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Exploring the Therapeutic Effects of Noninvasive Brain Stimulation on Motor Function, Cognition, and Quality of Life in Parkinson's Disease: A Systematic Review

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ABSTRACT

Background: Parkinson's Disease (PD) significantly impacts both cognition and quality of life, posing a substantial burden on patients and healthcare systems. However, there is hope on the horizon. Noninvasive brain stimulation (NIBS) has emerged as a potential therapeutic intervention with the power to mitigate these effects. While the evidence regarding its efficacy remains fragmented, the potential it holds is promising. Objective: The present review explores the effects of noninvasive brain stimulation on cognition and quality of life in patients with Parkinson's disease (PD). Methods: A comprehensive search was carried out in electronic databases to find pertinent articles on noninvasive brain stimulation, such as Transcranial direct stimulation (tDCS) and Transcranial Magnetic Stimulation (TMS), in patients with PD. The methodological quality of the included studies was checked using the PEDro scale. Results: A total of 11 studies were finally included in the studies published between 2012 and 2023. Results indicated that a complex relationship exists between cognition and noninvasive brain stimulation. Additionally, possible therapeutic benefits apart from cognition were identified when examining the quality of life in patients with PD. Conclusion: The present review highlights the complex relationship between quality of life and cognitive functioning. In addition, it summarizes the studies performed on noninvasive brain stimulation in PD. These therapies also proved potent in improving general well-being and cognitive domains. More research is needed to determine the best procedures and interventions with suitable therapeutic outcomes.

Keywords: Cognition, Brain stimulation, Parkinson's disease.

INTRODUCTION

Parkinson's Disease (PD) is a major challenge in the context of neurodegenerative illness affecting millions of people worldwide [1]. It is a progressive condition that results in motor symptoms such as bradykinesia, tremors, stiffness, and complex non-motor signs that significantly impair cognitive function and quality of life [2]. The pursuit of novel therapeutic approaches for PD has led to the increased exploration of noninvasive techniques as potential treatments [3]. Techniques such as Transcranial Direct current stimulation (TDS or tDCS) and Transcranial Magnetic Stimulation (TMS) gave patients with PD an innovative way of treatment for both physical and cognitive symptoms as they can change the activity in the brain without medications [4]. tDCS is a viable method for studying noninvasive brain stimulation techniques for a range of neurological symptoms, including PD [5]. A variety of motor and non-motor

symptoms are caused by PD, which is characterized by the gradual destruction of dopaminergic neurons in the substantia nigra [6]. Using tDCS for PD aims to change brain activity and potentially lessen the symptoms of illness [7].

tDCS involves the application of a low electrical current to the scalp, which modulates neuronal excitability [8]. The electrical current affects neurons' resting membrane potential, affecting the probability of action potential firing. [9]. The objective in relation to PD is to modify the neural circuits responsible for motor control and potentially alleviate non-motor symptoms by adjusting cortical excitability. [10]. Studies have investigated how tDCS affects motor symptoms such as stiffness and bradykinesia. [11,12]. On targeting motor area stimulation via tDCS, cortical excitability is increased with the possibility of improving motor function, from mild cognitive impairment to dementia, which is frequently linked to PD [13]. Previous studies investigated how tDCS affected potential cognitive functions, focusing on memory, attention, and executive functioning. [14,15]. tDCS holds promise as a noninvasive therapeutic modality for addressing both motor and non-motor symptoms in PD [16]. Researchers continue improving their knowledge of its mechanism of action, ideal stimulation levels, and long-term consequences. The addition of tDCS to patients with PD all-encompassing therapy opens up new avenues for enhancing their functional results and the quality of life as it develops [17].

TMS and tACS also gained popularity as noninvasive brain stimulation among patients with PD [18]. TMS provides a method for regulating neuronal activity by using electromagnetic induction to create electric currents in particular brain regions. In the realm of PD [19]. Studies on TMS have looked up it as a possible therapeutic intervention for both motor and non-motor disorders. [20,21]. Studies on TMS have investigated its effects on bradykinesia, tremor, or stiffness, among other motor symptoms. [22,23]. TMS seeks to modify the neural circuits responsible for motor control by focusing on the motor cortex, which may lessen symptoms related to dopaminergic dysfunction that characterizes PD [24]. In patients with PD, TMS can be utilized to measure and adjust cortical excitability. [25]. By focusing on particular regions involved in executive functions, attention, and memory, TMS can modify cognitive functions [23]. To better understand the therapeutic landscape of noninvasive brain stimulation in PD, this systematic review concentrates on how it may improve the general quality of life and cognitive harmony in people with PD. After an in-depth examination of the literature, the present review aims to clarify the current understanding, pinpoint areas of more investigation, and provide perspectives on the opportunities and difficulties posed by these novel approaches.

Detailed examination of studies that investigate how noninvasive brain stimulation affects motor symptoms, cognitive functions, and overall quality of life in patients with PD. The authors have unraveled the complexities in patients with PD and how these approaches are useful additions to the therapeutic function of noninvasive brain stimulation. By summarizing evidence from different studies, this review gives physicians, researchers, and policymakers a thorough picture of the state of noninvasive brain stimulation in PD.

METHODS

Registration

The current systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [26]. The review was registered in the International Prospective Registry of Systematic Reviews (PROSPERO) with CRD42024531872.

Selection Criteria

Inclusion Criteria:

1. Studies focusing on noninvasive brain stimulation as a treatment strategy in PD, 2. Studies exploring how noninvasive brain stimulation affects cognition and quality of life in patients with PD, 3. Randomized controlled or clinical trials were included 4. Studies which involved participants diagnosed with PD with standard diagnostic criteria, 5. Research articles written in English.

Exclusion Criteria:

1. Studies unrelated to noninvasive brain stimulation as a treatment strategy in PD, 2. Studies that do not focus on the effects of noninvasive brain stimulation on cognition and quality of life in patients with PD, 3. Studies with no significant findings or metrics of cognition and quality of life, 4. Research articles such as editorials, reviews, and viewpoints. These inclusion and exclusion criteria were used to make high-quality findings offering insightful information about the state of noninvasive brain stimulation therapy for PD, focusing on quality of life and cognition.

Types of Participants

Studies incorporated individuals above 40 years of age or older who had received a diagnosis through clinical Assessment or clinical definition. Participants were included regardless of their medication use, length of illness, presence of motor fluctuations, and length of treatment or degree of initial impairment.

Types of Interventions

The authors compared noninvasive stimulation techniques with any type of placebo or control intervention, such as sham tDCS or no intervention. The application of direct current to the brain for more than a minute was referred to as active tDCS and TMS. On the other hand, tDCS shams were described as brief, direct current stimulations that lasted under a minute.

Types of Outcome Measures

The primary outcomes encompassed the following criteria:

- Assessment of impairment/disability using the Unified Parkinson's Disease Rating Scale (UPDRS).
- Reduction in off time, denoting periods when medication does not control symptoms.
- Reduction in on-time with dyskinesia, indicating instances where symptoms are under control but involuntary muscle movements persist. We presented the primary outcome measures after the intervention phase and if data permitted, at least three months after the conclusion of said intervention phase.
    - Parkinson's Disease Quality of Life Questionnaire-39 (PDQ-39),
    - Montreal Cognitive Assessment (MoCA)
    - Hoehn and Yahr Criteria

The secondary outcomes comprised the following aspects such as specific assessments of impairment, Timed evaluations of gait, Measurements of stride length and cadence, Evaluation of bradykinesia in the upper extremity, assessment of the health-related quality of life, with

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potential outcome measures including safety and acceptability, dropout rates, occurrence of adverse events, encompassing instances of death from any cause.

Search Strategy

The search focused on key terms related to noninvasive brain stimulation techniques, including TMS and tDCS, in conjunction with Parkinson's disease, cognition, and quality of life. The search was conducted across major medical databases such as PubMed/MEDLINE, PEDro, Scopus, Embase, and Cochrane Library from 2012 to 2023. The inclusion criteria encompassed studies examining the therapeutic impact of noninvasive brain stimulation on cognitive function and quality of life in Parkinson's Disease. The search also extended to grey literature sources and Google Scholar. The strategy aimed to unveil a comprehensive understanding of the therapeutic landscape, incorporating a systematic review methodology to analyze and synthesize the available evidence. In addition, continuous monitoring and hand-searching of references were undertaken to ensure the retrieval of relevant and up-to-date studies.

Selection of Studies

Initially, titles and abstracts from records identified through electronic searches were screened to eliminate references that did not align with the predetermined inclusion criteria. Subsequently, the full-text versions of the remaining studies were retrieved. assessment of the relevance of these studies for inclusion based on predefined criteria related to study types, participants, and intervention aims, was carried out.

Data Extraction and Management

Checklists were employed to extract data on various aspects systematically, and the details were presented in the 'Characteristics of Included Studies' table. The aspects covered included methods of random sequence generation, allocation concealment methods, blinding of assessors, utilization of intention-to-treat (ITT) analysis, reporting of adverse effects and dropouts, notable differences in prognostic factors, participant details (country, number, age, gender, Parkinson's disease stage as per Hoehn and Yahr criteria at entry, 'on'/'off' state of dopaminergic medication, inclusion/exclusion criteria), comparison details (interventions in treatment and control groups, treatment duration, co-interventions in study groups), outcomes, and time points of measurement. Additionally, data on initial functional ability and initial function level were extracted and meticulously presented for each included study in a detailed table.

Assessment of Risk of Bias

The risk of bias was evaluated for the included trials per the guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions and Review Manager ver. 5.4. The assessment involved categorizing the risk of bias as either 'low,' 'high,' or 'unclear' for various domains, including random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, selective outcome reporting, incomplete outcome data, and other potential sources of bias. The Risk of bias is shown in figure 2.

Challenges Related to The Unit of Analysis

Both phases of randomized crossover trials were examined. In cases where the same study incorporated sham or active control groups exploring identical content, these groups were

combined into a unified entity for each (for instance, if the study utilized two sham control groups, we merged them to create a single group for comparison with the intervention group).

Data Synthesis

A random-effects model without consideration for the degree of heterogeneity was employed. Consequently, even in situations of heterogeneity, the conditions of a random-effects model approach were applied to avoid violations of the assumptions associated with a fixed-effects model.

Methodological Quality Assessment

The quality of evidence was evaluated utilizing the grading system developed by the Grading of Recommendations, Assessments, Development, and Evaluation (GRADE) collaboration. Employing the methodology outlined by the GRADE Working Group, the quality of the evidence assessment through a transparent framework that considered factors such as research design, implementation, imprecision, inconsistency, indirectness, and reporting bias. To facilitate the GRADE assessment process, the GRADE profiler software was utilized. A 'summary of findings' table was generated to articulate the quality of evidence for the primary comparison, specifically 'transcranial direct current stimulation (tDCS) versus sham tDCS.' In cases where reporting data for more than seven outcomes was necessary, we prioritized the outcomes with the highest significance in the 'Summary of findings' table, irrespective of data availability.

Sensitivity Analysis

A sensitivity analysis was conducted concerning the risk of bias in the included studies to evaluate the robustness of our findings. The strategy involved assessing the impact of studies that either inadequately stated or did not employ proper methods for (1) generating the randomization schedule, (2) ensuring allocation concealment, and (3) utilizing an intention-to-treat analysis.

RESULTS

From produced searches, a total of 4420 distinct records were initially identified. Following screening titles and abstracts, 4167 records we excluded and obtained the full text of the remaining 53 articles. After applying the search strategy and implementing inclusion and exclusion criteria, a thorough assessment led to conclude that 11 studies aligned with the inclusion criteria for the review. The flow of references is visually presented in Figure 1.

A study focused on a single session tDCS's immediate effects on PD's cognitive performance. The results of a Wilcoxon signed-ranks test revealed that there was no significant difference in the ability to detect changes in the Visual Working Memory (VWM) task, as measured by d-prime, between anodal tDCS and sham stimulation (P = .80). This suggests that the performance of the VWM task did not show an immediate impact with tDCS. For the go/no-go test, the mean reaction time (RT) did not significantly differ between the two conditions (P = .87), and the mean accuracy, around 82%, also exhibited no significant distinction between tDCS and sham stimulation (P = .78) [5]. ANOVA results indicated a significant Stimulation × Moment interaction for simple reaction time ($F_{1,19} = 5.248$; P = .034). The Stimulation × Moment interaction approached statistical significance for choice reaction time ($F_{1,19} = 3.711$; P = .069). Post hoc tests revealed that participants only decreased simple (P = .004, SRM = −0.73) and choice reaction times (P = .019, SRM = −0.57) after the aerobic exercise + active-tDCS session.

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In contrast, for the aerobic exercise + sham-tDCS session, no significant differences between pre-intervention and post-intervention assessments were observed for simple (P = .612, SRM = 0.11) or choice reaction times (P = .865, SRM = −0.04). ANOVA further indicated a moment's main effect for the Montreal Cognitive Assessment (MoCA) score (F1,19 = 8.779, P = .008), Trail Making Test part A (F1,19 = 37.156, P < .001), and Trail Making Test part B (F1,13 = 10.423, P = .007). Participants increased MoCA scores and reduced the time to complete Trail Making Test parts A and B after both intervention sessions [27].

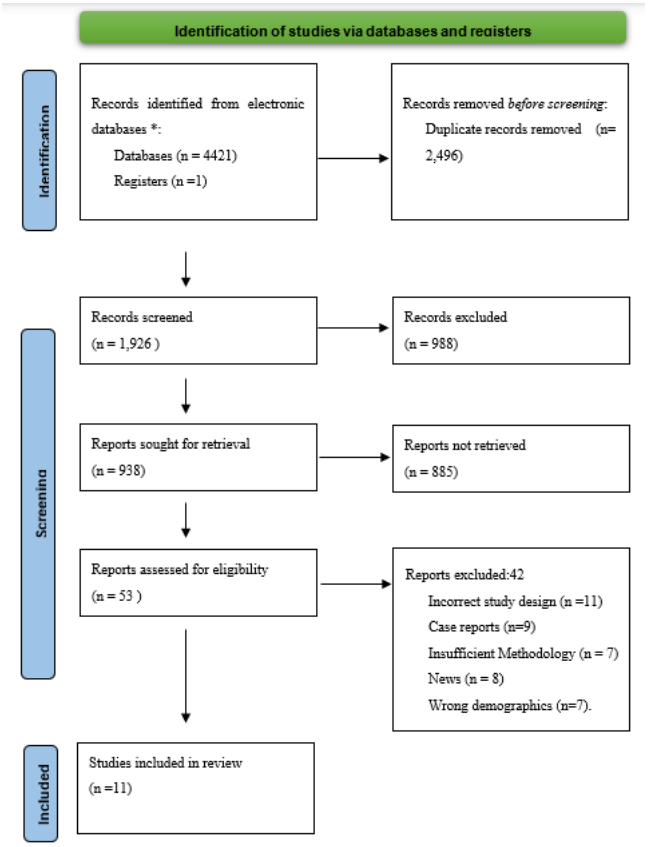

Figure 1: PRISMA Flow diagram of study selection in review.

The tDCS intervention employed in a study demonstrated improved walking speed and increased step length for patients with Parkinson's disease at 2, 4, and 8 weeks post-intervention. Only 5.7% of participants from groups 1 and 2 (2 out of 35) reported transient burning pain at the electrode attachment sites, a known occurrence that resolved spontaneously over time. Notably, no serious or severe adverse effects were observed with tDCS, distinguishing it from deep brain stimulation, which carries risks such as intracranial hemorrhage, cerebritis, seizures, and other surgery-related complications [28,29].

Compared to other brain stimulation techniques, tDCS stands out for its lower incidence of complications. The mechanisms and technical aspects of various brain stimulation methods, noting the absence of a definitive protocol for tDCS. A current intensity of 0.5 to 2 mA for approximately 20 minutes is commonly used, although the optimal number of sessions remains undefined. These findings affirm that tDCS, delivered through the scalp, can enhance the activity of motor neurons in the brain, promoting improved neural modulation and plasticity. The

physiological mechanism involves the penetration of tDCS deep into the cortex, effectively reaching specific neural networks like the cortico-subthalamic projection, which is crucial for motor coordination. The application of tDCS has the potential to calibrate and enhance neuronal networking, even in advanced stages of PD characterized by cortical and basal ganglion dysfunctions [28,30].

In individuals with PD, challenges in gait performance during dual tasks are exacerbated due to disease-related deficits and motor-cognitive interference. It is known that dual tasking imposes a cost on both healthy adults and people with PD. Previous research has suggested that tDCS can mitigate dual-task costs in young, healthy adults and independently enhance motor and cognitive processing in individuals with PD. Although the bi-hemispheric tDCS protocol did not significantly improve dual-task gait performance in a previous study, it did reduce the dual-task cost following active tDCS in our PD participants under dual-task conditions. This implies that a single session of bi-hemispheric tDCS seems to diminish the dual-task cost during gait, particularly in the presence of more complex secondary tasks. The ability to concurrently focus on both gait and a complex secondary task is associated with freezing of gait in individuals with PD and an increased risk of falls in those with cognitive impairment [31–33]. Patients with PD exhibited clinical motor improvement in the segmental Unified Parkinson's Disease Rating Scale (UPDRS III) hemibody sub-score related to the right-hand tasks (items 22–25) following active stimulation (post1), and this improvement persisted for at least 30 minutes (post2). The analysis using a 3×2 repeated-measures ANOVA on this score, considering the factors' session' [pre, post1, post2] and 'condition' [verum; sham], revealed significant results for 'condition' [$F=5.884$, $p=.038$], 'session' [$F=14.270$, $p < .001$], and 'condition*session' [$F=11.292$, $p=.004$]. Post-hoc analysis, incorporating Bonferroni correction, indicated a significant difference in the verum condition between 'pre vs. post1' ($t=4.801$, $p=.001$) and 'pre vs. post2' ($t=7.236$, $p=.000$). Conversely, in the sham condition, no significant difference was observed between 'pre vs. post1' ($t=1.105$, $p=.298$) and 'pre vs. post2' ($t=0.669$, $p=.520$). Although there was a marginal reduction in mean UPDRS III scores in the sham condition over time, it did not reach statistical significance. Furthermore, when comparing the effect of sham condition [sham_post2 – sham_pre] with the effect of verum condition [verum_post2 – verum_pre], a significant difference was found [sham (post2-pre) vs. verum (post2-pre): confidence interval [0.80548–4.19452], $t=3.337$, $p=.009$ (paired t-test)]. This suggests that the observed effect in the verum condition cannot be attributed to the slight difference between the pre and post2 sessions in the sham condition. Notably, the pre-stimulation baseline scores for sham and verum did not differ significantly [verum_pre vs. sham_pre: $t=-0.152$, $p=.882$ (paired t-test)] [11,31]. The demographic characteristics and detailed summary of included studies are shown in Tables 1 and 2.

Table 1: Demographic details of the included studies.

Author (Year)	Country	Study design	Total Patients	Mean Age (Years)
Joana B. Pereira et al (2013)	Spain	Randomized controlled trial	16	61.5 ±9.9
Pattarapol Yotnuengnit et al (2017)	Thailand	Experimental, double-blinded, randomized controlled trial	60	tDCS group= 64.4 ±7.8 Combination group = 68.2±9.8 PT group= 62.7±8.8
Alessandra Del Felice et al (2019)	Italy	Controlled cross-over clinical trial	20	45.14±14
Chad Swank et al. (2016)	United States	Randomized controlled trial	10	68.7 ± 10.2

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Anna Schoellmann et al (2019)	Germany	double-blind, randomized, sham-controlled trial	17	64.3 ± 11.4
Si-a Lee et al (2021)	Korea	Randomized controlled trial	30	EG = 12.07±3.71 CG = 13.47±1.77
Eduardo Lattari et al (2016)	Brazil	Randomized controlled trial	17	69.18 ± 9.98
Núbia Ribeiro Conceição et al (2021)	Brazil	randomized, double-blinded, sham-controlled crossover study	20	70.80 ± 7.87
Chi-ieong Lau et al (2019)	Taiwan	Randomized controlled trial	10	62.7 ± 6.6
Rosa Manenti et al (2018)	Italy	Randomized, placebo-controlled trial	22	StDCS plus Computerized Cognitive Training = 63.8±7.1 AtDCS plus Computerized Cognitive Training = 65.5±6.4
Yea-Ru Yang et al (2012)	Taiwan	Randomized controlled trial	20	EG= 65.20 ± 11.08 CG= 67.00 ± 13.21

Abbreviations: EG = Experimental Group, CG = Control Group, StDCS = Sham TDCS, AtDCS = Active tDCS

Table 2: Main findings from the studies included in the review

Author (Year)	Objective	Intervention	Outcome measures	Conclusion
Joana B. Pereira et al (2013)	Examine variations in the impacts generated by tDCS when applied to frontal and temporo-parietal areas on functional networks related to phonemic and semantic fluency in individuals with PD.	Participants underwent tDCS targeting the left dorsolateral prefrontal cortex (DLPFC) and left temporo-parietal cortex (TPC) in a counterbalanced order. Immediately after the stimulation, patients engaged in a verbal fluency paradigm within an fMRI scanner. Alterations caused by tDCS in the activation and deactivation patterns of task-related networks were examined using free-model independent component analyses (ICA).	UPDRS (Unified Parkinson's disease rating Scale), MMSE (Mini-mental state examination), GDS (Geriatric depression scale)	These results offer support for the notion that tDCS targeted at specific brain regions brings about alterations in large-scale functional networks, which form the basis for behavioral effects. This suggests the potential utility of tDCS in improving phonemic fluency in individuals with PD.
Pattarapol Yotnuengnit et al (2017)	The collective impact of tDCS and physical therapy on the walking ability of individuals diagnosed with PD.	In Group 1 (tDCS), participants underwent treatment involving solely anodal tDCS. Group 2 (combination) received a combined intervention consisting of anodal tDCS followed by physical therapy. Group 3 (PT) underwent a treatment regimen involving sham tDCS followed by physical therapy.	Walking speed, UPDRS	Either anodal tDCS or physical therapy alone, as well as their combination, can be employed as treatments to enhance the walking speed of patients with PDs. The observed effects persisted for around 8 weeks. However, the combined treatment did not demonstrate superiority over the individual use of either tDCS or physical therapy.
Alessandra Del Felice et al (2019)	The efficacy of personalized tACS combined with physical therapy in the treatment of motor and cognitive	The frequency and electrode position for tACS were personalized for each participant by comparing their EEG power spectra maps with normative data from our laboratory. The	UPDRS-III, EEG	Customized tACS in Parkinson's disease (PD) leads to enhancements in both motor and cognitive performance. These improvements are linked

	symptoms in patients with pd.	stimulation frequency was determined based on the EEG band exhibiting higher power spectra; specifically, when beta excess was observed on the EEG map, tACS was set at 4 Hz, and when theta excess was present, tACS was set at 30 Hz.		to a decrease in excessive fast EEG oscillations.
Chad Swank et al (2016)	The impact of a bilateral tDCS protocol on dual-task gait in individuals with PD.	Patients with PD underwent two sessions of a tDCS protocol, with one being active and the other sham, spaced seven days apart. The assignment of tDCS protocols was randomized, and participants were kept unaware of whether they were receiving the active or sham treatment. Following each tDCS session, participants engaged in both single and dual-task gait assessments. The tDCS intervention consisted of a single 20-minute session targeting the dorsolateral prefrontal cortex, with the left side as the anode and the right side as the cathode, applying a 2 mA current, while one session involved sham stimulation.	UPDRS, Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).	The bilateral tDCS protocol applied to individuals with PD did not result in a significant enhancement in dual-task gait. Nevertheless, there was a reduction in dual-task cost following tDCS, especially notable in the presence of a cognitive distractor. To draw more definitive conclusions about the effectiveness of our bilateral tDCS approach, a larger sample size is necessary.
Anna Schoellmann et al 2019	The impact of tDCS targeting the left sensorimotor area on clinical motor outcomes, fine motor performance of the right hand, and cortical activity and synchronization in the high beta range.	Examined patients with idiopathic PD and eleven appropriately matched healthy controls (HC) across two days while performing an isometric precision grip task and during rest. This evaluation took place both before and after administering 'verum' and 'sham' anodal tDCS sessions, each lasting 20 minutes with 1 mA intensity, using an anode at C3 and a cathode at Fp2. The assessment encompassed clinical outcomes, fine motor performance, and the analysis of both cortical frequency domain activity and corticocortical imaginary coherence.	EEG, UPDRS-III	Actual tDCS influenced the cortical network associated with PD, particularly during the integration of fine motor skills. In general, cortical oscillatory features in PD were not universally dysregulated but rather contingent upon motor processing.
Si-a Lee et al (2021)	The impact of tDCS on motor function, balance, and gait ability in individuals diagnosed with PD.	Visual cueing training was administered to both groups, with the experimental group receiving tDCS during visual training, and the control group undergoing sham tDCS concurrently with visual	UPDRS, Freezing of Gait Questionnaire (FOG-Q), Functional Gait Assessment (FGA)	Administering tDCS to the supplementary motor area in patients with Parkinson's disease proves beneficial as a supplementary intervention for the

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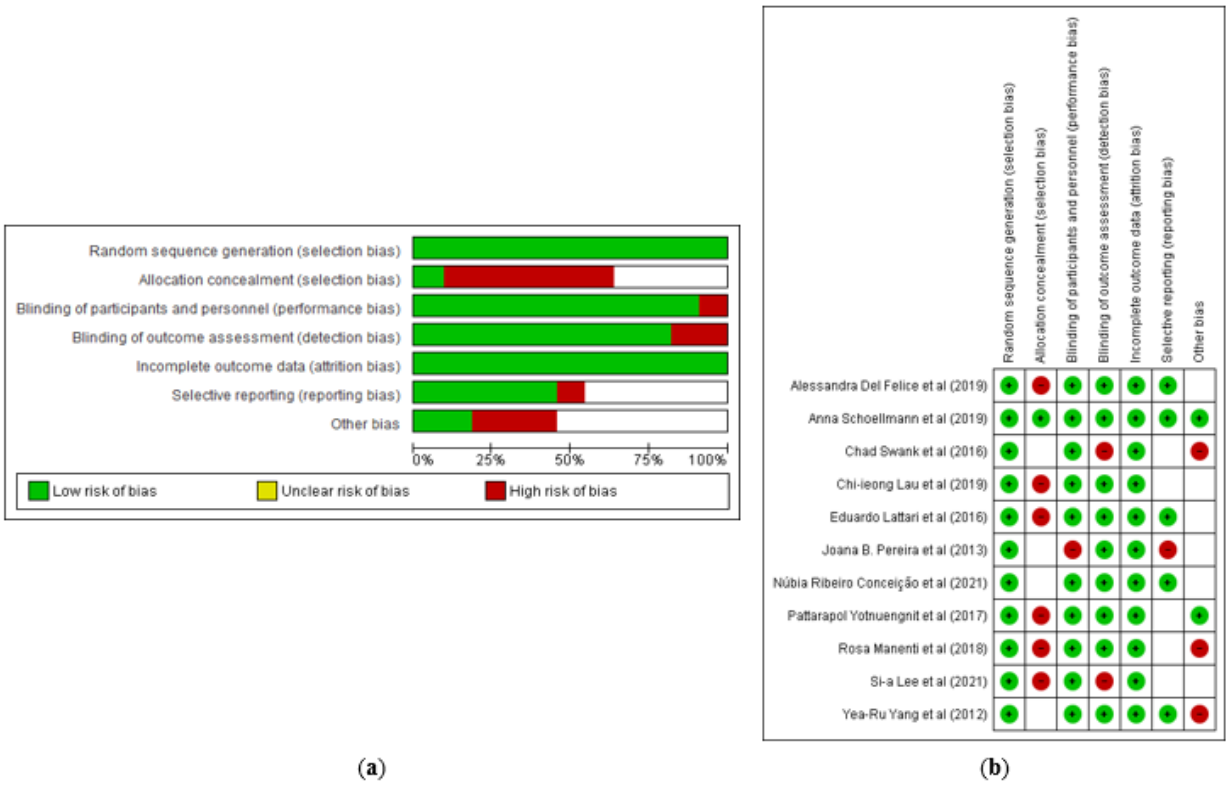
		training. All participants underwent pre-testing before the initial intervention, post-testing upon completing the entire 4-week intervention.		rehabilitation training of individuals with PD.
Eduardo Lattari et al (2016)	Investigating the impact of tDCS on the left dorsolateral prefrontal cortex (DLPFC) on the balance and functional mobility of individuals diagnosed with PD.	The anodal a-tDCS condition focused on the left DLPC, electrode position F3 and was administered for 20 minutes with a current intensity of 2 mA. In the sham-tDCS condition, the electrode position was maintained, but the stimulator was deactivated after 30 seconds.	Berg balance scale (BBS), The Dynamic Gait Index (DGI), Timed Upand Go (TUG)	Application of anodal-tDCS to the left DLPFC results in enhanced balance and functional mobility compared to sham-tDCS. The positive effects on functional mobility and balance observed with a-tDCS on the DLPFC may be attributed to the augmentation of compensatory mechanisms supporting motor function in individuals with PD.
Núbia Ribeiro Conceição et al (2021)	Impact of incorporating anodal tDCS over the prefrontal cortex (PFC) into a session of aerobic exercise on gait, cognition, and PFC activity during walking in individuals diagnosed with PD.	Participants engaged in two 30-minute sessions of moderate-intensity aerobic exercise (cycling) paired with distinct tDCS conditions—active or sham tDCS—separated by a week. Anodal tDCS was applied, with a magnitude of 2 mA for 20 minutes in the active-tDCS condition and 10 seconds in the sham-tDCS condition, targeting the PFC in the hemisphere more affected by PD. Evaluation of spatiotemporal gait parameters, cognitive functions, and PFC activity during walking occurred before and immediately after each session.	UPDRS-III, Montreal Cognitive Assessment (MoCA), fNIRS system (OctaMon fNIRS system, Artinis Medical Systems, Netherlands)	Incorporating anodal tDCS over the PFC into a session of aerobic exercise resulted in immediate favorable outcomes on gait variability, processing speed, and executive control of walking in individuals with PD.
Chi-ieong Lau et al (2019)	To investigate the immediate impact of a single session of tDCS on cognitive performance in individuals with PD.	patients with pds underwent two sessions in a counterbalanced sequence, experiencing 20 minutes of either 2 mA anodal tDCS or sham tDCS applied over the left dorsolateral prefrontal cortex (DLPFC). Concurrently, they engaged in visual working memory and go/no-go tasks during the stimulation.	Go/no-go test, UPDRS-III, Visual working memory (VWM),	A solitary session of tDCS does not yield improvements in visual working memory and inhibitory control in individuals with PD.
Rosa Manenti et al (2018)	To explore the impact of applying tDCS in conjunction with computerized cognitive training on cognitive functions and mood	Twenty-twopatients with pds were randomly allocated to two groups: one receiving active tDCS along with CCT, and the other receiving sham tDCS plus CCT. Each participant underwent a two-	Trail Making Test, Test of Attentional Performance, Stroop Test, Frontal Assessment Battery - FAB), Beck Depression	The combination of active tDCS and cognitive training proves to be an effective strategy for addressing mood and cognitive impairments in PD.

	disruptions among individuals diagnosed with PD.	week intervention involving daily 25-minute sessions of tDCS during CCT, which specifically targeted functions associated with the prefrontal cortex.	Inventory-II (BDI-II), Parkinson's Disease Quality of Life Questionnaire-39 (PDQ-39),	
Yea-Ru Yang et al (2012)	Examine the impact of high-frequency rTMS succeeded by treadmill training on cortical inhibition and locomotor function in individuals diagnosed with PD.	Study participants were subjected repetitive rTMS in the experimental group or sham rTMS in the control group, followed by a 30-minute treadmill training for a total of 12 sessions spanning over 4 weeks. The application of repetitive TMS involved a 5-Hz frequency targeting the leg area of the motor cortex contralateral to the more affected side, and each session lasted for 6 minutes.	EMG Timed up and go test	The amalgamation of rTMS and treadmill training amplifies the impact of treadmill training on the modulation of corticomotor inhibition and the enhancement of walking performance in individuals diagnosed PD.



(a) (b)

Figure 2: Risk of bias: (a) Risk of bias graph; (b) Risk of bias summary.

DISCUSSION

The systematic review undertaken in this study explores and synthesizes existing evidence on the therapeutic potential of noninvasive brain stimulation in the context of PD. The discussion of the findings provides valuable insights into the intersection of cognition and quality of life, shedding light on the broader therapeutic landscape for individuals with PD. The systematic review's findings contribute significantly to understanding the effects of noninvasive brain stimulation techniques on cognitive functions and overall quality of life in patients with PD. A

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complex picture regarding the therapeutic potential of tDCS is provided by an in-depth examination of pertinent studies, which highlights the impact of these interventions on subjective well-being and cognitive function among individuals with PD.

Cognitive Performance Analysis

Several significant findings are presented on the rapid impact of a single session of tDCS on cognitive performance in patients with PD. The influence on the VWM task, the go/no-go test, and pertinent metrics like accuracy and reaction time were all examined in the review's cognitive domain. Analyzing the VWM task with d-prime as a parameter showed no discernible difference between sham stimulation and anodal tDCS. This suggests the performance of VWM tasks using tDCS [5]. Similarly, there were no significant variations in the mean reaction times or accuracy between the two circumstances according to go/no-go test results. These results imply that cognitive performance in visual memory and reaction inhibition tasks may not be considerably affected, at least not after a single tDCS session. In a study, an interesting, intriguing element was noted when aerobic exercise was mixed with active tDCS and sham tDCS sessions. In this context, participants showed choice and single reaction time changes after active tDCS + aerobic exercise sessions, indicating a potential connection between tDCS and exercise in modulating motor responses [5,32]. The prospect of noninvasive brain stimulation to favorably affect cognitive functioning in patients with PD is one of the major findings of the present review [33]. Integrating findings from multiple trials suggests that tDCS improves certain areas of the cognitive domain, which could impact day-to-day functioning and general quality of life. This discovery is especially noteworthy considering the frequency of note-worthy deficits in PD and the consequent influence on the capacity to carry out routine tasks [34,35].

Motor Symptom Improvement

The observed improvement in motor clinical symptoms of patients with PD, especially in hemibody subscores associated with tasks requiring the right hand, supports the potential therapeutic benefits of tDCS in treating motor-related difficulties. Furthermore, the lack of significant side effects highlights the tDCS safety profile and sets it apart from more intrusive brain stimulation techniques. The bi-hemispheric tDCS procedure did not significantly increase overall gait performance. However, it did simultaneously lower the cost of dual-task activities, particularly when more complex dual activities are involved. The significant finding suggests that the possibility of tDCS particularly affects the cognitive-motor interference associated with the difficulties in dual tasking usually encountered by patients with PD [36].

tDCS Cognitive-Motor Interactions

The comprehensive description highlights the complex ways that tDCS affects cognitive and motor abilities in PD, stressing the importance of taking task-specific and environmental factors into account when evaluating outcomes [37]. Beyond just improving motor skills, tDCS may also positively affect cognitive-motor interactions, as shown by decreased dual-task costs [38]. The intricate connections between cognitive and motor functions are shed in findings among patients with PD [39]. Furthermore, the discussion also identifies the directions for future research, such as studies into the long-term implications of repeated tDCS sessions, the best stimulation parameter used, and possible synergistic effects with non-pharmacological therapies like aerobic exercise. This forward-looking approach deepens our understanding of the multifaceted impact of tDCS in PD patients. This will provide important insights into

developing new interventional protocols that address various complex challenges encountered by patients with neurodegenerative disorders. Beyond motor symptoms, TMS has notable effects on cognitive abilities and the general quality of life for those with PD [40]. The present review adds to the growing evidence that TACS therapies have benefitted patients with PD, apart from motor-related effects, by improving cognitive functions and possibly elevating their subjective well-being.

Cognition and Quality Enhancement

Incorporating treadmill training with repetitive motion training (rTMS) has improved walking ability in people with PD via modulating corticomotor inhibition. This indicates that the use of rTMS in conjunction with treadmill training improves brain circuits that influence motor control, improving brain circuits that influence motor control and thus improving walking performance in patients with PD. These results highlight the combined effect of therapeutic intervention significance for treating motor deficits linked to PD and suggest that it may have synergistic effects [29]. Furthermore, the review also explores the gains in cognition and subsequent improvement in quality of life. The discussion highlights the need to consider the immediate cognitive effects of noninvasive brain stimulation and the wider implications for the well-being and functional independence of patients with PD by combining data from various studies. As Parkinson's progresses, challenges in maintaining social interactions, managing treatment side effects, and coping with reduced autonomy also impact QoL. Therapeutic interventions, like noninvasive brain stimulation, aim to improve motor function, cognition, and emotional well-being, ultimately enhancing overall life satisfaction and reducing disease-related distress [36]. This all-encompassing viewpoint is consistent with the growing understanding of how neurodegenerative diseases affect cognition and quality of life.

LIMITATIONS

The limitations of the evaluated study include heterogeneity in outcome measures, limited sample sizes, and differences in stimulation protocols. Further extensive, carefully controlled trials and standardized procedures are required to address the robustness of reported effects. Furthermore, the discussion prospects of conducting additional trials to investigate ideal stimulation levels, enduring impacts, and possible collaborations with additional medical procedures.

FUTURE RECOMMENDATIONS

Future research on noninvasive brain stimulation for PD should prioritize the standardization of procedures, including uniform stimulation parameters and outcome assessments, to improve comparability between trials. Determining lasting benefits requires long-term studies. Nuanced insights will guide personalized treatment options obtained from stratification based on the severity of the condition. Evidence can be strengthened by utilizing large-scale multicenter trials investigating underlying neurophysiological mechanisms and experimenting with combining approaches with multimodal approaches. A complete understanding of treatment's impact can be obtained using patient-centered outcomes and comprehensive quality-of-life indicators. Efforts need to be directed toward implementing effective interventions in clinical settings and providing tailored and efficient approaches to improve cognitive functions and quality of life in patients with PD.

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CONCLUSIONS

The systematic review concludes by offering a thorough synthesis of the available data on noninvasive stimulation in PD, emphasizing the treatment potential to improve cognition and quality of life. Knowledge of therapeutic settings for people with PD is deepened by the detailed discussion of the results and the understanding of limitations of potential directions for further investigation. The foundation for further research and interventions targeted at improving cognitive results and boosting the general well-being of patients with PD.

Conflict of Interest: Author declare no conflict of interest.

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