters WV, de Bie RMA, Prent N, Bot M, *et al*. Motor effects of deep brain stimulation correlate with increased functional connectivity in Parkinson's disease: An MEG study. NeuroImage. Clinical. 2020; 26: 102225.
[112] Donoghue T, Voytek B. Automated meta-analysis of the event-related potential (ERP) literature. Scientific Reports. 2022; 12: 1867.
[113] Chen L, Oei TP, Zhou R. The cognitive control mechanism of improving emotion regulation: A high-definition tDCS and ERP study. Journal of Affective Disorders. 2023; 332: 19–28.
[114] Aparício LVM, Guarienti F, Razza LB, Carvalho AF, Fregni F, Brunoni AR. A Systematic Review on the Acceptability and Tolerability of Transcranial Direct Current Stimulation Treatment in Neuropsychiatry Trials. Brain Stimulation. 2016; 9: 671–681.
[115] Workman CD, Fietsam AC, Rudroff T. Tolerability and Blinding of Transcranial Direct Current Stimulation in People with Parkinson's Disease: A Critical Review. Brain Sciences. 2020; 10: 467.