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Title: Effects of Transcranial Direct Current Stimulation on EEG Mean Frequency and Motor Recovery in Chronic Stroke: A Randomized Controlled Study

Authors: Maryam Zolghadr¹, Javad Sarrafzadeh^{1,*}, Shohreh Noorizadeh Dehkordi¹, Saeed Talebian², Marzieh Yassin¹, Hassan Haddadzade Niri³

1. *Rehabilitation Research Center, Department of Physical Therapy, School of Rehabilitation, Iran University of Medical Sciences, Tehran, Iran*
2. *Department of Physical Therapy, School of Rehabilitation, Tehran University of Medical Sciences, Tehran, Iran*
3. *Department of Audiology, School of Rehabilitation, Iran University of Medical Sciences, Tehran, Iran*

***Corresponding Author:** Javad Sarrafzadeh, Rehabilitation Research Center, Department of Physical Therapy, School of Rehabilitation, Iran University of Medical Sciences, Tehran, Iran.
Email: sarrafzadehjavadt@gmail.com

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Abstract

Objectives: This study aimed to investigate the effects of transcranial direct current stimulation (tDCs) on resting-state electroencephalography (EEG) mean frequency and motor recovery in patients with chronic stroke.

Methods: Thirty individuals with chronic stroke were randomly allocated to receive either real or sham anodal tDCs combined with task-oriented training (TOT). The real-tDCs group received 2 mA anodal stimulation over the motor cortex for 20 minutes per session, five times per week, for three weeks. EEG mean frequency and the Fugl-Meyer Assessment (FMA) of the upper extremity were used as the main and secondary outcomes, respectively.

Results: Both groups demonstrated a gradual reduction in EEG mean frequency over time, with a more pronounced decrease in the sham group. This difference was statistically significant only at follow-up ($P = 0.02$). The FMA scores improved significantly in both groups ($P < 0.001$), with a greater improvement trend in the real-tDCs group; however, intergroup differences were not significant.

Conclusion: Although the association between EEG mean frequency and motor performance remains inconclusive, these findings suggest that anodal tDCs may modulate cortical activity and support motor recovery in chronic stroke patients.

Keywords: *transcranial direct current stimulation; task-oriented training; EEG mean frequency; motor recovery; stroke; neurorehabilitation*

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Introduction

Transcranial direct current stimulation (tDCS) has been widely applied to modulate cerebral cortical function (Accornero, Capozza, Pieroni, 2014; Matsumoto, Fujiwara, Takahashi, 2010; Nitsche, Cohen, Wassermann, 2008; Nitsche & Paulus, 2011; Polanía, Paulus, & Nitsche, 2012; Stagg & Nitsche, 2011; Zaehle, Beretta, Jäncke, 2011). Following stroke, the use of tDCS as a non-invasive neuromodulatory technique has shown promising potential for enhancing motor recovery. Randomized controlled trials (RCTs) investigating the effects of tDCS applied over the primary motor cortex (M1) in combination with rehabilitation have demonstrated its safety and its capacity to prime the motor system and augment therapy-induced gains across different stages of stroke recovery, including the acute (1-7 days), subacute (>7 days to 3 months), and chronic (>6 months) phases (Accornero et al., 2014; Salazar, Feng, Bonilha, 2023).

Despite these encouraging findings, there is still no clear consensus regarding the effects of tDCS on neural tissue or the extent to which these effects depend on electrode montage and the functional status of participants (Accornero et al., 2014). Moreover, variability in stroke lesion characteristics, stimulation protocols, and outcome assessment methods has limited the clinical translation of tDCS. Multiple factors, including corticospinal tract integrity, the type of adjunct therapy, and stimulation timing and intensity, appear to influence motor recovery outcomes following tDCS in stroke populations (Hsu, Lu, Lin, 2023).

Electroencephalography (EEG) provides a valuable means of assessing cortical activity following electrical and magnetic stimulation, enabling the investigation of cortico-cortical interactions and motor cortical dynamics without reliance on sensory pathways, subcortical structures, or descending motor pathways. Consequently, EEG-based measures are not directly confounded by corticospinal tract integrity when evaluating cortical responses to tDCS (Clancy, 1988; Niedermeyer, 2004). Nevertheless, previous stroke rehabilitation studies have predominantly relied on clinical scales such as the Fugl-Meyer Assessment (FMA) or the Modified Ashworth Scale (MAS) as well as task- and time-based measures including the Jebsen-Taylor Hand Function Test to evaluate intervention effects.

Accumulating evidence suggests that neuroplastic processes often unfold over extended timeframes, ranging from weeks to months or even years (Kandel, Schwartz, Jessell, 2000). Accordingly, exclusive reliance on functional outcome measures may be insufficient for capturing early or evolving neuroplastic changes induced by interventions such as non-invasive brain stimulation or intensive task practice. This temporal mismatch underscores the importance of incorporating neurophysiological measures when evaluating treatment efficacy. In recent years, neurophysiological biomarkers have gained increasing attention for predicting and characterizing the effects of rehabilitation and neuromodulatory interventions. Within this context, EEG represents a robust tool for exploring how tDCS influences motor and cognitive cortical networks by providing standardized, quantitative, and neurophysiology-based indices of brain activity (Fanciullacci, Bertolucci, Lamola, 2017; Gandolfi, Formaggio, Geroi, 2018). Advances in signal

processing techniques have further enhanced the analytical value of EEG, enabling more refined characterization of neural dynamics through quantitative EEG (qEEG) methods (Kim, Yang, & Kim, 2023; Tong & Thankor, 2009). QEEG facilitates the extraction of meaningful spectral features from EEG recordings and may assist clinicians in characterizing patients' neurophysiological states during recovery (Sebastián-Romagosa, Udina, Ortner, 2020).

Building on previous work that evaluated changes in relative EEG spectral power (delta to gamma bands) before and after tDCS intervention in stroke patients (Zolghadr, 2024), the present study extends this line of investigation by addressing additional neurophysiological and clinical outcomes that have not yet been explored. While earlier analyses focused primarily on spectral power alterations, other markers such as EEG mean frequency and their relationship to functional recovery remain largely unexamined. Despite the growing interest in qEEG, only a limited number of studies have quantitatively investigated cortical responses to tDCS (Morales-Quezada, 2014; Schestatsky, 2013; Marceglia, 2016; Liu, 2023; Mane, 2018; Wang, 2022). Although abnormal EEG patterns are well documented in stroke populations (Zhang, 2013), no study to date has systematically examined changes in EEG mean frequency following stroke or explored their association with functional motor outcomes.

Therefore, the objective of the present study was to investigate changes in EEG mean frequency before, immediately after, and three months following intervention with anodal or sham tDCS combined with Task-Oriented Training (TOT) in patients with stroke, alongside functional recovery assessed using the Fugl-Meyer Assessment.

Method and Material

Thirty patients with chronic ischemic stroke and upper-extremity hemiparesis, aged between 18 and 80 years, were recruited from a neurologic physiotherapy center. Demographic and clinical characteristics of the participants are presented in Table 1.

Table 1: Demographic and clinical characteristics of participants

Group	Age (year)	BMI* (Kg/m ²)	Gender (M/F)	Handedness	Involved side	Months since the stroke attack	Brunnstrom stage (n)
Case	58.46	27.60	7 / 8	12 Right	7 Right	Mean: 39 months	Stage 4 (8)
	(±13.79)	(±3.36)		3 Left	8 Left		Stage 5 (6)
Control	63.26	26.90	10 / 5	13 Right	10 Right	Mean: 36 months	Stage 4 (7)
	(±8.72)	(±3.09)		2 Left	5 Left		Stage 5 (5)
							Stage 6 (3)

* BMI, Body Mass Index

This study was conducted as a double-blind, randomized, sham-controlled trial to investigate the effects of anodal transcranial direct current stimulation (tDCs) combined with task-oriented training (TOT) on motor recovery in patients with chronic stroke. Participant recruitment and data collection were carried out between February 2022 and January 2023. All participants provided written informed consent prior to enrollment. The study protocol was approved by the Ethics Committee of Iran University of Medical Sciences, Tehran, Iran (Ethics Code: IR.IUMS.REC.1400.1122), and all procedures were conducted in accordance with the Declaration of Helsinki.

Task-oriented training was selected as the rehabilitation framework based on previous evidence indicating that adjunct neuromodulation combined with task-oriented training, rather than simple joint exercises, is more effective in improving upper-extremity motor function (Hsu et al., 2023). Participants with chronic stroke-related hemiparesis were enrolled in a 3-week intervention program consisting of 15 sessions (5 sessions per week), consistent with prior rehabilitation protocols (Adeagbo, Olawale, & Gbiri, 2021; Bornheim, Croisier, Maquet, 2020; Timmermans, Spooren, Kingma, 2010).

Participants were randomly assigned to one of two groups: an intervention group receiving real-anodal tDCs combined with TOT (case group) or a control group receiving sham tDCs combined with TOT. Thus, the effects of real tDCs were specifically compared with task-oriented training under sham stimulation conditions. Relative power across EEG frequency bands was assessed at baseline, immediately after completion of the 15 intervention sessions (3 weeks), and at the 15-week follow-up from the start of the intervention. The primary outcome measure was EEG mean frequency, while the secondary outcome measure was the Upper-Extremity Fugl-Meyer Assessment (UE-FMA). The study flowchart is shown in Figure 1.

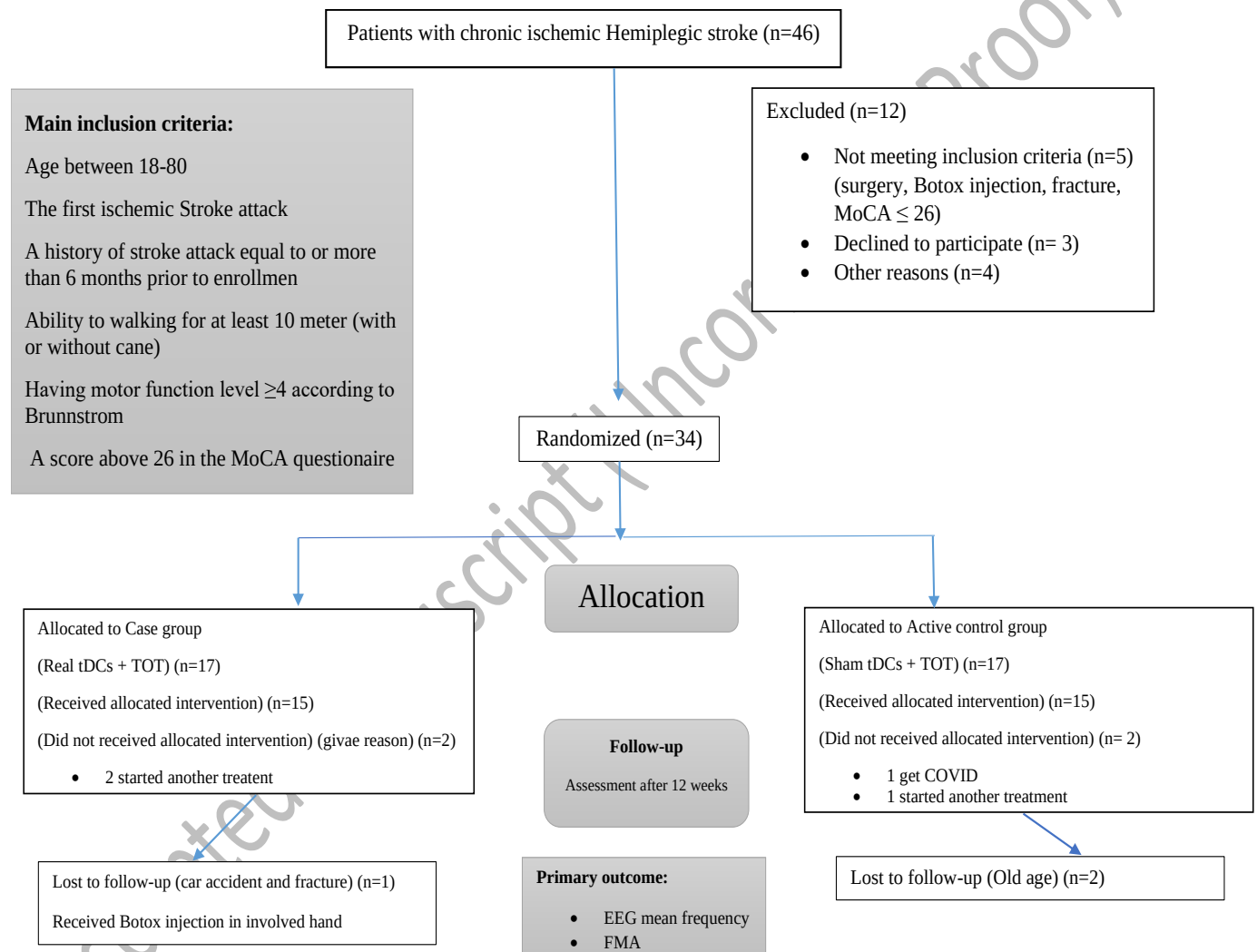
Eligibility Criteria

Inclusion criteria were: (i) hemiparesis resulting from a first-ever ischemic stroke confirmed by magnetic resonance imaging (MRI) or computed tomography (CT) scan; (ii) a minimum duration of 6 months since the unilateral stroke event (Bao, Wong, Leung, 2018; Rossiter, Boudrias, & Ward, 2014); (iii) ability to walk at least 10 m with or without an assistive device; (iv) upper-limb motor impairment at Brunnstrom recovery stage ≥ 4 (Kim, Jang, Roh, 2020); and (v) a score of ≥ 26 on the Montreal Cognitive Assessment (MoCA) (Rossiter et al., 2014).

Exclusion criteria included: (i) presence of other neurological disorders such as Dejerine–Roussy syndrome (Hu, Ji, Lu, 2018; Remsik, Williams Jr, Gjini, 2019); (ii) history of seizures within the previous two years or use of anticonvulsant medication within one month prior to study entry; (iii) botulinum toxin injection within 6 months before participation; (iv) contractures of the wrist or finger joints on the affected side; (v) moderate to severe depression (Beck Depression Inventory score ≥ 19) (Hu et al., 2018); (vi) painful shoulder, defined as a score ≤ 12 on the pain subsection

of the upper-extremity Fugl-Meyer Assessment; (vii) presence of a pacemaker or other ferromagnetic or electrical implants; (viii) use of medications acting on the central nervous system; (ix) pregnancy; (x) unwillingness or inability to complete the intervention or assessment sessions; (xi) significant skin irritation, concentration difficulties, or sleep disturbances related to tDCs; and (xii) known allergy to EEG electrode gel.

Fig. 1: Flow chart of research design (tDCs: trans Cranial Direct current stimulation); TOT: Task-Oriented Training; EEG: Electroencephalography



Sample size

G*Power software (Düsseldorf, Germany) was used for sample size estimation. A total sample size of 30 patients was estimated. Applied values in the application were included: the absolute or relative power quantity reported by previous studies (Remsik et al., 2019) (the primary outcome was mean frequency, which is calculated based on relative powers), $\alpha = 0.05$, power = 80%, the

standard Cohen's effect size (d) of 0.5, and number of groups =2. According to the allocation ratio (N2/N1) equal to one, 15 patients were considered for each group (case and control groups).

Concealment and randomization

Initial assessments were conducted after obtaining written consent from participants. The assessment process was conducted by a person who was unaware of the participants' group assignments. An independent researcher, not involved in outcome assessments, randomized the participants into either the active control group (sham tDCs with TOT) or the case group (real tDCs with TOT) on a 1:1 ratio. Based on a sample size of 30, as determined by previous studies, 15 double blocks were created using the online tool www.sealedenvelope.com. To ensure concealment, the type of tDCs was assigned by an analyst using sealed envelopes. During the randomization process, unique codes were assigned to these envelopes. Stratification was used to achieve an equal distribution of participants with right or left hemiplegia in both groups. The participants in both groups (case and control) were blinded to the group to which they were assigned. Data extraction and evaluation were carried out by a third individual who was also blinded to the group assignments and interventions. The allocation sequence, participant enrollment, and assignment to interventions were managed by an independent investigator who was not involved in the assessments, interventions, or any other part of the research. The treating physiotherapist who conducted interventions was blinded to the results of the measurements.

Intervention description

A professional and educated physiotherapist with 3 years of practical knowledge in the rehabilitation of stroke patients and who has completed courses on working with tDCs, performed all interventions. Interventions in both groups were administered for three weeks, 5 sessions per week, each taking 60 minutes.

Case group

All entrants were provided by tDCs, along with task-oriented therapeutic exercises for the upper extremity in both case and control groups. In the case group, Anodal-tDCs on the ipsilesional hemisphere (with Bilateral Bipolar non-balanced electrode montage) were applied concurrently with TOT for 20 minutes in each session, and then TOT continued for another 40 minutes without tDCs. The selected TOT in the current study includes 15 exercises aimed at active and accessory movements to improve the range of motion in the upper extremity joints, grasping skills, grasping and moving, and releasing objects. Before the start of the intervention, a comprehensive and comprehensible explanation was given to the participants about the importance of non-invasive brain stimulation, how this stimulation works, and its possible side effects. The anode electrode

was placed on the lesioned hemisphere (ipsilesional M1-C3/C4) and the cathode electrode on the contralesional supraorbital (Nitsche et al., 2008). The stimulation lasted for 20 minutes in each session, and during the intervention, the patient's physical and mental condition was carefully observed. The first 20 minutes of the intervention sessions were devoted to combining simultaneous TOT with the tDCs, and the remaining 40 minutes were spent only on task training. The stimulation applied before exercises (TOT) because according to the results of previous studies, applying tDCs before the start of motor exercises, compared to conditions where it is applied during or after movement training, contributes better therapeutic effects (Winstein, Stein, Arena, 2016). All interventions were accomplished in the first half of the day.

Active control group

In this group, participants received TOT in combination with sham tDCs, with the device settings and electrode placement identical to those of the case group. However, the stimulation protocol varied: the current intensity initially increased gradually from zero to 2 mA over 30-second, followed by a 20-minute pause. The current was then briefly restored for 30 seconds before the device was turned off. After that, TOT continued for an additional 40 minutes.

Outcomes

The mean frequency of EEG power spectrum was the primary outcome. The secondary outcome was sensory-motor function ability of upper limbs.

Primary outcome

Electroencephalography parameters were recorded and extracted as primary outcomes of this study. For this purpose, frequency domain analysis using the Fast Fourier Transform (FFT) algorithm was conducted to calculate absolute power ($\mu V^2/Hz$), relative power (%), and mean frequency (Hz) within each of the frequency sub-bands (delta, theta, alpha, beta, and gamma).

- Absolute Power: The absolute power of each frequency band is the integral of all power values within that band's frequency range.
- Relative Power: The relative power for each band is calculated by expressing the absolute power of that band as a percentage of the total absolute power of all frequency bands.
- Mean Frequency: The overall mean frequency was derived from the entire analyzed spectrum (1-30 Hz) (Yuvaraj, Murugappan, Mohamed Ibrahim, 2014).

In the present study, the EEG mean frequency was calculated based on the equation employed by Neri Accornero et al. (2014). They considered f_b (the brain rate) as a single value to simplify the statistical analysis of EEG mean frequency as a dependent value in their study. This index quickly measures the EEG overall mean frequency which encompasses the mean frequency for brain oscillatory activities across various frequency bands of the EEG power spectrum and is calculated as follows: $f_b = \sum f_i V_i / V$, where the index i denotes the frequency band (for delta $i = 1$, for theta $i = 2$, etc.); f_i represents the mean frequency in Hz for any band (in our arrangement, for delta $f_i =$

2.5, for theta $f_i = 6$, for alpha $f_i = 10.5$, for beta $f_i = 16.5$, and Gamma $f_i = 45$); V_i is the corresponding mean power in any frequency band, estimated according to the EEG raw data, and V is the sum of all V_i band potentials ($V = \sum V_i$). This equation facilitated the calculation of the general EEG mean frequency by converting the relative powers of the different frequency bands (Accornero et al., 2014).

Secondary outcomes

The Fugl-Meyer Assessment for the upper limb is a performance-based tool used to evaluate impairment. This assessment specifically evaluates sensory-motor function and describes motor recovery in present study. Scoring is based on the direct observation of the patient's performance. The total score for the upper limb is 126 points, distributed as follows: 66 points for upper limb motor function, 12 points for sensory function, 24 points for passive joint movements, and 24 points for joint pain (Malouin, Pichard, Bonneau, 1994).

Data collection

EEG signals were recorded by 64 channel amplifiers (MicroMed, Italy) according to the international 10/20 system (bandwidth is 0.2–70 Hz, the impedance ≤ 20 k Ω , and the sampling rate = 512 Hz), from 20 Ag/AgCl surface electrodes with a diameter of 6 mm which were placed in Fp, Fpz, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, and O2. The ground electrode was attached to the unaffected hand. The reference electrodes A1 and A2 were respectively stuck on the left and right earlobes. The signals were recorded by using a Medium-large EEG Cap in a magnetic-acoustic shielded module and during 3-minute resting (but conscious) state with closed eyes. The absolute and relative power of the EEG frequency spectrum were extracted from the raw EEG data. The mean frequency was then calculated based on the relative power of all frequency bands at baseline, post-treatment, and at the 3-month follow-up (Accornero et al., 2014).

Statistical analysis

Statistical analyses were performed using SPSS software (version 22.0) and sLORETA. An intention-to-treat approach was applied to account for participant dropouts. The reliability of QEEG measures was assessed using the intraclass correlation coefficient (ICC). A significance level of 0.05 was adopted for all analyses. Data normality was evaluated using the Kolmogorov–Smirnov test. Given the non-normal distribution of the data and the relatively small sample size, non-parametric statistical tests were employed. Quantitative demographic variables were compared between the intervention and control groups using the Mann Whitney U test.

Within-group comparisons of mean frequency and Fugl-Meyer Assessment (FMA) scores across the three assessment time points (T0: before intervention, T1: after intervention, and T2: follow-up) were conducted using the Friedman test. Between-group differences in outcome changes across these time points were examined using the Kruskal Wallis test.

Results

Changes in mean frequency were examined across the three assessment time points (Baseline, post-intervention, and follow-up) using the Friedman test. In both the intervention and control groups, mean frequency showed a gradual decrease from baseline to post-intervention and follow-up (intervention group: 12.86 ± 5.31 to 11.70 ± 2.32 Hz; control group: 12.50 ± 5.20 to 8.17 ± 4.95 Hz). However, these within-group changes did not reach statistical significance (Fig. 2).

Between-group comparisons based on the Kruskal Wallis test revealed no significant differences in mean frequency at baseline or immediately after the intervention. At the follow-up assessment, however, the difference between the two groups reached statistical significance ($P = 0.02$). The corresponding effect size was 0.38, suggesting a noticeable, though not large, effect (Table 2). Although declines in mean frequency were observed in both groups over time, the magnitude of reduction was more pronounced in the control group.

To compare sensory-motor function between the two groups, changes in FMA scores were calculated for three predefined contrasts: post-intervention relative to baseline (After-Before), follow-up relative to post-intervention (Follow-up-After), and follow-up relative to baseline (Follow-up-Before). Analysis using the Kruskal Wallis test indicated that improvements across these contrasts were generally greater in the intervention group than in the control group.

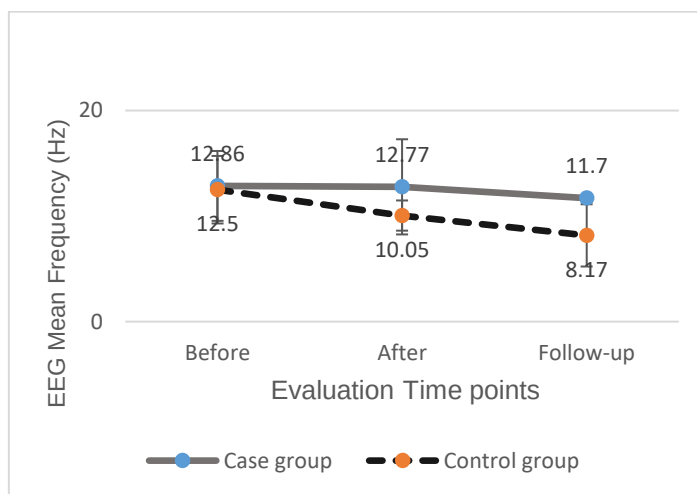
Sensory-motor performance was further evaluated using the Fugl-Meyer Assessment (FMA) as a secondary outcome measure (Table 3). Within-group analyses using the Friedman test demonstrated significant effects of time on both FMA Sensory and FMA Motor scores in the intervention and control groups. In the intervention group, time exerted a very large effect on FMA Sensory ($\chi^2 = 28.42$, $P < 0.001$, Kendall's $W = 0.95$) and FMA Motor scores ($\chi^2 = 26.81$, $P < 0.001$, Kendall's $W = 0.89$), reflecting highly consistent changes across the assessment time points. In the control group, the effect of time was large for both FMA Sensory ($\chi^2 = 20.77$, $P < 0.001$, Kendall's $W = 0.69$) and FMA Motor ($\chi^2 = 17.20$, $P < 0.001$, Kendall's $W = 0.57$), indicating less uniform, yet still meaningful, temporal changes (Table 4).

Table 2. Comparison of mean frequency between the two groups at three time points.

	Mean Frequency Before		Mean Frequency After		Mean Frequency Follow-up	
	case	control	case	control	case	Control
Mean frequency	12.86	12.50	12.77	10.05	11.7	8.17
Chi-Square	0.413		1.654		4.937	
Df	1		1		1	
Asymp. Sig.	0.520		0.198		*0.026	
Effect size (Transformation of η^2)	0.021		0.023		0.38	

*There was a significant difference in EEG mean frequency between case and control groups

Fig. 2. Changes in mean frequency across study time points (before intervention, after intervention, and three-month follow-up) in the case and control groups.



*Before: Before intervention, After: After intervention, Follow-up: 3 months after intervention.

Table 3. Comparison of FMA score changes between the two groups at three time points.

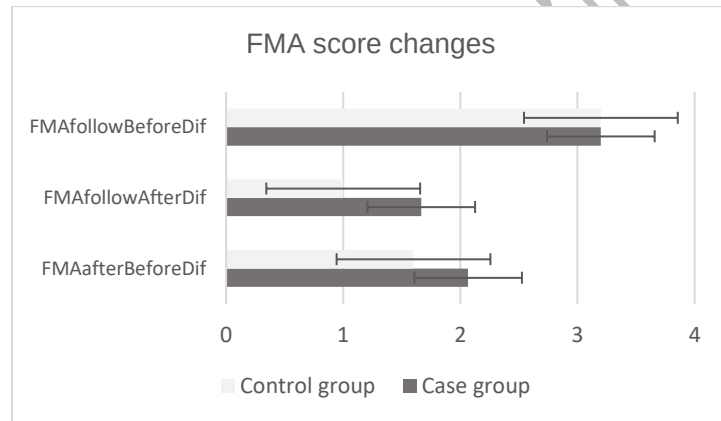
	FMA _{sens} After- Before difference	FMA _{sens} Follow-up- After difference	FMA _{sens} Follow-up-Before difference	FMA _{motor} After- Before difference	FMA _{motor} Follow-up- After difference	FMA _{motor} Followu-up- Before difference
Chi-Square	13.735	8.821	12.791	9.597	4.286	10.303
Df	1	1	1	1	1	1
Asymp. Sig.	.000	.003	.000	.002	.038	.001
Effect size (Transformation of η^2)	0.455	0.279	0.421	0.307	0.117	0.332

*After-Before: The FMA score at the end of the 15 sessions intervention, minus the pre-intervention FMA score

*Follow-up-After: The FMA score in the three-month follow-up, minus the FMA score at the end of the 15 sessions intervention

*Follow-up-Before: The FMA score in the three-month follow-up, minus the pre-intervention FMA score

Fig.3: FMA score changes during the study time points (before the intervention, after the intervention and three-month follow-up) in case and control group.



* FMA_{followBeforeDif}: The FMA score in the three-month follow-up, minus the pre-intervention FMA score.

*FMA_{followAfterDif}: The FMA score in the three-month follow-up, minus the FMA score at the end of the 15 sessions intervention

*FMA_{afterBeforeDif}: The FMA score at the end of the 15 sessions intervention minus the pre-intervention FMA score

Table 4: Friedman test results and effect sizes (Kendall's W) for FMA-Motor and FMA-Sensory scores

Group	outcome	Median (IQR)			χ^2 (Friedman)	(df)	p-value	Kendall's W
		B	A	F				
Case	FMA-Sensory	49.00	53.00	56.00	28.42	2	0.00	0.94
	FMA-Motor	46.00	53.00	54.00	26.81	2	0.00	0.89
Control	FMA-Sensory	56.00	56.00	58.00	20.77	2	0.00	0.69
	FMA-Motor	55.00	58.00	42.00	17.20	2	0.00	0.57

*In Median (IQR) column, B: Before intervention, A: After intervention and, F: Follow-up.

Discussion

This study aimed to investigate the effectiveness and added value of applying transcranial direct current stimulation (tDCs) as an adjunct to task-oriented training (TOT) in individuals with chronic stroke, with a particular focus on changes in EEG mean frequency and upper extremity motor performance as assessed by the UE-FMA.

Our findings demonstrated a decreasing trend in EEG mean frequency following the application of anodal tDCs over the primary motor cortex from pre-intervention to post-intervention and follow-up assessments. Nevertheless, this trend reached statistical significance only at the follow-up stage, suggesting that potential neuromodulatory effects of tDCs on resting-state cortical oscillatory dynamics may emerge gradually over time rather than immediately after intervention.

A major limitation of the present study is the relatively small sample size ($n = 30$), which may have reduced the statistical power to detect subtle group-level differences in EEG measures. This limitation is particularly relevant in the context of resting-state EEG recordings, as spontaneous cortical activity in individuals with chronic stroke is known to exhibit substantial inter-individual variability (Finnigan & van Putten, 2013; Thibaut, Simis, Battistella, 2017). Even so, Resting-state recordings provide a stable and standardized measure of baseline cortical oscillatory dynamics that is not influenced by task performance variability or motor execution limitations, which are particularly pronounced in stroke populations (Accornero et al., 2014; Boonstra, Nikolin, Meisener, 2016; Finnigan & van Putten, 2013). Mean frequency obtained during rest is widely regarded as a global index of tonic cortical excitability and thalamocortical integrity rather than task-evoked neural activity (Nunez & Srinivasan, 2006; Rossini, Burke, Chen, 2015). For this

reason, EEG mean frequency was evaluated during rest under standardized conditions, independent of behavioral demands (Nunez & Srinivasan, 2006). Consequently, the absence of robust group-level effects should be interpreted cautiously and may primarily reflect limited statistical power combined with the inherent variability of resting-state EEG in stroke populations (Finnigan, Walsh, Rose, 2007; Rossini et al., 2015). Despite these limitations, patients with chronic stroke in the intervention group appeared to benefit from the addition of anodal tDCs to task-oriented training involving, particularly at the follow-up stage, across both primary and secondary outcomes.

EEG mean frequency, represented as brain rate (f_b) (van Putten & Hofmeijer, 2016), was examined at different evaluation time points (T0, T1, and T2). In the control group, the observed pattern suggested a tendency toward slower cortical oscillatory activity following the application of sham tDCs over the primary motor cortex. This finding is consistent with previous work by Boonstra and colleagues (2016), who reported a significant reduction in EEG mean frequency following both active and sham tDCs (Boonstra et al., 2016). Similar cortical changes after tDCs have also been reported by other researchers, including increases in delta (Donaldson, Kirkovski, Yang, 2019) and theta power (Miller, Berger, & Sauseng, 2015; Zaehle, Beretta, et al., 2011; Zaehle, Sandmann, Thorne, 2011). Because, increased power in low-frequency bands shifts the mean frequency toward lower frequencies. In contrast, Accornero et al. (2014), using a bifrontal stimulation montage, reported a significant increase in EEG mean frequency after active tDCs, with no change following sham stimulation (Accornero et al., 2014). Likewise, studies targeting the prefrontal cortex have documented increases in beta activity (Pellegrino, Maran, Turco, 2018), decreases in theta power (Mondini, Mangia, & Cappello, 2018), or reductions in delta activity (Trujillo Diaz, Mastropietro, Scano, 2017). Although these studies did not explicitly calculate mean frequency, the reported changes in EEG frequency bands imply corresponding shifts in mean frequency. Such discrepancies across studies highlight the strong dependency of tDCs effects on stimulation parameters, target regions, baseline brain state, and experimental design. Importantly, previous evidence suggests that the physiological state of the brain during stimulation plays a critical role in shaping tDCs-induced plasticity (Boonstra et al., 2016). Antal et al. reported that both cognitive tasks and motor tasks modified plasticity induced by transcranial direct current stimulation. In comparison to the passive resting state, motor cortical excitability was greater after cathodal stimulation and lower following anodal stimulation when individuals completed

cognitive tasks during stimulation (Antal, Terney, Poreisz, 2007). Given that participants in the present study performed task-oriented (motor-cognitive) training concurrently with anodal or sham tDCs, a reduction in cortical excitability following stimulation was therefore expected. Additionally, resting-state EEG characteristics are influenced by recording conditions such as eye state (Wang, Li, Wang, 2022). Previous studies have shown marked differences between eyes-open and eyes-closed resting-state EEG, including shifts in alpha and beta activity and relative increases in lower-frequency power during eyes-closed conditions (Wang, Chen, Song, 2022; Zolghadr, Dehkordi, Sarrafzadeh, 2024). As EEG recordings in the present study were obtained with eyes closed, a reduction in alpha and beta power accompanied by an increase in lower-frequency activity was anticipated, contributing to the observed decrease in mean frequency. Moreover, anatomical variability across individuals may further account for heterogeneity in tDCs effects (van der Cruisen, Dooren, Schouten, 2022).

Despite the observed decreasing tendency in EEG mean frequency, the dominant frequency in stroke patients in the present study remained within the alpha range, which is generally considered a marker of relatively preserved cortical function. This observation aligns with previous findings indicating that abnormal post-stroke EEG patterns are often characterized by a shift of dominant frequency toward the delta range, whereas healthy individuals typically exhibit alpha-dominant activity (Zakaria, Valentine, & Mayza, 2021).

From a clinical perspective, statistical analyses revealed significant improvements in UE-FMA scores over time in both the intervention and control groups. The large Kendall's W values observed in the intervention group indicate highly consistent within-subject improvements across assessment time-points, whereas the control group demonstrated more variable temporal patterns. These findings suggest stable longitudinal motor recovery trends but do not, on their own, establish a definitive causal effect of tDCs.

Our results are broadly consistent with previous studies examining the combined effects of tDCs and task-oriented or functional training. Adeagbo et al. (2021) reported greater motor improvements (UE-FMA scores) following anodal tDCs compared with other stimulation conditions when combined with repetitive functional training, although the absence of a sham group limits direct comparison (Adeagbo et al., 2021). Similarly, Hsu et al. (2023) observed significantly greater gains in UE-FMA scores following real tDCs combined with task practice

compared to sham stimulation (Hsu et al., 2023). However, systematic reviews investigating the combination of priming strategies, including tDCs, with task-oriented training have yielded inconclusive results, with some studies reporting superiority of combined interventions and others finding comparable effects between real and sham conditions (da Silva, Ocamoto, Santos-Maia, 2020). Variability in sham stimulation protocols and study designs may partially account for these inconsistent findings.

Although no statistically significant correlation was observed between changes in EEG mean frequency and changes in UE-FMA scores in the present study, this does not imply a lack of relationship between these variables. Both measures exhibited changes that were directionally consistent with improvements in motor performance, particularly in the intervention group. Previous work has suggested that indices related to EEG mean frequency, such as spectral mobility, are associated with improvements in motor function as measured by the Fugl-Meyer scale (Singh, Pradhan, Bakshi, 2020). It means that an increase in mean frequency after stroke correlates with improved motor performance in these patients (Milani, Antonioni, Baroni, 2022; Simis, Doruk, Imamura, 2015; Singh et al., 2020). Mean frequency exhibited a gradual decline over time following both real and sham interventions in present study; however, this decline was less pronounced in the real anodal tDCs group. Consequently, greater improvements in sensorimotor performance were observed in patients receiving anodal tDCs. Taken together, these findings suggest that anodal tDCs may have attenuated the spontaneous decline in EEG mean frequency commonly associated with chronic stroke and aging, thereby contributing to more favorable motor outcomes (Singh et al., 2020). Future studies with larger sample sizes and task-related EEG designs may help reduce physiological variability and enhance the sensitivity for monitoring tDCs-induced cortical changes.

Finally, given the limited sample size of the present study, the statistical power to detect both inter-group and intra-group differences was constrained, and the results should therefore be interpreted with appropriate caution.

Conclusion

The quantitative EEG methods employed in this study may contribute to a better understanding of stroke-related neural changes and brain adaptation during rehabilitation. These approaches have the potential to detect variations in EEG biomarkers across the course of therapy, which could inform future therapeutic strategies and potentially support improved functional outcomes.

Anodal tDCs applied over the primary motor cortex using a bilateral, bipolar non-balanced electrode montage was associated with changes in resting-state EEG following stimulation. Analysis of EEG mean frequency suggested a slight decrease after active tDCs. Comparable alterations in resting-state EEG were also observed after sham stimulation and appeared more pronounced than those following active tDCs; however, these effects did not reach statistical significance, except at the follow-up assessment.

Although previous studies have suggested that improvements in motor function may be accompanied by increases in EEG mean frequency, the relationship between mean frequency and FMA scores in chronic stroke patients remains inconclusive. In the context of the present findings, anodal tDCs in the intervention group may have attenuated the decline in mean frequency over time, which was accompanied by greater improvements in FMA scores compared with the sham condition.

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Authors' Contributions

Conceptualization: Maryam Zolghadr, Javad Sarrafzadeh, Shohreh Noorizadeh Dehkordi

Methodology: Maryam Zolghadr, Shohreh Noorizadeh Dehkordi, Saeed Talebian

Formal Analysis: Maryam Zolghadr, Saeed Talebian

Investigation: Maryam Zolghadr, Shohreh Noorizadeh Dehkordi, Marzieh Yassin

Writing – Original Draft: Maryam Zolghadr, Saeed Talebian, Marzieh Yassin

Writing – Review & Editing: Shohreh Noorizadeh Dehkordi, Javad Sarrafzadeh, Marzieh Yassin

Resources: Hassan Haddadzade Niri

Supervision: Javad Sarrafzadeh

Project Administration: Maryam Zolghadr

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Trial Registration

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Declaration of interests

None. On behalf of all authors, the corresponding author states that there is no conflict of interest.

Competing Interests:

The authors declare that they have no competing interests.

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This work is based, in part, on the doctoral research conducted by the first author.

Consent to Publish

The authors have provided their consent for publication.

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